

	<b>DRUG SAFETY REPORT RDR No: 1132062</b>		
	<b>Roche / Genentech</b>		
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## **Executive Summary**

This Drug Safety Report (DSR) was prepared in response to a signal arising from the randomized study BO42864 (AcceleRET-Lung), wherein a fatal septic shock event was reported in a patient who had recently initiated pralsetinib therapy. The case included temporal association of the initiation of pralsetinib with the onset of neutropenia and severe bacterial pulmonary infection, suggestive of a plausible causal association. A study-wide review of fatal events following this episode identified a potential imbalance in severe infections, including fatal events, in the pralsetinib treatment arm vs the Standard of Care arm of AcceleRET-Lung that triggered this assessment.

Therefore, this DSR provides a comprehensive assessment of the severe infection adverse events (AE)s from AcceleRET-Lung and ARROW studies, and that of post marketing sources to evaluate a causal association between pralsetinib treatment and an increased risk of severe and fatal infections.

The Core Data Sheet (CDS) version 6.0 (dated September 2023) of pralsetinib enlists pneumonia, including fatal pneumonia, urinary tract infection (UTI), and cytopenia (neutropenia, leukopenia and lymphopenia) as very common adverse drug reactions. Infections are not included in the Warnings and Precautions section. The pralsetinib Core Risk Management Plan (cRMP; version 5.0) specifies infections as an important potential risk for the drug. This risk of infections may potentially be attributed to the mechanism of action of pralsetinib which causes reduced bone marrow cellularity, reduced hemoglobin, reduced reticulocytes, reduced lymphoid cellularity, and decreased lymphocyte counts<sup>1</sup>. Decreased blood cell counts have been observed in patients treated with pralsetinib, especially anemia, neutropenia, and thrombocytopenia. As cancer patients are already immunocompromised, neutropenia can put such patients at even greater risk of developing severe infections. Infections are also listed as an adverse drug reaction (ADR) for the other similar-in-class (SIC) molecule, selpercatinib. The European Union Summary of Product Characteristics (EU SmPC) of selpercatinib mentions pneumonia and UTI as ADRs, whereas the United States Package Insert (USPI) mentions pneumonia as an ADR and sepsis as a fatal ADR. Decreased lymphocyte, neutrophil, and white blood cell counts are also labeled as ADRs for selpercatinib.

In preclinical studies of pralsetinib, hematological abnormalities (reduced bone marrow cellularity, attributed to off-target Janus kinase [JAK 2] inhibition) and lymphoid effects (reduced lymphoid cellularity and decreased lymphocyte counts, attributed to stress response) were observed. Pralsetinib has been shown to inhibit JAK2 pathways as an off-target effect, but with lower affinity as compared to rearranged during transfection (RET) inhibition or compared to JAK inhibiting compounds with JAK-inhibition as a

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<sup>1</sup> Gavreto Core Risk Management Plan version 5.0, September 2023.

primary target<sup>1</sup>. JAK inhibition has the potential to suppress integral elements of the immune response. The risk of infection, including opportunistic infections, appears to be increased with all JAK inhibitors.<sup>2</sup>

Clinical data summarized in this report included study results from ARROW (BO42863) and the ongoing AcceleRET-Lung study (BO42864). AcceleRET-Lung presents the first opportunity to consider randomized safety data comparing pralsetinib with standard of care treatment options (platinum doublet ± pembrolizumab) in patients with RET fusion-positive non-small cell lung cancer (NSCLC). ARROW, on the other hand is non-randomized, open-label, study with no comparator arm. However, it is included in this report as it provides a larger dataset of patients and the current labelling documents for pralsetinib are based on the results of this study. For AcceleRET-Lung, the analysis population includes all patients who received any amount of study drug. Only adverse events that occurred during the main treatment period are included in these analyses; patients randomized to the control arm had the option to receive pralsetinib following disease progression.

The clinical study AcceleRET-Lung data review showed a crude reporting rate of 4.6% (5/108) for patients with fatal infection events (excluding COVID-19 events) and 21.3% (23/108) for patients with Grade 3 and 4 infection events in the pralsetinib treatment arm. The comparator treatment arm reported a 7.7% (8/104) rate for patients with Grade 3 and 4 infections, with no fatal infection events reported. A significant increase in the incidence proportion of severe infections (Grades 3-5) was observed in the pralsetinib treatment arm versus the standard of care arm (two-sided fisher's exact p=0.0004). Additional statistical testing using the Aalen-Johansen estimator was performed to account for the effect of time on treatment, as well as for the occurrences of end of treatment and/or death that are handled as competing events. In this analysis, a risk ratio of 3.33, 95% CI: [1.57 ,7.06] was estimated, indicating a higher risk in the pralsetinib arm<sup>3</sup>. An analysis of neutropenia and lymphopenia in AcceleRET-Lung suggests that these clinical events do not appear to account for the higher risk of infection in pralsetinib treated patients. Further, a total of 7 pralsetinib-treated patients presented with 8 AEs of severe opportunistic infections of which only 2 patients were receiving systemic corticosteroids prior to the onset of infection. This analysis suggested that prior corticosteroid use does not appear to be an inciting risk factor for the development of severe opportunistic infections in these patients. The evidence from the ARROW study showed an incidence of 3.2% for patients with fatal AEs while 24.4% for patients with Grade 3-4 infection events in pralsetinib treated arm.

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<sup>2</sup> Adas MA, Alveyn E, Cook E, Dey M, Galloway JB, Bechman K. The infection risks of JAK inhibition. *Expert Rev Clin Immunol*. 2022;18(3):253-261.

<sup>3</sup> Stegherr R, Beyermann J, Jehl V, Rufibach K, Leverkus F, Schmoor C, Friede T. Survival analysis for Adverse events with Varying follow-up times (SAVYY): Rationale and statistical concept of a meta-analytic study. *Biometrical Journal*. 2021; 63: 650–670.

An analysis of both the AcceleRET-Lung and ARROW studies revealed high incidence rates of severe infections in patients treated with pralsetinib. The infection rates were similar between the two studies. Notably, a clear imbalance in terms of severe (including fatal) infections has been emerged from AcceleRET-Lung study.

In pralsetinib treatment arm of AcceleRET-Lung, five fatal infection events (in 5 patients) including preferred terms (PT)s of pneumonia, lower respiratory tract infection, and sepsis, were reported. The time to onset ranged from 25 to 155 days (median: 51 days) for the fatal infection events. Furthermore, a total of 32 Grade 3-4 infection events (reported in 23 patients), with the time to onset ranging from 20 to 1001 days (median: 122 days), were reported in patients treated with pralsetinib. In the standard of care arm, no patients reported fatal infections. The median time to onset for Grade 3-4 severe infections in the comparator treatment group was 110.5 days (range: 7 to 528 days). The majority of the severe infection events (26/32; 81.2%) in the pralsetinib treated arm were manageable and the patients had recovered/ recovered with sequelae or were recovering.

Cumulative search (cut-off date: 05-Aug-2024) of the Company Safety Database for pralsetinib identified 806 cases reporting 923 AEs mapped to System Organ Class (SOC) "Infections and Infestations", using Medical Dictionary for Regulatory Activities (MedDRA) version 27.0. The focus of the analysis was to identify the cases reporting severe infection events reported with National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) grading of  $\geq 3$ . Of the total retrieved cases, 740 were serious cases reporting 794 serious AEs of interest, which were further analyzed. The 794 serious events included 86 Grade 5, 47 Grade 4, 311 Grade 3, 66 Grade 2, and 12 Grade 1 AEs. The remaining AEs (n=272) lacked severity grade information. Among the 444/794 events (in 387/740 cases) reporting Grade 3 or higher grades of severity, the most frequently reported PT was pneumonia (n=117), followed by Sepsis (n=45), Urinary tract infection (n=38), COVID 19 (n=30), COVID 19 pneumonia (n=16) and *Pneumocystis jirovecii* pneumonia (n=8). Furthermore, 86/794 AEs (82 cases) resulted in a fatal outcome and the cause of death was reported mainly as pneumonia (n=25), sepsis (n=19), and COVID-19 (n=18).

The 387 cases reporting grade  $\geq 3$  events (i.e. 444 events) were categorized as follows to evaluate a causal association between pralsetinib treatment and an increased risk of severe infection, and death due to infection:

- Category A, there were 2 cases with no alternative explanations, each involving a Grade 4 infection. The first case reported *Pneumocystis jirovecii* pneumonia, with a first dose latency of 65 days. The second case reported neutropenic sepsis, which occurred 1460 days after the first dose of pralsetinib. Both the events resolved following pralsetinib therapy interruption and introduction of corrective treatment. Positive rechallenge was not reported in any of these cases

- Category B, there were 301 cases with risk factors/alternative explanations including but not limited to pre-existing co-morbidities such as diabetes, lymphopenia, dyslipidemia, pre-existing infections, underlying cancer progression with multiple metastatic sites, chronic renal insufficiency and/or use of anticancer drugs like cisplatin, pemetrexed, gemcitabine, use of immunosuppressant drugs such as tocilizumab, methylprednisolone, prednisolone, dexamethasone, radiotherapy, hormonal therapy, and invasive medical procedures.
- Category C, 84 cases with insufficient information for causality analysis.

Of the 740 serious cases, 249 cases (reporting 272 events) lacked severity grading information for 1 or more AEs of infection. These cases were evaluated and it was found that 26 cases had additional risk factors such as underlying cancer progression and use of immunosuppressive medications, and the remaining 223 had insufficient information for a comprehensive analysis. Additionally, 73 of the 740 serious cases reported grade 1 or 2 infection.

Based on the evaluation of the comparative safety data from the AcceleRET-Lung study, it could be concluded that despite earlier evidence from the ARROW study and a plausible mechanism of action, a clear imbalance in terms of severe (including fatal) infections emerged only from the AcceleRET-Lung study. AcceleRET-Lung is a randomized study, thus it is reasonable to assume that disease-related susceptibility to severe infections (including fatal cases) is similar in both arms at study enrollment, however, a higher frequency and severity of infections in the pralsetinib-treated arm was observed compared to the standard of care cohort. Also, an analysis of neutropenia and lymphopenia in AcceleRET-Lung study suggested that these events do not appear to account for the higher risk of infection in pralsetinib treated patients. Similarly, prior systemic corticosteroid use does not appear to account for severe opportunistic infections in the pralsetinib arm of AcceleRET-Lung. These findings along with a comprehensive analysis of cumulative evidence from the company safety database and plausible mechanism of action for reduced cellular immune function, the Marketing Authorization Holder (MAH)<sup>4</sup> has determined that the risk classification for severe infections should be updated from an important potential risk to an important identified risk. Additionally, the MAH recommends inclusion of a statement on the risk of severe infections, including fatal and opportunistic infections, in the Warnings & Precautions for Gavreto, including in the CDS, local labels, and the Investigator's Brochure.

An Urgent Safety Measure (USM)- Dear Investigator Letter and Dear Health Care Provider Letter will be issued by the MAH to inform investigators and prescribers of the

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<sup>4</sup> For the purposes of this report, MAH refers exclusively to Roche, and MAH actions exclusively apply to Roche, as there are additional MAHs for Gavreto globally. For actions relating to clinical studies and clinical development, this refers to ongoing clinical studies where Roche/Genentech is the study sponsor. For actions relating to CDS, local labels, and DHCP, this exclusively relates to territories where Roche is the legal MAH, and/or conducts compassionate use programs or post-trial access

identification of this risk on the basis of this analysis. Study Protocols and the Pralsetinib Investigator's Brochure will be updated accordingly.

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<b>LIST OF ABBREVIATIONS</b>	
ADR	Adverse Drug Reaction
AE	Adverse Event
AER	Adverse Event Report (number)
AST	Aspartate aminotransferase
CARV	Community-acquired respiratory viruses
CDS	Core Data Sheet
CMV	Cytomegalovirus
COPD	Chronic Obstructive Pulmonary Disease
CPAP	Continuous Positive Airway Pressure
CT	Computerized tomography
cRMP	Core Risk Management Plan
DIBD	Developmental International Birth Date
DLP	Data Lock Point
DSR	Drug Safety Report
ECOG	Eastern Cooperative Oncology Group
EU	European Union
EU SmPC	European Union Summary of Product Characteristics
HSV	Herpes Simplex Virus
IL	Interleukin
JAK	Janus kinase
MAH	Marketing Authorization Holder
MedDRA	Medical Dictionary for Regulatory Activities
MTC	Medullary Thyroid Cancer
NCI-CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
NHF	High-flow nasal cannula
NOS	Not Otherwise Specified
NPPV	Non-invasive positive pressure ventilation
NSCLC	Non-small cell lung cancer
NSAE	Non-serious Adverse Event
PCR	Polymerase Chain Reaction
PEEP	Positive End Expiratory Pressure
PT	Preferred Term
PBRER	Periodic Benefit Risk Evaluation Report
RET	Rearranged during transfection
SAE	Serious Adverse Event
SOC	System Organ Class
SMQ	Standard MedDRA Query
Unk	Unknown
US	United States
USM	Urgent Safety Measure
USPI	United States Package Insert
VZV	Varicella Zoster Virus

## **1. INTRODUCTION**

The current Drug Safety Report (DSR) describing severe infections with pralsetinib (Gavreto<sup>®</sup>) is written in response to a signal arising from the randomized non-small cell lung cancer (NSCLC) study BO42864 (AcceleRET-Lung). The trigger for this safety review was a fatal septic shock event reported in a patient who had recently initiated pralsetinib therapy, with temporal association of onset of neutropenia and severe bacterial pulmonary infection, suggestive of plausible causal association with initiation of pralsetinib treatment. A study-wide review of fatal events following this episode identified a numerical imbalance in severe infections, including fatal events, in the pralsetinib treatment arm vs the Standard of Care arm of AcceleRET-Lung. This represents the first opportunity to evaluate the differentiated safety profile of pralsetinib from that of a standard of care therapy regimen through randomized treatment assignment. Prior studies of pralsetinib in cancer patients have followed a single-arm design where such comparative safety evaluations were not possible.

The signal for severe infections with pralsetinib, including fatal infections was considered validated as of 05 August 2024, and therefore a thorough review of infection related adverse events (AE)s was performed to determine whether a causal association exists between pralsetinib treatment and an increased risk of severe infection, including fatal infections, as compared to standard of care therapy options. Statistical analysis of Grade 3-5 infection AEs across the treatment arms of study BO42864 (AcceleRET-Lung) was also performed.

Of note, the current Gavreto labeling documents [Core Data Sheet (CDS, version 6.0 [Gavreto CDS](#)]), European Union (EU) Summary of Product Characteristics (SmPC, dated 09 May 2024 [[Gavreto SmPC](#)]), United States Product Information (USPI, August 2023 [[Gavreto USPI](#)]) describe the adverse drug reactions (ADR) of pneumonia (all grade- 22.4%; grade 3/4 - 13.1%) and urinary tract infections (all grade-14.8%; grade 3/4 - 4.4%), occurring in the ARROW (BO42863) study of Gavreto. Additionally, hematological conditions such as neutropenia, leukopenia and lymphopenia, which are known to be associated with increased susceptibility to infections, are listed as very commonly reported ADRs with Gavreto. Moreover, in the pralsetinib Core Risk Management Plan (cRMP), ‘severe infections’ constitute an important potential risk, given the drug’s mode of action [reduced bone marrow and lymphoid organ cellularity] ([Gavreto cRMP](#)). Furthermore, infections like pneumonia are also listed for the other approved similar-in-class (SIC) molecule, selpercatinib (Retevmo<sup>®</sup>) in its labelling documents- SmPC ([Selpercatinib SmPC](#)) and USPI ([Selpercatinib USPI](#)[Selpercatinib SmPC](#)) and USPI ([Selpercatinib USPI](#)) including common occurrences of Grade  $\geq 3$  infections.

The Warnings and Precautions section of Gavreto labeling documents does not include the risk of infections.

## **1.1 OBJECTIVES OF REPORT**

The purpose of this DSR is to determine if the available evidence indicates a causal association between pralsetinib administration and increased risk of severe (including fatal) infections and if any update to the reference safety information is warranted.

## **1.2 BACKGROUND**

### **1.2.1 Drug Background – Pralsetinib**

Pralsetinib is a highly potent and selective inhibitor of oncogenic rearranged during transfection (RET) fusion and mutant proteins. RET fusions are oncogenic drivers in 1-2% of NSCLC, 10-20% of papillary thyroid cancer and, at lower prevalence, below 1% across multiple other solid tumor types. Pralsetinib inhibits the ligand independent constitutive activation of the RET tyrosine kinase activity and therefore prevents downstream oncogenic cell signaling.

Pralsetinib was first granted marketing approval in the U.S. on 4 September 2020, which marks the IBD. As of the Data Lock Point (DLP) of the latest Periodic Benefit Risk Evaluation Report (PBRER) (3 March 2024), pralsetinib has been approved in 61 countries worldwide. As of September 2024, Pralsetinib has been deregistered in the majority of countries where it was initially authorized, after the decision was taken to discontinue global marketing and development of the program, except in the United States and Greater China. This action was not taken due to any efficacy or safety findings in patients treated with pralsetinib. As of the time of authoring of this report, the global safety database and Market Authorization Holder (MAH)<sup>5</sup> status in the EU and US have been transferred from Roche to Blueprint Medicines. Pralsetinib is available as hard capsules and the recommended dose is 400 mg once daily ([Gavreto PBRER](#)).

#### **1.2.1.1 Therapeutic Indications<sup>6</sup>**

##### *Non-Small Cell Lung Cancer*

Pralsetinib is indicated for the treatment of adult patients with RET fusion-positive, locally advanced or metastatic NSCLC ([Gavreto CDS](#)).

##### *Thyroid cancer*

Pralsetinib is indicated for the treatment of adult and pediatric patients 12 years of age and older with locally advanced or metastatic RET-mutant Medullary Thyroid Cancer (MTC) who require systemic therapy and locally advanced or metastatic RET fusion-

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<sup>5</sup> For the purposes of this report, MAH refers exclusively to Roche, and MAH actions exclusively apply to Roche, as there are additional MAHs for Gavreto globally. For actions relating to clinical studies and clinical development, this refers to ongoing clinical studies where Roche/Genentech is the study sponsor. For actions relating to CDS, local labels, and DHCP, this exclusively relates to territories where Roche is the legal MAH, and/or conducts compassionate use programs or post-trial access

<sup>6</sup> Approved indications Countrywide: EU only has NSCLC and US only has NSCLC and TC (not MTC).

positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate) ([Gavreto CDS](#)).

#### **1.2.1.2 Relevant Information in the core RMP**

Pralsetinib has been observed to cause hematological effects in both preclinical and clinical settings. These effects include reduced bone marrow cellularity, decreased hemoglobin levels, lowered reticulocyte counts, diminished lymphoid cellularity, and decreased lymphocyte counts. These changes, particularly prominent in the initial two weeks of treatment, are consistent with off target Janus kinase 2 (JAK 2) inhibition of pralsetinib. This risk is further compounded by patients' potentially immunocompromised state due to prior chemotherapy or their underlying malignancy. Clinical observations of patients treated with pralsetinib have shown decreases in blood cell counts, specifically anemia, neutropenia, and thrombocytopenia. Neutropenia, a known side effect of various tyrosine kinase inhibitors, including gefitinib, sorafenib, sunitinib, lenvatinib, and cabozantinib, is of particular concern as it can place patients at an even greater risk of developing severe infections ([Gavreto cRMP](#)).

#### **1.2.1.3 Patient Exposure**

Since the Developmental International Birth Date (DIBD) (20 December 2016), an estimated total of 1034 patients have received pralsetinib in clinical trial participation.

Since the IBD (i.e, 04 September 2020) until DLP of the latest PBRER (3 March 2024), an estimated cumulative total of 2,694 patients have received pralsetinib from marketing experience. Additionally, a total of 502 patients enrolled and 449 received pralsetinib through other therapeutic use like pre-approval access, compassionate use programs and expanded access programs ([Gavreto PBRER](#)).

#### **1.2.2 Background on Severe Infection**

Infectious diseases are illnesses caused by pathogens or their toxins, spread from infected people, animals, or contaminated objects to susceptible individuals.

Opportunistic infections arise when typically, harmless microorganisms including bacteria, fungi, viruses, or parasites become pathogenic in individuals with weakened immune systems. These infections exploit compromised host defenses, particularly in cases of immunodeficiency disorders, to cause disease where they normally would not ([Van Seventer and Hochberg, 2017](#)). Severe infections are defined as all preferred terms (PTs) from the Medical Dictionary for Regulatory Activities (MedDRA) system organ class (SOC) "Infections and infestations", when of severity Grade ≥3.

#### **1.2.2.1 The Epidemiological Triad: Agent–Host–Environment**

The epidemiological triad, a foundational model in understanding infectious disease causation suggests that such illnesses emerge from the interplay of three key elements: the pathogenic agent, the host, and environmental factors. This triad encompasses a diverse array of infectious agents, ranging from living parasites like helminths and protozoa to fungi and bacteria, as well as non-living entities such as viruses and prions.

Environmental conditions play a crucial role in determining whether a potential host encounters these pathogens, while the subsequent interactions between the agent and the host ultimately dictate the outcome of the exposure. This model thus provides a comprehensive framework for comprehending the multifaceted nature of infectious disease development and transmission ([Van Sechteren and Hochberg, 2017](#)).

### **1.2.2.2 Factors Responsible for Increased Susceptibility to Severe Infections in Solid Tumor Patients**

Cancer patients have an increased susceptibility to infections due to several factors. An overview of the main factors responsible are:

#### *Neutropenia*

Neutropenia remains the most common predisposing factor for infection in cancer patients and both the degree and the duration of neutropenia influence the development of infection. The currently accepted definition of neutropenia is an absolute neutrophil count of  $\leq 500/\text{mm}^3$ . Most serious infections, including bacteremia, develop during episodes of severe and prolonged neutropenia, and virtually every patient whose neutrophil count is less than  $100/\text{mL}$  for 3 weeks or more will develop an infection, indicating a direct relationship between the risk of infection and the duration of neutropenia. Neutropenic patients often fail to develop the characteristic signs and symptoms of infection, since they are unable to mount an adequate inflammatory response and infection can disseminate widely. The most common sites of infection in neutropenic patients include the lung, oropharynx, blood, urinary tract, skin, and soft tissues, including the perirectal area. Infections are generally caused by organisms already colonizing the patient.

#### *Immune Dysfunction*

The impact of cancer on the peripheral immune system is multifaceted, involving changes in hematopoiesis, alterations in cellular populations, and functional impairments across various immune lineages. The malignant state shifts bone marrow hematopoiesis towards increased production of immature neutrophils and monocytes. This occurs through an elevated frequency of hematopoietic stem cells and granulocyte monocyte progenitors. In some cases, this shift comes at the expense of dendritic cell precursors, which share common progenitors. The result is a systemic reduction in dendritic cells, driven by two main mechanisms. First, granulocyte colony stimulating factor stimulate signal transducer and activator of transcription-3 signaling while suppressing interferon regulatory factor-8. Second, vascular endothelial growth factor decreases nuclear factor-kappa B signaling. The bone marrow also experiences a decrease in T cell, B cell, and plasma cell populations. This reduction in lymphoid lineages further contributes to the overall immune dysregulation observed in cancer patients. Beyond quantitative changes, cancer also induces qualitative alterations in immune cell function. Notably, T cell populations and natural killer cells exhibit functional deficits in their response to stimuli.

This impaired responsiveness can significantly compromise the immune system's ability to mount effective anti-tumor responses ([Somasundaram et al. 2022](#)).

### Medications

Chemotherapeutic agents contribute to increased infection susceptibility through multiple pathways. One primary mechanism is the induction of severe mucositis, particularly in the gastrointestinal tract, which compromises the body's natural barriers. This damage facilitates the entry of microorganisms into tissues and the bloodstream. Additionally, myelosuppressive agents cause neutropenia, a well-documented risk factor for infections. Many chemotherapeutic drugs interfere with cell-mediated and humoral immunity, even when administered at doses that do not typically result in significant myelosuppression. Agents such as azathioprine, cyclosporin, mycophenolate mofetil, cyclophosphamide, and systemic corticosteroids fall into this category, elevating infection risk through their immunosuppressive effects. A range of other medications can cause milder impairment of immune function, particularly when used in combination with other agents. Methotrexate is one such example. Biological agents also play a role in modulating immune responses, potentially increasing infection susceptibility. These include tumor necrosis factor alpha antagonists like infliximab, etanercept, and adalimumab, as well as various interleukin (IL) antibodies. The latter group encompasses IL-12/23 antibodies (ustekinumab), IL-17 antibodies (secukinumab, ixekizumab, brodalumab), and IL-4 receptor antibodies (dupilumab). Furthermore, immunoglobulin E antibodies such as omalizumab, JAK receptor inhibitors like tofacitinib, and Phosphodiesterase E4 inhibitors such as apremilast can also contribute to immune suppression. The cumulative effect of these various agents, whether used alone or in combination, can significantly compromise the immune system's capacity to combat infections ([Somasundaram et al. 2022](#)).

### Medical Conditions and Lifestyle Factors

A range of medical conditions significantly elevate the risk of infections. These include metabolic disorders such as diabetes, respiratory diseases like Chronic Obstructive Pulmonary Disease (COPD), and various autoimmune disorders. Immunocompromised states also play a crucial role, encompassing conditions such as cystic fibrosis, Human Immunodeficiency Virus, and post-transplantation scenarios. Tobacco use, poor nutritional status, chronic stress, and insufficient sleep all contribute to weakened immune responses. Advanced age is another significant factor that can compromise the body's ability to fight off infections. Cancer patients face additional, specific challenges that contribute to their infection risk. The local effects of tumors, particularly metastases causing obstructions and disruption to normal anatomical barriers, can create environments conducive to infection. Moreover, the use of invasive devices (central venous catheters, urinary catheters, feeding tubes), altered microbial flora (due to broad-spectrum antibiotics), organ dysfunction, prolonged hospitalization and surgical procedures often increase the risk of infections in cancer patients ([Budisan et al. 2021](#)).

### **1.2.2.3 Common Types of Infections in Solid Tumor Patients and Their Management**

Infections in cancer patients exhibit diverse characteristics based on their anatomical location, source, and the duration of cancer treatment. In patients with solid tumors, the infectious organisms often mirror the individual's resident microflora at the specific infection site. Some infections in cancer patients follow seasonal patterns like those observed in the general population, however, other infections are opportunistic.

#### **Pneumonia**

Pneumonia poses a significant mortality risk in cancer patients, causing death directly through respiratory failure and sepsis, and indirectly by interrupting cancer treatments. Pneumonia has been reported to occur in 50–70% of patients with lung cancer. Cancer-related alterations in both immune function and lung structure increase the vulnerability of lung cancer patients to infections. The immune system is compromised not only by the cancer itself but also by the various treatments employed to combat it.

Simultaneously, cancer can cause structural changes in the lungs, such as airway obstructions, further exacerbating the risk of infection. This dual impact on immunity and lung architecture creates a complex environment that significantly enhances the susceptibility of lung cancer patients to a wide range of infectious complications. Diagnosis and management are complicated by immune impairments from both cancer and its treatments, the presence of multidrug-resistant organisms, and atypical clinical presentations. Cancer patients are susceptible to various types of pneumonia due to multiple immune defects affecting both innate and adaptive immunity. These defects, along with treatment-induced respiratory tract damage, increase infection risk. Accurate diagnosis requires careful evaluation of clinical, radiographic, and microbiological data, considering both community-acquired and nosocomial sources. Given the high risk of complications, empiric antimicrobial therapy is often initiated promptly when infection is suspected in these vulnerable patients.

#### ***Types of pneumonia***

*Community-Acquired Pneumonia* occurs in patients not recently hospitalized or in long-term care, with common pathogens including *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae*, *Pseudomonas* spp., and other Gram-negative bacteria, as well as atypical pathogens and viruses.

*Hospital-Acquired Pneumonia* develops 48+ hours after hospital admission and often involves multidrug-resistant organisms.

*Healthcare-Associated Pneumonia* occurs in patients with recent healthcare exposure and has a pathogen spectrum similar to late-onset HAP.

Ventilator-Associated Pneumonia affects patients on mechanical ventilation and is a high risk for intensive care patients.

Aspiration Pneumonia is caused by inhalation of orogastric or oropharyngeal contents and often involves anaerobic bacteria.

Post-obstructive Pneumonia occurs due to airway obstruction by solid tumors and is often polymicrobial. Pneumonia from Septic Emboli is caused by infected intravascular thrombi.

Pneumonia caused by opportunistic pathogens: *Pneumocystis jiroveci* pneumonia primarily affects patients with CD4 lymphocytopenia. Tuberculosis, can occur in immunosuppressed cancer patients, often as a reactivation of latent infection. Nontuberculous mycobacteria can cause chronic, indolent lung infections, with *M. avium-intracellulare* complex being a common cause. Invasive pulmonary aspergillosis is the most common fungal pneumonia in cancer patients, with risk factors including prolonged neutropenia and immunosuppressive therapies. Other opportunistic fungi, including non-*Aspergillus* molds, are increasingly problematic. Viral pneumonias, particularly those caused by cytomegalovirus (CMV), varicella-zoster virus (VZV), and respiratory viruses, are significant concerns in immunocompromised cancer patients ([Valvani et al. 2019](#), [Evans and Safdar 2011](#)).

### **Bacterial infections**

Gram-positive bacteria, particularly *Staphylococcus aureus*, *Streptococcus* species, and *Enterococcus* species, are responsible for the majority of infections in cancer patients. *S. aureus*, including methicillin susceptible and methicillin resistant strains, causes a range of infections treated with vancomycin or beta-lactams, respectively. *Streptococcus* species, including viridans group streptococci, *S. agalactiae*, and *S. pneumoniae*, commonly cause bacteremia and pneumonia, with treatments varying from cefepime to penicillins. *Enterococcus* infections, often resistant to vancomycin, pose significant challenges and are treated with daptomycin or linezolid. The prevalence of these infections in cancer patients, especially those associated with catheter use or compromised immune systems, emphasizes the need for careful management and appropriate antibiotic selection based on susceptibility testing and individual patient factors.

The most common gram-negative organisms include *Escherichia coli*, *Klebsiella* species, and *Pseudomonas aeruginosa*. *E. coli*, often causing urinary tract infections and bacteremia, is typically treated with carbapenems like meropenem or imipenem for extended spectrum beta lactamase producing strains, while plazomicin is an alternative for complicated urinary tract infections. *Klebsiella* species, especially *K. pneumoniae*, cause urinary tract and bloodstream infections, with carbapenem-resistant strains treated using a combination of tigecycline and piperacillin/tazobactam or ceftazidime-

avibactam with a carbapenem. *P. aeruginosa* infections, though declining due to prophylactic measures, remain severe and are treated with antipseudomonal beta-lactams such as piperacillin-tazobactam ([Delgado and Guddati 2021](#), [Seo et al. 2021](#)).

### **Fungal infections**

Fungal infections pose a significant threat to cancer patients, especially those with prolonged neutropenia. *Candida* species, primarily *Candida albicans*, cause invasive yeast infections, typically treated with fluconazole. However, fluconazole prophylaxis has led to an increase in *Aspergillus* infections, particularly *Aspergillus fumigatus*, which commonly causes pneumonia. *Aspergillus* is treated with azoles and echinocandins like caspofungin. Less common fungal pathogens include *Fusarium* and *Scedosporium* species ([Delgado and Guddati 2021](#), [Seo et al. 2021](#)).

### **Viral infections**

Viral infections are a significant concern for cancer patients, particularly those undergoing chemotherapy or transplantation. Herpes simplex virus (HSV) 1 and 2, VZV, and community-acquired respiratory viruses (CARVs) are the most common threats. HSV reactivations, frequent in chemotherapy patients, are treated with acyclovir. VZV reactivation causes herpes zoster, often months after treatment initiation, and may require prophylactic acyclovir. CARVs, including influenza, parainfluenza, and coronaviruses, pose a higher risk to neutropenic patients. The novel Severe Acute Respiratory Syndrome Coronavirus 2 has shown potentially more severe outcomes in cancer patients and has significantly impacted cancer management practices ([Delgado and Guddati 2021](#), [Seo et al. 2021](#)).

#### **1.2.2.4 Treatment recommendations**

Treatment recommendations for cancer patients at risk of infections focus on antibacterial, antifungal, and antiviral prophylaxis. For antibacterial prophylaxis, fluoroquinolones are recommended for high-risk patients (neutrophil count  $\leq 100$  cells/mm<sup>3</sup> for  $> 7$  days), with levofloxacin preferred for those at risk of *Streptococcus viridans* mucositis. Intermediate-risk patients require case-by-case evaluation, while low-risk patients generally don't need routine prophylaxis. Antifungal prophylaxis is recommended for patients with anticipated severe neutropenia lasting over 7 days, with fluconazole for those likely to develop mucositis and posaconazole or voriconazole for those at risk of invasive mold infections. *Pneumocystis pneumonia* prophylaxis with trimethoprim-sulfamethoxazole is advised for high-risk patients. Antiviral prophylaxis includes annual influenza vaccination, acyclovir or valacyclovir for HSV-seropositive patients undergoing allogeneic hematopoietic cell transplantation or acute leukemia induction, and entecavir or tenofovir for those at risk of hepatitis B reactivation ([Delgado and Guddati 2021](#), [Seo et al. 2021](#)).

## **2. METHODOLOGY OF ANALYSIS OF DATA**

### **2.1 RELEVANT TOXICOLOGY INFORMATION**

Toxicology data was reviewed for specific findings on infection or susceptibility information for infection in general.

### **2.2 ANALYSIS OF COMPANY SPONSORED CLINICAL TRIALS**

Pralsetinib is being investigated for use in the treatment of patients with RET fusion positive NSCLC, RET-altered thyroid cancer, and other RET fusion-positive solid tumors.

As of 3-Sept-2024, the clinical development program for pralsetinib consists of 8 ongoing company sponsored interventional trials (see [Table 1](#) for an overview of these clinical trials).

**Table 1 Overview of Company Sponsored Interventional Trials for Pralsetinib**

<b>Study Number</b>	<b>Study Title</b>	<b>Study Phase</b>	<b>Study Design [Randomisation, Blinding, Design, Comparison]</b>
BO41932	Tumor-agnostic precision immuno-oncology and somatic targeting rational for you (TAPISTRY) phase II platform trial	Phase II	1. Nonrandomized 2. Open label 3. Single Group 4. Non-Controlled
BO42863 (ARROW)	A Phase 1/2 Study of the Highly-selective RET Inhibitor, BLU-667, in Patients with Thyroid Cancer, Non-Small Cell Lung Cancer and Other Advanced Solid Tumors	Phase I/II	1. Nonrandomized 2. Open label 3. Non-Controlled
BO42864 (AcceleRET-Lung)	A phase III, randomized, open-label study of pralsetinib versus standard of care for first-line treatment of RET fusion-positive, metastatic non-small cell lung cancer	Phase III	1. Randomized 2. Open label 3. Parallel 4. Active Controlled
GP43164	A Phase 1, Two-arm, Open-label Study to Evaluate the Clinical Drug-Drug Interaction Potential of Pralsetinib in Combination with Sensitive Transporter Substrates, Sensitive CYP Substrates, or a Combined Oral Contraceptive in Patients with Advanced or Metastatic Solid Tumors that are not Responsive to Standard Therapies or for which there is no Effective Therapy	Phase I	1. N/A 2. Open label 3. Parallel 4. Non-Controlled
JO43175	A Phase I Study of Pralsetinib in Patients With RET Altered Solid Tumor	Phase I	1. Nonrandomized 2. Open label 3. Single Group 4. Non-Controlled

<b>Study Number</b>	<b>Study Title</b>	<b>Study Phase</b>	<b>Study Design [Randomisation, Blinding, Design, Comparison]</b>
JO43701	A Phase II Study of Pralsetinib in Patients with Previously Treated RET Fusion Positive Non-Small Cell Lung Cancer	Phase II	1. Nonrandomized 2. Open label 3. Single Group 4. Non-Controlled
ML41591	Nautika1: A Multicenter, Phase II, Neoadjuvant and Adjuvant Study of Multiple Therapies in Biomarker-Selected Patients with Resectable Stages Ib-III Non-Small Cell Lung Cancer	Phase II	1. Nonrandomized 2. Open label 3. Single Group 4. Non-Controlled
ML42439	Mytactic: An Open-Label Phase II Study Evaluating Targeted Therapies in Patients who have Advanced Solid Tumors With Genomic Alterations Or Protein Expression Patterns Predictive Of Response	Phase II	1. Nonrandomized 2. Open label 3. Parallel 4. Non-Controlled

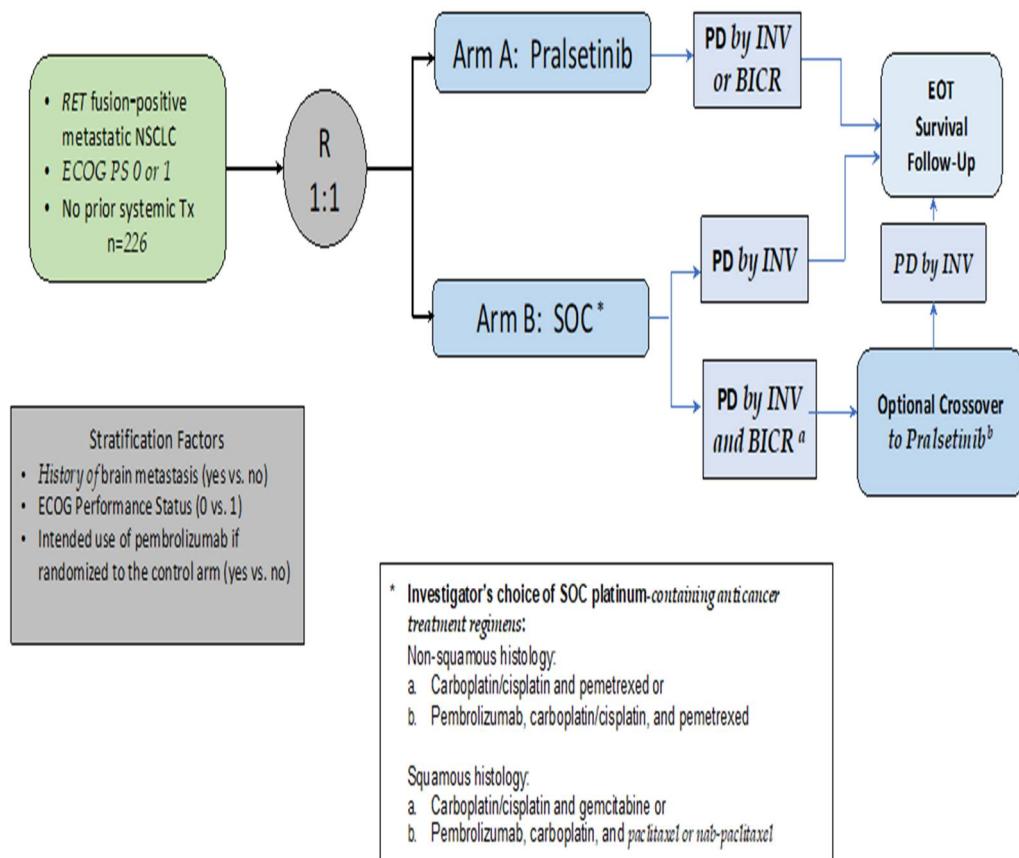
CYP: Cytochrome P450

Of the studies reported in [Table 1](#), BO42864 (AcceleRET-Lung) and BO42863 (ARROW) are included for trial case analysis. Safety data from the AcceleRET-Lung study triggered this analysis. Additionally, the ARROW study is being included as it provides a larger dataset of patients and the current labelling documents for Gavreto are based on the results of this study.

### **2.2.1      Study BO42864 (AcceleRET-Lung)**

A randomized, open label, parallel, active controlled, Phase III study of pralsetinib versus standard of care for first-line treatment of RET fusion-positive, metastatic NSCLC, is currently ongoing; however, a decision has been made to stop the study based on the decision taken by Blueprint Medicines to terminate marketing and development of Gavreto outside of the United States and Greater China, and following that decision, the study has been unblinded. The decision to terminate the study was not based on any findings related to efficacy or safety of pralsetinib in the trial participants. The safety population includes all patients who received any amount of study drug. Only adverse events that occurred during the main treatment period are included in these analyses; patients randomized to the control arm had the option to receive pralsetinib following disease progression. Please see [Figure 1](#) for study design.

**Figure 1 Flow Diagram of AcceleRET-LUNG Study**



BICR = blinded independent central review; ECOG PS = Eastern Cooperative Oncology Group Performance Status; EOT = end of treatment; INV = investigator; NSCLC = non-small cell lung cancer; PD = progressive disease; R = randomization; RET = rearranged during transfection; SOC = standard of care; tx = treatment

The AcceleRET-Lung study presents the first opportunity to consider randomized safety data comparing pralsetinib with standard of care treatment options (platinum doublet  $\pm$  pembrolizumab) in patients with RET fusion-positive NSCLC. The data used for DSR authoring was based on data extracted from the study's clinical database on 12 July 2024. The last patient was enrolled on 6 February 2024, hence this data-cut represents a relatively mature dataset for evaluating safety (212 safety evaluable patients in this analysis, from a planned enrollment of 226 patients). Note; however, that this dataset does not correspond to a formal data-cut for the study, so missing information and inconsistencies in the data are to be expected. The study was unblinded following the decision to terminate the study, allowing for a by treatment analysis of the data. Adverse Events were coded using MedDRA version 27.0.

## **2.2.2 Study BO42863 (ARROW)**

ARROW is a non-randomized, open-label, Phase I/II study of pralsetinib in patients with thyroid cancer, NSCLC and other advanced solid tumors. The study is ongoing, but completed enrolment in December 2021 and last patient last visit was on 21 March 2024.

The clinical cut-off date of the study used for DSR authoring was the latest available data-cut date of 04 March 2022<sup>7</sup>.

## **2.3 ANALYSIS OF COMPANY SAFETY DATABASE**

The Company Safety Database records information on the following:

- Reports from interventional clinical trials: all cases with Serious adverse events (SAEs) or some designate non-serious adverse events (NSAEs), where pralsetinib is considered “suspect”.
- Reports from unsolicited sources: including all serious and non-serious cases arising from spontaneous reports, scientific literature, Internet and digital media and other sources (e.g., newspapers and lay media).
- Reports from solicited sources other than interventional clinical trials: including all serious and non-serious cases arising from organized data collections systems, including non-interventional studies, market research, and patient support programs.

The database search criteria used in this report are outlined in [Table 2](#).

**Table 2 Summary of search criteria used**

Criteria	Search Criteria used in this report
Reporting period	Cumulative through 05 August 2024
Report sources:	Spontaneous/Literature/Clinical/All
Suspect drug(s):	Pralsetinib / Gavreto
MedDRA search terms (Version 27.0):	SOC “Infections and Infestations”.
Search type	Clinical trial/post-marketing/literature

### **2.3.1 Strategy for Case Analysis**

All the cases retrieved by the search strategy outlined above were screened. The focus of analysis was to identify cases reporting infection events with a Common Terminology Criteria for Adverse Events CTCAE severity grade of  $\geq 3$ .

All serious cases reporting infection events were individually reviewed to evaluate a causal association between pralsetinib treatment and an increased risk of severe infection, and death due to infection. These cases included infection events with severity

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<sup>7</sup> Serious events that have occurred after that date, will be reported in the section “evidence from Company Global Safety Database.

grade of  $\geq 3$ , as well as cases where information regarding the severity grade was not reported.

The individual case evaluation of serious cases included a review of the concurrent/underlying medical conditions and relevant concomitant medications known to be associated with infections, drug-event latency period, positive de-challenge/re-challenge, relevant laboratory measures, and/or event outcome.

Based on the medical review and strength of evidence, the cases were categorized as below:

- **Category A:** Cases with likely causal association with no other alternate explanation.
- **Category B:** Cases with additional risk factors or plausible alternate explanation/other etiology for infections.
- **Category C:** Cases with insufficient information to allow a meaningful causality assessment.

All non-Serious Adverse Events (NSAEs) of infections and AEs of infections with reported severity of Grade 1 and Grade 2, as retrieved from the Safety database, were summarized in an aggregate fashion without comprehensive review of the individual case narratives. For these lower-grade events, no risk factor analysis was conducted.

For cases where severity grading was not reported or was unclear, individual case narratives were meticulously reviewed to ascertain the severity or seriousness of the events. An overall aggregate summary has been provided for these cases with no further risk factor assessment. However, in instances where the narrative review identified infections of grade 3 or higher severity, a detailed risk factor analysis has been performed.

### **3. RESULTS**

#### **3.1 RELEVANT TOXICOLOGY RESULTS**

The toxicology program for pralsetinib to date consists of oral single- and repeat-dose toxicity studies with durations up to 13 weeks in rats and cynomolgus monkeys, in vitro and in vivo genotoxicity, embryo-fetal developmental toxicity, fertility and early embryonic development toxicity, in vitro and in vivo phototoxicity studies, in vitro safety pharmacology studies and a single dose cardiovascular safety study in rats. The main toxicities of pralsetinib observed in rat and/or monkeys included hematological abnormalities, effects on bony tissues, reproductive/developmental toxicities, metabolic perturbation, and effects on cardiovascular and gastrointestinal systems. With the exception of developmental toxicities, which were attributed to on-target RET inhibition, the majority of the pralsetinib-related toxicologic effects were attributed to off-target

kinase inhibition such as hematological abnormalities (reduced bone marrow cellularity) ([Gavreto cRMP](#)).

### **3.1.1 Hematologic and Lymphoid Systems**

The key common toxicities noted in rat and/or monkey at systemic exposures similar to clinical steady state exposures (Area Under Curve [AUC<sub>0-24</sub>]) at the 400 mg QD dose included hematological abnormalities (reduced bone marrow cellularity, reduced hemoglobin, reduced reticulocytes), and lymphoid effects (reduced lymphoid cellularity and decreased lymphocyte counts). These effects were dose-dependent and reversible. The primary cellular effects on the bone marrow and erythron parameters were attributed to off-target Janus kinase (JAK) 2 inhibition. The decreased cellularity of lymphoid organs corresponding with changes in the hemogram, notably decreased lymphocytes with increased neutrophils and monocytes was attributed to stress response rather than to pralsetinib-related off-target effects ([Gavreto cRMP](#)).

There are no other relevant toxicology results for this report.

## **3.2 EVIDENCE FROM COMPANY SPONSORED CLINICAL TRIALS**

### **3.2.1 AcceleRET-Lung Study**

In the clinical trial AcceleRET-Lung, as of 12 July 2024, 108 subjects received pralsetinib and 104 subjects received standard of care/ comparator treatment. A total of 14 subjects (14/108; 13.0%) in the pralsetinib treatment arm and 5 subjects (5/104; 4.8%) in comparator arm developed fatal AEs (see [Table 3](#)).

Of note, fatal infections are a subset of fatal AEs, i.e., out of the total fatal AEs, 5 fatal events were due to infections occurred in the pralsetinib arm while no fatal infection was observed in the Standard of Care arm. However, for comparative safety between the arms, [Table 4](#) presents the breakdown of all fatal events including fatal infections by broad medical concept.

**Table 3 Comparative Safety in the AcceleRET-Lung Study**

Medical Concept	Pralsetinib N=108	Standard of Care N=104
Total Fatal AEs	14 (13.0%)	5 (4.8%)
Fatal Infections	5 (4.6%)	0
Grade 3-4 Infections	25 <sup>a</sup> (23.1%)	10 (9.6%)

a: Two of the 25 patients also presented with Grade 5 AEs of infections. Hence the total number of unique patients who experienced events of infections would be 28.

Note: Percentages are based on N. MedDRA Version 27.0; Analysis includes COVID-19 AEs

Clinical Output Source:

root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/t\_ae\_ctc\_MAIN\_SE.out

**Table 4 Distribution of Fatal AEs by Selected Medical Concept in the AcceleRET-Lung study**

Medical Concept	Pralsetinib N=108	Standard of Care N=104
<b>Infection AEs</b> Preferred Terms: Pneumonia, Sepsis, Lower respiratory tract infection	5 (4.6%)	0
<b>Cardiac AEs</b> Preferred Terms: Cardio-respiratory arrest, Cardiac tamponade, Myocardial infarction)	2 (1.9%)	1 (1.0%)
<b>Respiratory AEs</b> Preferred Terms: Respiratory failure, dyspnoea, Interstitial lung disease, Pulmonary fibrosis, Pleural effusion, Pulmonary embolism)	5 (4.6%)	2 (1.9%)
Death NOS	1 (0.9%)	0
Pyrexia	1 (0.9%)	0
GI haemorrhage	0	1(1%)
Acute kidney injury	0	1(1%)

Note: Percentages are based on N. MedDRA Version 27.0.  
 NOS: Not Otherwise Specified  
 Clinical Output Source:  
[root/clinical\\_studies/RO7499790/CDT30380/BO42864/data\\_analysis/Adhoc\\_Analysis/prod/output/t\\_ae\\_ct\\_c\\_MAIN\\_SE.out](root/clinical_studies/RO7499790/CDT30380/BO42864/data_analysis/Adhoc_Analysis/prod/output/t_ae_ct_c_MAIN_SE.out)

The analysis of both the study arms was performed in relevance to infection related AEs. [Table 5](#) summarizes the distribution of Grade 3-5 infection AEs by MedDRA PT in pralsetinib treatment arm and comparator arm.

**Table 5 Distribution of Grade 3-5 Infection AEs by MedDRA Preferred Term in Pralsetinib Treatment Arm and Standard of Care Arm of the AcceleRET-Lung study**

Adverse Events MedDRA PT	Pralsetinib Treated Arm (N=108)		Standard of Care (N=104)	
	Grade 3-4 (%)	Grade 5 (%)	Grade 3-4 (%)	Grade 5 (%)
COVID-19	0	0	1 (1.0)	0
COVID-19 pneumonia	1 (0.9)	0	1 (1.0)	0
Pneumonia	7 (6.5)	3 (2.8)	4 (3.8)	0
<i>Pneumocystis jirovecii</i> pneumonia	3 (2.8)	0	0	0
Pneumonia cytomegaloviral	2 (1.9)	0	0	0

Adverse Events MedDRA PT	Pralsetinib Treated Arm (N=108)		Standard of Care (N=104)	
	Grade 3-4 (%)	Grade 5 (%)	Grade 3-4 (%)	Grade 5 (%)
Pneumonia legionella	1 (0.9)	0	0	0
Urinary tract infection	2 (1.9)	0	0	0
Herpes zoster	2 (1.9)	0	0	0
Respiratory tract infection	0	0	1 (1.0)	0
Lower respiratory tract infection	0	1 (0.9)	0	0
Infection	1 (0.9)	0	0	0
Sepsis	1 (0.9)	1 (0.9)	1(1.0)	0
Device related infection	2 (1.9)	0	0	0
Diverticulitis	0	0	1(1.0)	0
Escherichia infection	0	0	1(1.0)	0
Pyelonephritis	3 (2.8)	0	0	0
Urosepsis	1 (0.9)	0	0	0
Bronchopulmonary aspergillosis	1 (0.9)	0	0	0
Oesophageal candidiasis	1 (0.9)	0	0	0
Oesophageal infection	1 (0.9)	0	0	0
Pleural infection	1 (0.9)	0	0	0
Pseudomembranous colitis	1 (0.9)	0	0	0
Pyelonephritis acute	1 (0.9)	0	0	0
Q fever	1 (0.9)	0	0	0
Spontaneous bacterial peritonitis	1 (0.9)	0	0	0
Staphylococcal sepsis	1 (0.9)	0	0	0
<b>Total No. of AEs</b>	<b>36</b>	<b>5</b>	<b>12</b>	<b>0</b>

Adverse Events MedDRA PT	Pralsetinib Treated Arm (N=108)		Standard of Care (N=104)	
	Grade 3-4 (%)	Grade 5 (%)	Grade 3-4 (%)	Grade 5 (%)
Note: The row per each MedDRA PT contains numbers and percentages of patients (within each treatment arm), whereas the last row contains the total number of AEs.				
Note for Pralsetinib Arm: 11 patients presented with more than one AE (9 patients with 2 AEs each and 2 patients with 3 AEs). Hence, a total of 41 AEs were reported in 28 patients.				
Of these 36 Grade 3-4 AEs, 5 AEs were of Grade 4 severity with PTs as Sepsis (n=2) and Device related infection, Urosepsis and Pneumocystis jirovecii pneumonia (n=1 each)				
MedDRA Version 27.0				
Clinical Output Source: <a href="root/clinical_studies/RO7499790/CDT30380/BO42864/data_analysis/Adhoc_Analysis/prod/output/t_ae_ctc_MAIN_SE.out">root/clinical_studies/RO7499790/CDT30380/BO42864/data_analysis/Adhoc_Analysis/prod/output/t_ae_ctc_MAIN_SE.out</a>				

The most frequently reported PT with Grade 5 and Grade 3-4 infections was Pneumonia<sup>8</sup> (3/5; 60% and 13/34; 38.2% respectively).

The Grade 3-5 infection AEs in the pralsetinib arm have been described and analyzed in the following Section 3.2.1.1 and Section 3.2.1.2.

### 3.2.1.1 Infections leading to death (Grade 5)

A total of five (5/108; 4.6%) subjects developed five fatal events of infections in the pralsetinib treatment arm ([Table 3](#)). The reported PTs included Pneumonia (n=3), lower respiratory tract infection (n=1) and sepsis (n=1).

No fatal events related to infections were reported in the comparator treatment arm.

[Table 6](#) presents an overview of the subjects with fatal infections in the pralsetinib treatment arm:

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<sup>8</sup> Grade 3-4 Pneumonia includes PTs of Pneumonia (n=7), Pneumocystis jirovecii pneumonia (n=3), Pneumonia cytomegaloviral (n=2) and Pneumonia legionella (n=1).

**Table 6 Overview of Subjects with Fatal Infections in the Pralsetinib Treatment Arm for the AcceleRET-Lung study (N=5)**

Patient Number Age/Sex Ethnicity/Country Indication	MedDRA PT of Fatal AE Time to Event Onset (in days) Day of Death	Action taken with Pralsetinib Causality (as per investigator)
3302/012 57/Male Asian/Korea, republic of Non-small cell lung cancer	Pneumonia SD 58 SD 71	Drug withdrawn Not related
4201/002 <sup>9</sup> 76/Female Unknown/France Non-small cell lung cancer metastatic	Pneumonia SD 30 SD 39	Dose not changed Not related
4508/003 <sup>10</sup> 72/Male White/ Spain Non-small cell lung cancer metastatic	Sepsis SD 155 SD 155	Drug withdrawn Not related
4701/001 33/Female White/ United Kingdom Non-small cell lung cancer metastatic	Lower respiratory tract infection SD 51 SD 60	Drug withdrawn Related
7201/001 70/Female American Indian or Alaska native/ Costa Rica Non-small cell lung cancer metastatic	Pneumonia SD 25 SD 26	Dose not changed Not related

MedDRA Version 27.0. SD: Study Day

Clinical Output Source:

root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/l\_ae\_INVI\_NF\_SE.out

Of the five fatal infection events in pralsetinib arm 5/108 (4.6%), three fatal events of pneumonia were reported in 3/108 (2.8%) patients (2 females and one male), aged 57 to 76 years. These three events were reported from Costa Rica, France, and Korea, Republic of (n=1 each). All patients had received pralsetinib for non-small cell lung cancer/ metastatic. The time to onset ranged from 25, 30 and 58 days. All the three

<sup>9</sup> This patient also presented with Grade 3 AE of Pyelonephritis

<sup>10</sup> This patient presented with Grade 3 AE of Pseudomembranous colitis and Grade 4 Sepsis.

events were considered as not related to pralsetinib treatment by the study investigator (1 event of pneumonia was attributed to the underlying malignancy).

The remaining two fatal events reporting PT of lower respiratory tract infection and sepsis were reported in a 33-year-old female and 72-year-old male, respectively. These two events were reported from Spain and United Kingdom. Both patients had received pralsetinib for non-small cell lung cancer metastatic. The time to onset of these events was reported as 51 and 155 days, respectively. The therapy with pralsetinib was withdrawn for both the events. The study investigator assessed the event of sepsis as not related while lower respiratory tract infection as related to pralsetinib treatment.

These five fatal cases were also retrieved in Company Safety database and are described in detail below:

**AER 3172766 (PT: Pneumonia):** This clinical study case concerns a 69-year-old female patient (patient number: 7201001) who presented with bronchopneumonia, 24 days after starting therapy with pralsetinib for non-small cell lung cancer metastatic.

AEs concurrent to bronchopneumonia included urinary tract infection, mucosal inflammation, hyponatremia, leukopenia and lymphopenia.

Patient's medical history included dyspnea, hypertension, insomnia, hyponatremia, lactate dehydrogenase increased, leukocytosis, hypereosinophilia. She was a non-smoker. Concomitant medications included formoterol, budesonide-formoterol, clonazepam, loperamide, ciprofloxacin and saline solution.

On Cycle 1 Day 1, the patient received pralsetinib at a dose of 400 mg daily that was administered until Study Day 21. On Study Day 22, the pralsetinib dose was interrupted due to events of Grade 3 hyponatremia in conjunction with Grade 1 leukopenia and Grade 3 lymphopenia. Laboratory values were reported as lymphocyte count:  $1.5 \times 10^9/L$  (screening),  $0.28 \times 10^9/L$  (at Day 22), absolute neutrophil count was within normal limits. On Study Day 25, the patient presented with bronchopneumonia (initial severity Grade 3), and clinical deterioration with dyspnea, lack of appetite and general weakness, and was kept under observation in the hospital. She received cefotaxime as treatment. On Study Day 25, she died due to bronchopneumonia (Grade 5). No information on autopsy was provided.

The physician assessed the fatal bronchopneumonia as not related to pralsetinib. No additional information is available at this time.

***MAH Comment:*** *The patient developed pneumonia 24 days after pralsetinib treatment initiation; four days after the last dose of pralsetinib. However, patient's detailed clinical course, other investigations like bronchoscopy, sputum analysis, blood cultures and any*

*imaging studies while she was in the hospital were not reported. Additionally, it was unknown if an autopsy was performed or not.*

**AER 3313491 (PT: Sepsis):** This clinical study case concerns a 72-year-old male patient (patient number: 4508003) who developed cholangitis, pseudomembranous colitis, pleural effusion, episodes of sepsis after receiving treatment with pralsetinib for non-small cell lung cancer metastatic.

Patient's medical history included chronic obstructive pulmonary disease, dyspnea, rib cage pain (right side), bilirubin increased (all ongoing at baseline) and creatinine increased (past). Patient was a former smoker. Concomitant medications included paracetamol, salbutamol, olodaterol, atovaquone, amoxicillin, budesonide, calcium acetate and carbonate, trimethoprim-sulfamethazole, dexamethasone, diazepam, enoxaparin, insulin, ipratropium, lorazepam, magnesium, meropenem, methylprednisolone, metoclopramide, morphine, omeprazole, pantoprazole, ondansetron, salbutamol, tobramycin, tazobactam, tiotropium, tranexamic acid.

From Study Day 1 to Study Day 62, the patient received treatment with pralsetinib at a dose of 400 mg QD. On Study Day 63, pralsetinib treatment was interrupted due to Grade 2 cholangitis. The patient developed Grade 2 cholangitis and hypoxemia, leading to an ER admission on Study Day 64. Chest Computerized Tomography (CT) on Study Day 75, showed bilateral infiltrates. Subsequently, on Study Day 78, the patient developed Grade 4 sepsis of respiratory origin, Polymerase Chain Reaction (PCR) pneumocystis jirovecii positive, and was hospitalized due to worsening of respiratory condition (received trimethoprim/sulfamethoxazole treatment). On Study Day 100, Grade 3 pseudomembranous colitis was diagnosed after abdominal angiogram CT due to signs of colitis. On the same day he experienced hypovolemic shock associated with grade 4 thrombocytopenia and grade 4 anemia, reported by the investigator as probably related to the trimethoprim/sulfamethoxazole treatment. He was diagnosed with pseudomembranous colitis due to *Clostridium difficile* and started on Fidaxomicin. Pseudomembranous colitis was resolved on Study Day 123. On Study Day 117, the patient developed Grade 2 pleural effusion, with new respiratory worsening (due to pleural effusion and pulmonary superinfection), and underwent thoracentesis. Also concurrent Grade 4 anemia (since Study Day 101). All AEs, except anemia (ongoing), eventually resolved at latest by Study Day 126. On Study Day 127, pralsetinib was reintroduced at 400 mg, and the patient was discharged on Study Day 139. On Study Day 155, the patient developed Grade 5 sepsis and passed away. Autopsy status was unknown. The investigator assessed the cholangitis, pseudomembranous colitis, sepsis, pleural effusion as not related to pralsetinib while the investigator reported pulmonary superinfection as other suspected cause for the pleural effusion.

**MAH Comment:** *The patient presented with a medical history of increased bilirubin and therefore the concurrent condition of cholangitis could be an ongoing phenomenon from baseline. While hospitalized the patient received trimethoprim/sulfamethoxazole, which*

is known to cause *Clostridium difficile* infection including colitis. The patient's immunocompromised status as evidenced by the presence of *pneumocystis jirovecii*, advanced age and chronic obstructive pulmonary disease are potential risk factors for the progression into sepsis.

**AER 3355432 (PT: Pneumonia):** This case concerns a 76-year-old female patient (patient number: 4201002) who developed pyelonephritis, femoral neck fracture, fatal infectious pneumopathy after receiving treatment with pralsetinib for non-small cell lung cancer metastatic.

The patient's medical history included arterial hypertension, epilepsy, diabetes mellitus, severe osteoporosis, right scapulohumeral periarthritis, hypothyroidism, dyslipidemia, urinary tract infection, insomnia (all ongoing at baseline), pulmonary embolism (past), idiopathic pneumothorax (past). She was a non-smoker. Concomitant medications included atorvastatin, pantoprazole, perindopril, levothyroxine, apixaban, lamotrigine, propranolol, zopiclone.

On Study Day 1, the patient started therapy with oral pralsetinib 400 mg once a day. On Study Day 17, she developed pyelonephritis (Grade 3), accompanied by hyperthermia and chills, and was hospitalized. On Study Day 18, treatment with pralsetinib was interrupted. On the same day, the cyto-bacteriological examination of urine showed *Klebsiella pneumoniae* and an abdominal pelvic scan showed an acute bilateral pyelonephritis picture. She was treated with IV ceftriaxone, IV metronidazole, IV cefotaxime and oral acide clavulanique/amoxicillin. During hospitalization she also suffered from anaemia, which was treated by administration of 2 red blood cell units. On Study Day 24, treatment with pralsetinib was restarted at 400 mg and she was discharged from hospital on Study Day 28.

On Study Day 30, blood cultures were in progress with no detected organisms, a negative COVID test, and negative urinary legionella antigen. The pyelonephritis, hyperthermia, and chills were resolved. However, on the same day, she experienced a fall (Grade 3), femoral neck fracture (Grade 4), and was also found to have lung infection/ infectious pneumopathy/ right lower lobar pneumonia (Grade 3). Oxygen saturations were recorded as 85% on 15 litres of oxygen. Respiratory distress occurred due to right lower lobar pneumonia. She was given IV furosemide, oxygen therapy and antibiotics. Hip surgery was not possible due to her respiratory condition. After one week of antibiotic treatment her condition was still unfavourable. She was put on comfort care and she passed away on Study Day 39 due to infectious pneumopathy (Grade 5). No autopsy was performed.

The investigator assessed the causality between pyelonephritis, infectious pneumopathy and femoral neck fracture as not related to pralsetinib but related to disease under study.

**MAH Comment:** The patient reported a medical history of urinary tract infection which could have progressed to pyelonephritis. In addition, the patient was an elderly with diabetes and dyslipidemia, which are additional risk factors for the reported events.

**AER 3355845 (PT: Lower respiratory tract infection):** This case concerns a 33-year-old female patient (ID: 4701001) who died due to chest infection after receiving treatment with pralsetinib for non-small cell lung cancer metastatic.

Patient's medical history included ovarian cyst and anxiety (both ongoing at baseline). Relevant concurrent adverse events included cough and fatigue (both grade 1). Concomitant medication included amoxicillin/ clavulanate potassium.

On Study Day 1, the patient started treatment with pralsetinib at a dose of 400 mg daily. On Study Day 51, the patient developed chest infection (Initial: Grade 3 and progressing to Grade 5) with symptoms of worsening shortness of breath, cough, and fever. She started antibiotics (piperacillin/tazobactum, amoxicillin, metronidazole and gentamycin) but cough became worse and diarrhea ensued. On Study Day 57, pralsetinib was withdrawn in response to the AE of chest infection and she was admitted to a local hospital with worsening fatigue, dyspnea, diarrhea, and vomiting. Despite the hospital's best efforts, the patient's condition did not improve, and she passed away on Study Day 60. It was not reported if an autopsy was performed or not. Eastern Cooperative Oncology Group (ECOG) performance was 1 throughout study. No further information is available. The investigator assessed the chest infection as related to pralsetinib.

**MAH Comment:** As the event occurred within 51 days of pralsetinib initiation, a plausible causality could not be excluded. However, the concurrent worsening fatigue, diarrhea and vomiting probably due to broad spectrum antibiotics could have contributed to the fatal outcome. Further information with respect to the status of the ovarian cyst and any associated treatment was not available.

**AER 3428340 (PT: Pneumonia):** This case concerns a 57-year-old male patient (patient number: 3302012) who experienced lung infection and died after receiving treatment with pralsetinib for non-small cell lung cancer metastatic.

The patient's medical history included diabetes, developmental venous anomaly in left occipital lobe, peritumoral edema, anemia and aspartate aminotransferase (AST) increased (all ongoing at baseline). Other adverse events included constipation, dysgeusia, paraesthesia, alanine aminotransferase increased, blood creatinine increased (all concurrent) and dysuria (dysuria until study day 58). Concomitant medications included lactulose, pregabalin, magnesium oxide, sodium chloride, ursodeoxycholic acid, cefpodoxime proxetil and paracetamol.

On Study Day 1, the patient started therapy with pralsetinib at 400 mg daily. On Study Day 58, he developed a lung infection accompanied by a sore throat. Seven days' later

fever and cough started. On Study Day 69, he received the most recent pralsetinib dose prior to death. On the same day (unscheduled visit) he underwent investigations for pneumonia. Chest CT (non- contrast), respiratory virus test with result negative, *Pneumocystis jirovecii* PCR with positive result, atypical pneumonia pathogen multiplex RT-PCR showed negative, culture (blood, urine, sputum) was negative. Treatment with paracetamol and cefadroxil was started. Severe general weakness occurred, attributed by the investigator to the lung infection. On Study Day 71, event became serious and while receiving treatment at another hospital (ventilator care, inotropic treatment), the patient died due to lung infection. It was not reported if an autopsy was performed or not. Therapy was withdrawn in response to the lung infection. Relevant laboratory values: Absolute neutrophil count 5.26 (screening), 1.90 (Day 22), 3.01 (Day 43), 1.65 (Day 64), 2.20 (Day 69); lymphocyte count was within normal limits.

The physician assessed the lung infection as not related to pralsetinib while related to *Pneumocystis jirovecii* infection. No further information was reported.

**MAH Comment:** *The patient's medical history of diabetes is a risk factor for their immunocompromised state.*

### **3.2.1.2 Grade 3-4 Infections**

A total of 23 (23/108; 21.3%) patients in the pralsetinib treatment arm had a maximum Grade 3 or Grade 4 infection events (32 total events in these patients) in the AcceleRET-Lung study (excluding COVID-19 events). Of these 23 patients, 19/23 presented with 28 AEs corresponding to Grade 3 infections while 4/23 patients presented with 4 AEs corresponding to Grade 4 infections.

On the other hand, 8 (8/104; 7.7%) patients in the comparator treatment arm developed Grade 3-4 infection events.

An overview of the subjects with Grade 3 and Grade 4 infections in pralsetinib treatment arm is presented in [Appendix 2](#).

The review of these Grade 3 and Grade 4 AEs showed that for 18/32 events, therapy with pralsetinib was interrupted/ withdrawn/reduced, and was maintained for 13/32 events while action taken with pralsetinib was not applicable for remaining one AE. Of the 20 AEs for which pralsetinib therapy was modified, 13/18 resolved or resolved with sequelae while five (5/18) had not resolved. The time to onset was known for all the 32 AEs and ranged from 20 to 1001 days (with a median of 122 days). The reporting investigator assessed 23 AEs as not related and nine as related to the study drug i.e, pralsetinib.

Of note, 18<sup>11</sup> of these 23 clinical study cases have also been retrieved in the Safety database and are discussed in detail in Section 3.3.1. However, the remaining 5/23 cases (with patients' IDs 4307/004, 4517/001, 7301/006, 4208/004 and 4508/002) were not identified in the Company Safety database and hence a brief overview of these five cases is provided below:

These five cases reported 7 AEs (including four serious AEs of Urinary Tract infection [n=1], infection [n=1], Pneumonia [n=2] and three non-serious AEs of Oesophageal candidiasis, Bronchopulmonary aspergillosis and Oesophageal infection [n=1 each]). The cases concerned two male patients and three female patients, with age ranged from 58 to 79 years. The time to onset ranged from 52 to 1001 days (with a median of 280 days). For 6/7 events, pralsetinib dose was not changed while for 1/7 AE, action taken with pralsetinib was not applicable. All the events were reported as resolved and/or resolving. Four events were considered as not related while three as related to pralsetinib treatment by the study investigator.

### 3.2.1.3 Opportunistic Infections

The review of the data from AcceleRET-Lung for the presence of Grade 3-5 opportunistic infections was also performed. From the review, it has been identified that a total of 8 AEs related to opportunistic infections were reported in 7 patients (7/108; 6.5%) in pralsetinib treatment arm, however no patients in the standard of care arm presented with opportunistic infections (see [Table 7](#)).

- PTs of the opportunistic infections reported in pralsetinib arm included Pneumocystis jirovecii pneumonia (n=3); Pneumonia cytomegaloviral, (n=2); Pneumonia legionella, Bronchopulmonary aspergillosis and Oesophageal candidiasis (n=1 each).
- All these AEs were of Grade 3-4 severity.
- The time to onset observed for these AEs ranged from 26 to 280 days (with a median of 116.5 days). All of these AEs were reported as resolved/ resolved with sequelae.
- Of the 7 patients who developed opportunistic infections, only 2/7 patients had been taking systemic corticosteroids prior to the onset of the infection (see [Table 8](#))
- From this analysis, prior corticosteroid use does not appear to be an inciting risk factor for the development of severe opportunistic infections in pralsetinib treated patients in AcceleRET-Lung.

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<sup>11</sup> AER 3489162, AER 2951941, AER 2944253, AER 3107480, AER 3509451, AER 3355432, AER 3041085, AER 2790973, AER 3375129, AER 3278393, AER 3446811, AER 3330307, AER 3313491, AER 3363904, AER 3145942, AER 3072556, AER 2827699, AER 3384670, AER 3495267, and AER 3207649.

**Table 7 Summary of Severe Opportunistic Infections in AcceleRET-Lung**

MedDRA PT (SMQ: Opportunistic Infections <sup>1</sup> )	Pralsetinib (N=108)	Standard of Care (N=104)
Pneumocystis jirovecii pneumonia*	3	0
Pneumonia cytomegaloviral*	2	0
Pneumonia legionella	1	0
Bronchopulmonary aspergillosis	1	0
Oesophageal candidiasis	1	0
Total Number of Patients with at least one event	7	0

<sup>1</sup>Narrow search Terms  
\*One patient experienced both Pneumonia cytomegaloviral and Pneumocystis jirovecii pneumonia  
No patients incurred an opportunistic infection with Grade 5 severity.  
MedDRA Version 27.0. SMQ: Standard MedDRA Query  
Source: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/t\_ae OPPINF3\_MAIN\_SE\_12JUL2024\_42864.out

**Table 8 Summary of Corticosteroid Use in Patients with Severe Opportunistic Infections in AcceleRET-Lung**

Patient ID Opportunistic Infection PT Onset day/Duration	Corticosteroid Use Prior to AE Onset (Yes/No)	Corticosteroid Use at onset or during the opportunistic infection (Yes/No)	Corticosteroid Details
3301/008 Pneumonia cytomegaloviral SD 85 – 105	No	Yes (Onset and following the infection)	Methylprednisolone IV QD (SD 85 – 93) Prednisolone PO QD (SD 94 - 103)
3302/007 Pneumonia cytomegaloviral (SD 161 - ongoing) Pneumocystis jirovecii pneumonia (SD 161 - 193)	No	Yes During only	Prednisolone PO QD (SD 178 -186) Methylprednisolone sodium succinate IV (SD 186 – 190 BID; SD 210-211 QD 212 – 217 BID, SD 218 – 220 QD, SD 220 – 225 BID)
4410/008 Pneumonia legionella SD 26 - 62	No	No	–
4517/001 Bronchopulmonary aspergillosis SD 148 - 208	Yes Prior: Inhalational use only	Yes (During and following the infection)	Beclometasone dipropionate, formoterol, fumarate (SD: -143 – 208 inhalation QD)

Patient ID Opportunistic Infection PT Onset day/Duration	Corticosteroid Use Prior to AE Onset (Yes/No)	Corticosteroid Use at onset or during the opportunistic infection (Yes/No)	Corticosteroid Details
			Budesonide (SD: 46 – 49, inhalation PRN) Budesonide (SD 147 – 150 inhalation BID) Dexamethasone (SD 246 IV QD) Prednisone (SD 247- 291 PO QD); Budesonide (SD: 405- 436 Nasal BID); Methylprednisolone (SD: 405-406 IV TID); Prednisone (SD: 406- 408 IV QD)
4801/002 Pneumocystis jirovecii pneumonia SD 55 - 75	Yes	Yes (Following)	Fluticasone furoate, vilanterol trifenatate (SD: -68 - unk inhalation QD); Fluticasone furoate: SD: -37 – unk nasal PRN); Dexamethasone (SD: -20 to Unk PO QD; SD 64 – 72 IV BID; SD 74 – 75 PO QD)
7301/006 Oesophageal candidiasis (SD 280 – 301)	Yes	Yes (During)	Ciclesonide (SD: -39 – 376 inhalation QD) Prednisone (SD: 153 – 162 PO QD) Budesonide (SD 274 – unk inhalation, BID)
8411/001 Pneumocystis jirovecii pneumonia SD 66 - 127	No	Yes (Following)	methylprednisolone sodium succinate (SD: 69 – 71 IV QD) prednisolone (SD 72 – 88 IV QD) Prednisolone (SD 89 – 127 PO QD)

SD: Study Day; QD: once daily, BID: Twice daily; TID: Thrice daily; PO: per oral, IV: Intravenous; PRN: As needed; unk: Unknown

Source:

[root/clinical\\_studies/RO7499790/CDT30380/BO42864/data\\_analysis/Adhoc\\_Analysis/prod/output/l\\_cm\\_opp\\_inf\\_SE\\_12JUL2024\\_42864.out](root/clinical_studies/RO7499790/CDT30380/BO42864/data_analysis/Adhoc_Analysis/prod/output/l_cm_opp_inf_SE_12JUL2024_42864.out)

### 3.2.1.4 Analysis of Neutropenia and Lymphopenia Events in Patients with Grade 3-5 Infections

An analysis of neutropenia/lymphopenia events were also conducted as these conditions are associated with increased risk of infections in cancer patients, and are already ADRs for pralsetinib [Gavreto CDS]. For the 28 patients with  $\geq$ Grade 3 infections in pralsetinib treatment arm, a total of six (6/28; 21.4%) patients presented with events of neutropenia or neutrophil count decreased and lymphopenia or lymphopenia count decreased prior to the onset of severe infections. Of these, four (4/28; 14.3%) patients presented with neutrophil count decreased/ neutropenia and three (2/28; 7.1%) patients presented with lymphocyte count decreased/ lymphopenia (see [Table 9](#)). From this analysis, neutropenia and lymphopenia do not appear to be inciting risk factors for the development of Grade 3-5 infections in pralsetinib treated patients in AcceleRET-Lung.

**Table 9 Overview of Neutropenia and Lymphopenia Events in Patients Presenting with Grade 3-5 Infections in Pralsetinib Treatment Arm of AcceleRET-Lung**

MedDRA PT	Patients with $\geq$ Grade 3 Infections in Pralsetinib Treatment Arm (N=28)		
	< Grade 3 (%)	$\geq$ Grade 3 (%)	Total (%)
Neutrophil count decreased	2 (7.1)	1 (3.6)	3 (10.7)
Lymphocyte count decreased	1 (3.6)	0	1 (3.6)
Neutropenia	1 (3.6)	0	1 (3.6)
Lymphopenia	0	1 (3.6)	1 (3.6)

MedDRA Version 27.0

Source output:

root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/l\_ae\_inf3\_NEULYMPH\_SE\_12JUL2024\_42864.out

[Table 10](#) presents details of these events in six patients with  $\geq$ Grade 3 infections. None of the patients had a medical history of neutropenia or lymphopenia prior to start of pralsetinib treatment.

From the available data, it was identified that all of the six events were resolved or resolving prior to onset of Grade 3-5 infections.

**Table 10 Details of Neutropenia and Lymphopenia Events in Patients Presenting with Grade 3-5 Infections in the AcceleRET-Lung study**

Patient ID Infection AE MedDRA PT (Severity) Onset Day	Details of Neutropenia and Lymphopenia AE				History of Neutropenia and Lymphopenia	Status of neutrophil and lymphocyte counts at the start of study or baseline
	MedDRA PT (Severity)	Onset Day	Status of Events During the onset of $\geq$ Grade 3 Infection	AE Duration (in days)		
3302/007 Pneumocystis jirovecii pneumonia (Grade 3) SD 161  Pneumonia cytomegaloviral (Grade 3) SD 161	Lymphocyte count decreased (Grade 2)	SD 44	Resolved	21	None	Lab values* at screening visit (SD: -6): high neutrophil count ( $8.57 \times 10^3/\mu\text{L}$ (1.6 -7)), low lymphocyte count ( $1.02 \times 10^3/\mu\text{L}$ (1.1 -4.1))
4202/001 Staphylococcal sepsis (Grade 3) SD 290	Neutrophil count decreased (Grade 3)	SD 20	Resolved	10	None	Lab values at C1D1 (SD 1): normal neutrophil count ( $6.86 \times 10^9/\text{L}$ (1.5 -7)), low lymphocyte count ( $1.36 \times 10^9/\text{L}$ (1.5 - 4))
4307/004 Pneumonia (Grade 3) SD 825	Neutrophil count decreased (Grade 2)	SD 343	Resolved	64	None	Lab values at C1D1 (SD 1): normal neutrophil count ( $5.4 \times 10^9/\text{L}$ (1.8 - 7.55)), normal lymphocyte count ( $1.53 \times 10^9/\text{L}$ (1.5 - 4))

Patient ID Infection AE MedDRA PT (Severity) Onset Day	Details of Neutropenia and Lymphopenia AE				History of Neutropenia and Lymphopenia	Status of neutrophil and lymphocyte counts at the start of study or baseline
	MedDRA PT (Severity)	Onset Day	Status of Events During the onset of $\geq$ Grade 3 Infection	AE Duration (in days)		
8411/001 Pneumocystis jirovecii pneumonia (Grade 4) SD 66	Neutrophil count decreased (Grade 2))	SD 22	Resolved	13	None	Lab values* at screening (SD -21): normal neutrophil count ( $4.147 \times 10^9/L$ (1- 8)), normal lymphocyte count ( $1.305 \times 10^9/L$ (1 - 5))
4404/003 Herpes Zoster (Grade 3) SD 888 Spontaneous bacterial peritonitis (Grade 3) SD 888	Neutropenia (Grade 2)	SD 86	Resolving	—	None	Lab values at C1D1 (SD 1): normal neutrophil count ( $4.25 \times 10^9/L$ (1.5 - 7.7)), normal lymphocyte count ( $2.07 \times 10^9/L$ (1.1 – 4.5))
7201/001 Pneumonia SD 25	Lymphopenia (Grade 3)	SD 22	Resolving	—	None	Lab values* at screening: High neutrophil count ( $15.64 \times 10^9/L$ (2.5 - 7.7)), normal lymphocyte count ( $1.15 \times 10^9/L$ (1 - 5))

SD: Study Day. MedDRA Version: 27.0

\*No samples collected at day of first study drug administration

Source Output:

- [root/clinical\\_studies/RO7499790/CDT30380/BO42864/data\\_analysis/Adhoc\\_Analysis/prod/output/l\\_ae\\_inf3\\_NEULYMPH\\_SE\\_12JUL2024\\_42864.out](root/clinical_studies/RO7499790/CDT30380/BO42864/data_analysis/Adhoc_Analysis/prod/output/l_ae_inf3_NEULYMPH_SE_12JUL2024_42864.out)
- [root/clinical\\_studies/RO7499790/CDT30380/BO42864/data\\_analysis/Adhoc\\_Analysis/prod/output/l\\_inf3\\_SE\\_12JUL2024\\_42864.out](root/clinical_studies/RO7499790/CDT30380/BO42864/data_analysis/Adhoc_Analysis/prod/output/l_inf3_SE_12JUL2024_42864.out)

### **3.2.2        ARROW Study**

In this non-comparative trial, as of 04 March 2022, 590 patients have received at least one dose of pralsetinib (regardless of dose and indication). Of these patients, 299 were treated for metastatic RET-fusion NSCLC. An overview of key safety results for this population is provided in [Table 11](#) and are summarized below:

Overall, 588/590 patients (99.7%) in this population experienced an AE. A total of 485/590 patients (82.2%) experienced a Grade  $\geq 3$  AE.

A total of 376/590 patients (63.7%) experienced a SAE of which infection related SAEs were reported as Pneumonia in 77/590 (13.1%) patients, Sepsis in 24/590 (4.1%) patients, Urinary tract infection in 23/590 (3.9%) patients and Coronavirus infection in 20/590 (3.4%) patients.

Further, a total of 335/590 patients (56.8%) experienced a Grade  $\geq 3$  SAE. Of these Grade 3 SAEs of infections were reported in 125/590 patients (21.2%); Grade 4 AEs were reported in 19/590 patients (3.2%) and fatal AEs (Grade 5 AEs) were reported in 24/590 patients (4.1%) (see [Table 11](#)).

- The most frequently PTs of infections (Grade 3-4) observed were: Pneumonia (9.3%), Sepsis (3.2%), Urinary tract infection (3.6%), Coronavirus infection (2.5%) and Diverticulitis (1.0%). All the remaining PTs reported frequency of <1%.
- The most frequently PT with Grade 5 severity was Pneumonia (1.9%).
- Further, treatment-related Grade 5 AEs included pneumonia (3 patients) and pneumocystis jirovecii pneumonia (1 patient).
- Opportunistic infections reported in the study included pneumocystis jirovecii pneumonia (n=6), Herpes zoster (n=3), Pneumonia legionella (n=2), Bronchopulmonary aspergillosis (n=1), Pneumonia cytomegaloviral (n=1), Sinusitis aspergillus (n=1), Proteus infection (n=1), Oropharyngeal candidiasis (n=1), Klebsiella bacteraemia (n=1) and Atypical mycobacterial pneumonia (n=1). Majority of these infections were Grade 3 while pneumocystis jirovecii pneumonia and Pneumonia cytomegaloviral (n=1 each) were Grade 5.

[Table 11](#) presents an overview of the infection SAEs (with >1% frequency) by MedDRA PT and severity Grades. The remaining infection SAEs reported a frequency <1% and are presented in [Appendix 3](#).

**Table 11 Overview of Infection SAEs by MedDRA PT in the ARROW study**

MedDRA PT	Total Number of Patients (N=590)			
	Grade 3 AE (%)	Grade 4 AE (%)	Grade 5 AE (%)	Total* (%)
Patients with SAEs	125 (21.2)	19 (3.2)	24 (4.1))	183 (31.0)
Pneumonia	50 (8.5)	5 (<1)	11 (1.9)	77 (13.1)
Sepsis	11 (1.9)	8 (1.4)	4 (<1)	24 (4.1)
Urinary Tract Infection	20 (3.4)	1 (<1)	0	23 (3.9)
Corona virus infection	14 (2.4)	1 (<1)	5 (<1)	20 (3.4)
Diverticulitis	6 (1.0)	0	0	6 (1.0)
Pneumocystis jirovecii pneumonia	5 (<1)	0	1 (<1)	6 (1.0)

\*This total count also takes into account AEs of Grade 1 and Grade 2 severity.

MedDRA Version: 19.1

Source Output: Table 14.3.2.8.1.11 in Clinical Study Report 1113097 for ARROW Study

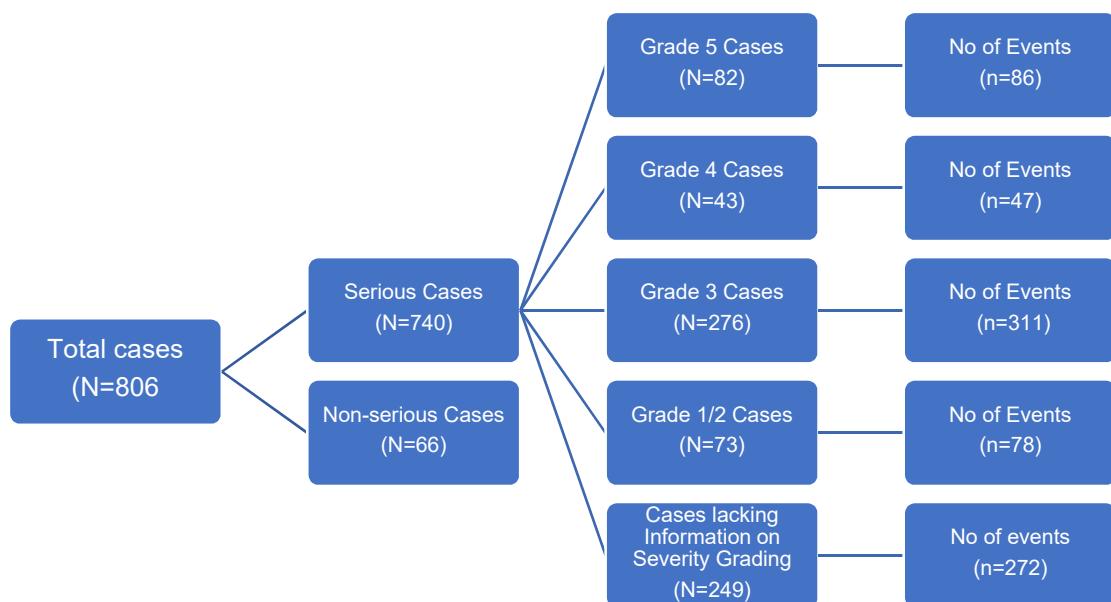
### 3.3 EVIDENCE FROM COMPANY SAFETY DATABASE

Cumulatively, a total of 806 cases reporting 923 AEs of interest were retrieved from Company Safety Database using the search strategy described in Section 2.3.1.

Of these 806 cases, 66 cases were non-serious while 740 cases were serious.

[Figure 2](#) presents disposition of the cases reporting infection AEs from the Company Safety Database.

**Figure 2 Disposition of Safety Database Cases Reporting Infection Events with Pralsetinib**



N denotes number of cases and n denotes number of events. One case may report more than 1 event of infection.

### 3.3.1 Serious Cases

A total of 740 serious cases reporting 854 AEs were retrieved from the safety database. Of these 854 AEs, 794 AEs (AEs of interest) were serious while 60 AEs were non-serious (NSAEs).

Out of the 60 NSAEs, four AEs were reported with Grade 2 severity while the severity grading for the remaining 56 AEs was not reported. These NSAEs were not assessed further.

This section focuses on the analysis of the SAEs reported from 740 cases. An overview of these SAEs with respect to severity is presented in [Table 12](#).

**Table 12 Distribution of SAEs by Severity Grade, for Cases treated with Pralsetinib from Safety Database (n=794)**

Severity Grade	Frequency of AEs (%)
Grade 5	86 (10.8)
Grade 4	47 (5.9)
Grade 3	311 (39.2)
Grade 2	66 (8.3)
Grade 1	12 (1.5)
Not reported	272 (34.3)

### 3.3.1.1 Cases with Grade 5 Infections

A total of 82 cases reported 86 fatal (Grade 5) AEs of interest. Eleven of these cases co-reported 12 non-fatal AEs<sup>12</sup> related to infection. Please note that 1 case may report more than one AE with or without fatal outcomes.

An overview of characteristics of these 82 cases reporting fatal infections is presented in [Table 13](#).

**Table 13 Summary of Characteristics of Cases Involving the Use of Pralsetinib and Reporting Fatal Infections from Safety Database (N=82)**

Characteristic	Number of Cases (%)	
<b>Primary Reporter Type</b>	Healthcare Professional	53 (64.6)
	Non-Healthcare Professional/Consumer	29 (35.4)
<b>Sex</b>	Male	51 (62.2)
	Female	27 (33.0)
	Not reported	4 (4.9)
<b>Age (Years)</b> Range: 34 to 87 Mean: 65.6 Median: 65	18 to 64 (Adult)	32 (39.0)
	≥ 65 (Elderly)	32 (39.0)
	Not reported	18 (22.0)
<b>Source</b>	Clinical Study	45 (54.9)
	Non-Interventional Study/Program	35 (42.7)
	Spontaneous	1 (1.2)

<sup>12</sup> These AEs include severity Grades as Grade 4 (n=4), Grade 3 (n=3), Grade 2 (n=1) while severity was not reported for 4 AEs.

Characteristic		Number of Cases (%)
	Literature - Non-Interventional Study/Program	1 (1.2)
Indication groups	Lung Cancer	60 (73.2)
	Thyroid Cancer	15 (18.3)
	Other malignancies	4 (4.9)
	Not reported	3 (3.7)

The below [Table 14](#) presents distribution of fatal infections by MedDRA PT.

**Table 14 Distribution of Fatal AEs by MedDRA PT from Safety Database (n=86)**

Preferred Term	Frequency (%)
Pneumonia	25 (29.1)
Sepsis	19 (22.1)
COVID-19	18 (20.9)
Septic shock	6 (7.0)
COVID-19 pneumonia	4 (4.6)
Pneumonia aspiration	3 (3.5)
Urosepsis	2 (2.3)
Pneumonia cytomegaloviral, Endocarditis bacterial, Infection, Pneumocystis jirovecii pneumonia, Lower respiratory tract infection, Urinary tract infection, Meningitis, Bronchitis, Peritonitis	1 each (39.6*)

MedDRA version: 27.0

\*Percentage is provided as combined for all the Preferred terms mentioned in the respective row.

### 3.3.1.1 Single Case Analysis

All the 82 cases reporting fatal infections were medically evaluated and assigned to the causality categories based on the strategy described in Section [2.3.1](#).

Upon review none of the cases were assessed as having a likely causal association between the fatal event and pralsetinib treatment (Category A= 0). Almost half of the cases were identified as either reporting potential risk factors/ alternate explanations for the event that led to a fatal outcome (Category B= 42/82; 51.2%) or the other half reported insufficient information to enable a comprehensive causality assessment (Category C= 40/82; 48.8%). They are further described below:

**Category A:** None of the cases had a clear causal association between the drug and the fatal event in the absence of any alternative risk factors.

**Category B:** Of the total, 42 cases reporting 43 infection events, reported risk factors/alternative explanations for the event that led to a fatal outcome. A few observations from the review of these cases are listed below:

- The most frequently reported PTs were Pneumonia (n=15), Sepsis (n=9), COVID 19 (n=5), septic shock (n=3) and Pneumonia aspiration (n=2).
- Among the 42 cases, 26 concerned males, 15 concerned females, and sex was not reported in the remaining 1 case.
- The first dose latency was < 1 month for 4 AEs, 1 to 3 months for 13 AEs and >3 months for the rest of the 26 AEs.
- The additional risk factors included pre-existing co-morbidities such as diabetes, lymphopenia, dyslipidemia, pre-existing recurrent urinary tract infections, pre-existing systemic bacteremia, asthma, COPD, underlying cancer progression and/or metastases to lung, brain, chronic renal insufficiency and/or use of anticancer drugs such as cisplatin, pemetrexed, gemcitabine, use of immunosuppressant drugs such as tocilizumab, methylprednisolone, prednisolone, dexamethasone, radiotherapy, fluticasone, mesalazine.
- Of the 42 cases, evidence of co-existing cytopenias including lymphopenia, neutropenia and leukopenia was identified in 47.6% (20/42) of these cases depicting the immunosuppressed state of the patient. The most commonly reported pathogens were Corona virus and *Staphylococcus aureus*. Other pathogens known to cause opportunistic infections were also reported including *Pneumocystis jirovecii*, Enterococcus, CMV, *Clostridium difficile*, *Klebsiella pneumoniae*, *Candida albicans*, *Streptococcus salivarius* and Actinomyces.
- Therapy with pralsetinib was interrupted/ withdrawn for 25 AEs of infections; however, the patients later died due to infection. Therapy with pralsetinib was maintained/not applicable for 1 AE, meanwhile therapy status of pralsetinib was not reported for the remaining 16 AEs.
- Autopsy details were not provided in any of the cases.
- The reported causality for these fatal events of infections was reported as related for 7 AEs, not related for 33 AEs while it was not reported for the remaining 3 AEs.

Please refer to [Appendix 4](#) for detailed analysis and line listings of these cases.

**Category C:** The remaining 40/82 (48.8%) cases reporting fatal infection events reported insufficient information regarding underlying medical conditions, concurrent conditions, concomitant medications, event course details, drug-event latency, laboratory findings, and/or autopsy findings to enable a comprehensive analysis.

Of note, five<sup>13</sup> of these 82 fatal cases were reported from study AcceleRET-Lung and had already been discussed and presented in Section 3.2.1.1. The narratives along with the case listings of the remaining 77 fatal cases are presented in [Appendix 4](#).

### 3.3.1.2 Cases with Grade 4 Infections

A total of 43 cases reporting 47 life-threatening AEs<sup>14</sup> or Grade 4 severity were retrieved from the Company Safety Database.

An overview of characteristics of these cases reporting life-threatening infections is presented in [Table 15](#).

**Table 15 Summary of Characteristics of Cases Involving the Use of Pralsetinib and Reporting Life-threatening Infections from the Safety Database (N=43)**

Characteristic		Number of Cases (%)
Primary Reporter Type	Healthcare Professional	32 (74.4)
	Non-Healthcare Professional/Consumer	11 (25.6)
Sex	Male	24 (55.8)
	Female	18 (41.9)
	Not reported	1 (2.3)
<b>Age (Years)</b> Range: 13 to 81 Mean: 59.2 Median: 60.5	< 18 (Pediatric)	1 (2.3)
	18 to 64 (Adult)	27 (62.8)
	≥ 65 (Elderly)	15 (34.9)
Source	Clinical Study	34 (79)
	Non-Interventional Study/Program	3 (7)
	Spontaneous	5 (11.6)
	Literature Study	1 (2.3)
Indication groups	Lung cancer	25 (58.1)
	Thyroid cancer	15 (34.9)
	Other malignancies	3 (7)
MedDRA version 27.0		

The below [Table 16](#) presents overview of these life-threatening infections by MedDRA PT.

<sup>13</sup> AER 3172766, AER 3313491, AER 3355432, AER 3355845 and AER 3428340.

<sup>14</sup> Along with 16 events of infections reported with severity as Grade 5 (n=4), Grade 3 (n=7), Grade 2 (n=3) and not reported (n=2).

**Table 16 Distribution of Grade 4 Infections by MedDRA PT from the Safety Database (n=47)**

Preferred Term	Count
Sepsis	13 (27.7)
Pneumonia	10 (21.3)
Pneumocystis jirovecii pneumonia	3 (6.4)
Septic shock, Urinary tract infection, Neutropenic sepsis	2 each (12.8*)
Pseudomembranous colitis, COVID-19, Arthritis infective, COVID-19 pneumonia, Staphylococcal scalded skin syndrome, Diverticulitis, Biliary Tract infection, Escherichia sepsis, Abdominal infection, Streptococcal bacteraemia, Opportunistic infection, Urosepsis, Pancreatic abscess, Peritonitis, Device related infection	1 each (32*)

\*Percentage is provided as combined for all the Preferred terms mentioned in the respective row.

#### **Event Outcome by Action Taken**

The event outcome was not reported for 3/47 (6.4%) events, 28/47 (59.6%) were resolved/resolved with sequelae, 5/47 (10.6%) were resolving, and 11/47 (23.4%) events did not resolve.

Therapy with pralsetinib was interrupted or withdrawn for 27 AEs and was maintained for 3 AEs while the action taken was not reported for 17 AEs. Of the 27 life-threatening infections for which pralsetinib was interrupted or withdrawn, 16/27 had resolved/resolved with sequelae, five (5/27) were resolving while five (5/27) had not resolved. The outcome of the remaining AEs was not reported.

- Though the 21/27 AEs which were resolved or resolving on therapy interruption or withdrawal, a positive dechallenge is confounded by the fact that the patients received corrective treatments (including but not limited to cefuroxime, gentamicin, meropenem, ceftriaxone, cefazolin, moxifloxacin, doxycycline).
- Positive rechallenge was not reported for any of the events.

##### **3.3.1.2.1 Single Case Analysis**

All the 43 cases reporting life threatening infections were medically evaluated and assigned to the causality categories based on the strategy described in Section 2.3.1.

Upon review of the cases reporting life threatening infections, two (2/43) cases were assessed as having a likely causal association between the event and pralsetinib treatment in the absence of alternative explanations (Category A), 36/43 cases were identified with reported risk factors/alternative explanations for the event (Category B)

and 5/43 were having insufficient information that could enable a comprehensive causality assessment (Category C).

**Category A:** Of the total 43 cases, two (2/43; 4.6%) cases were assessed as providing a likely association between pralsetinib and infections without contributory risk factors or alternative explanations reported in the case details. A brief overview of these cases is presented below:

- Both the cases reported from clinical studies and were medically confirmed.
- The PTs reported in these cases included *Pneumocystis jirovecii* pneumonia (n=1) and Neutropenic sepsis (n=1).
- The first dose latencies for the AEs were 65 and 1460 days.
- Both the events resolved following pralsetinib therapy interruption and introduction of corrective treatment which included levofloxacin, tazobactam/ piperacillin, steroid pulse therapy, meropenem.
- Positive rechallenge was not reported in any of these cases.
- Evidence of neutropenia was found in one case reporting neutropenic sepsis.
- The organisms identified in these 2 cases were *Pneumocystis jirovecii*, CMV and *Streptococcus pneumoniae*.
- The reporting investigator assessed *Pneumocystis jirovecii* pneumonia as related while neutropenic sepsis as not related to pralsetinib treatment.

The details of these cases are presented below:

**AER 3207649<sup>15</sup> (PT: *Pneumocystis jirovecii* pneumonia):** This clinical study case concerns a 74-year-old elderly male patient, (patient number: 8411001) who developed pneumocystis pneumonia and cholangitis whilst participating in BO42864, a phase III, randomized, open-label study of pralsetinib versus standard of care for first-line treatment of RET fusion positive, metastatic non-small cell lung cancer.

Concurrent conditions (baseline conditions and other concurrent adverse events with onset prior to the occurrence of *pneumocystis jirovecii* pneumonia) included arthralgia, cataract, cough, dyslipidaemia, hypertension, gastrooesophageal reflux disease, sinus tachycardia, blood creatinine increased (grade 1), alanine aminotransferase Increased (grade 1), AST Increased (grade 1).  
oncomitant medications included olmesartan medoxomil, probiotics, pirenoxine, tiquizium bromide, ketoprofen, dequalinium chloride, paracetamol, sodium gualenate hydrate, trichlormethiazide, bisoprolol, dextromethorphan hydrobromide hydrate and nifedipine.

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<sup>15</sup> The case AER 3207649 (Patient number: 8411/001) has also been reported in clinical outputs.

Thirteen days into therapy with pralsetinib (400 mg, once daily) the patient developed increased creatine phosphokinase, subsequent to which the therapy with pralsetinib was withdrawn. Six days later pralsetinib was restarted with dose reduced to 300 mg, once daily. Forty-six days later (Study day), the patient developed pneumocystis pneumonia (grade 2) with fever and was hospitalized. Laboratory tests included a CT scan that revealed shadows in both lungs that took the form of ground glass opacities; COVID-19 test was negative. C-reactive protein was elevated to 13, oxygen saturation was 98% in the sitting position, 88% in the supine position and pneumocystis carinii PCR test was positive. Treatment with levofloxacin, tazobactam and piperacillin infusion was started. Beta d glucan test results were found to be elevated at 273.4 and treatment was provided for suspected pneumocystis pneumonia. The patient's condition rapidly deteriorated within 24 hours of admission. Initially, he was on 1L/min oxygen, but his respiratory function had significantly worsened, necessitating an increase to 7L/min oxygen, which still failed to adequately compensate. Based on blood tests and X-rays, it was determined that the patient's pneumonia had progressed. The decline was attributed to either a pneumocystis infection or drug-induced lung injury. The patient required high-flow nasal cannula (NHF) at 50L/min with 80% oxygen. Blood gas analysis revealed: pH: 7.484, PaO<sub>2</sub>: 70.2 mmHg, and PaCO<sub>2</sub>: 31.7 mmHg, prompting a switch to non-invasive positive pressure ventilation (NPPV) at Grade 4. The patient was started on Continuous Positive Airway Pressure (CPAP) with Positive End Expiratory Pressure 4 (PEEP) at FiO<sub>2</sub> 80%. As the patient tolerated the treatment, settings were adjusted to PEEP6 at FiO<sub>2</sub> 70%. SpO<sub>2</sub> was maintained at high 90s. Subsequent blood gas analysis showed improvement: pH: 7.532, PO<sub>2</sub>: 169.8 mmHg, PCO<sub>2</sub>: 27.4 mmHg, Lactate: 0.87 mmol/L. Despite better oxygenation, the patient couldn't be weaned off NPPV. Treatment continued with tazobactam, piperacillin, and steroid pulse therapy was initiated. Three days later, the patient's respiratory status began to improve, allowing a reduction in oxygen support to NHF 40L/min at 50% to 40% oxygen. Chest imaging showed improvement in lung field shadows. However, new complications arose, including nausea and liver dysfunction. A contrast-enhanced CT scan revealed cholangitis, leading to the discontinuation of pralsetinib treatment. The patient was further managed for these conditions and discharged later, approximately one month after hospitalization, as he was recovering. Treatment was continued for pneumocystis pneumonia and he was followed up on an outpatient basis. On study day 127 the outcomes of pneumocystis pneumonia and cholangitis were resolved; chest x-ray showed no worsening, treatment for pneumocystis was discontinued.

The investigator additionally reported the adverse event of immune system disorders (non-serious, grade 3), with same onset and end date and same outcome (recovered/resolved) as pneumocystis jirovecii pneumonia. Further reported information included the following (verbatim text by the investigator):

IGG were in the 400s (study day 71), CMV-C7HRP 15/50,000 (study day 77), "patient is easily infected", "cellular immunosuppressive mechanisms are thought to be at work,

since the disease has changed mainly along the course of pneumocystis jirovecii pneumonia ". The patient was treated with Ganciclovir for I.V. infusion on study days 77 – 83.

The investigator assessed the SAEs pneumocystis jirovecii pneumonia, cholangitis and the non-serious AE immune system disorders (unk diagnosis) as related to pralsetinib.

**MAH Comment:** *The causal association between the event of pneumonia and pralsetinib cannot be excluded because of the observed drug-event latency combined with the absence of any alternative explanations,*

**AER 3327231 (PT: Neutropenic sepsis):** This clinical study case concerns a 58-year-old male patient (patient number: 1802002) who developed life threatening neutropenic sepsis whilst enrolled in BO42863, a phase 1/2 study of the highly-selective RET inhibitor, blu-667, in patients with thyroid cancer, NSCLC and other advanced solid tumors.

Concurrent conditions included community acquired pneumonia, back pain, gastroesophageal reflux disease, hypothyroidism, erectile dysfunction, constipation, low Vit. B12, and low iron. Concomitant medications included codeine phosphate, paracetamol, lansoprazole, levothyroxine, bisoprolol, calcium carbonate, cholecalciferol, alfacalcidol, salbutamol, sildenafil, naproxen, pregabalin, senna spp., docusate sodium, ferrous sulfate and hydroxycobalamin.

After 1660 days of therapy with pralsetinib, the patient was admitted to hospital with type 1 respiratory failure due to pneumonia caused by *Streptococcus pneumoniae*, associated with neutropenic sepsis, septic shock and bacteraemia. He was found to be hypoxic. His chest X ray showed right sided consolidation, neutrophil count was  $0.21 \times 10^9/L$  (range:  $1.57 - 7 \times 10^9/L$ ) and he was diagnosed with life threatening neutropenic sepsis (grade 4) with a likely chest source. On the same day, he was admitted to intensive care unit was intubated and antibiotic treatment with levofloxacin was administered. The next day, the dose of pralsetinib was interrupted in response to the life threatening neutropenic sepsis and he received treatment with ciprofloxacin, vancomycin, gentamicin, and norepinephrine. After 22 days of hospitalization, life threatening neutropenic sepsis was resolved.

The investigator assessed the life threatening neutropenic sepsis as unrelated to pralsetinib. Additionally, in the investigator's opinion the neutropenia was related to sepsis rather than IMP.

**MAH Comment:** *The event resolved on discontinuation of pralsetinib along with institution of corrective management. In absence of an alternative etiology and given the known safety profile of pralsetinib, the causative role of pralsetinib in this case of neutropenic sepsis cannot be excluded.*

**Category B:** Of the total, 36 (36/43; 83.7%) cases reporting 40 infection events were identified with risk factors/alternative explanations for the infections. A few observations from the review of these cases are listed below:

- The most reported PTs were Sepsis (n=14), Pneumonia (n=6) and Urinary tract infection (n=2).
- Of the 36 cases, 20 concerned males and 16 concerned female patients.
- The first dose latencies were < 3 months for 3 AEs, 1 to 3 months for 5 AEs, > 3 months for 1 AE and it was not reported for rest of the 31 AEs.
- The additional risk factors included pre-existing white blood cell count decreased, neutrophils decreased, ureteral catheterization/ stent placement, diabetic state, smoking, COPD, pre-existing pneumonia, diverticulitis, cellulitis, chronic kidney disease, cancer progression or metastases to lung and/or use of concomitant immunosuppressants such as dexamethasone, methylprednisolone, rituximab, bendamustine.
- Of the 20 infection events for which therapy with pralsetinib was either interrupted or withdrawn, 16 had resolved/ resolved with sequelae or were resolving while 4 had not resolved. Positive dechallenge in these was confounded by the fact that the patients received corrective treatment (IV antibiotics, meropenem, tazobactam/piperacillin, doxycycline, vancomycin, Rocephin®) for 15/16 AEs while information on corrective treatment was no reported in 1/16 case.
- None of the cases reported positive rechallenge.
- Evidence of co-existing cytopenia including lymphopenia, neutropenia and leukopenia was identified in 15/35 cases depicting the immunosuppressed state of the patient. Among these cases, the reported infections involved mostly respiratory system and urinary tract. The most common pathogen reported was *Staphylococcus aureus* followed by Corona virus and *Escherichia coli*. The opportunistic pathogens reported included *Klebsiella* species, *Pneumocystis jirovecii*, *Proteus mirabilis*, *Enterobacter* species and *Aspergillus*
- The reporter causality was reported as related for 8 AEs, not related for 25 AEs, and not reported/ unknown for the remaining 6 AEs.

**Category C:** The remaining 5/43 (11.6%) cases reporting infection events had insufficient information regarding underlying medical conditions, concurrent diseases, concomitant medications, event course details, and/or autopsy findings for a comprehensive analysis. This includes 1 case (AER 2980773) concerning a 13-year-old female patient who developed pulmonary hemorrhage, pneumonia and electrolyte imbalance 185 days after starting treatment with pralsetinib. Also, 1 case reported the PT of *Pneumocystis pneumonae* which is an opportunistic infection.

Please refer [Appendix 5](#) for the case listings of these cases.

### 3.3.1.3 Cases with Grade 3 Infections

A total of 276 cases reporting 311 Grade 3 AEs infections (along with 2 Grade 5 AEs and 8 Grade 4 AEs<sup>16</sup>) were retrieved from Company Safety Database.

An overview of characteristics of these cases reporting Grade 3 AEs is presented in [Table 17](#).

**Table 17 Summary of Characteristics of Cases Involving the Use of Pralsetinib and Reporting Grade 3 Infections from the Safety Database (N=276)**

Characteristic	Number of Cases (%)	
<b>Primary Reporter Type</b>	Healthcare Professional	214 (77.5)
	Non-Healthcare Professional/Consumer	62 (22.5)
<b>Sex</b>	Male	131 (47.5)
	Female	143 (51.8)
	Not reported	2 (0.7)
<b>Age (Years)</b> Range: 34 to 87 Mean: 65.6 Median: 65	18 to 64 (Adult)	149 (54.0)
	≥ 65 (Elderly)	126 (45.7)
	Not reported	1 (0.4)
<b>Source</b>	Clinical Study	258 (93.5)
	Non-Interventional Study/Program	16 (5.8)
	Spontaneous	2 (0.7)
<b>Indication groups</b>	Lung Cancer	141 (51.1)
	Thyroid Cancer	111 (40.2)
	Other malignancies	20 (7.2)
	Not reported	4 (1.4)
MeDRA version: 27.0		

<sup>16</sup> These Grade 4 AEs and Grade 5 AEs are already discussed in respective sections.

**Table 18 Distribution of Grade 3 Infections AEs by MedDRA PT from the Safety Database (n=311)**

Preferred Term	Frequency (%)
Pneumonia	82 (26.4)
Urinary tract infection	37 (11.9)
Sepsis, COVID-19 pneumonia	13 each (8.4*)
COVID-19	11 (3.5)
Pyelonephritis, Clostridium difficile colitis	7 each (4.4*)
Pneumocystis jirovecii pneumonia, Bacteraemia, Herpes zoster, Diverticulitis	6 each (7.6*)
Appendicitis, Pneumonia legionella	5 each (3.2*)
Urosepsis, Pneumonia aspiration, Cellulitis	4 each (3.9*)
Respiratory tract infection, Pneumonia staphylococcal, Pneumonia cytomegaloviral, Device related infection, Gastroenteritis, Urinary tract infection bacterial, Clostridium difficile infection	3 each (7*)
Pneumonia bacterial, Pseudomembranous colitis, Kidney infection, Pneumonia, Pyelonephritis acute, Hepatitis B reactivation, Diverticulitis intestinal perforated, Infection, Upper respiratory tract infection, Influenza, Urinary tract infection, Spontaneous bacterial peritonitis, Osteomyelitis, Pleural infection	2 each (8.4*)
Sinusitis aspergillus, Colonic abscess, Large intestine infection, Lower respiratory tract infection, Klebsiella infection, Epididymitis, Klebsiella urinary tract infection, Varicella, Proteus infection, Oropharyngeal candidiasis, Q fever, Escherichia sepsis, Atypical pneumonia, Peritonitis bacterial, Skin infection, Pharyngeal abscess, Staphylococcal sepsis, Cystitis, Intervertebral discitis, Haemophilus infection, Enterococcal bacteraemia, Cryptococcosis, Klebsiella bacteraemia, Bronchitis, Renal tuberculosis, Cholecystitis infective, Scrotal cellulitis, Arthritis infective, Septic arthritis staphylococcal, Bronchitis bacterial, Sinusitis bacterial, Cystitis, Spinal cord infection, Pneumonia haemophilus, Staphylococcal bacteraemia, Pneumonia influenza, Tonsillitis, Pneumonia klebsiella, Empyema, Appendicitis perforated, Pneumocystis jirovecii infection, Arthritis bacterial, Lymph node tuberculosis, Acute sinusitis, Meningitis bacterial, Enterobacter bacteremia	1 each (15.3*)

\*Percentage is provided as combined for all the Preferred terms mentioned in the respective row

### Cases reporting opportunistic infections

A total of 27 cases reported 28 PTs of opportunistic infections namely, Pneumocystis pneumonia, Herpes zoster (n=6), Pneumonia legionella (n=5), Pneumonia cytomegaloviral (n=3), Proteus, Varicella, Proteus infection, Klebsiella urinary tract infection, Cryptococcus, Sinusitis aspergillus, Klebsiella bacteremia, Pneumocystis jirovecii infection and Pneumonia klebsiella (n=1 each). The latency for the events ranged from 21 to 1825 days. The outcome for the events were resolved/resolved with sequelae in 25, not resolved in 1 and resolving in 1. In 6 of these 27 cases there was evidence of co-existing lymphopenia/leucopenia.

### Event outcome by action taken

[Table 19](#) presents the action taken with pralsetinib in response to the event.

**Table 19 Summary of Event Outcome by action taken for Grade 3 Infection AEs from Safety Database**

Event outcome	Action taken with the drug					
	Dose interrupted	Dose reduced	Drug withdrawn	Dose not changed	Not applicable	Not reported
Recovered/Resolved	159	1	4	40	10	32
Recovered/Resolved with sequelae	26	1	1	4	0	2
Not Recovered/Not resolved/Ongoing	14	1	3	1	2	1
Recovering/Resolving	3	0	0	2	0	2
Unknown	1	0	0	0	0	1
<b>Total</b>	<b>203</b>	<b>3</b>	<b>8</b>	<b>47</b>	<b>12</b>	<b>38</b>

Of the 214 events for which therapy with pralsetinib was interrupted, discontinued or dose reduced, 164 had resolved, 28 had resolved with sequelae and 3 were resolving. Of these 214 events, corrective treatment was received for 191 events, thus confounding the dechallenge information. Treatment included broad-spectrum antibiotics, antivirals, steroids, symptomatic management and corrective surgery.

#### 3.3.1.3.1 Single Case Analysis

All the 276 cases reporting Grade 3 infections were medically assessed and assigned to the causality categories based on the strategy described in Section [2.3.1](#).

Upon review of the cases reporting Grade 3 infections, none of the cases were evaluated as Category A, 236 cases reported either risk factors/alternate explanations

for the event (Category B) and for 40 cases there was insufficient information for a comprehensive causality assessment (Category C).

**Category B:** Of the total 276 cases, 236 cases (with 267 infection events) reported risk factors/alternative explanations for the AEs. A few observations from the review of these cases are listed below:

- The most reported PTs were Pneumonia (n=74) followed by Urinary tract infection (n=35), Sepsis and COVID 19 pneumonia (n=11).
- Of the 236 cases, 126 concerned females, 109 concerned males and sex was not reported for the remaining 1 case.
- The first dose latencies where reported were < 1 month for 29 AEs, 1 to 3 months for 46 AEs and > 3 months for 192 AEs.
- The additional risk factors included pre-existing co-morbidities such as diabetes, lymphopenia, dyslipidemia, pre-existing infections, asthma, COPD, underlying cancer progression and/or metastases to multiple sites, chronic renal insufficiency, renal stones and/or use of anticancer drugs like cisplatin, pemetrexed, gemcitabine; use of immunosuppressant drugs such as tocilizumab, methylprednisolone, prednisolone; dexamethasone, radiotherapy, fluticasone, mesalazine, hormonal therapy and invasive medical procedures.

Of the 236 cases, evidence of co-existing cytopenia including lymphopenia, neutropenia and leukopenia was identified in 90% (210/236) of these cases depicting the immunosuppressed state of the patient

- Among these 236 cases, the reported infections mostly involved respiratory system followed by urinary tract and gastrointestinal tract. In 101 of the 233 cases the organisms causing the infections were reported. The most common pathogens were *Escherichia coli*, Corona virus and *Staphylococcus aureus*. Some pathogens causing opportunistic infections were also reported like *Pneumocystis jirovecii*, *Enterococcus*, *Varicella zoster*, CMV, *Clostridium difficile*, *Klebsiella pneumoniae* and *Aspergillus*.
- The reporter causality for these Grade 3 events of infections was related for 32 AEs, not related for 234 AEs while it was not reported for the remaining 1 AE.

**Category C:** The remaining 40/231 (17.3%) cases reporting Grade 3 infection events had insufficient information regarding underlying medical conditions, concurrent diseases, concomitant medications and/or event course details to enable an adequate causality analysis for the events and pralsetinib.

Please refer [Appendix 6](#) for the case listings of these cases.

### **3.3.1.4 Cases lacking Information on Severity Grades for Infection**

A total of 249 cases with 272 AEs (including with 4 Grade 5 AEs<sup>17</sup>) did not report a severity grading for the AEs related to infection. A summary of these is provided below.

**Source and Demographics:** Among these 249 cases, majority (172/249) were from Non-Interventional Study Program, medically unconfirmed (206/249) and included an indication for lung cancer (198/249). Where reported (n=207), 110 cases concerned female patients and 97 cases concerned male patients. The age ranged from 34 to 85 years.

Among the AEs, Pneumonia was the most commonly reported PT (145/272), followed by Pneumocystis jirovecii pneumonia (6/272) and Pneumonia fungal (4/272). The first dose latency ranged from 0 to 1095 days. The action taken with the drug where reported was dose interrupted for 99 AEs, dose not changed for 75 AEs, drug withdrawn for 29 AEs, dose reduced for 4 AEs and not applicable for 5 AEs. The event outcome where reported was resolving/not resolved for 73 AEs and resolved in 49 AEs. The corrective treatment where reported were symptomatic management, antibiotics, anti-virals, anti-fungals, steroids and curative procedures.

Among the 249 cases 27 reported co-existing neutropenia/leukopenia/lymphopenia.

#### **Risk Factor Analysis:**

Upon review of the 249 cases lacking information on severity grades for infections, none of the AEs were assessed as having a likely causal association with pralsetinib. Of the total 249 cases, 26/249 reported risk factors/alternative explanations for the (Category B) AE while the remaining 223/249 lacked sufficient information on the clinical course, medical history, concurrent conditions or concomitant medications to medically assess the case (Category C). These are discussed below.

**Category A:** None of the cases had a likely association between the drug and the AE.

**Category B:** Of the total 249 cases, 26 cases (with 31 infection events) reported risk factors/alternative explanations for the AEs. A few observations from the review of these cases are listed below:

- The most frequently reported PT was Pneumonia (n=10), followed by Pulmonary tuberculosis (N=2).
- The additional risk factors included pre-existing co-morbidities such as diabetes, lymphopenia, dyslipidemia, pre-existing infections, COPD, underlying cancer progression and/or metastases to multiple sites, and/or use of immunosuppressant drugs such as methylprednisolone, prednisolone; dexamethasone, radiotherapy and invasive medical procedures.

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<sup>17</sup> These Grade 4 AEs and Grade 5 AEs are already discussed in respective sections.

- Of the 26 cases, evidence of cytopenia including lymphopenia, neutropenia and leukopenia was identified in 15.4% (4/26) of these cases. Among these 26 cases, the reported infections mostly involved respiratory system followed by gastro intestinal tract followed by skin and urinary tract. In 10 of the 26 cases the organisms causing the infections were reported. The pathogens were Corona virus, *Staphylococcus aureus*, *Pneumocystis jirovecii*, Mycobacterium, CMV, Cryptococcus, *Klebsiella pneumoniae* and hepatitis B virus.
- The reporter causality for these events of infections was related for 12 AEs, not related for 6 AEs while it was not reported for the remaining 13 AEs.

**Category C:** The remaining 223/249 cases had insufficient information regarding underlying medical conditions, concurrent diseases, concomitant medications and/or event course details to enable an adequate causality analysis for the events and pralsetinib.

Please refer [Appendix 7](#) for the case listings of these cases.

### **3.3.1.5 Cases with Grade 2 and 1 Infections**

A total of 73 cases with 78 AEs (along with 1 Grade 5 AE and 2 Grade 4 AEs<sup>18</sup>) reporting Grade 1 and 2 infections were reported from the Company Safety Database. An overview of these cases is provided below.

Among these 73 cases, majority (65/73) were from Clinical Study, were medically confirmed (49/73) and included an indication for lung cancer (42/73). Among these 73 cases, 37 concerned males and the remaining concerned female patients. The age ranged from 26 to 87 years.

Among the AEs, Pneumonia was the most commonly reported PT (20/78), followed by COVID 19 (5/78), Urinary tract infection and Gastroenteritis (each 4/78). The first dose latency for the AEs ranged from 4 to 1094 days.

These cases are not discussed further for any risk factor analysis as per strategy provided in Section [2.3.1](#). However, the case listings are provided in [Appendix 8](#).

### **3.3.2 Non-serious Cases**

A total of 66 non-serious cases reporting 69 NSAEs were retrieved from the safety database and an aggregate summary has been presented in this section. Most of the cases were reported from non-interventional study/program (N=45) followed by spontaneous (N=19) and literature spontaneous sources (N=2). Majority (84.8%; 56/66) of the cases were reported by consumers/ non-healthcare professionals while the remaining 15.2% (10/66) cases were reported by healthcare professionals. 33/66 cases concerned female patients, 27/66 concerned male patients while gender was not reported in remaining 6 cases. Age of the patients was reported in 42 cases (ranged

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<sup>18</sup> These Grade 4 AEs and Grade 5 AEs are already discussed in respective sections.

from 22 to 85 years with a median of 62.5 years) while age was not reported in remaining 24 cases.

Severity Grades were not reported for any of these NSAEs. The below [Table 20](#) presents an overview of these events by MedDRA PT.

**Table 20 Overview of NSAEs by MedDRA PT from the Safety Database (n=69)**

Preferred Term	Frequency (%)
COVID-19	10 (14.5)
Urinary tract infection	8 (11.6)
Paronychia	7 (10.1)
Nasopharyngitis, Herpes zoster	5 each (14.4*)
Infection	4 (5.8)
Pneumonia, Oral fungal infection, Laryngopharyngitis, Bacterial infection	2 each (9.6*)
Pulpitis dental, Oral herpes, Tinea infection, Genital herpes, Fungal infection, Herpes virus infection, Sinusitis, Abscess limb, Coronavirus infection, Cellulitis, Urinary tract infection, Pulmonary tuberculosis, Cystitis, Respiratory tract infection, Ear infection, Sinusitis fungal, Abscess, Tongue fungal infection, Oral candidiasis, Fungal skin infection, Fungal foot infection, Laryngitis	1 each (34*)

Note: Three cases reported more than one AE.

\*Percentage is provided as combined for all the Preferred terms mentioned in the respective row

MedDRA Version: 27.0

The first dose latency was reported for 27/69 (39.1%) AEs which ranged from 0 to 594 days with a median of 145 days. Latency from the first dose was unknown for the remaining AEs (60.9%; 42/69). The event outcome was not reported/unknown for 37 (37/69; 53.6%) events, 10 (10/69; 14.5%) had resolved, five (5/69; 7.2%) were resolving, and 17 (17/69; 24.6%) events did not resolve.

Risk factor analysis was not performed for these cases as per strategy provided in Section [2.3.1](#). The case line listings are presented in [Appendix 9](#).

### **3.3.3 Summary of Safety Results**

A search of the Company Safety Database for pralsetinib identified a total of 806 cases reporting 923 AEs of interest based on the MedDRA SOC, Infections and Infestations.

Of these 806 cases, 740 cases were serious and 66 were non-serious. As per the case analysis strategy described in Section [2.3.1](#), the 740 serious cases reporting 794 serious AEs of infection were further analyzed. Out of these 794 serious events, 86 were

Grade 5, 47 were Grade 4, 311 were Grade 3, 66 were Grade 2 and 12 were Grade 1 infections. For the remaining 272 AEs of infection (reported from 249 cases), severity grades were not reported. The key features of the 387 cases reporting ≥ Grade 3 AEs of infection (444/794) are summarized below:

- Out of the 387 cases, where reported, 199 were males and 181 were females.
- The most frequently reported PT was Pneumonia (117/444) followed by Sepsis (45/444), Urinary tract infection (38/444), COVID 19 (30/444), COVID 19 pneumonia (16/444) and *Pneumocystis jirovecii* pneumonia (8/444).
- A total of 86 events resulted in a fatal outcome and the PTs reported were Pneumonia (n=25), Sepsis (n=19), COVID 19 (n=18), Septic shock (n=6), COVID-19 pneumonia (n=4), Pneumonia aspiration (n=3), Urosepsis (n=2), Pneumonia cytomegaloviral, Endocarditis bacterial, Infection, *Pneumocystis jirovecii* pneumonia, Lower respiratory tract infection, Urinary tract infection, Meningitis, Bronchitis and Peritonitis (n=1 each).
- The outcome where reported was resolved/resolved with sequelae for more than half of the events (280/444), not resolved in 33/444 and resolving in 12/444 for the non-fatal events.
- The events resolved/resolved with sequelae or were resolving in half (222/444) of the events (reported in 281/387 cases) with therapy interruption or withdrawal of Pralsetinib. However, corrective treatment was received with broad-spectrum antibiotics, antivirals, steroids, symptomatic management and corrective surgery in 250/ 281 cases. There was no information on the same for rest of the 31 cases.
- The first dose latency ranged between 0 days to 1825 days for the majority (417/444) of the events.

The case categories of these 387 cases are summarized below:

#### **Category A cases:**

In a total of 2 cases reporting 2 Grade 4 AEs, no alternative explanations were identified for the events of infection. The PTs reported in these cases included *Pneumocystis jirovecii* pneumonia (n=1) and Neutropenic sepsis (n=1). The first dose latencies were 65 and 1460 days and both the events resolved following pralsetinib therapy interruption and with institution of corrective treatment. Evidence of co-existing neutropenia was there in 1 case reporting neutropenic sepsis. The causative organisms identified in these 2 cases were *Pneumocystis jirovecii*, CMV and *Streptococcus pneumoniae*.

#### **Category B cases:**

Of the total, 301 cases reporting 349 infection events (43 Grade 5, 40 Grade 4 and 267 Grade 3) reported additional risk factors which could have contributed to the reported infection. The most common PTs reported were Pneumonia (n=95) followed by Urinary tract infection (n=37) Sepsis (n=34) COVID 19 (n=14) and COVID 19 pneumonia (n=13).

The risk factors and/or alternate explanations included pre-existing co-morbidities such as diabetes, lymphopenia, dyslipidemia, pre-existing infections, underlying cancer progression with multiple metastatic sites, chronic renal insufficiency, co-existing fractures and/or use of anticancer drugs like cisplatin, pemetrexed, gemcitabine, use of immunosuppressant drugs such as tocilizumab, methylprednisolone, prednisolone, dexamethasone, radiotherapy, hormonal therapy and invasive medical procedures. Evidence of cytopenias including lymphopenia, neutropenia and leukopenia was identified in 82/301 cases.

**Category C cases:**

The remaining 84 cases had insufficient information regarding underlying medical conditions, concurrent diseases, concomitant medications, drug-event latency, diagnostic details and/or event course details for a comprehensive causality analysis for the events and pralsetinib.

For the remaining 249/740 cases reporting 272 AEs, information on severity grading was lacking. The most commonly reported PT was of Pneumonia and none of these cases were assessed as category A. Twenty-six cases were assessed as Category B with risk factors/alternative explanations (e.g., underlying cancer progression and use of immunosuppressive medications). The remaining 223 cases were assessed as Category C with insufficient information regarding underlying medical conditions, concurrent diseases, concomitant medications and/or event course details to enable an adequate causality analysis for the events and pralsetinib.

**4. DISCUSSION**

This DSR has been prepared in response to a signal arising from study AcceleRET-Lung where a patient presented with fatal septic shock with temporal association of onset of neutropenia, severe bacterial pulmonary infection, following start of pralsetinib therapy, suggesting plausible causal association with pralsetinib. This DSR provides a comprehensive assessment of the severe infection AEs in study AcceleRET-Lung and post marketing sources to evaluate a causal association between pralsetinib treatment and an increased risk of severe infection and death due to infection.

The CDS version 6.0 (dated September 2023) of pralsetinib specifies infections including pneumonia, fatal pneumonia and urinary tract infection as an adverse event for the drug. ‘Infections’ as a medical concept is not included in the Warnings and Precautions section of the CDS. The pralsetinib cRMP (version 5.0) specifies infections as an important potential risk for the drug. Note however that, these labelling documents of pralsetinib are based on the earlier evidence from the non-randomized, open label, single arm ARROW study.

Pralsetinib, given its mode of action, causes reduced bone marrow cellularity, reduced hemoglobin, reduced reticulocytes, reduced lymphoid cellularity and decreased

lymphocyte counts, and hence may be associated with an increased risk of infections. Decrease in blood cell counts was observed in patients treated with pralsetinib, especially anemia, neutropenia, and thrombocytopenia. As cancer patients are already immunocompromised, neutropenia can put such patients at even greater risk of developing severe infections. However, in the analysis of severe infections in AcceleRET-Lung, neither neutropenia nor lymphopenia appear to account for the increased risk of infection in pralsetinib treated patients. Infections (including Pneumonia and Urinary Tract Infection) are also listed as an ADR among the other SIC molecule selpercatinib.

In the pralsetinib preclinical studies, hematological abnormalities (reduced bone marrow cellularity, attributed to off-target JAK 2 inhibition) and lymphoid effects (reduced lymphoid cellularity and decreased lymphocyte counts, attributed to stress response) were observed. Pralsetinib has shown to inhibit JAK 2 pathways as an off-target but with lower potency compared to RET inhibition or compared to JAK inhibiting compounds with JAK inhibition as a primary target ([Gavreto cRMP](#)). JAK inhibition has the potential to suppress integral elements of the immune response. The risk of infection, including opportunistic infections, appears to be increased with all JAK inhibitors ([Adas et al. 2022](#)).

For the purpose of this DSR, clinical trial data analysis included review of study results from ARROW and AcceleRET-Lung study. AcceleRET-Lung presents the first opportunity to consider randomized safety data comparing pralsetinib with standard of care treatment options (platinum doublet ± pembrolizumab) while ARROW, on the other hand is non-randomized, open-label, study with no comparator arm. The review of the data from the clinical study AcceleRET-Lung revealed a crude reporting rate 4.6% (5/108) for patients with fatal infection events and 21.3% (23/108) for patients with Grade 3 and Grade 4 infection events in the pralsetinib treatment arm. On the contrary, no fatal or Grade 5 infection events were reported and 7.7% (8/104) was reported for Grade 3 and Grade 4 infections in the comparator treatment arm. A significant increase in the incidence proportion of severe infections (Grades 3-5) was observed in the pralsetinib treatment arm versus the standard of care arm (two- sided fisher's exact p=0.0004). Additional statistical testing using the Aalen-Johansen estimator was performed to account for the effect of time on treatment, as well as for the occurrences of end of treatment and/or death that are handled as competing events. In this analysis, a risk ratio of 3.33, 95% CI: [1.57 ,7.06] was estimated, indicating a higher risk in the pralsetinib arm ([Stegherr R et al. 2021](#)).

In pralsetinib treatment arm of AcceleRET-Lung, five fatal infection AEs (in 5 patients) were reported, including PTs of pneumonia (n=3), lower respiratory tract infection and sepsis (n=1 each), with time to onset ranging from 25 to 155 days (median 51 days). The study investigator assessed all the events except for lower respiratory tract infection as not related to pralsetinib treatment. On detailed analysis, case (AER 3355432) reporting pneumonia reported a medical history of urinary tract infection which could

have progressed to pyelonephritis (concurrently reported AE). The concurrent femoral neck fracture with prolonged hospitalization explains the patient's predisposition to a likely nosocomial opportunistic infection (*Klebsiella pneumoniae*). Moreover, the patient was elderly with diabetes, which is an additional risk factor. Another case (AER 3428340) also reported diabetes as a risk factor along with the immunocompromised state of the patient. The case (AER 3313491) reporting sepsis presented concurrent condition of cholangitis and concomitant use of trimethoprim/sulfamethoxazole as risk factors for the AEs in addition to immunocompromised status, elderly age and chronic obstructive pulmonary disease. For the remaining 2 cases, there was insufficient information regarding diagnostic details and/ or clinical course for an adequate medical assessment.

In pralsetinib treatment arm of AcceleRET-Lung, 32 Grade 3-4 infection events in 23 patients were reported. The reporting investigator assessed 23 AEs as not related while nine were reported as related to pralsetinib. The time to onset ranged from 20 to 1001 days (with a median of 122 days). In the standard of care arm of the study, no patients reported fatal infections. The median time to onset of severe infections (Grade 3-4) in this comparator treatment group was 110.5 days (range: 7 to 528 days). Further, a total of 7 pralsetinib-treated patients presented with 8 AEs of severe opportunistic infections of which only 2 patients were receiving systemic corticosteroids prior to the onset of infection. This analysis suggested that prior corticosteroid use does not appear to be an inciting risk factor for the development of severe opportunistic infections in these patients.

The majority of severe infection events in the pralsetinib treated arm (26/32; 81.2%) were manageable and the patients recovered/ recovered with sequelae/ recovering. These cases either presented additional risk factors for the events or were limited in information required for a comprehensive evaluation as the clinical data being used is not from a formal data cut.

However, note that the evidence from the ARROW study showed an incidence of 3.2% for patients with fatal infection AEs while 24.4% for patients with Grade 3-4 infection events in pralsetinib treated patients.

The cumulative search of the Company Safety Database retrieved a total of 806 cases. Out of these 806 cases, 740 serious cases reporting 794 serious adverse events (AEs) of infection were evaluated in detail. Of the 794 AEs, 444 were grade 3 or higher (from 387 cases), with pneumonia being the most common. A fatal outcome was reported for 86 events, primarily due to pneumonia (n=25), sepsis (n=19), and COVID-19 (n=18). Only 2/387 cases (Category A) showed a potential causal association with pralsetinib, lacking alternative explanations. These involved PTs of *Pneumocystis jirovecii* pneumonia (n=1), and neutropenic sepsis (n=1), both resolving after treatment interruption and with institution of corrective measures. Causative organisms identified in these 2 cases included *Pneumocystis jirovecii*, CMV and *Streptococcus pneumoniae*.

which projects an opportunistic infection picture owing to the immunocompromised state of the patients. Additionally, in 1/2 cases there was co-existing neutropenia which could have further increased the risk of infections. The majority (301/387 cases, Category B) reported risk factors or additional risk factors for infections, such as pre-existing comorbidities, cancer progression, and use of other immunosuppressive medications or medical interventions. The infections mostly involved the respiratory and urinary tract; and the organisms where reported were mostly corona virus, Escherichia coli, Staphylococcus aureus, herpes zoster, pneumocystis jirovecii, CMV and COVID 19 (SARS COV 2) which could be attributed to the low immunity of these patients. Cytopenias, including neutropenia, were co-reported in 82/300 cases, potentially increasing infection risk especially of the sites like lungs and urinary tract. Although more than half of the events resolved, the assessment of dechallenge information was confounded by the administration of corrective treatments. The remaining 84 cases (Category C) lacked sufficient information for causality analysis. An additional 249 cases with 272 AEs reported no severity grading, were assessed as Categories B (26/249) or C (223/249).

This review confirms that severe infections, including fatal outcomes, occur in increased frequency in patients treated with pralsetinib, however, the majority could be attributed to other factors.

## **5. OVERALL CONCLUSIONS**

The unblinding of AcceleRET-Lung has presented the first opportunity for the sponsor to evaluate the comparative safety of the important potential risk of severe infections with Gavreto against a standard of care treatment option in an equal disease setting. Prior to the unblinding, the Independent Data Monitoring Committee (iDMC) was providing safety review of this study. Despite earlier evidence from the ARROW study and a plausible mechanism of action, based on the evaluation of the comparative safety data from AcceleRET-Lung study, it could be concluded that a higher frequency and severity of infections was observed in the pralsetinib-treated cohort compared to the standard of care cohort. Also, an analysis of neutropenia and lymphopenia in AcceleRET-Lung study suggested that these events do not appear to account for the higher risk of infection in pralsetinib treated patients. Similarly, prior systemic corticosteroid use does not appear to account for severe opportunistic infections in the pralsetinib arm of AcceleRET-Lung. These findings along with a comprehensive analysis of cumulative evidence from the Company Safety Database, the study Sponsor and MAH have jointly determined that the risk classification for severe infections should be updated from an important potential risk to an important identified risk. In addition, the MAH recommends inclusion of increased risk of severe infections in the Warnings & Precautions for Gavreto, including in the Core Data Sheet, local labels, and the Investigator's Brochure. An Urgent Safety Measure (USM)-Dear Investigator Letter and Dear Health Care Provider Letter will be issued by the MAH to inform investigators and prescribers of the identification of this risk on the

basis of this analysis. Study Protocols and the Pralsetinib Investigator's Brochure will be updated accordingly.

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7. **APPENDICES**

## **Appendix 1    Clinical Trial Outputs**

Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE	Duration in Days	Crossover phase	Most Serious	Most Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>3301/004 - 73/F/Asian</b>										
Investigations										
Alanine aminotransferase increased		14SEP2022	22	43	No	No	MOD	Yes	3	2
Aspartate aminotransferase increased		14SEP2022	22	134	No	No	MOD	Yes	3	2
Infections and infestations										
Nasopharyngitis		14SEP2022	59	6	No	No	MILD	No	3	2
Investigations										
COVID-19		14SEP2022	100	7	No	No	MILD	No	3	2
Investigations										
Aspartate aminotransferase increased		14SEP2022	198		No	No	MILD	Yes	2	2
Investigations										
Nasopharyngitis		14SEP2022	297	67	No	No	MILD	No	3	2
<b>3301/006 - 57/M/Asian</b>										
Investigations										
Urinary tract infection		24MAY2023	267	8	No	No	MOD	No	3	2
<b>3301/008 - 67/F/Asian</b>										
Investigations										
Paronychia		17OCT2023	22		No	No	MILD	Yes	2	2
Investigations										
Pneumonia cytomegaloviral		17OCT2023	85	21	No	Yes	SEV	Yes	3	4
<b>3302/003 - 61/F/Asian</b>										
Investigations										
Alanine aminotransferase increased		27APR2021	15	8	No	No	MILD	Yes	3	2
Aspartate aminotransferase increased		27APR2021	15	143	No	No	MILD	Yes	3	2
Investigations										
Lymphocyte count decreased		27APR2021	127	24	No	No	MILD	Yes	3	2
Investigations										
Lymphocyte count decreased		27APR2021	157	22	No	No	MILD	Yes	3	2
<b>3302/004 - 71/M/Asian</b>										
Investigations										
Blood thyroid stimulating hormone increased		27APR2021	22	8	No	No	MILD	No	3	2
Platelet count decreased		27APR2021	22	107	No	No	SEV	Yes	3	3
Investigations										
Aspartate aminotransferase increased		27APR2021	86	8	No	No	MILD	Yes	3	2

Notes: Adverse Events are coded using MedDRA 27.0

For patients who crossed over, date of first Study Drug Administration is provided for the standard of care treatment in the main treatment period and for Pralsetinib in the crossover treatment period.

(1) Severity: MILD = Grade 1 - Mild, MOD = Grade 2 - Moderate, SEV = Grade 3 - Severe, LT = Grade 4 - Life Threatening, DEATH = Grade 5 - Death.

(2) Outcome: 1 = fatal; 2 = not recovered/not resolved; 3 = recovered/resolved; 4 = recovered/resolved with sequelae; 5 = recovering/resolving; 6 = unknown.

(3) Action taken: 1 = dose increased; 2 = dose not changed; 3 = dose reduced; 4 = drug interrupted; 5 = drug withdrawn; 6 = not applicable; 7 = unknown.

\* Study day derived from imputed onset date

\*\* Duration derived from imputed onset date and/or end date

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE Study Drug	Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
System Organ Class Preferred Term											
3302/004 - 71/M/Asian	Investigations										
	Aspartate aminotransferase increased	27APR2021	189	8	No	No	MILD	Yes	3	2	
	Infections and infestations										
	Pleural infection	27APR2021	204	73	No	Yes	SEV	No	3	4	
	Investigations										
	Platelet count decreased	27APR2021	204	21	No	No	MOD	No	3	2	
	Infections and infestations										
	Device related infection	27APR2021	214	16	No	Yes	SEV	No	3	2	
	Investigations										
	Blood creatinine increased	27APR2021	233	1	No	No	MOD	No	3	2	
	Investigations										
	Blood bicarbonate decreased	27APR2021	252		No	No	MOD	No	2	6	
	Investigations										
	Alanine aminotransferase increased	27APR2021	262		No	No	MILD	No	2	6	
	Aspartate aminotransferase increased	27APR2021	262	2	No	No	MILD	No	3	6	
	Neutrophil count decreased	27APR2021	262		No	No	LT	No	2	6	
	Platelet count decreased	27APR2021	262		No	No	LT	No	2	6	
3302/005 - 74/M/Asian	Investigations										
	Aspartate aminotransferase increased	10AUG2021	22	60	No	No	MILD	Yes	3	2	
	Investigations										
	Alanine aminotransferase increased	10AUG2021	64	14	No	No	MILD	Yes	3	2	
	Infections and infestations										
	Pneumonia	10AUG2021	65		No	Yes	SEV	No	2	5	
	Investigations										
	Alanine aminotransferase increased	10AUG2021	79	6	No	No	MILD	No	3	2	
	Investigations										
	Blood thyroid stimulating hormone decreased	10AUG2021	106		No	No	MILD	No	2	6	
3302/006 - 51/F/Asian	Investigations										
	Alanine aminotransferase increased	10AUG2021	147	23	No	No	MILD	Yes	3	2	
	Aspartate aminotransferase increased	10AUG2021	147	23	No	No	MILD	Yes	3	2	
	Investigations										
	Aspartate aminotransferase increased	10AUG2021	234	82	No	No	MILD	Yes	3	2	
	Blood cholesterol increased	10AUG2021	234	19	No	No	MILD	No	3	2	
	Blood lactate dehydrogenase increased	10AUG2021	234		No	No	MILD	No	2	2	
	Investigations										
	Aspartate aminotransferase increased	10AUG2021	424	39	No	No	MILD	Yes	3	2	
	Investigations										
	Aspartate aminotransferase increased	10AUG2021	546	45	No	No	MILD	Yes	3	2	

Notes: Adverse Events are coded using MedDRA 27.0

For patients who crossed over, date of first Study Drug Administration is provided for the standard of care treatment in the main treatment period and for Pralsetinib in the crossover treatment period.

(1) Severity: MILD = Grade 1 - Mild, MOD = Grade 2 - Moderate, SEV = Grade 3 - Severe, LT = Grade 4 - Life Threatening, DEATH = Grade 5 - Death.

(2) Outcome: 1 = fatal; 2 = not recovered/not resolved; 3 = recovered/resolved; 4 = recovered/resolved with sequelae; 5 = recovering/resolving; 6 = unknown.

(3) Action taken: 1 = dose increased; 2 = dose not changed; 3 = dose reduced; 4 = drug interrupted; 5 = drug withdrawn; 6 = not applicable; 7 = unknown.

\* Study day derived from imputed onset date

\*\* Duration derived from imputed onset date and/or end date

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE	Duration in Days	Crossover phase	Most Serious	Most Extreme Intensity (1)	Caused by Study Drug	Action Taken (2)	Action Taken (3)
<b>3302/006 - 51/F/Asian</b>										
Investigations										
Aspartate aminotransferase increased		10AUG2021	674	45	No	No	MILD	Yes	3	2
<b>3302/007 - 52/F/Asian</b>										
Investigations										
Alanine aminotransferase increased		23NOV2021	22	21	No	No	MILD	Yes	3	2
Aspartate aminotransferase increased		23NOV2021	22	21	No	No	MOD	Yes	3	2
Investigations										
Lymphocyte count decreased		23NOV2021	44	21	No	No	MOD	Yes	3	2
Investigations										
Urinary tract infection		23NOV2021	85	11	No	No	MOD	Yes	3	2
Investigations										
Aspartate aminotransferase increased		23NOV2021	127	42	No	No	MILD	Yes	3	2
Investigations										
Pneumocystis jirovecii pneumonia		23NOV2021	161	33	No	Yes	SEV	No	4	4
Pneumonia cytomegaloviral		23NOV2021	161		No	Yes	SEV	No	2	5
Investigations										
Aspartate aminotransferase increased		23NOV2021	210	2	No	No	MILD	Yes	3	2
<b>3302/012 - 57/M/Asian</b>										
Investigations										
Alanine aminotransferase increased		13JUL2023	22	43	No	No	MILD	Yes	3	2
Blood creatinine increased		13JUL2023	22		No	No	MILD	No	2	2
Investigations										
Pneumonia		13JUL2023	58	14	No	Yes	DEATH	No	1	5
<b>3302/013 - 67/F/Asian</b>										
Investigations										
Alanine aminotransferase increased		05DEC2023	22	43	No	No	MILD	Yes	3	2
Aspartate aminotransferase increased		05DEC2023	22	53	No	No	MILD	Yes	3	2
Investigations										
Pneumonia		05DEC2023	67	11	No	Yes	SEV	No	3	4
Pyelonephritis acute		05DEC2023	67	4	No	Yes	SEV	No	3	4

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup> Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Extreme Serious	Caused by Study Drug	Action Outcome (2) Taken (3)
3303/001 - 60/M/Asian							
Infections and infestations Pneumonia	17MAR2021	361	10	No	Yes	MOD	No 3 4
Investigations Neutrophil count decreased	17MAR2021	840	7	No	No	SEV	Yes 3 4
Investigations Neutrophil count decreased	17MAR2021	847		No	No	MOD	Yes 2 3
4101/001 - 64/M/White							
Investigations Neutrophil count decreased	09NOV2020	22	99	No	No	SEV	Yes 3 3
Investigations Blood creatinine increased	09NOV2020	64	8	No	No	MOD	Yes 3 2
Investigations Neutrophil count decreased	09NOV2020	162	43	No	No	SEV	Yes 3 3
Investigations Platelet count decreased	09NOV2020	183	22	No	No	MOD	Yes 3 2
Investigations Blood creatinine increased	09NOV2020	246	64	No	No	MILD	Yes 3 2
Infections and infestations COVID-19	09NOV2020	653	58	No	No	MOD	No 3 2
Infections and infestations Upper respiratory tract infection	09NOV2020	1177	6	No	No	MOD	No 3 2
4201/002 - 76/F/Unknown							
Infections and infestations Urinary tract infection	03MAY2023	13	4	No	No	MOD	No 3 2
Infections and infestations Pyelonephritis	03MAY2023	17	15	No	Yes	SEV	No 3 4
Infections and infestations Pneumonia	03MAY2023	30	10	No	Yes	DEATH	No 1 2
4201/003 - 56/M/Unknown							
Infections and infestations Lower respiratory tract infection	07JUL2023	46	18	No	No	MOD	No 3 2
Investigations Aspartate aminotransferase increased	07JUL2023	46	43	No	No	MILD	No 3 2

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE Study Drug	Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>4202/001 - 77/F/White</b>											
Investigations											
Neutrophil count decreased		12MAY2021		20	10	No	No	SEV	Yes	3	3
Infections and infestations											
Staphylococcal sepsis		12MAY2021		290	10	No	Yes	SEV	No	3	2
<b>4205/002 - 45/F/NOT REPORTED</b>											
Infections and infestations											
Tongue fungal infection		03AUG2022		106		No	No	MOD	No	2	2
Infections and infestations											
Gastroenteritis		03AUG2022		190	1	No	No	MILD	No	3	2
Investigations											
Alanine aminotransferase increased		03AUG2022		398	23	No	No	MILD	Yes	3	2
Aspartate aminotransferase increased		03AUG2022		398	23	No	No	MILD	Yes	3	2
<b>4205/004 - 78/F/White</b>											
Infections and infestations											
Tongue fungal infection		11APR2023		22	45	No	No	MILD	Yes	3	2
Investigations											
Weight increased		11APR2023		66		No	No	MILD	Yes	2	2
Investigations											
Blood creatine phosphokinase increased		11APR2023		148	21	No	No	MILD	Yes	3	2
Infections and infestations											
Viral infection		11APR2023		217	3	No	No	MILD	No	3	2
Infections and infestations											
Gastroenteritis		11APR2023		235*	31**	No	No	MOD	No	3	2
Investigations											
Blood creatine phosphokinase increased		11APR2023		274	22	No	No	MILD	Yes	3	2
Infections and infestations											
Localised infection		11APR2023		359		No	No	MILD	No	2	2
Investigations											
Blood creatine phosphokinase increased		11APR2023		359		No	No	MILD	Yes	2	2
<b>4206/001 - 71/F/NOT REPORTED</b>											
Investigations											
Alanine aminotransferase increased		29JUL2020		16	46	No	No	MILD	Yes	3	2
Aspartate aminotransferase increased		29JUL2020		16	28	No	No	MILD	Yes	3	2
Infections and infestations											
Oral fungal infection		29JUL2020		48	39	No	No	MILD	No	3	2
Pyelonephritis		29JUL2020		48	30	No	Yes	SEV	Yes	3	2

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE Study Drug	Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
4206/001 - 71/F/NOT REPORTED											
Investigations											
Alanine aminotransferase increased		29JUL2020	84	43	No	No	MILD	Yes	3	2	
Infections and infestations											
Pyelonephritis		29JUL2020	96	180	No	Yes	SEV	Yes	4	3	
Investigations											
Alanine aminotransferase increased		29JUL2020	189	44	No	No	MILD	Yes	3	2	
Infections and infestations											
Urinary tract infection		29JUL2020	332	86	No	No	MOD	Yes	3	3	
Investigations											
Urinary tract infection		29JUL2020	457	12	No	No	MILD	Yes	3	2	
Infections and infestations											
Urinary tract infection		29JUL2020	580	19	No	No	MILD	Yes	3	2	
Investigations											
Urinary tract infection		29JUL2020	603	10	No	No	MOD	Yes	3	2	
Infections and infestations											
Urinary tract infection		29JUL2020	631	678	No	No	MOD	Yes	3	2	
Investigations											
Alanine aminotransferase increased		29JUL2020	798	40	No	No	MILD	No	3	2	
Gamma-glutamyltransferase increased		29JUL2020	798	40	No	No	MILD	No	3	2	
4208/002 - 76/M/NOT REPORTED											
Investigations											
Blood creatine phosphokinase increased		06MAY2022	106		No	No	SEV	Yes	5	3	
Investigations											
Weight decreased		06MAY2022	149		No	No	MILD	No	2	2	
4208/004 - 73/F/Other											
Investigations											
Oesophageal infection		08NOV2022	52	16	No	No	SEV	Yes	3	2	
Oral fungal infection		08NOV2022	52	16	No	No	MOD	Yes	3	2	
Investigations											
Urinary tract infection		08NOV2022	55	8	No	No	MILD	No	3	2	
Investigations											
Pneumonia		08NOV2022	86	16	No	Yes	MOD	No	3	4	
Investigations											
Blood creatinine increased		08NOV2022	193		No	No	MOD	No	2	4	
Investigations											
Vascular device infection		08NOV2022	284	8	No	No	MOD	No	3	4	

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE	Duration in Days	Crossover phase	Most Serious	Most Extreme Intensity (1)	Caused by Study Drug	Action Taken (2)	Action Taken (3)
<b>System Organ Class Preferred Term</b>										
4209/001 - 52/F/White	Investigations									
	Alanine aminotransferase increased	04SEP2021	18		No	No	MILD	Yes	2	2
	Aspartate aminotransferase increased	04SEP2021	18	22	No	No	MILD	Yes	3	2
Infections and infestations										
	Fungal infection	04SEP2021	97	55	No	No	MILD	No	3	2
Investigations										
	Oxygen saturation decreased	04SEP2021	104	2	No	No	MOD	No	3	2
Infections and infestations										
	Pneumonia	04SEP2021	105	6	No	No	MOD	No	3	4
4210/001 - 67/M/Unknown	Investigations									
	Blood creatinine increased	10JAN2024	22		No	No	MOD	Yes	5	2
4307/001 - 58/M/White	Investigations									
	Neutrophil count decreased	30DEC2020	8	56	No	No	MOD	Yes	3	2
Investigations										
	White blood cell count decreased	30DEC2020	22	21	No	No	MOD	Yes	3	2
Investigations										
	White blood cell count decreased	30DEC2020	43	21	No	No	MILD	Yes	3	2
Investigations										
	White blood cell count decreased	30DEC2020	106	21	No	No	MILD	Yes	3	2
Investigations										
	White blood cell count decreased	30DEC2020	148	58	No	No	MILD	Yes	3	2
Infections and infestations										
	Urinary tract infection	30DEC2020	199	28	No	No	MOD	No	3	2
Infections and infestations										
	COVID-19	30DEC2020	311	26	No	No	MILD	No	3	2
Investigations										
	White blood cell count decreased	30DEC2020	581	45	No	No	MILD	Yes	3	2
4307/003 - 40/F/White	Investigations									
Infections and infestations										
	Bronchitis	28APR2021	80	32	No	No	MOD	Yes	3	2

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE	Duration in Days	Crossover phase	Most Serious	Most Extreme Intensity (1)	Caused by Study Drug	Action Taken (2)	Action Taken (3)
System Organ Class Preferred Term										
4307/004 - 59/F/White	Investigations									
	Neutrophil count decreased	21APR2021	21	43	No	No	SEV	Yes	3	3
	Platelet count decreased	21APR2021	21	43	No	No	MILD	Yes	3	2
	Investigations									
	White blood cell count decreased	21APR2021	35	29	No	No	SEV	Yes	3	2
	Investigations									
	Neutrophil count decreased	21APR2021	85	41	No	No	MOD	Yes	3	2
	White blood cell count decreased	21APR2021	85	41	No	No	MOD	Yes	3	2
	Infections and infestations									
	Fungal infection	21APR2021	126	28	No	No	MILD	No	3	2
	Investigations									
	Neutrophil count decreased	21APR2021	126	28	No	No	MILD	Yes	3	2
	White blood cell count decreased	21APR2021	126	49	No	No	MILD	Yes	3	2
	Infections and infestations									
	Urinary tract infection	21APR2021	153	17	No	No	MOD	Yes	3	2
	Investigations									
	Neutrophil count decreased	21APR2021	154	22	No	No	MOD	Yes	3	2
	Investigations									
	White blood cell count decreased	21APR2021	196	21	No	No	MILD	Yes	3	2
	Infections and infestations									
	Nasopharyngitis	21APR2021	212	26	No	No	MILD	No	3	2
	Investigations									
	White blood cell count decreased	21APR2021	259	63	No	No	MOD	Yes	3	2
	Investigations									
	Neutrophil count decreased	21APR2021	301	21	No	No	MOD	Yes	3	2
	Infections and infestations									
	Urinary tract infection	21APR2021	305	9	No	No	MOD	No	3	2
	Infections and infestations									
	Cystitis	21APR2021	314	8	No	No	MILD	No	3	2
	Investigations									
	Neutrophil count decreased	21APR2021	343	64	No	No	MOD	Yes	3	2
	White blood cell count decreased	21APR2021	343	169	No	No	MOD	Yes	3	2
	Infections and infestations									
	Respiratory tract infection	21APR2021	444	26	No	No	MOD	Yes	3	2
	Urinary tract infection	21APR2021	444	26	No	No	MOD	Yes	3	2
	Infections and infestations									
	Paronychia	21APR2021	470	170	No	No	MILD	No	3	2
	Infections and infestations									
	Nasopharyngitis	21APR2021	626	56	No	No	MILD	No	3	2
	Infections and infestations									
	Pneumonia	21APR2021	825	13	No	Yes	SEV	Yes	3	6

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race3 Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>4307/005 - 59/M/White</b>									
Investigations									
White blood cell count decreased	07JUL2021	43	23	No	No	MILD	No	3	2
Investigations									
White blood cell count decreased	07JUL2021	84	42	No	No	MILD	Yes	3	2
Infections and infestations									
Nasopharyngitis	07JUL2021	116	12	No	No	MILD	No	3	2
Investigations									
White blood cell count decreased	07JUL2021	169	20	No	No	MILD	Yes	3	2
Infections and infestations									
Nasopharyngitis	07JUL2021	175	15	No	No	MILD	No	3	2
Investigations									
White blood cell count decreased	07JUL2021	210	42	No	No	MILD	Yes	3	2
Investigations									
Neutrophil count decreased	07JUL2021	274	21	No	No	MOD	Yes	3	2
White blood cell count decreased	07JUL2021	274	21	No	No	MOD	Yes	3	2
Investigations									
White blood cell count decreased	07JUL2021	463	62	No	No	MOD	Yes	3	2
Investigations									
Neutrophil count decreased	07JUL2021	505	21	No	No	MOD	Yes	3	2
Investigations									
White blood cell count decreased	07JUL2021	547		No	No	MOD	Yes	2	2
Investigations									
Neutrophil count decreased	07JUL2021	631	51	No	No	MILD	Yes	3	2
Infections and infestations									
Nasopharyngitis	07JUL2021	682	21	No	No	MILD	No	3	2
<b>4312/001 - 77/M/White</b>									
Investigations									
White blood cell count decreased	09OCT2020	43		No	No	SEV	Yes	2	2
Infections and infestations									
Herpes zoster	09OCT2020	442	12	No	No	MOD	No	3	2
<b>4402/003 - 56/F/White</b>									
Infections and infestations									
Oral candidiasis	14DEC2022	33	27	No	No	MOD	No	3	2
Infections and infestations									
COVID-19	14DEC2022	44	8	No	No	MILD	No	3	2
Investigations									
Alanine aminotransferase increased	14DEC2022	169	43	No	No	MILD	No	3	2
Aspartate aminotransferase increased	14DEC2022	169	43	No	No	MILD	No	3	2

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Taken (3)
<b>4403/003 - 61/M/White</b>									
Investigations									
Blood bicarbonate decreased		28JUL2023	41	27	No	No	MILD	Yes	3
Investigations									
Amylase increased		28JUL2023	55	20	No	No	MOD	No	3
Blood phosphorus decreased		28JUL2023	55	20	No	No	MILD	No	3
Investigations									
Amylase increased		28JUL2023	61	14	No	No	MOD	No	3
Lipase increased		28JUL2023	61	56	No	No	MOD	No	3
Investigations									
Amylase increased		28JUL2023	95		No	No	MOD	No	5
		28JUL2023	95		No	No	MOD	No	5
Investigations									
Gamma-glutamyltransferase increased		28JUL2023	116		No	No	MILD	No	5
Lymphocyte count decreased		28JUL2023	116		No	No	MOD	No	5
Protein total decreased		28JUL2023	116		No	No	MILD	No	5
<b>4404/003 - 57/M/White</b>									
Investigations									
Platelet count decreased		23DEC2020	23	22	No	No	MOD	Yes	3
Infections and infestations									
Nasopharyngitis		23DEC2020	325	4	No	No	MILD	No	3
Investigations									
Aspartate aminotransferase increased		23DEC2020	443		No	No	MILD	No	5
Infections and infestations									
Gastroenteritis viral		23DEC2020	633	5	No	No	MOD	No	3
Infections and infestations									
COVID-19		23DEC2020	888	6	No	No	MILD	No	3
Herpes zoster		23DEC2020	888	9	No	Yes	SEV	No	3
Spontaneous bacterial peritonitis		23DEC2020	888	9	No	Yes	SEV	No	3
Infections and infestations									
Gastroenteritis		23DEC2020	1149	9	No	Yes	MOD	No	3
Infections and infestations									
Gastroenteritis		23DEC2020	1169	8	No	Yes	MOD	No	3
<b>4404/004 - 57/M/White</b>									
Investigations									
Blood alkaline phosphatase increased		05JAN2021	1		No	No	MILD	No	2

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup> Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Extreme Serious	Caused by Study Drug	Action Outcome (2) Taken (3)
4404/004 - 57/M/White Infections and infestations Cystitis	05JAN2021	22		No	No	MOD	No 5 2
4404/005 - 53/M/White Infections and infestations Device related infection	14APR2021	20	12	No	Yes	LT	No 3 4
Infections and infestations Cystitis	14APR2021	147	9	No	No	MILD	No 3 2
Investigations Alanine aminotransferase increased	14APR2021	191	28	No	No	MILD	Yes 3 2
Aspartate aminotransferase increased	14APR2021	191	28	No	No	MILD	Yes 3 2
Infections and infestations Escherichia urinary tract infection	14APR2021	314	9	No	No	MILD	No 3 2
Infections and infestations Cystitis	14APR2021	338	7	No	No	MOD	No 3 4
Infections and infestations Herpes zoster	14APR2021	386		No	No	MOD	No 5 5
Investigations Platelet count decreased	14APR2021	434		No	No	MILD	Yes 5 2
Investigations SARS-CoV-2 test positive	14APR2021	472		No	No	MILD	No 5 6
4404/009 - 68/M/White Infections and infestations COVID-19	02DEC2021	48	25	No	No	MILD	No 3 4
Investigations Transaminases abnormal	02DEC2021	107		No	No	MILD	Yes 5 2
Infections and infestations Urinary tract infection	02DEC2021	392	2	No	No	MILD	No 3 2
Investigations Blood creatinine increased	02DEC2021	400		No	No	MILD	Yes 5 2
4404/011 - 71/M/White Infections and infestations Paronychia	19AUG2022	84		No	No	MILD	Yes 5 2
Infections and infestations Infection	19AUG2022	146	17	No	No	MOD	No 3 4
Investigations Aspartate aminotransferase increased	19AUG2022	273		No	No	MILD	No 5 2

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE Study Drug	Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
4404/011 - 71/M/White	Infections and infestations O fever	19AUG2022	406	30	No	Yes	SEV	No	3	4	
	Infections and infestations Pneumonia	19AUG2022	636		No	Yes	SEV	No	2	4	
4404/012 - 46/M/White	Investigations Blood creatinine increased	21SEP2022	23		No	No	MILD	No	5	2	
	Transaminases increased	21SEP2022	23	293	No	No	MILD	Yes	3	2	
	Investigations Alanine aminotransferase increased	21SEP2022	86		No	No	MILD	Yes	5	2	
	Aspartate aminotransferase increased	21SEP2022	86		No	No	MILD	Yes	5	2	
	Investigations Pneumonia	21SEP2022	154	9	No	No	MOD	Yes	3	4	
	Infections and infestations Pneumonia	21SEP2022	210		No	No	MILD	Yes	5	2	
	Infections and infestations Pneumonia	21SEP2022	456	20	No	Yes	MOD	No	3	4	
	Investigations Transaminases increased	21SEP2022	524	85	No	No	MILD	Yes	3	4	
4406/001 - 60/M/White	Investigations Blood creatine phosphokinase increased	28APR2021	307	53	No	No	SEV	No	3	2	
	Infections and infestations Urinary tract infection	28APR2021	636	16	No	No	MILD	No	3	2	
4406/003 - 53/M/White	Investigations Aspartate aminotransferase increased	30MAR2022	23		No	No	MILD	Yes	2	2	
	White blood cell count decreased	30MAR2022	23		No	No	MILD	Yes	2	2	
	Investigations Blood creatinine increased	30MAR2022	148	22	No	No	MILD	No	3	2	
	Investigations Urinary tract infection	30MAR2022	568		No	Yes	SEV	No	5	2	
	Infections and infestations Nail infection	30MAR2022	583	15	No	No	MILD	Yes	3	2	
	Infections and infestations COVID-19	30MAR2022	644	7	No	No	MILD	No	3	2	

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race3 Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	Study Drug	Day of Onset	AE Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>4407/001 - 58/M/White</b>										
Investigations										
Blood cholesterol increased	11MAR2021	14		No	No	MOD	No	5	2	
Blood creatine phosphokinase increased	11MAR2021	14	220	No	No	MOD	Yes	3	2	
Investigations										
White blood cell count decreased	11MAR2021	22	131	No	No	MOD	Yes	3	2	
Infections and infestations										
Pharyngitis	11MAR2021	57	5	No	Yes	MOD	No	3	2	
Infections and infestations										
Herpes zoster	11MAR2021	756	7	No	No	MOD	No	3	4	
<b>4407/002 - 64/M/White</b>										
Investigations										
Alanine aminotransferase increased	07JUN2021	89	22	No	No	SEV	Yes	3	4	
Aspartate aminotransferase increased	07JUN2021	89	6	No	No	MOD	Yes	3	2	
Infections and infestations										
Pustule	07JUN2021	297	29	No	No	MOD	Yes	3	2	
<b>4407/003 - 70/F/White</b>										
Infections and infestations										
Cytomegalovirus infection	22OCT2021	86	10	No	No	MILD	No	3	2	
<b>4407/004 - 55/F/White</b>										
Infections and infestations										
Fungal infection	14JUN2022	149	8	No	No	MILD	No	3	2	
<b>4408/002 - 57/M/White</b>										
Infections and infestations										
Oropharyngeal candidiasis	02MAY2023	263	8	No	No	MILD	Yes	3	4	
<b>4410/001 - 41/F/White</b>										
Investigations										
Blood creatinine increased	04MAR2021	190	189	No	No	MILD	No	3	2	

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race3 Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>4410/001 - 41/F/White</b>									
Investigations Haemoglobin decreased	04MAR2021	232	147	No	No	MILD	Yes	3	2
<b>4410/003 - 63/M/White</b>									
Investigations and infestations COVID-19	25MAY2021	233	23	No	No	MILD	No	3	4
Investigations Blood bilirubin increased	25MAY2021	302	63	No	No	MILD	Yes	3	2
Investigations Weight increased	25MAY2021	659		No	No	MILD	No	2	2
Investigations and infestations Pharyngitis	25MAY2021	683	4	No	No	MILD	No	3	2
Investigations and infestations Erysipelas	25MAY2021	769	57	No	No	MOD	No	3	2
Investigations Blood creatinine increased	25MAY2021	890		No	No	MILD	No	2	2
<b>4410/004 - 67/M/White</b>									
Investigations Alanine aminotransferase increased	23JUL2021	46	147	No	No	MILD	Yes	3	2
Investigations Aspartate aminotransferase increased	23JUL2021	46	147	No	No	MILD	Yes	3	2
Investigations and infestations Pneumonia	23JUL2021	459	352	No	Yes	MOD	No	3	4
Investigations and infestations Urinary tract infection	23JUL2021	735		No	No	MILD	No	2	4
Investigations Neutrophil count decreased	23JUL2021	980		No	No	MILD	Yes	2	2
<b>4410/007 - 62/M/White</b>									
Investigations Aspartate aminotransferase increased	23SEP2022	22	21	No	No	MILD	No	3	2
Investigations Aspartate aminotransferase increased	23SEP2022	313	22	No	No	MILD	Yes	3	2
Investigations and infestations Blood glucose increased	23SEP2022	313		No	No	MILD	No	2	2
Investigations and infestations COVID-19	23SEP2022	346	7	No	No	MILD	No	3	4
Investigations Haemoglobin decreased	23SEP2022	355	106	No	No	MILD	Yes	3	2
Investigations Haemoglobin decreased	23SEP2022	589		No	No	MILD	Yes	2	2

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE	Most Extreme Intensity (1)	Caused by Study Drug	Action Taken (3)		
System Organ Class	MedDRA Preferred Term	Study Drug	Day of Onset	Duration in Days	Crossover phase	Serious	Outcome (2)	
4410/008 - 65/M/White	Infections and infestations							
	COVID-19 pneumonia	06MAR2023	26	37	No	Yes	SEV	No 3 4
	Pneumonia legionella	06MAR2023	26	37	No	Yes	SEV	No 4 4
	Infections and infestations							
	Pneumonia	06MAR2023	58		No	Yes	SEV	No 2 4
	Investigations							
	Blood creatinine increased	06MAR2023	148		No	No	MILD	No 2 2
	Infections and infestations							
	Severe acute respiratory syndrome	06MAR2023	238	9	No	No	MILD	No 3 4
4411/001 - 65/M/White	Investigations							
	Alanine aminotransferase increased	03APR2023	234	50	No	No	MILD	No 3 2
	Aspartate aminotransferase increased	03APR2023	234	50	No	No	MILD	No 3 2
	Investigations							
	Blood creatinine increased	03APR2023	381		No	No	MILD	No 5 2
4412/003 - 82/F/White	Infections and infestations							
	Pneumonia	05AUG2021	90	35	No	No	MILD	Yes 3 3
	Investigations							
	Transaminases increased	05AUG2021	713	66	No	No	MILD	No 3 2
	Investigations							
	Ejection fraction decreased	05AUG2021	785		No	No	MOD	No 2 4
4412/004 - 54/F/White	Investigations							
	Escherichia test positive	29NOV2022	32	21	No	No	MOD	No 3 4
	Investigations							
	Alanine aminotransferase increased	29NOV2022	37	9	No	No	MILD	No 3 2
	Investigations							
	Alanine aminotransferase increased	29NOV2022	73		No	No	MILD	Yes 2 2
	Aspartate aminotransferase increased	29NOV2022	73		No	No	MILD	Yes 2 2
	Infections and infestations							
	Urinary tract infection	29NOV2022	144	17	No	No	MOD	Yes 3 4

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race3 Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>4412/005 - 62/M/White</b>									
Investigations									
Alanine aminotransferase increased									
Aspartate aminotransferase increased									
Investigations									
Alanine aminotransferase increased									
Aspartate aminotransferase increased									
Investigations									
Alanine aminotransferase increased									
Aspartate aminotransferase increased									
Investigations									
Electrocardiogram QT prolonged									
Infections and infestations									
COVID-19									
Investigations									
Alanine aminotransferase increased									
Aspartate aminotransferase increased									
Investigations									
Blood creatinine increased									
<b>4412/008 - 56/F/White</b>									
Investigations									
Alanine aminotransferase increased									
Aspartate aminotransferase increased									
Blood alkaline phosphatase increased									
Investigations									
Blood lactate dehydrogenase increased									
Investigations									
Alanine aminotransferase increased									
Aspartate aminotransferase increased									
Investigations									
Neutrophil count decreased									
Investigations									
Alanine aminotransferase increased									
Aspartate aminotransferase increased									
Investigations									
Aspartate aminotransferase increased									

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race3 Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>4412/009 - 46/M/White</b>									
Investigations									
Alanine aminotransferase increased	06OCT2023	42	110	No	No	MILD	No	3	2
Aspartate aminotransferase increased	06OCT2023	42	117	No	No	MILD	No	3	2
Investigations									
Blood lactate dehydrogenase increased	06OCT2023	63	65	No	No	MILD	No	3	2
Investigations									
Streptococcus test positive	06OCT2023	77	7	No	No	MILD	No	3	2
Investigations									
Blood creatinine increased	06OCT2023	127	40	No	No	MILD	No	3	2
Infections and infestations									
Pneumonia	06OCT2023	167		No	No	MOD	No	2	4
Investigations									
Blood lactate dehydrogenase increased	06OCT2023	225	43	No	No	MILD	Yes	3	2
<b>4415/003 - 36/M/White</b>									
Infections and infestations									
COVID-19	04AUG2023	80	8	No	No	MOD	No	3	2
Infections and infestations									
Streptococcal infection	04AUG2023	188	8	No	No	MILD	No	3	2
Infections and infestations									
Cystitis	04AUG2023	213	2	No	No	MILD	No	3	2
<b>4505/001 - 50/F/White</b>									
Investigations									
Blood alkaline phosphatase increased	28JUL2021	22	22	No	No	MILD	No	3	2
Neutrophil count decreased	28JUL2021	22	38	No	No	SEV	Yes	3	3
Investigations									
Aspartate aminotransferase increased	28JUL2021	43	15	No	No	MILD	Yes	3	2
Blood creatinine increased	28JUL2021	43	8	No	No	MILD	Yes	3	2
Investigations									
Aspartate aminotransferase increased	28JUL2021	79	63	No	No	MILD	Yes	3	2
Neutrophil count decreased	28JUL2021	79	21	No	No	MILD	Yes	3	2
Investigations									
Alanine aminotransferase increased	28JUL2021	120	22	No	No	MILD	No	3	2
Neutrophil count decreased	28JUL2021	120	22	No	No	MOD	Yes	3	2
Investigations									
Alanine aminotransferase increased	28JUL2021	162	43	No	No	MILD	Yes	3	2
Aspartate aminotransferase increased	28JUL2021	162	190	No	No	MILD	Yes	3	2
Infections and infestations									
Upper respiratory tract infection	28JUL2021	187	24	No	No	MILD	No	3	2

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE	Duration in Days	Crossover phase	Most Serious	Most Extreme Intensity (1)	Caused by Study Drug	Action Taken (2)	Action Taken (3)
<b>4505/001 - 50/F/White</b>										
Investigations										
Neutrophil count decreased		28JUL2021	204	22	No	No	MOD	Yes	3	2
Investigations										
Alanine aminotransferase increased		28JUL2021	225	85	No	No	MILD	Yes	3	2
Investigations										
Neutrophil count decreased		28JUL2021	246	43	No	No	MOD	Yes	3	2
Investigations										
Alanine aminotransferase increased		28JUL2021	330	22	No	No	MILD	Yes	3	2
Infections and infestations										
COVID-19		28JUL2021	334	10	No	No	MILD	No	3	2
<b>4505/003 - 59/M/White</b>										
Investigations										
Alanine aminotransferase increased		14SEP2022	21	70	No	No	MILD	Yes	3	2
Investigations										
Blood creatine phosphokinase increased		14SEP2022	42	49	No	No	SEV	Yes	3	3
Investigations										
Amylase increased		14SEP2022	83	8	No	No	MILD	Yes	3	2
Aspartate aminotransferase increased		14SEP2022	83	8	No	No	MILD	Yes	3	2
Infections and infestations										
Nasopharyngitis		14SEP2022	131	45	No	No	MILD	No	3	2
Investigations										
Blood creatine phosphokinase increased		14SEP2022	133	57	No	No	SEV	Yes	3	3
Investigations										
Alanine aminotransferase increased		14SEP2022	154	36	No	No	MILD	Yes	3	2
Amylase increased		14SEP2022	154	22	No	No	MILD	Yes	3	2
Investigations										
Aspartate aminotransferase increased		14SEP2022	175	15	No	No	MILD	Yes	3	2
Investigations										
Amylase increased		14SEP2022	182	8	No	No	MILD	Yes	3	2
Investigations										
Amylase increased		14SEP2022	196	22	No	No	MILD	Yes	3	2
Lipase increased		14SEP2022	196	32	No	No	MILD	Yes	3	2
Investigations										
Blood creatine phosphokinase increased		14SEP2022	217		No	No	MILD	Yes	2	2
Investigations										
Alanine aminotransferase increased		14SEP2022	259	22	No	No	MILD	Yes	3	2
<b>4507/003 - 59/F/White</b>										
Investigations										
Amylase increased		30NOV2022	356	22	No	No	MOD	No	3	2
Lipase increased		30NOV2022	356		No	No	SEV	No	2	4

Notes: Adverse Events are coded using MedDRA 27.0

For patients who crossed over, date of first Study Drug Administration is provided for the standard of care treatment in the main treatment period and for Pralsetinib in the crossover treatment period.

(1) Severity: MILD = Grade 1 - Mild, MOD = Grade 2 - Moderate, SEV = Grade 3 - Severe, LT = Grade 4 - Life Threatening, DEATH = Grade 5 - Death.

(2) Outcome: 1 = fatal; 2 = not recovered/not resolved; 3 = recovered/resolved; 4 = recovered/resolved with sequelae; 5 = recovering/resolving; 6 = unknown.

(3) Action taken: 1 = dose increased; 2 = dose not changed; 3 = dose reduced; 4 = drug interrupted; 5 = drug withdrawn; 6 = not applicable; 7 = unknown.

\* Study day derived from imputed onset date

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE Study Drug	Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>4507/003 - 59/F/White</b>											
Investigations											
Amylase increased		30NOV2022	400				No	No	MILD	No	2
<b>4508/002 - 79/F/White</b>											
Investations and infestations											
Infection		24NOV2022	89				No	Yes	SEV	No	5
<b>4508/003 - 72/M/White</b>											
Investigations											
Blood creatinine increased		13JAN2023	21	105			No	No	MILD	No	3
Platelet count decreased		13JAN2023	21	102			No	No	SEV	No	3
Investigations											
Aspartate aminotransferase increased		13JAN2023	35	91			No	No	MILD	Yes	3
Investigations											
Bilirubin conjugated increased		13JAN2023	42	84			No	No	MILD	No	3
Investigations											
Blood bilirubin increased		13JAN2023	62	8			No	No	MOD	No	3
Investigations											
Weight decreased		13JAN2023	63	64			No	No	MOD	No	3
Infections and infestations											
Sepsis		13JAN2023	78	46			No	Yes	LT	No	3
Infections and infestations											
Pseudomembranous colitis		13JAN2023	100	24			No	Yes	SEV	No	3
Infections and infestations											
Sepsis		13JAN2023	155	1			No	Yes	DEATH	No	1
<b>4511/002 - 45/F/White</b>											
Investions and infestations											
Influenza		16DEC2022	23	21			No	No	MILD	No	3
Investions and infestations											
Pharyngitis		16DEC2022	155	78			No	No	MOD	No	3
<b>4511/004 - 44/M/White</b>											
Investigations											
Blood creatine phosphokinase increased		23NOV2023	22				No	No	MOD	Yes	2

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(1) Severity: MILD = Grade 1 - Mild, MOD = Grade 2 - Moderate, SEV = Grade 3 - Severe, LT = Grade 4 - Life Threatening, DEATH = Grade 5 - Death.

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(3) Action taken: 1 = dose increased; 2 = dose not changed; 3 = dose reduced; 4 = drug interrupted; 5 = drug withdrawn; 6 = not applicable; 7 = unknown.

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race3 Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>4517/001 - 58/M/White</b>									
Investigations									
Blood creatinine increased	22OCT2020	22	63	No	No	MILD	No	3	2
Infections and infestations									
Pneumocystis jirovecii pneumonia	22OCT2020	46	13	No	Yes	MOD	No	3	4
Investigations									
Blood lactate dehydrogenase increased	22OCT2020	146	63	No	No	MILD	No	3	2
Infections and infestations									
Atypical pneumonia	22OCT2020	147		No	Yes	MOD	No	2	2
Investigations									
Bronchopulmonary aspergillosis	22OCT2020	148	61	No	No	SEV	No	3	2
Infections and infestations									
Atypical pneumonia	22OCT2020	152	11	No	Yes	MOD	No	4	4
Investigations									
Alanine aminotransferase increased	22OCT2020	176	33	No	No	MILD	No	3	2
Investigations									
Blood creatinine increased	22OCT2020	372	72	No	No	MILD	No	3	2
Infections and infestations									
COVID-19	22OCT2020	693	24	No	No	MILD	No	3	2
Investigations									
Gastroenteritis	22OCT2020	864	14	No	No	MILD	No	3	2
Investigations									
Urinary tract infection	22OCT2020	1001	6	No	Yes	SEV	No	3	2
Investigations									
Nitrite urine present	22OCT2020	1121	22	No	No	MILD	No	3	2
Investigations									
Nasopharyngitis	22OCT2020	1171	4	No	No	MILD	No	3	2
<b>4517/003 - 76/F/White</b>									
Investigations									
Rhinitis	02JUN2022	8		No	No	MILD	No	5	2
Investigations									
COVID-19	02JUN2022	33	18	No	No	MILD	No	3	4
Investigations									
Herpes zoster	02JUN2022	183	12	No	No	MILD	No	3	2
Investigations									
Nasopharyngitis	02JUN2022	201	45	No	No	MOD	No	3	3
<b>4518/001 - 63/F/White</b>									
Investigations									
Alanine aminotransferase increased	01AUG2023	22	85	No	No	MILD	Yes	3	2
Aspartate aminotransferase increased	01AUG2023	22		No	No	MILD	Yes	2	2

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For patients who crossed over, date of first Study Drug Administration is provided for the standard of care treatment in the main treatment period and for Pralsetinib in the crossover treatment period.

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE Study Drug	Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>4518/001 - 63/F/White</b>											
Investigations											
Alanine aminotransferase increased		01AUG2023		127	23	No	No	MILD	Yes	3	2
<b>4601/001 - 61/F/White</b>											
Investigations											
Transaminases increased		10NOV2021		21	472	No	No	MOD	Yes	3	2
Infections and infestations											
Urinary tract infection		10NOV2021		103	6	No	No	MOD	No	3	2
Infections and infestations											
Otitis externa		10NOV2021		104	8	No	No	MILD	No	3	2
Infections and infestations											
Tularaemia		10NOV2021		113	35	No	No	MILD	No	3	2
Infections and infestations											
COVID-19		10NOV2021		235	9	No	No	MILD	No	3	2
Infections and infestations											
Urinary tract infection		10NOV2021		251	22	No	No	MILD	No	3	2
Investigations											
Blood creatine phosphokinase increased		10NOV2021		335	168	No	No	SEV	Yes	3	4
Infections and infestations											
Urinary tract infection		10NOV2021		395	23**	No	No	MOD	No	3	2
Investigations											
Blood creatine phosphokinase increased		10NOV2021		510	77	No	No	MOD	Yes	3	4
Infections and infestations											
Cystitis		10NOV2021		519	5	No	No	MILD	No	3	2
Investigations											
Blood cholesterol increased		10NOV2021		567	20	No	No	LT	No	3	2
Infections and infestations											
Pneumonia		10NOV2021		568	13	No	Yes	SEV	No	3	2
Infections and infestations											
Candida infection		10NOV2021		585	6	No	No	MILD	No	3	2
Infections and infestations											
Parainfluenzae virus infection		10NOV2021		588	66	No	No	MOD	No	3	4
Investigations											
Blood creatine phosphokinase increased		10NOV2021		596	36	No	No	SEV	Yes	3	3
Investigations											
Blood creatine phosphokinase increased		10NOV2021		653		No	No	MILD	Yes	2	2
Investigations											
Alanine aminotransferase increased		10NOV2021		674		No	No	MOD	Yes	2	2
Aspartate aminotransferase increased		10NOV2021		674		No	No	MOD	Yes	2	2
Infections and infestations											
Upper respiratory tract infection		10NOV2021		774	14	No	No	MILD	No	3	2
Infections and infestations											
Influenza		10NOV2021		882	9	No	No	MILD	No	3	2

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE	Duration in Days	Crossover phase	Most Serious	Most Extreme Intensity (1)	Caused by Study Drug	Action Taken (2)
System Organ Class Preferred Term	Study Drug Onset							Outcome (2)	Outcome (3)
4601/002 - 58/F/White									
Infections and infestations									
Upper respiratory tract infection	22NOV2021	32	4	No	No	MOD	No	3	2
Infections and infestations									
Upper respiratory tract infection	22NOV2021	109	11	No	No	MOD	No	3	2
Investigations									
Blood creatine phosphokinase increased	22NOV2021	124	96	No	No	SEV	Yes	3	3
Infections and infestations									
Lower respiratory tract infection	22NOV2021	219	10	No	No	MOD	Yes	3	2
Investigations									
Blood creatine phosphokinase increased	22NOV2021	242	110	No	No	MOD	Yes	3	2
Infections and infestations									
Urinary tract infection	22NOV2021	269	8	No	No	MOD	Yes	3	2
Infections and infestations									
COVID-19	22NOV2021	276	16	No	No	MILD	No	3	2
Infections and infestations									
Diverticulitis	22NOV2021	345	11	No	No	MOD	Yes	3	4
Infections and infestations									
Upper respiratory tract infection	22NOV2021	373	10	No	No	MOD	No	3	2
Investigations									
Blood creatine phosphokinase increased	22NOV2021	379	185	No	No	MOD	Yes	3	2
Blood creatinine increased	22NOV2021	379	19	No	No	MILD	No	3	2
Infections and infestations									
Upper respiratory tract infection	22NOV2021	418	21	No	No	MOD	Yes	3	2
Investigations									
Blood creatinine increased	22NOV2021	442	42	No	No	MILD	No	3	2
Infections and infestations									
Rhinitis	22NOV2021	470	32	No	No	MOD	No	3	2
4601/003 - 68/F/White									
Infections and infestations									
Gastroenteritis	14JUN2022	10	9	No	No	MOD	Yes	3	2
Infections and infestations									
Herpes zoster	14JUN2022	32	49	No	Yes	SEV	No	3	2
4701/001 - 33/F/White									
Infections and infestations									
Lower respiratory tract infection	21MAR2023	51	10	No	Yes	DEATH	Yes	1	5

Notes: Adverse Events are coded using MedDRA 27.0

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup> Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
4701/001 - 33/F/White Infections and infestations Oral candidiasis	21MAR2023	57		No	No	MOD	Yes	2	2
4702/002 - 69/M/Black or African American Investigations Blood creatinine increased	14JUN2023	6	35	No	No	MILD	No	3	2
Investigations Alanine aminotransferase increased	14JUN2023	22	8	No	No	LT	No	3	2
Investigations Alanine aminotransferase increased	14JUN2023	30	5	No	No	SEV	No	3	2
Investigations Alanine aminotransferase increased	14JUN2023	35	2	No	No	MOD	No	3	2
Investigations Alanine aminotransferase increased	14JUN2023	37	5	No	No	MILD	No	3	2
Investigations Aspartate aminotransferase increased	14JUN2023	77		No	No	MILD	No	2	2
Blood creatinine increased	14JUN2023	77		No	No	MILD	No	2	2
4703/002 - 51/F/Unknown Infections and infestations Cellulitis	24MAY2023	17		No	No	MOD	Yes	2	2
Paronychia	24MAY2023	17		No	No	MILD	Yes	2	2
Investigations Alanine aminotransferase increased	24MAY2023	22	37	No	No	MOD	Yes	3	2
Investigations Aspartate aminotransferase increased	24MAY2023	34	25	No	No	MOD	Yes	3	2
Infections and infestations Sepsis	24MAY2023	41		No	Yes	LT	No	2	2
Investigations Alanine aminotransferase increased	24MAY2023	58		No	No	MILD	Yes	2	2
4705/001 - 63/M/White Infections and infestations Lower respiratory tract infection	23FEB2022	50	5	No	No	MILD	No	3	2
Infections and infestations Lower respiratory tract infection	23FEB2022	93	8	No	No	MILD	No	3	2

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE Study Drug	Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>4705/003 - 76/F/White</b>											
Investigations											
Platelet count decreased		27JUL2023		27			No	No	MILD	No	5
											2
<b>4801/001 - 54/M/Black or African American</b>											
Investigations and infestations											
COVID-19		22JUL2021		236	8		No	No	MOD	No	3
											4
Investigations											
Neutrophil count decreased		22JUL2021		614	16		No	No	SEV	Yes	3
											4
Investigations and infestations											
Rash pustular		22JUL2021		625			No	No	MILD	No	2
											2
Investigations and infestations											
Nasopharyngitis		22JUL2021		925	5		No	No	MILD	No	3
											2
<b>4801/002 - 54/F/White</b>											
Investigations and infestations											
Oral candidiasis		07FEB2022		15	70		No	No	MOD	No	3
											2
Investigations and infestations											
Urinary tract infection		07FEB2022		43	16		No	No	MILD	No	3
											2
Investigations											
Blood creatinine increased		07FEB2022		43	15		No	No	MILD	No	3
											2
Transaminases increased		07FEB2022		43			No	No	MOD	Yes	2
											2
Investigations and infestations											
Pneumocystis jirovecii pneumonia		07FEB2022		55	21		No	Yes	SEV	Yes	3
											3
Investigations											
Neutrophil count decreased		07FEB2022		218	22		No	No	MOD	No	3
											2
Investigations											
Neutrophil count decreased		07FEB2022		242	14		No	No	SEV	No	3
											2
Investigations											
Neutrophil count decreased		07FEB2022		247	9		No	No	SEV	No	3
											2
Investigations											
Blood phosphorus decreased		07FEB2022		372	22		No	No	MOD	No	3
											2
Neutrophil count decreased		07FEB2022		372	22		No	No	MOD	No	3
											2
<b>5203/001 - 65/M/White</b>											
Investigations											
Alanine aminotransferase increased		02DEC2021		21	63		No	No	MILD	Yes	3
											2
Aspartate aminotransferase increased		02DEC2021		21			No	No	MILD	Yes	2
											2
Blood alkaline phosphatase increased		02DEC2021		21			No	No	MILD	No	2
											2
Blood lactate dehydrogenase increased		02DEC2021		21			No	No	MILD	No	2
											2

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE Study Drug	Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>5203/001 - 65/M/White</b>											
Investigations											
Blood phosphorus decreased		02DEC2021		63	64	No	No	MILD	No	3	2
Infections and infestations											
Genital herpes simplex		02DEC2021		98	34	No	No	MOD	No	3	2
Investigations											
Blood thyroid stimulating hormone decreased		02DEC2021		105		No	No	MILD	Yes	2	2
Infections and infestations											
COVID-19		02DEC2021		110	6	No	No	MILD	No	3	2
Investigations											
Blood albumin increased		02DEC2021		126		No	No	MILD	Yes	2	2
Infections and infestations											
Genital herpes simplex		02DEC2021		177	15	No	No	MILD	No	3	2
Investigations											
Genital herpes simplex		02DEC2021		293	21	No	No	MILD	No	3	2
Infections and infestations											
Gastrointestinal infection		02DEC2021		362	15	No	No	MOD	No	3	2
<b>5203/002 - 79/M/White</b>											
Investigations											
Infections and infestations											
Candida infection		02JUN2022		21	10	No	No	MOD	Yes	3	2
Investigations											
Alanine aminotransferase increased		02JUN2022		21		No	No	MILD	Yes	2	2
Aspartate aminotransferase increased		02JUN2022		21		No	No	MILD	Yes	2	2
Blood lactate dehydrogenase increased		02JUN2022		21		No	No	MILD	Yes	2	2
Investigations											
Blood phosphorus decreased		02JUN2022		26	37	No	No	MILD	Yes	3	2
Infections and infestations											
Candida infection		02JUN2022		63		No	No	MILD	Yes	2	2
Investigations											
Blood creatinine increased		02JUN2022		63		No	No	MILD	Yes	2	2
Blood phosphorus increased		02JUN2022		63	10	No	No	MILD	Yes	3	2
Glomerular filtration rate decreased		02JUN2022		63		No	No	MOD	Yes	2	2
Infections and infestations											
Pneumonia		02JUN2022		67	18	No	Yes	MOD	Yes	4	2
Investigations											
Blood phosphorus decreased		02JUN2022		76		No	No	MILD	Yes	2	2
<b>5401/001 - 69/F/White</b>											
Investigations											
Paronychia		10DEC2021		84	23	No	No	MILD	Yes	3	2

Notes: Adverse Events are coded using MedDRA 27.0

For patients who crossed over, date of first Study Drug Administration is provided for the standard of care treatment in the main treatment period and for Pralsetinib in the crossover treatment period.

(1) Severity: MILD = Grade 1 - Mild, MOD = Grade 2 - Moderate, SEV = Grade 3 - Severe, LT = Grade 4 - Life Threatening, DEATH = Grade 5 - Death.

(2) Outcome: 1 = fatal; 2 = not recovered/not resolved; 3 = recovered/resolved; 4 = recovered/resolved with sequelae; 5 = recovering/resolving; 6 = unknown.

(3) Action taken: 1 = dose increased; 2 = dose not changed; 3 = dose reduced; 4 = drug interrupted; 5 = drug withdrawn; 6 = not applicable; 7 = unknown.

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE	Duration in Days	Crossover phase	Most Serious	Most Extreme Intensity (1)	Caused by Study Drug	Action Taken (2)	Action Taken (3)
<b>5401/001 - 69/F/White</b>										
Investigations										
Alanine aminotransferase increased	10DEC2021	84	43	No	No	MOD	Yes	3	2	
Aspartate aminotransferase increased	10DEC2021	84	23	No	No	MILD	Yes	3	2	
Infections and infestations										
COVID-19	10DEC2021	100	7	No	No	MILD	No	3	2	
Investigations										
Gastroenteritis	10DEC2021	204	4	No	No	MILD	No	3	2	
Investigations										
Blood alkaline phosphatase increased	10DEC2021	232		No	No	SEV	No	2	2	
Investigations										
Electrocardiogram QT prolonged	10DEC2021	321	129	No	No	SEV	No	3	2	
<b>6602/060 - 58/F/White</b>										
Investigations										
Electrocardiogram QT prolonged	23JAN2024	15		No	No	SEV	Yes	5	4	
Investigations										
Alanine aminotransferase increased	23JAN2024	86	10	No	No	MILD	Yes	3	2	
Aspartate aminotransferase increased	23JAN2024	86		No	No	MILD	Yes	5	2	
<b>7201/001 - 70/F/American Indian or Alaska Native</b>										
Investigations										
Urinary tract infection	11JUL2022	19		No	No	MOD	No	5	2	
Investigations										
Pneumonia	11JUL2022	25	2	No	Yes	DEATH	No	1	2	
<b>7201/008 - 52/M/American Indian or Alaska Native</b>										
Investigations										
Urosepsis	07SEP2023	111		No	No	MOD	Yes	5	2	
Investigations										
Sinusitis	07SEP2023	211		No	No	MILD	Yes	5	2	
<b>7301/001 - 63/M/White</b>										
Investigations										
Gastroenteritis	12MAY2022	65	8	No	No	MOD	No	3	2	
Investigations										
COVID-19	12MAY2022	95	6	No	No	MILD	No	3	2	

Notes: Adverse Events are coded using MedDRA 27.0

For patients who crossed over, date of first Study Drug Administration is provided for the standard of care treatment in the main treatment period and for Pralsetinib in the crossover treatment period.

(1) Severity: MILD = Grade 1 - Mild, MOD = Grade 2 - Moderate, SEV = Grade 3 - Severe, LT = Grade 4 - Life Threatening, DEATH = Grade 5 - Death.

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(3) Action taken: 1 = dose increased; 2 = dose not changed; 3 = dose reduced; 4 = drug interrupted; 5 = drug withdrawn; 6 = not applicable; 7 = unknown.

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race3 Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
7301/003 - 67/M/American Indian or Alaska Native									
Investigations Blood creatinine increased	25MAY2022	147	56	No	No	MILD	Yes	3	2
7301/005 - 63/M/American Indian or Alaska Native									
Investigations Aspartate aminotransferase increased	31AUG2022	43	126	No	No	MILD	Yes	3	2
Investigations Blood creatinine increased	31AUG2022	147		No	No	MILD	Yes	5	2
Infections and infestations Lower respiratory tract infection	31AUG2022	159		No	No	MOD	No	5	4
Investigations Alanine aminotransferase increased	31AUG2022	190		No	No	MOD	Yes	5	2
Aspartate aminotransferase increased	31AUG2022	190		No	No	MOD	Yes	5	2
7301/006 - 64/M/American Indian or Alaska Native									
Infections and infestations COVID-19	07DEC2022	150	13	No	No	MOD	No	3	2
Investigations Alanine aminotransferase increased	07DEC2022	231	43	No	No	MILD	Yes	3	2
Aspartate aminotransferase increased	07DEC2022	231	43	No	No	MILD	Yes	3	2
Infections and infestations Oesophageal candidiasis	07DEC2022	280	22	No	No	SEV	No	3	2
Infections and infestations Helicobacter infection	07DEC2022	303	16	No	No	MOD	No	3	2
Infections and infestations Pneumonia	07DEC2022	368	10	No	Yes	SEV	Yes	3	2
Infections and infestations Upper respiratory tract infection	07DEC2022	414	7	No	No	MILD	No	3	2
7301/009 - 25/F/American Indian or Alaska Native									
Infections and infestations Gastroenteritis	23FEB2023	377	4	No	No	MILD	No	3	2

Notes: Adverse Events are coded using MedDRA 27.0

For patients who crossed over, date of first Study Drug Administration is provided for the standard of care treatment in the main treatment period and for Pralsetinib in the crossover treatment period.

(1) Severity: MILD = Grade 1 - Mild, MOD = Grade 2 - Moderate, SEV = Grade 3 - Severe, LT = Grade 4 - Life Threatening, DEATH = Grade 5 - Death.

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race3 Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
7301/012 - 65/F/American Indian or Alaska Native									
Investigations									
Alanine aminotransferase increased	25OCT2023	19			No	No	MOD	Yes	2
Aspartate aminotransferase increased	25OCT2023	19			No	No	MOD	Yes	2
Blood alkaline phosphatase increased	25OCT2023	19			No	No	MOD	Yes	2
Infections and infestations									
Urosepsis	25OCT2023	35			No	Yes	LT	Yes	2
7501/009 - 46/F/White									
Investigations									
Aspartate aminotransferase increased	19OCT2023	40	25		No	No	MILD	No	3
Investigations									
Platelet count decreased	19OCT2023	110	21		No	No	MILD	Yes	3
8402/001 - 81/F/Asian									
Infections and infestations									
Pneumonia	01FEB2024	12	10		No	Yes	MOD	Yes	3
Investigations									
Alanine aminotransferase increased	01FEB2024	28			No	No	SEV	Yes	5
Aspartate aminotransferase increased	01FEB2024	28			No	No	MOD	Yes	5
8407/001 - 64/F/Asian									
Investigations									
Neutrophil count decreased	07JUL2022	23	39		No	No	SEV	No	3
White blood cell count decreased	07JUL2022	23	39		No	No	MOD	No	3
Investigations									
Electrocardiogram QT prolonged	07JUL2022	82	8		No	No	SEV	Yes	3
White blood cell count decreased	07JUL2022	82	22		No	No	MOD	No	3
Investigations									
Neutrophil count decreased	07JUL2022	124	84		No	No	SEV	Yes	3
White blood cell count decreased	07JUL2022	124	84		No	No	SEV	Yes	3
Investigations									
Lymphocyte count decreased	07JUL2022	166	43		No	No	SEV	Yes	3
Investigations									
Lymphocyte count decreased	07JUL2022	229	145		No	No	SEV	Yes	3
Investigations									
Neutrophil count decreased	07JUL2022	271	43		No	No	MOD	Yes	3
White blood cell count decreased	07JUL2022	271	43		No	No	MOD	Yes	3

Notes: Adverse Events are coded using MedDRA 27.0

For patients who crossed over, date of first Study Drug Administration is provided for the standard of care treatment in the main treatment period and for Pralsetinib in the crossover treatment period.

(1) Severity: MILD = Grade 1 - Mild, MOD = Grade 2 - Moderate, SEV = Grade 3 - Severe, LT = Grade 4 - Life Threatening, DEATH = Grade 5 - Death.

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE Study Drug	Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<hr/>											
8408/001 - 45/M/Asian											
Investigations											
Alanine aminotransferase increased											
Aspartate aminotransferase increased											
Blood creatinine increased											
Neutrophil count decreased											
Investigations											
Alanine aminotransferase increased											
Aspartate aminotransferase increased											
Blood creatine phosphokinase increased											
Neutrophil count decreased											
Investigations											
Blood creatine phosphokinase increased											
Neutrophil count decreased											
Investigations											
Alanine aminotransferase increased											
Aspartate aminotransferase increased											
Investigations											
Blood creatine phosphokinase increased											
Investigations											
Aspartate aminotransferase increased											
Neutrophil count decreased											
Investigations											
Alanine aminotransferase increased											
Aspartate aminotransferase increased											
Investigations											
Blood creatine phosphokinase increased											
Investigations											
White blood cell count decreased											
Investigations											
Neutrophil count decreased											
Infections and infestations											
Pneumocystis jirovecii pneumonia											
<hr/>											

Notes: Adverse Events are coded using MedDRA 27.0

For patients who crossed over, date of first Study Drug Administration is provided for the standard of care treatment in the main treatment period and for Pralsetinib in the crossover treatment period.

(1) Severity: MILD = Grade 1 - Mild, MOD = Grade 2 - Moderate, SEV = Grade 3 - Severe, LT = Grade 4 - Life Threatening, DEATH = Grade 5 - Death.

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(3) Action taken: 1 = dose increased; 2 = dose not changed; 3 = dose reduced; 4 = drug interrupted; 5 = drug withdrawn; 6 = not applicable; 7 = unknown.

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race<sup>3</sup>

Adverse Event MedDRA

System Organ Class

Preferred Term

Date of First Study Administration	AE Study Drug	Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
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8411/001 - 75/M/Asian

Investigations

Amylase increased

19AUG2022 78 21 No No SEV No 3 2

Investigations

Lipase increased

19AUG2022 84 70 No No SEV No 3 2

Notes: Adverse Events are coded using MedDRA 27.0

For patients who crossed over, date of first Study Drug Administration is provided for the standard of care treatment in the main treatment period and for Pralsetinib in the crossover treatment period.

(1) Severity: MILD = Grade 1 - Mild, MOD = Grade 2 - Moderate, SEV = Grade 3 - Severe, LT = Grade 4 - Life Threatening, DEATH = Grade 5 - Death.

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(3) Action taken: 1 = dose increased; 2 = dose not changed; 3 = dose reduced; 4 = drug interrupted; 5 = drug withdrawn; 6 = not applicable; 7 = unknown.

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	Day of Onset	AE Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
System Organ Class Preferred Term										
3301/001 - 59/M/Asian										
Investigations										
Alanine aminotransferase increased		21JUN2021	22	493	No	No	SEV	No	3	2
Aspartate aminotransferase increased		21JUN2021	22	274	No	No	MOD	No	3	2
Infections and infestations										
COVID-19		21JUN2021	241	7	No	No	MILD	No	3	2
Investigations										
Aspartate aminotransferase increased		21JUN2021	323	228	Yes	No	MILD	No	3	2
Infections and infestations										
Herpes zoster		21JUN2021	820		Yes	No	MOD	No	2	4
3301/002 - 74/F/Asian										
Infections and infestations										
COVID-19		12JAN2022	145	7	No	No	SEV	No	3	2
Infections and infestations										
Vaginal infection		12JAN2022	155		No	No	MILD	No	2	2
3301/003 - 54/F/Asian										
Infections and infestations										
Nasopharyngitis		27JUL2022	127	49	No	No	MILD	No	3	2
Infections and infestations										
Herpes zoster		27JUL2022	164	27	No	No	MOD	No	3	2
3302/002 - 76/F/Asian										
Investigations										
Blood thyroid stimulating hormone decreased		26NOV2020	294	78	No	No	MILD	Yes	3	2
Investigations										
Blood creatinine increased		26NOV2020	371	23	Yes	No	MILD	Yes	3	2
Investigations										
Aspartate aminotransferase increased		26NOV2020	393	222	Yes	No	MILD	Yes	3	2
Neutrophil count decreased		26NOV2020	393	83	Yes	No	SEV	Yes	3	3
Investigations										
Lymphocyte count decreased		26NOV2020	401	15	Yes	No	MOD	Yes	3	2
Investigations										
Blood creatinine increased		26NOV2020	436	40	Yes	No	MILD	Yes	3	2
Investigations										
Blood creatinine increased		26NOV2020	496	22	Yes	No	MILD	Yes	3	2
Investigations										
Blood creatinine increased		26NOV2020	579	22	Yes	No	MILD	Yes	3	2

Notes: Adverse Events are coded using MedDRA 27.0

For patients who crossed over, date of first Study Drug Administration is provided for the standard of care treatment in the main treatment period and for Pralsetinib in the crossover treatment period.

(1) Severity: MILD = Grade 1 - Mild, MOD = Grade 2 - Moderate, SEV = Grade 3 - Severe, LT = Grade 4 - Life Threatening, DEATH = Grade 5 - Death.

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race3 Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
3302/002 - 76/F/Asian									
Investigations									
Aspartate aminotransferase increased	26NOV2020	616	4	Yes	No	MILD	No	3	6
Infections and infestations									
Oral candidiasis	26NOV2020	617		Yes	No	MOD	No	2	6
Investigations									
Blood bicarbonate decreased	26NOV2020	618		Yes	No	MOD	No	2	6
Infections and infestations									
COVID-19	26NOV2020	626	8	Yes	No	SEV	No	3	6
COVID-19 pneumonia	26NOV2020	626		Yes	No	SEV	No	2	6
3302/008 - 71/F/Asian									
Investigations									
Aspartate aminotransferase increased	17MAY2022	88	79	No	No	MILD	No	3	2
Infections and infestations									
Cystitis	17MAY2022	112	11	Yes	No	MOD	No	3	2
Investigations									
Platelet count decreased	17MAY2022	121		Yes	No	SEV	Yes	2	2
Infections and infestations									
Pneumonia	17MAY2022	162		Yes	Yes	LT	No	2	5
Investigations									
Aspartate aminotransferase increased	17MAY2022	167	7	Yes	No	MOD	No	3	6
Investigations									
Alanine aminotransferase increased	17MAY2022	171	2	Yes	No	MILD	No	3	6
Blood bicarbonate decreased	17MAY2022	171	3	Yes	No	MOD	No	3	6
Investigations									
Aspartate aminotransferase increased	17MAY2022	174		Yes	No	MOD	No	2	6
Investigations									
Alanine aminotransferase increased	17MAY2022	177		Yes	No	MILD	No	2	6
3302/009 - 58/M/Asian									
Investigations									
Blood bicarbonate decreased	06JAN2023	2	3	No	No	MOD	No	3	2
Investigations									
Neutrophil count decreased	06JAN2023	11	2	No	No	MOD	No	3	2
Infections and infestations									
COVID-19 pneumonia	06JAN2023	20	9	No	Yes	SEV	No	3	4
3302/010 - 79/F/Asian									
Infections and infestations									
Pneumonia	23MAR2023	291	45	No	No	MOD	No	3	2

Notes: Adverse Events are coded using MedDRA 27.0

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(1) Severity: MILD = Grade 1 - Mild, MOD = Grade 2 - Moderate, SEV = Grade 3 - Severe, LT = Grade 4 - Life Threatening, DEATH = Grade 5 - Death.

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(3) Action taken: 1 = dose increased; 2 = dose not changed; 3 = dose reduced; 4 = drug interrupted; 5 = drug withdrawn; 6 = not applicable; 7 = unknown.

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race <sup>3</sup> Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
3303/003 - 74/M/Asian									
Investigations Aspartate aminotransferase increased	26DEC2022	64	21	No	No	MOD	Yes	3	2
Investigations Alanine aminotransferase increased	26DEC2022	311		Yes	No	MILD	Yes	2	2
Investigations Aspartate aminotransferase increased	26DEC2022	311		Yes	No	SEV	Yes	2	3
Investigations Aspartate aminotransferase increased	26DEC2022	318	21	Yes	No	MILD	Yes	3	2
3303/004 - 65/M/Asian									
Investigations Neutrophil count decreased	04APR2023	288	42	Yes	No	MOD	Yes	3	2
Investigations Neutrophil count decreased	04APR2023	351		Yes	No	SEV	Yes	5	4
3304/001 - 67/M/Asian									
Investigations Neutrophil count decreased	15JAN2024	85	8	No	No	MOD	Yes	3	2
Investigations White blood cell count decreased	15JAN2024	85	8	No	No	MOD	Yes	3	2
4203/001 - 60/M/NOT REPORTED									
Investigations Weight decreased	03JAN2022	39		No	No	MOD	Yes	2	2
Investigations SARS-CoV-2 test positive	03JAN2022	85	8	No	No	MOD	No	3	2
4204/001 - 63/F/NOT REPORTED									
Investigations Alanine aminotransferase increased	20MAY2021	21		No	No	MOD	Yes	2	2
Investigations Transaminases increased	20MAY2021	21	384	No	No	MOD	Yes	3	2
Investigations Aspartate aminotransferase increased	20MAY2021	85	84	No	No	MILD	Yes	3	2
Investigations Blood lactate dehydrogenase increased	20MAY2021	106	194	No	No	MILD	Yes	3	2

Notes: Adverse Events are coded using MedDRA 27.0

For patients who crossed over, date of first Study Drug Administration is provided for the standard of care treatment in the main treatment period and for Pralsetinib in the crossover treatment period.

(1) Severity: MILD = Grade 1 - Mild, MOD = Grade 2 - Moderate, SEV = Grade 3 - Severe, LT = Grade 4 - Life Threatening, DEATH = Grade 5 - Death.

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race <sup>3</sup> Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>4204/001 - 63/F/NOT REPORTED</b>									
Infections and infestations									
COVID-19	20MAY2021	317	7	No	No	MILD	Yes	3	2
Infections and infestations									
Tongue fungal infection	20MAY2021	968		Yes	No	MOD	Yes	2	2
Investigations									
Alanine aminotransferase increased	20MAY2021	988		Yes	No	MILD	Yes	2	2
Aspartate aminotransferase increased	20MAY2021	988		Yes	No	MILD	Yes	2	2
Blood lactate dehydrogenase increased	20MAY2021	988		Yes	No	MILD	Yes	2	2
Gamma-glutamyltransferase increased	20MAY2021	988		Yes	No	MILD	Yes	2	2
<b>4205/003 - 73/F/NOT REPORTED</b>									
Infections and infestations									
Sinusitis	25NOV2022	107	35	No	No	MOD	No	3	2
Infections and infestations									
Bronchitis	25NOV2022	115	27	No	No	MOD	No	3	2
Investigations									
Kidney infection	25NOV2022	206		Yes	Yes	SEV	No	2	4
Infections and infestations									
Paronychia	25NOV2022	249		Yes	No	MILD	Yes	2	2
<b>4206/003 - 70/F/NOT REPORTED</b>									
Infections and infestations									
Rhinitis	14DEC2022	15	57	No	No	MILD	No	3	2
Investigations									
Gamma-glutamyltransferase increased	14DEC2022	21	100	No	No	MILD	No	3	2
Lymphocyte count decreased	14DEC2022	21	22	No	No	MILD	No	3	2
Infections and infestations									
Conjunctivitis	14DEC2022	44	29	No	No	MILD	Yes	3	2
Investigations									
Fungal infection	14DEC2022	51	22	No	No	MILD	Yes	3	2
Blood alkaline phosphatase increased	14DEC2022	69	45	No	No	MILD	Yes	3	2
Lymphocyte count decreased	14DEC2022	69	22	No	No	MILD	Yes	3	2
Investigations									
Neutrophil count decreased	14DEC2022	90	2	No	No	MILD	Yes	3	2
Investigations									
Alanine aminotransferase increased	14DEC2022	147	191	No	No	MILD	Yes	3	2
Aspartate aminotransferase increased	14DEC2022	147	191	No	No	MILD	Yes	3	2
Blood alkaline phosphatase increased	14DEC2022	147	213	No	No	MILD	Yes	3	2
Gamma-glutamyltransferase increased	14DEC2022	147	213	No	No	MILD	Yes	3	2
Infections and infestations									
Rhinitis	14DEC2022	151	4	No	No	MILD	No	3	2

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race3 Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>4206/003 - 70/F/NOT REPORTED</b>									
Infections and infestations Conjunctivitis	14DEC2022	170	232	No	No	MOD	Yes	3	2
Infections and infestations Viral infection	14DEC2022	216	5	No	No	MILD	No	3	2
Infections and infestations Fungal infection	14DEC2022	221	34	No	No	MILD	No	3	2
Infections and infestations Viral infection	14DEC2022	387	10	No	No	MILD	No	3	2
Investigations Alanine aminotransferase increased	14DEC2022	400	22	No	No	MILD	Yes	3	2
Gamma-glutamyltransferase increased	14DEC2022	400	22	No	No	MILD	Yes	3	2
<b>4208/001 - 36/M/NOT REPORTED</b>									
Investigations Weight increased	31MAR2021	1		No	No	MOD	No	2	2
Infections and infestations COVID-19	31MAR2021	283	2	No	No	MILD	No	3	2
<b>4208/003 - 70/F/NOT REPORTED</b>									
Infections and infestations Urinary tract infection	29SEP2022	16	4	No	No	MILD	No	3	2
Infections and infestations Escherichia infection	29SEP2022	54	3	No	No	MILD	No	3	2
Investigations Alanine aminotransferase increased	29SEP2022	86	21	No	No	MILD	No	3	2
Gamma-glutamyltransferase increased	29SEP2022	86		No	No	MOD	No	2	2
Infections and infestations Conjunctivitis	29SEP2022	126*	59**	No	No	MILD	No	3	2
Investigations Alanine aminotransferase increased	29SEP2022	170	45**	No	No	MILD	No	3	2
<b>4208/005 - 60/F/Other</b>									
Infections and infestations Herpes zoster	15MAR2023	66	43**	No	No	MOD	Yes	3	2
Investigations Blood creatinine increased	15MAR2023	394		No	No	MILD	Yes	2	2

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race <sup>3</sup> Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	Study Drug	Day of Onset	AE Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>4211/001 - 65/M/NOT REPORTED</b>										
Investigations										
Alanine aminotransferase increased	28JUN2021	19	43	No	No	MILD	Yes	3	2	
Aspartate aminotransferase increased	28JUN2021	19	22	No	No	MILD	Yes	3	2	
Investigations										
Weight decreased	28JUN2021	144	12	No	No	MILD	No	3	2	
<b>4213/001 - 58/F/NOT REPORTED</b>										
Investigations										
Blood creatinine increased	15FEB2022	309	283	No	No	MOD	No	3	2	
Investigations										
Blood creatinine increased	15FEB2022	360	232	Yes	No	MOD	No	3	2	
Investigations										
Blood creatine phosphokinase increased	15FEB2022	528	190	Yes	No	MOD	No	3	2	
<b>4213/002 - 77/M/NOT REPORTED</b>										
Investigations										
Lymphocyte count decreased	16JAN2024	22		No	No	MOD	Yes	2	2	
<b>4214/005 - 55/M/NOT REPORTED</b>										
Investigations										
Neutrophil count decreased	24AUG2022	55	9	No	No	LT	Yes	3	2	
Platelet count decreased	24AUG2022	55	4	No	No	MOD	Yes	3	2	
Investigations										
Blood creatinine increased	24AUG2022	261	55	Yes	No	MILD	Yes	3	2	
Investigations										
Alanine aminotransferase increased	24AUG2022	441	8	Yes	No	MOD	Yes	3	4	
<b>4214/006 - 62/M/NOT REPORTED</b>										
Investigations										
Weight decreased	15MAY2023	43	29	No	No	MOD	No	3	2	
Investigations										
Alanine aminotransferase increased	15MAY2023	111	48	No	No	SEV	Yes	3	5	

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race <sup>3</sup> Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug	Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Taken (2) Outcome (2)	Action Taken (3)
<b>4303/001 - 79/M/White</b>										
Investigations Neutrophil count decreased	10MAY2021	43	8	No	No	SEV	Yes	3	4	
Investigations Neutrophil count decreased	10MAY2021	115	10	No	No	SEV	Yes	3	4	
Investigations White blood cell count decreased	10MAY2021	136	36	No	No	MOD	Yes	3	2	
Infections and infestations COVID-19	10MAY2021	276	15	No	No	MILD	No	3	4	
<b>4307/002 - 68/F/White</b>										
Infections and infestations Infection	12MAR2021	51	5	No	No	MOD	Yes	3	2	
Investigations Platelet count decreased	12MAR2021	54	8	No	No	MOD	Yes	3	2	
Infections and infestations Nasopharyngitis	12MAR2021	412	8	No	No	MILD	Yes	3	2	
Investigations Conjunctivitis	12MAR2021	426	9	No	No	MOD	No	3	2	
Infections and infestations COVID-19	12MAR2021	519	36	No	No	MOD	No	3	2	
Infections and infestations Urinary tract infection	12MAR2021	532	6	No	No	MOD	No	3	2	
Infections and infestations Oropharyngeal candidiasis	12MAR2021	538	17	No	No	MOD	No	3	2	
<b>4312/002 - 61/M/White</b>										
Infections and infestations Conjunctivitis	26OCT2020	79	170**	No	No	MILD	Yes	3	2	
Investigations Blood alkaline phosphatase increased	26OCT2020	270	98	No	No	MILD	No	3	2	
Investigations White blood cell count decreased	26OCT2020	367	22	Yes	No	MOD	Yes	3	2	
<b>4312/003 - 48/F/White</b>										
Investigations Alanine aminotransferase increased	30DEC2020	50	155	No	No	SEV	Yes	3	2	
Aspartate aminotransferase increased	30DEC2020	50	155	No	No	MILD	Yes	3	2	
Infections and infestations Conjunctivitis	30DEC2020	141	166**	No	No	MILD	Yes	3	2	

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race <sup>3</sup> Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug	Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
4312/003 - 48/F/White Infections and infestations COVID-19	30DEC2020	385	32	No	No	MILD	No	3	6	
4313/001 - 60/F/White Infections and infestations Urinary tract infection	08JUL2021	106	22	No	No	MOD	No	3	2	
Infections and infestations Urinary tract infection	08JUL2021	148	64	No	No	MOD	No	3	2	
Infections and infestations Oral herpes	08JUL2021	511	7	No	No	MILD	No	3	2	
4402/002 - 43/F/White Infections and infestations Nasopharyngitis	17OCT2022	145		No	No	MILD	No	2	2	
4403/001 - 62/F/White Investigations Amylase increased	19JUL2021	190		Yes	No	MOD	No	5	2	
Investigations Platelet count decreased	19JUL2021	191	35	Yes	No	SEV	No	3	2	
Infections and infestations Urinary tract infection	19JUL2021	194		Yes	No	MOD	No	5	2	
Infections and infestations Cytomegalovirus infection	19JUL2021	208	18	Yes	No	MOD	No	3	2	
Epstein-Barr virus infection	19JUL2021	208	18	Yes	No	MOD	No	3	2	
4404/002 - 61/F/White Infections and infestations Conjunctivitis	06NOV2020	28		No	No	MILD	No	2	2	
Investigations Alanine aminotransferase increased	06NOV2020	42	42	No	No	MILD	Yes	3	2	
Aspartate aminotransferase increased	06NOV2020	42	42	No	No	MILD	Yes	3	2	
Infections and infestations COVID-19	06NOV2020	757		No	No	MILD	No	5	2	

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE Study Drug	Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>4404/006 - 59/F/White</b>											
Investigations											
Platelet count decreased		06MAY2021	64	6	No	No	MILD	Yes	3	2	
Infections and infestations											
COVID-19		06MAY2021	343		No	No	MILD	No	5	4	
Investigations											
Conjunctivitis		06MAY2021	356		No	No	MILD	No	5	2	
Investigations											
Transaminases increased		06MAY2021	492		No	No	MILD	Yes	5	2	
Infections and infestations											
Influenza		06MAY2021	761		Yes	No	MILD	No	5	4	
<b>4404/007 - 48/M/White</b>											
Investigations											
Alanine aminotransferase increased		05OCT2021	1		No	No	MILD	No	5	2	
Aspartate aminotransferase increased		05OCT2021	1		No	No	MILD	No	5	2	
Infections and infestations											
Gastrointestinal infection		05OCT2021	179	3	No	No	MILD	No	3	2	
Investigations											
Pneumonia		05OCT2021	209	2	No	Yes	SEV	No	3	4	
Infections and infestations											
Pneumonia		05OCT2021	211		No	No	SEV	No	5	2	
Investigations											
Weight decreased		05OCT2021	239		No	No	MILD	No	5	5	
<b>4404/008 - 73/F/White</b>											
Investigations											
Platelet count decreased		21OCT2021	85	22	No	No	MILD	Yes	3	3	
<b>4404/010 - 48/F/White</b>											
Investigations											
Platelet count decreased		15MAR2022	190		Yes	No	MILD	Yes	5	2	
<b>4406/004 - 49/M/White</b>											
Investigations											
Conjunctivitis		07MAR2023	126	24	No	No	MILD	Yes	3	2	
Infections and infestations											
COVID-19		07MAR2023	215		No	No	MILD	No	2	2	

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race3 Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>4406/004 - 49/M/White</b>									
Investigations Blood creatinine increased	07MAR2023	267		No	No	MOD	Yes	2	4
<b>4407/007 - 43/F/White</b>									
Investigations Alanine aminotransferase increased Aspartate aminotransferase increased	03MAY2023 03MAY2023	19 19	10 10	No No	No No	MILD MILD	No No	3 3	3 3
<b>4407/008 - 59/F/White</b>									
Investigations Alanine aminotransferase increased Aspartate aminotransferase increased Gamma-glutamyltransferase increased	07SEP2023 07SEP2023 07SEP2023	13 13 13	10	No No No	No No No	MOD MILD SEV	Yes Yes Yes	2 3 2	3 3 3
Infections and infestations Herpes zoster	07SEP2023	230		No	No	MOD	No	2	4
<b>4410/002 - 59/F/White</b>									
Investigations Haemoglobin decreased	22MAR2021	54	141	No	No	MOD	Yes	3	2
<b>4410/009 - 55/F/White</b>									
Infections and infestations Conjunctivitis	28DEC2023	112		No	No	MILD	Yes	2	2
<b>4412/001 - 65/F/White</b>									
Investigations Blood creatinine increased	29APR2021	369		No	No	MILD	No	2	2
Infections and infestations Conjunctivitis	29APR2021	503		No	No	MILD	Yes	2	2
<b>4412/002 - 57/M/White</b>									
Infections and infestations Dermo-hypodermitis	05AUG2021	209		No	No	MOD	No	2	2

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE	Most Extreme Intensity (1)	Caused by Study Drug	Action Taken (3)
System Organ Class	MedDRA Preferred Term	Study Drug Onset	Duration in Days	Crossover phase	Serious	Outcome (2)
4412/002 - 57/M/White	Investigations					
	Blood creatinine increased	05AUG2021	524	No	No	MOD
	Investigations					
	Blood magnesium decreased	05AUG2021	859	26	Yes	No
	Investigations					
	Aspartate aminotransferase increased	05AUG2021	884	Yes	No	MILD
4412/007 - 53/M/White	Investigations					
	Haemoglobin decreased	28JUN2023	205	27	No	No
4415/002 - 59/M/White	Infections and infestations					
	COVID-19	15JUN2023	93	6	No	No
4503/001 - 63/F/White	Investigations					
	Alanine aminotransferase increased	09MAR2023	64	105	No	No
	Infections and infestations					
	Diverticulitis	09MAR2023	179	9	No	SEV
	Investigations					
	Diverticulitis	09MAR2023	188	17	No	No
	Investigations					
	Respiratory tract infection	09MAR2023	261	9	No	MOD
4505/002 - 83/F/White	Investigations					
	Neutrophil count decreased	09JUN2022	22	8	No	No
	Investigations					
	Neutrophil count decreased	09JUN2022	50	7	No	No
	Investigations					
	Neutrophil count decreased	09JUN2022	78	15	No	MOD
	Investigations					
	Neutrophil count decreased	09JUN2022	134	29	No	No
	Infections and infestations					
	Oral herpes	09JUN2022	286	45	No	No
	Investigations					
	COVID-19	09JUN2022	474	3	No	MOD
					No	No

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race3 Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug	Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
4505/002 - 83/F/White Infections and infestations Pneumonia	09JUN2022	528	10	No	Yes	SEV	No	3	5	
4506/002 - 74/M/White Investigations Alanine aminotransferase increased	07AUG2023	8	77	No	No	SEV	Yes	3	3	
Aspartate aminotransferase increased	07AUG2023	8	14	No	No	MOD	Yes	3	3	
Investigations Aspartate aminotransferase increased	07AUG2023	85	23	No	No	MILD	Yes	3	2	
Investigations Alanine aminotransferase increased	07AUG2023	108	105	No	No	MILD	Yes	3	2	
Infections and infestations COVID-19	07AUG2023	191	22	No	No	MILD	No	3	2	
4508/001 - 64/F/White Investigations Alanine aminotransferase increased	05MAR2021	62		No	No	SEV	Yes	2	2	
Investigations Aspartate aminotransferase increased	05MAR2021	83	19	No	No	MOD	Yes	3	2	
Gamma-glutamyltransferase increased	05MAR2021	83		No	No	SEV	No	2	2	
Investigations Blood creatinine increased	05MAR2021	95	3	No	No	MILD	Yes	3	2	
Investigations Aspartate aminotransferase increased	05MAR2021	123	14	No	No	MILD	Yes	3	2	
Investigations Aspartate aminotransferase increased	05MAR2021	158	24	No	No	MILD	Yes	3	2	
Investigations Aspartate aminotransferase increased	05MAR2021	202		No	No	MILD	Yes	2	2	
Infections and infestations Respiratory tract infection	05MAR2021	231		No	Yes	SEV	No	2	6	
4511/001 - 42/F/White Investigations Neutrophil count decreased	16FEB2022	106	7	No	No	SEV	Yes	3	4	
Infections and infestations Onychomycosis	16FEB2022	197	22	No	No	MILD	Yes	3	2	
Infections and infestations Respiratory tract infection	16FEB2022	392	21	No	No	MILD	No	3	2	
Investigations Blood creatinine increased	16FEB2022	519	82	Yes	No	MILD	Yes	3	2	

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race <sup>3</sup> Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>4511/001 - 42/F/White</b>									
Infections and infestations Viral infection	16FEB2022	528	11	Yes	No	MILD	No	3	2
Infections and infestations COVID-19	16FEB2022	622	22	Yes	No	MILD	No	3	2
<b>4512/001 - 55/F/White</b>									
Infections and infestations Conjunctivitis	14JAN2021	9	13	No	No	MILD	Yes	3	2
Infections and infestations Conjunctivitis	14JAN2021	36	8	No	No	MILD	Yes	3	2
Infections and infestations Respiratory tract infection	14JAN2021	719	24	Yes	No	MILD	No	3	2
<b>4512/002 - 70/M/White</b>									
Infections and infestations Urinary tract infection	03MAY2022	27	13	No	No	MOD	No	3	2
Infections and infestations Escherichia infection	03MAY2022	42	24	No	Yes	SEV	No	3	2
Infections and infestations Respiratory tract infection	03MAY2022	165	6	No	No	MILD	No	3	2
Infections and infestations COVID-19	03MAY2022	190	8	No	No	MILD	No	3	4
Infections and infestations Pyuria	03MAY2022	217	43	No	No	MILD	No	3	2
Infections and infestations Escherichia infection	03MAY2022	239	21	No	No	MILD	No	3	2
Infections and infestations Bacteraemia	03MAY2022	282	6	No	No	MILD	No	3	4
<b>4512/003 - 72/M/White</b>									
Investigations Gamma-glutamyltransferase increased	30NOV2022	402	20	Yes	No	MOD	No	3	2
<b>4517/009 - 37/F/White</b>									
Infections and infestations Urinary tract infection	14MAR2023	15	51	No	No	MOD	No	3	2
Infections and infestations COVID-19	14MAR2023	90	4	No	No	MILD	No	3	2

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race <sup>3</sup> Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>4517/009 - 37/F/White</b>									
Investigations Neutrophil count decreased	14MAR2023	175	16	No	Yes	SEV	No	3	2
4702/001 - 53/M/White									
Investigations Blood creatinine increased	17FEB2022	104	190	No	No	MILD	Yes	3	2
Infections and infestations COVID-19	17FEB2022	137	9	No	No	MILD	No	3	2
Infections and infestations Nasopharyngitis	17FEB2022	369	5	No	No	MILD	No	3	2
4703/001 - 47/F/Black or African American									
Investigations Groin abscess	10DEC2020	23*	153**	No	No	MILD	Yes	3	2
Investigations Weight decreased	10DEC2020	126	85	No	No	MILD	No	3	2
Infections and infestations Conjunctivitis	10DEC2020	140	302	No	No	MOD	Yes	3	4
Infections and infestations Skin infection	10DEC2020	602		Yes	No	MILD	Yes	2	2
Infections and infestations Urinary tract infection	10DEC2020	920	5	Yes	No	MOD	No	3	2
4706/001 - 74/M/Other									
Infections and infestations Sepsis	07OCT2022	7	7	No	Yes	SEV	Yes	3	6
4903/003 - 68/F/White									
Infections and infestations Vulvovaginal candidiasis	27JAN2022	97	4	No	No	MOD	Yes	3	2
Infections and infestations Urinary tract infection	27JAN2022	127	33	No	No	MOD	No	3	4
Investigations Aspartate aminotransferase increased	27JAN2022	204	37	Yes	No	MILD	Yes	3	2
Infections and infestations Blood alkaline phosphatase increased	27JAN2022	204	37	Yes	No	MOD	Yes	3	2
Infections and infestations Pneumonia legionella	27JAN2022	240	12	Yes	Yes	SEV	No	3	4

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE	Duration in Days	Crossover phase	Most Serious	Most Extreme Intensity (1)	Caused by Study Drug	Action Action Taken (3)	Action Outcome (2)
System Organ Class	Preferred Term	Study Drug Onset								
4903/003 - 68/F/White	Infections and infestations Oropharyngeal candidiasis	27JAN2022	241	7	Yes	No	MOD	No	3	2
	Investigations Blood creatinine increased	27JAN2022	302	21	Yes	No	MILD	No	3	2
	Investigations Blood thyroid stimulating hormone increased	27JAN2022	323		Yes	No	MILD	Yes	2	2
	Infections and infestations Urinary tract infection	27JAN2022	393	8	Yes	No	MOD	No	3	2
	Infections and infestations Urinary tract infection	27JAN2022	408	9	Yes	No	MOD	No	3	2
4903/004 - 38/M/White	Investigations Alanine aminotransferase increased	25FEB2022	182	42	No	No	MILD	Yes	3	2
	Investigations Blood thyroid stimulating hormone decreased	25FEB2022	350	65	No	No	MILD	Yes	3	2
5202/001 - 57/M/Asian	Investigations Neutrophil count decreased	04MAY2021	827	9	Yes	No	MOD	Yes	3	2
5202/003 - 48/F/White	Investigations Alanine aminotransferase increased	29SEP2021	23	8	No	No	MOD	Yes	3	2
	Investigations Aspartate aminotransferase increased	29SEP2021	23	8	No	No	MOD	Yes	3	3
	Investigations Alanine aminotransferase increased	29SEP2021	44	21	No	No	MOD	Yes	3	4
	Investigations Aspartate aminotransferase increased	29SEP2021	55	10	No	No	MOD	Yes	3	4
	Infections and infestations COVID-19	29SEP2021	276*	31**	Yes	No	MILD	No	3	2
5202/004 - 65/M/White	Infections and infestations COVID-19	19NOV2021	80	9	No	No	MILD	No	3	2
	Infections and infestations Pneumonia	19NOV2021	720	16	Yes	No	MOD	No	3	2

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race <sup>3</sup> Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug	Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Taken (2) Outcome (2)	Action Taken (3)
5202/005 - 66/M/Black or African American										
Infections and infestations										
COVID-19	13JAN2022	13	8	No	No	MILD	No	3	2	
Investigations										
Blood creatinine increased	13JAN2022	216		No	No	MILD	Yes	2	5	
Investigations										
Blood alkaline phosphatase increased	13JAN2022	601	39	Yes	No	MILD	Yes	3	2	
Investigations										
Neutrophil count decreased	13JAN2022	790	28	Yes	No	MOD	Yes	3	2	
Infections and infestations										
Pneumonia	13JAN2022	808	11	Yes	Yes	SEV	No	3	4	
5202/009 - 58/M/White										
Infections and infestations										
COVID-19	03AUG2023	164	5	No	No	MILD	No	3	2	
5203/003 - 74/M/White										
Investigations										
White blood cell count decreased	14APR2023	21	28	No	No	MILD	Yes	3	2	
Infections and infestations										
Pneumonia	14APR2023	37	6	No	Yes	SEV	No	3	2	
Infections and infestations										
Urinary tract infection	14APR2023	60		No	No	MILD	No	2	2	
Infections and infestations										
Epididymitis	14APR2023	63	14	No	No	MILD	No	3	2	
Infections and infestations										
Epididymitis	14APR2023	211	7	No	No	MOD	No	3	2	
Infections and infestations										
COVID-19	14APR2023	230	8	No	No	MILD	No	3	2	
Infections and infestations										
Nasopharyngitis	14APR2023	238	21	No	No	MILD	No	3	2	
Infections and infestations										
Respiratory tract infection	14APR2023	249	5	No	No	MILD	No	3	2	
Infections and infestations										
Burn infection	14APR2023	294	9	No	No	MOD	No	3	2	
Infections and infestations										
Epididymitis	14APR2023	390	4	No	No	MILD	No	3	2	

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race <sup>3</sup> Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
5301/001 - 67/M/White									
Investigations									
Neutrophil count decreased	08FEB2022	8	15	No	No	SEV	Yes	3	3
Infections and infestations									
Nasopharyngitis	08FEB2022	249	6	No	No	MILD	No	3	2
Infections and infestations									
Nasopharyngitis	08FEB2022	329	5	No	No	MILD	No	3	2
Infections and infestations									
COVID-19 pneumonia	08FEB2022	409	6	No	No	MOD	No	3	2
6301/001 - 73/F/White									
Investigations									
Blood pressure increased	12APR2023	28	1	No	No	MOD	Yes	3	4
Infections and infestations									
Conjunctivitis	12APR2023	72	3	No	No	MOD	Yes	3	2
Infections and infestations									
Conjunctivitis	12APR2023	83	3	No	No	MOD	Yes	3	5
Infections and infestations									
Urinary tract infection	12APR2023	104	5	No	No	MOD	No	3	2
6601/002 - 40/M/White									
Infections and infestations									
Pneumonia	02SEP2021	3	45	No	No	MOD	No	3	2
Infections and infestations									
Tooth infection	02SEP2021	40	8	No	No	MOD	No	3	2
6602/039 - 25/F/White									
Investigations									
Blood lactate dehydrogenase increased	26JUN2023	37	59	No	No	MILD	No	3	2
Investigations									
Alanine aminotransferase increased	26JUN2023	116	47	No	No	MOD	No	3	2
Aspartate aminotransferase increased	26JUN2023	116	47	No	No	MILD	No	3	2
Investigations									
Blood lactate dehydrogenase increased	26JUN2023	198		No	No	MILD	No	5	2
Infections and infestations									
COVID-19	26JUN2023	263	19	Yes	Yes	MOD	No	3	4

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race3 Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
<b>6602/051 - 67/F/White</b>									
Investigations Gamma-glutamyltransferase increased	15NOV2023	20	24	No	No	MILD	No	3	2
<b>6602/053 - 62/M/White</b>									
Investigations Bilirubin conjugated increased	07DEC2023	21	13	No	No	MILD	Yes	3	4
Blood alkaline phosphatase increased	07DEC2023	21	13	No	No	MOD	Yes	3	4
Gamma-glutamyltransferase increased	07DEC2023	21	16	No	No	SEV	Yes	3	4
Investigations Blood lactate dehydrogenase increased	07DEC2023	36	35	No	No	SEV	Yes	3	4
<b>6604/025 - 70/M/White</b>									
Investigations Blood albumin decreased	02MAR2023	3		No	No	MOD	No	2	2
Blood uric acid increased	02MAR2023	3	2	No	No	MILD	No	3	2
Lymphocyte count decreased	02MAR2023	3		No	No	LT	Yes	2	2
Investigations Gamma-glutamyltransferase increased	02MAR2023	4		No	No	MOD	Yes	2	2
Investigations Platelet count decreased	02MAR2023	6		No	No	MOD	Yes	2	2
<b>7201/002 - 64/F/American Indian or Alaska Native</b>									
Infections and infestations Upper respiratory tract infection	11AUG2022	156	8	No	No	MILD	No	3	2
<b>7201/004 - 62/M/American Indian or Alaska Native</b>									
Investigations Weight decreased	13OCT2022	22	427	No	No	MOD	Yes	3	2
Infections and infestations Gastroenteritis	13OCT2022	87	14	No	No	MOD	No	3	2
Investigations Alanine aminotransferase increased	13OCT2022	489	43	Yes	No	MILD	Yes	3	2
Aspartate aminotransferase increased	13OCT2022	489	43	Yes	No	MILD	Yes	3	2

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\*\* Duration derived from imputed onset date and/or end date

Program: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/program/l\_ae.sas

Output: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/l\_ae\_INVINF\_SE.out

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race <sup>3</sup> Adverse Event MedDRA System Organ Class Preferred Term	Date of First Study Administration	AE Study Drug Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
7201/004 - 62/M/American Indian or Alaska Native									
Infections and infestations Urinary tract infection	13OCT2022	593	8	Yes	No	MOD	No	3	2
7201/007 - 74/F/American Indian or Alaska Native									
Investigations Alanine aminotransferase increased Aspartate aminotransferase increased	16AUG2023 16AUG2023	231 231	22 22	No No	No No	MILD MILD	No No	3 3	2 2
7301/011 - 71/F/American Indian or Alaska Native									
Infections and infestations Respiratory tract infection viral	16AUG2023	231		No	No	MOD	No	2	2
8001/001 - 61/F/Asian									
Investigations Alanine aminotransferase increased Aspartate aminotransferase increased Blood alkaline phosphatase increased	08AUG2022 08AUG2022 08AUG2022	22 22 22	213 213 155	No No No	No No No	MILD MILD MILD	Yes Yes Yes	3 3 3	2 2 2
8001/003 - 43/M/Asian									
Infections and infestations Pneumonia	11NOV2022	11	14	No	No	SEV	No	3	2
Investigations Cytomegalovirus test positive	11NOV2022	15	8	No	No	MILD	No	3	2
Infections and infestations Herpes simplex	11NOV2022	18	5	No	No	MOD	No	3	2
Investigations Blood creatine phosphokinase increased	11NOV2022	123		Yes	No	MILD	No	2	2
Infections and infestations COVID-19	11NOV2022	170		Yes	No	MILD	No	5	2
Infections and infestations Oral candidiasis	11NOV2022	537		Yes	No	MILD	No	2	2
8405/001 - 44/F/Asian									
Infections and infestations Periodontitis	03JUN2022	89	467	No	No	MOD	No	3	2

Notes: Adverse Events are coded using MedDRA 27.0

For patients who crossed over, date of first Study Drug Administration is provided for the standard of care treatment in the main treatment period and for Pralsetinib in the crossover treatment period.

(1) Severity: MILD = Grade 1 - Mild, MOD = Grade 2 - Moderate, SEV = Grade 3 - Severe, LT = Grade 4 - Life Threatening, DEATH = Grade 5 - Death.

(2) Outcome: 1 = fatal; 2 = not recovered/not resolved; 3 = recovered/resolved; 4 = recovered/resolved with sequelae; 5 = recovering/resolving; 6 = unknown.

(3) Action taken: 1 = dose increased; 2 = dose not changed; 3 = dose reduced; 4 = drug interrupted; 5 = drug withdrawn; 6 = not applicable; 7 = unknown.

\* Study day derived from imputed onset date

\*\* Duration derived from imputed onset date and/or end date

Program: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/program/l\_ae.sas

Output: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/l\_ae\_INVINF\_SE.out

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Listing of Investigations and Infections and Infestations Adverse Events, Safety-Evaluable Patients  
Protocol: BO42864

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race <sup>3</sup>	Adverse Event MedDRA	Date of First Study Administration	AE Study Drug	Day of Onset	Duration in Days	Crossover phase	Most Serious	Extreme Intensity (1)	Caused by Study Drug	Action Outcome (2)	Action Taken (3)
System Organ Class Preferred Term											
8405/001 - 44/F/Asian	Investigations										
	Alanine aminotransferase increased	03JUN2022	127	169	No	No	MOD	Yes	3	2	
8405/002 - 48/F/Asian	Investigations										
	Aspartate aminotransferase increased	18APR2023	4		No	No	MOD	Yes	2	2	
	Investigations										
	Alanine aminotransferase increased	18APR2023	7	15	No	No	MILD	Yes	3	2	
	Investigations										
	Alanine aminotransferase increased	18APR2023	42		No	No	MOD	Yes	2	2	
8406/001 - 67/M/Asian	Infections and infestations										
	Oral candidiasis	05JUL2022	43	170	No	No	MILD	Yes	3	2	
	Infections and infestations										
	Herpes ophthalmic	05JUL2022	155	144	No	No	MOD	Yes	3	4	
	Herpes zoster	05JUL2022	155	15	No	No	MOD	Yes	3	4	
	Infections and infestations										
	Pneumonia	05JUL2022	451		Yes	No	MILD	Yes	2	2	
8407/002 - 78/F/Asian	Infections and infestations										
	Influenza	08FEB2023	295	18	No	No	MOD	No	3	2	

Notes: Adverse Events are coded using MedDRA 27.0

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(1) Severity: MILD = Grade 1 - Mild, MOD = Grade 2 - Moderate, SEV = Grade 3 - Severe, LT = Grade 4 - Life Threatening, DEATH = Grade 5 - Death.

(2) Outcome: 1 = fatal; 2 = not recovered/not resolved; 3 = recovered/resolved; 4 = recovered/resolved with sequelae; 5 = recovering/resolving; 6 = unknown.

(3) Action taken: 1 = dose increased; 2 = dose not changed; 3 = dose reduced; 4 = drug interrupted; 5 = drug withdrawn; 6 = not applicable; 7 = unknown.

\* Study day derived from imputed onset date

\*\* Duration derived from imputed onset date and/or end date

Program: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/program/l\_ae.sas  
Output: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/l\_ae\_INVINF\_SE.out  
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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade -  
 Cross Over Period, Safety-Evaluable Patients  
 Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=35)
- Any adverse events -	- Any Grade -	33 (94.3%)
	Grade 1-2	11 (31.4%)
	1	3 ( 8.6%)
	2	8 (22.9%)
	Grade 3-4	19 (54.3%)
	3	14 (40.0%)
	4	5 (14.3%)
	Grade 5	3 ( 8.6%)
Investigations	-	
- Overall -	- Any Grade -	19 (54.3%)
	Grade 1-2	14 (40.0%)
	1	7 (20.0%)
	2	7 (20.0%)
	Grade 3-4	5 (14.3%)
	3	5 (14.3%)
Aspartate aminotransferase increased	- Any Grade -	8 (22.9%)
	Grade 1-2	7 (20.0%)
	1	6 (17.1%)
	2	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Alanine aminotransferase increased	- Any Grade -	5 (14.3%)
	Grade 1-2	5 (14.3%)
	1	4 (11.4%)
	2	1 ( 2.9%)
Blood creatinine increased	- Any Grade -	5 (14.3%)
	Grade 1-2	5 (14.3%)
	1	4 (11.4%)
	2	1 ( 2.9%)
Neutrophil count decreased	- Any Grade -	4 (11.4%)
	Grade 1-2	2 ( 5.7%)
	2	2 ( 5.7%)
	Grade 3-4	2 ( 5.7%)
	3	2 ( 5.7%)
Platelet count decreased	- Any Grade -	3 ( 8.6%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
	Grade 3-4	2 ( 5.7%)
	3	2 ( 5.7%)
Blood alkaline phosphatase increased	- Any Grade -	2 ( 5.7%)
	Grade 1-2	2 ( 5.7%)
	1	1 ( 2.9%)
	2	1 ( 2.9%)
Blood bicarbonate decreased	- Any Grade -	2 ( 5.7%)
	Grade 1-2	2 ( 5.7%)
	2	2 ( 5.7%)

Investigator text for AEs encoded using MedDRA version 27.0. All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.

To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.

Percentages are based on N in the column headings.

Only AEs with onset during the cross-over period are displayed in this output.

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Output: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/t\_ae\_ctc\_XOVER\_SE.out

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade -  
 Cross Over Period, Safety-Evaluable Patients  
 Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=35)
Blood creatine phosphokinase increased	- Any Grade -	2 ( 5.7%)
	Grade 1-2	2 ( 5.7%)
	1	1 ( 2.9%)
	2	1 ( 2.9%)
Gamma-glutamyltransferase increased	- Any Grade -	2 ( 5.7%)
	Grade 1-2	2 ( 5.7%)
	1	1 ( 2.9%)
	2	1 ( 2.9%)
Amylase increased	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Blood lactate dehydrogenase increased	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Blood magnesium decreased	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Blood thyroid stimulating hormone increased	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Lymphocyte count decreased	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
White blood cell count decreased	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Infections and infestations		
- Overall -	- Any Grade -	18 (51.4%)
	Grade 1-2	13 (37.1%)
	1	6 (17.1%)
	2	7 (20.0%)
	Grade 3-4	5 (14.3%)
	3	4 (11.4%)
	4	1 ( 2.9%)
COVID-19	- Any Grade -	5 (14.3%)
	Grade 1-2	4 (11.4%)
	1	3 ( 8.6%)
	2	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Pneumonia	- Any Grade -	4 (11.4%)
	Grade 1-2	2 ( 5.7%)
	1	1 ( 2.9%)
	2	1 ( 2.9%)
	Grade 3-4	2 ( 5.7%)
	3	1 ( 2.9%)
	4	1 ( 2.9%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade -  
 Cross Over Period, Safety-Evaluable Patients  
 Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=35)
Urinary tract infection	- Any Grade -	4 (11.4%)
	Grade 1-2	4 (11.4%)
	2	4 (11.4%)
Oral candidiasis	- Any Grade -	2 ( 5.7%)
	Grade 1-2	2 ( 5.7%)
	1	1 ( 2.9%)
	2	1 ( 2.9%)
COVID-19 pneumonia	- Any Grade -	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Cystitis	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Cytomegalovirus infection	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Epstein-Barr virus infection	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Herpes zoster	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Influenza	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Kidney infection	- Any Grade -	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Oropharyngeal candidiasis	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Paronychia	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Pneumonia legionella	- Any Grade -	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Respiratory tract infection	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Skin infection	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Tongue fungal infection	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade -  
 Cross Over Period, Safety-Evaluable Patients  
 Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=35)
Viral infection	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Gastrointestinal disorders	- Any Grade -	16 (45.7%)
- Overall -	Grade 1-2	16 (45.7%)
	1	10 (28.6%)
	2	6 (17.1%)
Constipation	- Any Grade -	9 (25.7%)
	Grade 1-2	9 (25.7%)
	1	7 (20.0%)
	2	2 ( 5.7%)
Nausea	- Any Grade -	4 (11.4%)
	Grade 1-2	4 (11.4%)
	1	2 ( 5.7%)
	2	2 ( 5.7%)
Abdominal pain upper	- Any Grade -	3 ( 8.6%)
	Grade 1-2	3 ( 8.6%)
	1	2 ( 5.7%)
	2	1 ( 2.9%)
Diarrhoea	- Any Grade -	3 ( 8.6%)
	Grade 1-2	3 ( 8.6%)
	1	2 ( 5.7%)
	2	1 ( 2.9%)
Dry mouth	- Any Grade -	3 ( 8.6%)
	Grade 1-2	3 ( 8.6%)
	1	3 ( 8.6%)
Stomatitis	- Any Grade -	3 ( 8.6%)
	Grade 1-2	3 ( 8.6%)
	2	3 ( 8.6%)
Abdominal pain	- Any Grade -	2 ( 5.7%)
	Grade 1-2	2 ( 5.7%)
	1	1 ( 2.9%)
	2	1 ( 2.9%)
Haemorrhoids	- Any Grade -	2 ( 5.7%)
	Grade 1-2	2 ( 5.7%)
	1	1 ( 2.9%)
	2	1 ( 2.9%)
Vomiting	- Any Grade -	2 ( 5.7%)
	Grade 1-2	2 ( 5.7%)
	1	1 ( 2.9%)
	2	1 ( 2.9%)
Abdominal discomfort	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade -  
 Cross Over Period, Safety-Evaluable Patients  
 Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=35)
Ascites	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Eruption	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Food poisoning	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Oesophagitis	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Salivary hypersecretion	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Toothache	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Respiratory, thoracic and mediastinal disorders		
- Overall -	- Any Grade -	16 (45.7%)
	Grade 1-2	10 (28.6%)
	1	5 (14.3%)
	2	5 (14.3%)
Cough	Grade 3-4	6 (17.1%)
	3	4 (11.4%)
	4	2 ( 5.7%)
Pneumonitis	- Any Grade -	7 (20.0%)
	Grade 1-2	7 (20.0%)
	1	7 (20.0%)
Dysphonia	- Any Grade -	5 (14.3%)
	Grade 1-2	4 (11.4%)
	2	4 (11.4%)
Dyspnoea	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Interstitial lung disease	- Any Grade -	2 ( 5.7%)
	Grade 1-2	2 ( 5.7%)
	1	2 ( 5.7%)
	- Any Grade -	2 ( 5.7%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	4	1 ( 2.9%)
	- Any Grade -	2 ( 5.7%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade -  
 Cross Over Period, Safety-Evaluable Patients  
 Protocol: BO42864

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=35)
Pleural effusion	- Any Grade -	2 ( 5.7%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Pneumothorax	- Any Grade -	2 ( 5.7%)
	Grade 3-4	2 ( 5.7%)
	3	1 ( 2.9%)
	4	1 ( 2.9%)
Pulmonary embolism	- Any Grade -	2 ( 5.7%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Bronchopleural fistula	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Lung disorder	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Nasal congestion	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Pleuritic pain	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Reflux laryngitis	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Rhinorrhoea	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
General disorders and administration site conditions		
- Overall -	- Any Grade -	15 (42.9%)
	Grade 1-2	13 (37.1%)
	1	9 (25.7%)
	2	4 (11.4%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
	Grade 5	1 ( 2.9%)
Asthenia	- Any Grade -	6 (17.1%)
	Grade 1-2	5 (14.3%)
	1	2 ( 5.7%)
	2	3 ( 8.6%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade -  
 Cross Over Period, Safety-Evaluable Patients  
 Protocol: BO42864

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=35)
Face oedema	- Any Grade -	4 (11.4%)
	Grade 1-2	4 (11.4%)
	1	4 (11.4%)
Oedema peripheral	- Any Grade -	4 (11.4%)
	Grade 1-2	4 (11.4%)
	1	3 (8.6%)
	2	1 (2.9%)
Pyrexia	- Any Grade -	3 (8.6%)
	Grade 1-2	3 (8.6%)
	1	2 (5.7%)
	2	1 (2.9%)
Chest pain	- Any Grade -	2 (5.7%)
	Grade 1-2	2 (5.7%)
	1	2 (5.7%)
Mucosal inflammation	- Any Grade -	2 (5.7%)
	Grade 1-2	2 (5.7%)
	1	1 (2.9%)
	2	1 (2.9%)
Death	- Any Grade -	1 (2.9%)
	Grade 5	1 (2.9%)
Fatigue	- Any Grade -	1 (2.9%)
	Grade 1-2	1 (2.9%)
	1	1 (2.9%)
Influenza like illness	- Any Grade -	1 (2.9%)
	Grade 1-2	1 (2.9%)
	1	1 (2.9%)
Oedema	- Any Grade -	1 (2.9%)
	Grade 1-2	1 (2.9%)
	2	1 (2.9%)
Pain	- Any Grade -	1 (2.9%)
	Grade 1-2	1 (2.9%)
	1	1 (2.9%)
Swelling	- Any Grade -	1 (2.9%)
	Grade 1-2	1 (2.9%)
	2	1 (2.9%)
Blood and lymphatic system disorders	- Any Grade -	14 (40.0%)
- Overall -	Grade 1-2	7 (20.0%)
	1	2 (5.7%)
	2	5 (14.3%)
	Grade 3-4	7 (20.0%)
	3	7 (20.0%)

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Output: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/t\_ae\_ctc\_XOVER\_SE.out

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade -  
 Cross Over Period, Safety-Evaluable Patients  
 Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=35)
Anaemia	- Any Grade -	7 (20.0%)
	Grade 1-2	5 (14.3%)
	1	2 ( 5.7%)
	2	3 ( 8.6%)
	Grade 3-4	2 ( 5.7%)
	3	2 ( 5.7%)
Neutropenia	- Any Grade -	7 (20.0%)
	Grade 1-2	4 (11.4%)
	1	1 ( 2.9%)
	2	3 ( 8.6%)
	Grade 3-4	3 ( 8.6%)
	3	3 ( 8.6%)
Leukopenia	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Lymphopenia	- Any Grade -	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Pancytopenia	- Any Grade -	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Nervous system disorders		
- Overall -	- Any Grade -	13 (37.1%)
	Grade 1-2	12 (34.3%)
	1	10 (28.6%)
	2	2 ( 5.7%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Dysgeusia	- Any Grade -	7 (20.0%)
	Grade 1-2	7 (20.0%)
	1	5 (14.3%)
	2	2 ( 5.7%)
Headache	- Any Grade -	3 ( 8.6%)
	Grade 1-2	3 ( 8.6%)
	1	3 ( 8.6%)
Paraesthesia	- Any Grade -	2 ( 5.7%)
	Grade 1-2	2 ( 5.7%)
	1	2 ( 5.7%)
Balance disorder	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Hypoesthesia	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Neuralgia	- Any Grade -	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade -  
 Cross Over Period, Safety-Evaluable Patients  
 Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=35)
Neuropathy peripheral	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Sciatica	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Taste disorder	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Metabolism and nutrition disorders		
- Overall -	- Any Grade -	12 (34.3%)
	Grade 1-2	10 (28.6%)
	1	6 (17.1%)
	2	4 (11.4%)
	Grade 3-4	2 ( 5.7%)
	3	2 ( 5.7%)
Decreased appetite	- Any Grade -	3 ( 8.6%)
	Grade 1-2	3 ( 8.6%)
	1	1 ( 2.9%)
	2	2 ( 5.7%)
Hypophosphataemia	- Any Grade -	3 ( 8.6%)
	Grade 1-2	3 ( 8.6%)
	2	3 ( 8.6%)
Hypoalbuminaemia	- Any Grade -	2 ( 5.7%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Hyponatraemia	- Any Grade -	2 ( 5.7%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Cell death	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Diabetes mellitus	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Hyperglycaemia	- Any Grade -	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Hyperkalaemia	- Any Grade -	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade -  
 Cross Over Period, Safety-Evaluable Patients  
 Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=35)
Hyperphosphatasæmia	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Hyperuricaæmia	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Hypocalcaæmia	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Hypoglycaæmia	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Hypokalaæmia	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Increased appetite	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Musculoskeletal and connective tissue disorders		
- Overall -	- Any Grade -	12 (34.3%)
	Grade 1-2	12 (34.3%)
	1	6 (17.1%)
	2	6 (17.1%)
Arthralgia	- Any Grade -	4 (11.4%)
	Grade 1-2	4 (11.4%)
	1	4 (11.4%)
Back pain	- Any Grade -	2 ( 5.7%)
	Grade 1-2	2 ( 5.7%)
	2	2 ( 5.7%)
Bone pain	- Any Grade -	2 ( 5.7%)
	Grade 1-2	2 ( 5.7%)
	1	1 ( 2.9%)
	2	1 ( 2.9%)
Myalgia	- Any Grade -	2 ( 5.7%)
	Grade 1-2	2 ( 5.7%)
	1	1 ( 2.9%)
	2	1 ( 2.9%)
Hypercreatinaæmia	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Limb mass	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Muscular weakness	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade -  
 Cross Over Period, Safety-Evaluable Patients  
 Protocol: BO42864

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=35)
Neck pain	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Osteoarthritis	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Pain in extremity	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Pubic pain	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Vascular disorders		
- Overall -	- Any Grade -	12 (34.3%)
	Grade 1-2	9 (25.7%)
	1	4 (11.4%)
	2	5 (14.3%)
	Grade 3-4	3 ( 8.6%)
	3	3 ( 8.6%)
Hypertension	- Any Grade -	10 (28.6%)
	Grade 1-2	8 (22.9%)
	1	3 ( 8.6%)
	2	5 (14.3%)
	Grade 3-4	2 ( 5.7%)
	3	2 ( 5.7%)
Blood pressure inadequately controlled	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Capillary fragility	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Hypotension	- Any Grade -	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
No Coding available		
- Overall -	- Any Grade -	10 (28.6%)
	Grade 1-2	6 (17.1%)
	1	3 ( 8.6%)
	2	3 ( 8.6%)
	Grade 3-4	3 ( 8.6%)
	3	2 ( 5.7%)
	4	1 ( 2.9%)
	Grade 5	1 ( 2.9%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade -  
 Cross Over Period, Safety-Evaluable Patients  
 Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=35)
No Coding available	- Any Grade -	10 (28.6%)
	Grade 1-2	6 (17.1%)
	1	3 ( 8.6%)
	2	3 ( 8.6%)
	Grade 3-4	3 ( 8.6%)
	3	2 ( 5.7%)
	4	1 ( 2.9%)
	Grade 5	1 ( 2.9%)
Skin and subcutaneous tissue disorders		
- Overall -	- Any Grade -	9 (25.7%)
	Grade 1-2	9 (25.7%)
	1	8 (22.9%)
	2	1 ( 2.9%)
Rash	- Any Grade -	4 (11.4%)
	Grade 1-2	4 (11.4%)
	1	4 (11.4%)
Alopecia	- Any Grade -	2 ( 5.7%)
	Grade 1-2	2 ( 5.7%)
	1	2 ( 5.7%)
Dermatitis	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Dermatitis acneiform	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Dry skin	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Hair growth abnormal	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Hirsutism	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Nail dystrophy	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Nail ridging	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Palmar-plantar erythrodysesthesia syndrome	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Pruritus	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade -  
 Cross Over Period, Safety-Evaluable Patients  
 Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=35)
Skin reaction	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Skin ulcer	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Reproductive system and breast disorders		
- Overall -	- Any Grade -	6 (17.1%)
	Grade 1-2	6 (17.1%)
	1	2 ( 5.7%)
	2	4 (11.4%)
Erectile dysfunction	- Any Grade -	2 ( 5.7%)
	Grade 1-2	2 ( 5.7%)
	1	1 ( 2.9%)
	2	1 ( 2.9%)
Prostatitis	- Any Grade -	2 ( 5.7%)
	Grade 1-2	2 ( 5.7%)
	2	2 ( 5.7%)
Intermenstrual bleeding	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Vulvovaginal dryness	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Eye disorders		
- Overall -	- Any Grade -	5 (14.3%)
	Grade 1-2	5 (14.3%)
	1	4 (11.4%)
	2	1 ( 2.9%)
Eyelid oedema	- Any Grade -	4 (11.4%)
	Grade 1-2	4 (11.4%)
	1	3 ( 8.6%)
	2	1 ( 2.9%)
Dry eye	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Injury, poisoning and procedural complications		
- Overall -	- Any Grade -	4 (11.4%)
	Grade 1-2	2 ( 5.7%)
	1	1 ( 2.9%)
	2	1 ( 2.9%)
	Grade 3-4	2 ( 5.7%)
	3	2 ( 5.7%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade -  
 Cross Over Period, Safety-Evaluable Patients  
 Protocol: BO42864

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=35)
Lumbar vertebral fracture	- Any Grade -	2 ( 5.7%)
	Grade 3-4	2 ( 5.7%)
	3	2 ( 5.7%)
Clavicle fracture	- Any Grade -	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Eyelid abrasion	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Limb injury	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Rib fracture	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Skin abrasion	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Cardiac disorders		
- Overall -	- Any Grade -	3 ( 8.6%)
	Grade 1-2	2 ( 5.7%)
	1	2 ( 5.7%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Cardiac failure	- Any Grade -	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Extrasystoles	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Palpitations	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Endocrine disorders		
- Overall -	- Any Grade -	3 ( 8.6%)
	Grade 1-2	3 ( 8.6%)
	1	1 ( 2.9%)
	2	2 ( 5.7%)
Adrenal insufficiency	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Hyperthyroidism	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade -  
 Cross Over Period, Safety-Evaluable Patients  
 Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=35)
Hypothyroidism	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Thyroiditis	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Hepatobiliary disorders	- Any Grade -	3 ( 8.6%)
- Overall -	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
	Grade 3-4	2 ( 5.7%)
	3	1 ( 2.9%)
	4	1 ( 2.9%)
Hepatic cytolysis	- Any Grade -	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Hepatic pain	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)
Hypertransaminasaemia	- Any Grade -	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	4	1 ( 2.9%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	- Any Grade -	3 ( 8.6%)
- Overall -	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
	Grade 5	1 ( 2.9%)
Cancer pain	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	2	1 ( 2.9%)
Metastases to central nervous system	- Any Grade -	1 ( 2.9%)
	Grade 5	1 ( 2.9%)
Thyroid adenoma	- Any Grade -	1 ( 2.9%)
	Grade 3-4	1 ( 2.9%)
	3	1 ( 2.9%)
Psychiatric disorders	- Any Grade -	2 ( 5.7%)
- Overall -	Grade 1-2	2 ( 5.7%)
	1	2 ( 5.7%)
Irritability	- Any Grade -	1 ( 2.9%)
	Grade 1-2	1 ( 2.9%)
	1	1 ( 2.9%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade -  
 Cross Over Period, Safety-Evaluable Patients  
 Protocol: BO42864

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=35)
Libido decreased	- Any Grade - Grade 1-2 1	1 ( 2.9%) 1 ( 2.9%) 1 ( 2.9%)
Ear and labyrinth disorders	- Any Grade - Grade 1-2 2	1 ( 2.9%) 1 ( 2.9%) 1 ( 2.9%)
Vertigo	- Any Grade - Grade 1-2 2	1 ( 2.9%) 1 ( 2.9%) 1 ( 2.9%)
Renal and urinary disorders	- Any Grade - Grade 1-2 2	1 ( 2.9%) 1 ( 2.9%) 1 ( 2.9%)
Urinary tract obstruction	- Any Grade - Grade 1-2 2	1 ( 2.9%) 1 ( 2.9%) 1 ( 2.9%)

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 output/t\_ae\_ctc\_XOVER\_SE.out  
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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
- Any adverse events -	- Any Grade -	108 ( 100%)	104 ( 100%)	212 ( 100%)
	Grade 1-2	25 (23.1%)	45 (43.3%)	70 (33.0%)
	1	5 ( 4.6%)	6 ( 5.8%)	11 ( 5.2%)
	2	20 (18.5%)	39 (37.5%)	59 (27.8%)
	Grade 3-4	69 (63.9%)	54 (51.9%)	123 (58.0%)
	3	62 (57.4%)	47 (45.2%)	109 (51.4%)
	4	7 ( 6.5%)	7 ( 6.7%)	14 ( 6.6%)
	Grade 5	14 (13.0%)	5 ( 4.8%)	19 ( 9.0%)
Gastrointestinal disorders				
- Overall -	- Any Grade -	84 (77.8%)	78 (75.0%)	162 (76.4%)
	Grade 1-2	71 (65.7%)	71 (68.3%)	142 (67.0%)
	1	36 (33.3%)	33 (31.7%)	69 (32.5%)
	2	35 (32.4%)	38 (36.5%)	73 (34.4%)
	Grade 3-4	13 (12.0%)	6 ( 5.8%)	19 ( 9.0%)
	3	13 (12.0%)	6 ( 5.8%)	19 ( 9.0%)
	Grade 5	0	1 ( 1.0%)	1 ( 0.5%)
Constipation	- Any Grade -	46 (42.6%)	30 (28.8%)	76 (35.8%)
	Grade 1-2	45 (41.7%)	30 (28.8%)	75 (35.4%)
	1	31 (28.7%)	22 (21.2%)	53 (25.0%)
	2	14 (13.0%)	8 ( 7.7%)	22 (10.4%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Nausea	- Any Grade -	20 (18.5%)	48 (46.2%)	68 (32.1%)
	Grade 1-2	19 (17.6%)	48 (46.2%)	67 (31.6%)
	1	13 (12.0%)	24 (23.1%)	37 (17.5%)
	2	6 ( 5.6%)	24 (23.1%)	30 (14.2%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Diarrhoea	- Any Grade -	40 (37.0%)	22 (21.2%)	62 (29.2%)
	Grade 1-2	36 (33.3%)	19 (18.3%)	55 (25.9%)
	1	18 (16.7%)	12 (11.5%)	30 (14.2%)
	2	18 (16.7%)	7 ( 6.7%)	25 (11.8%)
	Grade 3-4	4 ( 3.7%)	3 ( 2.9%)	7 ( 3.3%)
	3	4 ( 3.7%)	3 ( 2.9%)	7 ( 3.3%)
Stomatitis	- Any Grade -	15 (13.9%)	8 ( 7.7%)	23 (10.8%)
	Grade 1-2	14 (13.0%)	8 ( 7.7%)	22 (10.4%)
	1	9 ( 8.3%)	3 ( 2.9%)	12 ( 5.7%)
	2	5 ( 4.6%)	5 ( 4.8%)	10 ( 4.7%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Vomiting	- Any Grade -	10 ( 9.3%)	11 (10.6%)	21 ( 9.9%)
	Grade 1-2	10 ( 9.3%)	11 (10.6%)	21 ( 9.9%)
	1	6 ( 5.6%)	6 ( 5.8%)	12 ( 5.7%)
	2	4 ( 3.7%)	5 ( 4.8%)	9 ( 4.2%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Abdominal pain	- Any Grade -	11 (10.2%)	8 ( 7.7%)	19 ( 9.0%)
	Grade 1-2	8 ( 7.4%)	8 ( 7.7%)	16 ( 7.5%)
	1	6 ( 5.6%)	4 ( 3.8%)	10 ( 4.7%)
	2	2 ( 1.9%)	4 ( 3.8%)	6 ( 2.8%)
	Grade 3-4	3 ( 2.8%)	0	3 ( 1.4%)
	3	3 ( 2.8%)	0	3 ( 1.4%)
Abdominal pain upper	- Any Grade -	10 ( 9.3%)	9 ( 8.7%)	19 ( 9.0%)
	Grade 1-2	10 ( 9.3%)	9 ( 8.7%)	19 ( 9.0%)
	1	7 ( 6.5%)	8 ( 7.7%)	15 ( 7.1%)
	2	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)
Dry mouth	- Any Grade -	14 (13.0%)	4 ( 3.8%)	18 ( 8.5%)
	Grade 1-2	14 (13.0%)	4 ( 3.8%)	18 ( 8.5%)
	1	10 ( 9.3%)	3 ( 2.9%)	13 ( 6.1%)
	2	4 ( 3.7%)	1 ( 1.0%)	5 ( 2.4%)
Dyspepsia	- Any Grade -	8 ( 7.4%)	3 ( 2.9%)	11 ( 5.2%)
	Grade 1-2	8 ( 7.4%)	3 ( 2.9%)	11 ( 5.2%)
	1	7 ( 6.5%)	0	7 ( 3.3%)
	2	1 ( 0.9%)	3 ( 2.9%)	4 ( 1.9%)
Dysphagia	- Any Grade -	4 ( 3.7%)	2 ( 1.9%)	6 ( 2.8%)
	Grade 1-2	4 ( 3.7%)	2 ( 1.9%)	6 ( 2.8%)
	1	4 ( 3.7%)	2 ( 1.9%)	6 ( 2.8%)
Gastrooesophageal reflux disease	- Any Grade -	4 ( 3.7%)	2 ( 1.9%)	6 ( 2.8%)
	Grade 1-2	4 ( 3.7%)	2 ( 1.9%)	6 ( 2.8%)
	1	4 ( 3.7%)	1 ( 1.0%)	5 ( 2.4%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Aphthous ulcer	- Any Grade -	1 ( 0.9%)	4 ( 3.8%)	5 ( 2.4%)
	Grade 1-2	1 ( 0.9%)	4 ( 3.8%)	5 ( 2.4%)
	1	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	2	0	2 ( 1.9%)	2 ( 0.9%)
Ascites	- Any Grade -	4 ( 3.7%)	0	4 ( 1.9%)
	Grade 1-2	3 ( 2.8%)	0	3 ( 1.4%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Odynophagia	- Any Grade -	2 ( 1.9%)	2 ( 1.9%)	4 ( 1.9%)
	Grade 1-2	2 ( 1.9%)	2 ( 1.9%)	4 ( 1.9%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Abdominal discomfort	- Any Grade -	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	Grade 1-2	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	1	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
Abdominal distension	- Any Grade -	3 ( 2.8%)	0	3 ( 1.4%)
	Grade 1-2	3 ( 2.8%)	0	3 ( 1.4%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	2 ( 1.9%)	0	2 ( 0.9%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Haemorrhoids	- Any Grade -	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	Grade 1-2	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
	2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Toothache	- Any Grade -	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	Grade 1-2	0	2 ( 1.9%)	2 ( 0.9%)
	2	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Flatulence	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
Haematochezia	- Any Grade -	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 1-2	0	2 ( 1.9%)	2 ( 0.9%)
	1	0	2 ( 1.9%)	2 ( 0.9%)
Oral pain	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Abdominal pain lower	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Anal haemorrhage	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Apical granuloma	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Benign pancreatic hyperenzymaemia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Dental caries	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Enteritis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Enterocolitis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Gastric hypomotility	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Gastrointestinal disorder	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Gastrointestinal haemorrhage	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 5	0	1 ( 1.0%)	1 ( 0.5%)
Gastrointestinal mucosa hyperaemia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Gingival bleeding	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Hiatus hernia	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Intestinal obstruction	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Intestinal perforation	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Intra-abdominal haematoma	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Lip dry	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Lip haemorrhage	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Oesophageal discomfort	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Oral dysaesthesia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Pancreatic pseudocyst	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Pancreatitis acute	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Paraesthesia oral	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Peritoneal disorder	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Proctalgia	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Rectal fissure	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Rectal haemorrhage	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Salivary hypersecretion	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Upper gastrointestinal haemorrhage	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
General disorders and administration site conditions	- Overall -	74 (68.5%)	81 (77.9%)	155 (73.1%)
	Grade 1-2	63 (58.3%)	72 (69.2%)	135 (63.7%)
	1	38 (35.2%)	37 (35.6%)	75 (35.4%)
	2	25 (23.1%)	35 (33.7%)	60 (28.3%)
	Grade 3-4	9 ( 8.3%)	9 ( 8.7%)	18 ( 8.5%)
	3	9 ( 8.3%)	9 ( 8.7%)	18 ( 8.5%)
	Grade 5	2 ( 1.9%)	0	2 ( 0.9%)
Asthenia	- Any Grade -	26 (24.1%)	38 (36.5%)	64 (30.2%)
	Grade 1-2	24 (22.2%)	34 (32.7%)	58 (27.4%)
	1	15 (13.9%)	16 (15.4%)	31 (14.6%)
	2	9 ( 8.3%)	18 (17.3%)	27 (12.7%)
	Grade 3-4	2 ( 1.9%)	4 ( 3.8%)	6 ( 2.8%)
	3	2 ( 1.9%)	4 ( 3.8%)	6 ( 2.8%)
Fatigue	- Any Grade -	19 (17.6%)	23 (22.1%)	42 (19.8%)
	Grade 1-2	16 (14.8%)	21 (20.2%)	37 (17.5%)
	1	8 ( 7.4%)	12 (11.5%)	20 ( 9.4%)
	2	8 ( 7.4%)	9 ( 8.7%)	17 ( 8.0%)
	Grade 3-4	3 ( 2.8%)	2 ( 1.9%)	5 ( 2.4%)
	3	3 ( 2.8%)	2 ( 1.9%)	5 ( 2.4%)
Pyrexia	- Any Grade -	24 (22.2%)	11 (10.6%)	35 (16.5%)
	Grade 1-2	23 (21.3%)	10 ( 9.6%)	33 (15.6%)
	1	16 (14.8%)	10 ( 9.6%)	26 (12.3%)
	2	7 ( 6.5%)	0	7 ( 3.3%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 5	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Oedema peripheral	- Any Grade -	14 (13.0%)	14 (13.5%)	28 (13.2%)
	Grade 1-2	14 (13.0%)	14 (13.5%)	28 (13.2%)
	1	11 (10.2%)	10 ( 9.6%)	21 ( 9.9%)
	2	3 ( 2.8%)	4 ( 3.8%)	7 ( 3.3%)
Mucosal inflammation	- Any Grade -	8 ( 7.4%)	12 (11.5%)	20 ( 9.4%)
	Grade 1-2	8 ( 7.4%)	12 (11.5%)	20 ( 9.4%)
	1	5 ( 4.6%)	9 ( 8.7%)	14 ( 6.6%)
	2	3 ( 2.8%)	3 ( 2.9%)	6 ( 2.8%)
Chest pain	- Any Grade -	7 ( 6.5%)	9 ( 8.7%)	16 ( 7.5%)
	Grade 1-2	7 ( 6.5%)	8 ( 7.7%)	15 ( 7.1%)
	1	7 ( 6.5%)	5 ( 4.8%)	12 ( 5.7%)
	2	0	3 ( 2.9%)	3 ( 1.4%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Pain	- Any Grade -	4 ( 3.7%)	9 ( 8.7%)	13 ( 6.1%)
	Grade 1-2	3 ( 2.8%)	9 ( 8.7%)	12 ( 5.7%)
	1	3 ( 2.8%)	5 ( 4.8%)	8 ( 3.8%)
	2	0	4 ( 3.8%)	4 ( 1.9%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Oedema	- Any Grade -	3 ( 2.8%)	5 ( 4.8%)	8 ( 3.8%)
	Grade 1-2	3 ( 2.8%)	5 ( 4.8%)	8 ( 3.8%)
	1	2 ( 1.9%)	4 ( 3.8%)	6 ( 2.8%)
	2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Malaise	- Any Grade -	4 ( 3.7%)	2 ( 1.9%)	6 ( 2.8%)
	Grade 1-2	2 ( 1.9%)	2 ( 1.9%)	4 ( 1.9%)
	1	2 ( 1.9%)	2 ( 1.9%)	4 ( 1.9%)
	Grade 3-4	2 ( 1.9%)	0	2 ( 0.9%)
	3	2 ( 1.9%)	0	2 ( 0.9%)
Face oedema	- Any Grade -	5 ( 4.6%)	0	5 ( 2.4%)
	Grade 1-2	5 ( 4.6%)	0	5 ( 2.4%)
	1	5 ( 4.6%)	0	5 ( 2.4%)
Influenza like illness	- Any Grade -	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	Grade 1-2	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	1	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
Chills	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
General physical health deterioration	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Illness	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Swelling face	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
Catheter site pain	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Chest discomfort	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Death	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 5	1 ( 0.9%)	0	1 ( 0.5%)
Feeling abnormal	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Gait disturbance	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Ill-defined disorder	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Non-cardiac chest pain	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Peripheral swelling	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Serositis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Suprapubic pain	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Vaccination site swelling	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Investigations				
- Overall -	- Any Grade -	73 (67.6%)	56 (53.8%)	129 (60.8%)
	Grade 1-2	48 (44.4%)	42 (40.4%)	90 (42.5%)
	1	30 (27.8%)	23 (22.1%)	53 (25.0%)
	2	18 (16.7%)	19 (18.3%)	37 (17.5%)
	Grade 3-4	25 (23.1%)	14 (13.5%)	39 (18.4%)
	3	22 (20.4%)	12 (11.5%)	34 (16.0%)
	4	3 ( 2.8%)	2 ( 1.9%)	5 ( 2.4%)

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Output: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/t\_ae\_ctc\_MAIN\_SE.out

Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Aspartate aminotransferase increased	- Any Grade -	43 (39.8%)	18 (17.3%)	61 (28.8%)
	Grade 1-2	43 (39.8%)	18 (17.3%)	61 (28.8%)
	1	33 (30.6%)	12 (11.5%)	45 (21.2%)
	2	10 ( 9.3%)	6 ( 5.8%)	16 ( 7.5%)
Alanine aminotransferase increased	- Any Grade -	38 (35.2%)	21 (20.2%)	59 (27.8%)
	Grade 1-2	34 (31.5%)	16 (15.4%)	50 (23.6%)
	1	27 (25.0%)	10 ( 9.6%)	37 (17.5%)
	2	7 ( 6.5%)	6 ( 5.8%)	13 ( 6.1%)
	Grade 3-4	4 ( 3.7%)	5 ( 4.8%)	9 ( 4.2%)
	3	3 ( 2.8%)	5 ( 4.8%)	8 ( 3.8%)
	4	1 ( 0.9%)	0	1 ( 0.5%)
Blood creatinine increased	- Any Grade -	25 (23.1%)	8 ( 7.7%)	33 (15.6%)
	Grade 1-2	25 (23.1%)	8 ( 7.7%)	33 (15.6%)
	1	21 (19.4%)	5 ( 4.8%)	26 (12.3%)
	2	4 ( 3.7%)	3 ( 2.9%)	7 ( 3.3%)
Neutrophil count decreased	- Any Grade -	15 (13.9%)	9 ( 8.7%)	24 (11.3%)
	Grade 1-2	5 ( 4.6%)	3 ( 2.9%)	8 ( 3.8%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	2	4 ( 3.7%)	2 ( 1.9%)	6 ( 2.8%)
	Grade 3-4	10 ( 9.3%)	6 ( 5.8%)	16 ( 7.5%)
	3	9 ( 8.3%)	5 ( 4.8%)	14 ( 6.6%)
	4	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Platelet count decreased	- Any Grade -	8 ( 7.4%)	5 ( 4.8%)	13 ( 6.1%)
	Grade 1-2	6 ( 5.6%)	5 ( 4.8%)	11 ( 5.2%)
	1	4 ( 3.7%)	2 ( 1.9%)	6 ( 2.8%)
	2	2 ( 1.9%)	3 ( 2.9%)	5 ( 2.4%)
	Grade 3-4	2 ( 1.9%)	0	2 ( 0.9%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
	4	1 ( 0.9%)	0	1 ( 0.5%)
White blood cell count decreased	- Any Grade -	8 ( 7.4%)	3 ( 2.9%)	11 ( 5.2%)
	Grade 1-2	5 ( 4.6%)	3 ( 2.9%)	8 ( 3.8%)
	1	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	2	3 ( 2.8%)	2 ( 1.9%)	5 ( 2.4%)
	Grade 3-4	3 ( 2.8%)	0	3 ( 1.4%)
	3	3 ( 2.8%)	0	3 ( 1.4%)
Blood alkaline phosphatase increased	- Any Grade -	6 ( 5.6%)	4 ( 3.8%)	10 ( 4.7%)
	Grade 1-2	5 ( 4.6%)	4 ( 3.8%)	9 ( 4.2%)
	1	4 ( 3.7%)	3 ( 2.9%)	7 ( 3.3%)
	2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Blood creatine phosphokinase increased	- Any Grade -	10 ( 9.3%)	0	10 ( 4.7%)
	Grade 1-2	4 ( 3.7%)	0	4 ( 1.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	3 ( 2.8%)	0	3 ( 1.4%)
	Grade 3-4	6 ( 5.6%)	0	6 ( 2.8%)
	3	6 ( 5.6%)	0	6 ( 2.8%)
Blood lactate dehydrogenase increased	- Any Grade -	6 ( 5.6%)	3 ( 2.9%)	9 ( 4.2%)
	Grade 1-2	6 ( 5.6%)	2 ( 1.9%)	8 ( 3.8%)
	1	6 ( 5.6%)	2 ( 1.9%)	8 ( 3.8%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Gamma-glutamyltransferase increased	- Any Grade -	2 ( 1.9%)	7 ( 6.7%)	9 ( 4.2%)
	Grade 1-2	2 ( 1.9%)	4 ( 3.8%)	6 ( 2.8%)
	1	2 ( 1.9%)	2 ( 1.9%)	4 ( 1.9%)
	2	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 3-4	0	3 ( 2.9%)	3 ( 1.4%)
	3	0	3 ( 2.9%)	3 ( 1.4%)
Weight decreased	- Any Grade -	2 ( 1.9%)	6 ( 5.8%)	8 ( 3.8%)
	Grade 1-2	2 ( 1.9%)	6 ( 5.8%)	8 ( 3.8%)
	1	1 ( 0.9%)	3 ( 2.9%)	4 ( 1.9%)
	2	1 ( 0.9%)	3 ( 2.9%)	4 ( 1.9%)
Lymphocyte count decreased	- Any Grade -	4 ( 3.7%)	3 ( 2.9%)	7 ( 3.3%)
	Grade 1-2	3 ( 2.8%)	2 ( 1.9%)	5 ( 2.4%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	2	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 3-4	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
	4	0	1 ( 1.0%)	1 ( 0.5%)
Transaminases increased	- Any Grade -	4 ( 3.7%)	2 ( 1.9%)	6 ( 2.8%)
	Grade 1-2	4 ( 3.7%)	2 ( 1.9%)	6 ( 2.8%)
	1	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	2	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
Amylase increased	- Any Grade -	4 ( 3.7%)	0	4 ( 1.9%)
	Grade 1-2	3 ( 2.8%)	0	3 ( 1.4%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Blood phosphorus decreased	- Any Grade -	4 ( 3.7%)	0	4 ( 1.9%)
	Grade 1-2	4 ( 3.7%)	0	4 ( 1.9%)
	1	3 ( 2.8%)	0	3 ( 1.4%)
	2	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Blood thyroid stimulating hormone decreased	- Any Grade -	2 ( 1.9%)	2 ( 1.9%)	4 ( 1.9%)
	Grade 1-2	2 ( 1.9%)	2 ( 1.9%)	4 ( 1.9%)
	1	2 ( 1.9%)	2 ( 1.9%)	4 ( 1.9%)
Electrocardiogram QT prolonged	- Any Grade -	4 ( 3.7%)	0	4 ( 1.9%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	3 ( 2.8%)	0	3 ( 1.4%)
	3	3 ( 2.8%)	0	3 ( 1.4%)
Haemoglobin decreased	- Any Grade -	2 ( 1.9%)	2 ( 1.9%)	4 ( 1.9%)
	Grade 1-2	2 ( 1.9%)	2 ( 1.9%)	4 ( 1.9%)
	1	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Lipase increased	- Any Grade -	4 ( 3.7%)	0	4 ( 1.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	2 ( 1.9%)	0	2 ( 0.9%)
	3	2 ( 1.9%)	0	2 ( 0.9%)
Blood bicarbonate decreased	- Any Grade -	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 1-2	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Blood cholesterol increased	- Any Grade -	3 ( 2.8%)	0	3 ( 1.4%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	4	1 ( 0.9%)	0	1 ( 0.5%)
Weight increased	- Any Grade -	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 1-2	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Bilirubin conjugated increased	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Blood bilirubin increased	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
SARS-CoV-2 test positive	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Blood albumin decreased	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Blood albumin increased	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Blood glucose increased	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Blood phosphorus increased	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Blood pressure increased	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Blood thyroid stimulating hormone increased	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Blood uric acid increased	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Cytomegalovirus test positive	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Ejection fraction decreased	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Escherichia test positive	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Glomerular filtration rate decreased	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Nitrite urine present	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Oxygen saturation decreased	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Protein total decreased	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Streptococcus test positive	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Transaminases abnormal	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Infections and infestations				
- Overall -	- Any Grade -	73 (67.6%)	52 (50.0%)	125 (59.0%)
	Grade 1-2	45 (41.7%)	42 (40.4%)	87 (41.0%)
	1	15 (13.9%)	21 (20.2%)	36 (17.0%)
	2	30 (27.8%)	21 (20.2%)	51 (24.1%)
	Grade 3-4	23 (21.3%)	10 ( 9.6%)	33 (15.6%)
	3	19 (17.6%)	10 ( 9.6%)	29 (13.7%)
	4	4 ( 3.7%)	0	4 ( 1.9%)
	Grade 5	5 ( 4.6%)	0	5 ( 2.4%)
COVID-19	- Any Grade -	21 (19.4%)	20 (19.2%)	41 (19.3%)
	Grade 1-2	21 (19.4%)	19 (18.3%)	40 (18.9%)
	1	17 (15.7%)	16 (15.4%)	33 (15.6%)
	2	4 ( 3.7%)	3 ( 2.9%)	7 ( 3.3%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Pneumonia	- Any Grade -	19 (17.6%)	6 ( 5.8%)	25 (11.8%)
	Grade 1-2	9 ( 8.3%)	2 ( 1.9%)	11 ( 5.2%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	8 ( 7.4%)	2 ( 1.9%)	10 ( 4.7%)
	Grade 3-4	7 ( 6.5%)	4 ( 3.8%)	11 ( 5.2%)
	3	7 ( 6.5%)	4 ( 3.8%)	11 ( 5.2%)
	Grade 5	3 ( 2.8%)	0	3 ( 1.4%)
Urinary tract infection	- Any Grade -	17 (15.7%)	8 ( 7.7%)	25 (11.8%)
	Grade 1-2	15 (13.9%)	8 ( 7.7%)	23 (10.8%)
	1	5 ( 4.6%)	2 ( 1.9%)	7 ( 3.3%)
	2	10 ( 9.3%)	6 ( 5.8%)	16 ( 7.5%)
	Grade 3-4	2 ( 1.9%)	0	2 ( 0.9%)
	3	2 ( 1.9%)	0	2 ( 0.9%)
Nasopharyngitis	- Any Grade -	8 ( 7.4%)	6 ( 5.8%)	14 ( 6.6%)
	Grade 1-2	8 ( 7.4%)	6 ( 5.8%)	14 ( 6.6%)
	1	7 ( 6.5%)	6 ( 5.8%)	13 ( 6.1%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Conjunctivitis	- Any Grade -	0	13 (12.5%)	13 ( 6.1%)
	Grade 1-2	0	13 (12.5%)	13 ( 6.1%)
	1	0	9 ( 8.7%)	9 ( 4.2%)
	2	0	4 ( 3.8%)	4 ( 1.9%)
Herpes zoster	- Any Grade -	6 ( 5.6%)	4 ( 3.8%)	10 ( 4.7%)
	Grade 1-2	4 ( 3.7%)	4 ( 3.8%)	8 ( 3.8%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	3 ( 2.8%)	4 ( 3.8%)	7 ( 3.3%)
	Grade 3-4	2 ( 1.9%)	0	2 ( 0.9%)
	3	2 ( 1.9%)	0	2 ( 0.9%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Gastroenteritis	- Any Grade -	8 ( 7.4%)	1 ( 1.0%)	9 ( 4.2%)
	Grade 1-2	8 ( 7.4%)	1 ( 1.0%)	9 ( 4.2%)
	1	4 ( 3.7%)	0	4 ( 1.9%)
	2	4 ( 3.7%)	1 ( 1.0%)	5 ( 2.4%)
Respiratory tract infection	- Any Grade -	1 ( 0.9%)	5 ( 4.8%)	6 ( 2.8%)
	Grade 1-2	1 ( 0.9%)	4 ( 3.8%)	5 ( 2.4%)
	1	0	3 ( 2.9%)	3 ( 1.4%)
	2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Upper respiratory tract infection	- Any Grade -	5 ( 4.6%)	1 ( 1.0%)	6 ( 2.8%)
	Grade 1-2	5 ( 4.6%)	1 ( 1.0%)	6 ( 2.8%)
	1	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)
	2	2 ( 1.9%)	0	2 ( 0.9%)
Cystitis	- Any Grade -	5 ( 4.6%)	0	5 ( 2.4%)
	Grade 1-2	5 ( 4.6%)	0	5 ( 2.4%)
	1	3 ( 2.8%)	0	3 ( 1.4%)
	2	2 ( 1.9%)	0	2 ( 0.9%)
Lower respiratory tract infection	- Any Grade -	5 ( 4.6%)	0	5 ( 2.4%)
	Grade 1-2	4 ( 3.7%)	0	4 ( 1.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	3 ( 2.8%)	0	3 ( 1.4%)
	Grade 5	1 ( 0.9%)	0	1 ( 0.5%)
Paronychia	- Any Grade -	5 ( 4.6%)	0	5 ( 2.4%)
	Grade 1-2	5 ( 4.6%)	0	5 ( 2.4%)
	1	5 ( 4.6%)	0	5 ( 2.4%)
Fungal infection	- Any Grade -	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)
	Grade 1-2	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)
	1	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)
Oral candidiasis	- Any Grade -	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)
	Grade 1-2	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
	2	3 ( 2.8%)	0	3 ( 1.4%)
Pneumocystis jirovecii pneumonia	- Any Grade -	4 ( 3.7%)	0	4 ( 1.9%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	3 ( 2.8%)	0	3 ( 1.4%)
	3	2 ( 1.9%)	0	2 ( 0.9%)
	4	1 ( 0.9%)	0	1 ( 0.5%)
COVID-19 pneumonia	- Any Grade -	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	3	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)

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Output: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/t\_ae\_ctc\_MAIN\_SE.out

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Infection	- Any Grade -	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Influenza	- Any Grade -	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 1-2	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Pharyngitis	- Any Grade -	3 ( 2.8%)	0	3 ( 1.4%)
	Grade 1-2	3 ( 2.8%)	0	3 ( 1.4%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	2 ( 1.9%)	0	2 ( 0.9%)
Rhinitis	- Any Grade -	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 1-2	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Sepsis	- Any Grade -	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 3-4	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
	4	1 ( 0.9%)	0	1 ( 0.5%)
Bronchitis	Grade 5	1 ( 0.9%)	0	1 ( 0.5%)
- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)	
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Candida infection	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Device related infection	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 3-4	2 ( 1.9%)	0	2 ( 0.9%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
	4	1 ( 0.9%)	0	1 ( 0.5%)
Diverticulitis	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Escherichia infection	- Any Grade -	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Gastrointestinal infection	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)

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Output: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/t\_ae\_ctc\_MAIN\_SE.out

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Oral fungal infection	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Oral herpes	- Any Grade -	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 1-2	0	2 ( 1.9%)	2 ( 0.9%)
	1	0	2 ( 1.9%)	2 ( 0.9%)
Oropharyngeal candidiasis	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Pneumonia cytomegaloviral	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 3-4	2 ( 1.9%)	0	2 ( 0.9%)
	3	2 ( 1.9%)	0	2 ( 0.9%)
Pyelonephritis	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 3-4	2 ( 1.9%)	0	2 ( 0.9%)
	3	2 ( 1.9%)	0	2 ( 0.9%)
Sinusitis	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Tongue fungal infection	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Urosepsis	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	4	1 ( 0.9%)	0	1 ( 0.5%)
Viral infection	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Atypical pneumonia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Bacteraemia	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Bronchopulmonary aspergillosis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Burn infection	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)

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Output: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/t\_ae\_ctc\_MAIN\_SE.out

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Cellulitis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Cytomegalovirus infection	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Dermo-hypodermatitis	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Epididymitis	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Erysipelas	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Escherichia urinary tract infection	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Gastroenteritis viral	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Genital herpes simplex	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Groin abscess	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Helicobacter infection	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Herpes ophthalmic	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Herpes simplex	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Localised infection	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Nail infection	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Oesophageal candidiasis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)

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Output: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/t\_ae\_ctc\_MAIN\_SE.out

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Oesophageal infection	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Onychomycosis	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Otitis externa	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Parainfluenzae virus infection	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Periodontitis	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Pleural infection	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Pneumonia legionella	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Pseudomembranous colitis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Pustule	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Pyelonephritis acute	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Pyuria	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Q fever	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Rash pustular	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Respiratory tract infection viral	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Severe acute respiratory syndrome	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Spontaneous bacterial peritonitis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Staphylococcal sepsis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Streptococcal infection	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Tooth infection	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Tularaemia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Vaginal infection	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Vascular device infection	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Vulvovaginal candidiasis	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Blood and lymphatic system disorders				
- Overall -				
	- Any Grade -	62 (57.4%)	54 (51.9%)	116 (54.7%)
	Grade 1-2	36 (33.3%)	32 (30.8%)	68 (32.1%)
	1	9 ( 8.3%)	7 ( 6.7%)	16 ( 7.5%)
	2	27 (25.0%)	25 (24.0%)	52 (24.5%)
	Grade 3-4	26 (24.1%)	22 (21.2%)	48 (22.6%)
	3	22 (20.4%)	18 (17.3%)	40 (18.9%)
	4	4 ( 3.7%)	4 ( 3.8%)	8 ( 3.8%)
Anaemia	- Any Grade -	49 (45.4%)	45 (43.3%)	94 (44.3%)
	Grade 1-2	36 (33.3%)	32 (30.8%)	68 (32.1%)
	1	14 (13.0%)	9 ( 8.7%)	23 (10.8%)
	2	22 (20.4%)	23 (22.1%)	45 (21.2%)
	Grade 3-4	13 (12.0%)	13 (12.5%)	26 (12.3%)
	3	11 (10.2%)	12 (11.5%)	23 (10.8%)
	4	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)

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```
Program: root/clinical_studies/RO7499790/CDT30380/BO42864/data_analysis/Adhoc_Analysis/prod/
         program/t_ae_ctc.sas
Output: root/clinical_studies/RO7499790/CDT30380/BO42864/data_analysis/Adhoc_Analysis/prod/
        output/t_ae_ctc_MAIN_SE.out
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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Neutropenia	- Any Grade -	26 (24.1%)	19 (18.3%)	45 (21.2%)
	Grade 1-2	15 (13.9%)	10 ( 9.6%)	25 (11.8%)
	1	6 ( 5.6%)	4 ( 3.8%)	10 ( 4.7%)
	2	9 ( 8.3%)	6 ( 5.8%)	15 ( 7.1%)
	Grade 3-4	11 (10.2%)	9 ( 8.7%)	20 ( 9.4%)
	3	11 (10.2%)	7 ( 6.7%)	18 ( 8.5%)
	4	0	2 ( 1.9%)	2 ( 0.9%)
Leukopenia	- Any Grade -	12 (11.1%)	5 ( 4.8%)	17 ( 8.0%)
	Grade 1-2	10 ( 9.3%)	3 ( 2.9%)	13 ( 6.1%)
	1	7 ( 6.5%)	2 ( 1.9%)	9 ( 4.2%)
	2	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)
	Grade 3-4	2 ( 1.9%)	2 ( 1.9%)	4 ( 1.9%)
	3	2 ( 1.9%)	2 ( 1.9%)	4 ( 1.9%)
Thrombocytopenia	- Any Grade -	4 ( 3.7%)	11 (10.6%)	15 ( 7.1%)
	Grade 1-2	2 ( 1.9%)	7 ( 6.7%)	9 ( 4.2%)
	1	2 ( 1.9%)	5 ( 4.8%)	7 ( 3.3%)
	2	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 3-4	2 ( 1.9%)	4 ( 3.8%)	6 ( 2.8%)
	3	0	3 ( 2.9%)	3 ( 1.4%)
	4	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
Lymphopenia	- Any Grade -	5 ( 4.6%)	1 ( 1.0%)	6 ( 2.8%)
	Grade 1-2	4 ( 3.7%)	1 ( 1.0%)	5 ( 2.4%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
	2	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Febrile neutropenia	- Any Grade -	1 ( 0.9%)	4 ( 3.8%)	5 ( 2.4%)
	Grade 3-4	1 ( 0.9%)	4 ( 3.8%)	5 ( 2.4%)
	3	0	3 ( 2.9%)	3 ( 1.4%)
	4	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Leukocytosis	- Any Grade -	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 1-2	0	2 ( 1.9%)	2 ( 0.9%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Febrile bone marrow aplasia	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Thrombocytosis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)

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Output: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/t\_ae\_ctc\_MAIN\_SE.out

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
<b>Respiratory, thoracic and mediastinal disorders</b>				
- Overall -	- Any Grade -	58 (53.7%)	48 (46.2%)	106 (50.0%)
	Grade 1-2	43 (39.8%)	41 (39.4%)	84 (39.6%)
	1	27 (25.0%)	24 (23.1%)	51 (24.1%)
	2	16 (14.8%)	17 (16.3%)	33 (15.6%)
	Grade 3-4	10 ( 9.3%)	5 ( 4.8%)	15 ( 7.1%)
	3	8 ( 7.4%)	5 ( 4.8%)	13 ( 6.1%)
	4	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 5	5 ( 4.6%)	2 ( 1.9%)	7 ( 3.3%)
Cough	- Any Grade -	28 (25.9%)	10 ( 9.6%)	38 (17.9%)
	Grade 1-2	26 (24.1%)	10 ( 9.6%)	36 (17.0%)
	1	22 (20.4%)	7 ( 6.7%)	29 (13.7%)
	2	4 ( 3.7%)	3 ( 2.9%)	7 ( 3.3%)
	Grade 3-4	2 ( 1.9%)	0	2 ( 0.9%)
	3	2 ( 1.9%)	0	2 ( 0.9%)
Dyspnoea	- Any Grade -	16 (14.8%)	19 (18.3%)	35 (16.5%)
	Grade 1-2	15 (13.9%)	15 (14.4%)	30 (14.2%)
	1	7 ( 6.5%)	11 (10.6%)	18 ( 8.5%)
	2	8 ( 7.4%)	4 ( 3.8%)	12 ( 5.7%)
	Grade 3-4	1 ( 0.9%)	3 ( 2.9%)	4 ( 1.9%)
	3	1 ( 0.9%)	3 ( 2.9%)	4 ( 1.9%)
	Grade 5	0	1 ( 1.0%)	1 ( 0.5%)
Epistaxis	- Any Grade -	11 (10.2%)	3 ( 2.9%)	14 ( 6.6%)
	Grade 1-2	11 (10.2%)	2 ( 1.9%)	13 ( 6.1%)
	1	8 ( 7.4%)	2 ( 1.9%)	10 ( 4.7%)
	2	3 ( 2.8%)	0	3 ( 1.4%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Pneumonitis	- Any Grade -	13 (12.0%)	0	13 ( 6.1%)
	Grade 1-2	11 (10.2%)	0	11 ( 5.2%)
	1	6 ( 5.6%)	0	6 ( 2.8%)
	2	5 ( 4.6%)	0	5 ( 2.4%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	4	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 5	1 ( 0.9%)	0	1 ( 0.5%)
Pleural effusion	- Any Grade -	5 ( 4.6%)	6 ( 5.8%)	11 ( 5.2%)
	Grade 1-2	2 ( 1.9%)	6 ( 5.8%)	8 ( 3.8%)
	1	0	3 ( 2.9%)	3 ( 1.4%)
	2	2 ( 1.9%)	3 ( 2.9%)	5 ( 2.4%)
	Grade 3-4	2 ( 1.9%)	0	2 ( 0.9%)
	3	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 5	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Pulmonary embolism	- Any Grade -	6 ( 5.6%)	5 ( 4.8%)	11 ( 5.2%)
	Grade 1-2	4 ( 3.7%)	3 ( 2.9%)	7 ( 3.3%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
	2	2 ( 1.9%)	3 ( 2.9%)	5 ( 2.4%)
	Grade 3-4	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	3	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 5	0	1 ( 1.0%)	1 ( 0.5%)
Interstitial lung disease	- Any Grade -	4 ( 3.7%)	2 ( 1.9%)	6 ( 2.8%)
	Grade 1-2	3 ( 2.8%)	2 ( 1.9%)	5 ( 2.4%)
	1	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 5	1 ( 0.9%)	0	1 ( 0.5%)
Oropharyngeal pain	- Any Grade -	5 ( 4.6%)	1 ( 1.0%)	6 ( 2.8%)
	Grade 1-2	5 ( 4.6%)	1 ( 1.0%)	6 ( 2.8%)
	1	3 ( 2.8%)	0	3 ( 1.4%)
	2	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
Dysphonia	- Any Grade -	3 ( 2.8%)	2 ( 1.9%)	5 ( 2.4%)
	Grade 1-2	3 ( 2.8%)	2 ( 1.9%)	5 ( 2.4%)
	1	3 ( 2.8%)	2 ( 1.9%)	5 ( 2.4%)
Haemoptysis	- Any Grade -	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	4	1 ( 0.9%)	0	1 ( 0.5%)
Dyspnoea exertional	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
Nasal congestion	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
Nasal dryness	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Nasal inflammation	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Respiratory failure	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 5	1 ( 0.9%)	0	1 ( 0.5%)
Allergic cough	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Alveolitis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Bronchospasm	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Chronic obstructive pulmonary disease	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Haemothorax	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Hiccups	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Hypoxia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Lung opacity	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Nasal obstruction	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Painful respiration	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Pharyngeal inflammation	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Pleural thickening	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Pleuritic pain	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Pneumothorax	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Productive cough	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Pulmonary fibrosis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 5	1 ( 0.9%)	0	1 ( 0.5%)
Pulmonary toxicity	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Rhinorrhoea	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Sputum discoloured	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Wheezing	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Nervous system disorders				
- Overall -	- Any Grade -	55 (50.9%)	45 (43.3%)	100 (47.2%)
	Grade 1-2	50 (46.3%)	41 (39.4%)	91 (42.9%)
	1	39 (36.1%)	30 (28.8%)	69 (32.5%)
	2	11 (10.2%)	11 (10.6%)	22 (10.4%)
Dysgeusia	Grade 3-4	5 ( 4.6%)	4 ( 3.8%)	9 ( 4.2%)
	3	5 ( 4.6%)	4 ( 3.8%)	9 ( 4.2%)
	- Any Grade -	26 (24.1%)	9 ( 8.7%)	35 (16.5%)
	Grade 1-2	26 (24.1%)	9 ( 8.7%)	35 (16.5%)
Paraesthesia	1	24 (22.2%)	9 ( 8.7%)	33 (15.6%)
	2	2 ( 1.9%)	0	2 ( 0.9%)
	- Any Grade -	14 (13.0%)	5 ( 4.8%)	19 ( 9.0%)
	Grade 1-2	14 (13.0%)	5 ( 4.8%)	19 ( 9.0%)
Headache	1	11 (10.2%)	5 ( 4.8%)	16 ( 7.5%)
	2	3 ( 2.8%)	0	3 ( 1.4%)
	- Any Grade -	8 ( 7.4%)	10 ( 9.6%)	18 ( 8.5%)
	Grade 1-2	8 ( 7.4%)	10 ( 9.6%)	18 ( 8.5%)
Neuropathy peripheral	1	8 ( 7.4%)	8 ( 7.7%)	16 ( 7.5%)
	2	0	2 ( 1.9%)	2 ( 0.9%)
	- Any Grade -	8 ( 7.4%)	9 ( 8.7%)	17 ( 8.0%)
	Grade 1-2	8 ( 7.4%)	7 ( 6.7%)	15 ( 7.1%)
Dizziness	1	8 ( 7.4%)	6 ( 5.8%)	14 ( 6.6%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	2 ( 1.9%)	2 ( 0.9%)
	3	0	2 ( 1.9%)	2 ( 0.9%)
Sciatica	- Any Grade -	7 ( 6.5%)	9 ( 8.7%)	16 ( 7.5%)
	Grade 1-2	7 ( 6.5%)	9 ( 8.7%)	16 ( 7.5%)
	1	6 ( 5.6%)	5 ( 4.8%)	11 ( 5.2%)
	2	1 ( 0.9%)	4 ( 3.8%)	5 ( 2.4%)
Syncope	- Any Grade -	8 ( 7.4%)	2 ( 1.9%)	10 ( 4.7%)
	Grade 1-2	8 ( 7.4%)	2 ( 1.9%)	10 ( 4.7%)
	1	7 ( 6.5%)	1 ( 1.0%)	8 ( 3.8%)
	2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
- Any Grade -	3 ( 2.8%)	2 ( 1.9%)	5 ( 2.4%)	
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)
	3	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Balance disorder	- Any Grade -	3 ( 2.8%)	0	3 ( 1.4%)
	Grade 1-2	3 ( 2.8%)	0	3 ( 1.4%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	2 ( 1.9%)	0	2 ( 0.9%)
Peripheral sensory neuropathy	- Any Grade -	3 ( 2.8%)	0	3 ( 1.4%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Ageusia	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Neurotoxicity	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Polyneuropathy	- Any Grade -	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 1-2	0	2 ( 1.9%)	2 ( 0.9%)
	1	0	2 ( 1.9%)	2 ( 0.9%)
Tremor	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Amnesia	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Anosmia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Brain oedema	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Carpal tunnel syndrome	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Cognitive disorder	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Dysaesthesia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Hypoesthesia	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Hypogeausia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)

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Program: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/program/t\_ae\_ctc.sas

Output: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/t\_ae\_ctc\_MAIN\_SE.out

Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Hypokinesia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Intracranial pressure increased	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Lethargy	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Memory impairment	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Post herpetic neuralgia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Seizure	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Somnolence	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Taste disorder	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Transient ischaemic attack	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Metabolism and nutrition disorders				
- Overall -				
	- Any Grade -	53 (49.1%)	42 (40.4%)	95 (44.8%)
	Grade 1-2	40 (37.0%)	37 (35.6%)	77 (36.3%)
	1	24 (22.2%)	23 (22.1%)	47 (22.2%)
	2	16 (14.8%)	14 (13.5%)	30 (14.2%)
	Grade 3-4	13 (12.0%)	5 ( 4.8%)	18 ( 8.5%)
	3	12 (11.1%)	5 ( 4.8%)	17 ( 8.0%)
	4	1 ( 0.9%)	0	1 ( 0.5%)
Decreased appetite				
	- Any Grade -	20 (18.5%)	22 (21.2%)	42 (19.8%)
	Grade 1-2	19 (17.6%)	22 (21.2%)	41 (19.3%)
	1	10 ( 9.3%)	13 (12.5%)	23 (10.8%)
	2	9 ( 8.3%)	9 ( 8.7%)	18 ( 8.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Hypokalaemia	- Any Grade -	10 ( 9.3%)	7 ( 6.7%)	17 ( 8.0%)
	Grade 1-2	8 ( 7.4%)	6 ( 5.8%)	14 ( 6.6%)
	1	6 ( 5.6%)	6 ( 5.8%)	12 ( 5.7%)
	2	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 3-4	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	3	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
Hypophosphataemia	- Any Grade -	11 (10.2%)	3 ( 2.9%)	14 ( 6.6%)
	Grade 1-2	8 ( 7.4%)	3 ( 2.9%)	11 ( 5.2%)
	1	4 ( 3.7%)	2 ( 1.9%)	6 ( 2.8%)
	2	4 ( 3.7%)	1 ( 1.0%)	5 ( 2.4%)
	Grade 3-4	3 ( 2.8%)	0	3 ( 1.4%)
	3	3 ( 2.8%)	0	3 ( 1.4%)
Hypocalcaemia	- Any Grade -	8 ( 7.4%)	4 ( 3.8%)	12 ( 5.7%)
	Grade 1-2	7 ( 6.5%)	4 ( 3.8%)	11 ( 5.2%)
	1	6 ( 5.6%)	2 ( 1.9%)	8 ( 3.8%)
	2	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Hypoalbuminaemia	- Any Grade -	6 ( 5.6%)	2 ( 1.9%)	8 ( 3.8%)
	Grade 1-2	5 ( 4.6%)	2 ( 1.9%)	7 ( 3.3%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	2	4 ( 3.7%)	1 ( 1.0%)	5 ( 2.4%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Hyponatraemia	- Any Grade -	7 ( 6.5%)	1 ( 1.0%)	8 ( 3.8%)
	Grade 1-2	3 ( 2.8%)	0	3 ( 1.4%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	4 ( 3.7%)	1 ( 1.0%)	5 ( 2.4%)
	3	4 ( 3.7%)	1 ( 1.0%)	5 ( 2.4%)
Hyperglycaemia	- Any Grade -	2 ( 1.9%)	5 ( 4.8%)	7 ( 3.3%)
	Grade 1-2	1 ( 0.9%)	4 ( 3.8%)	5 ( 2.4%)
	1	1 ( 0.9%)	4 ( 3.8%)	5 ( 2.4%)
	Grade 3-4	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	3	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Cell death	- Any Grade -	5 ( 4.6%)	0	5 ( 2.4%)
	Grade 1-2	4 ( 3.7%)	0	4 ( 1.9%)
	1	3 ( 2.8%)	0	3 ( 1.4%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Hyperkalaemia	- Any Grade -	5 ( 4.6%)	0	5 ( 2.4%)
	Grade 1-2	4 ( 3.7%)	0	4 ( 1.9%)
	1	3 ( 2.8%)	0	3 ( 1.4%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Hypomagnesaemia	- Any Grade -	1 ( 0.9%)	4 ( 3.8%)	5 ( 2.4%)
	Grade 1-2	1 ( 0.9%)	4 ( 3.8%)	5 ( 2.4%)
	1	1 ( 0.9%)	3 ( 2.9%)	4 ( 1.9%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Dehydration	- Any Grade -	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	0	2 ( 1.9%)	2 ( 0.9%)
	3	0	2 ( 1.9%)	2 ( 0.9%)
Hyperphosphataemia	- Any Grade -	3 ( 2.8%)	0	3 ( 1.4%)
	Grade 1-2	3 ( 2.8%)	0	3 ( 1.4%)
	1	3 ( 2.8%)	0	3 ( 1.4%)
Hypertriglyceridaemia	- Any Grade -	3 ( 2.8%)	0	3 ( 1.4%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	4	1 ( 0.9%)	0	1 ( 0.5%)
Hyperuricaemia	- Any Grade -	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 1-2	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	1	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
Hypercholesterolaemia	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
Hypoglycaemia	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
Vitamin D deficiency	- Any Grade -	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 1-2	0	2 ( 1.9%)	2 ( 0.9%)
	1	0	2 ( 1.9%)	2 ( 0.9%)
Diabetic metabolic decompensation	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Hyperamylasaemia	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Hypercalcaemia	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Hypernatraemia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Hyperphosphatasia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Increased appetite	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Iron deficiency	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Malnutrition	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Musculoskeletal and connective tissue disorders	- Overall -			
	- Any Grade -	43 (39.8%)	41 (39.4%)	84 (39.6%)
	Grade 1-2	39 (36.1%)	37 (35.6%)	76 (35.8%)
	1	32 (29.6%)	21 (20.2%)	53 (25.0%)
	2	7 ( 6.5%)	16 (15.4%)	23 (10.8%)
	Grade 3-4	4 ( 3.7%)	4 ( 3.8%)	8 ( 3.8%)
	3	4 ( 3.7%)	4 ( 3.8%)	8 ( 3.8%)
Back pain	- Any Grade -	13 (12.0%)	14 (13.5%)	27 (12.7%)
	Grade 1-2	13 (12.0%)	11 (10.6%)	24 (11.3%)
	1	9 ( 8.3%)	7 ( 6.7%)	16 ( 7.5%)
	2	4 ( 3.7%)	4 ( 3.8%)	8 ( 3.8%)
	Grade 3-4	0	3 ( 2.9%)	3 ( 1.4%)
	3	0	3 ( 2.9%)	3 ( 1.4%)
Arthralgia	- Any Grade -	11 (10.2%)	15 (14.4%)	26 (12.3%)
	Grade 1-2	11 (10.2%)	15 (14.4%)	26 (12.3%)
	1	10 ( 9.3%)	6 ( 5.8%)	16 ( 7.5%)
	2	1 ( 0.9%)	9 ( 8.7%)	10 ( 4.7%)
Myalgia	- Any Grade -	15 (13.9%)	10 ( 9.6%)	25 (11.8%)
	Grade 1-2	13 (12.0%)	10 ( 9.6%)	23 (10.8%)
	1	13 (12.0%)	8 ( 7.7%)	21 ( 9.9%)
	2	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 3-4	2 ( 1.9%)	0	2 ( 0.9%)
	3	2 ( 1.9%)	0	2 ( 0.9%)
Pain in extremity	- Any Grade -	9 ( 8.3%)	4 ( 3.8%)	13 ( 6.1%)
	Grade 1-2	9 ( 8.3%)	4 ( 3.8%)	13 ( 6.1%)
	1	7 ( 6.5%)	4 ( 3.8%)	11 ( 5.2%)
	2	2 ( 1.9%)	0	2 ( 0.9%)
Musculoskeletal chest pain	- Any Grade -	2 ( 1.9%)	7 ( 6.7%)	9 ( 4.2%)
	Grade 1-2	1 ( 0.9%)	7 ( 6.7%)	8 ( 3.8%)
	1	1 ( 0.9%)	6 ( 5.8%)	7 ( 3.3%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Bone pain	- Any Grade -	4 ( 3.7%)	1 ( 1.0%)	5 ( 2.4%)
	Grade 1-2	4 ( 3.7%)	1 ( 1.0%)	5 ( 2.4%)
	1	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)
	2	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Muscle spasms	- Any Grade -	4 ( 3.7%)	0	4 ( 1.9%)
	Grade 1-2	4 ( 3.7%)	0	4 ( 1.9%)
	1	4 ( 3.7%)	0	4 ( 1.9%)
Hypercreatininaemia	- Any Grade -	3 ( 2.8%)	0	3 ( 1.4%)
	Grade 1-2	3 ( 2.8%)	0	3 ( 1.4%)
	1	3 ( 2.8%)	0	3 ( 1.4%)
Muscular weakness	- Any Grade -	3 ( 2.8%)	0	3 ( 1.4%)
	Grade 1-2	3 ( 2.8%)	0	3 ( 1.4%)
	1	3 ( 2.8%)	0	3 ( 1.4%)
Osteoarthritis	- Any Grade -	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	Grade 1-2	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	0	2 ( 1.9%)	2 ( 0.9%)
Flank pain	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
Intervertebral disc protrusion	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Joint range of motion decreased	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Limb discomfort	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
Neck pain	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Osteonecrosis	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Tendonitis	- Any Grade -	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 1-2	0	2 ( 1.9%)	2 ( 0.9%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Arthritis	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Connective tissue disorder	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Foot deformity	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Groin pain	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Joint swelling	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Mobility decreased	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Muscle fatigue	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Muscle tightness	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Musculoskeletal discomfort	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Musculoskeletal disorder	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Myopathy	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Osteoporosis	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Pain in jaw	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Pathological fracture	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Pubic pain	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Rheumatoid arthritis	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Spinal pain	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)

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Output: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/t\_ae\_ctc\_MAIN\_SE.out

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
<b>Skin and subcutaneous tissue disorders</b>				
- Overall -	- Any Grade -	45 (41.7%)	36 (34.6%)	81 (38.2%)
	Grade 1-2	45 (41.7%)	35 (33.7%)	80 (37.7%)
	1	37 (34.3%)	25 (24.0%)	62 (29.2%)
	2	8 ( 7.4%)	10 ( 9.6%)	18 ( 8.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Rash	- Any Grade -	16 (14.8%)	12 (11.5%)	28 (13.2%)
	Grade 1-2	16 (14.8%)	11 (10.6%)	27 (12.7%)
	1	14 (13.0%)	8 ( 7.7%)	22 (10.4%)
	2	2 ( 1.9%)	3 ( 2.9%)	5 ( 2.4%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Pruritus	- Any Grade -	5 ( 4.6%)	10 ( 9.6%)	15 ( 7.1%)
	Grade 1-2	5 ( 4.6%)	10 ( 9.6%)	15 ( 7.1%)
	1	5 ( 4.6%)	8 ( 7.7%)	13 ( 6.1%)
	2	0	2 ( 1.9%)	2 ( 0.9%)
Alopecia	- Any Grade -	7 ( 6.5%)	5 ( 4.8%)	12 ( 5.7%)
	Grade 1-2	7 ( 6.5%)	5 ( 4.8%)	12 ( 5.7%)
	1	6 ( 5.6%)	5 ( 4.8%)	11 ( 5.2%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Dry skin	- Any Grade -	4 ( 3.7%)	4 ( 3.8%)	8 ( 3.8%)
	Grade 1-2	4 ( 3.7%)	4 ( 3.8%)	8 ( 3.8%)
	1	4 ( 3.7%)	4 ( 3.8%)	8 ( 3.8%)
Hypertrichosis	- Any Grade -	7 ( 6.5%)	0	7 ( 3.3%)
	Grade 1-2	7 ( 6.5%)	0	7 ( 3.3%)
	1	6 ( 5.6%)	0	6 ( 2.8%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Erythema	- Any Grade -	2 ( 1.9%)	4 ( 3.8%)	6 ( 2.8%)
	Grade 1-2	2 ( 1.9%)	4 ( 3.8%)	6 ( 2.8%)
	1	2 ( 1.9%)	3 ( 2.9%)	5 ( 2.4%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Hyperhidrosis	- Any Grade -	3 ( 2.8%)	0	3 ( 1.4%)
	Grade 1-2	3 ( 2.8%)	0	3 ( 1.4%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Night sweats	- Any Grade -	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 1-2	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	1	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
Skin discolouration	- Any Grade -	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 1-2	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	1	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
Skin disorder	- Any Grade -	0	3 ( 2.9%)	3 ( 1.4%)
	Grade 1-2	0	3 ( 2.9%)	3 ( 1.4%)
	1	0	2 ( 1.9%)	2 ( 0.9%)
	2	0	1 ( 1.0%)	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Dermatitis	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Eczema	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Erythrosis	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Nail dystrophy	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
Rash maculo-papular	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Rosacea	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Seborrhoeic dermatitis	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Skin exfoliation	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Skin hyperpigmentation	- Any Grade -	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 1-2	0	2 ( 1.9%)	2 ( 0.9%)
	1	0	2 ( 1.9%)	2 ( 0.9%)
Acne	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Actinic keratosis	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Blister	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Cutaneous vasculitis	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Decubitus ulcer	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Dermatitis acneiform	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Erythema multiforme	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Hyperkeratosis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Nail bed bleeding	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Nail disorder	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Nail ridging	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Onychalgia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Onychoclasia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Onycholysis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Palmar-plantar erythrodysesthesia syndrome	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Papule	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Penile ulceration	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Rash papular	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Skin fissures	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Skin irritation	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Stevens-Johnson syndrome	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
<b>Vascular disorders</b>				
- Overall -	- Any Grade -	38 (35.2%)	16 (15.4%)	54 (25.5%)
	Grade 1-2	22 (20.4%)	13 (12.5%)	35 (16.5%)
	1	10 ( 9.3%)	4 ( 3.8%)	14 ( 6.6%)
	2	12 (11.1%)	9 ( 8.7%)	21 ( 9.9%)
	Grade 3-4	16 (14.8%)	3 ( 2.9%)	19 ( 9.0%)
	3	15 (13.9%)	3 ( 2.9%)	18 ( 8.5%)
	4	1 ( 0.9%)	0	1 ( 0.5%)
Hypertension	- Any Grade -	33 (30.6%)	4 ( 3.8%)	37 (17.5%)
	Grade 1-2	19 (17.6%)	3 ( 2.9%)	22 (10.4%)
	1	7 ( 6.5%)	1 ( 1.0%)	8 ( 3.8%)
	2	12 (11.1%)	2 ( 1.9%)	14 ( 6.6%)
	Grade 3-4	14 (13.0%)	1 ( 1.0%)	15 ( 7.1%)
	3	13 (12.0%)	1 ( 1.0%)	14 ( 6.6%)
	4	1 ( 0.9%)	0	1 ( 0.5%)
Haematoma	- Any Grade -	3 ( 2.8%)	3 ( 2.9%)	6 ( 2.8%)
	Grade 1-2	3 ( 2.8%)	3 ( 2.9%)	6 ( 2.8%)
	1	3 ( 2.8%)	0	3 ( 1.4%)
	2	0	3 ( 2.9%)	3 ( 1.4%)
Hypotension	- Any Grade -	4 ( 3.7%)	1 ( 1.0%)	5 ( 2.4%)
	Grade 1-2	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)
	1	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Thrombosis	- Any Grade -	0	3 ( 2.9%)	3 ( 1.4%)
	Grade 1-2	0	2 ( 1.9%)	2 ( 0.9%)
	2	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Deep vein thrombosis	- Any Grade -	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 1-2	0	2 ( 1.9%)	2 ( 0.9%)
	2	0	2 ( 1.9%)	2 ( 0.9%)
Embolism	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Capillary fragility	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Hot flush	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Lymphoedema	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Orthostatic hypertension	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Orthostatic hypotension	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Peripheral artery thrombosis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Thrombophlebitis migrans	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Eye disorders				
- Overall -	- Any Grade -	19 (17.6%)	21 (20.2%)	40 (18.9%)
	Grade 1-2	15 (13.9%)	21 (20.2%)	36 (17.0%)
	1	14 (13.0%)	17 (16.3%)	31 (14.6%)
	2	1 ( 0.9%)	4 ( 3.8%)	5 ( 2.4%)
	Grade 3-4	4 ( 3.7%)	0	4 ( 1.9%)
	3	4 ( 3.7%)	0	4 ( 1.9%)
Vision blurred	- Any Grade -	5 ( 4.6%)	5 ( 4.8%)	10 ( 4.7%)
	Grade 1-2	5 ( 4.6%)	5 ( 4.8%)	10 ( 4.7%)
	1	5 ( 4.6%)	4 ( 3.8%)	9 ( 4.2%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Lacrimation increased	- Any Grade -	0	7 ( 6.7%)	7 ( 3.3%)
	Grade 1-2	0	7 ( 6.7%)	7 ( 3.3%)
	1	0	6 ( 5.8%)	6 ( 2.8%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Dry eye	- Any Grade -	0	4 ( 3.8%)	4 ( 1.9%)
	Grade 1-2	0	4 ( 3.8%)	4 ( 1.9%)
	1	0	3 ( 2.9%)	3 ( 1.4%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Eyelid oedema	- Any Grade -	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)
	Grade 1-2	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)
	1	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)
Periorbital oedema	- Any Grade -	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 1-2	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	1	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
Visual impairment	- Any Grade -	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Eye pruritus	- Any Grade -	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 1-2	0	2 ( 1.9%)	2 ( 0.9%)
	1	0	2 ( 1.9%)	2 ( 0.9%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Keratitis	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 3-4	2 ( 1.9%)	0	2 ( 0.9%)
	3	2 ( 1.9%)	0	2 ( 0.9%)
Ocular hyperaemia	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
Xerophthalmia	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Blepharospasm	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Cataract	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Corneal erosion	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Diplopia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Eye disorder	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Eye haemorrhage	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Eye pain	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Foreign body sensation in eyes	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Noninfective conjunctivitis	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Periorbital swelling	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Scleral disorder	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Swelling of eyelid	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)

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Output: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/t\_ae\_ctc\_MAIN\_SE.out

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Ulcerative keratitis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Visual acuity reduced	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Renal and urinary disorders				
- Overall -	- Any Grade -	22 (20.4%)	15 (14.4%)	37 (17.5%)
	Grade 1-2	15 (13.9%)	13 (12.5%)	28 (13.2%)
	1	8 ( 7.4%)	7 ( 6.7%)	15 ( 7.1%)
	2	7 ( 6.5%)	6 ( 5.8%)	13 ( 6.1%)
	Grade 3-4	7 ( 6.5%)	1 ( 1.0%)	8 ( 3.8%)
	3	7 ( 6.5%)	0	7 ( 3.3%)
	4	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 5	0	1 ( 1.0%)	1 ( 0.5%)
Dysuria	- Any Grade -	7 ( 6.5%)	2 ( 1.9%)	9 ( 4.2%)
	Grade 1-2	7 ( 6.5%)	2 ( 1.9%)	9 ( 4.2%)
	1	6 ( 5.6%)	1 ( 1.0%)	7 ( 3.3%)
	2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Acute kidney injury	- Any Grade -	5 ( 4.6%)	2 ( 1.9%)	7 ( 3.3%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	5 ( 4.6%)	0	5 ( 2.4%)
	3	5 ( 4.6%)	0	5 ( 2.4%)
	Grade 5	0	1 ( 1.0%)	1 ( 0.5%)
Renal failure	- Any Grade -	3 ( 2.8%)	4 ( 3.8%)	7 ( 3.3%)
	Grade 1-2	2 ( 1.9%)	3 ( 2.9%)	5 ( 2.4%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
	2	2 ( 1.9%)	2 ( 1.9%)	4 ( 1.9%)
	Grade 3-4	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
	4	0	1 ( 1.0%)	1 ( 0.5%)
Urinary retention	- Any Grade -	4 ( 3.7%)	1 ( 1.0%)	5 ( 2.4%)
	Grade 1-2	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Haematuria	- Any Grade -	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)
	Grade 1-2	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Chronic kidney disease	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Glycosuria	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Hydronephrosis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Leukocyturia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Micturition urgency	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Nephritis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Nephropathy toxic	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Proteinuria	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Renal cyst	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Renal impairment	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Renal vein thrombosis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Strangury	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Urinary tract inflammation	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Urinary tract obstruction	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Urinary tract pain	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
No Coding available				
- Overall -	- Any Grade -	23 (21.3%)	8 ( 7.7%)	31 (14.6%)
	Grade 1-2	23 (21.3%)	7 ( 6.7%)	30 (14.2%)
	1	13 (12.0%)	4 ( 3.8%)	17 ( 8.0%)
	2	10 ( 9.3%)	3 ( 2.9%)	13 ( 6.1%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
No Coding available	- Any Grade -	23 (21.3%)	8 ( 7.7%)	31 (14.6%)
	Grade 1-2	23 (21.3%)	7 ( 6.7%)	30 (14.2%)
	1	13 (12.0%)	4 ( 3.8%)	17 ( 8.0%)
	2	10 ( 9.3%)	3 ( 2.9%)	13 ( 6.1%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Psychiatric disorders				
- Overall -	- Any Grade -	16 (14.8%)	13 (12.5%)	29 (13.7%)
	Grade 1-2	14 (13.0%)	13 (12.5%)	27 (12.7%)
	1	11 (10.2%)	10 ( 9.6%)	21 ( 9.9%)
	2	3 ( 2.8%)	3 ( 2.9%)	6 ( 2.8%)
	Grade 3-4	2 ( 1.9%)	0	2 ( 0.9%)
	3	2 ( 1.9%)	0	2 ( 0.9%)
Insomnia	- Any Grade -	4 ( 3.7%)	7 ( 6.7%)	11 ( 5.2%)
	Grade 1-2	4 ( 3.7%)	7 ( 6.7%)	11 ( 5.2%)
	1	4 ( 3.7%)	5 ( 4.8%)	9 ( 4.2%)
	2	0	2 ( 1.9%)	2 ( 0.9%)
Anxiety	- Any Grade -	5 ( 4.6%)	4 ( 3.8%)	9 ( 4.2%)
	Grade 1-2	5 ( 4.6%)	4 ( 3.8%)	9 ( 4.2%)
	1	4 ( 3.7%)	3 ( 2.9%)	7 ( 3.3%)
	2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Confusional state	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Adjustment disorder with depressed mood	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Agitation	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Depressed mood	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Depression	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Irritability	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Libido decreased	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Sleep disorder	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Suicide attempt	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Injury, poisoning and procedural complications	- Overall -	13 (12.0%)	14 (13.5%)	27 (12.7%)
	- Any Grade -	8 ( 7.4%)	13 (12.5%)	21 ( 9.9%)
	Grade 1-2	6 ( 5.6%)	7 ( 6.7%)	13 ( 6.1%)
	1	2 ( 1.9%)	6 ( 5.8%)	8 ( 3.8%)
	2	5 ( 4.6%)	1 ( 1.0%)	6 ( 2.8%)
	Grade 3-4	4 ( 3.7%)	1 ( 1.0%)	5 ( 2.4%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Fall	- Any Grade -	1 ( 0.9%)	5 ( 4.8%)	6 ( 2.8%)
	Grade 1-2	0	5 ( 4.8%)	5 ( 2.4%)
	1	0	2 ( 1.9%)	2 ( 0.9%)
	2	0	3 ( 2.9%)	3 ( 1.4%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Thermal burn	- Any Grade -	0	3 ( 2.9%)	3 ( 1.4%)
	Grade 1-2	0	2 ( 1.9%)	2 ( 0.9%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Infusion related reaction	- Any Grade -	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 1-2	0	2 ( 1.9%)	2 ( 0.9%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Joint dislocation	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Rib fracture	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Skin abrasion	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
Ankle fracture	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Bone contusion	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Contusion	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Femoral neck fracture	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	4	1 ( 0.9%)	0	1 ( 0.5%)
Femur fracture	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Foot fracture	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Foreign body in eye	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Fracture displacement	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Head injury	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Injury	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Limb injury	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Pelvic fracture	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Peripancreatic fluid collection	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Procedural pain	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Radiation oedema	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Stress fracture	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Subdural haematoma	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Sunburn	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Vascular access site pain	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Cardiac disorders				
- Overall -	- Any Grade -	8 ( 7.4%)	17 (16.3%)	25 (11.8%)
	Grade 1-2	3 ( 2.8%)	13 (12.5%)	16 ( 7.5%)
	1	3 ( 2.8%)	8 ( 7.7%)	11 ( 5.2%)
	2	0	5 ( 4.8%)	5 ( 2.4%)
	Grade 3-4	3 ( 2.8%)	3 ( 2.9%)	6 ( 2.8%)
	3	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	4	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	Grade 5	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
Atrial fibrillation	- Any Grade -	2 ( 1.9%)	2 ( 1.9%)	4 ( 1.9%)
	Grade 1-2	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Palpitations	- Any Grade -	0	4 ( 3.8%)	4 ( 1.9%)
	Grade 1-2	0	4 ( 3.8%)	4 ( 1.9%)
	1	0	4 ( 3.8%)	4 ( 1.9%)
Tachycardia	- Any Grade -	0	4 ( 3.8%)	4 ( 1.9%)
	Grade 1-2	0	4 ( 3.8%)	4 ( 1.9%)
	1	0	2 ( 1.9%)	2 ( 0.9%)
	2	0	2 ( 1.9%)	2 ( 0.9%)
Angina pectoris	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Cardiac tamponade	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	4	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 5	1 ( 0.9%)	0	1 ( 0.5%)

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Output: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/t\_ae\_ctc\_MAIN\_SE.out

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Pericardial effusion	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	4	1 ( 0.9%)	0	1 ( 0.5%)
Acute myocardial infarction	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Bradycardia	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Cardio-respiratory arrest	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 5	1 ( 0.9%)	0	1 ( 0.5%)
Myocardial infarction	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 5	0	1 ( 1.0%)	1 ( 0.5%)
Myocarditis	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	4	0	1 ( 1.0%)	1 ( 0.5%)
Pericarditis	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Restrictive cardiomyopathy	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Sinus bradycardia	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Ventricular extrasystoles	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Hepatobiliary disorders	- Overall -	11 (10.2%)	14 (13.5%)	25 (11.8%)
	- Any Grade -	11 (10.2%)	14 (13.5%)	25 (11.8%)
	Grade 1-2	7 ( 6.5%)	9 ( 8.7%)	16 ( 7.5%)
	1	6 ( 5.6%)	7 ( 6.7%)	13 ( 6.1%)
	2	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	Grade 3-4	4 ( 3.7%)	5 ( 4.8%)	9 ( 4.2%)
	3	4 ( 3.7%)	5 ( 4.8%)	9 ( 4.2%)
Hypertransaminasaemia	- Any Grade -	5 ( 4.6%)	7 ( 6.7%)	12 ( 5.7%)
	Grade 1-2	5 ( 4.6%)	6 ( 5.8%)	11 ( 5.2%)
	1	5 ( 4.6%)	4 ( 3.8%)	9 ( 4.2%)
	2	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Hepatic cytolysis	- Any Grade -	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Hepatotoxicity	- Any Grade -	0	3 ( 2.9%)	3 ( 1.4%)
	Grade 1-2	0	2 ( 1.9%)	2 ( 0.9%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Cholangitis	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Cholecystitis	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 3-4	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	3	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
Hyperbilirubinaemia	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
Drug-induced liver injury	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Hepatic artery thrombosis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Hepatic failure	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Hepatitis	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Liver disorder	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Ear and labyrinth disorders	- Overall -	10 ( 9.3%)	8 ( 7.7%)	18 ( 8.5%)
	- Any Grade -	10 ( 9.3%)	8 ( 7.7%)	18 ( 8.5%)
	Grade 1-2	10 ( 9.3%)	8 ( 7.7%)	18 ( 8.5%)
	1	8 ( 7.4%)	8 ( 7.7%)	16 ( 7.5%)
	2	2 ( 1.9%)	0	2 ( 0.9%)
Vertigo	- Any Grade -	4 ( 3.7%)	4 ( 3.8%)	8 ( 3.8%)
	Grade 1-2	4 ( 3.7%)	4 ( 3.8%)	8 ( 3.8%)
	1	3 ( 2.8%)	4 ( 3.8%)	7 ( 3.3%)
	2	1 ( 0.9%)	0	1 ( 0.5%)

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AEs with onset during the cross-over period are not displayed in this output.

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Tinnitus	- Any Grade -	3 ( 2.8%)	2 ( 1.9%)	5 ( 2.4%)
	Grade 1-2	3 ( 2.8%)	2 ( 1.9%)	5 ( 2.4%)
	1	2 ( 1.9%)	2 ( 1.9%)	4 ( 1.9%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Ear pain	- Any Grade -	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 1-2	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	1	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
Deafness bilateral	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
External ear pain	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Hypoacusis	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Reproductive system and breast disorders				
- Overall -				
	- Any Grade -	11 (10.2%)	3 ( 2.9%)	14 ( 6.6%)
	Grade 1-2	10 ( 9.3%)	3 ( 2.9%)	13 ( 6.1%)
	1	9 ( 8.3%)	2 ( 1.9%)	11 ( 5.2%)
	2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Erectile dysfunction	- Any Grade -	5 ( 4.6%)	0	5 ( 2.4%)
	Grade 1-2	5 ( 4.6%)	0	5 ( 2.4%)
	1	4 ( 3.7%)	0	4 ( 1.9%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Vaginal haemorrhage	- Any Grade -	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	Grade 1-2	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
	1	2 ( 1.9%)	1 ( 1.0%)	3 ( 1.4%)
Pelvic pain	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Adnexa uteri cyst	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Benign prostatic hyperplasia	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Prostatic disorder	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Prostatitis	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Endocrine disorders	- Overall -			
	- Any Grade -	3 ( 2.8%)	10 ( 9.6%)	13 ( 6.1%)
	Grade 1-2	3 ( 2.8%)	9 ( 8.7%)	12 ( 5.7%)
	1	2 ( 1.9%)	2 ( 1.9%)	4 ( 1.9%)
	2	1 ( 0.9%)	7 ( 6.7%)	8 ( 3.8%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Hypothyroidism	- Any Grade -	3 ( 2.8%)	9 ( 8.7%)	12 ( 5.7%)
	Grade 1-2	3 ( 2.8%)	8 ( 7.7%)	11 ( 5.2%)
	1	2 ( 1.9%)	4 ( 3.8%)	6 ( 2.8%)
	2	1 ( 0.9%)	4 ( 3.8%)	5 ( 2.4%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Hyperthyroidism	- Any Grade -	0	3 ( 2.9%)	3 ( 1.4%)
	Grade 1-2	0	3 ( 2.9%)	3 ( 1.4%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	2 ( 1.9%)	2 ( 0.9%)
Hypophysitis	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	- Overall -			
	- Any Grade -	6 ( 5.6%)	6 ( 5.8%)	12 ( 5.7%)
	Grade 1-2	4 ( 3.7%)	3 ( 2.9%)	7 ( 3.3%)
	1	3 ( 2.8%)	1 ( 1.0%)	4 ( 1.9%)
	2	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	Grade 3-4	2 ( 1.9%)	3 ( 2.9%)	5 ( 2.4%)
	3	2 ( 1.9%)	3 ( 2.9%)	5 ( 2.4%)
Anogenital warts	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	2 ( 1.9%)	0	2 ( 0.9%)
Cancer pain	- Any Grade -	1 ( 0.9%)	1 ( 1.0%)	2 ( 0.9%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Anal cancer	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Endometrial adenocarcinoma	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Lipoma	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Neoplasm	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
Non-small cell lung cancer	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Paraneoplastic syndrome	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Skin papilloma	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	2	0	1 ( 1.0%)	1 ( 0.5%)
Tumour pain	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 3-4	0	1 ( 1.0%)	1 ( 0.5%)
	3	0	1 ( 1.0%)	1 ( 0.5%)
Immune system disorders				
- Overall -	- Any Grade -	1 ( 0.9%)	2 ( 1.9%)	3 ( 1.4%)
	Grade 1-2	0	2 ( 1.9%)	2 ( 0.9%)
	1	0	2 ( 1.9%)	2 ( 0.9%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Contrast media reaction	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Drug hypersensitivity	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Immune system disorder	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Surgical and medical procedures				
- Overall -	- Any Grade -	2 ( 1.9%)	0	2 ( 0.9%)
	Grade 1-2	2 ( 1.9%)	0	2 ( 0.9%)
	1	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Abdominal cavity drainage	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	2	1 ( 0.9%)	0	1 ( 0.5%)
Tooth extraction	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 1-2	1 ( 0.9%)	0	1 ( 0.5%)
	1	1 ( 0.9%)	0	1 ( 0.5%)

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Adverse Events by System Organ Class and Preferred Term and by Highest NCI CTCAE Grade - Main Treatment Period, Safety-Evaluable Patients  
Protocol: BO42864

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MedDRA System Organ Class MedDRA Preferred Term	Grade	Pralsetinib (N=108)	Standard of Care (N=104)	All Patients (N=212)
Congenital, familial and genetic disorders				
- Overall -	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Hydrocele	- Any Grade -	0	1 ( 1.0%)	1 ( 0.5%)
	Grade 1-2	0	1 ( 1.0%)	1 ( 0.5%)
	1	0	1 ( 1.0%)	1 ( 0.5%)
Product issues				
- Overall -	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)
Device dislocation	- Any Grade -	1 ( 0.9%)	0	1 ( 0.5%)
	Grade 3-4	1 ( 0.9%)	0	1 ( 0.5%)
	3	1 ( 0.9%)	0	1 ( 0.5%)

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Listing of Baseline Neutrophil and Lymphocyte Lab Values and Medical History of Neutropenia and Lymphopenia events for Patients with  
 Grade 3-5 Infections  
 Protocol: BO42864  
 Snapshot date: 12th July 2024

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race Lab Test Name	Visit Name	Lab Result	Standard Lab Units	Reference Range Low	Reference Range High	History of Neutropenia or Lymphopenia
3301/008 - 67/F/Asian Lymphocytes	CYCLE 1 DAY 1	D				
Neutrophils	CYCLE 1 DAY 1	5.78	10 <sup>9</sup> /L	1.8	7.8	
3302/004 - 71/M/Asian Lymphocytes	SCREENING	0.71	10 <sup>9</sup> /L	1.1	4.1	
Neutrophils	SCREENING	6.12	10 <sup>9</sup> /L	1.7	7	
3302/005 - 74/M/Asian Lymphocytes	CYCLE 1 DAY 1	1.73	10 <sup>9</sup> /L	1.1	4.1	
Neutrophils	CYCLE 1 DAY 1	5.35	10 <sup>9</sup> /L	1.7	7	
3302/007 - 52/F/Asian Lymphocytes	SCREENING	1.02	10 <sup>9</sup> /L	1.1	4.1	
Neutrophils	SCREENING	8.57	10 <sup>9</sup> /L	1.6	7	
3302/012 - 57/M/Asian Lymphocytes	SCREENING	2.3	10 <sup>9</sup> /L	1.1	4.1	
Neutrophils	SCREENING	5.26	10 <sup>9</sup> /L	1.7	7	
3302/013 - 67/F/Asian Lymphocytes	CYCLE 1 DAY 1	1.98	10 <sup>9</sup> /L	1.1	4.1	
Neutrophils	CYCLE 1 DAY 1	9.44	10 <sup>9</sup> /L	1.6	7	
4201/002 - 76/F/Unknown Lymphocytes	SCREENING	2.1	10 <sup>9</sup> /L	1	4	
Neutrophils	SCREENING	4.47	10 <sup>9</sup> /L	1.8	7.5	
4202/001 - 77/F/White Lymphocytes	CYCLE 1 DAY 1	1.36	10 <sup>9</sup> /L	1.5	4	
Neutrophils	CYCLE 1 DAY 1	6.86	10 <sup>9</sup> /L	1.5	7	
4206/001 - 71/F/NOT REPORTED Lymphocytes	CYCLE 1 DAY 1	2.25	10 <sup>9</sup> /L	1	4	
Neutrophils	CYCLE 1 DAY 1	4.05	10 <sup>9</sup> /L	1.8	7.5	
4208/004 - 73/F/Other Lymphocytes	CYCLE 1 DAY 1	2.1	10 <sup>9</sup> /L	1.2	4	
Neutrophils	CYCLE 1 DAY 1	4.5	10 <sup>9</sup> /L	1.5	7	

Patients with Grade 3-5 Infections during the main period of treatment are included in this output

Program: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/program/l\_inf3.sas

Output: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/l\_inf3\_SE\_12JUL2024\_42864.out

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Listing of Baseline Neutrophil and Lymphocyte Lab Values and Medical History of Neutropenia and Lymphopenia events for Patients with  
 Grade 3-5 Infections  
 Protocol: BO42864  
 Snapshot date: 12th July 2024

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race Lab Test Name	Visit Name	Lab Result	Standard Lab Units	Reference Range Low	Reference Range High	History of Neutropenia or Lymphopenia
4307/004 - 59/F/White Lymphocytes	CYCLE 1 DAY 1	1.53	10 <sup>9</sup> /L	1.5	4	
Neutrophils	CYCLE 1 DAY 1	5.4	10 <sup>9</sup> /L	1.8	7.55	
4404/003 - 57/M/White Lymphocytes	CYCLE 1 DAY 1	2.07	10 <sup>9</sup> /L	1.1	4.5	
Neutrophils	CYCLE 1 DAY 1	4.25	10 <sup>9</sup> /L	1.5	7.7	
4404/005 - 53/M/White Lymphocytes	CYCLE 1 DAY 1	1.69	10 <sup>9</sup> /L	1.1	4.5	
Neutrophils	CYCLE 1 DAY 1	5.52	10 <sup>9</sup> /L	1.5	7.7	
4404/011 - 71/M/White Lymphocytes	CYCLE 1 DAY 1	1.41	10 <sup>9</sup> /L	1.1	4	
Neutrophils	CYCLE 1 DAY 1	4.86	10 <sup>9</sup> /L	1.5	7.7	
4406/003 - 53/M/White Lymphocytes	CYCLE 1 DAY 1	0.7	10 <sup>9</sup> /L	1	4.8	
Neutrophils	CYCLE 1 DAY 1	5.7	10 <sup>9</sup> /L	1.8	7.7	
4410/008 - 65/M/White Lymphocytes	CYCLE 1 DAY 1	1.82	10 <sup>9</sup> /L	1.13	3.37	
Neutrophils	CYCLE 1 DAY 1	3.88	10 <sup>9</sup> /L	1.81	6.74	
4508/002 - 79/F/White Lymphocytes	CYCLE 1 DAY 1	1.7	10 <sup>9</sup> /L	1.2	3.5	
Neutrophils	CYCLE 1 DAY 1	13.8	10 <sup>9</sup> /L	2	7	
4508/003 - 72/M/White Lymphocytes	CYCLE 1 DAY 1	6.6	10 <sup>9</sup> /L	1.2	3.5	
Neutrophils	CYCLE 1 DAY 1	6.7	10 <sup>9</sup> /L	2	7	
4517/001 - 58/M/White Lymphocytes	SCREENING	1.77	10 <sup>9</sup> /L	1.2	3.4	
Neutrophils	SCREENING	2.95	10 <sup>9</sup> /L	1.5	7.5	
4601/001 - 61/F/White Lymphocytes	CYCLE 1 DAY 1	1.29	10 <sup>9</sup> /L	1.5	4	
Neutrophils	CYCLE 1 DAY 1	4.99	10 <sup>9</sup> /L	1.4	8	

Patients with Grade 3-5 Infections during the main period of treatment are included in this output

Program: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/program/l\_inf3.sas

Output: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/l\_inf3\_SE\_12JUL2024\_42864.out

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Listing of Baseline Neutrophil and Lymphocyte Lab Values and Medical History of Neutropenia and Lymphopenia events for Patients with  
 Grade 3-5 Infections  
 Protocol: BO42864  
 Snapshot date: 12th July 2024

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race Lab Test Name	Visit Name	Lab Result	Standard Lab Units	Reference Range Low	Reference Range High	History of Neutropenia or Lymphopenia
4601/003 - 68/F/White Lymphocytes	SCREENING	0.57	10 <sup>9</sup> /L	1.5	4	
Neutrophils	SCREENING	4	10 <sup>9</sup> /L	1.4	8	
4701/001 - 33/F/White Lymphocytes	CYCLE 1 DAY 1	1.1	10 <sup>9</sup> /L	1.5	4	
Neutrophils	CYCLE 1 DAY 1	12.3	10 <sup>9</sup> /L	2	7.5	
4703/002 - 51/F/Unknown Lymphocytes	CYCLE 1 DAY 1	3.1	10 <sup>9</sup> /L	1.2	3.5	
Neutrophils	CYCLE 1 DAY 1	17.4	10 <sup>9</sup> /L	1.5	7	
4801/002 - 54/F/White Lymphocytes	CYCLE 1 DAY 1	0.8	10 <sup>9</sup> /L	1.5	3.5	
Neutrophils	CYCLE 1 DAY 1	12.6	10 <sup>9</sup> /L	2	7.5	
7201/001 - 70/F/American Indian or Alaska Native Lymphocytes	SCREENING	1.15	10 <sup>9</sup> /L	1	5	
Neutrophils	SCREENING	15.64	10 <sup>9</sup> /L	2.5	7.725	
7301/006 - 64/M/American Indian or Alaska Native Lymphocytes	CYCLE 1 DAY 1	1.45	10 <sup>9</sup> /L	0.9	2.9	
Neutrophils	CYCLE 1 DAY 1	6.49	10 <sup>9</sup> /L	1.7	7	
7301/012 - 65/F/American Indian or Alaska Native Lymphocytes	SCREENING	0.37	10 <sup>9</sup> /L	0.9	2.9	
Neutrophils	SCREENING	2.08	10 <sup>9</sup> /L	1.7	7	
8411/001 - 75/M/Asian Lymphocytes	SCREENING	1.305	10 <sup>9</sup> /L	1	5	
Neutrophils	SCREENING	4.147	10 <sup>9</sup> /L	1	8	

Patients with Grade 3-5 Infections during the main period of treatment are included in this output

Program: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/program/l\_inf3.sas

Output: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/l\_inf3\_SE\_12JUL2024\_42864.out

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Listing of Baseline Neutrophil and Lymphocyte Lab Values and Medical History of Neutropenia and Lymphopenia events for Patients with  
 Grade 3-5 Infections  
 Protocol: BO42864  
 Snapshot date: 12th July 2024

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race Lab Test Name	Visit Name	Lab Result	Standard Lab Units	Reference Range Low	Reference Range High	History of Neutropenia or Lymphopenia
4404/007 - 48/M/White Lymphocytes	CYCLE 1 DAY 1	0.94	10 <sup>9</sup> /L	1.1	4.5	
Neutrophils	CYCLE 1 DAY 1	6.26	10 <sup>9</sup> /L	1.5	7.7	
4503/001 - 63/F/White Lymphocytes	CYCLE 1 DAY 1	1.6	10 <sup>9</sup> /L	1.1	3.5	
Neutrophils	CYCLE 1 DAY 1	6.58	10 <sup>9</sup> /L	1.8	7.4	
4505/002 - 83/F/White Lymphocytes	SCREENING	0.5	10 <sup>9</sup> /L	1.3	3.5	
Neutrophils	SCREENING	2.5	10 <sup>9</sup> /L	1.8	7.5	
4508/001 - 64/F/White Lymphocytes	SCREENING	0.8	10 <sup>9</sup> /L	1.2	3.5	
Neutrophils	SCREENING	6.4	10 <sup>9</sup> /L	2	7	
4512/002 - 70/M/White Lymphocytes	CYCLE 1 DAY 1	2.1	10 <sup>9</sup> /L	1.2	5	
Neutrophils	CYCLE 1 DAY 1	5.3	10 <sup>9</sup> /L	1.4	7.5	
4706/001 - 74/M/Other Lymphocytes	CYCLE 1 DAY 1	1	10 <sup>9</sup> /L	1	4.5	
Neutrophils	CYCLE 1 DAY 1	7.3	10 <sup>9</sup> /L	1.7	7.5	
5203/003 - 74/M/White Lymphocytes	CYCLE 1 DAY 1					
Neutrophils	CYCLE 1 DAY 1	2.8	10 <sup>9</sup> /L	1.4	7.7	
8001/003 - 43/M/Asian Lymphocytes	SCREENING	1	10 <sup>9</sup> /L	1	4	
Neutrophils	SCREENING	7.3	10 <sup>9</sup> /L	2	8	

Patients with Grade 3-5 Infections during the main period of treatment are included in this output

Program: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/program/l\_inf3.sas

Output: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/l\_inf3\_SE\_12JUL2024\_42864.out

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Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race Medication Name	Medication Start Date	Medication End Date	Study Start Day	Study End Day	Dose	Frequency	Route of Administration	Indication
3301/008 - 67/F/Asian METHYLPREDNISOLONE PREDNISOLONE	09JAN2024 18JAN2024	17JAN2024 27JAN2024	85 94	93 103	QD QD		INTRAVENOUS ORAL	ADVERSE EVENT ADVERSE EVENT
3302/007 - 52/F/Asian PREDNISOLONE	19MAY2022	27MAY2022	178	186	QD		ORAL	ADVERSE EVENT
METHYLPREDNISOLONE SODIUM SUCCINATE	27MAY2022	31MAY2022	186	190	BID		INTRAVENOUS	ADVERSE EVENT
METHYLPREDNISOLONE SODIUM SUCCINATE	20JUN2022	21JUN2022	210	211	QD		INTRAVENOUS	ADVERSE EVENT
METHYLPREDNISOLONE SODIUM SUCCINATE	22JUN2022	27JUN2022	212	217	BID		INTRAVENOUS	ADVERSE EVENT
METHYLPREDNISOLONE SODIUM SUCCINATE	28JUN2022	30JUN2022	218	220	QD		INTRAVENOUS	ADVERSE EVENT
METHYLPREDNISOLONE SODIUM SUCCINATE	30JUN2022	05JUL2022	220	225	BID		INTRAVENOUS	ADVERSE EVENT
4517/001 - 58/M/White BECLOMETASONE DIPROPIONATE;FORMOTEROL FUMARATE	01JUN2020	17MAY2021	-143	208	QD		RESPIRATORY (INHALATION)	MEDICAL HISTORY
BUDESONIDE	06DEC2020	09DEC2020	46	49	PRN		RESPIRATORY (INHALATION)	ADVERSE EVENT
BUDESONIDE	17MAR2021	20MAR2021	147	150	BID		RESPIRATORY (INHALATION)	ADVERSE EVENT
DEXAMETHASONE	24JUN2021	24JUN2021	246	246	QD		INTRAVENOUS	ADVERSE EVENT
PREDNISONE	25JUN2021	08AUG2021	247	291	QD		ORAL	ADVERSE EVENT
BUDESONIDE	30NOV2021	31DEC2021	405	436	BID		NASAL	ADVERSE EVENT
METHYLPREDNISOLONE	30NOV2021	01DEC2021	405	406	TID		INTRAVENOUS	ADVERSE EVENT
PREDNISONE	01DEC2021	03DEC2021	406	408	QD		INTRAVENOUS	ADVERSE EVENT
4801/002 - 54/F/White FLUTICASONE FUROATE:VILANTEROL TRIFENATATE	01DEC2021		-68*		QD		RESPIRATORY (INHALATION)	MEDICAL HISTORY
FLUTICASONE FUROATE	01JAN2022		-37*		PRN		NASAL	MEDICAL HISTORY
DEXAMETHASONE	18JAN2022		-20		QD		ORAL	MEDICAL HISTORY
DEXAMETHASONE	11APR2022	19APR2022	64	72	BID		INTRAVENOUS	ADVERSE EVENT
DEXAMETHASONE	21APR2022	22APR2022	74	75	QD		ORAL	ADVERSE EVENT
7301/006 - 64/M/American Indian or Alaska Native CICLESONIDE	29OCT2022	17DEC2023	-39	376	QD		RESPIRATORY (INHALATION)	MEDICAL HISTORY
PREDNISONE	08MAY2023	17MAY2023	153	162	QD		ORAL	ADVERSE EVENT
BUDESONIDE	06SEP2023		274		BID		RESPIRATORY (INHALATION)	ADVERSE EVENT
8411/001 - 75/M/Asian METHYLPREDNISOLONE SODIUM SUCCINATE	26OCT2022	28OCT2022	69	71	QD		IV	ADVERSE EVENT
PREDNISOLONE	29OCT2022	14NOV2022	72	88	QD		IV	ADVERSE EVENT
PREDNISOLONE	15NOV2022	23DEC2022	89	127	QD		ORAL	ADVERSE EVENT

\* Study day derived from imputed medication start date.

Patients with only Opportunistic Infections AEs with onset during the cross-over period are not considered in this output

Program: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/program/l\_cm\_oppinf.sas  
Output: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/l\_cm\_oppinf\_SE\_12JUL2024\_42864.out  
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Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race	Adverse Event MedDRA	Date of First Study Administration	AE	Most Extreme	Action Taken					
System Organ Class	Preferred Term	Study Drug	Day of Onset	Duration in Days	Crossover phase	Serious	CTCAE Grade	Caused by Study Drug	Outcome (1)	Action Taken (2)
3302/004 - 71/M/Asian Investigations Neutrophil count decreased		27APR2021	262	No	No	4	No	2	6	
3302/007 - 52/F/Asian Investigations Lymphocyte count decreased		23NOV2021	44	21	No	No	2	Yes	3	2
4201/002 - 76/F/Unknown Blood and lymphatic system disorders Lymphopenia		03MAY2023	21	5	No	No	1	Yes	3	2
4202/001 - 77/F/White Investigations Neutrophil count decreased		12MAY2021	20	10	No	No	3	Yes	3	3
4208/004 - 73/F/Other Blood and lymphatic system disorders Lymphopenia		08NOV2022	86	28**	No	No	1	Yes	3	2
4307/004 - 59/F/White Investigations Neutrophil count decreased		21APR2021	21	43	No	No	3	Yes	3	3
Investigations Neutrophil count decreased		21APR2021	85	41	No	No	2	Yes	3	2
Investigations Neutrophil count decreased		21APR2021	126	28	No	No	1	Yes	3	2
Investigations Neutrophil count decreased		21APR2021	154	22	No	No	2	Yes	3	2
Investigations Neutrophil count decreased		21APR2021	301	21	No	No	2	Yes	3	2
Investigations Neutrophil count decreased		21APR2021	343	64	No	No	2	Yes	3	2

Notes: Adverse Events are coded using MedDRA 27.0

For patients who crossed over, date of first Study Drug Administration is provided for the standard of care treatment in the main treatment period and for Pralsetinib in the crossover treatment period.

(1) Outcome: 1 = fatal; 2 = not recovered/not resolved; 3 = recovered/resolved; 4 = recovered/resolved with sequelae; 5 = recovering/resolving; 6 = unknown.

(2) Action taken: 1 = dose increased; 2 = dose not changed; 3 = dose reduced; 4 = drug interrupted; 5 = drug withdrawn; 6 = not applicable; 7 = unknown.

\* Study day derived from imputed onset date

\*\* Duration derived from imputed onset date and/or end date

Patients with Grade 3-5 Infections during the main period of treatment are included in this output

Program: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/program/l\_ae\_inf3.sas

Output: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/l\_ae\_inf3\_NEULYMPH\_SE\_12JUL2024\_42864.out

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## Listing of Neutropenia and Lymphopenia events for Patients with Grade 3-5 Infections

Protocol: BO42864

Snapshot date: 12th July 2024

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race	Adverse Event MedDRA	Date of First Study Administration	AE	Most Extreme	Action Taken			
System Organ Class Preferred Term	Study Drug	Day of Onset	Duration in Days	Crossover phase	CTCAE Grade	Caused by Study Drug	Outcome (1)	Outcome (2)
<b>4404/003 - 57/M/White</b>								
Blood and lymphatic system disorders								
Neutropenia		23DEC2020	23	22	No	No	2	Yes 3 2
Blood and lymphatic system disorders								
Neutropenia		23DEC2020	86		No	No	2	Yes 5 2
<b>4404/005 - 53/M/White</b>								
Blood and lymphatic system disorders								
Neutropenia		14APR2021	434		No	No	3	Yes 5 2
<b>4410/008 - 65/M/White</b>								
Blood and lymphatic system disorders								
Neutropenia		06MAR2023	117	8	No	No	3	Yes 3 4
Blood and lymphatic system disorders								
Neutropenia		06MAR2023	169	22	No	No	2	Yes 3 2
<b>4517/001 - 58/M/White</b>								
Blood and lymphatic system disorders								
Neutropenia		22OCT2020	161	7	No	No	3	No 3 2
Blood and lymphatic system disorders								
Neutropenia		22OCT2020	610	26	No	No	2	Yes 3 4
<b>4801/002 - 54/F/White</b>								
Investigations								
Neutrophil count decreased		07FEB2022	218	22	No	No	2	No 3 2
Investigations								
Neutrophil count decreased		07FEB2022	242	14	No	No	3	No 3 2
Investigations								
Neutrophil count decreased		07FEB2022	247	9	No	No	3	No 3 2
Investigations								
Neutrophil count decreased		07FEB2022	372	22	No	No	2	No 3 2

Notes: Adverse Events are coded using MedDRA 27.0

For patients who crossed over, date of first Study Drug Administration is provided for the standard of care treatment in the main treatment period and for Pralsetinib in the crossover treatment period.

(1) Outcome: 1 = fatal; 2 = not recovered/not resolved; 3 = recovered/resolved; 4 = recovered/resolved with sequelae; 5 = recovering/resolving; 6 = unknown.

(2) Action taken: 1 = dose increased; 2 = dose not changed; 3 = dose reduced; 4 = drug interrupted; 5 = drug withdrawn; 6 = not applicable; 7 = unknown.

\* Study day derived from imputed onset date

\*\* Duration derived from imputed onset date and/or end date

Patients with Grade 3-5 Infections during the main period of treatment are included in this output

Program: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/program/l\_ae\_inf3.sas

Output: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/l\_ae\_inf3\_NEULYMPH\_SE\_12JUL2024\_42864.out

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## Listing of Neutropenia and Lymphopenia events for Patients with Grade 3-5 Infections

Protocol: BO42864

Snapshot date: 12th July 2024

Treatment: Pralsetinib (N=108)

Center/Patient ID - Age/Sex/Race		Adverse Event MedDRA	Date of First Study Administration	AE	Most Extreme				Action Taken (2)					
System Organ Class	Preferred Term				Study Drug	Day of Onset	Duration in Days	Crossover phase	Serious	CTCAE Grade	Caused by Study Drug	Outcome (1)		
7201/001 - 70/F/American Indian or Alaska Native														
Blood and lymphatic system disorders														
Lymphopenia														
8411/001 - 75/M/Asian														
Investigations														
Neutrophil count decreased														

Notes: Adverse Events are coded using MedDRA 27.0

For patients who crossed over, date of first Study Drug Administration is provided for the standard of care treatment in the main treatment period and for Pralsetinib in the crossover treatment period.

(1) Outcome: 1 = fatal; 2 = not recovered/not resolved; 3 = recovered/resolved; 4 = recovered/resolved with sequelae; 5 = recovering/resolving; 6 = unknown.

(2) Action taken: 1 = dose increased; 2 = dose not changed; 3 = dose reduced; 4 = drug interrupted; 5 = drug withdrawn; 6 = not applicable; 7 = unknown.

\* Study day derived from imputed onset date

\*\* Duration derived from imputed onset date and/or end date

Patients with Grade 3-5 Infections during the main period of treatment are included in this output

Program: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/program/l\_ae\_inf3.sas

Output: root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/l\_ae\_inf3\_NEULYMPH\_SE\_12JUL2024\_42864.out

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## Listing of Neutropenia and Lymphopenia events for Patients with Grade 3-5 Infections

Protocol: BO42864

Snapshot date: 12th July 2024

Treatment: Standard of Care (N=104)

Center/Patient ID - Age/Sex/Race	Adverse Event MedDRA	Date of First Study Administration	AE	Most Extreme	Action			
System Organ Class Preferred Term	Study Drug	Day of Onset	Duration in Days	Crossover phase	CTCAE Grade	Caused by Study Drug	Outcome (1)	Action Taken (2)
4503/001 - 63/F/White Blood and lymphatic system disorders Lymphopenia		09MAR2023	22	No	No	2	Yes	5
4505/002 - 83/F/White Investigations Neutrophil count decreased		09JUN2022	22	8	No	No	1	Yes
Investigations Neutrophil count decreased		09JUN2022	50	7	No	No	3	Yes
Investigations Neutrophil count decreased		09JUN2022	78	15	No	No	2	Yes
Investigations Neutrophil count decreased		09JUN2022	134	29	No	No	2	Yes
4512/002 - 70/M/White Blood and lymphatic system disorders Neutropenia		03MAY2022	53	25	No	No	3	Yes

Notes: Adverse Events are coded using MedDRA 27.0

For patients who crossed over, date of first Study Drug Administration is provided for the standard of care treatment in the main treatment period and for Pralsetinib in the crossover treatment period.

(1) Outcome: 1 = fatal; 2 = not recovered/not resolved; 3 = recovered/resolved; 4 = recovered/resolved with sequelae; 5 = recovering/resolving; 6 = unknown.

(2) Action taken: 1 = dose increased; 2 = dose not changed; 3 = dose reduced; 4 = drug interrupted; 5 = drug withdrawn; 6 = not applicable; 7 = unknown.

\* Study day derived from imputed onset date

\*\* Duration derived from imputed onset date and/or end date

Patients with Grade 3-5 Infections during the main period of treatment are included in this output

Program: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/program/l\_ae\_inf3.sas

Output: root/clinical\_studies/R07499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/l\_ae\_inf3\_NEULYMPH\_SE\_12JUL2024\_42864.out

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## Appendix 2    Overview of Subjects with Grade 3 and 4 Infections in AcceleRET-Lung study

The below Table presents an overview of Subjects with Grade 3 and Grade 4 Infections in Pralsetinib Treatment Arm of the AcceleRET-Lung study (N=23)

Patient number Age/Sex Ethnicity/Country Indication	MedDRA PT (Grading) Time to Event Onset (in days) Outcome	Action taken with Pralsetinib Causality (as per investigator)
3301/008 67/Female Asian/ Korea, Republic Of Non-small cell lung cancer	Pneumonia cytomegaloviral (Grade 3) SD 85 Resolved	Drug interrupted Related
3302/004 71/ Male Asian/ Korea, republic Of Small cell lung cancer	Pleural infection (Grade 3) SD 204 Resolved	Drug interrupted Not related
	Device related infection (Grade 3) SD 214 Resolved	Dose not changed Not related
3302/005 74/Male Asian/ Korea, republic Of Non-small cell lung cancer	Pneumonia (Grade 3) SD 65 Not resolved	Drug withdrawn Not related
3302/007 52/Female Asian/ Korea, republic Of Non-small cell lung cancer metastatic	Pneumocystis jirovecii pneumonia (Grade 3) SD 161 Resolved with sequelae	Drug interrupted Not related
	Pneumonia cytomegaloviral (Grade 3) SD 161 Not resolved	Drug withdrawn Not related
3302/013 67/Female Asian// Korea, republic Of Non-small cell lung cancer metastatic	Pneumonia (Grade 3) SD 67 Resolved	Drug interrupted Not related
	Pyelonephritis acute (Grade 3) SD 67 Resolved	Drug interrupted Not related

Patient number Age/Sex Ethnicity/Country Indication	MedDRA PT (Grading) Time to Event Onset (in days) Outcome	Action taken with Pralsetinib Causality (as per investigator)
4202/001 77/Female White/ France Non-small cell lung cancer	Staphylococcal sepsis (Grade 3) SD 290 Resolved	Dose not changed Not related
4206/001 71/Female Unknown/ France Non-small cell lung cancer	Pyelonephritis (Grade 3) SD 48 Resolved Pyelonephritis (Grade 3) SD 96 Resolved with sequelae	Dose not changed Related Dose reduced Related
4208/004 73/Female	Oesophageal infection (Grade 3) SD 52 Resolved	Dose not changed Related
4307/004 59/Female White	Pneumonia (Grade 3) SD 825 Resolved	Not applicable Related
4404/003 57/Male White/ Italy Non-small cell lung cancer metastatic	Herpes Zoster (Grade 3) SD 888 Resolved Spontaneous bacterial peritonitis (Grade 3) SD 888 Resolved	Drug interrupted Not related Drug interrupted Not related
4404/011 71/Male White/ Italy Non-small cell lung cancer metastatic	Q fever (Grade 3) SD 406 Resolved Pneumonia (Grade 3) SD 636 Not resolved	Drug interrupted Not related Drug interrupted Not related
4406/003 53/Male White/ Italy Non-small cell lung cancer metastatic	Urinary tract infection (Grade 3) SD 568 Resolving	Dose not changed Not related

Patient number Age/Sex Ethnicity/Country Indication	MedDRA PT (Grading) Time to Event Onset (in days) Outcome	Action taken with Pralsetinib Causality (as per investigator)
4410/008 65/Male White/Italy Non-small cell lung cancer metastatic	Pneumonia legionella (Grade 3) SD 26 Resolved with sequelae  Pneumonia (Grade 3) SD 58 Not resolved	Drug interrupted Not related  Drug interrupted Not related
4508/002 79/Female White	Infection (Grade 3) SD 89 Resolving	Dose not changed Not related
4517/001 58/Male White	Urinary tract infection (Grade 3) SD 1001 Resolved  Bronchopulmonary aspergillosis (Grade 3) SD 148 Resolved	Dose not changed Not related  Dose not changed Not related
4601/001 61/Female White/Switzerland Non-small cell lung cancer metastatic	Pneumonia (Grade 3) SD 568 Resolved	Dose not changed Not related
4601/003 68/Female White/Switzerland Non-small cell lung cancer metastatic	Herpes Zoster (Grade 3) SD 32 Resolved	Dose not changed Not related
4801/002 54/Female White/ United Kingdom Non-small cell lung cancer metastatic	Pneumocystis jirovecii pneumonia (Grade 3) SD 55 Resolved	Dose reduced Related
7301/006 64/Male American Indian or Alaska Native	Oesophageal candidiasis (Grade 3) SD 280 Resolved  Pneumonia (Grade 3) SD 368 Resolved	Dose not changed Not related  Dose not changed Related

Patient number Age/Sex Ethnicity/Country Indication	MedDRA PT (Grading) Time to Event Onset (in days) Outcome	Action taken with Pralsetinib Causality (as per investigator)
4404/005 53/Male White/ Italy Non-small cell lung cancer metastatic	Device related infection (Grade 4) SD 20 Resolved	Drug Interrupted Not related
4703/002 51/Female Unknown/ United Kingdom Non-small cell lung cancer metastatic	Sepsis (Grade 4) SD 41 Not resolved	Dose not changed Not related
7301/012 65/ Female American Indian or Alaska Native/ Mexico Non-small cell lung cancer metastatic	Urosepsis (Grade 4) SD 35 Not resolved	Drug Interrupted Related
8411/001 Japan Non-small cell lung cancer metastatic	Pneumocystis jirovecii pneumonia (Grade 4) SD 66 Resolved	Drug withdrawn Related

MedDRA Version 27.0. SD: Study Day

Clinical Output Source:

root/clinical\_studies/RO7499790/CDT30380/BO42864/data\_analysis/Adhoc\_Analysis/prod/output/l\_ae\_INVI  
NF\_SE.out

### Appendix 3      Overview of Grade 3-5 Infection AEs by MedDRA PT in ARROW Study

The below Table (continued from [Table 11](#)) summarizes the Grade 3-5 infection AEs by MedDRA PT which were observed in ARROW study. The below mentioned AEs reported a frequency of < 1%.

MedDRA PT	Total Number of Patients (N=590)			
	Grade 3 AE (%)	Grade 4 AE (%)	Grade 5* AE (%)	Total* (%)
Patients with SAEs	125 (21.2)	19 (3.2)	24 (4.1))	183 (31.0)
Bacteraemia	3 (< 1)	0	0	5 (< 1)
Appendicitis	4 (< 1)	0	0	4 (< 1)
Cellulitis	3 (< 1)	0	0	4 (< 1)
Clostridium difficile colitis	4 (< 1)	0	0	4 (< 1)
Pyelonephritis	4 (< 1)	0	0	4 (< 1)
Urosepsis	1 (< 1)	2 (< 1)	1 (< 1)	4 (< 1)
Gastroenteritis	2 (< 1)	0	0	3 (< 1)
Herpes zoster	3 (< 1)	0	0	3 (< 1)
Lung infection	3 (< 1)	0	0	3 (< 1)
Pneumonia influenzal	1 (< 1)	0	0	3 (< 1)
Upper respiratory tract infection	2 (< 1)	0	0	3 (< 1)
Urinary tract infection bacterial	3 (< 1)	0	0	3 (< 1)
Escherichia sepsis	2 (< 1)	0	0	2 (< 1)
Escherichia urinary tract infection	0	0	0	2 (< 1)
Hepatitis B	2 (< 1)	0	0	2 (< 1)
Lymph node tuberculosis	1 (< 1)	0	0	2 (< 1)
Pneumonia legionella	2 (< 1)	0	0	2 (< 1)
Pneumonia staphylococcal	2 (< 1)	0	0	2 (< 1)
Pneumonia viral	1 (< 1)	1 (< 1)	0	2 (< 1)
Respiratory tract infection	2 (< 1)	0	0	2 (< 1)

MedDRA PT	Total Number of Patients (N=590)			
	Grade 3 AE (%)	Grade 4 AE (%)	Grade 5* AE (%)	Total* (%)
Septic shock	0	2 (< 1)	0	2 (< 1)
Skin infection	1 (< 1)	0	0	2 (< 1)
Abdominal infection	1 (< 1)	0	0	1 (< 1)
Appendicitis perforated	1 (< 1)	0	0	1 (< 1)
Arthritis bacterial	1 (< 1)	0	0	1 (< 1)
Arthritis infective	1 (< 1)	0	0	1 (< 1)
Atypical mycobacterial pneumonia	1 (< 1)	0	0	1 (< 1)
Bronchitis	1 (< 1)	0	0	1 (< 1)
Bronchitis bacterial	1 (< 1)	0	0	1 (< 1)
Bronchopulmonary aspergillosis	0	0	0	1 (< 1)
Cellulitis of male external genital organ	1 (< 1)	0	0	1 (< 1)
Cholecystitis infective	1 (< 1)	0	0	1 (< 1)
Cystitis	1 (< 1)	0	0	1 (< 1)
Device related infection	1 (< 1)	0	0	1 (< 1)
Empyema	1 (< 1)	0	0	1 (< 1)
Enterobacter bacteraemia	1 (< 1)	0	0	1 (< 1)
Enterococcal bacteraemia	1 (< 1)	0	0	1 (< 1)
Epididymitis	1 (< 1)	0	0	1 (< 1)
Escherichia bacteraemia	0	0	0	1 (< 1)
Infectious colitis	1 (< 1)	0	0	1 (< 1)
Influenza	1 (< 1)	0	0	1 (< 1)
Kidney infection	1 (< 1)	0	0	1 (< 1)
Klebsiella bacteraemia	1 (< 1)	0	0	1 (< 1)
Lower respiratory tract infection	1 (< 1)	0	0	1 (< 1)
Meningitis	0	0	1 (< 1)	1 (< 1)

MedDRA PT	Total Number of Patients (N=590)			
	Grade 3 AE (%)	Grade 4 AE (%)	Grade 5* AE (%)	Total* (%)
Meningitis enterococcal	0	1 (< 1)	0	1 (< 1)
Neutropenic sepsis	0	1 (< 1)	0	1 (< 1)
Oropharyngeal candidiasis	1 (< 1)	0	0	1 (< 1)
Osteomyelitis	1 (< 1)	0	0	1 (< 1)
Pancreatic abscess	0	1 (< 1)	0	1 (< 1)
Pleural infection	1 (< 1)	0	0	1 (< 1)
Pneumonia bacterial	1 (< 1)	0	0	1 (< 1)
Pneumonia cytomegaloviral	0	0	1 (< 1)	1 (< 1)
Pneumonia haemophilus	1 (< 1)	0	0	1 (< 1)
Proteus infection	1 (< 1)	0	0	1 (< 1)
Pseudomembranous colitis	1 (< 1)	0	0	1 (< 1)
Psoas abscess	1 (< 1)	0	0	1 (< 1)
Pyelonephritis acute	1 (< 1)	0	0	1 (< 1)
Renal tuberculosis	1 (< 1)	0	0	1 (< 1)
Septic arthritis staphylococcal	1 (< 1)	0	0	1 (< 1)
Sinusitis aspergillus	1 (< 1)	0	0	1 (< 1)
Sinusitis bacterial	1 (< 1)	0	0	1 (< 1)
Staphylococcal bacteraemia	1 (< 1)	0	0	1 (< 1)
Streptococcal bacteraemia	1 (< 1)	0	0	1 (< 1)
This total count also takes into account AEs of Grade 1 and Grade 2 severity.				
MedDRA Version: 19.1				
Source Output: Table 14.3.2.8.1.11 in Clinical Study Report 1113097 for ARROW Study				

**Appendix 4      Summaries of the Cases Reporting Grade 5 Infections from  
the Company Safety Database (N=77)**

## Category B (N=38)

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
2858632 57 Not reported ITALY Non-Interventional Study/Program Healthcare professional	Pneumonia Sepsis Grade 5	92 NR	(1) PRALSETINIB (S)  (2) RAMIPRIL (C)  (3) ZOLEDRONIC ACID (C)  (4) CISPLATIN (C)  (5) PEMETREXED (C)  (6) OXYGEN (T)  (7) CEFTRIAXONE SODIUM (T)	Dose interrupted  Dose interrupted N/A  N/A N/A  N/A Fatal  Fatal	"AER 2858632 (PT: Pneumonia, Sepsis)  This non-interventional study case concerned a 57-year-old patient (sex unspecified) from Italy who developed pneumonia and sepsis while receiving treatment with pralsetinib for non-small cell lung cancer and lung neoplasm malignant. The patient's medical history and past drugs were not reported. Concurrent conditions included bone metastasis. Concomitant medications included ramipril, zoledronic acid, cisplatin and pemetrexed. Maternal family history included myocardial infarction.  After 29 days of starting treatment with pralsetinib (400 mg daily), the patient developed hypertension. An unspecified duration later, the pralsetinib dose was reduced to 300 mg daily. After 92 days of starting treatment with pralsetinib, the patient developed pneumonia and fever. The next day, the patient was hospitalized due to persistent fever and dyspnea. Upon admission, the patient's temperature was 37.2°C and oxygen saturation was critically low at 69%. Initial CT scan confirmed the diagnosis of pneumonia. A CT scan without contrast detected extensive parenchymal blob in the lower right lobe and significant left pleural effusion. The treatment regimen included oxygen therapy with continuous positive airway pressure, steroids, ceftriaxone and left pleural drainage. A follow-up CT scan showed no pulmonary embolism. Blood tests indicated severe sepsis, likely secondary to pneumonia, with markedly elevated procalcitonin, C-reactive protein and creatinine levels. After 92 days of starting treatment with pralsetinib, the patient died due to pneumonia and sepsis. An autopsy was not performed. The physician did not report the causality between fatal pneumonia and fatal sepsis with pralsetinib."

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
					Though the patient developed pneumonia and sepsis while being treated with pralsetinib, the events could be explained the immunocompromised state due to the progression of underlying malignancy and the co-administration of medications like cisplatin and pemetrexed.
3018085 70 Male TURKIYE Non-Interventional Study/Program Healthcare professional	COVID-19 Grade 5	41	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	"AER 3018085 (PT: COVID-19)  This non-interventional study case concerned a 70-year-old male from Turkey who developed COVID-19, 41 days after starting treatment with pralsetinib for non-small cell lung cancer. The patient's medical history, concomitant medications or past drugs were not reported. Concurrent conditions include hypertension, benign prostatic hyperplasia and bronchial asthma. After 41 days of starting treatment with pralsetinib, the patient was tested positive for COVID 19 and was hospitalized due to respiratory distress associated with COVID-19. After 77 days of starting treatment with pralsetinib, the patient died due to COVID-19. It was not reported if an autopsy was performed. The physician assessed the COVID-19 as not related to pralsetinib."  Though the patient developed COVID 19 41 days after starting pralsetinib, the occurrence of event could be explained by the elderly age and concurrent condition of bronchial asthma
3065813 64 Female ITALY Non-Interventional Study/Program	Sepsis Abdominal abscess Grade 5	NR NR Grade 5	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (S)  (3) BISOPROLOL (S)  (4) FUROSEMIDE (S)	N/A N/A N/A N/A	This spontaneous case concerns a 64-year-old female patient who developed sepsis and abdominal abscess, unspecified duration after initiating therapy with pralsetinib for thyroid cancer. Concomitant medications included pantoprazole, however no past medical history, past drugs, concurrent conditions were reported. After an unspecified duration, the patient developed sepsis for which the patient was hospitalized. Reportedly, the patient developed abdominal abscess which was likely to be a

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
gram Healthcare professional	NR		(5) METHYLPREDNISOLONE (S)  (6) APIXABAN (S)  (7) PANTOPRAZOLE SODIUM SESQUIHYDRATE (C)	N/A Fatal  Not Reported	complication of pancreatic resection surgery. After approximately 6 months of the initiation of pralsetinib, the patient died due to sepsis. It was unknown if an autopsy was performed or not.  The time to onset of sepsis and abdominal abscess in relation to pralsetinib therapy is not reported. The medical history of pancreatic resection surgery explains the development of abdominal abscess and sepsis as post surgical complications of major abdominal surgery. Additionally, history of recurrent urinary tract infection and pre-existing systemic bacteremia are possible risk factors.
2710528 77 Female FRANCE Clinical Study Healthcare professional	Septic shock  Staphylococcal scalded skin syndrome Grade 5  Grade 4	109  109	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) MESALAZINE (C)  (4) PREDNISOLONE (C)  (5) CEFAZOLIN (T)  (6) CLINDAMYCIN (T)	Dose interrupted  Dose interrupted N/A  Negative N/A  N/A Fatal  Not Recovered/Not Resolved/Ongoing	"AER 2710528 (PT: Septic shock, Staphylococcal scaled skin syndrome):  This clinical study case concerned a 77-year-old female (patient number: PAAP667029002) from France who developed septic shock and scaled skin syndrome, 109 days after starting therapy with pralsetinib for non-small cell lung cancer. The patient's medical history included cervical surgery and total thyroidectomy. Concurrent conditions included high blood pressure, dysplasia, and diarrhea. Concomitant medications included levothyroxine, mesalazine, and prednisolone. Past drugs included temozolomide, selpercatinib, capecitabine and vandetanib. The patient had no history of skin infection. The patient's baseline laboratory values were within normal range for white blood cells and absolute neutrophil count and the patient had dysphagia due to local relapse. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg daily and received till Study Day 109. On Study Day 109, after receiving the most recent dose, the patient developed Grade 4 scaled skin syndrome (skin desquamation onset was noted

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
					<p>three days prior) and Grade 5 septic shock and was hospitalized. Upon admission, the patient presented with tachycardia, fever, oxygen supply of 25% and body surface desquamation including anal and genital mucosa lesions. Laboratory tests revealed hemoglobin of 7.39 g/dL (reference range 12.0-15.0), WBC of 0.30 g/L (reference range 4.0-11.0), platelet count of 100 g/L (reference range 150-400), and the hemoculture for staphylococcus was positive. According to the investigator's assessment, the patient developed septic shock due to scalded skin syndrome, which was caused by a staphylococcus infection. Later during the hospitalization, it was observed that the skin desquamation had affected 40% of the patient's body surface and the origin of staphylococcal infection was determined to be the skin. The patient received treatment with intravenous cefazolin and clindamycin. On Study Day 110, the patient passed away due to septic shock. No autopsy was performed. The physician assessed the septic shock and scalded skin syndrome as related to pralsetinib."</p> <p>The occurrence of the events could be explained by the patient's immunocompromised state due to the use of prednisolone and mesalazine. Furthermore the co-existing pancytopenia and the elderly age of the patient could have contributed to the events as well.</p>
2714685 58 Male CHINA Clinical Study Healthcare	Pneumonia Grade 5	263	(1) PRALSETINIB (S)  (2) CELECOXIB (C)  (3) MONTMORILLONITE (C)  (4) IBUPROFEN (C)	Drug interrupted N/A N/A Fatal	<p>AER 2714685 (PT: Pneumonia):</p> <p>This clinical study case concerned a 58-year-old male (patient number: 6305003) from China who developed pneumonia, 263 days after starting therapy with pralsetinib for non-small cell lung cancer. The patient's concurrent conditions included right shoulder pain, cough, fever, lymph node metastases, bone metastases, and diarrhea. Concomitant medications included celecoxib, montmorillonite, and ibuprofen. Past drugs included</p>

AER Number	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
professional			(5) CEFRADINE (T)  (6) DOXOFYLLINE (T)  (7) AZITHROMYCIN (T)  (8) TERBUTALINE SULFATE (T)  (9) BUDESONIDE (T)  (10) GLUCOSE (T)		pemetrexed, and cisplatin. The patient had no history of neutropenia or pneumonia. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg daily and received till Study Day 263. On Study Day 252, the patient's absolute neutrophil count (ANC) was reported as 4.5x10 <sup>9</sup> /L. On Study Day 261, the patient experienced cough and fever and on Study Day 263, the patient developed Grade 5 pneumonia. The patient exhibited symptoms including fever (39.4 °C), cough, production of white sputum, and mild chest distress. A chest CT scan revealed patchy shadows on bilateral lungs, predominantly on the right lung. Two pneumonia lesions, local atelectasis of the right middle lobe and bilateral pleural effusion with limited thickening of the left pleura was also observed. The patient was diagnosed with right lung pneumonia on the same day. Treatment medications for pneumonia included cefradine, doxofylline, glucose injection, azithromycin, terbutaline (inhalation) and budesonide. On the same day, the patient died due to pneumonia. An autopsy was not performed. According to the investigator's assessment, there was no evidence for underlying disease progression and there was no available data on COVID-19. Therapy with pralsetinib was withdrawn in response to pneumonia. The physician assessed the fatal pneumonia as not related to pralsetinib. The occurrence of pneumonia could be explained by the underlying disease progression as evidenced by the metastasis to multiple sites. Additionally, the contributory role of the patient's past medication with pemetrexed and cisplatin could not be completely ruled out, even though the exact dates are not reported.
3298701 Not reported Male CHINA	COVID-19 pneumonia Grade 5	511	(1) PRALSETINIB (S)	N/A N/A N/A Fatal	This non-interventional program case concerns a male patient of unknown age, who developed covid-19 pneumonia, 511 days after initiating therapy with pralsetinib for lung cancer. No past medical history past, drugs, concurrent conditions and concomitant medications were reported. After 511 days of

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
Non-Interventional Study/Program Non-healthcare professional					<p>initiating therapy with pralsetinib, the patient developed covid-19 pneumonia due to which the patient passed away. It was unknown if an autopsy was performed or not.</p> <p>The event of pneumonia developed almost 1.5 years after initiation of treatment with pralsetinib, which is an unduly long latency for a causative infection to appear. Secondly, concurrent thrombocytopenia and leukopenia in the setting of covid-19 infection and underlying disease progression are possible risk factors for the event severity and outcome.</p>
2717111 71 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Sepsis  COVID-19 pneumonia  Pneumonia staphylococcal Grade 5  Grade 3  Grade 3	50  20  47	(1) PRALSETINIB (S)  (2) BACLOFEN (C)  (3) LEVETIRACETAM (C)  (4) LEVOTHYROXINE (C)  (5) METOPROLOL TARTRATE (C)  (6) ONDANSETRON (C)  (7) RIVAROXABAN (C)  (8) AMLODIPINE (C)  (9) DOCUSATE (C)  (10) FLUTICASONE (C)  (11) GABAPENTIN (C)	N/A  Dose interrupted  Dose interrupted N/A  Negative  Negative N/A  N/A  N/A Fatal  Not Recovered/Not Resolved/Ongoing  Not Recovered/Not Resolved/Ongoing	<p>AER 2717111 (PT: Sepsis, COVID-19 pneumonia, Pneumonia staphylococcal):</p> <p>This clinical study case concerned a 71-year-old male (patient number: 2613013) from the USA who developed sepsis, COVID-19 pneumonia, pneumonia staphylococcal while receiving treatment with pralsetinib for papillary thyroid cancer. The patient's medical history included mumps, rubella, varicella, rubella, fracture of arm and smoking and surgical history included arthroscopy of knee, appendectomy, spine surgery, arthroscopy of shoulder, total knee arthroplasty. Concurrent medical condition included acquired hypothyroidism, allergic rhinitis, benign prostatic hyperplasia, eyeglasses, hyperlipidemia, hypertensive disorder, hypothyroid, malignant tumor of thyroid gland, metastasis to vertebral column of unknown primary, osteoarthritis, paraplegia, pulmonary embolism, secondary malignant neoplasm of bone, secondary malignant neoplasm of brain, sinus infection, snores, spinal cord compression, supraventricular tachycardia, tobacco user and total knee joint prosthesis. Concomitant medications included baclofen, levetiracetam, levothyroxine, metoprolol, ondansetron, rivaroxaban, amlodipine, docusate, fluticasone, gabapentin, nitrofurantoin, oxybutynin, tizanidine, senna, macrogol 3350,</p>

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
			(12) NITROFURANTOIN (C)  (13) OXYBUTYNIN (C)  (14) TIZANIDINE (C)  (15) IPRATROPIUM BROMIDE\ SALBUTAMOL SULFATE (C)  (16) DEXAMETHASONE (T)  (17) REMDESIVIR (T)  (18) RIVAROXABAN (T)  (19) PARACETAMOL (T)  (20) FERROUS SULFATE (T)  (21) IBUPROFEN (T)  (22) LEVETIRACETAM (T)  (23) MACROGOL 3350 (T)  (24) OXYBUTYNIN HYDROCHLORIDE (T)  (25) SENNA SPP. (T)		ipratropium\salbutamol, guaifenesin and ferrous sulfate. The patient had an oncology history of papillary thyroid cancer, colon polyp and thyroid cancer along with cancer treatment regimens and prior cancer surgeries. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 300 mg (frequency unspecified) and received till Study Day 20. On Study Day 20, the patient experienced the first episode COVID-19 pneumonia (Grade 3) with symptoms including sore throat, headache, cough, fever, and mild diarrhea and was hospitalized. Laboratory tests confirmed COVID-19 infection and revealed various abnormalities, including low sodium levels and elevated liver enzymes. A chest x-ray showed mild bilateral infiltrates with small effusions. The patient was treated with intravenous fluids and paracetamol. On Study Day 21, further tests revealed elevated C-reactive protein, low hemoglobin, and persistently low sodium levels. Treatment with pralsetinib was interrupted on the same day. On Study Day 30, the patient was recovering from COVID-19 pneumonia and was discharged. Pralsetinib was restarted at 300 mg on Study Day 31. On Study Day 35, the patient experienced a second episode of COVID-19 pneumonia (Grade 3), leading to hospital re-admission. Despite a negative PCR test, chest CT showed bilateral COVID-type infiltrates. Laboratory results indicated various abnormalities, including elevated liver enzymes and inflammatory markers. During this hospitalization, the patient received additional treatments, including empiric bacterial treatment with levofloxacin and respiratory therapies. Pralsetinib was interrupted again on Study Day 36. On Study Day 39, the patient was discharged and the second episode of COVID-19 pneumonia resolved. Pralsetinib was restarted at 300 mg on Study Day 40, however by Study Day 43, the patient experienced a third episode of COVID-19 pneumonia (Grade 3) and laboratory results showed various abnormalities, including liver enzyme elevations and coagulation irregularities. Pralsetinib was discontinued again on the same

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
			(26) SODIUM CHLORIDE (T)  (27) BENZONATATE (T)  (28) VANCOMYCIN (T)		day. On Study Day 45, the patient was hospitalized again due to chronic hypoxic respiratory failure. On Study Day 46, laboratory results revealed low hemoglobin levels, low Lymphocyte counts and elevated inflammatory markers, electrolyte imbalances, particularly hyponatremia. On the same day, the third episode COVID-19 pneumonia resolved. On Study Day 47, the patient was diagnosed with Grade 3 pneumonia staphylococcal and eventually the patient developed Grade 5 sepsis. Intravenous vancomycin treatment was initiated, but sepsis persisted. Sputum culture results revealed a significant presence of methicillin-resistant staphylococcus aureus (MRSA). On Study Day 50, the patient died due to sepsis. No autopsy was performed. The physician assessed the episodes of COVID-19 pneumonia, pneumonia MRSA, and sepsis as not related to pralsetinib.  The patient had multiple co-morbidities like highly advanced malignancies including secondaries, multiple past surgeries, paraplegic state and radiotherapy which could explain the occurrence of the events
2717955 82 Male KOREA, REPUBLIC OF Clinical Study Healthcare professional	Pneumonia Grade 5	577	(1) PRALSETINIB (S)  (2) METFORMIN (C)  (3) CALCIUM CARBONATE\COLECALCI FEROL (C)  (4) LEVOTHYROXINE SODIUM (C)  (5) LACTULOSE (C)  (6) MAGNESIUM OXIDE (C)	Drug interrupted N/A N/A Fatal	AER 2717955 (PT: Pneumonia):  This clinical study case concerned an 82-year-old male (patient number: 6103008) from Korea, Republic Of who developed pneumonia, 577 days after starting therapy with pralsetinib for medullary thyroid cancer. The patient's concurrent conditions included urinary tract infection, complete atrioventricular block, hypertension, diabetes mellitus, metastasis to the lungs, hypothyroidism, and left renal stone. Medical history or past drugs were not reported. The patient's prior cancer treatment included stereotactic radiosurgery and radiotherapy of ilium and surgeries included near total thyroidectomy, bilateral modified radical neck dissection, and total thyroidectomy with central compartment node dissection. Concomitant medications included metformin, calcium carbonate\colecalciferol,

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
			(7) ALFACALCIDOL (C)  (8) CODEINE PHOSPHATE\IBUPROFEN\PARACETAMOL (C)  (9) CANDESARTAN CILEXETIL (C)  (10) CARVEDILOL (C)  (11) ACETYLSALICYLIC ACID (C)  (12) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (13) RED BLOOD CELLS (T)  (14) MEROPENEM (T)  (15) LEVOFLOXACIN (T)  (16) TEICOPLANIN (T)  (17) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)  (18) MOXIFLOXACIN HYDROCHLORIDE (T)		levothyroxine, lactulose, magnesium oxide, alfacalcidol, codeine phosphate\ibuprofen\paracetamol, candesartan, carvedilol and aspirin. The patient had no history of pneumonia or any other infection. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg (frequency unspecified) and received till Study Day 576. The patient's neutrophil and platelet counts were within normal range on Study Day 576. Subsequently, the patient experienced hematochezia following which the patient's hemoglobin levels and platelet counts decreased. The patient received piperacillin/tazobactam for infection prophylaxis along with packed red blood cell. The patient's COVID-19 PCR test was negative. A high-resolution CT scan of chest revealed a newly developed ground-glass opacities at both lungs, suggesting possible atypical pneumonia along with small amounts of bilateral pleural effusion, subsegmental atelectasis at both lower lobe and slightly increased tumor burden. Subsequently, on Study Day 577, the patient developed Grade 5 pneumonia. The hemoglobin level was maintained at 10.9 g/dL (reference range 13.0-17.4 g/dL). Antibiotics administered to treat pneumonia included meropenem, levofloxacin, teicoplanin, and sulfamethoxazole(trimethoprim along with high oxygen treatment. The patient exhibited low partial pressure of oxygen (PO2) and oxygen saturation, accompanied by elevated C-reactive protein (CRP) levels and low white blood cell count. No causative pathogen of pneumonia was identified. Over the course of treatment from Study Day 578 to 579, the patient's condition fluctuated, with some improvements in oxygen levels and white blood cell count, but persistent low hemoglobin levels and platelet counts. Lung radiographs showed deterioration, and the patient's oxygen demand increased and oxygen saturation continued to decrease despite maintenance of hyperbaric oxygen therapy. The patient received various treatments, including albumin, vitamins, and respiratory medications. On

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					<p>Study Day 579, moxifloxacin was administered for pneumonia, however the patient's blood tests indicated that oxygenation levels and cell count remained below normal ranges. On the same day, the patient died due to pneumonia. An autopsy was not performed. Therapy with pralsetinib was discontinued in response to pneumonia. The physician assessed pneumonia as not related to pralsetinib.</p> <p>The patient was diabetic and of advanced age with progression of underlying malignancy. He also had prior radiotherapy and co-existing cytopenia which predisposed the patient to infections</p>
2720338 84 Female CHINA Clinical Study Healthcare professional	Pneumonia aspiration Grade 5	3	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (C)  (3) SODIUM (C)	Drug interrupted N/A N/A Fatal	<p>AER 2720338 (PT: Pneumonia aspiration):</p> <p>This clinical study case concerned an 84-year-old female (patient number: 6317004) from China who developed aspiration pneumonia, 3 days after starting therapy with pralsetinib for poorly differentiated thyroid carcinoma. The patient's concurrent conditions included thyroid carcinoma, hypertension, diabetes, chronic gastritis, room premature beats, anemia and complete right bundle branch block. Concomitant medications included levothyroxine and sodium. No medical history and past drugs were reported. The patient had no history of cancer treatment. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg daily and received till Study Day 3. On Study Day 3, after receiving the most recent dose, the patient developed Grade 3 aspiration pneumonia. The patient presented to the emergency room with choking on eating and a fever of 39°C. The baseline CT scan revealed a soft tissue mass on the left side of trachea. During the initial physical examination, a neck mass was also observed. It was reported that the compression of the esophagus by the tumor was causing the patient to choke while eating which eventually led to pneumonia aspiration. The patient was treated with anti-infective medications and nutritional support treatment during hospitalization. On Study Day 4, the patient was unable to take</p>

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					<p>pralsetinib due pneumonia aspiration and therefore, therapy with pralsetinib was suspended. On Study Day 12, the pneumonia aspiration worsened to grade 5 and the patient died in the hospital due to pneumonia aspiration. The autopsy was not performed. The physician assessed the aspiration pneumonia as not related to pralsetinib.</p> <p>The event occurred due to aspiration of food due to the choking effect of the underlying malignancy. There was also no lab investigations reported to prove an infective etiology.</p>
2724802 54 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia aspiration Grade 5	756	(1) PRALSETINIB (S)  (2) ESOMEPRAZOLE (C)  (3) PIOGLITAZONE (C)  (4) PRAMIPEXOLE (C)  (5) TIOTROPIUM BROMIDE (C)  (6) CANNABIS SATIVA (C)  (7) CALCITRIOL (C)  (8) SALBUTAMOL (C)  (9) LEVOTHYROXINE (C)  (10) SERTRALINE (C)  (11) BUDESONIDE\FORMOTE ROL (C)	Drug interrupted N/A N/A Fatal	<p>AER 2724802 (PT: Pneumonia aspiration):</p> <p>This clinical study case concerned a 54-year-old male (patient number: 2610005) from the USA who developed aspiration pneumonia, 756 days after starting therapy with pralsetinib for non small cell lung cancer. The patient's medical history included lymphadenopathy, hematochezia, shingles, unintended weight loss, left shoulder pain, bilateral neck pain, right inguinal hernia repair, heavy alcohol use, tobacco use, bilateral leg pain, depression, intermittent night sweats, percutaneous endoscopic gastrostomy tube placement, left hip pain, pneumonia, intermittent generalized edema, stridor, sensation of chest pressure, heart palpitations, and flashing lights. Concurrent conditions included mucositis, percutaneous endoscopic gastrostomy tube placement, intermittent diarrhea, hypothyroidism, left sided neck stiffness, neuropathy in face, chronic dysphagia, chronic productive cough, chronic aspiration, left true vocal cord paralysis, hypercholesterolemia, chronic obstructive pulmonary disease, intermittent fatigue, chronic sore throat, type 2 diabetes mellitus, restless leg syndrome, insomnia, gastroesophageal reflux disease, intermittent dizziness, intermittent arthralgia, hypertension, migraine headache, hypokalemia, generalized weakness, nausea, intermittent dry heaves, and bilateral hand tremor. Concomitant medications included esomeprazole, pioglitazone, pramipexole, tiotropium</p>

AER Number	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
			(12) CALCIUM\COLECALCIFEROL (C)  (13) SILDENAFIL (C)  (14) FLUCONAZOLE (C)  (15) NYSTATIN (C)  (16) PREDNISONE (C)  (17) AMLODIPINE (C)  (18) GABAPENTIN (C)  (19) PARACETAMOL (T)  (20) EPINEPHRINE (T)  (21) NOREPINEPHRINE BITARTRATE (T)  (22) IOHEXOL (T)  (23) FENTANYL (T)  (24) MIDAZOLAM (T)  (25) PIPERACILLIN\TAZOBACTAM (T)  (26) BUSPIRONE (T)		bromide, cannabis sativa, calcitriol, salbutamol, levothyroxine, sertraline, budesonide/formoterol, calcium/colecalciferol, paracetamol, sildenafil, fluconazole, nystatin, prednisone, amlodipine, and gabapentin. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 300 mg daily. On Study Day 753, the patient experienced worsened difficulty breathing with associated wheezing, and the patient was on 3 L of continuous oxygen at home. From Study Day 754 to 755, the oxygen requirement was increased to 5 L. On Study Day 756, the patient developed Grade 4 pneumonia aspiration and anemia with oxygen needs rising to 8L. The patient's condition rapidly deteriorated, leading to an emergency response. Initially conscious but cyanotic upon EMS arrival, the patient became unresponsive and pulseless. After extensive resuscitation efforts, including six rounds of CPR and epinephrine administration, spontaneous circulation was restored. At the emergency department, the patient was intubated but remained unresponsive, later developing hypotension and bradycardia with minimal neurological responses. On Study Day 757, the patient had second occurrence of pneumonia aspiration (Grade 5). Comprehensive laboratory tests revealed multiple abnormalities, including elevated lactate, acidosis, hypoxemia, anemia, electrolyte imbalances, hyperglycemia, elevated liver enzymes, positive urine bacteria, blood culture showing <i>Actinomyces naeslundii</i> and elevated cardiac markers, though without signs of myocardial infarction. Imaging studies showed no pulmonary embolism but did show mild ground-glass opacities in both lungs with dependent atelectasis, potentially indicative of pulmonary edema or atypical pneumonia, along with rib fractures likely from CPR. Sputum culture indicated normal upper respiratory flora, while the gram stain of the lower respiratory culture showed a significant presence of gram-positive cocci. Treatment medications included epinephrine, norepinephrine, iohexol, fentanyl, midazolam, piperacillin/tazobactam, acetaminophen,

AER Number	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
			(27) ENOXAPARIN (T)  (28) LEVETIRACETAM (T)  (29) MAGNESIUM SULFATE (T)  (30) POTASSIUM CHLORIDE (T)  (31) INSULIN LISPRO (T)  (32) SODIUM PHOSPHATE (T)  (33) PROPOFOL (T)  (34) FAMOTIDINE (T)  (35) LORAZEPAM (T)		buspirone, enoxaparin, levetiracetam, magnesium sulfate, potassium chloride, insulin lispro, sodium phosphate, propofol, famotidine, and lorazepam. On the same day, the patient died due to respiratory failure secondary to aspiration pneumonia. Autopsy was not performed. The dose of pralsetinib was interrupted in response to the aspiration pneumonia. The physician assessed the event of aspiration pneumonia as not related to pralsetinib. The patient had multiple co morbidities like pre-existing pneumonia/mucositis/COPD, history of multiple aspirations and diabetes. He was also in an immunocompromised state as evidenced by the presence of
2727739 59 Female FRANCE Clinical Study Healthcar e profession al	Pneumonia Grade 5	99	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) PARACETAMOL (C)  (4) GABAPENTIN (C)  (5) ALPRAZOLAM (C)  (6) ZOLPIDEM (C)  (7) PANTOPRAZOLE (C)	Drug interrupted N/A N/A Fatal	AER 2727739 (PT: Pneumonia):  This clinical study case concerned a 59-year-old female (patient number: 1701008) from France who developed pneumonia, 99 days after starting therapy with pralsetinib for thyroid cancer, non-small cell lung cancer and neoplasm. The patient's medical history included knee pain, lumbar pain, constipation, dyspnea, hoarseness of voice, fatigue, left upper limb pain, chest pain, thyroidectomy, and cardiac arrest. Concurrent conditions included pleurisy, cough, anorexia, anxiety, left upper limb paresthesia, deglutition disorder, hypothyroidism, diarrhea, papillary carcinoma of the thyroid, progressive disease, intermittent mucus sputum, hyperphosphatemia, and oral

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			(8) LOPERAMIDE (C)  (9) SEVELAMER (C)  (10) SODIUM BICARBONATE (C)		mucositis. Concomitant medications included levothyroxine, paracetamol, gabapentin, alprazolam, zolpidem, pantoprazole, loperamide, sevelamer, and sodium bicarbonate. The patient's previous cancer therapy regimen included lenvatinib and external beam radiotherapy. The patient had no history of infectious diseases. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg (frequency unspecified) and received till Study Day 99. On Study Day 99, the patient was presented to the emergency room due to Grade 5 pneumonia with the symptoms including fever and dyspnea. On admission, physical examination showed crepitus in right lung and a chest X-ray revealed opacity consistent with right middle lobe lung infection. The patient was treated with antibiotics on the same day and pralsetinib was discontinued. The patient's hematology test revealed severe leucopenia and thrombocytopenia and the subsequent blood culture test was positive for streptococcus pneumoniae. On Study Day 100, the patient's laboratory results revealed severe metabolic acidosis from blood gas analysis, significant anemia, leukopenia, and thrombocytopenia. The patient also showed elevated inflammatory markers, abnormal coagulation, impaired liver function, and electrolyte imbalances including hyponatremia, hypochloremia, hypocalcemia, and hyperphosphatemia. Cardiac stress was indicated by elevated troponin and NT-proBNP levels and high lactic acid levels were observed. On the same day, the patient underwent cardiac arrest. The patient was resuscitated however, the neurological recovery was poor and the patient died on the same day. The cardiac arrest was not considered the primary cause of death, given that the patient's absolute neutrophil count had been normal at baseline. It was not reported if autopsy was performed or not. The physician assessed causality of fatal pneumonia as not related to pralsetinib. The patient was in an immunosuppressive state due to the

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
					underlying progressive malignancy. This is also confirmed by the existence of leukopenia and the bacteria, Streptococcus pneumoniae, which is an opportunistic pathogen. Moreover, the patient had also received prior radiotherapy and lenvatinib, the contributory role of which could not be completely ruled out.
2733812 66 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	COVID-19 Grade 5	764	(1) PRALSETINIB (S)  (2) SULFAMETHOXAZOLE/TRIMETHOPRIM (C)  (3) ATORVASTATIN (C)  (4) FUROSEMIDE (C)  (5) POTASSIUM CHLORIDE (C)  (6) LEVOTHYROXINE (C)  (7) PARACETAMOL (C)  (8) SALBUTAMOL (C)  (9) AZITHROMYCIN (C)  (10) CEFTRIAXONE (C)  (11) DEXAMETHASONE SODIUM PHOSPHATE (C)  (12) ENOXAPARIN (C)  (13) REMDESIVIR (C)	Drug interrupted N/A N/A Fatal	"AER 2733812 (PT: COVID-19):  This clinical study case concerned a 66-year-old male (patient number: 2605009) from the USA who developed COVID-19, 764 days after starting therapy with pralsetinib for medullary thyroid cancer. The patient's medical history included partial thyroidectomy. Concurrent conditions included diabetes, hypercholesterolemia, hypertension, postoperative hypothyroidism, ankle fracture, medullary thyroid cancer, UTI, hyperlipidemia, radical dissection neck, thyroidectomy and neck selective lymph node dissection. Concomitant medications included atorvastatin, furosemide, sulfamethoxazole/trimethoprim, potassium chloride, and levothyroxine. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg daily and received till Study Day 764. On Study Day 764, the patient developed Grade 3 COVID-19 and was hospitalized. Initial symptoms began on Study Day 760, progressing to fever, shortness of breath, chills, body aches, sore throat, headache, and a dry cough. Upon hospitalization, the patient's blood pressure was slightly low, patient had a mild fever and the respiratory rate was elevated. The dose of pralsetinib was interrupted in response to the COVID-19 with no improvement observed after the interruption. On Study Day 765, the patient presented with fever, nausea, and generalized body pain, along with slightly elevated vital signs and abnormal lab results, particularly elevated AST and low RBC and HGB. Pralsetinib was suspended until discharge. Over the following days until Study Day 771, fibrinogen and procalcitonin levels were significantly elevated. On Study Day 775, the patient

AER Number	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
			(14) SODIUM CHLORIDE (C)  (15) LEVOTHYROXINE (C)  (16) FUROSEMIDE (C)  (17) AMLODIPINE (C)  (18) ATORVASTATIN (C)  (19) GLIPIZIDE (C)  (20) ACETYLSALICYLIC ACID (C)  (21) PARACETAMOL (C)		was intubated due to hypoxic respiratory failure. The patient's hemoglobin levels dropped and a blood transfusion was administered. The results of the CT scans revealed fibrosis, while blood and respiratory cultures showed no growth. From Study Day 780 to 782, the patient received methylprednisolone treatment. However, by Study Day 788, a urine culture indicated an abnormal growth of <i>Candida glabrata</i> . On Study Day 799, the patient developed a right pneumothorax, requiring chest tube placement. On Study Day 809, CT scans of the chest, abdomen, and pelvis were performed due to persistent leukocytosis and respiratory failure. The chest CT revealed diffuse interstitial changes, reticular nodular densities, and a small left pleural effusion, while abdominal/pelvic scans showed gallstones, a distended gallbladder, and minor renal abnormalities. Over the following days, the patient's condition deteriorated, with atrial fibrillation, elevated WBC counts, and the development of a left pneumothorax necessitating additional chest tube placement. Chest X-rays on subsequent days showed bilateral chest tubes and pneumothoraxes and the patient required increasing oxygen support. Lab results on Study Day 819 indicated elevated inflammatory markers. The final chest X-ray revealed severe bilateral lung infiltration, persistent pneumothoraxes, and multiple medical devices in place, including endotracheal and nasogastric tubes, drainage catheters, and chest tubes. On Study Day 820 to 822, the patient's laboratory results showed persistently elevated inflammatory markers, including ferritin, CRP, and D-dimer, along with abnormal liver function and blood cell counts. On Study Day 822, an X-ray revealed a resolved right pneumothorax but a small left pneumothorax, with severe lung scarring and infiltration from interstitial lung disease, particularly on the right side. The patient required high oxygen support and positive end-expiratory pressure. Medical records noted cytopenia in multiple cell lines and active problems including hyponatremia, leukocytosis, anemia, COVID-19 acute

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					<p>respiratory distress syndrome, and acute hypoxic respiratory failure. On Study Day 823, despite stable vital signs, the patient passed away due to COVID-19. It was not reported if an autopsy was performed. The physician assessed the COVID-19 as not related to pralsetinib."</p> <p>The patient had other risk factors predisposing to COVID 19, namely, diabetes, dyslipidemia, which eventually aggravated to respiratory distress/acute hypoxic respiratory failure and death</p>
2734968 74 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	COVID-19 Grade 5	434	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) DOCUSATE SODIUM\SENNOSIDE A+B (C)  (4) MACROGOL 3350 (C)  (5) DOCUSATE SODIUM (C)  (6) ACETYLSALICYLIC ACID (C)  (7) CALCIUM CARBONATE (C)  (8) PARACETAMOL (C)  (9) CARMELLOSE (C)  (10) COLECALCIFEROL	NR Unknown N/A Fatal	<p>"AER 2734968 (PT: COVID-19):</p> <p>This clinical study case concerned a 74-year-old female (patient number: 2614006) from the USA who developed COVID-19, 430 days after starting therapy with pralsetinib for papillary thyroid cancer. The patient's medical history included renal stones, hematuria, nausea, tonsillectomy, cholecystectomy, left knee replacement, right rotator cuff repair, carpal tunnel surgery, trigger thumb surgery, middle finger surgery, dental implants and cataract surgery. Concurrent conditions included hypothyroidism, hoarseness, dysphagia, postmenopausal, knee pain, surgery, metastatic papillary thyroid cancer, total thyroidectomy, radiotherapy and progressive disease. Concomitant medications included macrogol 3350, levothyroxine, docusate/sennoside a+b, docusate, acetylsalicylic acid, calcium carbonate, paracetamol, carmellose, cholecalciferol, cyanocobalamin, melatonin, loperamide, and iodine. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 200 mg (frequency unspecified). On Study Day 430, prior to initiating Cycle 15, the patient was tested positive for COVID-19 (Grade 5). On Study Day 434, the patient was hospitalized due to worsening symptoms, including balance difficulties and severe hypoxia (oxygen saturation 70%). During hospitalization, the patient was diagnosed with hypoxia, acute hypoxic respiratory failure</p>

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			(C)  (11) CYANOCOBALAMIN (C)  (12) MELATONIN (C)  (13) LOPERAMIDE HYDROCHLORIDE (C)  (14) IODINE (C)  (15) REMDESIVIR (T)  (16) DEXAMETHASONE (T)  (17) VANCOMYCIN (T)  (18) CEFEPIME (T)  (19) DOXYCYCLINE (T)		secondary to COVID-19, and MRSA pneumonia. Treatment medications included oxygen therapy, remdesivir, dexamethasone, and convalescent plasma for COVID-19, and antibiotics including vancomycin, cefepime, and oral doxycycline for MRSA pneumonia. Despite the interventions, the patient remained hypoxic. After consultation with pulmonary specialist and considering her overall life situation, the patient was discharged to hospice care on Study Day 444. The patient ultimately passed away on Study Day 539 due to long-term effects of COVID-19. An autopsy was not performed. The physician assessed the COVID-19 as unrelated to pralsetinib."  The patient was of elderly age group, and had undergone surgery and radiotherapy concurrently. Additionally, there was also progression of underlying disease and ultimately patient died due to long term effects of COVID
2735872 54 Female KOREA, REPUBLIC OF Clinical Study Healthcare professional	Urosepsis Grade 5	57	(1) PRALSETINIB (S)  (2) ERDOSTEINE (C)  (3) CODEINE (C)  (4) MAGNESIUM OXIDE (C)  (5) RIVAROXABAN (C)  (6) PARACETAMOL (C)	Drug interrupted N/A N/A Fatal	"AER 2735872 (PT: Urosepsis):  This clinical study case concerned a 54-year-old female (patient number: 6102009) from Korea, Republic of who developed urosepsis, 57 days after starting therapy with pralsetinib for non-small cell lung cancer. The patient's medical history included tumor thrombosis in superior vena cava thrombosis. Concurrent conditions included pericardial effusion, productive cough, pleural effusion, fever, and constipation. Concomitant medications included erdosteine, codeine, magnesium oxide, rivaroxaban, paracetamol, dalteparin, ammonium chloride/chlorphenamine/dihydrocodeine/methylephedrine. On

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			(7) DALTEPARIN SODIUM (C)  (8) AMMONIUM CHLORIDE\CHLORPHEN AMINE MALEATE\DIHYDROCOD EINE BITARTRATE\METHYLEP HEDRINE HYDROCHLORIDE-DL (C)  (9) LEVOFLOXACIN (T)  (10) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)		Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg (frequency unspecified) and received till Study Day 56. On Study Day 57, the patient developed Grade 5 urosepsis and was hospitalized with moderate dyspnea and intermittent fever (39°C). Blood and urine cultures revealed Escherichia coli infection. A CT chest scan revealed increased loculated effusion in the left lower hemothorax. Treatment with levofloxacin and piperacillin/tazobactam was initiated. On Study Day 58, the patient underwent left percutaneous catheter drainage for increased pleural effusion. On the same day, the patient received her third cycle of pralsetinib. However, pralsetinib treatment was discontinued on Study Day 68. On Study Day 69, the patient died due to fatal urosepsis and underlying non-small cell lung cancer. An autopsy was not performed. The investigator assessed the causality of fatal urosepsis as not related to pralsetinib.  The patient had a an advanced underlying disease which led to even superiot venecaval thrombosis along with concurrent pericardial and pleural effusion. The patient was also in an immunosuppressant state as per the presence of Escherichia coli in blood and urine culture. This could have led to urosepsis and ultimately death of the patient
2752094 63 Female UNITED STATES OF AMERICA Non-Interventional	Bronchitis Grade 5	50	(1) PRALSETINIB (S)  (2) RIVAROXABAN (C)  (3) LORAZEPAM (C)  (4) BUSPIRONE (C)  (5) LEVOFLOXACIN (T)	Drug interrupted N/A N/A Fatal	"AER 2752094 (PT: Bronchitis)  This non-interventional study case concerned a 63-year-old female from the USA who developed bronchitis, 50 days after starting treatment with pralsetinib for non-small cell lung cancer. The patient's medical history included bronchoscopy. Concurrent conditions included pneumonia and right lower lung collapse. Concomitant medications included rivaroxaban, lorazepam and buspirone. Past drugs included carboplatin, pemetrexed, atorvastatin and pembrolizumab. The patient had a history of

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Study/Program Healthcare professional					<p>residual swallowing issues due to stroke, fatigue and recurrent aspiration pneumonia prior to pralsetinib treatment.</p> <p>After 50 days of starting treatment with pralsetinib (400 mg daily), the patient developed bronchial infection (Grade 5) and fatigue (Grade 3). Three days later, the patient experienced stroke (Grade 2) exhibiting symptoms including increased confusion and inability to use left hand. Two days later, a CT scan of chest, abdomen and pelvis revealed an almost complete response to treatment with no evidence of a pneumonia. The patient was subsequently treated for suspected bronchitis. Blood tests on the same day showed an elevated white blood cell count and pralsetinib therapy was temporarily suspended. The following day, during a scheduled clinic visit, the patient reported continued inability to use left hand and displayed a left-sided facial droop. The patient had a productive cough along with loss of appetite. The patient was prescribed with levofloxacin for the treatment of infection along with intravenous fluids for rehydration. After 75 days of receiving the first dose pralsetinib, the patient died. The cause of death was presumed as bronchial infection. An autopsy was not performed. The physician assessed the causality of fatal bronchial infection as possibly related to pralsetinib."</p> <p>The concurrent pneumonia/collapse of the lung with history of recurrent aspiration pneumonia and stroke must have contributed to the event of bronchitis.</p>
2767594 68 Male UNITED STATES OF	COVID-19 Grade 5	679	(1) PRALSETINIB (S)  (2) COLECALCIFEROL (C)  (3) CURCUMA LONGA (C)	Drug interrupted N/A N/A Fatal	<p>"AER 2767594 (PT: COVID-19):</p> <p>This clinical study case concerned a 68-year-old male (patient number: 2608011) from the USA who developed COVID-19, 678 days after starting therapy with pralsetinib for non-small cell lung cancer. The patient's medical history included hepatitis A,</p>

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AMERICA Clinical Study Healthcare professional			(4) BRIMONIDINE TARTRATE\BRINZOLAMI DE (C)  (5) ASCORBIC ACID (C)  (6) ACETYLSALICYLIC ACID (C)  (7) CITRUS X AURANTIUM\RUBUS FRUTICOSUS\VACCINIUM MYRTILLUS\VITIS VINIFERA (C)  (8) PARACETAMOL (C)  (9) SILYBUM MARIANUM (C)  (10) UBIDECARENONE (C)  (11) AMLODIPINE (C)  (12) NEBIVOLOL (C)  (13) CARVEDILOL (C)  (14) ENOXAPARIN (C)  (15) HYDROCHLOROTHIAZIDE (C)		arthrosis, and arthroplasty of hip. Concurrent conditions included glaucoma, hypercholesterolemia, hypertension, pain, neutropenia, hair growth increased, muscle stiffness, diarrhea, fatty liver, neuropathy, lymphopenia, anorexia, gram-positive bacterial infection, hypokalemia, and hyponatremia. Concomitant medications included colecalciferol, curcuma longa, brimonidine/brinzolamide, ascorbic acid, acetylsalicylic acid, citrus aurantium/rubus fruticosus/vaccinium myrtillus/vitis vinifera, paracetamol, silybum marianum, ubidecarenone, amlodipine, nebivolol, carvedilol, enoxaparin, hydrochlorothiazide, lisinopril, nebivolol, metoprolol, latanoprost, timolol, acetylsalicylic acid, docosate, famotidine, bisacodyl, magnesium hydroxide, naloxone, glyceryl trinitrate, oxycodone, cefazolin, vancomycin, Moderna Covid-19 Vaccine, dexamethasone, ceftriaxone, diphenhydramine, cefepime, Vitamin B complex, and probiotic. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 300 mg (frequency unspecified) received till Study Day 678. On Study Day 678, after receiving the most recent dose, the patient tested positive for COVID 19 (Grade 3). Therapy with pralsetinib was temporarily suspended. On Study Day 679, the patient developed shortness of breath and was hospitalized the following day with COVID-19 infection and toxic metabolic encephalopathy. The patient's condition rapidly deteriorated, requiring intubation and dialysis in the intensive care unit. Despite aggressive treatment, including intravenous fluids, vancomycin, remdesivir, and dexamethasone, the patient developed renal failure and other complications. Blood cultures revealed Clostridium ramosum and Streptococcus salivarius infections for which the patient received treatment with ampicillin/subbactam and amoxicillin/clavulanic acid. The laboratory data revealed low white blood cell count and red blood cell count, normal hemoglobin, hematocrit, and platelet count. The mean corpuscular volume (MCV), mean corpuscular

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			(16) LISINOPRIL (C)  (17) NEBIVOLOL HYDROCHLORIDE (C)  (18) METOPROLOL (C)  (19) LATANOPROST (C)  (20) TIMOLOL (C)  (21) ACETYLSALICYLIC ACID (C)  (22) DOCUSATE SODIUM (C)  (23) FAMOTIDINE (C)  (24) BISACODYL (C)  (25) MAGNESIUM HYDROXIDE (C)  (26) NALOXONE (C)  (27) GLYCERYL TRINITRATE (C)  (28) OXYCODONE (C)  (29) CEFAZOLIN (C)		<p>hemoglobin (MCH), and MCH concentration were slightly elevated. Differential counts showed low lymphocytes and monocytes, with normal neutrophils. The blood cultures indicated gram-positive rods and <i>Streptococcus sanguinis</i>. The coronavirus CoV-2 PCR test was positive, confirming COVID-19 infection. From Study Day 681 to 684, the patient's laboratory results showed a fluctuating pattern. White blood cell counts ranged from low to normal, while red blood cell counts remained consistently below normal range. Hemoglobin levels declined slightly from 13.3 to 11.4 g/dL, and hematocrit decreased from 38.2% to 32.9%. MCV was consistently elevated and MCH and MCHC values were slightly above normal range, while RDW remained stable. On Study Day 685, the patient was discharged. The first episode of COVID-19 infection was considered resolved with sequelae on the same day, however, it was reported that the patient was later readmitted for a second episode of COVID-19 infection (Grade 5). On Study Day 714, the patient was extubated and removed from dialysis and shortly after, the patient died due to COVID-19. An autopsy was not performed. The physician assessed the episodes of COVID-19 infection as not related to pralsetinib."</p> <p>The pre-existing cytopenia and the presence of opportunistic pathogens in blood culture like <i>Clostridium ramosum</i> and <i>Streptococcus salivarius</i>, showcases the patient's immunosuppressive state. This along with the contributory effect from concurrent dyslipidemia must have predisposed the patient to the event of covid</p>

AER Number	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
			(30) VANCOMYCIN (C)  (31) DEXAMETHASONE (C)  (32) CEFTRIAXONE (C)  (33) DIPHENHYDRAMINE HYDROCHLORIDE (C)  (34) CEFEPIME HYDROCHLORIDE (C)		
2783335 60 Male UNITED STATES OF AMERICA Non-Interventional Study/Program Healthcare professional	Septic shock Grade 5	52	(1) PRALSETINIB (S)  (2) PREDNISONE (C)  (3) DIHYDROCODEINE (C)  (4) OXYGEN (C)  (5) HEPARIN (C)	NR Unknown N/A Fatal	<p>"AER 2783335 (PT: Septic shock)</p> <p>This non-interventional study case concerned a 60-year-old male from the USA who developed septic shock, 52 days after starting treatment with pralsetinib for non-small cell lung cancer. The patient's medical history was not reported. Concurrent conditions included hypertension, cerebral ischemia, dyspnea and pulmonary embolism. Concomitant medications included prednisone, dihydrocodeine, oxygen and heparin. The patient's prior cancer treatment regimens included pembrolizumab, RET-KIF5B and carboplatin+paclitaxel.</p> <p>Approximately 2.5 months before initiating treatment with pralsetinib, a CT scan revealed both clinical and pathological disease progression along with an asymptomatic pulmonary embolism. After 11 days of starting treatment with pralsetinib, the patient was hospitalized due to an ischemic attack. After 52 days of starting treatment with pralsetinib, the patient developed septic shock (Grade 5). A chest CT scan showed high inflammatory indices and inflammatory pulmonary thickening. The patient presented with fever, severe dyspnea and was treated with empiric antibiotics and high-flow oxygen therapy.</p>

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					<p>Despite the interventions, the patient's condition progressively worsened. Eventually, the patient died due to septic shock accompanied by paraneoplastic infection symptoms including thrombocytopenia and reduced fibrinogen levels. An autopsy was not performed. The physician assessed the septic shock as not related to pralsetinib."</p> <p>The patient's underlying disease was in a progressive state as confirmed by the CT scan findings.. This along with the pre-existing cerebral ishemia, pulmonary embolism and concurrent paraneoplastic disseminated intravascular coagulationmust have led to the event of septic shock.</p>
2791607 59 Female KOREA, REPUBLIC OF Clinical Study Healthcare professional	Sepsis Grade 5	170	(1) PRALSETINIB (S)  (2) DIAZEPAM (C)  (3) NORTRIPTYLINE HYDROCHLORIDE (C)	Drug interrupted N/A N/A Fatal	<p>"AER 2791607 (PT: Sepsis):</p> <p>This clinical study case concerned a 59-year-old female (patient number: 6101001) from Korea, Republic of who developed sepsis, 170 days after starting therapy with pralsetinib for non-small cell lung cancer. The patient's medical history included hypertension and cholecystitis acute. Concurrent conditions included anxiety, hypothyroidism, productive cough, musculoskeletal pain, decreased appetite, dyspnea and cholecystectomy. Concomitant medications included diazepam, and nortriptyline. Past drugs included cisplatin, pemetrexed, gemcitabine, docetaxel and tyrosine-kinase inhibitor therapy with sitravatinib. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg daily. On Study Day 170, after receiving the most recent dose, the patient developed Grade 5 sepsis, requiring hospitalization. The patient presented with a high fever of 39.6°C and abnormal laboratory results, including low sodium, chloride, phosphate, calcium, and albumin levels, and elevated alkaline phosphatase levels. A CT scan on Study Day 171 revealed active arterial bleeding at the gallbladder bed with a small hematoma, increased fluid collection, and possible</p>

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					<p>bile leakage. There were also signs of portal vein thrombosis and suspected hepatic artery occlusion with ischemic changes in liver segments. Blood cultures detected Klebsiella pneumoniae, leading to the temporary interruption of pralsetinib. Over the next few days from Study Day 172 to Study Day 176, the patient's condition worsened. Elevated C-reactive protein levels were observed, and additional blood cultures revealed Vancomycin-Resistant Enterococci (VRE) and Enterococcus faecium. The patient received various antibiotics, including meropenem, vancomycin, and linezolid for infection and sepsis. An abdominal percutaneous catheter drainage was also performed. Eventually, on Study Day 177, the patient died due to worsening of septic condition. Autopsy was not performed. The physician assessed the fatal sepsis as not related to pralsetinib."</p> <p>The patient had history of cholecystitis and at the time pf presentation to hospital, there was active arterial bleeding at the gallbladder bed with possible bile leak along with segmental ischemia of the liver. This along with the presence of Klebsiella pneumoneae, vancomycin resistant enterococci and enterococcus faecium (which depicts the immunosuppressed state of the patient) must have led to sepsis and death.</p>
2793440 63 Male FRANCE Clinical Study Healthcare professional	Pneumonia Grade 5	NR	(1) PRALSETINIB (S)  (2) FENTANYL (C)  (3) MORPHINE (C)  (4) PREDNISOLONE (C)  (5) TAMSULOSIN (C)  (6) TINZAPARIN SODIUM	NR Unknown N/A Fatal	<p>"AER 2793440 (PT: Pneumonia):</p> <p>This clinical study case concerned a 63-year-old male (patient number: 1701004) from France who developed pneumonia, 87 days after starting therapy with pralsetinib for non-small cell lung cancer. The patient's medical history was not reported. Concurrent conditions included intermittent headache, fatigue, cough, hemoptysis, dyspnea, myalgia, back pain, dizziness, psychomotor retardation, and lymphocytopenia. Concomitant medications included fentanyl, morphine, prednisolone, tamsulosin, tinzaparin, levetiracetam, alprazolam, naloxegol,</p>

AER Number	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
			(C)  (7) LEVETIRACETAM (C)  (8) ALPRAZOLAM (C)  (9) NALOXEGOL (C)  (10) PARACETAMOL (C)  (11) POTASSIUM CHLORIDE (C)  (12) AMOXICILLIN\CLAVULANATE POTASSIUM (T)  (13) DOCUSATE SODIUM (T)  (14) MACROGOL 4000 (T)  (15) MORPHINE SULFATE (T)  (16) MORPHINE SULFATE (T)  (17) MICONAZOLE (T)  (18) PARACETAMOL (T)  (19) PREDNISOLONE METASULFOBENZOATE		paracetamol and potassium chloride. Past drugs included cisplatin, pemetrexed disodium and nivolumab. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg daily. On Study Day 87, the patient presented with dyspnea and fever and was diagnosed with lung infection (Grade 5) which required hospitalization. Upon hospitalization, vital signs showed high blood pressure and tachycardia, with a decreased blood count. The patient exhibited cough, confusion and a high C-reactive protein (CRP) level. A chest X-ray confirmed pneumonia in the right lung base. Initial treatment included oxygen therapy and amoxicillin/clavulanate. The patient also received alprazolam, docusate sodium, macrogol, morphine, miconazole, paracetamol, prednisolone, tamsulosin, levetiracetam and tinzaparin. On Study Day 95, the patient experienced a recurrence of symptoms, including increased CRP, hepatic cytolysis, and abdominal pain. A CT scan revealed abscessed pneumonia in the right lower lobe with possible pulmonary infarction. Antibiotic therapy was changed to levofloxacin, resulting in clinical stability but with significant fatigue and continued oxygen dependence. Physical examination revealed limited mobility and neurological issues including psychomotor retardation, disorientation, memory disorders, anxiety, and left hemiplegia. Cardiopulmonary examination indicated tachycardia and diminished breath sounds in the right lung field with major crackles. Abdominal examination showed tenderness and pain, likely exacerbated by constipation. On Study Day 106, further testing revealed a positive PCR analysis for pneumocystis in the bronchoalveolar lavage (BAL) fluid. Treatment with tazobactam and ciprofloxacin was initiated. By Study Day 110, pneumocystis infection was confirmed, along with severe lymphocytopenia. Treatment with trimethoprim/sulfamethoxazole was initiated. A neurological episode occurred on Study Day 115, initially suspected as encephalitis, but later attributed to either an epileptic seizure or morphine overdose. An emergency CT scan

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			SODIUM (T)  (20) TAMSULOSIN (T)  (21) LEVETIRACETAM (T)  (22) LEVOFLOXACIN (T)		<p>of the brain showed no bleeding, and antiviral treatment was stopped. The patient remained hospitalized until Study Day 127, then was transferred to a palliative care unit. The patient's condition continued to deteriorate, with ongoing pneumonitis and confusion requiring tiapride. Due to the patient's severely compromised state and significant muscle wasting, the study drug was not resumed. On Study Day 150, the patient died due to lung infection. An autopsy was not performed. The physician assessed the lung infection as not related to pralsetinib."</p> <p>The patient was immunosuppressed as evidenced by the pre-existing lymphopenia and concurrent prednisolone use. Additionally, presence of pneumocystis was confirmed in the bronchioalveolar fluid which further shows compromised immunity which eventually led to fatal pneumonia.</p>
2799134 57 Male KOREA, REPUBLIC OF Clinical Study Healthcare professional	Pneumonia Grade 5	40	(1) PRALSETINIB (S)  (2) ACETYLSALICYLIC ACID (C)  (3) NALOXONE HYDROCHLORIDE\OXYCODONE HYDROCHLORIDE (C)  (4) OXYCODONE (C)  (5) HALOPERIDOL (C)  (6) LEVAMLODIPINE BESILATE\TELMISARTAN (C)	Drug interrupted N/A N/A Fatal	<p>"AER 2799134 (PT: Pneumonia):</p> <p>This clinical study case concerned a 57-year-old male (patient number: 6101006) from Korea, Republic Of who developed pneumonia, 40 days after starting therapy with pralsetinib for non-small cell lung cancer. The patient's medical history included percutaneous coronary intervention. Concurrent conditions included dyslipidemia, unstable angina, hypertension, glucose intolerance, and constipation. Concomitant medications included acetylsalicylic acid, naloxone/oxycodone, oxycodone, haloperidol, levamldipine/telmisartan, tamsulosin, valsartan, levamlodipine, quetiapine, lactulose, finasteride, ceftriaxone, propacetamol, norepinephrine, levofloxacin, rosuvastatin, and losartan. Past drugs included cisplatin, pemetrexed, gemcitabine, and docetaxel. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg daily. On Study Day 37, the patient experienced back pain followed by fever two days later which was treated with ibuprofen. The</p>

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			(7) TAMSULOSIN (C)  (8) VALSARTAN (C)  (9) LEVAMLODIPINE (C)  (10) QUETIAPINE (C)  (11) FINASTERIDE (C)  (12) CEFTRIAXONE (C)  (13) PROPACETAMOL (C)  (14) NOREPINEPHRINE (C)  (15) LEVOFLOXACIN (C)  (16) LACTULOSE (C)  (17) LOSARTAN (C)  (18) ROSUVASTATIN (C)  (19) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (20) LEVOFLOXACIN (T)		patient was hospitalized on Study Day 40 due to back pain, cough and fever. The CT scan showed multifocal patchy consolidations, with ground glass opacities in both upper lungs and right middle along with and large amount of bilateral pleural effusion with passive atelectasis. The patient was diagnosed with first episode of pneumonia (Grade 3) on the same day and started on intravenous antibiotic. Blood cultures showed the presence of <i>Staphylococcus aureus</i> . Disease progression was observed on Study Day 59 through an MRI of the brain. On Study Day 63, the patient's vital signs and blood tests were conducted revealing elevated liver enzymes, low albumin, and abnormal blood cell counts. The pneumonia was treated with multiple medications including propacetamol, levofloxacin, tazoperan, and morphine, while ibuprofen was administered for fever. The patient recovered from first episode of pneumonia with sequelae and was discharged from the hospital on the same day with a reduced dosage of pralsetinib at 300 mg. The dose was interrupted and the last dose of the pralsetinib prior to the event was on Study Day 75. On Study Day 76, the patient developed second episode of pneumonia (Grade 5) which was confirmed by a CT scan of the chest. The following day, the patient was hospitalized for intravenous antibiotic treatment. Treatment for pneumonia included piperacillin/tazobactam and levofloxacin, and pralsetinib was restarted at 300 mg. On Study Day 87, the patient was discharged with stationary dyspnea. On the same day the event first episode of pneumonia was recovered. On Study Day 99, pralsetinib was stopped. The patient visited ER due to hemoptysis and aggravation of dyspnea. A CT scan of the chest showed aggravated pneumonia and increased irregular ground glass opacity and consolidation in both lungs. On Study Day 100, a decision was made to discontinue pralsetinib and the patient was withdrawn from the study due to no further benefits. Eventually, the patient died due to pneumonia. An autopsy was not performed. The physician

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					<p>assessed both episodes of pneumonia as not related to pralsetinib."</p> <p>The patient had several risk factors for the occurrence of the the infectious event of pneumonia including disease progression, dyslipidemia and glucose intolerance. Moreover, the presence of <i>Staphylococcus aureus</i>, denotes the immunocompromised state of the patient.</p>
2799253 81 Male FRANCE Clinical Study Healthcar e profession al	Pneumocys tis jirovecii pneumonia Grade 5	43	(1) PRALSETINIB (S)  (2) INDAPAMIDE\PERINDOP RIL (C)  (3) INDAPAMIDE\PERINDOP RIL (C)  (4) METFORMIN HYDROCHLORIDE\SITAG LIPTIN PHOSPHATE MONOHYDRATE (C)  (5) ACETYLSALICYLATE LYSINE (C)  (6) VERAPAMIL (C)  (7) ROSUVASTATIN CALCIUM (C)  (8) LEVOTHYROXINE SODIUM (C)	Drug interrupted N/A N/A Fatal	<p>"AER 2799253 (PT: Pneumocystis jirovecii pneumonia):</p> <p>This clinical study case concerned an 81-year-old male (patient number: 1706001) from France who developed pneumocystis jirovecii pneumonia, 43 days after starting therapy with pralsetinib for medullary thyroid cancer. The patient's medical history included thyroidectomy. Concurrent conditions included sleep disorder, thermal burn, lumbalgia, arterial hypertension, hypothyroidism, insulin dependent diabetic, vitamin D deficiency, hypomagnesaemia, mouth mycosis, hypocalcemia and prostatitis. Concomitant medications included indapamide/perindopril, metformin/sitagliptin, acetylsalicylate lysine, verapamil, rosuvastatin calcium, levothyroxine, calcium carbonate, tocopherol, glycine max seed oil/persea americana oil, calcitriol, ceftriaxone, magnesium, glimepiride and insulin detemir. Past drugs included glimepiride, insulin detemir and vandetanib. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg (frequency unspecified) and received till Study Day 25. On Study Day 25, the pralsetinib dose was interrupted due to persistent asthenia. On Study Day 33, the patient developed lymphopenia, followed by a significant increase in C-reactive protein (CRP) by Study Day 40. On Study Day 42, the patient presented with depression, anxiety along with muscle weakness. An electrocardiogram revealed sinus tachycardia and a urine dipstick showed hematuria and</p>

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			(9) CALCIUM CARBONATE (C)  (10) TOCOPHERYL ACETATE (C)  (11) GLYCINE MAX SEED OIL\PERSEA AMERICANA OIL (C)  (12) CALCITRIOL (C)  (13) CEFTRIAXONE SODIUM (C)  (14) MAGNESIUM (C)  (15) GLIMEPIRIDE (C)  (16) INSULIN DETEMIR (C)  (17) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)  (18) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)		<p>proteinuria. A CT scan led to a diagnosis of acute interstitial pneumonitis, showing ground-glass opacities and areas of consolidation predominantly in the peri-hilar region. Treatment with pralsetinib was restarted at a reduced dose of 300 mg due to renal insufficiency. On Study Day 43, the patient developed Grade 5 pneumocystis jiroveci pneumonia, requiring hospitalization. Laboratory results showed elevated liver enzymes and CRP levels continued to rise. On Study Day 44, a bronchial lavage smear revealed cysts of pneumocystis jirovecii confirming the diagnosis for which the patient received treatment with sulfamethoxazole/trimethoprim. On same day, treatment with pralsetinib was stopped due to pneumonitis. Laboratory results on Study Day 45 showed further increases in CRP and liver enzymes. By Study Day 46, the patient was admitted to ICU and treatment included piperacillin/tazobactam and oxygen therapy. A chest CT angiogram ruled out pulmonary embolism but showed clear intensification of interstitial lung disease predominantly affecting the upper lobes. On Study Day 56, the patient died due to respiratory insufficiency secondary to pneumocystis jirovecii pneumonia. An autopsy was not performed. The investigator reported that the event pneumocystis jiroveci pneumonia was possibly related to pralsetinib."</p> <p>The patient was of elderly age with evidence of an immunocompromised state like diabetes, vitamin D deficiency, mouth mycosis and co-existing lymphopenia. The bronchoalveolar smear also revealed pneumocystis jirovecii which is an opportunistic infection, thus providing an alternative etiology for the event.</p>
2800088 69 Female	Pneumonia Grade 5	230	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)	Drug interrupted N/A	"AER 2800088 (PT: Pneumonia):  This clinical study case concerned a 69-year-old female (patient

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UNITED STATES OF AMERICA Clinical Study Healthcare professional			(3) DILTIAZEM (C)  (4) ATORVASTATIN (C)  (5) LEVETIRACETAM (C)  (6) METOPROLOL SUCCINATE (C)  (7) CEFPODOXIME (T)  (8) DOXYCYCLINE (T)  (9) VANCOMYCIN HYDROCHLORIDE (T)  (10) CEFEPIME HYDROCHLORIDE (T)  (11) LEVOFLOXACIN (T)	N/A Fatal	number: 2603018) from the USA who developed pneumonia, 217 days after starting therapy with pralsetinib for non-small cell lung cancer. The patient's medical history was not reported. Concurrent conditions included chronic renal insufficiency, seizure, hypothyroidism and hypertension. Concomitant medications included levothyroxine, diltiazem, atorvastatin, levetiracetam and metoprolol. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 300 mg daily which was later adjusted to 200 mg daily by Study Day 180. On Study Day 195, laboratory results revealed abnormalities in various blood cell counts, including low white blood cells, hemoglobin, and lymphocytes. A CT scan on Study Day 217 showed multifocal opacities in the chest. By Study Day 220, the patient developed symptomatic pneumonia with fever and productive cough, for which antibiotics (cefpodoxime and doxycycline) were prescribed. Despite initial improvement, the patient continued to experience worsening dyspnea, associated with nausea, vomiting and worsening fatigue. Neutropenia was noted on Study Day 222, leading to the suspension of pralsetinib on Study Day 224. On Study Day 229, following bronchoscopy, the patient was diagnosed with Grade 3 pneumonia, which worsened to Grade 5 and required hospitalization. A diagnostic bronchoscopy revealed the presence of Alcaligenes faecalis, rare Candida albicans and pus. A CT pulmonary angiogram revealed worsening of airway narrowing and multiple new patchy opacities in both lungs prominently within right lower lobe along with slight increase of a small pericardial effusion. The patient was treated with vancomycin, cefepime and levofloxacin and eventually required mechanical ventilation. The patient's laboratory tests revealed low counts for red blood cells, lymphocytes, platelets, low levels of hemoglobin, with neutrophil percentage elevated but absolute neutrophil count within normal range. On Study Day 238, the patient died due to pneumonia after withdrawal of ventilator support. An autopsy was not performed. The

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					<p>investigator assessed pneumonia as related to pralsetinib."</p> <p>The patients concurrent conditions like chronic kidney diseases and seizure have propensity to predispose the patient to infections, Additionally the identification of opportunistic pathogens like Alcaligenes faecalis and rare Candida species also confirms the underlying immunosuppression.</p>
2800321 48 Male UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Pneumonia Grade 5	210	(1) PRALSETINIB (S)  (2) PARACETAMOL (C)  (3) AMLODIPINE BESILATE (C)  (4) CETIRIZINE HYDROCHLORIDE (C)  (5) ENOXAPARIN SODIUM (C)  (6) FLUTICASONE PROPIONATE (C)  (7) OMEGA-3 FATTY ACIDS (C)  (8) OMEPRAZOLE (C)  (9) OXYCODONE (C)  (10) TRAZODONE HYDROCHLORIDE (C)	Drug interrupted N/A N/A Fatal	<p>"AER 2800321 (PT: Pneumonia):</p> <p>This clinical study case concerned a 48-year-old male (patient number: 2603003) from the USA who developed pneumonia, 210 days after starting therapy with pralsetinib for non-small cell lung cancer.</p> <p>The patient's medical history was not reported. Concurrent conditions included insomnia, cellulitis of arm, hypophosphatemia, reflux gastritis, allergic rhinitis, diverticulitis intestinal, essential hypertension and thrombosis. Concomitant medications included paracetamol, amlodipine, cetirizine, enoxaparin, fluticasone, omega-3 fatty acids, omeprazole, oxycodone, trazodone, lidocaine, potassium phosphate monobasic/sodium phosphate dibasic/sodium phosphate monobasic and atezolizumab. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 200 mg daily and received till Study Day 193. Since enrolment, the patient had experienced ALT increase, abdominal discomfort, dry skin, hypophosphatemia and neuropathy. On Study Day 51, the patient experienced worsening diverticulitis. A progression biopsy was performed on Study Day 182. Due to disease progression, pralsetinib treatment was discontinued on Study Day 193 and the patient began chemotherapy with atezolizumab on Study Day 196. On Study Day 210, the patient developed Grade 5 pneumonia presenting with high fever, shortness of</p>

AER Number	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
			(11) LIDOCAINE (C)  (12) POTASSIUM PHOSPHATE MONOBASIC\SODIUM PHOSPHATE DIBASIC\SODIUM PHOSPHATE MONOBASIC (ANHYDROUS) (C)  (13) ATEZOLIZUMAB (C)  (14) PARACETAMOL (T)  (15) CETIRIZINE (T)  (16) ENOXAPARIN (T)  (17) FLUTICASONE PROPIONATE (T)  (18) OMEPRAZOLE (T)  (19) OXYCODONE (T)  (20) SODIUM CHLORIDE (T)  (21) POTASSIUM PHOSPHATE MONOBASIC\SODIUM PHOSPHATE DIBASIC\SODIUM		<p>breath, right sided lower rib pain radiating to the back, and fatigue. A chest X-ray revealed right middle lobe consolidation and septal thickening at the site of prior lung cancer, raising concerns about disease recurrence. Treatment with cefepime was initiated. On Study Day 211, a CT scan of the chest showed multiple solid pulmonary nodules indicating metastatic disease, new mediastinal lymphadenopathy and a small to moderate right pleural effusion. The patient received treatment with acetaminophen, cetirizine, enoxaparin, fluticasone, omeprazole, oxycodone, sodium chloride, potassium phosphate monobasic/sodium phosphate dibasic/sodium phosphate monobasic and trazodone to manage symptoms. Over the next few days, the patient's treatment regimen was adjusted with the addition of vancomycin, ibuprofen, polyethylene glycol, senna, lidocaine patch, magnesium sulphate, and potassium chloride. A chest X-ray on Study Day 216 revealed bilateral pleural effusion with worsening atelectasis in the lower lobes, increased consolidation in the right lower lobe due to pneumonia and persistent consolidation in the middle lobe representing progressive metastatic disease. On Study Day 234, the patient died due to progressive disease. An autopsy was not performed. The physician assessed the causality of pneumonia as not related to pralsetinib."</p> <p>The patient had other co-morbidities like thrombosis, diverticulitis, reflux gastritis and there was underlying disease progression as well. The concomitant medications like atezolizumab and fluticasone must have also contributed to this event</p>

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome	Narrative MAH Comment
			PHOSPHATE MONOBASIC (ANHYDROUS) (T) (22) TRAZODONE (T) (23) VANCOMYCIN (T) (24) IBUPROFEN (T) (25) MACROGOL (T) (26) SENNA SPP. (T) (27) LIDOCAINE (T) (28) MAGNESIUM SULFATE (T) (29) POTASSIUM CHLORIDE (T)		
2800553 64 Female HONG KONG Clinical Study Non- healthcare profession al	Pneumonia Grade 5	64	(1) PRALSETINIB (S) (2) CODEINE PHOSPHATE (C) (3) AMLODIPINE BEZILATE (C) (4) CODEINE PHOSPHATE\PSUEDOEPHEDRINE HYDROCHLORIDE\TRIPROLIDINE	Drug interrupted N/A N/A Fatal	"AER 2800553 (PT: Pneumonia):  This clinical study case concerned a 64-year-old female (patient number: 6401001) from Hong Kong who developed pneumonia, 64 days after starting therapy with pralsetinib for lung neoplasm malignant. The patient's medical history included bilateral salpingo-oophorectomy. Concurrent conditions included hemangioma of liver, hepatic cyst, hydrosalpinx and ovarian cyst. Concomitant medications included codeine, amlodipine, codeine/pseudoephedrine/triprolidine, aluminum/magnesium hydroxide and simeticone. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg daily and received till Study Day 64. At the baseline, the patient had

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
			HYDROCHLORIDE (C)  (5) SIMETICONE (C)		<p>massive right pleural effusion, cough and pleuritic chest wall pain. A CT scan on Study Day 53 indicated a partial response to treatment. On Study Day 64, the patient developed Grade 5 pneumonia presenting with generalized weakness, fever (39°C), malaise, dyspnea and chills. The patient was non-neutropenic on admission and did not present significant lung finding during the physical examination. The patient was hospitalized and given oxygen therapy and broad-spectrum antibiotics for pneumonia management. Various tests, including COVID-19, multiplex PCR for respiratory pathogens, urine culture, and blood culture were all negative. A chest x-ray revealed a new, dense consolidation in the right upper lobe. Despite broad-spectrum antibiotic treatment, the patient's chest condition failed to improve, leading to respiratory failure requiring non-invasive ventilation support. On Study Day 73, the patient died due to pneumonia. The cause of death was reported as pneumonia and lung cancer. No autopsy was performed. The investigator assessed pneumonia as related to pralsetinib."</p> <p>Though the event of pneumonia had occurred after 2 months of pralsetinib therapy, the pre-existing massive pleural effusion must have contributed to it.</p>
2802164 87 Male UNITED STATES OF AMERICA Clinical Study Non-healthcare	Sepsis  Urinary tract infection Grade 5  Grade 2	10  10	(1) PRALSETINIB (S)  (2) AMLODIPINE (C)  (3) LISINOPRIL (C)  (4) SILODOSIN (C)  (5) DUTASTERIDE (C)  (6) LEVOTHYROXINE (C)	NR  NR Unknown  Unknown N/A  N/A Fatal	<p>"AER 2802164 (PT: Sepsis, Urinary tract infection):</p> <p>This clinical study case concerned an 87-year-old male (patient number: 2605004) from the USA who developed sepsis and urinary tract infection, 10 days after starting therapy with pralsetinib for medullary thyroid cancer. The patient's medical history was not reported. Concurrent conditions included encephalopathy, metastases to bone, metastases to liver, metastases to lung, hypothyroidism, pneumonitis, shoulder pain, hypertension, skin lesion excision, gastric ulcer, runny nose, thyroidectomy total, neck dissection and mucositis. Concomitant</p>

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
professional			(7) FINASTERIDE (C)  (8) FAMOTIDINE (C)  (9) CEFEPIME HYDROCHLORIDE (T)  (10) ACICLOVIR (T)  (11) HALOPERIDOL (T)  (12) VANCOMYCIN (T)  (13) MORPHINE (T)	Not Recovered/Not Resolved/Ongoing	medications included amlodipine, lisinopril, silodosin, dutasteride, levothyroxine, finasteride and famotidine. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 200 mg (frequency unspecified) and received till Study Day 10. On Study Day 10, the patient developed Grade 5 sepsis, Grade 3 acute encephalopathy and Grade 2 urinary tract infection. The patient's laboratory results revealed negative results for bacterial or viral etiology in the lumbar puncture, a negative herpes simplex virus test, and negative blood and CSF cultures. A urine culture showed a presence of Enterococcus faecalis. The patient was started on cefepime for sepsis, aciclovir as empiric therapy and haloperidol and olanzapine for agitation prophylaxis. On Study Day 11, a CT of the head showed mild cerebral atrophy along with small hyperintensity and small left calcified meningioma. The following day, vancomycin was added to the patient's sepsis treatment. An EEG showed signs of diffuse cerebral dysfunction, possibly indicating toxic-metabolic encephalopathy or medication effects. On Study Day 14, the patient was started on ampicillin for sepsis. The patient's blood tests revealed mostly normal values with slightly low blood urea nitrogen, creatinine, calcium, and protein levels along with slightly elevated glucose levels. On Study Day 19, heparin was administered for deep vein thrombosis prophylaxis. On Study Day 20, a rapid response team was called due to breathing difficulties and non-responsiveness. The patient was found to have hyponatremia, hypomagnesemia, and likely aspiration. Given the patient's advanced illness and rapid decline, it was decided to focus on comfort end-of-life care. The patient was transferred to hospice care, with additional medications provided for symptom management including ipratropium bromide, salbutamol, glycopyrrolate, lorazepam and morphine. The patient was unresponsive except for pain withdrawal and had cool extremities. On Study Day 22, the patient experienced significant seizures and high-grade fevers, initiating the

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
					<p>administration of ketorolac. On the same day, the patient died due to sepsis. An autopsy was not performed. The physician assessed the causality of sepsis and urinary tract infection as not related to pralsetinib."</p> <p>Though the event occurred 10 days after therapy initiation with pralsetinib, the overall status of the patient was declining with toxic metabolic encephalopathy and metastasis to multiple sites.. Urine culture showed presence of Enterococcus faecalis which is an opportunistic pathogen denoting the immunosuppressive state of the patient. These factors must have led to the progression to sepsis</p>
3403972 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia Grade 5	418	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	<p>AER 3403972 (PT: Pneumonia): This non-interventional study case concerns a male patient who developed pneumonia, 418 days after initiating therapy with pralsetinib for malignant lung neoplasm. No medical history, past drugs, concurrent conditions and concomitant medications were reported. After 378 days of initiating therapy with pralsetinib, the patient developed metastases to bone. After 418 days of therapy onset, the patient developed lung infection, which was suspected due to white blood cell low after chemotherapy, and died on the same day. It was unknown if an autopsy was performed or not.</p> <p>The underlying disease progression as evidenced by the bone metastasis must have contributed to the occurrence of the event. Additionally, the white blood cells count was also low denoting the patient's immunosuppressed state.</p>
2802325 66 Female SPAIN Clinical Study Healthcar	Pneumonia cytomegaloviral Grade 5	33	(1) PRALSETINIB (S)  (2) DEXAMETHASONE (C)  (3) NYSTATIN (C)  (4) TINZAPARIN (C)	Drug interrupted N/A N/A Fatal	<p>"AER 2802325 (PT: Pneumonia cytomegaloviral):</p> <p>This clinical study case concerned a 66-year-old female (patient number: 1605001) from Spain who developed pneumonia cytomegaloviral, 32 days after starting therapy with pralsetinib for non-small cell lung cancer. The patient's medical history included skin lesion and ex-smoker. Concurrent conditions</p>

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
e professional			(5) GANCICLOVIR (T)		<p>included asthenia, deafness, cough, blurred vision, hypothyroidism and oral thrush. Concomitant medications included dexamethasone, nystatin and tinzaparin. The patient's baseline laboratory tests showed all blood cell counts and percentages were within normal ranges, except for a slightly elevated neutrophil percentage. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg (frequency unspecified) and received till Study Day 26. On Study Day 26, the pralsetinib dose was interrupted due to events of dizziness and inability to walk. On Study Day 28, the patient was diagnosed with Grade 4 pulmonary thromboembolism through CT angiography and was hospitalized. Upon admission, the patient presented with symptoms of hypoxemia, head blunting, tachypnea, dyspnea and dizziness. Upon admission, the patient's laboratory tests revealed normal blood cell counts and differentials, with all measured parameters falling within typical ranges. The thoracic CT angiogram revealed centered mediastinal structures without pathologically sized lymph nodes. The scan identified filling defects compatible with pulmonary embolism, affecting both the right and left sides of the pulmonary arterial system with laminar morphology, which could suggest chronic thrombus. The pulmonary parenchyma appeared heterogeneous with a mosaic pattern and multiple laminar atelectasis, but no clear evidence of pulmonary infarction. An infiltrative tumor lesion was also observed in the peritracheal and peribronchial regions. On Study Day 32, the patient developed Grade 5 cytomegalovirus (CMV) pneumonia during hospitalization which was confirmed by a microbiology study conducted with a blood sample revealing CMV infection. It was reported that the patient received steroids which could predispose to this opportunistic CMV pneumonia infection. The patient was started on ganciclovir. Laboratory tests conducted on the same day showed slightly low hemoglobin, hematocrit, and erythrocyte counts, which further decreased by Study Day</p>

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					<p>36. A follow-up thoracic CT angiogram on Study Day 37 showed resolution of the previously observed pulmonary embolism related filling defects. However, the appearance of patchy areas of increased density with a ground-glass pattern in both lung fields, suggesting either an inflammatory/infectious process or drug toxicity. The scan also revealed progression of the infiltrative tumor lesion and the appearance of bilateral pleural effusion. The patient received tinzaparin as treatment for the pulmonary thromboembolism. On Study Day 39, the patient died due to respiratory insufficiency resulting from CMV pneumonia. No autopsy was performed. The investigator reported that the event of CMV pneumonia was not related to pralsetinib."</p> <p>The patient had an underlying disease progression and chronic pulmonary embolism which could have predisposed to infection. There was also co-existing lymphopenia, oral thrush, concurrent usage of dexamethasne and the presence of cytomegalovirus which confirms the event to be attributed to the comromised immune status of the patient.</p>
2802368 71 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia aspiration  Neutropenic sepsis Grade 5  Grade 4	320  307	(1) PRALSETINIB (S)  (2) ACETYLSALICYLIC ACID (C)  (3) ATENOLOL (C)  (4) BETACAROTENE (C)  (5) CHLORTALIDONE (C)  (6) CIPROFLOXACIN (C)  (7) METRONIDAZOLE (C)	Dose interrupted  Dose interrupted N/A  Negative N/A  N/A Fatal  Not Recovered/Not Resolved/Ongoing	<p>"AER 2802368 (PT: Pneumonia aspiration, Neutropenic sepsis):</p> <p>This clinical study case concerned a 71-year-old male (patient number: 2601049) from the USA who developed pneumonia aspiration and neutropenic sepsis while receiving treatment with pralsetinib for medullary thyroid cancer. The patient's oncology history included medullary thyroid cancer, metastases to the liver, bladder cancer, secondary malignant neoplasm of lymph nodes of multiple sites, endocrine neoplasia and parathyroid tumor. Previous surgeries included tonsillectomy, sinus surgery, colonoscopy, cataract extraction and bilateral knee replacement. Concurrent conditions included atrial fibrillation, cerebrovascular accident, deep vein thrombosis, cataract, colonic polyps, dyslipidemia, hypertension, irritable bowel syndrome,</p>

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
			(8) PANTOPRAZOLE (C)  (9) SIMVASTATIN (C)  (10) APIXABAN (C)  (11) VANCOMYCIN (T)  (12) CEFAZOLIN (T)		osteoarthritis of knee, allergy to penicillin, renal stone, pheochromocytoma and pruritic skin rash. Concomitant medications included acetylsalicylic acid, atenolol, betacarotene, chlortalidone, ciprofloxacin, metronidazole, pantoprazole, simvastatin and apixaban. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg daily which was temporarily interrupted on Study Day 115. On Study Day 136, pralsetinib was restarted at the same dose level and interrupted again on Study Day 306. On Study Day 302, a CT scan showed an enlarged low-attenuation structure surrounding the left humeral head and proximal humerus and suspecting hemorrhage. Subsequently, a chest CT showed a new small left and right pleural effusion. On Study Day 304, laboratory tests indicated anemia (Grade 3) and the patient reported intermittent left upper extremity edema. The patient received a blood transfusion on Study Day 305, which raised the hemoglobin level. The following day, the patient developed a high fever of 104.2°F. On Study Day 307, the patient was hospitalized with Grade 4 neutropenic sepsis, presenting with altered mentation, fever, left shoulder pain, and arm swelling. Additional symptoms included a reducible umbilical hernia and possible left lower lobe pneumonia. Upon admission, the patient's vital signs were elevated, and laboratory tests revealed various abnormalities, including low sodium, elevated BUN and creatinine, and abnormal liver function tests. Blood and urine cultures were positive for <i>Staphylococcus aureus</i> , leading to antibiotic treatment with ceferime and vancomycin. The chest X-ray findings revealed small opacities in the left basilar region of the lung, possibly indicating atelectasis, with or without concomitant airspace disease along with a small amount of fluid in the left pleural space, suggesting pneumonia. An ultrasound revealed the presence of deep vein thrombosis. Further examinations on Study Drug 308 and 309 revealed severely reduced systolic function with global hypokinesia and septic arthritis. The patient

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
					<p>continued treatment with intravenous vancomycin and cefazolin. On Study Day 311, the patient experienced altered mental state with dysarthria along with stroke resulting from chronic atrial fibrillation (Grade 3). During hospitalization, the patient developed acute renal failure. An MRI of the brain revealed multiple small strokes secondary to atrial fibrillation and acute ischemia infarction. Initially, anticoagulation was withheld due to thrombocytopenia, however, apixaban was later administered once the thrombocytopenia improved. By Study Day 313, the patient's creatinine levels peaked, indicating Grade 1 acute kidney injury. On Study Day 320, the patient experienced acute respiratory failure secondary to aspiration pneumonia (Grade 5) and upper gastrointestinal hemorrhage (Grade 4). A chest x-ray showed airspace disease in bilateral lung bases, with layering considering aspiration pneumonia. The patient died on the same day due to acute respiration failure secondary to inspiration pneumonia, complicated with a possible upper GI bleeding, atrial fibrillation resulting in stroke and complicated with methicillin-resistant <i>Staphylococcus aureus</i> bacteremia. No autopsy was performed. The physician assessed the events aspiration pneumonia and neutropenic sepsis as not related to pralsetinib. "</p> <p>There was multiple co-morbidities present in the patient like cerebro vascular accident, deep vein thrombosis dyslipidemia, multiple neoplasms including secondary metastasis. He was also concomitantly taking prednisolone thus decreasing the immunity of the patient. Patient also had co-existing pancytopenia depicting his immunosuppressed state.</p>
2998728 71 Female UNITED STATES	Meningitis Grade 5	617	(1) PRALSETINIB (S)  (2) CEFEPIME HYDROCHLORIDE (C)	Drug interrupted N/A N/A Fatal	<p>"AER 2998728 (PT: Meningitis):</p> <p>This clinical study case concerned a 71-year-old female (patient number: 2613018) from the USA who developed meningitis, 589 days after starting therapy with pralsetinib for non-small cell lung</p>

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
OF AMERICA Clinical Study Healthcare professional			(3) ATENOLOL (C)  (4) BRIMONIDINE TARTRATE\TIMOLOL MALEATE (C)  (5) BIMATOPROST (C)  (6) PREDNISOLONE ACETATE (C)  (7) SUCRALFATE (C)  (8) PARACETAMOL (C)  (9) CETIRIZINE (C)  (10) HYDRALAZINE (C)  (11) MAGNESIUM SULFATE (C)  (12) POTASSIUM CHLORIDE (C)		cancer. The patient's medical history included microdiscectomy, mastectomy, breast reconstruction, surgery, hysterectomy, lumbar laminectomy, tonsillectomy, port insertion, chest tube insertion, chest pain, joint pain and meningitis. Concurrent conditions included delirium, fever, confusion, breast biopsy, biopsy, drug allergy, anemia, anxiety, breast cancer, cataract, glaucoma, hypertension, neck pain, cervical radiculopathy, lumbar radiculopathy, peripheral neuropathy, normocytic anemia, essential hypertension, acute kidney injury, hypokalemia, high anion gap metabolic acidosis, hypocalcemia and empyema. Concomitant medications included cefepime, atenolol, brimonidine/timolol, bimatoprost, prednisolone, sucralfate, paracetamol, cetirizine, hydralazine, magnesium sulfate and potassium chloride.  On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg (frequency unspecified). On Study Day 533, a chest X-ray revealed a new cavitary lung lesion, possibly due to aspiration after intubation for microdiscectomy. The patient was hospitalized on Study Day 537 for L3/L4 microdiscectomy followed by tissue plasminogen activator treatment. A pleural drain was placed and the patient's vital signs and laboratory results were noted, including elevated blood pressure, respiratory rate and blood markers. On Study Day 589, the patient developed first episode of Grade 4 meningitis, presenting with altered mental status, fever, lethargic, tachycardic and tachypneic, leading to a sepsis alert due to empyema, hydropneumothorax and abnormal urine with a suspected pulmonary source. An epidural abscess was identified at L3-L4 and broad-spectrum antibiotics were administered. Despite various complications, including delirium, a trapped lung and a distended bladder, initial CT scans showed no acute abnormalities. The patient's urinalysis was positive for protein, urine culture was positive for enterococcus and candida and a

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
					CT scan of chest and pelvis showed moderate right-sided hydropneumothorax. The patient received balsam peru-castor oil, bimatoprost, brimonidine/timolol, calcium gluconate, gentamicin, heparin, miconazole nitrate, mirtazapine, and valacyclovir for the treatment of meningitis. Pralsetinib treatment was suspended on the same day. On Study Day 590, the patient was obtunded, tachypneic with coarse bilateral upper breath sounds and diminished lung fields bilaterally. Imaging revealed a significant fluid collection at the surgical site, and the patient was placed on a positive pressure ventilator. On Study Day 591, the patient experienced elevated C-reactive protein and a positive enterococcus culture, with MRI showing a post-operative fluid collection. Clinical examination was consistent with meningitis, raising concerns about an iatrogenic cerebrospinal fluid leak secondary to infection. The patient was hospitalized on the next day with fever and underwent various procedures, including IR-guided aspiration and antibiotic treatments with vancomycin, ampicillin and ceftriaxone for iatrogenic meningitis. On Study Day 593, the patient underwent surgical interventions for wound repair and lumbar drain placement. The patient developed encephalopathy secondary to meningitis along with cavitary lung lesion and right empyema. On Study Day 601, the patient experienced oropharyngeal dysphagia requiring tube feeding and the patient received heparin for deep vein thrombosis prophylaxis. On Study Day 615, the patient was discharged after her prolonged hospitalization. On Study Day 617, the patient developed second episode of meningitis (Grade 5) along with lower abdominal pain, constipation, nausea, emesis and an acute confusion. The patient's vital signs were normal and laboratory tests revealed elevated levels of potassium, BUN, creatinine, AST, lipase, and lactate, along with an increased anion gap and white blood cell count. Imaging studies revealed cholelithiasis and pleural effusion and the patient received laxatives for constipation. On Study Day 623, the patient had

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					<p>agonal breathing and was unresponsive. On the same day, the patient died due to second episode of meningitis. Autopsy information was not available. The investigator assessed the episode of meningitis as not related to pralsetinib."</p> <p>The patient had a chest tube in situ for pleural effusion and also history of microdissection of lumbar vertebrae which could have been the cause for infection. Additionally the pathogen isolated was enterococcus whihc is an opportunistic one stating the immunosuppressed state of the patient with additional contribution from the concomitant prednisolone use.</p>
3004963 59 Male CHINA Clinical Study Healthcare professional	Pneumonia Grade 5	730	(1) PRALSETINIB (S)	N/A N/A N/A Fatal	<p>"AER 3004963 (PT: Pneumonia):</p> <p>This clinical study case concerned a 59-year-old male (patient number: 6308001) from China who developed pneumonia, 750 days after starting therapy with pralsetinib for non-small cell lung cancer. The patient's medical history and concomitant medications were not reported. Concurrent conditions included hepatitis B, hoarse voice, constipation, meningioma, proteinuria, hypertension and palliative therapy. The patient's prior cancer treatment regimens included chemotherapy with pemetrexed and cisplatin, docetaxel, gemcitabine, bevacizumab and radiotherapy.</p> <p>On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg daily received till Study Day 307. On Study Day 308, pralsetinib was reintroduced at a reduced dose of 300 mg which continued until Study Day 319. The last dose of pralsetinib prior to the event onset was not reported. An unspecified duration later, the brain MRI revealed a lacunar cerebral infarction in both frontal and parietal lobes. On Study Day 750, the patient developed Grade 5 pneumonia, presenting with sudden change of consciousness, agitation, restlessness,</p>

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					<p>slurred speech along with distortion of commissure and the patient was hospitalized. A CT scan revealed bilateral breast cavity effusion, a significantly reduced right lung volume with an ill-defined hilar mass and intermediate bronchial truncation, right lung middle lobe atelectasis, suggesting potential malignant neoplastic lesions. New multiple plaques were observed in both lungs, indicating possible inflammation. The scan also showed aortic and coronary atherosclerotic changes, as well as left renal and hepatic cysts, potential intrahepatic bile duct calculi or calcification foci, and subcapsular liver calcification foci. Additionally, an abnormal bone density was observed in multiple vertebrae and bilateral ribs suggesting possible metastasis. Upon admission, the patient's vital signs were noted and a non-invasive respiratory assistance was initiated along with a comprehensive treatment regimen including antibiotics, antispasmodics, antiasthmatics, antiarrhythmics, anti-shock and symptomatic treatment. On Study Day 753, the patient's dyspnea worsened along with blurred consciousness requiring endotracheal intubation. The following day, the patient was declared clinically dead after continuous chest compressions and intermittent intravenous injection of epinephrine. The patient died due to pneumonia and circulatory failure. An autopsy was not performed. The investigator assessed the pneumonia as not related to pralsetinib."</p> <p>The patient developed pneumonia after 2 years of initiation with pralsetinib. Additionally, there is underlying disease progression as evidenced by multiple vertebral metastasis. The concurrent condition of cerebral ischemia could also predispose to infections.</p>
3054582 56 Male	Sepsis Grade 5	142	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)	N/A N/A	"This clinical study case concerns a 56-year-old male patient who developed sepsis, 142 days after initiating therapy with pralsetinib for Medullary thyroid carcinoma. The patient's past

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
UNITED STATES OF AMERICA Clinical Study Healthcare professional			(3) ATOVAQUONE (T)  (4) DEXAMETHASONE (T)  (5) MICAFUNGIN (T)  (6) NYSTATIN (T)  (7) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (8) HYDROMORPHONE (T)  (9) LORAZEPAM (T)	N/A Fatal	<p>oncology history included RET mutant (RET fusion 918T) Medullary thyroid carcinoma (diagnosed in 30/Dec/2013). His prior cancer treatment regimens and surgeries were not reported. Concomitant medications included levothyroxine and concurrent condition included hypothyroidism. No medical history and past drugs were reported. After 142 days of initiating therapy with pralsetinib, the patient experienced the serious adverse event (SAE) of Sepsis (Grade 3). The patient was admitted due to unable to talk, interact, and decreased food ingestion. On admission, the patient presented with vital signs suggestive of sepsis, including tachycardia (pulse 138), tachypnea (respiratory rate 29), and fever (38.6°C). Laboratory results further supported a sepsis diagnosis, revealing elevated lactate (2.95 mmol/L), arterial blood gas abnormalities (pH 7.58, PO2 73 mmHg, HCO3 34.8 mmol/L, BE 12.6 mmol/L), anemia (hemoglobin 8.0 g/dL, hematocrit 24.0%), neutrophilia (8.79 K/uL), lymphopenia (0.20 K/uL), and significantly elevated procalcitonin (828.08 ng/mL). Additional findings included hyponatremia (131 mmol/L), hypoalbuminemia (1.4 g/dL), elevated liver enzymes (AST 147 U/L, alkaline phosphatase 250 U/L), and prolonged PT (15.2 s) with elevated INR (1.3). Imaging studies revealed patchy airspace opacification suspicious for atypical infection or multifocal pneumonia, although blood cultures showed no growth after 5 days of incubation. After 20 days of hospitalization, the patient died. It was unknown if an autopsy was performed or not.</p> <p>The Investigator assessed the sepsis as not related to pralsetinib."</p> <p>Although an event of sepsis is reported during treatment with pralsetinib, the definitive diagnosis cannot be ascertained with a negative blood culture 5 days after incubation. Moreover, CT</p>

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					Angio Pulmonary with Contrast revealed rounded mucous retention cyst or polyps within the right maxillary sinus with the largest on axial image 3 measuring 18 mm, along with suspicious for atypical infection or multifocal pneumonia. The pre-existing sinusitis could be a plausible source of infection.
3171448 70 Male KOREA, REPUBLIC OF Clinical Study Healthcare professional	Pneumonia Grade 5	747	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) AMLODIPINE (C)  (4) AMBROXOL (T)  (5) FAMOTIDINE (T)  (6) AMOXICILLIN\CLAVULANATE POTASSIUM (T)  (7) AZITHROMYCIN (T)  (8) PARACETAMOL (T)	Dose not changed N/A N/A Fatal	<p>This clinical study case concerns a 70-year-old male patient who developed pneumonia, 747 days after initiating therapy with pralsetinib for non-small cell lung cancer. Concomitant medications included levothyroxine, amlodipine and no medical history, past drugs, concurrent conditions were reported. After 747 days of initiating therapy with pralsetinib, patient was diagnosed with pneumonia (grade 2) and was hospitalized. The CT chest was performed which showed increased multi local ground glass opacities in both lungs (esp BLL) which was pneumonia probably. There was no change of small consolidative lesion inside the LUL bulla, emphysema, reticular opacities, bronchiectasis in both lungs and no significant mediastinal lymphadenopathy. A day later, this episode of pneumonia was resolved. After 1072 days of the initial therapy with pralsetinib, the patient developed second episode of fatal pneumonia. It was not reported whether autopsy was performed or not.</p> <p>The event of pneumonia developed more than 2 years after initiation of treatment with pralsetinib, which is an unduly long latency for a causative infection to appear. Secondly, the patient had an underlying advanced malignancy, which in addition to the elderly age could have contributed to the immunosuppression predisposing the patient to pneumonia.</p>
3269568 50 Male CHINA	COVID-19 Grade 5	1095	(1) PRALSETINIB (S)  (2) ACETYLCYSTEINE (C)	Drug interrupted Negative N/A Fatal	" This clinical study case concerns a 50-year-old male patient who developed covid-19, 1095 days after initiating therapy with pralsetinib for non- small cell lung cancer. Past medical history included non-infectious pneumonia and concomitant medications

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Clinical Study Healthcare professional			(3) DIAMMONIUM GLYCRRHIZINATE (C)  (4) HEPARIN SODIUM (C)  (5) TERBUTALINE SULFATE (C)  (6) THYMALFASIN (C)  (7) UBIDECARENONE (C)  (8) POTASSIUM CHLORIDE (C)  (9) PYRIDOXINE HYDROCHLORIDE (C)  (10) SODIUM CHLORIDE (C)  (11) BENZYL PENICILLIN SODIUM (C)  (12) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (C)  (13) AMBROXOL HYDROCHLORIDE (C)  (14) SPIRONOLACTONE (C)		<p>included acetylcysteine, diammonium glycrrhizinate, heparin sodium, terbutaline sulfate, thymalfasin (Thymopeptides), ubidecarenone, potassium chloride, pyridoxine hydrochloride (Vitamin B6), sodium chloride, benzylpenicillin sodium, piperacillin sodium; tazobactam sodium, ambroxol hydrochloride, spironolactone, tocilizumab, clostridium butyricum, bromhexine hydrochloride, midazolam, omeprazole sodium, propofol, remifentanil hydrochloride, ascorbic acid (Vitamin C), , fluconazole (Fluconazole And Sodium Chloride), voriconazole, sulfamethoxazole, tigecycline, metaraminol tartrate (Metaraminol Bitartrate), norepinephrine bitartrate, ephedrine hydrochloride. No past drugs and concurrent conditions were reported.</p> <p>After 1015 days of initiating therapy with pralsetinib, the patient developed non-infectious pneumonia, CTCAE grade 1, due to which study drug was interrupted. Approximately 13 days later, the patient returned to the site and the investigator found that non-infectious pneumonia had improved, and the study drug was resumed.</p> <p>After 1095 days of initiating therapy with pralsetinib, the patient developed cough and fever reaching to 38 degrees Celsius and tested positive for COVID antigen nucleic acid test. The event progressed from grade2 to grade 4 and most extreme severity: grade 5 and the drug was temporarily interrupted. Two days after the diagnosis, the patient's CT (Computed tomography) scan showed pneumonia. The patient felt no discomfort and cough stopped and the patient resumed the study drug dose of 200 mg. As the COVID-19 became serious, the patient was hospitalized, and the study drug was again interrupted. On day 16 of diagnosis, novel coronavirus nucleic acid detection showed masculine. On day 19, the patient was transferred to the department the intensive care medicine for continued treatment and on the next day, the patient was transferred to ICU with</p>

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			(15) TOCILIZUMAB (C) (16) CLOSTRIDIUM BUTYRICUM (C) (17) BROMHEXINE HYDROCHLORIDE (C) (18) MIDAZOLAM (C) (19) OMEPRAZOLE SODIUM (C) (20) PROPOFOL (C) (21) REMIFENTANIL HYDROCHLORIDE (C) (22) ASCORBIC ACID (C) (23) FLUCONAZOLE (C) (24) VORICONAZOLE (C) (25) SULFAMETHOXAZOLE (C) (26) TIGECYCLINE (C) (27) METARAMINOL TARTRATE (C) (28) NOREPINEPHRINE		<p>intubation. Later, the patient was found with constipation and his novel coronavirus nucleic acid detection showed masculine Xray showed pneumonia. On day 28 of the event onset, the patient was declared dead. It was unknown if an autopsy was performed or not. "</p> <p>The event of pneumonia developed 3 years after initiation of treatment with pralsetinib, which is an unduly long latency for a causative infection to appear. Moreover the infection was reported as non-infectious to begin with and the patient tested positive for COVID-19 which explains the event. Moreover, the concurrent condition of diabetes could have added to the severity and to a fatal outcome.</p>

AER Number	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
			BITARTRATE (C) (29) EPHEDRINE HYDROCHLORIDE (C) (30) GLYCYRRHIZA GLABRA (T) (31) DEXAMETHASONE SODIUM PHOSPHATE (T) (32) ACETYL CYSTEINE (T) (33) BUDESONIDE (T) (34) NIRMATRELVIR\RITONAVIR (T) (35) CEFTRIAXONE SODIUM (T) (36) DIPROPHYLLINE (T) (37) ACARBOSE (T) (38) DAPAGLIFLOZIN (T) (39) GLIPIZIDE (T) (40) INSULIN NOS (T)		
3277885 69	Pneumonia Grade 5	23	(1) PRALSETINIB (S)	NR Unknown	This clinical study case concerns a 69-year-old female patient who developed pneumonia, 23 days after initiating therapy with

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Female KOREA, REPUBLIC OF Clinical Study Healthcare professional			(2) LOSARTAN POTASSIUM (C)  (3) ATORVASTATIN CALCIUM TRIHYDRATE (C)  (4) SARPOGRELATE (C)  (5) LACTULOSE (C)  (6) AMLODIPINE BESILATE\CHLORTALIDO NETELmisartan (C)  (7) DEXAMETHASONE (C)  (8) PANTOPRAZOLE (C)  (9) BENZYDAMINE (C)  (10) GLUCONATE SODIUM\MAGNESIUM CHLORIDE\POTASSIUM CHLORIDE\SODIUM ACETATE\SODIUM CHLORIDE (C)	N/A Fatal	<p>pralsetinib for metastatic cecal cancer. Past medical history included acute appendicitis GR4, concurrent conditions included hypertension grade 2, hyperlipidemia grade 2, peripheral sensory neuropathy grade 2, constipation grade 2, alopecia grade 2, pulmonary thromboembolism grade 1, former alcohol use, osteoporosis, creatinine increased and concomitant medications included losartan potassium, atorvastatin calcium trihydrate, sarogrelate, lactulose, amlodipine besilate;chlortalidone;telmisartan (True Set), dexamethasone, pantoprazole, benzydamine, gluconate sodium;magnesium chloride;potassium chloride;sodium acetate;sodium chloride (Plasma Solution A). The patient had no history of tobacco use and no past drugs were reported. After 23 days of initiating therapy with pralsetinib, the patient was diagnosed with pneumonia on chest CT (initial and most extreme NCI-CTCAE grade: 5). On the same day the AE became serious, and subject was hospitalized at nearby hospital. On day 24 of the diagnosis, the patient died of aggravated pneumonia. The relevant medical records and other details (autopsy) were refused to be provided by the family.</p> <p>The patient developed pneumonia 23 days into therapy with pralsetinib which has a compatible temporal plausibility. the aggravation of this condition can be explained by his underlying metastatic cancer and concomitant steroid therapy. The circumstances leading to death are not very clear as autopsy details were unavailable. However, pulmonary embolism is a possible risk factor.</p>
3410782 69 Male TAIWAN, PROVINCE	Sepsis Grade 5	43	(1) PRALSETINIB (S)  (2) BENZBROMARONE (C)	N/A N/A N/A Fatal	AER 3410782 (PT: Sepsis): This clinical study case concerns a 69-year-old male patient who developed sepsis, 43 days after initiating therapy with pralsetinib for gastro-oesophageal cancer. Past medical history included thyroidectomy and concurrent conditions included gastroesophageal reflux disease, chronic

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
E OF CHINA Clinical Study Healthcare professional			(3) LEVOTHYROXINE SODIUM (C)  (4) TENOFOVIR ALAFENAMIDE FUMARATE (C)  (5) EZETIMIBE\SIMVASTATIN (C)  (6) FAMOTIDINE (C)  (7) SENNOSIDE A+B (C)  (8) MORPHINE (C)  (9) BUPRENORPHINE HYDROCHLORIDE (C)  (10) PARACETAMOL (C)  (11) NOSCAPINE (C)  (12) CLINDAMYCIN (C)  (13) GEMCITABINE (C)  (14) FILGRASTIM (T)  (15) NOREPINEPHRINE (T)  (16) VASOPRESSIN (T)		hepatitis B, hypertension, hyperlipidemia, hyperuricemia, former alcohol user, former tobacco user and constipation. Concomitant medications included benz bromarone, levothyroxine sodium, tenofovir alafenamide fumarate, ezetimibe; simvastatin, famotidine, sennoside, morphine, paracetamol, noscapine, clindamycin, temgesic and gemcitabine as maintenance. No past drugs were reported. AER 3410782 (PT: Sepsis): This clinical study case concerns a 69-year-old male patient who developed sepsis, 43 days after initiating therapy with pralsetinib for gastroesophageal cancer. Past medical history included thyroidectomy and concurrent conditions included gastroesophageal reflux disease, chronic hepatitis B, hypertension, hyperlipidemia, hyperuricemia, former alcohol user, former tobacco user and constipation. Concomitant medications included benz bromarone, levothyroxine sodium, tenofovir alafenamide fumarate, ezetimibe; simvastatin, famotidine, sennoside, morphine, paracetamol, noscapine, clindamycin, temgesic and gemcitabine as maintenance. No past drugs were reported. After 42 days of initiating therapy with pralsetinib, the patient was hospitalized for grade 3 intracerebral hemorrhage after experiencing confusion and changes in consciousness. A brain CT- angiography revealed a left anterior communicating artery aneurysm and a brain MRI showed a left temporooccipital acute intraparenchymal hemorrhage with intraventricular extension, complicated with hemohydrocephalus, and cerebral subarachnoid hemorrhage probably related to acute infarcts involving the left cerebellum, bilateral temporooccipital regions, and left centrum semiovale. The dose of pralsetinib was interrupted in response to the intracerebral hemorrhage. On the same day, laboratory results showed a white blood cell count of 5600/ $\mu$ L, hemoglobin of 9.7 g/dL, and platelet count of 49,000/ $\mu$ L. After 43 days of therapy initiation, the patient developed grade 4 neutropenia (ANC: 194/ $\mu$ L) and grade 4 sepsis. The patient received subcutaneous filgrastim for

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					<p>neutropenia and hemodynamic support with norepinephrine and vasopressin for sepsis. Further laboratory tests revealed a white cell count of 100/<math>\mu</math>L, hemoglobin level of 8.2 g/dL, platelet count of 86,000/<math>\mu</math>L, C-reactive protein of 73.8 mg/L, procalcitonin of 41.97 ng/mL, BUN/creatinine of 31/1.46 mg/dL, albumin level of 1.9 g/dL, segmented neutrophils 44%, band forms 4% (ANC: 48/<math>\mu</math>L), and lactate level of 4.8 mmol/L. The patient's Glasgow Coma Scale was E3VEM4, and the PaO<sub>2</sub>/FiO<sub>2</sub> ratio was 44.6 mmHg. A diagnosis of septic shock was made based on the sequential organ failure assessment (SOFA) score of 13 and lactate level of 4.8 mmol/L. Despite intensive care measures, including hemodynamic support, antibiotic therapy, and continuous venovenous hemofiltration, the patient's condition deteriorated rapidly. On day 44, the patient experienced worsening hemodynamics, respiratory failure, and oliguria. Arterial blood gas analysis showed mixed respiratory and metabolic acidosis with pH level 7.165. The patient underwent endotracheal intubation with mechanical ventilation, anticonvulsant therapy, and continued hemodynamic support. After 45 days of initiating therapy with pralsetinib, passed away in the hospital due to sepsis. An autopsy was not performed. The Investigator assessed sepsis as related to pralsetinib. The patient had history of hyperlipidemia and chronic hepatitis B which could act as contributing factors to infections. Concomitant use of gemcitabine could also suppress the patient's immunity. Additionally, the patient had a rupture of brain aneurysm with intracranial hemorrhage which eventually led to sepsis and death. Furthermore the co-existing neutropenia also shows the low immunity in the patient.</p>
3525056 Not reported Male KOREA,	Sepsis Grade 5	1825	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	AER 3525056 (PT: Sepsis): This non-interventional program case concerns a male patient of unknown age, who developed sepsis, 1825 days after initiating therapy with pralsetinib for non-small cell lung cancer (NSCLC). No medical history, past drugs, concurrent conditions and concomitant medications were

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REPUBLIC OF Non-Interventional Study/Program Non-healthcare professional					<p>reported. After 1825 days of therapy initiation with the drug, while hospitalized in a nursing facility due to lumbar fracture, the patient experienced a sudden change in vital signs and developed sepsis. After 1826 days of initiating therapy with pralsetinib, the patient dies due to sepsis. An autopsy was not performed.</p> <p>The occurrence of sepsis could be attributed to the lumbar fracture encountered by the patient in the absence of other factors.</p>
3502024 76 Male BRAZIL Clinical Study Healthcare professional	Endocarditis bacterial Grade 5	363	(1) PRALSETINIB (S)  (2) DABIGATRAN (C)  (3) LEVETIRACETAM (C)  (4) ALLOPURINOL (C)  (5) DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE (C)  (6) INSULIN ISOPHANE NOS (C)  (7) BISOPROLOL (C)  (8) VENLAFAKINE (C)	NR Unknown N/A Fatal	<p>AER 3502024 (PT: Endocarditis bacterial): This clinical study case concerns a 76-year-old male patient who developed Endocarditis bacterial, 363 days after initiating therapy with pralsetinib for Pancreatic carcinoma metastatic. Patient's concurrent conditions included cavernous sinus thrombosis, diabetes mellitus, hyperuricemia, depression, systemic arterial hypertension, left anterior fascicular block. Concomitant medications included dabigatran, levetiracetam, allopurinol, dapagliflozin propanediol monohydrate, isophane insulin, bisoprolol, venlafaxine. No medical history and past drugs were reported. He had no history of alcohol use and tobacco use. After 363 days of initiating therapy with pralsetinib, the patient presented to the hospital with malaise, hypotension, and fever, consistent with sepsis. Blood culture tests revealed growth of enterococci, and subsequent echocardiogram tests showed a suspicious image indicative of fatal bacterial endocarditis. The patient underwent antibiotic treatment guided by blood culture results but showed no clinical improvement. During hospitalization, in consultation with the family, non-invasive support was chosen. No procedures or surgeries were performed. After 384 days of therapy initiation with pralsetinib, the patient died due to fatal bacterial endocarditis. It was unknown if an autopsy was performed or not. The investigator</p>

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					assessed the fatal bacterial endocarditis as not related to pralsetinib but related to unspecified other causes. The patient had concurrent conditions of cavernous sinus thrombosis and diabetes predisposing him to infections. Additionally presence of enterococcus shows an opportunistic picture owing to the patient's immunosuppression.
10000015712 57 Male TAIWAN, PROVINC E OF CHINA Clinical Study Non- healthcare profession al	Septic shock Grade 5	251	(1) PRALSETINIB (S)  (2) METFORMIN (C)  (3) MORPHINE (C)  (4) AMLODIPINE BESILATE (C)  (5) DIMETICON (C)  (6) SENNOSIDE A+B (C)  (7) CISAPRIDE (C)  (8) VALSARTAN (C)  (9) RABEPRAZOLE SODIUM (C)  (10) BENZBROMARONE (C)  (11) FEXOFENADINE HYDROCHLORIDE (C)  (12) FUROSEMIDE (C)	Drug interrupted N/A N/A Fatal	AER 10000015712 (PT: Endocarditis bacterial): This clinical study case concerns a 57-year-old male patient who developed Septic shock, 251 days after initiating therapy with pralsetinib for cholangiocarcinoma. Past medical history included neutropenic fever. Concurrent conditions included intrahepatic cholangiocarcinoma, diabetes mellitus, gouty, bone pain, cough, tinea over right foot, hypertension, constipation, mucositis, alcohol use and tobacco user. Concomitant products included metformin, morphine, amlodipine besilate, dimeticone, cisapride, sennoside a+b, rabeprazole sodium, valsartan, fexofenadine hydrochloride, benz bromarone, furosemide, methylprednisolone, paracetamol and valsartan, rolikan, meropenem, vitacal, vasopressin, norepinephrine, hydrocortisone, teicoplanin, levofloxacin, nicort oral gel, liq brown mixture, furosemide, tramadol, meropenem, heparin sod, midazolam, fentanyl, filgrastim m300, pot chloride, anidulafungin, cisatracurium, fludrocortisone acetate, pantoprazole, albumin, cal chloride, prismsol, epinephrine, chlorpheniramine. No past drugs were reported. After 251 days of initiating therapy with pralsetinib, the patient presented to the hospital with progressive dyspnea and laboratory data revealed acute kidney injury, elevated CRP level, severe lactic acidosis (lactate of 147 mmol/L), neutropenia (WBC 340/ $\mu$ L). The patient received rolikan 40 amp and was intubated due to dyspnea. Norepinephrine was administered at 20 mL/hr, and the patient was transferred for further care. Empirical antibiotic therapy with meropenem was initiated, and nephrology was consulted for continuous venovenous hemofiltration in view of metformin-associated lactic acidosis, profound septic shock,

AER Number	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
			(13) PARACETAMOL (C)  (14) METHYL PREDNISOLONE (C)  (15) VALSARTAN (C)  (16) SODIUM BICARBONATE (C)  (17) MEROPENEM (C)  (18) CALCIUM (C)  (19) NOREPINEPHRINE (C)  (20) HYDROCORTISONE (C)  (21) LEVOFLOXACIN (C)  (22) TEICOPLANIN (C)  (23) TRAMADOL (C)  (24) VASOPRESSIN (C)  (25) HEPARIN (C)  (26) MIDAZOLAM (C)  (27) FENTANYL (C)		and acute kidney injury. Treatment included vasopressors (norepinephrine, vasopressin, and epinephrine) and broad-spectrum antibiotics (meropenem, teicoplanin, and anidulafungin). Despite maximum vasopressor support, blood pressure remained low (70-80 mmHg). Oxygenation was poor (PaO <sub>2</sub> 70.8 mmHg on 100% FiO <sub>2</sub> , SpO <sub>2</sub> 70-80%). Sodium bicarbonate was administered for metabolic acidosis. Chest X-ray revealed bilateral infiltrates, and lung auscultation revealed diffuse bilateral crackles. Bedside echocardiography showed normal cardiac function without effusions. After 252 days of initiating therapy with pralsetinib, the patient died due to septic shock. No autopsy was performed. Pralsetinib therapy was interrupted in response to the septic shock and acute kidney injury. The investigator assessed both the septic shock and acute kidney injury as unrelated to pralsetinib. The use of concomitant steroids, concurrent diabetes and co-existing neutropenia suggests an immunosuppressive state of the patient. These factors complicated with acute kidney injury must have led to septic shock and eventually death.

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
			(28) ANIDULAFUNGIN (C)  (29) CISATRACURIUM (C)  (30) FLUDROCORTISONE ACETATE (C)  (31) PANTOPRAZOLE (C)  (32) ALBUMIN HUMAN (C)  (33) CALCIUM CHLORIDE (C)  (34) EPINEPHRINE (C)  (35) CHLORPHENAMINE (C)  (36) FILGRASTIM (T)  (37) POTASSIUM CHLORIDE (T)  (38) METHYLPREDNISOLONE (T)  (39) CALCIUM CHLORIDE\GLUCOSE MONOHYDRATE\LACTIC ACID\MAGNESIUM CHLORIDE\POTASSIUM		

AER Number	Event Preferred Term of Interest*	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
			CHLORIDE\ SODIUM BICARBONATE\ SODIUM CHLORIDE (T)		

## Category C (N=39)

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
2831146 71 Female UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Sepsis Grade 5	210	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	"AER 2831146 (PT: Sepsis)  This spontaneous case concerned a 71-year-old female from the USA who developed sepsis, 210 days after starting treatment with pralsetinib for thyroid cancer. The patient's medical history, concurrent conditions, concomitant medications or past drugs were not reported. After 210 days of starting treatment with pralsetinib, the patient died. Prior to the death, the patient had a port inserted for chemotherapy administration, which led to the development of sepsis. It was not reported if an autopsy was performed. The physician did not report the causality of contracted sepsis with pralsetinib."
2883830 64 Female ARGENTINA Non-Interventional Study/Program Non-healthcare professional	Sepsis Grade 5	NR	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	"AER 2883830 (PT: Sepsis)  This non-interventional study case concerned a 64-year-old female from Argentina who developed sepsis, after an unspecified duration of starting treatment with pralsetinib for lung neoplasm malignant. The patient's medical history, concurrent conditions, concomitant medications and past drugs were not reported. An unspecified duration after starting treatment with pralsetinib, the patient developed sepsis originating from the urinary system, which subsequently led to multiple organ failure. An unspecified duration later, the patient died due to sepsis. An autopsy was not performed. The physician assessed the sepsis as not related to pralsetinib."

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2902724 83 Female CHILE Non-Interventional Study/Program Healthcare professional	Pneumonia* Sepsis NR Grade 5	0 0	(1) ALECTINIB (S)  (2) PRALSETINIB (S)	NR  NR Unknown  Unknown N/A  N/A Not Reported  Fatal	"AER 2902724 (PT: Pneumonia, Sepsis)  This non-interventional study case concerned an 83-year-old female from Chile who developed pneumonia and sepsis on the same day of starting treatment with pralsetinib for non-small cell lung cancer. The patient's medical history, concurrent conditions and concomitant medications were not reported. Co-suspect medication included alectinib. Past drugs included pemetrexed and carboplatin. Approximately 6 months prior to beginning pralsetinib treatment, the patient developed disease progression while receiving alectinib therapy. On the same day pralsetinib treatment was started, the patient was hospitalized due to neutropenia, pneumonia and sepsis leading to subsequent death on the same day. It was not reported if an autopsy was performed. The physician did not report the causality of sepsis and pneumonia with pralsetinib."
2917567 82 Female ITALY Non-Interventional Study/Program Healthcare professional	Urosepsis Grade 5	42	(1) PRALSETINIB (S)  (2) ACENOCOUMAROL (C)  (3) DIGOXIN (C)	Drug interrupted N/A N/A Fatal	"AER 2917567 (PT: Urosepsis)  This non-interventional study case concerned an 82-year-old female from Italy who developed urosepsis, 42 days after starting treatment with pralsetinib for lung adenocarcinoma. The patient's medical history and past drugs were not reported. Concurrent conditions included atrial fibrillation. Concomitant medications included acenocoumarol and digoxin. After 42 days of starting treatment with pralsetinib, the patient developed urosepsis. The following day, laboratory tests revealed Escherichia coli in the urine culture and Staphylococcus aureus in the blood culture. After 45 days of starting treatment with pralsetinib, the patient died due to urosepsis. An autopsy was not performed. The physician did not report a causality between urosepsis and pralsetinib."
2919622 54 Female	COVID-19 Grade 5	466	(1) PRALSETINIB (S)	NR Unknown	"AER 2919622 (PT: COVID-19)  This non-interventional study case concerned a 54-year-old

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
NETHERLANDS Non-Interventional Study/Program Non-healthcare professional				N/A Fatal	<p>female from Netherlands who developed COVID-19, 466 days after starting treatment with pralsetinib for an unspecified indication. The patient's medical history, concurrent conditions, concomitant medications and past drugs were not reported.</p> <p>After 466 days of starting treatment with pralsetinib, the patient developed COVID-19 which eventually led to hospitalization due to respiratory distress caused by COVID-19. The patient's condition deteriorated over the course of a week. After 479 days of starting treatment with pralsetinib, the patient died. It was not reported if an autopsy was performed. The physician assessed the COVID-19 as not related to pralsetinib."</p>
2938014 55 Male KOREA, REPUBLIC OF Non-Interventional Study/Program Non-healthcare professional	Pneumonia Grade 5	23	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	<p>"AER 2938014 (PT: Pneumonia)</p> <p>This non-interventional study case concerned a 55-year-old male from Korea, Republic Of who developed pneumonia, 23 days after starting treatment with pralsetinib for non-small cell lung cancer. The patient's medical history, concurrent conditions, concomitant medications and past drugs were not reported.</p> <p>After 23 days of starting treatment with pralsetinib, the patient experienced dyspnea which gradually worsened and eventually the patient was diagnosed with infectious pneumonia. Five days later, a chest posteroanterior X-ray revealed new pneumonia in both lungs and an increase in bilateral pleural effusion. Blood tests showed positive results for mycoplasma pneumonia and aspergillus antibodies. Blood cultures showed no growth after five days, and the procalcitonin level was within the normal range. After 32 days of starting treatment with pralsetinib, the patient died. It was not reported if an autopsy was performed. The other health care professional assessed the infectious pneumonia as not related to pralsetinib."</p>

AER Number	Event Preferred Term of Interest*	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
2941403 63 Female HUNGARY Non-Interventional Study/Program Healthcare professional	Herpes virus infection  Peritonitis  NR  Grade 5	78  NR	(1) PRALSETINIB (S)	Dose interrupted  Dose interrupted N/A N/A NR  Fatal	"AER 2941403 (PT: Herpes virus infection, Peritonitis)  This non-interventional study case concerned a 63-year-old female from Hungary who developed herpes virus infection and peritonitis while receiving treatment with pralsetinib for non-small cell lung cancer. The patient's medical history, concurrent conditions, concomitant medications and past drugs were not reported. After 27 days of starting treatment with pralsetinib, the patient developed stomatitis. Fifty-one days later, the patient developed muscle hemorrhage, anemia, thrombocytopenia, rash accompanied by herpes virus infection, neutropenia, elevated transaminases level, necrotizing skin lesion on the forearm and back of the knee. After 146 days of starting treatment with pralsetinib, the patient developed another episode of muscle hemorrhage, anemia and thrombocytopenia and the patient was hospitalized. The outcome was not reported for any of the events. Treatment with pralsetinib was stopped one month before the patient's death due to blood count abnormalities. The patient's blood count abnormalities showed signs of improvement, although the patient still had anemia and thrombocytopenia. Subsequently, the patient developed peritonitis, ascites, heart failure and non-infectious gastroenteritis. The patient was hospitalized one day before death where muscle hemorrhage was diagnosed based on the diagnostic tests. Eventually, after 146 days of starting treatment with pralsetinib, the patient died. An autopsy revealed heart failure as the direct cause of death, with underlying malignant neoplasm of the upper lobe, bronchus, peritonitis, ascites, and non-infectious gastroenteritis as indirect causes. The physician did not report a causality of herpes virus infection and peritonitis."
2958644 Not reported Not	Urinary tract infection  Sepsis	NR  NR	(1) PRALSETINIB (S)	N/A  N/A N/A	"AER 2958644 (PT: Urinary tract infection, Sepsis)  This non-interventional study case concerned a patient of unspecified demographics from India who developed urinary

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
reported INDIA Non-Interventional Study/Program Healthcare professional	Grade 5 Grade 5			N/A N/A N/A Fatal Fatal	tract infection and sepsis, after an unspecified duration of starting treatment with pralsetinib for non-small cell lung cancer. The patient's medical history, concurrent conditions, concomitant medications and past drugs were not reported. An unspecified duration after starting treatment with pralsetinib, the patient died due to urinary tract infection and sepsis. No additional information was provided. It was not reported if an autopsy was performed. The physician assessed the causality between fatal urinary tract infection and sepsis and pralsetinib as not related."
2967108 63 Female ITALY Non-Interventional Study/Program Healthcare professional	Pneumonia Sepsis Grade 5	106 106	(1) PRALSETINIB (S)  (2) PANTOPRAZOLE SODIUM SESQUIHYDRATE (C)  (3) FUROSEMIDE (C)  (4) BISOPROLOL FUMARATE (C)  (5) AMLODIPINE BESILATE (C)  (6) ZOLPIDEM (C)	NR NR Unknown Unknown N/A N/A Fatal Fatal	"AER 2967108 (PT: Pneumonia, Sepsis)  This non-interventional study case concerned a 63-year-old female from Italy who developed pneumonia and sepsis, 106 days after starting treatment with pralsetinib for non-small cell lung cancer. The patient's medical history, concurrent conditions and past drugs were not reported. Concomitant medications included pantoprazole, furosemide, bisoprolol, amlodipine and zolpidem. The patient had a history of immunotherapy as part of a previous clinical trial. The patient began treatment with pralsetinib at a dose of 400 mg daily. Thirty-five days after starting pralsetinib therapy, the patient experienced fever and mucositis leading to the interruption of the pralsetinib until next 19 days. The treatment was resumed at a reduced dose of 300 mg daily. Subsequently, the patient was hospitalized due to clinical deterioration and diagnosis of pneumonia. After 106 days of starting treatment with pralsetinib, the patient died due to respiratory failure secondary to pneumonia and sepsis. An autopsy was not performed. The physician assessed the pneumonia and sepsis as not related with pralsetinib."

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
2979775 86 Male ITALY Non-Interventional Study/Program Healthcare professional	Sepsis Grade 5	NR	(1) PRALSETINIB (S)	N/A N/A N/A Fatal	"AER 2979775 (PT: Sepsis)  This non-interventional study case concerned an 86-year-old male from Italy who developed sepsis, after an unspecified duration of starting treatment with pralsetinib for non-small cell lung cancer. The patient's medical history, concurrent conditions, concomitant medications and past drugs were not reported. An unspecified duration after starting treatment with pralsetinib, the patient developed bone marrow toxicity, hepatotoxicity, hypertension, severe sepsis and bowel obstruction. Subsequently the patient died due to sepsis, likely originating from a urinary source and bowel obstruction. It was not reported if an autopsy was performed. The physician assessed the causality of severe sepsis as not related to pralsetinib."
3009924 66 Male CHINA Non-Interventional Study/Program Non-healthcare professional	COVID-19 Grade 5	365	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	"AER 3009924 (PT: COVID-19)  This non-interventional study case concerned a 66-year-old male from China who developed COVID-19, approximately 2 years after starting treatment with pralsetinib for lung neoplasm malignant. The patient's medical history, concurrent conditions and concomitant medications were not reported. After 13 days of starting treatment with pralsetinib, the patient developed muscular weakness. One year later, the patient experienced anemia. Two months following the onset of anemia, the patient experienced constipation. Approximately 2 years after starting treatment with pralsetinib, the patient died due to an infection with COVID-19. No autopsy details were reported. The consumer assessed the infection with COVID-19 not related with pralsetinib."

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3032892 76 Male ITALY Non-Interventional Study/Program Healthcare professional	Septic shock Grade 5	NR	(1) PRALSETINIB (S)  (2) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (3) VANCOMYCIN (T)  (4) FUROSEMIDE (T)  (5) SOTROVIMAB (T)	N/A N/A N/A Fatal	This spontaneous case concerns a 76-year-old male patient who experienced fatal septic shock at an unknown time during treatment with pralsetinib for non-small cell lung cancer. No medical history, past drugs, concurrent conditions and concomitant medications were reported. After an unspecified duration of starting treatment with pralsetinib, the patient developed septic shock. After approximately 20 months of receiving pralsetinib, the patient was emergently hospitalized for septic shock, which was reported as non-drug related, and subsequently died. An autopsy was not performed.
3064805 63 Not reported SPAIN Non-Interventional Study/Program Healthcare professional	COVID-19 Grade 5	NR	(1) PRALSETINIB (S)	N/A N/A N/A Fatal	This non-interventional study case concerns an adult patient who developed covid-19 infection at an unspecified duration after initiating therapy with pralsetinib for unknown indication. No medical history, past drugs, concurrent conditions and concomitant medications were reported. On an unspecified date, the patient contracted COVID-19 infection and subsequently, passed away on an unknown date due to the COVID-19 infection. It was unknown if an autopsy was performed or not.
3096526 76 Male ITALY Non-Interventional Study/Program Healthcare professional	Pneumonia  Sepsis Grade 5	NR  NR  Grade 5	(1) PRALSETINIB (S)	Dose interrupted  Dose interrupted N/A  N/A N/A N/A	This non-interventional study case concerns a 75-year-old male patient who developed pneumonia and sepsis, unspecified duration after initiating therapy with pralsetinib for thyroid cancer. Past drugs included vandetanib (Vandetanib), past medical history included total thyroidectomy, however, no concurrent conditions and concomitant medications were reported. After an unspecified duration, the patient developed bronchopneumonia and secondary sepsis. The patient came for an appointment due to a clinical worsening with mnemonic and was hospitalized on the next day and approximately 9 days later the patient died. Autopsy was not performed. The dose of pralsetinib was

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
				Fatal Fatal	interrupted in response to the bronchopneumonia and sepsis.
3188187 Not reported Not reported ITALY Literature - Non-Interventional Study/Program Healthcare professional	Sepsis Grade 5	NR	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	This literature - non-interventional program case concerns a patient of unknown demographics who developed sepsis, unspecified duration after initiating therapy with pralsetinib for non-small cell lung cancer. No medical history, concomitant medications, concurrent conditions and investigation reports were reported. After an unspecified duration, the patient developed sepsis and died due to it. There was lack of information about circumstances leading to sepsis and clinical history of the patient. It was unknown if autopsy was performed or not.
2708994 63 Male TAIWAN, PROVINCE OF CHINA Clinical Study Healthcare professional	Sepsis  Pneumonia Grade 5  Grade 4	835  833	(1) PRALSETINIB (S)	N/A  Doseinterrupted N/A  Positive N/A  N/A Fatal  Recovered/Resolved With Sequelae	AER 2708994 (PT: Sepsis, Pneumonia):  This clinical study case concerned a 63-year-old male (patient number: 6201002) from Taiwan, Province of China who developed sepsis and pneumonia while receiving treatment with pralsetinib for medullary thyroid cancer. The patient's medical history, past drugs, concurrent conditions and concomitant medications were not reported. The patient had no history of infectious diseases.  On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg (frequency unspecified) received till Study Day 8. On Study Day 21, pralsetinib was reintroduced at a reduced dose of 300 mg. The last dose prior the event onset was not reported. On Study Day 783, the patient's laboratory test results showed low absolute neutrophil count, low white blood cell counts and low hemoglobin levels. On Study Day 832, the

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
					patient experienced fever, cough, rhinorrhea and dizziness. The following day, the patient developed Grade 4 pneumonia leading to a temporary interruption of pralsetinib treatment. The patient had mild dyspnea with clear consciousness and was sent to the emergency department on the same day. A chest x-ray showed increased right lower lobe infiltration along with elevated heart rate, low oxygen saturation and rapid respiratory rate. The patient's condition deteriorated rapidly, with severe desaturation, necessitating intubation. A chest CT scan showed pneumonia at right middle lobe along with infection and inflammatory changes in both lungs and bilateral pulmonary emphysema leading to hospitalization. Additional laboratory tests showed positive results for influenza A + B rapid screening and elevated high sensitivity C-reactive protein. Following admission, the patient developed profound shock. Treatment included administration of inotropes and empirical broad-spectrum antibiotics. Peripheral cyanosis was observed, and due to refractory lactate acidosis, continuous veno-venous hemofiltration was initiated. On Study Day 835, it was reported that the pneumonia had resolved with sequelae, and the patient was discharged. On the same day, the patient died due to sepsis (Grade 5). Blood culture results revealed the presence of Escherichia coli and multiple organ failure was noted. No autopsy was performed. The investigator assessed pneumonia and sepsis as not related to pralsetinib.
3289005 Not reported Male CHINA Non-Interventional Study/Program	Pneumonia Grade 5	128	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	This non-interventional program case concerns a male patient of unknown age, who developed pneumonia, 128 days after initiating therapy with pralsetinib for lung cancer. No past medical history, past drugs, concurrent conditions and concomitant medications were reported. After 128 days of initiating therapy with pralsetinib, the patient developed pneumonia. After 105 days of the event onset, the patient died due to it. It was unknown if an autopsy was performed or not.

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Healthcare professional					
3289099 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	COVID-19 Grade 5	NR	(1) PRALSETINIB (S)	Dose interrupted Unknown Unknown Fatal	This patient support program case concerns a female patient of unknown age, who developed covid-19, unspecified duration after initiating therapy with pralsetinib for an unknown indication. No medical history, past drugs, concurrent conditions and concomitant medications were reported. After an unspecified duration of starting treatment with pralsetinib, the patient developed COVID-19. Therapy with pralsetinib was withdrawn in response to the covid-19, due to economic reasons. On an unknown date, the patient died due to Covid-19, being the primary cause. However, the discontinuation of the drug due to economic reason was considered as second cause of death. It was unknown if an autopsy was performed or not.
3292683 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	COVID-19 Grade 5	90	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	This non-interventional program case concerns a male patient of unknown age, who developed covid-19, approximately 3 months after initiating therapy with pralsetinib for lung cancer. No medical history, past drug, concurrent condition and concomitant medications were reported. After approximately 3 months of initiating therapy with pralsetinib, the patient developed covid-19. Unspecified duration after the event onset, the patient died due to it. It was unknown if an autopsy was performed or not.
3295424 Not reported Male CHINA Non-	COVID-19 Grade 5	90	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	This non-interventional program case concerns a male patient of unknown age, who developed covid-19, 90 days after initiating therapy with pralsetinib for an unknown indication. No past medical history, past drugs, concurrent conditions and concomitant medications were reported. After 90 days of initiating therapy with pralsetinib, the patient developed covid-19

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
Interventional Study/Program Non-healthcare professional					and died on the same day. It was unknown if an autopsy was performed or not.
3295666 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	COVID-19 Grade 5	255	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	This non-interventional program case concerns a male patient of unknown age, who developed covid-19, 255 days after initiating therapy with pralsetinib for lung cancer. No medical history, past drug, concurrent conditions, concomitant medications were reported. After 255 days of initiating therapy with pralsetinib, the patient developed covid-19 and died on the same day. It was unknown if an autopsy was performed or not.
3300030 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	COVID-19 Grade 5	312	(1) PRALSETINIB (S)	N/A N/A N/A Fatal	This non-interventional program case concerns a male patient of unknown age, who developed covid-19, 312 days after initiating therapy with pralsetinib for lung cancer. No past medical history, past drugs, concurrent conditions and concomitant medications were reported. After 312 days of initiating therapy with pralsetinib, the patient tested for SARS-CoV-2 test and results showed that he developed COVID-19. Reportedly, the patient died on the same day due to covid-19. It was unknown if an autopsy was performed or not.

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3317344 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	COVID-19 Grade 5	NR	(1) PRALSETINIB (S)	Dose interrupted Unknown Unknown Fatal	This non-interventional program case concerns a female patient of unknown age, who developed covid-19, unspecified duration after initiating therapy with pralsetinib for lung cancer. No medical history, past drugs, concurrent conditions and concomitant medications were reported. After an unspecified duration of starting treatment with pralsetinib, the patient developed COVID-19. Approximately 2 years after initiating the therapy with drug, the patient died due to Covid-19. It was unknown whether autopsy was performed or not.
2732122 78 Male CHINA Clinical Study Healthcare professional	Pneumonia Grade 5	48	(1) PRALSETINIB (S)  (2) CEFOPERAZONE SODIUM\SULBACTAM SODIUM (C)  (3) BUDESONIDE (C)  (4) TERBUTALINE SULFATE (C)  (5) ACETYLCYSTEINE (C)  (6) IBUPROFEN (C)	Drug interrupted N/A N/A Fatal	AER 2732122 (PT: Pneumonia):  This clinical study case concerned a 78-year-old male (patient number: 6301010) from China who developed pneumonia, 48 days after starting therapy with pralsetinib for lung adenocarcinoma. The patient's medical history, concurrent conditions and past drugs were not reported. Concomitant medications included cefoperazone/sulbactam, budesonide, terbutaline, acetylcysteine and ibuprofen.  On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg daily received till Study Day 42. The pralsetinib dose was temporarily interrupted due to events of Grade 3 hyponatremia and Grade 3 hypophosphatemia. On Study Day 46, the patient was hospitalized for symptomatic treatment. The following day, the patient experienced fever along with cough, sputum, shortness of breath and fatigue. Treatment included high-dose oxygen inhalation, ibuprofen and antibiotics. Blood test on the same day revealed hypophosphatemia. Additional laboratory tests showed low values of total protein and albumin, slightly low sodium and potassium, and markedly low inorganic phosphorus. Liver enzymes and renal function tests appeared

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					normal. Cardiac enzymes showed some elevation, particularly lactic dehydrogenase and α-hydroxybutyric dehydrogenase. The blood test revealed low hemoglobin and platelet count. Blood cultures were negative for bacterial and fungal growth after 5 days. On Study Day 48, the patient developed Grade 4 pneumonia with hemoptysis. Treatment medications included budesonide, terbutaline, acetylcysteine, imipenem/cilastatin and hemocoagulase. Tests conducted on the same day revealed elevated levels of C-reactive protein and procalcitonin, while the fungus D-glucose test was negative. A chest radiograph showed right lung cancer and bilateral pneumonia. Despite ongoing treatment, the patient's condition deteriorated and the patient insisted to be discharged. On Study Day 49, the patient was discharged with a prescription for ambroxol. The patient died at home on Study Day 50 and the cause of death was considered as aggravated pneumonia. It was not reported if an autopsy was performed. The physician assessed the causality of pneumonia as not related to pralsetinib.

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2732378 55 Male GERMANY Clinical Study Healthcare professional	COVID-19 pneumonia Grade 5	353	(1) PRALSETINIB (S)  (2) ZOLEDRONIC ACID MONOHYDRATE (C)  (3) CALCIUM CARBONATE\COLECALCIFEROL (C)	Drug interrupted N/A N/A Fatal	<p>AER 2732378 (PT: COVID-19 pneumonia):</p> <p>This clinical study case concerned a 55-year-old male (patient number: 1207002) from Germany who developed COVID-19 pneumonia, 353 days after starting therapy with pralsetinib for non-small cell lung cancer. The patient's medical history, concurrent conditions and past drugs were not reported. Concomitant medications included zoledronic acid and calcium carbonate/colecalciferol</p> <p>On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg daily and received till Study Day 353. Since Study Day 344, the patient reported flu-like symptoms without fever or breathing difficulties, however, by Study Day 352, the patient's general condition worsened with increased shortness of breath. On Study Day 353, the patient developed Grade 5 COVID-19 pneumonia and was hospitalized. The following day, the patient was transferred to intensive care unit and received non-invasive ventilation through upper airway. The patient was intubated and needed catecholamine therapy. Eventually, the patient's condition deteriorated and he developed a septic shock and kidney failure. On Study Day 367, the patient became cardiopulmonary unstable and died due to COVID-19 pneumonia. An autopsy was not performed. The physician assessed the COVID-19 pneumonia as not related to pralsetinib.</p>
3331438 Not reported Male CHINA Non-Interventional Study/Program	COVID-19 Grade 5	40	(1) PRALSETINIB (S)	Dose interrupted Unknown Unknown Fatal	<p>This non-interventional program case concerns a male patient of unknown age, who developed covid-19, 40 days after initiating therapy with pralsetinib for lung cancer. No medical history, past drugs, concurrent conditions and concomitant medications were reported. After 40 days of initiating therapy with pralsetinib, the patient developed covid-19 and died on the same day. It was unknown if an autopsy was performed or not.</p>

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
Non-healthcare professional					
3332326 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Sepsis Grade 5	208	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	This non-interventional program case concerns a female patient of unknown age, who developed sepsis, 208 days after initiating therapy with pralsetinib for lung cancer. No medical history, past drugs, concurrent conditions and concomitant medications were reported. After 208 days of initiating therapy with pralsetinib, the patient died due to septicaemia. It was unknown if an autopsy was performed or not. The stop date of pralsetinib was unknown.
3349877 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Infection Grade 5	68	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	AER 3349877 (PT: Infection): This non-interventional study case concerns a male patient who developed infection, 68 days after initiating therapy with pralsetinib for malignant lung neoplasm. No medical history, past drugs, concurrent conditions and concomitant medications were reported. After 68 days of initiating therapy with pralsetinib, the patient developed an unspecified infection and died due to it. It was unknown if an autopsy was performed or not.
3351851 Not reported Male CHINA	COVID-19 pneumonia Grade 5	656	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	AER 3351851 (PT: COVID-19 pneumonia): This non-interventional study case concerns a male patient who developed COVID-19 pneumonia, 656 days after initiating therapy with pralsetinib for malignant lung neoplasm. No medical history, past drugs, concurrent conditions and concomitant

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
Non-Interventional Study/Program Non-healthcare professional					medications were reported. After 68 days of initiating therapy with pralsetinib, the patient developed a thrombosis leg and Covid-19 pneumonia and was hospitalized. After 738 days of the initial therapy with pralsetinib, the patient passed away due to COVID-19 pneumonia. It was unknown if an autopsy was performed or not.
3360718 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia  Pneumonia Grade 5  NR	24	(1) PRALSETINIB (S)	Dose not changed N/A N/A Fatal  Recovering/Resolving	AER 3360718 (PT: Pneumonia): This non-interventional study case concerns a male patient who developed pneumonia, 24 days after initiating therapy with pralsetinib for malignant lung neoplasm. No medical history, past drugs, concurrent conditions and concomitant medications were reported. After 24 days of initiating therapy with pralsetinib, the patient developed obstructive pneumonia. After 31 days of therapy onset, the patient developed platelet high. After an unspecified duration of starting treatment with the drug, the patient developed lung infection and died due to it after 87 days of therapy initiation. It was unknown if an autopsy was performed or not.
2800706 60 Male UNITED STATES OF AMERICA Non-Interventional Study/Program Non-	Septic shock  Grade 5	52	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	"AER 2800706 (PT: Septic shock)  This non-interventional study case concerned a 60-year-old male from the USA who developed septic shock, 52 days after starting treatment with pralsetinib for non-small cell lung cancer. The patient's medical history, concomitant medications or past drugs were not reported. Concurrent conditions included bone metastasis. Concurrent conditions included hypertension. The patient started treatment with pralsetinib at a dose of 400 mg which discontinued on the same day. After 11 days of starting treatment with pralsetinib, the patient was hospitalized due to an ischemic attack. After 52 days of starting treatment with pralsetinib, the patient died due to septic shock (Grade 5). An

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healthcare professional					autopsy was not performed. The physician assessed the septic shock as not related to pralsetinib."
3413196 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	COVID-19 Grade 5	348	(1) PRALSETINIB (S)	Dose interrupted Unknown Unknown Fatal	AER 3413196 (PT: COVID-19): This non-interventional study case concerns a male patient who developed COVID-19, 348 days after initiating therapy with pralsetinib for malignant lung neoplasm. No medical history, past drugs, concurrent conditions and concomitant medications were reported. After 348 days of initiating therapy with pralsetinib, the patient developed covid-19 and died on the same day. It was unknown if an autopsy was performed or not.
2803254 59 Male CHINA Clinical Study Healthcare professional	Pneumonia Grade 5	474	(1) PRALSETINIB (S)	Drug interrupted N/A N/A Fatal	"AER 2803254 (PT: Pneumonia):  This clinical study case concerned a 59-year-old male (patient number: 6317001) from China who developed pneumonia, 474 days after starting therapy with pralsetinib for medullary thyroid cancer. The patient's medical history, concomitant medications and past drugs were not reported. Concurrent conditions included hypercholesterolemia and hypertriglyceridemia.  The patient's baseline laboratory tests conducted six days before starting pralsetinib treatment showed that both the white blood cell count and neutrophil count were within their respective normal ranges. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 400 mg daily which was temporarily interrupted on Study Day 22. On Study Day 28, pralsetinib was reintroduced at a reduced dose of 300 mg. On Study Day 474, the patient developed Grade 3 pneumonia accompanied by fever. The last dose of pralsetinib was taken on Study Day 475. That same day, due to fever and difficulty breathing, the patient

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					was sent to hospital for emergency care. On Study Day 476, the patient died due to pneumonia which was progressed to Grade 5. An autopsy was not performed. The physician assessed the causality of pneumonia as not related to pralsetinib."
2889538 54 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	COVID-19 Grade 5	5	(1) PRALSETINIB (S)  (2) PREDNISONE (T)  (3) SALBUTAMOL (T)	Drug interrupted Negative N/A Fatal	"AER 2889538 (PT: COVID-19):  This clinical study case concerned a 54-year-old female (patient number: 2608015) from the USA who developed COVID-19 infection, 5 days after starting therapy with pralsetinib for lung neoplasm malignant and non-small cell lung cancer. The patient's medical history, concurrent conditions, concomitant medications and past drugs were not reported. On Cycle 1 Day 1, the patient received study drug pralsetinib at a dose of 300 mg (frequency unspecified) and received till Study Day 421. On Study Day 426, the patient developed first episode of Grade 3 COVID-19 and was hospitalized due to exacerbated dyspnea related to COVID-19. The treatment regimen included a six-day course of prednisone and albuterol. On Study Day 444, the patient recovered with sequelae from the first episode of COVID-19. On Study Day 445, the patient developed second episode of COVID-19 infection (Grade: 5). On same day, the patient died due to second episode of COVID-19 infection. The autopsy report was not available. The physician assessed COVID-19 as not related to pralsetinib."
2896004 45 Male UNITED STATES OF AMERICA Clinical Study	COVID-19 Grade 5	658	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	"AER 2896004 (PT: COVID-19):  This clinical study case concerned a 45-year-old male (patient number: 2610015) from the USA who developed COVID-19 infection, 655 days after starting therapy with pralsetinib for thyroid cancer . The patient's medical history, concurrent conditions, concomitant medications and past drugs were not reported.  On Cycle 1 Day 1, the patient received study drug pralsetinib at

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
Healthcare professional					a dose of 400 mg (frequency unspecified). On Study Day 655, the patient was tested positive for COVID-19 with a critically low oxygen saturation of 35%. Despite recommendation to seek emergency care due to critically low oxygen levels, the patient opted for home health services with intravenous fluids and oxygen. On Study Day 658, the patient died due to Grade 5 Covid-19. It was not reported if an autopsy was performed. The physician assessed COVID-19 as not related to pralsetinib."
3260660 74 Male SPAIN Clinical Study Healthcare professional	COVID-19 pneumonia Grade 5	81	(1) PRALSETINIB (S)	Drug interrupted N/A N/A Fatal	This clinical study case concerns a male patient, who developed COVID-19 pneumonia, 81 days after initiating therapy with pralsetinib for non- small cell lung cancer. No medical history, past drugs, concurrent conditions and concomitant medications were reported. After 81 days of starting therapy with pralsetinib, the patient tested positive for COVID-19 in antigen test. Subsequently, progressive worsening with cough and dyspnea. The patient developed g3 lung infection not related to the treatment/disease (covid 19). Ten days after the diagnosis, the patient was hospitalized. The PCR was positive for COVID-19 and the chest x-ray showed bilateral infiltrates compatible with pneumonia. The patient required oxygen with facemask to maintain saturation above 90%. The patient remained in hospital for treatment and follow up. Therapy with pralsetinib was withdrawn in response to the event. After 118 days of starting therapy, the patient died due to covid19 pneumonia. Autopsy details were unknown.
3414427 73 Male KOREA, REPUBLIC OF Clinical Study	Pneumonia Grade 5	1460	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	AER 3414427 (PT: Pneumonia):  This clinical study case concerns a 73-year-old male patient who developed pneumonia, 1460 days after initiating therapy with pralsetinib for Non-small cell lung cancer. No medical history, past drugs, concurrent conditions and concomitant medications were reported. After 1460 days of initiating therapy with pralsetinib, the patient developed pneumonia and his condition deteriorated rapidly, resulting in death within hours of the ER

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
Healthcare professional					visit. The direct cause of death was listed as septic shock in the death certificate, however the investigator assessed that infectious pneumonia occurred initially, followed by sepsis, leading to fatal shock. The investigator further assessed pneumonia as unrelated to pralsetinib and related to the disease under study (NSCLC). It was unknown if an autopsy was performed or not.
3565442 72 Male ITALY Clinical Study Non-healthcare professional	Pneumonia Grade 5	634	(1) PRALSETINIB (S)	NR Unknown N/A Fatal	AER 3565442 (PT: Pneumonia): This clinical study case concerns a 72-year-old male patient who developed Pneumonia, 634 days after initiating therapy with pralsetinib for Non-small cell lung cancer metastatic. No medical history, past drugs, concurrent conditions and concomitant medications were reported. After 634 days of initiating therapy with pralsetinib, the patient developed pneumonia and was hospitalized. The dose of pralsetinib was interrupted in response to this event. After 696 days of therapy initiation with the drug, the patient's condition deteriorated and died due to pneumonia. It is unknown if an autopsy was performed. The investigator assessed the fatal pneumonia as not related to pralsetinib.
100000091 22 51 Male FRANCE Clinical Study Non-healthcare professional	Septic shock Grade 5	16	(1) PRALSETINIB (S)  (2) METHADONE (C)  (3) OXYCODONE (C)  (4) FENTANYL CITRATE (C)  (5) PARACETAMOL (C)  (6) OXYCODONE HYDROCHLORIDE (C)  (7) PIPERACILLIN SODIUM\TAZOBACTAM	Drug interrupted N/A N/A Fatal	AER 10000009122 (PT: Septic shock): This clinical study case concerns a 51-year-old male patient who developed sepsis, 43 days after initiating therapy with pralsetinib for gastro-oesophageal cancer. The patient's concomitant medications included methadone, oxycodone, fentanyl citrate, paracetamol, Sondalis and oxycodone hydrochloride. No medical history, past products, concurrent conditions were reported. After 16 days of initiating therapy with pralsetinib, the patient developed septic shock and was hospitalized with symptoms of grade 1 febrile syndrome with nausea, vomiting, diarrhea, and chills following laboratory tests showing a neutrophil count of 49/mm <sup>3</sup> and platelet count of 49,000/mm <sup>3</sup> (normal range: 150,000-400,000/mm <sup>3</sup> ). A chest scan showed bilateral pneumopathy, and blood cultures were positive for Klebsiella pneumoniae and Pseudomonas aeruginosa. Pralsetinib therapy was temporarily

AER Number Age (in Years) Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome	Narrative MAH Comment
			SODIUM (T) (8) SPIRAMYCIN (T) (9) NOREPINEPHRINE BITARTRATE (T) (10) OXYGEN (T) (11) CEFEPIME (T) (12) MEROPENEM (T) (13) DAPTOMYCIN (T) (14) AMIKACIN (T) (15) MIDAZOLAM (T)		interrupted in response to the septic shock. The patient received treatment with piperacillin-tazobactam, norepinephrine, and oxygen (3 L/min). After 21 days of therapy initiation, cefepime (2 g every 8 hours) was added to the treatment regimen. After 23 days of starting therapy with the study drug, chest radiography revealed an infectious focus on the left side. After 25 days of therapy initiation, the treatment was escalated to include meropenem (6 g once daily), daptomycin, amikacin, and midazolam (5 mg). After 26 days of initiating therapy with pralsetinib the patient died due to septic shock. It was not reported whether an autopsy was performed. The investigator assessed fatal septic shock as related to pralsetinib

**Appendix 5 Case Listings Reporting Grade 4 Infections from the Company Safety Database (N=43)**

## Category B (N=36)

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
2799576 25 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Sepsis  Urinary tract infection bacterial Grade 4  Grade 3	843  843	(1) PRALSETINIB (S)  (2) HYDROCHLOROTHIAZIDE (C)  (3) ONDANSETRON (C)  (4) ZINC SULFATE (C)  (5) CARVEDILOL (C)  (6) HYDRALAZINE HYDROCHLORIDE (C)  (7) AMLODIPINE BESILATE (C)  (8) CALCIUM CARBONATE (C)  (9) ESOMEPRAZOLE (C)  (10) TRAMADOL (C)  (11) PARACETAMOL (C)  (12) CALCITRIOL (C)  (13) FAMOTIDINE (C)  (14) HYDROCHLOROTHIAZIDE (C)  (15) LACTOBACILLUS ACIDOPHILUS (C)  (16) MAGNESIUM HYDROXIDE (C)	Dose not changed  Dose not changed N/A  N/A N/A  N/A Recovered/Resolv ed  Recovered/Resolv ed

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(17) PREDNISONE (C) (18) LEVOTHYROXINE SODIUM (C) (19) TAMSULOSIN (C) (20) SOLIFENACIN SUCCINATE (C) (21) CEFUROXIME (T) (22) MEROPENEM (T) (23) GENTAMICIN (T) (24) SODIUM CHLORIDE (T) (25) SOLIFENACIN (T) (26) TAMSULOSIN (T) (27) PROMETHAZINE (T) (28) PARACETAMOL (T) (29) CALCITRIOL (T) (30) FAMOTIDINE (T) (31) LACTOBACILLUS ACIDOPHILUS (T) (32) PREDNISONE (T) (33) HYDRALAZINE (T)	

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(34) LABETALOL (T)	
2799609 72 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Sepsis  Pneumonia Grade 4  Grade 3	276  276	(1) PRALSETINIB (S)  (2) PARACETAMOL (C)  (3) CETIRIZINE HYDROCHLORIDE (C)  (4) FEXOFENADINE (C)  (5) ACETYLSALICYLIC ACID (C)  (6) XYLITOL (C)  (7) VANCOMYCIN (T)  (8) CEFEPIME (T)  (9) AMOXICILLIN\CLAVULANIC ACID (T)  (10) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)	Dose interrupted  Dose interrupted Pos  Pos NA  NA Resolved  Resolved With Sequelae
2799612 57 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Urosepsis Grade 4	27	(1) PRALSETINIB (S)  (2) OXYCODONE (C)  (3) DEXAMETHASONE (C)  (4) HYDROMORPHONE (C)  (5) MACROGOL (C)  (6) SENNA SPP. (C)  (7) SIMETICONE (C)	NR Unknown N/A Resolved

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(8) RIVAROXABAN (C) (9) ALOE VERA (C) (10) ASCORBIC ACID (C) (11) CETIRIZINE (C) (12) COLECALCIFEROL (C) (13) TARAXACUM OFFICINALE (C) (14) LACTOBACILLUS ACIDOPHILUS\PECTIN (C) (15) MAGNESIUM CITRATE (C) (16) MELATONIN (C) (17) PYRIDOXINE HYDROCHLORIDE (C) (18) VITAMIN B1 NOS (C) (19) SERENOA REPENS (C)	
2800259 60 Female CHINA Clinical Study Healthcare professional	Pneumonia Grade 4	87	(1) PRALSETINIB (S) (2) LEVOTHYROXINE SODIUM (C) (3) CALCIUM CARBONATE\COLECALCIFEROL (C) (4) CALCITRIOL (C) (5) CEFMETAZOLE (C)	Drug withdrawn Pos NA Resolving

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(6) CEFOPERAZONE\SULBACTAM (C)  (7) AMBROXOL HYDROCHLORIDE (C)  (8) ACETYLCYSTEINE (C)  (9) OSELTAMIVIR (C)  (10) BACILLUS LICHENFORMIS (C)  (11) MONTMORILLONITE (C)  (12) CEFMETAZOLE SODIUM (C)  (13) MEROPENEM (T)  (14) CASPOFUNGIN (T)  (15) TEICOPLANIN (T)  (16) GANCICLOVIR (T)	
2800338 61 Male UNITED STATES OF AMERICA Clinical Study Non-Healthcare professional	Sinusitis bacterial  Sepsis Grade 3  Grade 4	68	(1) PRALSETINIB (S)  (2) PARACETAMOL (C)  (3) CLOBETASOL (C)  (4) HYDROCORTISONE (C)  (5) LEVETIRACETAM (C)  (6) LEVOTHYROXINE (C)  (7) LIDOCAINE\PRILOCAINE (C)	Dose interrupted  Dose interrupted Positive  Positive Negative  Negative Recovered/Resolved

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(8) ZOLPIDEM (C) (9) OXYCODONE (C) (10) MACROGOL 3350 (C) (11) DIPHENHYDRAMINE HYDROCHLORIDE (C) (12) SODIUM CHLORIDE (C) (13) TAMSULOSIN (C) (14) CEFEPIME (T) (15) AMPICILLIN (T) (16) VANCOMYCIN (T) (17) ACICLOVIR (T) (18) CEFTRIAXONE (T)	Recovered/Resolved
2800591 60 Male ITALY Clinical Study Non-Healthcare professional	COVID-19 Grade 4	182	(1) PRALSETINIB (S) (2) ESOMEPRAZOLE (C) (3) ZOLPIDEM (C) (4) LEVOTHYROXINE (C) (5) LOPERAMIDE (C) (6) PARACETAMOL (C)	Dose interrupted Pos Neg Resolved

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(7) HYDROXYCHLOROQUINE (T) (8) LOPINAVIR\RITONAVIR (T) (9) IBUPROFEN (T) (10) PARACETAMOL (T) (11) COBICISTAT (T) (12) CALCIUM GLUCONATE (T) (13) CALCIUM CARBONATE (T) (14) POTASSIUM CHLORIDE (T)	
2801025 25 Female UNITED STATES OF AMERICA Clinical Study Non-Healthcare professional	Sepsis  Urinary tract infection Grade 4  Grade 3	675  675	(1) PRALSETINIB (S) (2) BISACODYL (C) (3) HYDROCHLOROTHIAZIDE (C) (4) ONDANSETRON (C) (5) CARVEDILOL (C) (6) HYDRALAZINE HYDROCHLORIDE (C) (7) AMLODIPINE BESILATE (C) (8) CALCIUM CARBONATE (C) (9) ZINC SULFATE (C) (10) ESOMEPRAZOLE (C)	Dose interrupted  Dose interrupted Positive  Positive N/A  N/A Recovered/Resolv ed  Recovered/Resolv ed

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(11) FUROSEMIDE (C)  (12) PARACETAMOL (C)  (13) PARACETAMOL (C)  (14) CALCITRIOL (C)  (15) OXYCODONE HYDROCHLORIDE\PARACETAMOL (C)  (16) PREDNISONE (C)  (17) TRAMADOL (C)	
2802351 52 Male UNITED STATES OF AMERICA Clinical Study Non-Healthcare professional	Pneumonia  Streptococcal bacteraemia Grade 3  Grade 4	95  95	(1) PRALSETINIB (S)  (2) AMLODIPINE (C)  (3) ESOMEPRAZOLE (C)  (4) GABAPENTIN (C)  (5) LEVOTHYROXINE (C)  (6) PIOGLITAZONE (C)  (7) POTASSIUM CHLORIDE (C)  (8) PRAMIPEXOLE (C)  (9) FORMOTEROL FUMARATE\MOMETASONE FUROATE (C)  (10) TIOTROPIUM BROMIDE MONOHYDRATE (C)	Dose not changed  Dose not changed N/A  N/A N/A  N/A Recovered/Resolv ed  Recovered/Resolv ed

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(11) CANNABIS SATIVA (C)  (12) PROCHLORPERAZINE (C)  (13) CALCITRIOL (C)  (14) SERTRALINE (C)  (15) SALBUTAMOL (C)	
2971567 76 Female CHINA Spontaneous Non-Healthcare professional	Pneumonia Grade 4	NR	(1) PRALSETINIB (S)	NR Unknown N/A Unknown
3021613 63 Female INDIA Non- Interventional Study/Program Healthcare professional	Urinary tract infection  Sepsis  Urosepsis Grade 4  Grade 4  Grade 3	NR  NR  NR	(1) PRALSETINIB (S)  (2) BENDAMUSTINE (C)  (3) RITUXIMAB (C)	NR  NR  NR Unknown  Unknown Unknown N/A  N/A  N/A Not Recovered/Not Resolved/Ongoing

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
				Not Recovered/Not Resolved/Ongoing  Recovered/Resolved
3063053 62 Male FRANCE Non- Interventional Study/Program Healthcare professional	Sepsis Grade 4	54	(1) PRALSETINIB (S)  (2) AMITRIPTYLINE HYDROCHLORIDE (C)  (3) LEVETIRACETAM (C)  (4) HYDROCORTISONE (C)  (5) RIVAROXABAN (C)  (6) LEVOTHYROXINE SODIUM (C)	NR Unkown N/A Not Recovered/Not Resolved/Ongoing
3068416 70 Male AUSTRIA Spontaneous Healthcare professional	Opportunistic infection Grade 4	53	(1) PRALSETINIB (S)  (2) CANDESARTAN (C)	NR Unkown N/A Recovered/Resolved With Sequelae
3157218 45 Female FRANCE Spontaneous Non-Healthcare professional	Pneumocystis jirovecii pneumonia Grade 4	92	(1) PRALSETINIB (S)  (2) RITUXIMAB (S)  (3) LAMOTRIGINE (C)  (4) FERROUS SULFATE (C)  (5) BACLOFEN (C)	Drug withdrawn Pos NA Resolving

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(6) ESCITALOPRAM (C)  (7) PANTOPRAZOLE (C)	
10000023673 76 Male JAPAN Clinical Study Non-Healthcare professional	Biliary tract infection Grade 4	716	(1) PRALSETINIB (S)  (2) RIVAROXABAN (C)  (3) AMLODIPINE BESILATE (C)  (4) BORIC ACID\POTASSIUM CHLORIDE\SODIUM BICARBONATE\SODIUM CHLORIDE\SODIUM PHOSPHATE (C)  (5) HEPARINOID (C)  (6) AZOSEMIDE (C)	Dose interrupted Positive N/A Recovered/Resolved
2709786 62 Male CHINA Clinical Study Non-Healthcare professional	Pneumonia Grade 4	14	(1) PRALSETINIB (S)  (2) ACARBOSE (C)  (3) IRBESARTAN (C)  (4) IBUPROFEN (C)  (5) MOXIFLOXACIN HYDROCHLORIDE (C)  (6) MEROPENEM (C)  (7) ATORVASTATIN CALCIUM (C)  (8) ACETYLSALICYLIC ACID (C)  (9) CEFTRIAXONE SODIUM (T)	NR Unknown N/A Not Recovered/Not Resolved/Ongoing

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
2882278 81 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Abdominal infection Grade 4	1460	(1) PRALSETINIB (S)  (2) CARVEDILOL (C)  (3) AMLODIPINE (C)  (4) APIXABAN (C)  (5) CALCIUM (C)  (6) COLECALCIFEROL (C)  (7) DOCUSATE SODIUM (C)  (8) ESTRADIOL (C)  (9) FAMOTIDINE (C)  (10) FERROUS GLUCONATE (C)  (11) LEVOTHYROXINE (C)  (12) LOSARTAN (C)  (13) MELATONIN (C)  (14) OMEPRAZOLE (C)  (15) ONDANSETRON (C)  (16) PROPAFENONE (C)  (17) SERTRALINE (C)	Drug interrupted Positive N/A Recovering/Resolving

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(18) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)	
2902742 76 Male GERMANY Clinical Study Healthcare professional	Pancreatic abscess Grade 4	612	(1) PRALSETINIB (S)  (2) BISOPROLOL FUMARATE (C)  (3) SIMVASTATIN (C)  (4) RAMIPRIL (C)  (5) AMLODIPINE (C)  (6) PANTOPRAZOLE (C)  (7) ALLOPURINOL (C)  (8) METAMIZOLE SODIUM (C)  (9) ACETYLSALICYLIC ACID (C)  (10) CLOPIDOGREL (C)  (11) HYDROMORPHONE (C)	Dose not changed N/A N/A Recovered/Resolved
2934155 55 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Sepsis  Pneumonia Grade 4  Grade 2	884  884	(1) PRALSETINIB (S)  (2) IPRATROPIUM BROMIDE\SALBUTAMOL SULFATE (C)  (3) NAPROXEN (C)	Dose interrupted  Dose interrupted Positive  Positive N/A  N/A Recovered/Resolved

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
				Recovered/Resolv ed
3155215 61 Male FRANCE Literature Study Non-Healthcare professional	Diverticulitis  Peritonitis Grade 4  Grade 4	NR  NR	(1) PRALSETINIB (S)	Dose interrupted  Dose interrupted Positive  Positive N/A  N/A Recovered/Resolv ed  Recovered/Resolv ed
3205188 75 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Arthritis infective Grade 4	1460	(1) PRALSETINIB (S)  (2) GABAPENTIN (C)  (3) AMLODIPINE (C)  (4) LIDOCAINE\PRILOCAINE (C)  (5) OXYCODONE (C)  (6) ZOLPIDEM (C)  (7) ESTROGENS CONJUGATED (C)  (8) LISINOPRIL (C)	Drug interrupted Positive N/A Recovered/Resolv ed With Sequelae

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(9) RIVAROXABAN (C)  (10) CLOBETASOL (C)  (11) ESTRADIOL (C)  (12) ESTROGENS CONJUGATED (C)	
3257483 59.0247 Male CHINA Clinical Study Healthcare professional	Pneumonia Grade 4	76	(1) PRALSETINIB (S)  (2) METHYLSPREDNISOLONE SODIUM SUCCINATE (C)  (3) ASCORBIC ACID (C)  (4) AMBROXOL HYDROCHLORIDE (C)  (5) PARACETAMOL (C)  (6) ACETYLCYSTEINE (C)  (7) AMINOPHYLLINE (C)  (8) LEVOTHYROXINE SODIUM (C)  (9) BETAMETHASONE SODIUM PHOSPHATE (C)  (10) BENIDIPINE HYDROCHLORIDE (C)  (11) IMMUNOGLOBULIN HUMAN NORMAL (C)  (12) LEVOFLOXACIN (C)  (13) CINEOLE\DIPIENTEN\PINENE (C)  (14) AMINOPHYLLINE (C)	Drug interrupted Positive  Recovered/Resolved With Sequelae

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(15) DEXAMETHASONE SODIUM PHOSPHATE (C) (16) RABEPRAZOLE SODIUM (C) (17) ULINASTATIN (C) (18) LOW MOLECULAR WEIGHT HEPARIN (C) (19) THYMALFASIN (C) (20) AZVUDINE (C) (21) CILASTATIN SODIUM\IMIPENEM (C) (22) BARICITINIB (C) (23) AMLODIPINE BESILATE (C) (24) SUFENTANIL CITRATE (C)	
3270069 79 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia  Sepsis Grade 3  Grade 4	909  1125	(1) PRALSETINIB (S) (2) LEVOFLOXACIN (C) (3) SULFAMETHOXAZOLE\TRIMETHOPRIM (C) (4) AMIODARONE (C)	Dose interrupted  Dose interrupted Positive  Positive N/A  N/A Recovered/Resolved  Recovering/Resolving

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3273536 53 Female KOREA, REPUBLIC OF Clinical Study Healthcare professional	COVID-19 pneumonia  Grade 4	1460	(1) PRALSETINIB (S)  (2) FERROUS SULFATE (C)  (3) LEVETIRACETAM (C)  (4) DEXAMETHASONE (C)  (5) LACOSAMIDE (C)  (6) PARACETAMOL (C)  (7) SALBUTAMOL (T)	Drug interrupted Negative N/A Not Recovered/Not Resolved/Ongoing
3384670 51 Female UNITED KINGDOM Clinical Study Healthcare professional	Sepsis Grade 4	40	(1) PRALSETINIB (S)  (2) LEVETIRACETAM (C)  (3) SERTRALINE (C)  (4) PROPRANOLOL (C)  (5) OMEPRAZOLE (C)  (6) PARACETAMOL (C)  (7) FLUCLOXACILLIN (C)  (8) DEXAMETHASONE (C)  (9) CHLORAMPHENICOL (C)  (10) PARAFFIN (C)  (11) BENZALKONIUM CHLORIDE\CHLORHEXIDINE	Drug interrupted Negative N/A Not Recovered/Not Resolved/Ongoing

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			HYDROCHLORIDE\ISOPROPYL MYRISTATE\PARAFFIN, LIQUID (C) (12) ONDANSETRON (C) (13) FAMOTIDINE (C) (14) AMOXICILLIN (T) (15) CLARITHROMYCIN (T) (16) AMIKACIN (T) (17) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T) (18) METHYLPREDNISOLONE (T)	
2710528 77 Female FRANCE Clinical Study Healthcare professional	Septic shock  Staphylococcal scalded skin syndrome Grade 5  Grade 4	109  109	(1) PRALSETINIB (S) (2) LEVOTHYROXINE (C) (3) MESALAZINE (C) (4) PREDNISOLONE (C) (5) CEFAZOLIN (T) (6) CLINDAMYCIN (T)	Dose interrupted  Dose interrupted N/A  Negative N/A  N/A Fatal  Not Recovered/Not Resolved/Ongoing
2802368 71 Male UNITED STATES OF	Pneumonia aspiration  Neutropenic sepsis Grade 5	320  307	(1) PRALSETINIB (S) (2) ACETYLSALICYLIC ACID (C) (3) ATENOLOL (C)	Dose interrupted  Dose interrupted N/A

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
AMERICA Clinical Study Healthcare professional	Grade 4		(4) BETACAROTENE (C)  (5) CHLORTALIDONE (C)  (6) CIPROFLOXACIN (C)  (7) METRONIDAZOLE (C)  (8) PANTOPRAZOLE (C)  (9) SIMVASTATIN (C)  (10) APIXABAN (C)  (11) VANCOMYCIN (T)  (12) CEFAZOLIN (T)	Negative N/A  N/A Fatal  Not Recovered/Not Resolved/Ongoing
3313491 73 Male SPAIN Clinical Study Healthcare professional	Pseudomembranous colitis  Sepsis  Grade 4  Grade 5	99  77	(1) PRALSETINIB (S)  (2) FIDAXOMICIN (T)	N/A  N/A N/A  N/A  Recovered/Resolv ed  Fatal
2711859 53	Sepsis Grade 4	632	(1) PRALSETINIB (S)	NR Unkown

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Female UNITED STATES OF AMERICA Clinical Study Healthcare professional			(2) SENNOSIDE A+B (C)  (3) LISINOPRIL (C)  (4) DICLOFENAC (C)  (5) GABAPENTIN (C)  (6) NYSTATIN (C)  (7) OXYCODONE HYDROCHLORIDE (C)  (8) MACROGOL 3350 (C)  (9) ENOXAPARIN SODIUM (C)  (10) APIXABAN (C)  (11) MORPHINE (C)  (12) MORPHINE SULFATE (C)	N/A Not Recovered/Not Resolved/Ongoing
2714692 38 Male CHINA Clinical Study Healthcare professional	Septic shock Grade 4	389	(1) PRALSETINIB (S)  (2) SODIUM BICARBONATE (C)  (3) OXYCODONE HYDROCHLORIDE (C)  (4) TRAMADOL (C)  (5) CARBAZOCHEM (C)  (6) IMIPENEM (C)  (7) CILASTATIN (C)	N/A N/A N/A Not Recovered/Not Resolved/Ongoing

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(8) BICYCLOL (C) (9) ADEMETHIONINE (T) (10) GLUTATHIONE (T) (11) ARGININE GLUTAMATE (T) (12) OXYGEN (T) (13) LEVOTHYROXINE SODIUM (T) (14) DOPAMINE (T) (15) ATROPINE (T) (16) EPINEPHRINE (T) (17) NOREPINEPHRINE (T)	
2726273 73 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Sepsis  Urinary tract infection Grade 4  Grade 3	267  267	(1) PRALSETINIB (S) (2) AMLODIPINE (C) (3) CETIRIZINE (C) (4) ESOMEPRAZOLE (C) (5) IBUPROFEN (C) (6) SITAGLIPTIN (C) (7) LEVOTHYROXINE (C)	Drug withdrawn  Drug withdrawn Positive  Positive N/A  N/A Recovered/Resolv ed  Recovered/Resolv ed

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(8) MAGNESIUM OXIDE (C)  (9) ROSUVASTATIN (C)  (10) SIMVASTATIN (C)  (11) TELMISARTAN (C)  (12) METFORMIN HYDROCHLORIDE\SITAGLIPTIN PHOSPHATE MONOHYDRATE (C)  (13) METFORMIN (C)  (14) CEFTRIAXONE (T)  (15) VANCOMYCIN (T)	
2785472 58 Male TAIWAN, PROVINCE OF CHINA Clinical Study Healthcare professional	Pneumonia  Septic shock Grade 4  Grade 4	563	(1) PRALSETINIB (S)  (2) VALSARTAN (C)  (3) CLOBETASOL PROPIONATE (C)  (4) LEVOTHYROXINE SODIUM (C)  (5) TAMSULOSIN HYDROCHLORIDE (C)  (6) OXYBUTYNIN HYDROCHLORIDE (C)  (7) AMBROXOL HYDROCHLORIDE (C)  (8) NAPROXEN (C)  (9) LOPERAMIDE HYDROCHLORIDE (C)	Drug withdrawn  Drug withdrawn NA  NA  NA  NA Unknown  Unknown

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(10) TRANEXAMIC ACID (C)  (11) BACLOFEN (C)  (12) BISACODYL (C)  (13) DICLOXA CILLIN SODIUM MONOHYDRATE (C)  (14) ESOMEPRAZOLE (C)  (15) LOPERAMIDE HYDROCHLORIDE (C)	
2792289 32 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Sepsis  Urinary tract infection Grade 4  Grade 4	460  459	(1) PRALSETINIB (S)  (2) AMLODIPINE (C)  (3) DENOSUMAB (C)  (4) FLUDROCORTISONE (C)  (5) HYDROCORTISONE (C)  (6) POTASSIUM CHLORIDE (C)  (7) DOXYCYCLINE (C)  (8) LEVOTHYROXINE (C)  (9) MAGNESIUM HYDROXIDE (C)  (10) FUROSEMIDE (C)  (11) ALBUMIN HUMAN (T)  (12) CEFTRIAXONE (T)	NR Unkown N/A Recovered/Resolv ed  Recovered/Resolv ed

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(13) CEFALEXIN (T) (14) LEVOFLOXACIN (T) (15) PIPERACILLINTAZOBACTAM (T) (16) VANCOMYCIN (T) (17) HYDROCORTISONE (T) (18) HYDROCORTISONE SODIUM SUCCINATE (T) (19) PROPRANOLOL (T) (20) SEVELAMER CARBONATE (T) (21) VASOPRESSIN (T) (22) MAGNESIUM SULFATE (T) (23) METHYLPREDNISOLONE (T)	
2793160 52 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Sepsis Grade 4	306	(1) PRALSETINIB (S) (2) ALPRAZOLAM (C) (3) SENNOSIDE A+B (C) (4) ENOXAPARIN SODIUM (C) (5) LISINOPRIL (C) (6) NIFEDIPINE (C)	Dose interrupted positive Negative  Recovered/Resolved

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(7) FENTANYL CITRATE (C)  (8) APIXABAN (C)  (9) ONDANSETRON (C)	
2796030 59 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Sepsis  Bacteraemia Grade 4  Grade 2	7  10	(1) PRALSETINIB (S)  (2) CALCIUM CARBONATE (C)  (3) OXYGEN (C)  (4) LEVOTHYROXINE (C)  (5) RANITIDINE (C)  (6) ROSUVASTATIN (C)  (7) LACOSAMIDE (C)  (8) LEVETIRACETAM (C)  (9) LORAZEPAM (C)  (10) ONDANSETRON (C)  (11) PANTOPRAZOLE (C)  (12) MACROGOL (C)  (13) CEFEPIME HYDROCHLORIDE (T)  (14) VANCOMYCIN HYDROCHLORIDE (T)	NR Unkown N/A Recovered/Resolv ed With Sequelae  Recovered/Resolv ed
2797006 66	Pneumonia Grade 4	288	(1) PRALSETINIB (S)	NR Unkown

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Male ITALY Clinical Study Healthcare professional			(2) PIOGLITAZONE (C)  (3) INSULIN GLARGINE (C)  (4) LANSOPRAZOLE (C)  (5) MANIDIPINE (C)  (6) RAMIPRIL (C)  (7) PREDNISONE (C)  (8) ALLOPURINOL (C)  (9) INSULIN LISPRO (C)  (10) OMEPRAZOLE (C)  (11) AMOXICILLIN TRIHYDRATE\CLAVULANATE POTASSIUM (C)  (12) LEVOFLOXACIN (T)  (13) CEFTRIAXONE (T)  (14) METHYL PREDNISOLONE (T)  (15) FUROSEMIDE (T)  (16) BETAMETHASONE (T)  (17) PARACETAMOL (T)  (18) PARACETAMOL (T)	N/A Recovered/Resolv ed

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
2797521 66 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Escherichia sepsis  Escherichia bacteraemia Grade 4  Grade 2	212  212	(1) PRALSETINIB (S)  (2) MORPHINE SULFATE (C)  (3) MACROGOL 3350 (C)  (4) SENNOSIDE A+B (C)  (5) SALBUTAMOL (C)  (6) SODIUM CHLORIDE (C)  (7) SERTRALINE HYDROCHLORIDE (C)  (8) PARACETAMOL (C)  (9) ONDANSETRON (C)  (10) MEROPENEM (T)  (11) SALBUTAMOL (T)  (12) SALBUTAMOL (T)  (13) ACETYLSALICYLIC ACID (T)  (14) MUPIROCIN (T)  (15) CEFTRIAXONE (T)	NR Unkown N/A Recovered/Resolv ed  Recovered/Resolv ed

## Category C (N=5)

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
2827699 54 Male ITALY Clinical Study Healthcare professional	Device related infection Grade 4	(1) (1) 19	(1) PRALSETINIB (S)  (2) TEICOPLANIN (T)  (3) SULFAMETHOXAZOLE\TRIMETH OPRIM (T)	Recovered/Resolved
2980773 13 Female UNITED STATES OF AMERICA Spontaneous Healthcare professional	Pneumonia Grade 4	185	(1) PRALSETINIB (S)  (2) CALCITRIOL (C)	Drug interrupted Positive NA Recovering/Resolving
3067477 60 Female GERMANY Spontaneous Non-Healthcare professional	Pneumocystis jirovecii pneumonia Grade 4	80	(1) PRALSETINIB (S)	NR Unkown N/A Recovered/Resolved
3205767 Not reported Not reported CHINA Non-Interventional Study/Program Non-Healthcare professional	Pneumonia Grade 4	195	(1) PRALSETINIB (S)	Dose interrupted Negative N/A Not Recovered/Not Resolved/Ongoing
2708994 63 Male	Sepsis  Pneumonia	835  833	(1) PRALSETINIB (S)	N/A  Doseinterrupted

AER Number Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
TAIWAN, PROVINCE OF CHINA Clinical Study Healthcare professional	Grade 5  Grade 4			N/A  Positive N/A  N/A Fatal  Recovered/Resolved With Sequelae

**Appendix 6 Case Listings Reporting Grade 3 Infections from the Company Safety Database (N=276)**

**Category B (N=236)**

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
2790973 72 Female FRANCE Clinical Study Healthcare professional	Pyelonephritis Grade 3	47	(1) PRALSETINIB (S)  (2) METFORMIN (C)  (3) IRBESARTAN (C)  (4) SIMVASTATIN (C)  (5) COLECALCIFEROL (C)  (6) OMEPRAZOLE (C)  (7) PARACETAMOL (C)  (8) TINZAPARIN SODIUM (C)  (9) AMOXICILLIN (C)  (10) NITROFURANTOIN (C)  (11) LEVOFLOXACIN (C)  (12) CEFTRIAXONE SODIUM (C)  (13) NORFLOXACIN (C)  (14) BISOPROLOL (C)  (15) OFLOXACIN (C)  (16) PROMESTRIENE (C)	Dose reduced Positive N/A Recovered/Resolved With Sequelae

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(17) ALFUZOSIN HYDROCHLORIDE (C)  (18) MECILLINAM (C)  (19) RIVAROXABAN (C)  (20) OFLOXACIN (C)	
2944253 74 Male KOREA, REPUBLIC OF Clinical Study Healthcare professional	Pneumonia Grade 3	64	(1) PRALSETINIB (S)  (2) ALANINE\ARGININE\CALCIUM CHLORIDE\CYSTEINE HYDROCHLORIDE\GLUCOSE\GLYCINE\HISTIDINE\ISOLE UCINE\LEUCINE\LYSINE ACETATE\MAGNESIUM CHLORIDE\METHIONINE\PHENYLALANINE\POTASSIUM CHLORIDE\POTASSIUM PHOSPHATE MONOBASIC\PROLINE\SERINE\SODIUM ACETATE\SODIUM CHLORIDE\THREONINE\TRYPTOPHAN\VALINE (C)  (3) CHROMIC CHLORIDE\COPPER SULFATE\MANGANESE SULFATE\ZINC SULFATE (C)  (4) FERROUS SULFATE (C)  (5) PREGABALIN (C)  (6) MAGNESIUM OXIDE (C)  (7) URSOODEOXYCHOLIC ACID (C)  (8) ACETYLSALICYLIC ACID (C)  (9) PANTOPRAZOLE SODIUM SESQUIHYDRATE (C)  (10) LACTULOSE (C)	Dose interrupted Negative N/A Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			<p>(11) ORNITHINE ASPARTATE (C)</p> <p>(12) ALANINE\ARGININE\CALCIUM CHLORIDE DIHYDRATE\FISH OIL\GLUCOSE MONOHYDRATE\GLYCINE\GLYCINE MAX OIL\HISTIDINE\ISOLEUCINE\LEUCINE\LYSINE HYDROCHLORIDE\MAGNESIUM SULFATE HEPTAHYDRATE\MEDIUM-CHAIN TRIGLYCERIDES\METHIONINE\OLEA EUROPAEA OIL\PHENYLALANINE\POTASSIUM CHLORIDE\PROLINE\SERINE\SODIUM ACETATE TRIHYDRATE\SODIUM GLYCEROPHOSPHATE\THREONINE\TRYPTOPHAN\TYRO SINE\VALINE\ZINC SULFATE HEPTAHYDRATE (C)</p> <p>(13) CALCIUM POLYSTYRENE SULFONATE (C)</p> <p>(14) MUPIROCIN (C)</p> <p>(15) GLYCEROL (C)</p> <p>(16) POTASSIUM PHOSPHATE MONOBASIC (C)</p> <p>(17) INSULIN HUMAN (C)</p> <p>(18) ZOLPIDEM TARTRATE (C)</p> <p>(19) ALBUMIN HUMAN (C)</p> <p>(20) FUROSEMIDE (C)</p> <p>(21) PHENYLEPHRINE HYDROCHLORIDE\TROPICAMIDE (C)</p>	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(22) POLYCARBOPHIL CALCIUM (C) (23) CHLORPHENAMINE MALEATE (C) (24) PRUCALOPRIDE SUCCINATE (C) (25) ARIPIPRAZOLE (C) (26) CODEINE (C) (27) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T) (28) LEVOFLOXACIN (T) (29) SULFAMETHOXAZOLE\TRIMETHOPRIM (T) (30) METHYLSPREDNISOLONE SODIUM SUCCINATE (T) (31) SALBUTAMOL SULFATE (T) (32) IPRATROPIUM BROMIDE (T) (33) ACETYL CYSTEINE (T) (34) OXYGEN (T) (35) GANCICLOVIR (T) (36) SULFAMETHOXAZOLE\TRIMETHOPRIM (T) (37) METHYLSPREDNISOLONE SODIUM SUCCINATE (T) (38) FLUCONAZOLE (T)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(39) MEROPENEM (T)  (40) TEICOPLANIN (T)	
2951941 72 Male KOREA, REPUBLIC OF Clinical Study Healthcare professional	Device related infection  Pleural infection Grade 3  Grade 3	213  203	(1) PRALSETINIB (S)  (2) FERROUS SULFATE (C)  (3) MAGNESIUM OXIDE (C)  (4) CODEINE (C)  (5) PANTOPRAZOLE SODIUM SESQUIHYDRATE (C)  (6) LEVOTHYROXINE SODIUM (C)  (7) LACTULOSE (C)  (8) FEBUXOSTAT (C)  (9) URSODEOXYCHOLIC ACID (C)  (10) LOPERAMIDE (C)  (11) BENZYDAMINE HYDROCHLORIDE (C)  (12) ZOLPIDEM TARTRATE (C)  (13) CHOLINE ALFOSCERATE (C)  (14) CEFTRIAXONE (C)  (15) ALBUMIN HUMAN (C)	NR  NR Unknown  Unknown N/A  N/A Recovered/Resolved  Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(16) FUROSEMIDE (C) (17) SULFAMETHOXAZOLE\TRIMETHOPRIM (C) (18) CEFPODOXIME PROXETIL (C) (19) ERDOSTEINE (C) (20) PREDNISOLONE (C) (21) LACTULOSE (C) (22) PARACETAMOL (C) (23) PROPACETAMOL (C) (24) ALANINE\ARGININE\CALCIUM CHLORIDE DIHYDRATE\FISH OIL\GLUCOSE MONOHYDRATE\GLYCINE\GLYCINE MAX OIL\HISTIDINE\ISOLEUCINE\LEUCINE\LYSINE HYDROCHLORIDE\MAGNESIUM SULFATE HEPTAHYDRATE\MEDIUM-CHAIN TRIGLYCERIDES\METHIONINE\OLEA EUROPAEA OIL\PHENYLALANINE\POTASSIUM CHLORIDE\PROLINE\SERINE\SODIUM ACETATE TRIHYDRATE\SODIUM GLYCEROPHOSPHATE\THREONINE\TRYPTOPHAN\TYRO SINE\VALINE\ZINC SULFATE HEPTAHYDRATE (C) (25) TRANEXAMIC ACID (C) (26) FAMOTIDINE (C) (27) LEVOTHYROXINE SODIUM (C)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			<p>(28) ALANINE\ARGININE\CALCIUM CHLORIDE\FISH OIL\GLUCOSE MONOHYDRATE\GLYCINE\GLYCINE MAX SEED OIL\HISTIDINE\ISOLEUCINE\LEUCINE\LYSINE ACETATE\MAGNESIUM SULFATE\MEDIUM-CHAIN TRIGLYCERIDES\METHIONINE\OLEA EUROPAEA OIL\PHENYLALANINE\POTASSIUM CHLORIDE\PROLINE\SERINE\SODIUM ACETATE\SODIUM GLYCEROPHOSPHATE\TAURINE\THREONINE\TRYPTOPHAN\TYROSINE\VALINE\ZINC SULFATE (C)</p> <p>(29) CHROMIC CHLORIDE\COPPER SULFATE\MANGANESE SULFATE\ZINC SULFATE (C)</p> <p>(30) DIOSMECTITE (C)</p> <p>(31) MEGESTROL ACETATE (C)</p> <p>(32) CIPROFLOXACIN (C)</p> <p>(33) FOLIC ACID (C)</p> <p>(34) COBAMAMIDE (C)</p> <p>(35) PALONOSETRON HYDROCHLORIDE (C)</p> <p>(36) APREPITANT (C)</p> <p>(37) DEXAMETHASONE (C)</p> <p>(38) PEMETREXED DISODIUM HEMIPENTAHYDRATE (C)</p> <p>(39) CARBOPLATIN (C)</p>	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(40) SODIUM BICARBONATE (C) (41) VITIS VINIFERA SEED (C) (42) LOPERAMIDE (C) (43) CHLORPHENAMINE MALEATE (C) (44) FILGRASTIM (C) (45) DIMETHYL 4,4'-BIPHENYLDICARBOXYLATE\URSODEOXYCHOLIC ACID (C) (46) RED BLOOD CELLS (C) (47) PLATELETS, CONCENTRATED (C) (48) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T) (49) LEVOFLOXACIN (T) (50) SULFAMETHOXAZOLE\TRIMETHOPRIM (T) (51) METHYLSPREDNISOLONE SODIUM SUCCINATE (T) (52) TEICOPLANIN (T) (53) CEFPODOXIME PROXETIL (T) (54) SODIUM BICARBONATE (T) (55) CALCIUM POLYSTYRENE SULFONATE (T)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(56) GLUCOSE (T)  (57) INSULIN HUMAN (T)  (58) CALCIUM POLYSTYRENE SULFONATE (T)  (59) CALCIUM POLYSTYRENE SULFONATE (T)  (60) FUROSEMIDE (T)  (61) ALBUMIN HUMAN (T)  (62) SODIUM BICARBONATE (T)  (63) SODIUM CHLORIDE (T)  (64) PARACETAMOL (T)  (65) TAZOBACTAM (T)  (66) FLUCONAZOLE (T)  (67) CASPOFUNGIN ACETATE (T)  (68) TEICOPLANIN (T)  (69) PROPACETAMOL HYDROCHLORIDE (T)  (70) PARACETAMOL (T)  (71) BLOOD PLASMA (T)  (72) OXYGEN (T)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(73) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (74) FLUCONAZOLE (T)  (75) CIPROFLOXACIN (T)	
2727438 80 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	COVID-19 pneumonia Grade 3	182	(1) PRALSETINIB (S)  (2) DEXTROMETHORPHAN HYDROBROMIDE\GUAIFENESIN (C)  (3) IPRATROPIUM (C)  (4) LORAZEPAM (C)  (5) OMEPRAZOLE (C)  (6) PROCHLORPERAZINE (C)  (7) CAMPHOR\MENTHOL (C)  (8) PARACETAMOL (C)  (9) MEGLUMINE GADOTERATE (C)  (10) IOHEXOL (C)  (11) COLECALCIFEROL (C)  (12) NYSTATIN (C)	Dose not changed N/A N/A Recovered/Resolved
2762461 65 Not reported CHINA Spontaneous	Pneumonia Grade 3	14	(1) PRALSETINIB (S)	Dose interrupted Negative N/A Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decallenge Rechallenge Event Outcome
Healthcare professional				
2765097 73 Female UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Pneumonia Grade 3	509	(1) PRALSETINIB (S)  (2) CALCIUM CARBONATE (C)  (3) ESTRADIOL (C)  (4) LANSOPRAZOLE (C)  (5) LEVOTHYROXINE (C)  (6) METOPROLOL (C)  (7) NAPROXEN SODIUM (C)  (8) RIVAROXABAN (C)  (9) DOXYCYCLINE HYCLATE (C)  (10) CHLORHEXIDINE (C)  (11) FLECAINIDE (C)  (12) LORATADINE (C)  (13) ACETYLSALICYLIC ACID (C)  (14) CAFFEINE (C)  (15) PARACETAMOL (C)  (16) CHLORHEXIDINE (C)	Dose not changed N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(17) LACTOBACILLUS ACIDOPHILUS (C)  (18) MAGNESIUM HYDROXIDE (C)  (19) COLECALCIFEROL (C)  (20) TRIAMCINOLONE (C)  (21) DICYCLOVERINE (C)  (22) PARACETAMOL (C)  (23) CHLORHEXIDINE (T)  (24) ULOBETASOL (T)  (25) FUROSEMIDE (T)	
2798611 48 Female KOREA, REPUBLIC OF Clinical Study Healthcare professional	Pneumonia Grade 3	183	(1) PRALSETINIB (S)  (2) LEVOFLOXACIN (T)  (3) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)	N/A N/A N/A Not Recovered/Not Resolved/Ongoing
2798893 70 Male SPAIN Clinical Study Healthcare professional	Renal tuberculosis Grade 3	125	(1) PRALSETINIB (S)  (2) VERAPAMIL HYDROCHLORIDE (C)  (3) ISONIAZID (T)  (4) RIFAMPICIN (T)  (5) PYRAZINAMIDE (T)	Dose interrupted Positive N/A Recovered/Resolve d With Sequelae

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(6) ETHAMBUTOL (T)  (7) PREDNISONE (T)	
2798895 39 Male GERMANY Clinical Study Healthcare professional	Pneumocystis jirovecii pneumonia Grade 3	21	(1) PRALSETINIB (S)  (2) BISOPROLOL (C)  (3) AMLODIPINE (C)  (4) RANITIDINE (C)  (5) HYDROCORTISONE (C)  (6) LEVOTHYROXINE (C)  (7) MORPHINE (C)  (8) PREGABALIN (C)  (9) TORASEMIDE (C)  (10) CHLORHEXIDINE GLUCONATE\MACROGOL\SACCHARIN SODIUM\SODIUM BICARBONATE\SODIUM EDETATE (C)  (11) TETRACAIN (C)  (12) AMPHOTERICIN B (C)  (13) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)  (14) TORASEMIDE (T)	Dose interrupted Positive N/A Recovered/Resolved With Sequelae

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(15) PREDNISOLONE (T)  (16) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (17) PENTAMIDINE ISETHIONATE (T)  (18) DOXYLAMINE SUCCINATE\FOLIC ACID\PYRIDOXINE HYDROCHLORIDE (T)	
2798919 52 Female UNITED KINGDOM Clinical Study Healthcare professional	Tonsillitis Grade 3	100	(1) PRALSETINIB (S)  (2) APIXABAN (C)  (3) CALCIUM CARBONATE (C)  (4) SENNA SPP. (C)  (5) HYPROMELLOSE (C)  (6) DENOSUMAB (C)  (7) MACROGOL (C)  (8) SEA WATER (C)	Dose not changed N/A N/A Recovered/Resolved
2799041 58 Female FRANCE Clinical Study Healthcare professional	Pyelonephritis Grade 3	162	(1) PRALSETINIB (S)  (2) MEROPENEM (T)  (3) FOSFOMYCIN TROMETAMOL (T)	Dose interrupted Positive N/A Recovered/Resolved
2799071 59 Female FRANCE	Pneumonia Grade 3	196	(1) PRALSETINIB (S)  (2) AMOXICILLIN\CLAVULANATE POTASSIUM (T)	Dose interrupted Positive N/A

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
Clinical Study Healthcare professional			(3) VANCOMYCIN (T)	Recovered/Resolve d
2799103 73 Male UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Urinary tract infection Grade 3	219	(1) PRALSETINIB (S)  (2) GABAPENTIN (C)  (3) LEVOTHYROXINE SODIUM (C)  (4) LORAZEPAM (C)  (5) MACROGOL 3350 (C)  (6) ALENDRONATE SODIUM (C)  (7) BISOPROLOL FUMARATE (C)  (8) LISINOPRIL DIHYDRATE (C)  (9) ASCORBIC ACID\ CUPRIC OXIDE\ DL-ALPHA TOCOPHERYL ACETATE\ XANTOFYL\ ZEAXANTHIN\ ZINC OXIDE (C)  (10) CALCIUM (C)  (11) CEFTAZIDIME (T)  (12) METRONIDAZOLE (T)  (13) PARACETAMOL (T)  (14) ENOXAPARIN SODIUM (T)	NR Unknown N/A Recovered/Resolve d With Sequelae
2799112 60	Pyelonephritis Grade 3	41	(1) PRALSETINIB (S)	NR Unknown

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
Female FRANCE Clinical Study Healthcare professional			(2) HYDROCORTISONE (C)  (3) PARACETAMOL (C)  (4) FLUDROCORTISONE (C)  (5) MANIDIPINE (C)  (6) TINZAPARIN SODIUM (C)  (7) NICARDIPINE HYDROCHLORIDE (C)  (8) NICARDIPINE HYDROCHLORIDE (C)  (9) SODIUM CHLORIDE (C)  (10) OXYCODONE HYDROCHLORIDE (C)  (11) RED BLOOD CELLS (C)  (12) SODIUM POLYSTYRENE SULFONATE (C)  (13) LIDOCAINE (C)  (14) CALCIUM CARBONATE (C)  (15) POTASSIUM (C)  (16) ONDANSETRON (C)  (17) DOMPERIDONE (C)  (18) CALCIUM CHLORIDE (C)	N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(19) PLATELETS, HUMAN BLOOD (C)  (20) GLUCOSE (C)  (21) PIPERACILLIN\TAZOBACTAM (T)  (22) AMOXICILLIN (T)  (23) AMOXICILLIN (T)	
2799197 65 Male KOREA, REPUBLIC OF Clinical Study Healthcare professional	Pneumonia Grade 3	32	(1) PRALSETINIB (S)  (2) METFORMIN HYDROCHLORIDE (C)  (3) HYDROCHLOROTHIAZIDE\VALSARTAN (C)  (4) LACTULOSE (C)  (5) PSEUDOEPHEDRINE HYDROCHLORIDE (C)  (6) AMMONIUM CHLORIDE\CHLORPHENAMINE MALEATE\DIHYDROCODEINE BITARTRATE\METHYLEPHEDRINE HYDROCHLORIDE-DL (C)  (7) DEXAMETHASONE (C)  (8) MEGESTROL ACETATE (C)  (9) INSULIN HUMAN (C)  (10) POTASSIUM PHOSPHATE MONOBASIC (C)  (11) PROPACETAMOL HYDROCHLORIDE (C)	Dose interrupted Positive N/A Recovered/Resolved With Sequelae

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(12) PETHIDINE (C)  (13) PETHIDINE HYDROCHLORIDE (T)  (14) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (15) MOXIFLOXACIN HYDROCHLORIDE (T)  (16) AMBROXOL ACEFYLLINATE (T)  (17) AMBROXOL HYDROCHLORIDE (T)  (18) POTASSIUM PHOSPHATE MONOBASIC (T)	
2799576 25 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Sepsis  Urinary tract infection bacterial Grade 4  Grade 3	843  843	(1) PRALSETINIB (S)  (2) HYDROCHLOROTHIAZIDE (C)  (3) ONDANSETRON (C)  (4) ZINC SULFATE (C)  (5) CARVEDILOL (C)  (6) HYDRALAZINE HYDROCHLORIDE (C)  (7) AMLODIPINE BESILATE (C)  (8) CALCIUM CARBONATE (C)  (9) ESOMEPRAZOLE (C)  (10) TRAMADOL (C)  (11) PARACETAMOL (C)	Dose not changed  Dose not changed N/A  N/A N/A  N/A Recovered/Resolved  Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(12) CALCITRIOL (C) (13) FAMOTIDINE (C) (14) HYDROCHLOROTHIAZIDE (C) (15) LACTOBACILLUS ACIDOPHILUS (C) (16) MAGNESIUM HYDROXIDE (C) (17) PREDNISONE (C) (18) LEVOTHYROXINE SODIUM (C) (19) TAMSULOSIN (C) (20) SOLIFENACIN SUCCINATE (C) (21) CEFUROXIME (T) (22) MEROPENEM (T) (23) GENTAMICIN (T) (24) SODIUM CHLORIDE (T) (25) SOLIFENACIN (T) (26) TAMSULOSIN (T) (27) PROMETHAZINE (T) (28) PARACETAMOL (T)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(29) CALCITRIOL (T)  (30) FAMOTIDINE (T)  (31) LACTOBACILLUS ACIDOPHILUS (T)  (32) PREDNISONE (T)  (33) HYDRALAZINE (T)  (34) LABETALOL (T)	
2799578 26 Female UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Urinary tract infection  Klebsiella bacteraemia Grade 3  Grade 3	865  865	(1) PRALSETINIB (S)  (2) SULFAMETHOXAZOLE\TRIMETHOPRIM (C)	Dose not changed  Dose not changed N/A  N/A N/A  N/A Recovered/Resolved  Recovered/Resolved
2799584 52 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia  Sepsis Grade 3  Grade 3	310  310	(1) PRALSETINIB (S)  (2) ALLOPURINOL (C)  (3) AMLODIPINE BESILATE (C)  (4) SIMETICONE (C)	Dose interrupted  Dose interrupted Positive  Positive N/A

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(5) CLOTRIMAZOLE (C) (6) CLONIDINE (C) (7) ERGOCALCIFEROL (C) (8) FLUOXETINE HYDROCHLORIDE (C) (9) GABAPENTIN (C) (10) LEVOTHYROXINE SODIUM (C) (11) LIDOCAINE (C) (12) LISINOPRIL (C) (13) LOPERAMIDE HYDROCHLORIDE (C) (14) LORATADINE (C) (15) DIPHENHYDRAMINE\LIDOCAINE (C) (16) MORPHINE SULFATE (C) (17) MORPHINE SULFATE (C) (18) ONDANSETRON (C) (19) MACROGOL 3350 (C) (20) PROMETHAZINE (C) (21) SIMETICONE (C)	N/A Recovered/Resolved Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(22) TRIAMCINOLONE ACETONIDE (C)  (23) FAMOTIDINE (C)  (24) MUPIROCIN (C)  (25) TRIAMCINOLONE ACETONIDE (C)  (26) ATROPINE SULFATE\DIPIENOXYLATE HYDROCHLORIDE (C)  (27) MICONAZOLE NITRATE (C)  (28) SALBUTAMOL SULFATE (C)  (29) NYSTATIN (C)  (30) ALPRAZOLAM (C)	
2799585 31 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia Grade 3	19	(1) PRALSETINIB (S)  (2) PREDNISONE (C)  (3) AMLODIPINE (C)  (4) PARACETAMOL (C)  (5) CALCIUM ASCORBATE (C)  (6) CALCITRIOL (C)  (7) CALCIUM CITRATE\COLECALCIFEROL (C)  (8) COLECALCIFEROL (C)	N/A N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(9) FLUDROCORTISONE (C)  (10) LEVOTHYROXINE (C)  (11) DOCUSATE SODIUM (C)  (12) MAGNESIUM CITRATE (C)  (13) AMOXICILLIN\CLAVULANATE POTASSIUM (T)  (14) VANCOMYCIN (T)  (15) CEFEPIME (T)  (16) HYDROCODONE BITARTRATE\PARACETAMOL (T)	
2799593 58 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pleural infection Grade 3	117	(1) PRALSETINIB (S)  (2) LORAZEPAM (C)  (3) LOSARTAN POTASSIUM (C)  (4) PANTOPRAZOLE (C)  (5) VANCOMYCIN (T)  (6) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)	Dose not changed N/A N/A Recovered/Resolved
2799598 70 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Urinary tract infection Grade 3	49	(1) PRALSETINIB (S)  (2) AMOXICILLIN\CLAVULANATE POTASSIUM (C)  (3) ENOXAPARIN (C)  (4) METOPROLOL TARTRATE (C)	Dose not changed N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(5) DALTEPARIN (C) (6) PARACETAMOL (C) (7) VANCOMYCIN (C) (8) PANTOPRAZOLE (C) (9) PIPERACILLIN\TAZOBACTAM (C) (10) FLUTICASONE PROPIONATE (C) (11) SENNA SPP. (C) (12) MACROGOL (C) (13) OXYCODONE (C) (14) MAGNESIUM HYDROXIDE (C) (15) LEVOTHYROXINE (C) (16) LEVETIRACETAM (C) (17) ERGOCALCIFEROL (C) (18) DOCUSATE SODIUM (C) (19) BISACODYL (C) (20) BACLOFEN (C) (21) SODIUM CHLORIDE (C)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(22) CEFEPIME (C)  (23) D-MANNOSE (C)  (24) LEVOFLOXACIN (C)  (25) CEFEPIME HYDROCHLORIDE (T)	
2799599 60 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Urinary tract infection Grade 3	393	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (C)  (3) PANTOPRAZOLE SODIUM SESQUIHYDRATE (C)  (4) FUROSEMIDE (C)  (5) METOPROLOL (C)  (6) CANNABIS SATIVA (C)  (7) LOPERAMIDE HYDROCHLORIDE (C)  (8) CALCIUM CARBONATE (C)  (9) PANTOPRAZOLE (C)  (10) LEVOTHYROXINE (C)  (11) FUROSEMIDE (C)  (12) BENZONATATE (C)  (13) ONDANSETRON (C)  (14) PROCHLORPERAZINE (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(15) CANNABIDIOL (C) (16) NITROFURANTOIN (C) (17) AMOXICILLIN\CLAVULANATE POTASSIUM (T) (18) LEVOFLOXACIN (T) (19) CEFEPIME (T) (20) PIPERACILLIN\TAZOBACTAM (T) (21) ERTAPENEM (T) (22) LACTULOSE (T) (23) PSEUDOEPHEDRINE (T)	
2799609 72 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Sepsis  Pneumonia Grade 4  Grade 3	276  276	(1) PRALSETINIB (S) (2) PARACETAMOL (C) (3) CETIRIZINE HYDROCHLORIDE (C) (4) FEXOFENADINE (C) (5) ACETYLSALICYLIC ACID (C) (6) XYLITOL (C) (7) VANCOMYCIN (T) (8) CEFEPIME (T)	Dose interrupted  Dose interrupted Pos  Pos NA  NA Resolved  Resolved With Sequelae

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(9) AMOXICILLIN\CLAVULANIC ACID (T)  (10) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)	
2799610 67 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Clostridium difficile colitis  Enterobacter bacteraemia Grade 3  Grade 3	29  664	(1) PRALSETINIB (S)	Dose interrupted  Dose interrupted Pos  Pos Neg  Neg Resolved  Resolved
2799615 67 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Sepsis Grade 3	37	(1) PRALSETINIB (S)  (2) AMITRIPTYLINE (C)  (3) AMLODIPINE (C)  (4) HYDROCORTISONE (C)  (5) LEVOTHYROXINE (C)  (6) FISH OIL (C)  (7) ONDANSETRON (C)  (8) PROMETHAZINE (C)  (9) TRAMADOL (C)  (10) MACROGOL 3350 (C)	Dose interrupted Positive N/A Recovered/Resolved With Sequelae

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(11) RAMIPRIL (C) (12) MAGNESIUM HYDROXIDE (C) (13) SENNA SPP. (C) (14) AMLODIPINE BESILATE (C) (15) ENOXAPARIN SODIUM (C) (16) KETOROLAC TROMETHAMINE (C) (17) LEVOTHYROXINE SODIUM (C) (18) LEVOTHYROXINE SODIUM (C) (19) DOCUSATE SODIUM\SENNNA ALEXANDRINA (C) (20) TRAMADOL HYDROCHLORIDE (C) (21) VANCOMYCIN HYDROCHLORIDE (C) (22) ALBUMIN HUMAN (C) (23) POTASSIUM CHLORIDE (C) (24) FUROSEMIDE (C) (25) IOHEXOL (C) (26) ERTAPENEM SODIUM (C) (27) METHYLSPREDNISOLONE SODIUM SUCCINATE (C)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
2799616 71 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumocystis jirovecii pneumonia Grade 3	607	(1) PRALSETINIB (S)  (2) DOCUSATE SODIUM (C)  (3) PARACETAMOL (C)  (4) ONDANSETRON (C)  (5) PROCHLORPERAZINE (C)  (6) GLUCOSAMINE (C)  (7) COLECALCIFEROL (C)  (8) FOLIC ACID (C)  (9) FERROUS SULFATE (C)  (10) DIPHENHYDRAMINE (C)  (11) PREDNISONE (C)  (12) CYANOCOBALAMIN (C)  (13) KETOCONAZOLE (C)  (14) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)	Dose interrupted Positive N/A Recovered/Resolved
2799628 58 Female UNITED STATES OF AMERICA Clinical Study	Pneumonia Grade 3	305	(1) PRALSETINIB (S)  (2) AZELASTINE (C)  (3) CALCIUM CARBONATE (C)  (4) CETIRIZINE (C)	Dose interrupted Positive Unknown Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
Healthcare professional			(5) FORMOTEROL FUMARATE\MOMETASONE FUROATE (C)  (6) ESCITALOPRAM (C)  (7) LORAZEPAM (C)  (8) QUINAPRIL (C)  (9) RIVAROXABAN (C)  (10) MEROPENEM (T)	
2800335 68 Female UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Sepsis  Pneumonia Grade 3  Grade 3	44  44	(1) PRALSETINIB (S)  (2) FLUTICASONE\SALMETEROL (C)  (3) COLECALCIFEROL (C)  (4) FAMOTIDINE (C)  (5) LEVOTHYROXINE (C)  (6) MORPHINE (C)  (7) NAPROXEN (C)  (8) OXYCODONE (C)  (9) PROCHLORPERAZINE (C)  (10) DOCUSATE SODIUM\SENNOSIDE A+B (C)  (11) SALBUTAMOL (C)	Dose interrupted  Dose interrupted Positive  Positive N/A  N/A Recovered/Resolved  Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(12) CANNABIDIOL (C) (13) LORATADINE (C) (14) IPRATROPIUM\SALBUTAMOL (C) (15) BENZOCAINE (C) (16) APIXABAN (C) (17) GUAIFENESIN (C) (18) METHYLSPREDNISOLONE (C) (19) DOXYCYCLINE (C) (20) ROFLUMILAST (C) (21) CICLESONIDE (C) (22) SPREDNISONE (C) (23) TRIAMCINOLONE (C) (24) VANCOMYCIN (C) (25) AZITHROMYCIN (C) (26) CEFTRIAXONE (C) (27) SODIUM CHLORIDE (C) (28) ENOXAPARIN (C)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(29) GUAIFENESIN (C) (30) BENZONATATE (C) (31) FUROSEMIDE (C) (32) DOCUSATE SODIUM (C) (33) TIOTROPIUM (C) (34) LEVOFLOXACIN (C) (35) METRONIDAZOLE (C) (36) MACROGOL 3350 (C) (37) POTASSIUM CHLORIDE (C) (38) IOPAMIDOL (C) (39) ACETYLSALICYLIC ACID (C) (40) AMOXICILLIN\CLAVULANATE POTASSIUM (T) (41) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T) (42) VANCOMYCIN (T) (43) PARACETAMOL (T) (44) ONDANSETRON (T) (45) IBUPROFEN (T)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(46) DICLOFENAC (T)	
2800336 47 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia staphylococcal Grade 3	101	(1) PRALSETINIB (S)  (2) OMEPRAZOLE (C)  (3) ATORVASTATIN CALCIUM (C)  (4) WARFARIN (C)  (5) HYDROCODONE BITARTRATE\PARACETAMOL (C)  (6) COLECALCIFEROL (C)  (7) CALCIUM\MAGNESIUM\ZINC (C)  (8) BISOPROLOL FUMARATE (C)  (9) MIRTAZAPINE (C)  (10) ZOLEDRONIC ACID MONOHYDRATE (C)  (11) LISINOPRIL (C)  (12) SALBUTAMOL (C)  (13) FUROSEMIDE (C)  (14) MACROGOL 3350 (C)  (15) LEVOTHYROXINE (C)  (16) POTASSIUM CHLORIDE (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(17) MAGNESIUM OXIDE (C)  (18) VANCOMYCIN (T)  (19) CEFTAZIDIME (T)  (20) CEFEPIME (T)	
2800338 61 Male UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Sinusitis bacterial  Sepsis Grade 3  Grade 4	68	(1) PRALSETINIB (S)  (2) PARACETAMOL (C)  (3) CLOBETASOL (C)  (4) HYDROCORTISONE (C)  (5) LEVETIRACETAM (C)  (6) LEVOTHYROXINE (C)  (7) LIDOCAINE\PRILOCaine (C)  (8) ZOLPIDEM (C)  (9) OXYCODONE (C)  (10) MACROGOL 3350 (C)  (11) DIPHENHYDRAMINE HYDROCHLORIDE (C)  (12) SODIUM CHLORIDE (C)  (13) TAMSULOSIN (C)	Dose interrupted  Dose interrupted Positive  Positive Negative  Negative Recovered/Resolved  Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(14) CEFEPIME (T)  (15) AMPICILLIN (T)  (16) VANCOMYCIN (T)  (17) ACICLOVIR (T)  (18) CEFTRIAXONE (T)	
2800345 66 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia legionella Grade 3	448	(1) PRALSETINIB (S)  (2) PARACETAMOL (C)  (3) ENOXAPARIN (C)  (4) LEVOTHYROXINE (C)  (5) SENNA SPP. (C)  (6) SODIUM CHLORIDE (C)  (7) ERGOCALCIFEROL (C)  (8) LEVOTHYROXINE SODIUM (C)  (9) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (10) LEVOFLOXACIN (T)  (11) MINOCYCLINE (T)  (12) METRONIDAZOLE (T)  (13) POTASSIUM CHLORIDE (T)	Dose interrupted Positive Unknown Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
2800533 58 Male SINGAPORE Clinical Study Non-healthcare professional	Pneumonia Grade 3	300	(1) PRALSETINIB (S)  (2) ACETYLSALICYLIC ACID (C)  (3) ATORVASTATIN (C)  (4) BISOPROLOL (C)  (5) LEVETIRACETAM (C)  (6) NIFEDIPINE (C)  (7) FAMOTIDINE (C)	N/A N/A N/A Not Recovered/Not Resolved/Ongoing
2800564 42 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia  Clostridium difficile colitis Grade 3  Grade 3	958  173	(1) PRALSETINIB (S)  (2) AMITRIPTYLINE (C)  (3) ASCORBIC ACID (C)  (4) BACLOFEN (C)  (5) BUPIVACAINE (C)  (6) CALCIUM CARBONATE (C)  (7) COLECALCIFEROL (C)  (8) DIMENHYDRINATE (C)  (9) DIPHENHYDRAMINE HYDROCHLORIDE (C)  (10) FOLIC ACID (C)  (11) EMPAGLIFLOZIN (C)	Dose not changed  Dose interrupted N/A  Positive N/A  Negative Recovered/Resolved  Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(12) LAMOTRIGINE (C) (13) LEVOTHYROXINE (C) (14) PREGABALIN (C) (15) MAGNESIUM OXIDE (C) (16) MORPHINE (C) (17) ONDANSETRON (C) (18) OXYCODONE (C) (19) PIOGLITAZONE HYDROCHLORIDE (C) (20) THIAMINE (C) (21) ZINC (C) (22) COLECALCIFEROL (C) (23) ATROPINE SULFATE\DIPIENOXYLATE HYDROCHLORIDE (C) (24) LOPERAMIDE HYDROCHLORIDE (C) (25) MORPHINE SULFATE (C)	
2800565 64 Female UNITED STATES OF AMERICA	Pneumonia Grade 3	56	(1) PRALSETINIB (S) (2) BENZONATATE (C) (3) CEFTRIAXONE SODIUM (C)	Dose interrupted Positive Negative Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
Clinical Study Non-healthcare professional			(4) OTHER COUGH SUPPRESSANTS AND EXPECTORANTS (C)  (5) LEVOFLOXACIN (C)  (6) BUTALBITAL\CAFFEINE\PARACETAMOL (C)	
2800607 60 Female KOREA, REPUBLIC OF Clinical Study Non-healthcare professional	Bacteraemia Grade 3	68	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) URSOODEOXYCHOLIC ACID (C)  (4) AMLODIPINE BESILATE\OLMESARTAN MEDOXOMIL (C)  (5) CIPROFLOXACIN (T)  (6) CEFTRIAXONE (T)  (7) CEFPODOXIME (T)  (8) PARACETAMOL (T)  (9) ARGININE HYDROCHLORIDE\IBUPROFEN (T)	Dose interrupted Positive N/A Recovered/Resolved With Sequelae
2800658 70 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Appendicitis perforated Grade 3	221	(1) PRALSETINIB (S)  (2) AMLODIPINE BESILATE (C)  (3) ACETYLSALICYLIC ACID (C)  (4) ATORVASTATIN CALCIUM (C)  (5) LEVOTHYROXINE SODIUM (C)	Dose interrupted Positive Negative Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(6) UBIDECARENONE (C) (7) FISH OIL (C) (8) GLUCOSAMINE SULFATE (C) (9) ENOXAPARIN (C) (10) MACROGOL 3350 (C) (11) POTASSIUM CHLORIDE (C) (12) VITAMIN B COMPLEX (C) (13) ONDANSETRON (C) (14) OXYCODONE (C) (15) METRONIDAZOLE (T) (16) CEFTRIAXONE (T)	
2800660 73 Male NETHERLANDS Non-Interventional Study/Program Non-healthcare professional	Pneumonia Grade 3	4	(1) PRALSETINIB (S) (2) ACETYLCYSTEINE (C) (3) APIXABAN (C) (4) BARNIDIPINE (C) (5) CICLESONIDE (C) (6) DIGOXIN (C)	Dose not changed N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(7) EPLERENONE (C)  (8) FORMOTEROL (C)  (9) FOSINOPRIL (C)  (10) FUROSEMIDE (C)  (11) METOPROLOL (C)  (12) PANTOPRAZOLE SODIUM SESQUIHYDRATE (C)  (13) TIOTROPIUM (C)  (14) VENLAFAXINE (C)	
2800693 56 Male KOREA, REPUBLIC OF Clinical Study Non-healthcare professional	Pneumonia haemophilus Grade 3	569	(1) PRALSETINIB (S)  (2) PROPACETAMOL HYDROCHLORIDE (T)  (3) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (4) LEVOFLOXACIN (T)  (5) LENOGRASTIM (T)	Dose interrupted Positive N/A Recovered/Resolved With Sequelae
2800694 56 Female SPAIN Clinical Study Non-healthcare professional	Large intestine infection Grade 3	238	(1) PRALSETINIB (S)  (2) OMEPRAZOLE (C)  (3) EDOXABAN TOSILATE (C)  (4) PREGABALIN (C)  (5) LORAZEPAM (C)	Dose interrupted Positive Negative Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(6) MEROPENEM (T)  (7) ERTAPENEM (T)	
2800696 65 Male SPAIN Clinical Study Non-healthcare professional	Urinary tract infection Grade 3	271	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) BISOPROLOL (C)  (4) ACETYLSALICYLIC ACID (C)  (5) TAMSULOSIN (C)	Dose not changed N/A N/A Recovered/Resolved
2800703 51 Female ITALY Non-Interventional Study/Program Non-healthcare professional	Clostridium difficile colitis Grade 3	21	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) CALCITRIOL (C)  (4) LEVETIRACETAM (C)  (5) FENTANYL (C)  (6) METRONIDAZOLE (C)	Drug withdrawn Negative N/A Not Recovered/Not Resolved/Ongoing
2800717 79 Female KOREA, REPUBLIC OF Clinical Study Non-healthcare professional	Empyema Grade 3	23	(1) PRALSETINIB (S)  (2) CODEINE (C)  (3) AMBROXOL (C)  (4) AMLODIPINE (C)  (5) SODIUM CHLORIDE (C)  (6) TEPRENONE (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			<p>(7) URSODEOXYCHOLIC ACID (C)</p> <p>(8) DIOSMECTITE (C)</p> <p>(9) ALLIUM SATIVUM OIL\DIMETHYL 4,4'-BIPHENYLDICARBOXYLATE (C)</p> <p>(10) ALANINE\ARGININE\CALCIUM CHLORIDE\FISH OIL\GLUCOSE MONOHYDRATE\GLYCINE\GLYCINE MAX SEED OIL\HISTIDINE\ISOLEUCINE\LEUCINE\LYSINE ACETATE\MAGNESIUM SULFATE\MEDIUM-CHAIN TRIGLYCERIDES\METHIONINE\OLEA EUROPAEA OIL\PHENYLALANINE\POTASSIUM CHLORIDE\PROLINE\SERINE\SODIUM ACETATE\SODIUM GLYCEROPHOSPHATE\TAURINE\THREONINE\TRYPTOP HAN\TYROSINE\VALINE\ZINC SULFATE (C)</p> <p>(11) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (C)</p> <p>(12) VALACICLOVIR (C)</p> <p>(13) MUPIROCIN (C)</p> <p>(14) ACICLOVIR (C)</p> <p>(15) POTASSIUM CHLORIDE (C)</p> <p>(16) AMBROXOL HYDROCHLORIDE (C)</p> <p>(17) MORPHINE SULFATE (C)</p> <p>(18) GLUCOSE (C)</p>	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(19) DICLOFENAC (T)  (20) CEFTRIAXONE (T)  (21) PETHIDINE (T)  (22) AMBROXOL ACEFYLLINATE (T)  (23) ZALTOPROFEN (T)  (24) TRAMADOL (T)  (25) METRONIDAZOLE (T)	
2800731 69 Female UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Pneumonia legionella Grade 3	625	(1) PRALSETINIB (S)  (2) AMLODIPINE (C)  (3) LEVOTHYROXINE SODIUM (C)  (4) FAMOTIDINE (C)  (5) FUROSEMIDE (C)  (6) AMLODIPINE BESILATE (C)  (7) ALPRAZOLAM (C)  (8) METOPROLOL SUCCINATE (C)  (9) OSELTAMIVIR PHOSPHATE (T)  (10) CEFALEXIN (T)  (11) AZITHROMYCIN (T)	Dose interrupted Negative N/A Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(12) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)	
2800736 34 Female UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Pneumonia Grade 3	763	(1) PRALSETINIB (S)  (2) LISINOPRIL (C)  (3) APIXABAN (C)  (4) DEXTROMETHORPHAN HYDROBROMIDE\PARACETAMOL\PSEUDOEPHEDRINE HYDROCHLORIDE (C)  (5) PSEUDOEPHEDRINE HYDROCHLORIDE (C)  (6) MAGNESIUM OXIDE (C)  (7) LEVOTHYROXINE SODIUM (C)  (8) FERROUS SULFATE (C)  (9) POTASSIUM CHLORIDE (C)  (10) ETHINYLESTRADIOL\NORETHISTERONE ACETATE (C)  (11) LORAZEPAM (C)  (12) ATROPINE (C)  (13) CALCIUM CARBONATE (C)  (14) ERTAPENEM SODIUM (T)  (15) VANCOMYCIN (T)	Dose interrupted Positive Unknown Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
2800740 62 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Influenza  Bronchitis bacterial Grade 3  Grade 3	517  517	(1) PRALSETINIB (S)  (2) HYDROCHLOROTHIAZIDE\TRIAMTERENE (C)	Dose interrupted  Dose interrupted Positive  Positive Negative  Negative Recovered/Resolved  Recovered/Resolved
2800761 71 Male UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Herpes zoster Grade 3	582	(1) PRALSETINIB (S)  (2) GABAPENTIN (C)  (3) LEVOTHYROXINE (C)  (4) TAMSULOSIN (C)  (5) COLECALCIFEROL (C)  (6) LISINOPRIL (C)  (7) PENTOXIFYLLINE (C)  (8) COLLAGENASE (C)  (9) TRAMADOL (C)  (10) DOCUSATE SODIUM (C)	Dose interrupted Positive N/A Recovered/Resolved With Sequelae

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(11) MACROGOL (C)  (12) ONDANSETRON (C)  (13) DIPHENHYDRAMINE HYDROCHLORIDE (C)  (14) HEPARIN (C)  (15) ACICLOVIR (C)	
2800843 61 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Cellulitis Grade 3	420	(1) PRALSETINIB (S)  (2) PANTOPRAZOLE SODIUM SESQUIHYDRATE (C)  (3) TAMSULOSIN HYDROCHLORIDE (C)  (4) DIPHENHYDRAMINE HYDROCHLORIDE (C)  (5) VITAMIN B COMPLEX (C)  (6) BETAMETHASONE DIPROPIONATE\CLOTRIMAZOLE (C)  (7) METFORMIN (C)	NR Unknown N/A Recovered/Resolved
2800865 33 Male UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Sepsis  Urinary tract infection  Pyelonephritis Grade 3  Grade 3  Grade 3	444  444  444	(1) PRALSETINIB (S)  (2) MACROGOL 3350 (C)  (3) LINACLOTIDE (C)  (4) PARACETAMOL (C)  (5) CALCITRIOL (C)  (6) CALCIUM CITRATE\COLECALCIFEROL (C)	Dose interrupted  Dose interrupted  Dose interrupted Positive  Positive  Positive N/A

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(7) COLECALCIFEROL (C) (8) FLUDROCORTISONE (C) (9) LEVOTHYROXINE (C) (10) PREDNISONE (C) (11) HYDROCODONE BITARTRATE\PARACETAMOL (C) (12) HYDROCORTISONE (C) (13) PARACETAMOL (C) (14) AMLODIPINE (C) (15) DOCUSATE SODIUM\SENNOSIDE A+B (C) (16) HEPARIN (C) (17) SODIUM CHLORIDE (C) (18) SACCHAROMYCES BOULARDII (C) (19) OXYBUTYNIN HYDROCHLORIDE (C) (20) SENNOSIDE A+B (C) (21) SULFAMETHOXAZOLE\TRIMETHOPRIM (C) (22) DIPHENHYDRAMINE\LIDOCAINE (C) (23) SODIUM CHLORIDE (T)	N/A N/A Recovered/Resolve d Recovered/Resolve d Recovered/Resolve d

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(24) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (25) OXYBUTYNIN HYDROCHLORIDE (T)  (26) NOREPINEPHRINE (T)  (27) METHYLPREDNISOLONE SODIUM SUCCINATE (T)	
2800872 67 Female UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Clostridium difficile colitis  Pneumonia aspiration Grade 3  Grade 3	726  730	(1) PRALSETINIB (S)  (2) ASCORBIC ACID (C)  (3) CALCIUM\COLECALCIFEROL (C)  (4) CEFDINIR (C)  (5) CELECOXIB (C)  (6) COLECALCIFEROL (C)  (7) CYANOCOBALAMIN (C)  (8) DICLOFENAC (C)  (9) DIPHENHYDRAMINE (C)  (10) DOCUSATE SODIUM (C)  (11) FUROSEMIDE (C)  (12) GABAPENTIN (C)  (13) PROBIOTICS NOS (C)	Dose interrupted  Dose interrupted Positive  Positive N/A  N/A Recovered/Resolved  Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(14) LEVOTHYROXINE (C) (15) DIPHENHYDRAMINE\LIDOCAINE (C) (16) MELATONIN (C) (17) OMEPRAZOLE (C) (18) OMEPRAZOLE (C) (19) CETIRIZINE HYDROCHLORIDE (C) (20) ONDANSETRON (C) (21) CIPROFLOXACIN (C) (22) VANCOMYCIN (T) (23) METRONIDAZOLE (T) (24) CEFEPIME (T)	
2800875 32 Male UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Urinary tract infection Grade 3	486	(1) PRALSETINIB (S) (2) LINACLOTIDE (C) (3) METHYLPREDNISOLONE SODIUM SUCCINATE (C) (4) FLUDROCORTISONE (C) (5) LEVOTHYROXINE (C) (6) PREDNISONE (C) (7) PARACETAMOL (C)	Dose interrupted Positive Unknown Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(8) OXYBUTYNIN (C) (9) ENOXAPARIN (C) (10) DOCUSATE SODIUM (C) (11) FLUCONAZOLE (C) (12) SODIUM CHLORIDE (C) (13) AMOXICILLIN (C) (14) ERTAPENEM (T) (15) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)	
2800887 32 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Urinary tract infection Grade 3	534	(1) PRALSETINIB (S) (2) SENNOSIDE A+B (C) (3) PARACETAMOL (C) (4) CALCIUM ASCORBATE (C) (5) CALCITRIOL (C) (6) CALCIUM CITRATE\COLECALCIFEROL (C) (7) COLECALCIFEROL (C) (8) FLUDROCORTISONE (C) (9) PREDNISONE (C)	Dose interrupted Positive Negative Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(10) DIPHENHYDRAMINE\LIDOCAINE (C)  (11) LEVOTHYROXINE (C)  (12) HYDROCODONE BITARTRATE\PARACETAMOL (C)  (13) AMLODIPINE (C)  (14) DOCUSATE SODIUM\SENNOSIDE A+B (C)  (15) MACROGOL 3350 (C)  (16) LINACLOTIDE (C)  (17) OXYBUTYNIN HYDROCHLORIDE (C)  (18) SACCHAROMYCES BOULARDII (C)  (19) ONDANSETRON (C)	
2800893 68 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia Grade 3	1095	(1) PRALSETINIB (S)  (2) APIXABAN (C)  (3) DOCUSATE (C)  (4) KETOCONAZOLE (C)  (5) LEVOTHYROXINE (C)  (6) OXYCODONE (C)  (7) PREGABALIN (C)  (8) SENNOSIDE A+B (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(9) ERGOCALCIFEROL (C)	
2800896 25 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Proteus infection Grade 3	912	(1) PRALSETINIB (S)  (2) HYDROCHLOROTHIAZIDE (C)  (3) ONDANSETRON (C)  (4) ZINC SULFATE (C)  (5) CARVEDILOL (C)  (6) HYDRALAZINE HYDROCHLORIDE (C)  (7) AMLODIPINE BESILATE (C)  (8) CALCIUM CARBONATE (C)  (9) ESOMEPRAZOLE (C)  (10) TRAMADOL (C)	Dose interrupted Positive Negative Recovered/Resolved
2800897 58 Male TAIWAN, PROVINCE OF CHINA Clinical Study Healthcare professional	Sinusitis aspergillus Grade 3	918	(1) PRALSETINIB (S)  (2) TETRACYCLINE HYDROCHLORIDE (C)  (3) FEXOFENADINE HYDROCHLORIDE (C)  (4) HYDROTALCITE (C)  (5) GENTAMICIN SULFATE (C)  (6) BRIMONIDINE TARTRATE\TIMOLOL MALEATE (C)  (7) NEOSTIGMINE METILSULFATE (C)	Dose not changed N/A N/A Recovered/Resolved With Sequelae

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(8) ACETYL CYSTEINE (C) (9) BROTIZOLAM (C) (10) TRAVOPROST (C) (11) PARACETAMOL (C) (12) AMOXICILLIN\CLAVULANATE POTASSIUM (C) (13) NAPROXEN (C) (14) AMPHOTERICIN B (T) (15) ASCORBIC ACID (T) (16) ISAVUCONAZOLE (T)	
2800899 59 Female UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Arthritis bacterial Grade 3	41	(1) PRALSETINIB (S) (2) AMLODIPINE (C) (3) LOSARTAN (C) (4) RIVAROXABAN (C) (5) TRAMADOL (C) (6) ATORVASTATIN (C) (7) VENLAFAXINE (C) (8) DENOSUMAB (C)	Dose interrupted Positive Unknown Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
2801025 25 Female UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Sepsis  Urinary tract infection Grade 4  Grade 3	675  675	(1) PRALSETINIB (S)  (2) BISACODYL (C)  (3) HYDROCHLOROTHIAZIDE (C)  (4) ONDANSETRON (C)  (5) CARVEDILOL (C)  (6) HYDRALAZINE HYDROCHLORIDE (C)  (7) AMLODIPINE BESILATE (C)  (8) CALCIUM CARBONATE (C)  (9) ZINC SULFATE (C)  (10) ESOMEPRAZOLE (C)  (11) FUROSEMIDE (C)  (12) PARACETAMOL (C)  (13) PARACETAMOL (C)  (14) CALCITRIOL (C)  (15) OXYCODONE HYDROCHLORIDE\PARACETAMOL (C)  (16) PREDNISONE (C)  (17) TRAMADOL (C)	Dose interrupted  Dose interrupted Positive  Positive N/A  N/A Recovered/Resolved  Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
2801047 73 Female FRANCE Non-Interventional Study/Program Non-healthcare professional	Pyelonephritis Grade 3	38	(1) PRALSETINIB (S)  (2) CELIPIROLOL (C)  (3) INDAPAMIDE (C)  (4) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (5) CEFOTAXIME (T)  (6) OFLOXACIN (T)  (7) RACECADOTRIL (T)  (8) LOPERAMIDE (T)	N/A N/A N/A Recovered/Resolved
2801052 44 Female UNITED KINGDOM Clinical Study Non-healthcare professional	Lower respiratory tract infection Grade 3	335	(1) PRALSETINIB (S)  (2) BETAMETHASONE (C)  (3) LEVETIRACETAM (C)  (4) VALPROATE SODIUM (C)  (5) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)	Dose interrupted Positive Unknown Recovered/Resolved
2801053 79 Female UNITED KINGDOM Non-Interventional Study/Program Non-healthcare professional	Urinary tract infection Grade 3	161	(1) PRALSETINIB (S)  (2) SIMVASTATIN (C)  (3) METFORMIN (C)  (4) OMEPRAZOLE (C)  (5) DOXAZOSIN MESILATE (C)	N/A N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(6) CETIRIZINE (C)  (7) LETROZOLE (C)  (8) CANDESARTAN (C)  (9) RANITIDINE (C)  (10) AMOXICILLIN (T)  (11) GENTAMICIN (T)	
2802005 79 Female UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Urinary tract infection Grade 3	796	(1) PRALSETINIB (S)  (2) LORAZEPAM (C)  (3) LEVOTHYROXINE SODIUM (C)  (4) AMLODIPINE BESILATE (C)  (5) APIXABAN (C)  (6) LOSARTAN POTASSIUM (C)  (7) SERTRALINE (C)  (8) CARVEDILOL (C)  (9) OMEPRAZOLE (C)  (10) CYCLOBENZAPRINE (C)  (11) CALCIUM CARBONATE\COLECALCIFEROL (C)  (12) COLECALCIFEROL (C)	Dose interrupted Positive Unknown Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(13) PROPAFENONE (C)  (14) CEFUROXIME (T)  (15) CEFEPIME (T)  (16) CEFTRIAXONE (T)  (17) METRONIDAZOLE (T)	
2802013 80 Female UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Diverticulitis Grade 3	1095	(1) PRALSETINIB (S)  (2) LORAZEPAM (C)  (3) LEVOTHYROXINE SODIUM (C)  (4) AMLODIPINE BESILATE (C)  (5) APIXABAN (C)  (6) LOSARTAN POTASSIUM (C)  (7) SERTRALINE (C)  (8) CARVEDILOL (C)  (9) OMEPRAZOLE (C)  (10) CYCLOBENZAPRINE (C)  (11) CALCIUM CARBONATE\COLECALCIFEROL (C)  (12) COLECALCIFEROL (C)	Dose interrupted Positive Unknown Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(13) PROPAFENONE (C)  (14) METRONIDAZOLE (T)  (15) CEFTRIAXONE (T)	
2802023 74 Male SINGAPORE Clinical Study Non-healthcare professional	Pneumonia Grade 3	44	(1) PRALSETINIB (S)  (2) AMLODIPINE (C)  (3) METHYLPREDNISOLONE (T)  (4) PARACETAMOL (T)  (5) MEROPENEM (T)  (6) LEVOFLOXACIN (T)  (7) SALBUTAMOL (T)  (8) IPRATROPIUM BROMIDE\SALBUTAMOL SULFATE (T)  (9) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)	Dose interrupted Positive N/A Recovered/Resolved
2802048 57 Female SINGAPORE Clinical Study Non-healthcare professional	Sepsis Grade 3	33	(1) PRALSETINIB (S)  (2) AMLODIPINE (C)  (3) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (4) VANCOMYCIN (T)  (5) MEROPENEM (T)  (6) ACETYLSALICYLIC ACID (T)	Drug withdrawn Negative N/A Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(7) DEXAMETHASONE PHOSPHATE (T)	
2802118 68 Female UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Clostridium difficile colitis Grade 3	1095	(1) PRALSETINIB (S)  (2) PARACETAMOL (C)  (3) CEFALEXIN (C)  (4) LEVOFLOXACIN (C)  (5) ERYTHROMYCIN (C)  (6) CLARITHROMYCIN (C)  (7) METRONIDAZOLE (C)  (8) FEXOFENADINE HYDROCHLORIDE (C)  (9) FERROUS SULFATE (C)  (10) FLUDROCORTISONE (C)  (11) HYDROCORTISONE (C)  (12) LEVOTHYROXINE (C)  (13) MAGNESIUM OXIDE (C)  (14) MONTELUKAST SODIUM (C)  (15) HYDROCODONE BITARTRATE\PARACETAMOL (C)  (16) TOPIRAMATE (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(17) RIVAROXABAN (C)  (18) METOCLOPRAMIDE HYDROCHLORIDE (C)  (19) MORPHINE SULFATE (C)  (20) ONDANSETRON (C)  (21) VANCOMYCIN (T)	
2802120 57 Male TAIWAN, PROVINCE OF CHINA Clinical Study Non-healthcare professional	Septic arthritis staphylococcal  Grade 3	194	(1) PRALSETINIB (S)  (2) VALSARTAN (C)  (3) CLOBETASOL PROPIONATE (C)  (4) LEVOTHYROXINE SODIUM (C)  (5) TAMSULOSIN HYDROCHLORIDE (C)  (6) CEFUROXIME (C)  (7) OXYBUTYNIN HYDROCHLORIDE (C)  (8) AMBROXOL HYDROCHLORIDE (C)  (9) NAPROXEN (C)  (10) TRANEXAMIC ACID (C)  (11) ALGELDRATE (C)  (12) ALBUMIN HUMAN (C)  (13) BETHANECHOL CHLORIDE (C)	Dose not changed N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(14) HYDROTALCITE (C) (15) MAGNESIUM OXIDE (C) (16) MORPHINE (C) (17) POTASSIUM GLUCONATE (C) (18) SENNOSIDE A+B CALCIUM (C) (19) PARACETAMOL\TRAMADOL HYDROCHLORIDE (C) (20) DEXTROMETHORPHAN HYDROBROMIDE (C) (21) PARACETAMOL (T) (22) DICLOFENAC (T) (23) MEPHENOXALONE (T) (24) CHLORZOXAZONE (T) (25) BACLOFEN (T) (26) DICLOXACILLIN SODIUM MONOHYDRATE (T)	
2802122 83 Male SINGAPORE Clinical Study Non-healthcare professional	Cystitis Grade 3	298	(1) PRALSETINIB (S) (2) CEFUROXIME (C) (3) AMLODIPINE (C) (4) ACETYLSALICYLIC ACID (C)	Dose interrupted Positive Unknown Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(5) CEFEPIME (T)  (6) MEROPENEM (T)	
2802315 67 Female UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Clostridium difficile colitis  Pneumonia Grade 3  Grade 3	473  473	(1) PRALSETINIB (S)  (2) MONTELUKAST SODIUM (C)  (3) LEVOTHYROXINE SODIUM (C)  (4) HYDROCORTISONE (C)  (5) FLUDROCORTISONE ACETATE\FRAMYCTIN SULFATE\GRAMICIDIN (C)  (6) TOPIRAMATE (C)  (7) RIVAROXABAN (C)  (8) SALBUTAMOL (C)  (9) PANTOPRAZOLE SODIUM SESQUIHYDRATE (C)  (10) GABAPENTIN (C)  (11) CYANOCOBALAMIN (C)  (12) MACROGOL 3350 (C)  (13) HYDROCODONE BITARTRATE\PARACETAMOL (C)  (14) MELATONIN (C)  (15) MACROGOL\PROPYLENE GLYCOL\SIMETICONE\SORBIC ACID\SORBITOL\WHITE	Dose interrupted  Dose interrupted Positive  Positive N/A  N/A Recovered/Resolve d  Recovered/Resolve d

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			SOFT PARAFFIN (C) (16) POTASSIUM CHLORIDE (C) (17) LORAZEPAM (C) (18) CODEINE (C) (19) FLUTICASONE PROPIONATE (C) (20) IPRATROPIUM BROMIDE (C) (21) FORMOTEROL FUMARATE\MOMETASONE FUROATE (C) (22) PARACETAMOL (T) (23) DOXYCYCLINE (T) (24) VANCOMYCIN (T) (25) FIDAXOMICIN (T) (26) METOPROLOL (T)	
2802351 52 Male UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Pneumonia  Streptococcal bacteraemia Grade 3  Grade 4	95	(1) PRALSETINIB (S) (2) AMLODIPINE (C) (3) ESOMEPRAZOLE (C) (4) GABAPENTIN (C) (5) LEVOTHYROXINE (C)	Dose not changed Dose not changed N/A N/A N/A N/A Recovered/Resolve

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(6) PIOGLITAZONE (C) (7) POTASSIUM CHLORIDE (C) (8) PRAMIPEXOLE (C) (9) FORMOTEROL FUMARATE\MOMETASONE FUROATE (C) (10) TIOTROPIUM BROMIDE MONOHYDRATE (C) (11) CANNABIS SATIVA (C) (12) PROCHLORPERAZINE (C) (13) CALCITRIOL (C) (14) SERTRALINE (C) (15) SALBUTAMOL (C)	d Recovered/Resolved
2802359 71 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Diverticulitis Grade 3	15	(1) PRALSETINIB (S) (2) NAPROXEN SODIUM (C) (3) RIVAROXABAN (C) (4) DOXYCYCLINE (C) (5) CHLORHEXIDINE GLUCONATE (C) (6) LEVOTHYROXINE SODIUM (C) (7) FLECAINIDE ACETATE (C)	Dose interrupted Positive Unknown Recovered/Resolved With Sequelae

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(8) LANSOPRAZOLE (C)  (9) LORATADINE (C)  (10) PARACETAMOL (C)  (11) ACETYLSALICYLIC ACID\CAFFEINE (C)  (12) ESTRADIOL (C)  (13) CHLORHEXIDINE (C)  (14) METRONIDAZOLE (C)  (15) PROMETHAZINE (C)  (16) AZTREONAM (T)	
2802367 59 Female FRANCE Clinical Study Non-healthcare professional	Urinary tract infection Grade 3	29	(1) PRALSETINIB (S)  (2) MEROPENEM TRIHYDRATE (T)  (3) CIPROFLOXACIN (T)  (4) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)	Dose interrupted Positive Unknown Recovered/Resolved
2811141 65 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia Grade 3	279	(1) PRALSETINIB (S)  (2) DIPHENHYDRAMINE HYDROCHLORIDE\PARACETAMOL (C)  (3) DOCUSATE SODIUM (C)  (4) LEVOTHYROXINE (C)  (5) VANCOMYCIN (T)	Dose not changed N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(6) CEFEPIME (T)	
2812765 61 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia Grade 3	767	(1) PRALSETINIB (S)  (2) CEFTRIAXONE (T)  (3) AZITHROMYCIN (T)  (4) DEXAMETHASONE (T)  (5) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)	Dose interrupted Positive Negative Recovered/Resolved
2830078 63 Female CHINA Clinical Study Healthcare professional	Pneumonia Pneumonia Grade 3 Grade 3	270 978	(1) PRALSETINIB (S)  (2) LEVOFLOXACIN HYDROCHLORIDE (T)  (3) PIPERACILLIN SODIUM\SULBACTAM SODIUM (T)  (4) MONTELUKAST SODIUM (T)  (5) DICLOFENAC SODIUM (T)  (6) POTASSIUM CHLORIDE (T)  (7) ASCORBIC ACID (T)  (8) PYRIDOXINE HYDROCHLORIDE (T)  (9) COIX LACRYMA-JOBI VAR. MA-YUEN SEED (T)  (10) AMBROXOL HYDROCHLORIDE (T)  (11) ISOLEUCINE\LEUCINE\VALINE (T)	Drug withdrawn  Dose not changed Positive  N/A N/A  N/A Recovered/Resolved  Recovered/Resolved
2841030 56	Pyelonephritis Grade 3	522	(1) PRALSETINIB (S)	Dose not changed N/A

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
Female SPAIN Clinical Study Healthcare professional			(2) TRIMETHOPRIM (C)  (3) SULFAMETHOXAZOLE (C)  (4) MEROPENEM (T)  (5) ERTAPENEM (T)	N/A Recovered/Resolved
2849630 72 Male SPAIN Clinical Study Healthcare professional	Cellulitis Grade 3	807	(1) PRALSETINIB (S)	Dose interrupted Positive N/A Recovered/Resolved With Sequelae
2871834 58 Female TAIWAN, PROVINCE OF CHINA Clinical Study Healthcare professional	Pneumonia Grade 3	555	(1) PRALSETINIB (S)  (2) PARACETAMOL\TRAMADOL HYDROCHLORIDE (C)  (3) AMLODIPINE BESILATE (C)  (4) METOPROLOL SUCCINATE (C)  (5) ESOMEPRAZOLE (C)  (6) LEVOTHYROXINE SODIUM (C)  (7) AMOXICILLIN\CLAVULANATE POTASSIUM (C)  (8) DOXYCYCLINE (C)  (9) NEOMYCIN (C)  (10) MAGNESIUM OXIDE (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(11) ENTECAVIR (C) (12) FUROSEMIDE (C) (13) SERTACONAZOLE NITRATE (C) (14) HYDROCORTISONE ACETATE (C) (15) DEXTROMETHORPHAN HYDROBROMIDE (C) (16) DIMETICON (C) (17) FLUCONAZOLE (C) (18) FAMOTIDINE (C) (19) DIMETICON (C) (20) DIOSMECTITE (C) (21) MOSAPRIDE CITRATE (C) (22) HYDROTALCITE (C) (23) PREDNISOLONE (C) (24) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T) (25) PARACETAMOL (T)	
2880117 56 Male UNITED KINGDOM	COVID-19 Grade 3	1095	(1) PRALSETINIB (S) (2) LANSOPRAZOLE (C) (3) LEVOTHYROXINE (C)	Dose interrupted Positive Negative Recovered/Resolve d With Sequelae

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
Clinical Study Healthcare professional			(4) BISOPROLOL (C)  (5) CALCIUM CARBONATE (C)  (6) ALFACALCIDOL (C)  (7) SALBUTAMOL (C)  (8) SILDENAFIL (C)  (9) TERBINAFINE (C)	
3021613 63 Female INDIA Non-Interventional Study/Program Healthcare professional	Urinary tract infection  Sepsis  Urosepsis Grade 4  Grade 4  Grade 3	NR  NR  NR	(1) PRALSETINIB (S)  (2) BENDAMUSTINE (C)  (3) RITUXIMAB (C)	NR  NR  NR Unknown  Unknown N/A  N/A N/A Not Recovered/Not Resolved/Ongoing  Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
				Recovered/Resolved
2708978 55 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	COVID-19 pneumonia Grade 3	969	(1) PRALSETINIB (S)  (2) CALCIUM CITRATE (S)  (3) LOPERAMIDE (C)  (4) METOPROLOL SUCCINATE (C)  (5) LEVOTHYROXINE SODIUM (C)  (6) CALCITRIOL (C)  (7) PARACETAMOL (C)  (8) BENZONATATE (C)	Dose interrupted Positive N/A Recovered/Resolved
2728572 55 Female FRANCE Non-Interventional Study/Program Non-healthcare professional	COVID-19 Grade 3	100	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (C)  (3) PROPRANOLOL (C)  (4) AMLODIPINE (C)  (5) VALSARTAN (C)  (6) HYDROCORTISONE (C)	NR Unknown N/A Recovering/Resolving
2746101 71 Male CHINA	Pneumonia Grade 3	12	(1) PRALSETINIB (S)  (2) ATORVASTATIN (C)	Dose not changed N/A N/A

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
Clinical Study Non-healthcare professional			(3) METOPROLOL (C)  (4) ACETYLSALICYLIC ACID (C)  (5) SALBUTAMOL (C)  (6) SALMETEROL (C)  (7) DOXAZOSIN (C)	Recovered/Resolve d
2759488 58 Male SPAIN Clinical Study Non-healthcare professional	Diverticulitis Grade 3	374	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) CALCITRIOL (C)  (4) HYDROCORTISONE (C)  (5) OMEPRAZOLE (C)	Dose interrupted Positive N/A Recovered/Resolve d
2788519 35 Male GERMANY Clinical Study Non-healthcare professional	Appendicitis Grade 3	462	(1) PRALSETINIB (S)  (2) PIPERACILLIN (C)  (3) ENOXAPARIN SODIUM (C)  (4) PANTOPRAZOLE SODIUM SESQUIHYDRATE (C)  (5) RED BLOOD CELLS (C)  (6) LEVOTHYROXINE (C)  (7) COLECALCIFEROL (C)  (8) ACETYLSALICYLIC ACID (C)	Dose interrupted Positive N/A Recovered/Resolve d

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
2788564 65 Male SPAIN Clinical Study Non-healthcare professional	Urinary tract infection Grade 3	100	(1) PRALSETINIB (S)  (2) TAMSULOSIN (C)  (3) PYRIDOSTIGMINE BROMIDE (C)  (4) LEVOTHYROIDINE (C)  (5) ESOMEPRAZOLE (C)  (6) BISOPROLOL (C)  (7) ACETYLSALICYLIC ACID (C)  (8) TICAGRELOR (C)  (9) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (10) FOSFOMYCIN (T)  (11) COLECALCIFEROL (T)	Dose interrupted Positive N/A Recovered/Resolved
2788591 50 Female CHINA Clinical Study Non-healthcare professional	Pneumonia Grade 3	155	(1) PRALSETINIB (S)  (2) RED BLOOD CELLS (C)  (3) IRON (C)  (4) ERYTHROPOIETIN HUMAN (C)  (5) CABOZANTINIB (C)  (6) MOXIFLOXACIN (T)  (7) CEFOPERAZONE\SULBACTAM SODIUM (T)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(8) IRON POLYSACCHARIDE COMPLEX (T)  (9) RECOMBINANT HUMAN THROMBOPOIETIN (T)  (10) ALBUMIN HUMAN (T)  (11) FUROSEMIDE (T)	
2788594 58 Male SPAIN Clinical Study Non-healthcare professional	COVID-19 pneumonia Grade 3	282	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) HYDROCORTISONE (C)  (4) BISOPROLOL (C)  (5) OMEPRAZOLE (C)  (6) AZITHROMYCIN (T)  (7) TOCILIZUMAB (T)  (8) OSeltamivir (T)  (9) HYDROXYCHLOROQUINE (T)  (10) CEFTRIAZONE (T)	Dose interrupted Positive N/A Recovered/Resolved
2788680 67 Male CHINA Clinical Study Non-healthcare professional	Urinary tract infection Grade 3	212	(1) PRALSETINIB (S)  (2) TAMSULOSIN HYDROCHLORIDE (T)  (3) FINASTERIDE (T)  (4) CEFOPERAZONE SODIUM (T)	Dose not changed N/A N/A Recovered/Resolved With Sequelae

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(5) SULBACTAM SODIUM (T)  (6) LEVOFLOXACIN (T)  (7) SODIUM CHLORIDE (T)  (8) POTASSIUM CHLORIDE (T)  (9) CEFTEZOLE SODIUM (T)	
2791305 74 Male NETHERLANDS Clinical Study Non-healthcare professional	Urinary tract infection Grade 3	14	(1) PRALSETINIB (S)  (2) TRAMADOL (C)  (3) HYDROCHLOROTHIAZIDE (C)  (4) TIOTROPIUM BROMIDE MONOHYDRATE (C)  (5) SIMVASTATIN (C)  (6) FLUTICASONE PROPIONATE\SALMETEROL XINAFOATE (C)  (7) PANTOPRAZOLE (C)  (8) CLOPIDOGREL (C)  (9) RISEDRONIC ACID (C)  (10) TOBRAMYCIN (T)  (11) CLINDAMYCIN (T)	Dose not changed N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
2887244 64 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Urinary tract infection  Sepsis Grade 3  Grade 3	1095  1095	(1) PRALSETINIB (S)  (2) ALPRAZOLAM (C)  (3) AMLODIPINE BESILATE (C)  (4) ACETYLSALICYLIC ACID (C)  (5) CLONIDINE HYDROCHLORIDE (C)  (6) DENOSUMAB (C)  (7) LEVOTHYROXINE (C)  (8) LISINOPRIL (C)  (9) MUPIROCIN (C)  (10) PREGABALIN (C)  (11) APIXABAN (C)	Dose interrupted  Dose interrupted Positive  Positive N/A  N/A Recovered/Resolve d  Recovered/Resolve d
2893222 82 Female FRANCE Non-Interventional Study/Program Non-healthcare professional	Spinal cord infection Grade 3	57	(1) PRALSETINIB (S)  (2) PERINDOPRIL (C)  (3) LEVOTHYROXINE SODIUM (C)	Dose interrupted Positive N/A Recovering/Resolving
2905621 74 Male UNITED STATES OF AMERICA	Pneumonia Grade 3	966	(1) PRALSETINIB (S)  (2) REMDESIVIR (C)  (3) APIXABAN (C)	Dose interrupted Positive N/A Recovered/Resolve d

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
Clinical Study Healthcare professional				
2911849 37 Male CHINA Clinical Study Healthcare professional	Pneumocystis jirovecii pneumonia Grade 3	349	(1) PRALSETINIB (S)  (2) GANCICLOVIR (C)  (3) IMMUNOGLOBULIN HUMAN NORMAL (C)  (4) ALBUMIN HUMAN (C)  (5) CALCIUM (C)  (6) POTASSIUM CITRATE (C)  (7) LORATADINE (C)  (8) CETIRIZINE (C)  (9) RABEPRAZOLE (C)  (10) THIAMAZOLE (C)  (11) PROPRANOLOL (C)  (12) DIAMMONIUM GLYCYRRHIZINATE (C)  (13) URSODEOXYCHOLIC ACID (C)  (14) LOPERAMIDE (C)  (15) LEUCOGEN (C)  (16) MOXIFLOXACIN HYDROCHLORIDE (T)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(17) CEFTRIAXONE SODIUM (T)  (18) DEXAMETHASONE SODIUM PHOSPHATE (T)  (19) VORICONAZOLE (T)  (20) CASPOFUNGIN ACETATE (T)  (21) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)  (22) CEFOPERAZONE SODIUM (T)  (23) SULBACTAM SODIUM (T)	
2933058 63 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	COVID-19 Grade 3	681	(1) PRALSETINIB (S)  (2) DOXYCYCLINE (C)  (3) PARACETAMOL (C)  (4) RIVAROXABAN (C)  (5) DEXTROMETHORPHAN HYDROBROMIDE (T)  (6) GUAIFENESIN (T)  (7) DEXAMETHASONE (T)  (8) RIVAROXABAN (T)	Dose not changed N/A N/A Recovered/Resolved
2941299 66 Female UNITED STATES OF AMERICA	Pneumonia Grade 3	722	(1) PRALSETINIB (S)  (2) PARACETAMOL (C)  (3) LAMOTRIGINE (C)	Dose interrupted Positive N/A Recovered/Resolved With Sequelae

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
Clinical Study Healthcare professional			(4) ATROPINE SULFATE\DIPIENOXYLATE HYDROCHLORIDE (C)  (5) CALCITRIOL (C)  (6) PARACETAMOL (T)  (7) LAMOTRIGINE (T)  (8) ATROPINE SULFATE\DIPIENOXYLATE HYDROCHLORIDE (T)  (9) CALCITRIOL (T)  (10) LEVOFLOXACIN (T)	
2950270 55 Female UNITED KINGDOM Clinical Study Healthcare professional	Pneumonia Grade 3	95	(1) PRALSETINIB (S)  (2) AMOXICILLIN (C)  (3) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)	Dose interrupted Negative N/A Not Recovered/Not Resolved/Ongoing
2951586 68 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Acute sinusitis Grade 3	1253	(1) PRALSETINIB (S)  (2) PARACETAMOL (T)  (3) CEFEPIME (T)  (4) VANCOMYCIN (T)  (5) CEFPODOXIME (T)	Dose interrupted Positive Unknown Recovered/Resolve d

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
2960715 59 Male SPAIN Clinical Study Healthcare professional	Pneumonia Grade 3	876	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (C)  (3) CALCITRIOL (C)  (4) HYDROCORTISONE (C)  (5) FLUDROCORTISONE (C)  (6) OMEPRAZOLE (C)  (7) LORAZEPAM (C)  (8) BISOPROLOL (C)  (9) ALLOPURINOL (C)  (10) COLECALCIFEROL (C)  (11) TELMISARTAN (C)  (12) PRAVASTATIN (C)  (13) CEFIXIME (T)	Dose interrupted Positive Negative Recovered/Resolved
2972605 71 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia Grade 3	556	(1) PRALSETINIB (S)  (2) ALPRAZOLAM (C)  (3) ATENOLOL (C)  (4) BRIMONIDINE TARTRATE\TIMOLOL MALEATE (C)  (5) CALCIUM\COLECALCIFEROL (C)	Dose interrupted Positive N/A Recovering/Resolving

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(6) CYCLOBENZAPRINE HYDROCHLORIDE (C) (7) BIMATOPROST (C) (8) OMEPRAZOLE (C) (9) OXYCODONE HYDROCHLORIDE (C) (10) PREDNISOLONE ACETATE (C) (11) DOCUSATE SODIUM\SENNOSIDE A+B (C) (12) SUCRALFATE (C) (13) VALACICLOVIR HYDROCHLORIDE (C) (14) ACETYLSALICYLIC ACID (C)	
2979246 36 Male GERMANY Clinical Study Healthcare professional	Respiratory tract infection Grade 3	1095	(1) PRALSETINIB (S) (2) LEVOTHYROXINE (C) (3) CALCITRIOL (C) (4) RAMIPRIL (C) (5) CALCIUM BROMIDE (C) (6) SODIUM PERCHLORATE (C) (7) ZOLEDRONIC ACID MONOHYDRATE (C) (8) ESOMEPRAZOLE (C)	Dose not changed N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(9) AMOXICILLIN (T)  (10) CLAVULANATE POTASSIUM (T)	
2979290 60 Male NETHERLANDS Clinical Study Healthcare professional	Hepatitis B reactivation  Escherichia sepsis Grade 3  Grade 3	629  631	(1) PRALSETINIB (S)  (2) AMLODIPINE (C)  (3) SIMVASTATIN (C)  (4) METOPROLOL (C)  (5) OMEPRAZOLE (C)  (6) CLINDAMYCIN (C)  (7) SILDENAFIL CITRATE (C)  (8) SODIUM CHLORIDE (C)  (9) TENOFOVIR DISOPROXIL FUMARATE (T)  (10) CEFTRIAXONE (T)  (11) CIPROFLOXACIN (T)	Dose interrupted  Dose interrupted Positive  Positive N/A  N/A Recovered/Resolved  Recovered/Resolved
2988503 60 Female SPAIN Clinical Study Healthcare professional	COVID-19 pneumonia Grade 3	673	(1) PRALSETINIB (S)  (2) PREGABALIN (C)  (3) ZOLPIDEM (C)  (4) ESCITALOPRAM (C)  (5) BEMIPARIN (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(6) REMDESIVIR (T)  (7) TOCILIZUMAB (T)	
3022018 65 Male KOREA, REPUBLIC OF Clinical Study Healthcare professional	COVID-19 pneumonia Grade 3	87	(1) PRALSETINIB (S)  (2) PARACETAMOL (C)  (3) HEPARIN SODIUM (C)  (4) BENZYDAMINE HYDROCHLORIDE (C)  (5) INOSINE PRANOBEX (C)  (6) ACETYLCYSTEINE (C)  (7) BEPOTASTINE NICOTINATE (C)  (8) PELUBIPROFEN (C)  (9) REBAMIPIDE (C)  (10) REBAMIPIDE (C)  (11) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (12) SODIUM CHLORIDE (T)  (13) PIPERACILLIN\TAZOBACTAM (T)  (14) PROPACETAMOL HYDROCHLORIDE (T)  (15) ERDOSTEINE (T)  (16) LEVOFLOXACIN (T)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(17) AMMONIUM CHLORIDE\CHLORPHENAMINE MALEATE\DIHYDROCODEINE BITARTRATE\METHYLEPHEDRINE HYDROCHLORIDE-DL (T)	
3025451 27 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Urinary tract infection  Klebsiella urinary tract infection  COVID-19 Grade 3  Grade 3  Grade 3	342  342  342	(1) PRALSETINIB (S)  (2) CEFEPIME (T)	Dose interrupted  Dose interrupted  Dose interrupted Positive  Positive  Positive Unknown  Unknown Recovered/Resolve d  Recovered/Resolve d  Recovered/Resolve d
3041085 78 Female FRANCE Clinical Study	Staphylococcal sepsis Grade 3	289	(1) PRALSETINIB (S)  (2) TINZAPARIN SODIUM (C)  (3) MACROGOL 3350\POTASSIUM CHLORIDE\SODIUM BICARBONATE\SODIUM CHLORIDE (C)	Dose not changed N/A N/A Recovered/Resolve d

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
Healthcare professional			(4) PARACETAMOL (C)  (5) TRAMADOL HYDROCHLORIDE (C)  (6) MIANSERIN (C)  (7) SUFENTANIL (C)  (8) CEFAZOLIN SODIUM (T)	
3048492 61 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia Grade 3	1095	(1) PRALSETINIB (S)  (2) ZOLPIDEM TARTRATE (C)  (3) ATORVASTATIN CALCIUM (C)  (4) CITALOPRAM HYDROBROMIDE (C)  (5) GUAIFENESIN (C)  (6) PROCHLORPERAZINE (C)  (7) DEXBROMPHENIRAMINE MALEATE\DEXTROMETHORPHAN HYDROBROMIDE\PSEUDOEPHEDRINE HYDROCHLORIDE (C)  (8) MACROGOL 3350 (C)  (9) PROGESTERONE (C)  (10) SENNA SPP. (C)  (11) ALPRAZOLAM (C)	Dose interrupted Positive Negative Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(12) LEVOFLOXACIN (T)	
3053461 45 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia Grade 3	82	(1) PRALSETINIB (S)  (2) PARACETAMOL (C)  (3) SALBUTAMOL (C)  (4) LEVOTHYROXINE (C)	Dose interrupted Positive Unknown Recovered/Resolved
3072556 55 Female UNITED KINGDOM Clinical Study Healthcare professional	Pneumocystis jirovecii pneumonia Grade 3	54	(1) PRALSETINIB (S)  (2) MORPHINE SULFATE PENTAHYDRATE (C)  (3) FLUTICASONE FUROATE (C)  (4) LEVOTHYROXINE SODIUM (C)  (5) NYSTATIN (C)  (6) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (7) VANCOMYCIN (T)  (8) MEROPENEM (T)  (9) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)  (10) DEXAMETHASONE (T)	Dose interrupted Positive Unknown Recovered/Resolved
3073175 49 Female SPAIN Clinical Study	Pneumonia Grade 3	87	(1) PRALSETINIB (S)  (2) LEVOFLOXACIN (C)	Dose not changed N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
Healthcare professional				
3073178 69 Male KOREA, REPUBLIC OF Clinical Study Healthcare professional	COVID-19 pneumonia Grade 3	12	(1) PRALSETINIB (S)  (2) CHLORPHENAMINE MALEATE (C)  (3) AMLODIPINE (C)  (4) GLUCONATE SODIUM\MAGNESIUM CHLORIDE\POTASSIUM CHLORIDE\SODIUM ACETATE\SODIUM CHLORIDE (C)  (5) PANTOPRAZOLE (C)  (6) ENOXAPARIN (C)  (7) TRAMADOL (C)  (8) METOCLOPRAMIDE (C)  (9) ALMAGATE (C)  (10) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (11) PARACETAMOL (T)  (12) LEVOFLOXACIN (T)  (13) DEXAMETHASONE (T)  (14) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)  (15) REMDESIVIR (T)	Dose interrupted Positive Negative Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(16) LACTULOSE (T)  (17) AMBROXOL (T)	
3077668 54 Male GERMANY Clinical Study Healthcare professional	COVID-19 pneumonia Grade 3	794	(1) PRALSETINIB (S)  (2) CANDESARTAN (C)  (3) INFLUENZA VACCINE INACT SPLIT 4V (C)  (4) DICLOFENAC (C)  (5) CURCUMIN (C)  (6) PANTOPRAZOLE (C)  (7) DENOSUMAB (C)  (8) CALCIUM (C)  (9) METAMIZOLE (C)  (10) FLUPREDNIDENE ACETATE\ MICONAZOLE NITRATE (C)  (11) CLOTRIMAZOLE (C)  (12) ENOXAPARIN (T)	Dose not changed N/A N/A Recovered/Resolved With Sequelae
3107480 53 Female KOREA, REPUBLIC OF Clinical Study	Pneumocystis jirovecii pneumonia  Pneumonia cytomegaloviral Grade 3	161  161	(1) PRALSETINIB (S)  (2) CEFRADINE (C)  (3) FAMOTIDINE (C)  (4) POLYCARBOPHIL CALCIUM (C)	Dose interrupted  Dose interrupted Positive  Negative N/A

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Healthcare professional	Grade 3		(5) AMINO ACIDS NOS\CALCIUM\GLUCOSE\MAGNESIUM\POTASSIUM\SODIUM (C) (6) METHYLPREDNISOLONE SODIUM SUCCINATE (C) (7) FUROSEMIDE (C) (8) TEICOPLANIN (C) (9) GANCICLOVIR (C) (10) BROMHEXINE HYDROCHLORIDE (C) (11) MAGNESIUM OXIDE (C) (12) URSODEOXYCHOLIC ACID (C) (13) ADENINE HYDROCHLORIDE\CARNITINE OROTATE\CYANOCOBALAMIN\LIVER\PYRIDOXINE HYDROCHLORIDE\RIBOFLAVIN (C) (14) LACTULOSE (C) (15) SODIUM BICARBONATE (C) (16) BENZYDAMINE HYDROCHLORIDE (C) (17) CEFPODOXIME PROXETIL (C) (18) NOREPINEPHRINE (C) (19) INSULIN HUMAN (C)	N/A Recovered/Resolved With Sequelae  Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(20) PARACETAMOL (C) (21) LEVOFLOXACIN (T) (22) SULFAMETHOXAZOLE\TRIMETHOPRIM (T) (23) PREDNISOLONE (T) (24) CEPPODOXIME PROXETIL (T) (25) CEFIDINIR (T) (26) METHYL PREDNISOLONE SODIUM SUCCINATE (T) (27) LEVOFLOXACIN (T) (28) LEVODROPROPIZINE (T) (29) ERDOSTEINE (T) (30) SULFAMETHOXAZOLE\TRIMETHOPRIM (T) (31) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T) (32) CODEINE (T) (33) FLUCONAZOLE (T) (34) ACETYLCYSTEINE (T) (35) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T) (36) CORYDALIS YANHUSUO TUBER\IPOMOEA NIL SEED	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(T)  (37) IPRATROPIUM BROMIDE (T)	
3112750 71 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia Grade 3	NR	(1) PRALSETINIB (S)  (2) AMLODIPINE\BENAZEPRIL (C)  (3) LEVOTHYROXINE SODIUM (C)  (4) IMIQUIMOD (C)  (5) LOTEPEREDNOL ETABONATE (C)  (6) TADALAFIL (C)  (7) IPRATROPIUM BROMIDE\SALBUTAMOL SULFATE (T)  (8) AMPICILLIN SODIUM\SULBACTAM SODIUM (T)  (9) AMOXICILLIN\CLAVULANATE POTASSIUM (T)	Dose interrupted Positive Unknown Recovered/Resolved
3136179 66 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pseudomembranous colitis  Urinary tract infection bacterial Grade 3  Grade 3	752  752	(1) PRALSETINIB (S)  (2) CLINDAMYCIN (C)  (3) VANCOMYCIN (C)  (4) LEVOFLOXACIN (C)  (5) METRONIDAZOLE (C)  (6) FIDAXOMICIN (C)  (7) BEZLOTOXUMAB (C)	Dose interrupted  Dose interrupted Positive  Positive N/A  N/A Recovered/Resolved  Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(8) CEFEPIME (C)  (9) METRONIDAZOLE (C)	
3150236 90 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Colonic abscess  Clostridium difficile infection Grade 3  Grade 3	56  196	(1) PRALSETINIB (S)  (2) ATORVASTATIN (C)  (3) BACLOFEN (C)  (4) FISH OIL (C)  (5) DRONABINOL (C)  (6) OXYCODONE\PARACETAMOL (C)  (7) MORPHINE (C)  (8) MELATONIN (C)  (9) LEVOFLOXACIN (C)  (10) SIMETICONE (C)  (11) NYSTATIN (C)  (12) POTASSIUM (C)  (13) TAMSULOSIN (C)  (14) MIRABEGRON (C)  (15) SOLIFENACIN (C)  (16) TAMSULOSIN HYDROCHLORIDE (C)	Dose not changed  Dose interrupted N/A  Negative N/A  Unknown Recovered/Resolved  Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(17) RED BLOOD CELLS (C) (18) MACROGOL 3350 (C) (19) AMOXICILLIN\CLAVULANIC ACID (C) (20) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T) (21) SODIUM CHLORIDE (T) (22) CIPROFLOXACIN (T) (23) METRONIDAZOLE (T) (24) AMOXICILLIN\CLAVULANATE POTASSIUM (T) (25) ATROPINE SULFATE\DIPIENOXYLATE HYDROCHLORIDE (T) (26) AMOXICILLIN (T) (27) FLUCONAZOLE (T) (28) CEFEPIME (T) (29) SULFAMETHOXAZOLE\TRIMETHOPRIM (T) (30) METRONIDAZOLE (T) (31) LOPERAMIDE HYDROCHLORIDE (T) (32) VANCOMYCIN (T)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
3161561 80 Male NETHERLANDS Clinical Study Healthcare professional	Pneumonia Grade 3	67	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) RIVAROXABAN (C)  (4) OMEPRAZOLE (C)  (5) TRAMADOL (C)  (6) DOXYCYCLINE (T)  (7) CEFTRIAZONE (T)	Dose interrupted Positive N/A Recovered/Resolved With Sequelae
3165353 56 Female GERMANY Clinical Study Healthcare professional	Osteomyelitis Grade 3	743	(1) PRALSETINIB (S)  (2) MACROGOL 3350\POTASSIUM CHLORIDE\SODIUM BICARBONATE\SODIUM CHLORIDE (C)  (3) CLOMIFENE CITRATE (C)  (4) DEXAMETHASONE (C)  (5) INSULIN GLARGINE (C)  (6) INSULIN GLULISINE (C)  (7) METHOCARBAMOL (C)  (8) ZOLEDRONIC ACID MONOHYDRATE (C)  (9) CEFUROXIME (T)	Dose interrupted Positive Unknown Recovered/Resolved
3169545 61 Female	Pneumonia Grade 3	459	(1) PRALSETINIB (S)  (2) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)	Dose not changed N/A N/A

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
GERMANY Clinical Study Healthcare professional			(3) PREDNISOLONE (T)	Recovered/Resolved
3177824 57 Female CHINA Clinical Study Healthcare professional	Urinary tract infection Grade 3	866	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (C)  (3) CALCIUM CARBONATE (C)  (4) PANTOPRAZOLE (C)  (5) PIPERACILLIN\TAZOBACTAM (C)  (6) CALCIUM GLUCONATE (C)  (7) ALFACALCIDOL (C)  (8) ACARBOSE (C)  (9) MEGESTROL ACETATE (C)  (10) POTASSIUM CHLORIDE (C)  (11) ASCORBIC ACID (C)  (12) PYRIDOXINE HYDROCHLORIDE (C)  (13) POTASSIUM CHLORIDE (C)  (14) INSULIN NOS (C)  (15) GLUTATHIONE (C)	Dose interrupted Positive Unknown Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(16) CILASTATIN SODIUM\IMIPENEM (C)  (17) VALACICLOVIR HYDROCHLORIDE (C)  (18) GABAPENTIN (C)  (19) MECOBALAMIN (C)  (20) ACICLOVIR (C)  (21) CLOTRIMAZOLE\UREA (C)  (22) KETOROLAC TROMETHAMINE (C)  (23) ROSUVASTATIN CALCIUM (C)  (24) CALCIUM GLUCONATE (C)  (25) CEFOPERAZONE SODIUM\SULBACTAM SODIUM (T)	
3187619 68 Female PORTUGAL Clinical Study Healthcare professional	Pneumonia legionella Grade 3	57	(1) PRALSETINIB (S)  (2) PIPERACILLIN (C)  (3) TAZOBACTAM (C)  (4) MORPHINE (C)  (5) NYSTATIN (C)  (6) METAMIZOLE MAGNESIUM (C)  (7) FLUCONAZOLE (C)  (8) ONDANSETRON (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(9) PARACETAMOL (C)  (10) AMOXICILLIN\CLAVULANIC ACID (C)	
3189337 69 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	COVID-19 Grade 3	1460	(1) PRALSETINIB (S)  (2) REMDESIVIR (C)  (3) FOLIC ACID (C)  (4) OXYMETAZOLINE (C)  (5) FUROSEMIDE (C)  (6) HYDROCORTISONE (C)	NR Unknown N/A Recovered/Resolved
3193488 71 Female GERMANY Clinical Study Healthcare professional	Diverticulitis intestinal perforated Grade 3	29	(1) PRALSETINIB (S)  (2) POTASSIUM IODIDE (C)  (3) HYDROCHLOROTHIAZIDE (C)  (4) CITRIC ACID\POTASSIUM BICARBONATE\POTASSIUM CITRATE (C)  (5) AMPICILLIN (C)  (6) SULBACTAM (C)  (7) METHIONINE (T)	NR Unknown N/A Recovered/Resolved
3208425 72 Female KOREA, REPUBLIC OF	Pneumonia Grade 3	62	(1) PRALSETINIB (S)  (2) TELMISARTAN (C)  (3) AMLODIPINE BESILATE (C)	Dose interrupted Negative N/A Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
Clinical Study Healthcare professional			(4) ROSUVASTATIN CALCIUM (C) (5) EZETIMIBE (C) (6) CALCIUM CARBONATE\COLECALCIFEROL (C) (7) URSODEOXYCHOLIC ACID (C) (8) NALOXONE HYDROCHLORIDE\OXYCODONE HYDROCHLORIDE (C) (9) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T) (10) SULFAMETHOXAZOLE\TRIMETHOPRIM (T) (11) FLUCONAZOLE (T) (12) METHYLSPREDNISOLONE SODIUM SUCCINATE (T) (13) SALBUTAMOL SULFATE (T) (14) ACETYLCYSTEINE (T) (15) LEVOFLOXACIN (T) (16) MEROPENEM (T) (17) GANCICLOVIR (T) (18) TEICOPLANIN (T) (19) IPRATROPIUM BROMIDE (T)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
3214967 65 Male KOREA, REPUBLIC OF Clinical Study Healthcare professional	Influenza Grade 3	258	(1) PRALSETINIB (S)  (2) SACCHAROMYCES BOULARDII (C)  (3) ITOPRIDE HYDROCHLORIDE (C)  (4) MAGNESIUM OXIDE (C)  (5) MELATONIN (C)  (6) TRAZODONE (C)  (7) PREGABALIN (C)  (8) LEVOTHYROXINE SODIUM (C)  (9) CARVEDILOL (C)  (10) AMLODIPINE BESILATE (C)  (11) CANDESARTAN CILEXETIL (C)  (12) FOLIC ACID (C)  (13) ALANINE\ARGININE\ASPARTIC ACID\CYSTEINE\GLUTAMIC ACID\GLYCINE\HISTIDINE\ISOLEUCINE\LEUCINE\LYSINE ACETATE\METHIONINE\PHENYLALANINE\PROLINE\SERI NE\THREONINE\TRYPTOPHAN\TYROSINE\VALINE (C)  (14) GLUCOSE (C)  (15) LACTULOSE (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(16) ERTAPENEM SODIUM (T)	
3222777 73 Female KOREA, REPUBLIC OF Clinical Study Healthcare professional	Cellulitis Grade 3	143	(1) PRALSETINIB (S)  (2) ACECLOFENAC (C)  (3) EUGENOL\GLYCINE\LEVOMENTHOL\SODIUM BICARBONATE (C)  (4) LOPERAMIDE HYDROCHLORIDE (C)  (5) PARACETAMOL\TRAMADOL HYDROCHLORIDE (C)  (6) CODEINE PHOSPHATE\IBUPROFEN\PARACETAMOL (C)  (7) AMLODIPINE BESILATE\CHLORTALIDONE\TELMISARTAN (C)  (8) GLUCONATE SODIUM\MAGNESIUM CHLORIDE\POTASSIUM CHLORIDE\SODIUM ACETATE\SODIUM CHLORIDE (C)  (9) GLUCOSE (C)  (10) TRAMADOL HYDROCHLORIDE (C)  (11) SODIUM CHLORIDE (C)  (12) PARACETAMOL (C)  (13) ALBUMIN HUMAN (C)  (14) METOCLOPRAMIDE (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(15) ESOMEPRAZOLE (C) (16) MAGNESIUM SULFATE (C) (17) CALCIUM GLUCONATE (C) (18) POTASSIUM PHOSPHATE MONOBASIC (C) (19) FUROSEMIDE (C) (20) ACICLOVIR (C) (21) REMDESIVIR (C) (22) CHLORHEXIDINE GLUCONATE (C) (23) FENTANYL (C) (24) POTASSIUM CHLORIDE\SODIUM CHLORIDE (C) (25) CHLORPHENAMINE MALEATE\DIHYDROCODEINE BITARTRATE\GUAIFENESIN\METHYLEPHEDRINE HYDROCHLORIDE-DL (C) (26) ERDOSTEINE (C) (27) NOREPINEPHRINE (T) (28) CEFAZOLIN (T) (29) MEROPENEM TRIHYDRATE (T) (30) TEICOPLANIN (T)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(31) HYDROCORTISONE SODIUM SUCCINATE (T)  (32) CEFTRIAXONE SODIUM (T)  (33) METRONIDAZOLE (T)  (34) DOXYCYCLINE (T)  (35) MUPIROCIN (T)  (36) ACICLOVIR (T)	
3225257 66 Male BRAZIL Clinical Study Healthcare professional	Urinary tract infection  Cystitis Grade 3  Grade 3	210  220	(1) PRALSETINIB (S)  (2) ROSUVASTATIN (C)  (3) COLECALCIFEROL (C)  (4) METAMIZOLE SODIUM (C)  (5) LACTULOSE (C)  (6) LOSARTAN (C)  (7) CALCITRIOL (C)  (8) CALCIUM CARBONATE\COLECALCIFEROL (C)  (9) APIXABAN (C)  (10) METOPROLOL (C)  (11) METFORMIN (C)	Dose interrupted  Dose interrupted Positive  Positive N/A  N/A Recovered/Resolve d With Sequelae  Recovered/Resolve d With Sequelae

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(12) LEVOTHYROXINE (C) (13) PROPAFENONE HYDROCHLORIDE (C) (14) BUDESONIDE\FORMOTEROL FUMARATE (C) (15) METAMIZOLE SODIUM (C) (16) PARACETAMOL (C) (17) DICLOFENAC (C) (18) TAMSULOSIN (C) (19) CIPROFLOXACIN (T) (20) TAMSULOSIN HYDROCHLORIDE (T)	
3235328 68 Female TAIWAN, PROVINCE OF CHINA Clinical Study Healthcare professional	Urinary tract infection Grade 3	195	(1) PRALSETINIB (S) (2) AMLODIPINE BESILATE\VALSARTAN (C) (3) NEBIVOLOL (C) (4) SENNOSIDE A+B (C) (5) LEVOTHYROXINE SODIUM (C) (6) SITAGLIPTIN (C) (7) ROSUVASTATIN (C) (8) DIMETICON (C) (9) DIPHENHYDRAMINE (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(10) BISACODYL (C) (11) POTASSIUM GLUCONATE (C) (12) THIAMINE (C) (13) PARACETAMOL (C) (14) PIOGLITAZONE (C) (15) ACETYL CYSTEINE (C) (16) ALBUMIN HUMAN (C) (17) AMBROXOL (C) (18) DIOSMECTITE (C) (19) FUROSEMIDE (C) (20) IPRATROPIUM BROMIDE\SALBUTAMOL SULFATE (C) (21) POTASSIUM CHLORIDE (C) (22) MORPHINE (C) (23) PROPACETAMOL (C) (24) AMPICILLIN\SULBACTAM (C) (25) DOXYCYCLINE (C) (26) FLUCONAZOLE (C)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(27) MEROPENEM (C) (28) PIPERACILLIN\TAZOBACTAM (C) (29) AMLODIPINE (C) (30) ZINC OXIDE (C) (31) CEFACLOR (T) (32) CEFIXIME (T) (33) CEFTRIAXONE (T) (34) PIPERACILLIN\TAZOBACTAM (T) (35) CIPROFLOXACIN (T) (36) CEFEPIME (T)	
3235960 69 Female TAIWAN, PROVINCE OF CHINA Clinical Study Healthcare professional	Pneumonia  Pneumonia aspiration Grade 3  Grade 3	209  246	(1) PRALSETINIB (S) (2) AMLODIPINE BESILATE\VALSARTAN (C) (3) NEBIVOLOL (C) (4) SITAGLIPTIN (C) (5) ROSUVASTATIN (C) (6) DIMETICON (C) (7) CEFACLOR (C)	Dose not changed  Dose interrupted Positive  Negative N/A  N/A Recovered/Resolved  Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(8) CEFIXIME (C) (9) CEFTRIAXONE (C) (10) PIPERACILLIN (C) (11) CEFEPIME (C) (12) BISACODYL (C) (13) POTASSIUM GLUCONATE (C) (14) THIAMINE (C) (15) PARACETAMOL (C) (16) DIPHENHYDRAMINE (C) (17) SENNOSIDE A+B (C) (18) PIOGLITAZONE (C) (19) DIOSMECTITE (C) (20) POTASSIUM CHLORIDE (C) (21) PROPACETAMOL (C) (22) FUROSEMIDE (C) (23) AMLODIPINE (C) (24) ZINC OXIDE (C)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(25) RED BLOOD CELLS (C) (26) LENVATINIB (C) (27) CIPROFLOXACIN (T) (28) AMPICILLIN SODIUM\SULBACTAM SODIUM (T) (29) SULBACTAM (T) (30) ACETYL CYSTEINE (T) (31) ALBUMIN HUMAN (T) (32) AMBROXOL (T) (33) IPRATROPIUM (T) (34) MORPHINE (T) (35) AMPICILLIN\SULBACTAM (T) (36) DOXYCYCLINE (T) (37) FLUCONAZOLE (T) (38) MEROPENEM (T) (39) PIPERACILLIN\TAZOBACTAM (T)	
3241415 53 Male FRANCE Clinical Study	Intervertebral discitis Grade 3	109	(1) PRALSETINIB (S) (2) TESTOSTERONE ENANTHATE (C) (3) OXYCODONE HYDROCHLORIDE (C)	Dose reduced Negative N/A Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
Healthcare professional			(4) PREDNISOLONE METASULFOBENZOATE SODIUM (C)  (5) AMITRIPTYLINE HYDROCHLORIDE (C)  (6) POTASSIUM CHLORIDE (C)  (7) CALCIUM CARBONATE (C)  (8) METHADONE (C)  (9) HYDROCORTISONE (C)  (10) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (C)  (11) CIPROFLOXACIN (C)  (12) ENOXAPARIN SODIUM (C)  (13) ONDANSETRON (C)  (14) SULFAMETHOXAZOLE\TRIMETHOPRIM (C)  (15) AMOXICILLIN (C)  (16) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (17) TOBRAMYCIN (T)  (18) CIPROFLOXACIN (T)	
3253616 79 Female SPAIN	Infection Grade 3	88	(1) PRALSETINIB (S)  (2) MEROPENEM (T)	Dose not changed N/A N/A

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
Clinical Study Healthcare professional			(3) DAPTOMYCIN (T)  (4) DALBAVANCIN (T)  (5) CIPROFLOXACIN (T)  (6) DOXYCYCLINE (T)	Recovering/Resolvin g
3254775 34 Male CHINA Clinical Study Healthcare professional	Pneumonia Grade 3	52	(1) PRALSETINIB (S)  (2) ARTEMISIA ANNUA HERB\GARDENIA JASMINOIDES FRUIT\LONICERA JAPONICA FLOWER BUD (C)  (3) CEFOPERAZONE SODIUM\SULBACTAM SODIUM (C)  (4) METOCLOPRAMIDE (C)  (5) AMBROXOL HYDROCHLORIDE (C)  (6) POTASSIUM CHLORIDE (C)  (7) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (C)  (8) DEXAMETHASONE SODIUM PHOSPHATE (C)  (9) ESOMEPRAZOLE MAGNESIUM (C)  (10) LOW MOLECULAR WEIGHT HEPARIN, CALCIUM SALT (C)  (11) DICLOFENAC SODIUM (C)  (12) KETOROLAC TROMETHAMINE (C)  (13) ZOLEDRONIC ACID (C)	Dose interrupted Positive Unknown Recovered/Resolve d

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
3270069 79 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia  Sepsis Grade 3  Grade 4	909  1125	(1) PRALSETINIB (S)  (2) LEVOFLOXACIN (C)  (3) SULFAMETHOXAZOLE\TRIMETHOPRIM (C)  (4) AMIODARONE (C)	Dose interrupted  Dose interrupted Positive  Positive N/A  N/A Recovered/Resolved  Recovering/Resolving
3283245 68 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Urinary tract infection Grade 3	1095	(1) PRALSETINIB (S)  (2) OXYCODONE (C)  (3) GABAPENTIN (C)  (4) TIZANIDINE (C)  (5) VANCOMYCIN (T)  (6) CEFEPIME (T)  (7) CEFDINIR (T)  (8) AMOXICILLIN\CLAVULANATE POTASSIUM (T)  (9) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (10) FAMOTIDINE (T)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(11) METOCLOPRAMIDE (T)  (12) ONDANSETRON (T)	
3300007 66 Male BRAZIL Clinical Study Non-healthcare professional	COVID-19 Grade 3	309	(1) PRALSETINIB (S)  (2) ROSUVASTATIN (C)  (3) COLECALCIFEROL (C)  (4) LOSARTAN (C)  (5) METAMIZOLE SODIUM (C)  (6) LACTULOSE (C)  (7) CALCITRIOL (C)  (8) CALCIUM CARBONATE\COLECALCIFEROL (C)  (9) APIXABAN (C)  (10) BUDESONIDE\FORMOTEROL FUMARATE (C)  (11) METOPROLOL (C)  (12) PARACETAMOL (C)  (13) METFORMIN (C)  (14) DICLOFENAC (C)  (15) PROPAFENONE HYDROCHLORIDE (C)  (16) TRIMETHOPRIM,SULFAMETHOXAZOLE (C)	Dose interrupted Positive N/A Recovered/Resolved With Sequelae

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(17) BUDESONIDE\FORMOTEROL FUMARATE (C)  (18) TAMSULOSIN (C)  (19) LEVOTHYROXINE (C)  (20) REMDESIVIR (T)  (21) CEFTRIAXONE (T)  (22) METHYLSPREDNISOLONE (T)  (23) PARACETAMOL (T)  (24) CLARITHROMYCIN (T)	
3310666 38 Male GERMANY Clinical Study Healthcare professional	Atypical pneumonia  Pneumonia  Grade 3  Grade 3	1510  1526	(1) PRALSETINIB (S)  (2) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (C)  (3) VANDETANIB (C)	Dose interrupted  Dose interrupted Positive  Positive Positive  Positive Recovered/Resolved  Recovered/Resolved
3315664 56 Female JAPAN	Sepsis Grade 3	11	(1) PRALSETINIB (S)  (2) METOCLOPRAMIDE (C)	Dose interrupted Positive N/A

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
Clinical Study Healthcare professional			(3) BACILLUS MESENTERICUS\CLOSTRIDIUM BUTYRICUM\ENTEROCOCCUS FAECALIS (C)  (4) FENTANYL CITRATE (C)  (5) HYDROMORPHONE HYDROCHLORIDE (C)  (6) LOXOPROFEN SODIUM DIHYDRATE (C)  (7) REBAMIPIDE (C)  (8) FEXOFENADINE HYDROCHLORIDE (C)  (9) PARACETAMOL (C)  (10) MIRTAZAPINE (C)  (11) HYDROCORTISONE (C)  (12) SODIUM GUALENATE HYDRATE (C)  (13) MOSAPRIDE CITRATE (C)  (14) LEMBOREXANT (C)  (15) HEPARINOID (C)  (16) BETAMETHASONE VALERATE (C)  (17) THIAMAZOLE (C)  (18) DICLOFENAC SODIUM (C)  (19) FERRIC SODIUM CITRATE (C)	Recovered/Resolv ed

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(20) OXYCODONE HYDROCHLORIDE TRIHYDRATE (C) (21) LANSOPRAZOLE (C) (22) CALCIUM POLYSTYRENE SULFONATE (C) (23) AMLODIPINE BESILATE (C) (24) ESOMEPRAZOLE (C) (25) GUAIAZULENE (C) (26) BLOOD, WHOLE (T) (27) CALCIUM CHLORIDE DIHYDRATE\POTASSIUM CHLORIDE\SODIUM CHLORIDE\SODIUM LACTATE (T) (28) PIPERACILLIN\TAZOBACTAM (T) (29) PARACETAMOL (T) (30) OMEPRAZOLE (T) (31) CLOSTRIDIUM BUTYRICUM (T) (32) CLAVULANATE POTASSIUM (T) (33) AMOXICILLIN TRIHYDRATE (T) (34) RED BLOOD CELLS, LEUCOCYTE DEPLETED (T)	
3328401 43 Male	Gastroenteritis Grade 3	259	(1) PRALSETINIB (S) (2) BUDESONIDE\FORMOTEROL FUMARATE (C)	Dose not changed N/A N/A

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
SPAIN Clinical Study Healthcare professional			(3) METOCLOPRAMIDE (C)  (4) DEXKETOPROFEN TROMETAMOL (C)  (5) OXYCODONE (C)  (6) NALOXONE (C)  (7) FENTANYL (C)  (8) SITAGLIPTIN (C)  (9) CIPROFLOXACIN (T)	Recovered/Resolved
3355841 61 Female CHINA Clinical Study Healthcare professional	Pneumonia Grade 3	985	(1) PRALSETINIB (S)  (2) METHOXYPHENAMINE (C)  (3) DEXTROMETHORPHAN HYDROBROMIDE (C)  (4) ACETYL CYSTEINE (C)  (5) MONTELUKAST SODIUM (C)  (6) BROMHEXINE HYDROCHLORIDE (C)	Dose interrupted Positive N/A Recovered/Resolved With Sequelae
3363793 52 Female UNITED KINGDOM Clinical Study Healthcare professional	Staphylococcal bacteraemia Grade 3	571	(1) PRALSETINIB (S)  (2) ALFACALCIDOL (C)  (3) BISACODYL (C)  (4) LEVOTHYROXINE (C)  (5) PREGABALIN (C)	NR Unknown N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(6) BECLOMETASONE DIPROPIONATE (C) (7) SERTRALINE (C) (8) FOLIC ACID (C) (9) SALBUTAMOL (C) (10) LANSOPRAZOLE (C) (11) BETAMETHASONE VALERATE\FUSIDIC ACID (T) (12) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)	
3363904 63 Female SWITZERLAND Clinical Study Healthcare professional	Pneumonia Grade 3	567	(1) PRALSETINIB (S) (2) METAMIZOLE (C) (3) LOSARTAN (C) (4) ROSUVASTATIN (C) (5) ESCITALOPRAM (C) (6) METFORMIN (C) (7) PANTOPRAZOLE (C) (8) INSULIN NOS (C) (9) LERCANIDIPINE (C) (10) PREGABALIN (C)	NR Unknown N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(11) AMITRIPTYLINE (C)  (12) CEFTRIAXONE SODIUM (T)	
3364578 65 Male KOREA, REPUBLIC OF Clinical Study Healthcare professional	Herpes zoster Grade 3	467	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (C)  (3) FOLIC ACID (C)  (4) TAMSULOSIN HYDROCHLORIDE (C)  (5) BETHANECHOL CHLORIDE (C)  (6) AMLODIPINE BESILATE (C)  (7) CANDESARTAN CILEXETIL (C)  (8) ACICLOVIR (T)  (9) GABAPENTIN (T)  (10) TRAMADOL (T)  (11) PARACETAMOL\TRAMADOL HYDROCHLORIDE (T)	Dose interrupted Positive N/A Recovered/Resolved
3374277 73 Female IRELAND Clinical Study Healthcare professional	Kidney infection Grade 3	206	(1) PRALSETINIB (S)  (2) CEFTRIAXONE SODIUM (T)  (3) AMIKACIN (T)  (4) AMOXICILLIN (T)	Dose not changed N/A N/A Not Recovered/Not Resolved/Ongoing
3375129 60 Male	Spontaneous bacterial peritonitis	887 887	(1) PRALSETINIB (S)	Dose interrupted  Dose interrupted

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
ITALY Clinical Study Non-healthcare professional	Herpes zoster Grade 3  Grade 3			Positive  Positive N/A  N/A Recovered/Resolve d  Recovered/Resolve d
3410119 40 Male AUSTRALIA Clinical Study Healthcare professional	Urinary tract infection Grade 3	47	(1) PRALSETINIB (S)  (2) TEMAZEPAM (C)  (3) CALCIUM (C)  (4) COLECALCIFEROL (C)  (5) SERTRALINE (C)  (6) TRAMADOL (C)  (7) CODEINE PHOSPHATE\PARACETAMOL (C)  (8) PREGABALIN (C)  (9) IRON (C)  (10) MACROGOL 3350\POTASSIUM CHLORIDE\SODIUM BICARBONATE\SODIUM CHLORIDE (C)  (11) AMLODIPINE (C)	Dose interrupted Positive N/A Recovered/Resolve d

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(12) PARACETAMOL (C) (13) OXYCODONE HYDROCHLORIDE (C) (14) AMOXICILLIN\CLAVULANIC ACID (C) (15) METOCLOPRAMIDE (C) (16) CLARITHROMYCIN (C) (17) AMITRIPTYLINE (C) (18) CALCITRIOL (C) (19) METFORMIN (C) (20) AZITHROMYCIN (T) (21) CEFAZOLIN (T) (22) CEFTRIAXONE (T) (23) ENOXAPARIN (T) (24) MAGNESIUM ASPARTATE (T) (25) METHYL PREDNISOLONE (T) (26) PANTOPRAZOLE (T) (27) PIPERACILLIN\TAZOBACTAM (T) (28) FENTANYL (T)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(29) ONDANSETRON (T)  (30) PROPOFOL (T)  (31) SUXAMETHONIUM (T)  (32) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)  (33) CEFALEXIN (T)  (34) PREDNISOLONE (T)	
3473059 67 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Peritonitis bacterial Grade 3	1825	(1) PRALSETINIB (S)  (2) CEFEPIME (T)  (3) VANCOMYCIN (T)	Dose not changed N/A N/A Recovered/Resolved
3474000 54 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia  Grade 3	71	(1) PRALSETINIB (S)  (2) ERGOCALCIFEROL (C)  (3) TRIAMCINOLONE ACETONIDE (C)  (4) DOCUSATE\SENNA ALEXANDRINA (C)  (5) ENOXAPARIN SODIUM (C)  (6) TRAMADOL (C)  (7) GABAPENTIN (C)  (8) AMPICILLIN SODIUM\SULBACTAM SODIUM (C)	Dose not changed N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(9) FAMOTIDINE (C) (10) MAGNESIUM HYDROXIDE (C) (11) ONDANSETRON (C) (12) CELECOXIB (C) (13) HYDROMORPHONE HYDROCHLORIDE (C) (14) PARACETAMOL (C) (15) BISACODYL (C) (16) KETOROLAC TROMETHAMINE (C) (17) SACCHAROMYCES BOULARDII (C)	
3489162 67 Female KOREA, REPUBLIC OF Clinical Study Healthcare professional	Pneumonia cytomegaloviral Grade 3	84	(1) PRALSETINIB (S) (2) DIHYDROCODEINE BITARTRATE (C) (3) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (C) (4) LEVOFLOXACIN (C) (5) AMBROXOL HYDROCHLORIDE (C) (6) PARACETAMOL (C) (7) METHYLPREDNISOLONE (C) (8) ESOMEPRAZOLE (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(9) CODEINE PHOSPHATE (C) (10) SULFAMETHOXAZOLE\TRIMETHOPRIM (C) (11) FENTANYL (C) (12) POTASSIUM PHOSPHATE MONOBASIC (C) (13) ZOLPIDEM TARTRATE (C) (14) QUETIAPINE FUMARATE (C) (15) CHLORPHENAMINE MALEATE (C) (16) METOCLOPRAMIDE (C) (17) MEGESTROL ACETATE (C) (18) POTASSIUM CHLORIDE (C) (19) PREDNISOLONE (C) (20) TRAMADOL HYDROCHLORIDE (C) (21) PREGABALIN (C) (22) MELATONIN (C) (23) CILOSTAZOL (C)	
3495221 65 Male MEXICO Clinical Study	Pneumonia Grade 3	367	(1) PRALSETINIB (S) (2) LERCANIDIPINE (C) (3) LEVOFLOXACIN (T)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
Non-healthcare professional				
3495267 65 Female MEXICO Clinical Study Healthcare professional	Urosepsis Grade 3	34	(1) PRALSETINIB (S)  (2) ESOMEPRAZOLE (C)  (3) PREGABALIN (C)  (4) SIMVASTATIN (C)  (5) TELMISARTAN (C)  (6) DIMETICON\ MAGALDRATE (C)  (7) METFORMIN (C)  (8) FILGRASTIM (T)	Dose interrupted Negative N/A Not Recovered/Not Resolved/Ongoing
3499350 64 Male TAIWAN, PROVINCE OF CHINA Clinical Study Non-healthcare professional	Cryptococcosis Grade 3	230	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (C)  (3) FLUVASTATIN (C)  (4) DEXTROMETHORPHAN (C)  (5) AMBROXOL HYDROCHLORIDE (C)  (6) FEXOFENADINE (C)  (7) OLMESARTAN (C)  (8) TETRACYCLINE (C)  (9) GENTAMICIN (C)	Dose not changed N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(10) PARACETAMOL (C) (11) ACETYLCYSTEINE (C) (12) SULTAMICILLIN (C) (13) CEFAZOLIN SODIUM (C) (14) CELECOXIB (C) (15) AMOXICILLIN\CLAVULANIC ACID (C) (16) CALCIUM CHLORIDE\POTASSIUM CHLORIDE\SODIUM LACTATE (C) (17) GLUCOSE MONOHYDRATE\SODIUM CHLORIDE (C) (18) ESOMEPRAZOLE (C) (19) NALBUPHINE HYDROCHLORIDE (C) (20) MAGNESIUM OXIDE (C) (21) SENNOSIDE A+B (C) (22) NEBIVOLOL (C) (23) ESOMEPRAZOLE MAGNESIUM (C) (24) NIRMATRELVIR\RITONAVIR (C) (25) FLUCONAZOLE (T)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
3500851 57 Male TAIWAN, PROVINCE OF CHINA Clinical Study Healthcare professional	Pneumonia Grade 3	94	(1) PRALSETINIB (S)  (2) METFORMIN HYDROCHLORIDE (C)  (3) AMLODIPINE BESILATE (C)  (4) LINAGLIPTIN (C)  (5) DIMETICON (C)  (6) MORPHINE (C)  (7) LANSOPRAZOLE (C)  (8) SERTACONAZOLE NITRATE (C)  (9) SENNOSIDE A+B (C)  (10) ACETYLCYSTEINE (C)  (11) MOSAPRIDE CITRATE (C)  (12) VALSARTAN (C)  (13) MAGNESIUM OXIDE (C)  (14) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (C)  (15) NYSTATIN (C)  (16) CLINDAMYCIN (C)  (17) RABEPRAZOLE SODIUM (C)	Dose reduced Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(18) GLYCRRHIZA GLABRA EXTRACT\PAPAVER SOMNIFERUM\PIMPINELLA ANISUM OIL (C)  (19) CEFIXIME (C)  (20) NYSTATIN (C)  (21) FEXOFENADINE HYDROCHLORIDE (C)  (22) CLINDAMYCIN (C)  (23) AMOXICILLIN\CLAVULANIC ACID (C)  (24) CEFIXIME (C)	
3524202 66 Male KOREA, REPUBLIC OF Clinical Study Healthcare professional	Appendicitis Grade 3	738	(1) PRALSETINIB (S)  (2) CARVEDILOL (C)  (3) TAMSULOSIN HYDROCHLORIDE (C)  (4) BETHANECHOL CHLORIDE (C)  (5) SACCHAROMYCES BOULARDII (C)  (6) ITOPRIDE HYDROCHLORIDE (C)  (7) MAGNESIUM OXIDE (C)  (8) MELATONIN (C)  (9) TRAZODONE (C)  (10) PREGABALIN (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(11) LANSOPRAZOLE (C) (12) LEVOTHYROXINE SODIUM (C) (13) NIRMATRELVIR\RITONAVIR (C) (14) CEFTRIAZONE SODIUM (C) (15) BROMHEXINE HYDROCHLORIDE (C) (16) COPTIS SPP. RHIZOME\HEDERA HELIX LEAF (C) (17) AMLODIPINE BESILATE (C) (18) CANDESARTAN CILEXETIL (C) (19) FOLIC ACID (C) (20) PROTAMINE SULFATE (C) (21) ERTAPENEM SODIUM (C) (22) ACICLOVIR (C) (23) GABAPENTIN (C) (24) PARACETAMOL\TRAMADOL HYDROCHLORIDE (C) (25) LACTULOSE (C)	
3548756 69 Male NETHERLANDS Clinical Study	Pneumonia Grade 3	228	(1) PRALSETINIB (S) (2) CARBOPLATIN (S) (3) PEMETREXED (S)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
Non-healthcare professional			(4) PARACETAMOL (C)  (5) AMLODIPINE (C)  (6) ENALAPRIL (C)  (7) MACROGOL (C)  (8) AMOXICILLIN TRIHYDRATE\CLAVULANATE POTASSIUM (T)  (9) VANCOMYCIN (T)  (10) CEFTAZIDIME (T)	
2717111 71 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Sepsis  COVID-19 pneumonia  Pneumonia staphylococcal Grade 5  Grade 3  Grade 3	50  20  47	(1) PRALSETINIB (S)  (2) BACLOFEN (C)  (3) LEVETIRACETAM (C)  (4) LEVOTHYROXINE (C)  (5) METOPROLOL TARTRATE (C)  (6) ONDANSETRON (C)  (7) RIVAROXABAN (C)  (8) AMLODIPINE (C)  (9) DOCUSATE (C)  (10) FLUTICASONE (C)	N/A  Dose interrupted  Dose interrupted N/A  Negative  Negative N/A  N/A  N/A  Fatal  Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(11) GABAPENTIN (C) (12) NITROFURANTOIN (C) (13) OXYBUTYNIN (C) (14) TIZANIDINE (C) (15) IPRATROPIUM BROMIDE\SALBUTAMOL SULFATE (C) (16) DEXAMETHASONE (T) (17) REMDESIVIR (T) (18) RIVAROXABAN (T) (19) PARACETAMOL (T) (20) FERROUS SULFATE (T) (21) IBUPROFEN (T) (22) LEVETIRACETAM (T) (23) MACROGOL 3350 (T) (24) OXYBUTYNIN HYDROCHLORIDE (T) (25) SENNA SPP. (T) (26) SODIUM CHLORIDE (T) (27) BENZONATATE (T)	Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(28) VANCOMYCIN (T)	
3355432 77 Female FRANCE Clinical Study Healthcare professional	Pyelonephritis  Pneumonia Grade 3  Grade 5	16  29	(1) PRALSETINIB (S)  (2) ATORVASTATIN (C)  (3) PANTOPRAZOLE (C)  (4) PERINDOPRIL (C)  (5) LEVOTHYROXINE SODIUM (C)  (6) APIXABAN (C)  (7) LAMOTRIGINE (C)  (8) PROPRANOLOL (C)  (9) ZOPICLONE (C)  (10) CEFTRIAXONE (T)  (11) METRONIDAZOLE (T)  (12) CEFOTAXIME (T)  (13) FUROSEMIDE (T)  (14) SPIRAMYCIN (T)  (15) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)	Dose interrupted  NR Positive  Unknown Unknown  Unknown Recovered/Resolved  Fatal

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(16) CEFEPIME (T)	
2711982 71 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia Grade 3	819	(1) PRALSETINIB (S)  (2) AMLODIPINE BESILATE (C)  (3) ACETYLSALICYLIC ACID (C)  (4) ATORVASTATIN CALCIUM (C)  (5) UBIQUINOL (C)  (6) FISH OIL (C)  (7) LEVOTHYROXINE SODIUM (C)  (8) VITAMIN B COMPLEX (C)  (9) DEXAMETHASONE (T)  (10) REMDESIVIR (T)  (11) AZITHROMYCIN (T)	Dose interrupted Positive Negative Recovered/Resolved
2713020 35 Female CHINA Clinical Study Healthcare professional	Pneumonia Grade 3	285	(1) PRALSETINIB (S)  (2) CALCIUM CARBONATE (C)  (3) COLECALCIFEROL (C)  (4) LEUCOGEN (C)	Dose interrupted Positive N/A Recovered/Resolved With Sequelae
2713199 55 Female	Device related infection Grade 3	21	(1) PRALSETINIB (S)	Dose interrupted Positive Unknown

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
GERMANY Clinical Study Healthcare professional				Recovered/Resolved With Sequelae
2713664 66 Female CHINA Clinical Study Healthcare professional	Pneumonia Grade 3	63	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (C)  (3) ASCORBIC ACID (T)  (4) PYRIDOXINE HYDROCHLORIDE (T)  (5) POTASSIUM CHLORIDE (T)  (6) CEFACLOR (T)	NR Unknown N/A Recovered/Resolved
2714763 27 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Urinary tract infection  Sepsis Grade 3	941  1072	(1) PRALSETINIB (S)  (2) HYDROCHLOROTHIAZIDE (C)  (3) ONDANSETRON (C)  (4) ZINC SULFATE (C)  (5) CARVEDILOL (C)  (6) HYDRALAZINE HYDROCHLORIDE (C)  (7) AMLODIPINE BESILATE (C)  (8) CALCIUM CARBONATE (C)  (9) ESOMEPRAZOLE MAGNESIUM (C)  (10) TRAMADOL (C)	Dose interrupted  Dose interrupted Positive  Positive Negative  Negative Recovered/Resolved  Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(11) PARACETAMOL (C) (12) VACCINIUM SPP. (C) (13) DOCUSATE SODIUM (C) (14) ERGOCALCIFEROL (C) (15) ESCITALOPRAM OXALATE (C) (16) HYDROCHLOROTHIAZIDE (C) (17) LACTOBACILLUS ACIDOPHILUS (C) (18) LACTULOSE (C) (19) LORAZEPAM (C) (20) NITROFURANTOIN (C) (21) ONDANSETRON (C) (22) CALCIUM CARBONATE (C) (23) ESOMEPRAZOLE (C) (24) ESOMEPRAZOLE (C) (25) LEVOFLOXACIN (T) (26) HYDROCHLOROTHIAZIDE (T) (27) METOPROLOL TARTRATE (T)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
2715770 55 Female CHINA Clinical Study Healthcare professional	Pneumonia Grade 3	94	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (C)  (3) PIPERACILLIN\TAZOBACTAM (T)	N/A N/A N/A Recovered/Resolved
2716421 33 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Urinary tract infection Grade 3	625	(1) PRALSETINIB (S)  (2) PARACETAMOL (C)  (3) CALCIUM ASCORBATE (C)  (4) CALCITRIOL (C)  (5) CALCIUM CITRATE\COLECALCIFEROL (C)  (6) COLECALCIFEROL (C)  (7) FLUDROCORTISONE (C)  (8) PREDNISONE (C)  (9) LEVOTHYROXINE (C)  (10) DIPHENHYDRAMINE\LIDOCAINE (C)  (11) HYDROCODONE BITARTRATE\PARACETAMOL (C)  (12) AMLODIPINE (C)  (13) DOCUSATE SODIUM\SENNOSIDE A+B (C)  (14) MACROGOL 3350 (C)	NR Unknown N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(15) LINACLOTIDE (C)  (16) MACROGOL (C)	
2716423 58 Male CHINA Clinical Study Healthcare professional	Pneumonia Grade 3	327	(1) PRALSETINIB (S)  (2) ENTECAVIR (C)  (3) NIFEDIPINE (C)  (4) IRON POLYSACCHARIDE COMPLEX (C)	Dose not changed N/A N/A Recovered/Resolved
2717065 31 Male CHINA Clinical Study Healthcare professional	Appendicitis Grade 3	176	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) SODIUM CHLORIDE (T)  (4) CEFUROXIME SODIUM (T)  (5) PETHIDINE HYDROCHLORIDE (T)  (6) ORNIDAZOLE (T)	Dose interrupted Positive N/A Recovered/Resolved
2717177 73 Female FRANCE Non-Interventional Study/Program Healthcare professional	Clostridium difficile infection  Klebsiella infection Grade 3  Grade 3	118  38	(1) PRALSETINIB (S)  (2) SPIRONOLACTONE (C)  (3) CELIPIROLOL (C)  (4) INDAPAMIDE (C)  (5) LANSOPRAZOLE (C)  (6) VANCOMYCIN (T)	Dose interrupted  Dose interrupted Positive  Positive N/A  N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(7) PIPERACILLIN (T)  (8) OXYGEN (T)  (9) CEFOTAXIME (T)  (10) OFLOXACIN (T)  (11) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)	Recovered/Resolve d
2717198 55 Female FRANCE Non-Interventional Study/Program Healthcare professional	Pneumonia aspiration Grade 3	130	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) PROPRANOLOL (C)  (4) NICARDIPINE (C)  (5) IRBESARTAN (C)  (6) HYDROCORTISONE (C)  (7) ATEZOLIZUMAB (C)  (8) RUCAPARIB (C)  (9) ALFACALCIDOL (C)  (10) FOLIC ACID (C)  (11) PARACETAMOL (C)  (12) PAROXETINE HYDROCHLORIDE (C)  (13) MIRTAZAPINE (C)	Dose not changed N/A N/A Recovered/Resolve d

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(14) GABAPENTIN (C)  (15) AMITRIPTYLINE HYDROCHLORIDE (C)  (16) OXYCODONE HYDROCHLORIDE (C)  (17) OXYCODONE HYDROCHLORIDE (C)  (18) DESLORATADINE (C)  (19) LEVOCETIRIZINE DIHYDROCHLORIDE (C)	
2718490 60 Male FRANCE Clinical Study Healthcare professional	COVID-19 Grade 3	469	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (C)  (3) RED BLOOD CELLS (T)	Dose interrupted Positive N/A Recovered/Resolved
2718745 35 Female CHINA Clinical Study Healthcare professional	Pneumonia Grade 3	367	(1) PRALSETINIB (S)  (2) LOXOPROFEN (T)  (3) PIDOTIMOD (T)  (4) CEFUROXIME SODIUM (T)  (5) FLUCONAZOLE\ SODIUM CHLORIDE (T)  (6) DESARMILLARIA TABESCENS (T)  (7) CALCIUM GLUCONATE\ GLUCOSE\ MAGNESIUM CHLORIDE\ POTASSIUM CHLORIDE\ SODIUM ACETATE\ SODIUM CHLORIDE\ SODIUM CITRATE (T)	Dose not changed N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(8) POTASSIUM CHLORIDE (T)  (9) SODIUM CHLORIDE (T)  (10) REBAMIPIDE (T)  (11) SODIUM BICARBONATE (T)	
2718767 55 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Respiratory tract infection  Oropharyngeal candidiasis  Grade 3  Grade 3	552  552	(1) PRALSETINIB (S)  (2) SALBUTAMOL (C)  (3) AMOXICILLIN (C)  (4) AZITHROMYCIN (C)  (5) AZITHROMYCIN (C)  (6) COLECALCIFEROL (C)  (7) FINASTERIDE (C)  (8) CODEINE PHOSPHATE\GUAIFENESIN (C)  (9) LEVOTHYROXINE (C)  (10) LOPERAMIDE HYDROCHLORIDE (C)  (11) GUAIFENESIN (C)  (12) OMEPRAZOLE (C)  (13) ONDANSETRON (C)	Dose interrupted  Dose interrupted Positive  Positive N/A  N/A Recovered/Resolved  Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(14) PREDNISONE (C)  (15) SILDENAFIL (C)  (16) RACEPINEFRINE (T)  (17) FLUCONAZOLE (T)  (18) NYSTATIN (T)  (19) DEXAMETHASONE (T)  (20) CEFTRIAXONE SODIUM (T)	
2719938 72 Female KOREA, REPUBLIC OF Clinical Study Healthcare professional	Lymph node tuberculosis Grade 3	214	(1) PRALSETINIB (S)  (2) AMLODIPINE (C)  (3) CEFOTAXIME (T)  (4) PROPACETAMOL (T)  (5) TIROPRAMIDE (T)  (6) BORNEOL\CAMPHENE\CINEOLE\MENTHOL\MENTHONE\PINENE (T)  (7) URSODEOXYCHOLIC ACID (T)  (8) CIMETROPIUM (T)  (9) METOCLOPRAMIDE (T)  (10) SODIUM CHLORIDE (T)	Dose interrupted  Positive Positive Recovered/Resolved With Sequelae

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(11) POTASSIUM PHOSPHATE (T) (12) POTASSIUM CHLORIDE (T) (13) CHLORPHENAMINE (T) (14) PARACETAMOL (T) (15) LEVOFLOXACIN (T) (16) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T) (17) MEROPENEM (T) (18) VANCOMYCIN (T) (19) PETHIDINE (T) (20) ISONIAZID (T) (21) PIPERACILLIN\TAZOBACTAM (T) (22) RIFAMPICIN (T) (23) ETHAMBUTOL (T) (24) PYRIDOXINE (T) (25) PYRAZINAMIDE (T) (26) TRAMADOL (T) (27) MOXIFLOXACIN (T)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(28) CYCLOSERINE (T)	
2723220 54 Female GERMANY Clinical Study Healthcare professional	Pneumonia Grade 3	80	(1) PRALSETINIB (S)  (2) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (3) AZITHROMYCIN (T)	Dose interrupted positive N/A Recovered/Resolved
2724343 75 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Urinary tract infection Grade 3	995	(1) PRALSETINIB (S)  (2) FOSFOMYCIN TROMETAMOL (C)  (3) PIPERACILLIN (T)  (4) CIPROFLOXACIN (T)  (5) METHENAMINE HIPPURATE (T)  (6) ASCORBIC ACID (T)	Dose interrupted positive N/A Recovered/Resolved
2725078 42 Male GERMANY Clinical Study Healthcare professional	Pneumonia bacterial Grade 3	32	(1) PRALSETINIB (S)  (2) COLECALCIFEROL (C)  (3) METOPROLOL (C)  (4) CALCIUM (C)  (5) AMOXICILLIN\CLAVULANIC ACID (T)  (6) CLARITHROMYCIN (T)  (7) AMPICILLIN SODIUM\SULBACTAM SODIUM (T)	N/A N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(8) METAMIZOLE (T)  (9) LEVOTHYROXINE (T)  (10) CALCITRIOL (T)	
2725485 78 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia Grade 3	441	(1) PRALSETINIB (S)  (2) CEFPODOXIME (T)	Drug withdrawn Negative N/A Not Recovered/Not Resolved/Ongoing
2726036 67 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Clostridium difficile colitis  Pseudomembranous colitis  Urinary tract infection bacterial Grade 3  Grade 3  Grade 3	752 752 752	(1) PRALSETINIB (S)  (2) MELATONIN (C)  (3) DIPHENHYDRAMINE (C)  (4) DOCUSATE SODIUM (C)  (5) LEVOTHYROXINE (C)  (6) ONDANSETRON (C)  (7) CETIRIZINE (C)  (8) OMEPRAZOLE (C)  (9) OMEPRAZOLE (C)  (10) DICLOFENAC SODIUM (C)  (11) FIDAXOMICIN (C)	Dose interrupted  Dose interrupted  Dose interrupted NA  Positive  Positive NA  Positive  Positive Unknown  Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(12) METRONIDAZOLE (C)  (13) LEVOFLOXACIN (C)  (14) CEFEPIME (C)  (15) BEZLOTOXUMAB (C)  (16) VANCOMYCIN (T)  (17) METRONIDAZOLE (T)	Recovered/Resolve d
2726273 73 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Sepsis  Urinary tract infection Grade 4  Grade 3	267  267	(1) PRALSETINIB (S)  (2) AMLODIPINE (C)  (3) CETIRIZINE (C)  (4) ESOMEPRAZOLE (C)  (5) IBUPROFEN (C)  (6) SITAGLIPTIN (C)  (7) LEVOTHYROXINE (C)  (8) MAGNESIUM OXIDE (C)  (9) ROSUVASTATIN (C)  (10) SIMVASTATIN (C)  (11) TELMISARTAN (C)	Drug withdrawn  Drug withdrawn Positive  Positive N/A  N/A Recovered/Resolve d  Recovered/Resolve d

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(12) METFORMIN HYDROCHLORIDE\SITAGLIPTIN PHOSPHATE MONOHYDRATE (C)  (13) METFORMIN (C)  (14) CEFTRIAXONE (T)  (15) VANCOMYCIN (T)	
2726810 78 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	COVID-19 pneumonia Grade 3	609	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) PROMETHAZINE (C)  (4) COLECALCIFEROL (C)  (5) DOCUSATE SODIUM (C)  (6) PARACETAMOL (T)  (7) BENZONATATE (T)  (8) DEXTROMETHORPHAN\GUAIFENESIN (T)  (9) PANTOPRAZOLE (T)  (10) DIPHENHYDRAMINE\HYDROCORTISONE\NYSTATIN (T)  (11) DEXAMETHASONE (T)  (12) ONDANSETRON (T)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
2726821 70 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Urinary tract infection Grade 3	517	(1) PRALSETINIB (S)  (2) ALLOPURINOL (C)  (3) ATORVASTATIN (C)  (4) DULAGLUTIDE (C)  (5) INSULIN GLARGINE (C)  (6) COLECALCIFEROL (C)  (7) ACETYLSALICYLIC ACID (C)  (8) ZOLPIDEM (C)  (9) ALPRAZOLAM (C)  (10) HEPARIN (C)  (11) INSULIN LISPRO (C)  (12) LORAZEPAM (C)  (13) AZITHROMYCIN (C)  (14) PREDNISONE (C)	NR Unknown N/A Recovered/Resolved
2729104 71 Male UNITED STATES OF AMERICA Clinical Study	COVID-19 pneumonia Grade 3	819	(1) PRALSETINIB (S)  (2) AMLODIPINE BESILATE (C)  (3) ACETYLSALICYLIC ACID (C)  (4) ATORVASTATIN CALCIUM (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
Healthcare professional			(5) UBIDECARENONE (C)  (6) FISH OIL (C)  (7) LEVOTHYROXINE SODIUM (C)  (8) VITAMIN B COMPLEX (C)	
2729523 46 Male CHINA Clinical Study Healthcare professional	Urinary tract infection Grade 3	218	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (C)	NR Unknown N/A Not Recovered/Not Resolved/Ongoing
2729531 55 Female CHINA Clinical Study Healthcare professional	Pneumonia Grade 3	13	(1) PRALSETINIB (S)  (2) OLMESARTAN MEDOXOMIL (C)  (3) INDAPAMIDE (C)  (4) AMLODIPINE BESILATE (C)  (5) METHYLPREDNISOLONE SODIUM SUCCINATE (C)  (6) RABEPRAZOLE SODIUM (C)  (7) TRAMADOL (C)  (8) CATEQUENTINIB (C)  (9) ZOLEDRONIC ACID (C)  (10) FUROSEMIDE (C)	Dose interrupted Negative N/A Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(11) CALCIUM GLUCONATE (C)  (12) GLUCOSE (C)  (13) INSULIN NOS (C)	
2733973 54 Female ITALY Clinical Study Healthcare professional	Pneumonia Grade 3	83	(1) PRALSETINIB (S)  (2) DEXAMETHASONE (C)  (3) COLECALCIFEROL (C)  (4) MAGNESIUM HYDROXIDE (C)  (5) ANASTROZOLE (C)  (6) LANSOPRAZOLE (C)  (7) CARVEDILOL (C)  (8) AMLODIPINE (C)  (9) AMBROXOL (C)  (10) DIHYDROCODEINE (C)  (11) AMILORIDE\HYDROCHLOROTHIAZIDE (C)  (12) LEVOFLOXACIN (T)  (13) HYDROCHLOROTHIAZIDE\IRBESARTAN (T)  (14) FLUORESCEIN (T)	Drug withdrawn Positive N/A Recovered/Resolved With Sequelae

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(15) PARACETAMOL (T)	
2734973 67 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Arthritis infective Grade 3	609	(1) PRALSETINIB (S)  (2) PARACETAMOL (C)  (3) AMOXICILLIN (C)  (4) MELOXICAM (C)  (5) METOPROLOL (C)  (6) OXYCODONE (C)  (7) METOPROLOL SUCCINATE (C)  (8) HYDROCHLOROTHIAZIDE (T)  (9) ACETYLSALICYLIC ACID (T)  (10) DOCUSATE SODIUM (T)  (11) FAMOTIDINE (T)  (12) SODIUM CHLORIDE (T)  (13) DIPHENHYDRAMINE (T)  (14) MORPHINE (T)  (15) NALOXONE (T)  (16) CEFEPIME (T)	Dose interrupted positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(17) VANCOMYCIN (T)  (18) POTASSIUM CHLORIDE (T)	
2737755 87 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Urinary tract infection Grade 3	158	(1) PRALSETINIB (S)	N/A N/A N/A Recovered/Resolved
2739010 61 Female KOREA, REPUBLIC OF Clinical Study Healthcare professional	Herpes zoster Grade 3	29	(1) PRALSETINIB (S)  (2) CALCIUM CHLORIDE\GLUCOSE\POTASSIUM CHLORIDE\SODIUM CHLORIDE\SODIUM LACTATE (C)  (3) ARTEMISIA ARGYI (C)  (4) DICLOFENAC SODIUM (C)  (5) ACICLOVIR (T)  (6) GABAPENTIN (T)  (7) PARACETAMOL (T)  (8) CHLORPHENAMINE MALEATE (T)  (9) BROMELAINS (T)  (10) ACICLOVIR (T)  (11) CALAMINE (T)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(12) AMOXICILLIN SODIUM\CLAVULANATE POTASSIUM (T)	
2739673 75 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Urosepsis Grade 3	695	(1) PRALSETINIB (S)  (2) METHENAMINE HIPPURATE (C)  (3) ASCORBIC ACID (C)  (4) VANCOMYCIN (T)  (5) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (6) AMPICILLIN (T)	Dose interrupted Positive N/A Recovered/Resolved
2740001 46 Female KOREA, REPUBLIC OF Clinical Study Healthcare professional	Pneumonia cytomegaloviral Grade 3	22	(1) PRALSETINIB (S)  (2) CALCIUM CITRATE\COLECALCIFEROL (C)  (3) CALCITRIOL (C)  (4) SILYBUM MARIANUM (C)  (5) MUPIROCIN (C)	NR Unknown N/A Recovered/Resolved
2740296 54 Male UNITED STATES OF AMERICA Non-Interventional Study/Program Healthcare professional	Pneumonia Grade 3	247	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (C)  (3) OXYCODONE HYDROCHLORIDE (C)  (4) VANCOMYCIN (C)  (5) CALCITRIOL (C)	NR Unknown N/A Recovered/Resolved
2740809 62 Female	Upper respiratory tract infection Grade 3	136	(1) PRALSETINIB (S)  (2) CALCIUM (C)	Dose interrupted Positive Negative

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
CHINA Clinical Study Healthcare professional			(3) LEVOFLOXACIN (C)  (4) ZINC GLUCONATE (C)  (5) AMBROXOL HYDROCHLORIDE (C)  (6) OMEPRAZOLE SODIUM (C)  (7) SODIUM CHLORIDE (C)  (8) DEXAMETHASONE SODIUM PHOSPHATE (C)  (9) CHYMOTRYPSIN (C)  (10) GENTAMICIN SULFATE (C)  (11) MEGESTROL (C)  (12) POTASSIUM CHLORIDE (C)  (13) METOCLOPRAMIDE (C)  (14) LANSOPRAZOLE (C)	Recovered/Resolve d
2742023 59 Female KOREA, REPUBLIC OF Clinical Study Healthcare professional	Hepatitis B reactivation Grade 3	88	(1) PRALSETINIB (S)  (2) URSOODEOXYCHOLIC ACID (C)  (3) SILYBUM MARIANUM (C)  (4) ORNITHINE ASPARTATE (T)  (5) ENTECAVIR (T)	Dose interrupted Positive Unknown Recovered/Resolve d

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
2744401 77 Female TAIWAN, PROVINCE OF CHINA Clinical Study Healthcare professional	Kidney infection  Urinary tract infection Grade 3  Grade 3	157  198	(1) PRALSETINIB (S)  (2) MAGNESIUM OXIDE (C)  (3) ZOLPIDEM TARTRATE (C)  (4) PARACETAMOL (C)  (5) BACLOFEN (C)  (6) PARACETAMOL\TRAMADOL HYDROCHLORIDE (C)  (7) AMLODIPINE BESILATE (C)  (8) DENOSUMAB (C)  (9) CEFTRIAZONE SODIUM (C)  (10) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (C)  (11) MEROPENEM (C)  (12) CEFTRIAZONE (C)  (13) FUROSEMIDE (C)  (14) POTASSIUM GLUCONATE (T)  (15) PROCHLORPERAZINE MALEATE (T)	Dose interrupted  Dose interrupted Positive  N/A N/A  N/A Recovered/Resolve d  Recovered/Resolve d
2744633 31 Female CHINA Clinical Study	Gastroenteritis Grade 3	326	(1) PRALSETINIB (S)  (2) PANTOPRAZOLE (T)  (3) MONTMORILLONITE (T)	NR Unknown N/A Recovered/Resolve d

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
Healthcare professional				
2747622 67 Female SINGAPORE Clinical Study Healthcare professional	Pneumonia Grade 3	113	(1) PRALSETINIB (S)  (2) CODEINE PHOSPHATE (C)  (3) PREDNISOLONE (C)  (4) COLECALCIFEROL (C)  (5) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (6) DOXYCYCLINE (T)	Dose interrupted Positive Negative Recovered/Resolved
2752277 32 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Urinary tract infection Grade 3	325	(1) PRALSETINIB (S)  (2) PARACETAMOL (C)  (3) CALCITRIOL (C)  (4) CALCIUM CITRATE\COLECALCIFEROL (C)  (5) COLECALCIFEROL (C)  (6) FLUDROCORTISONE (C)  (7) LEVOTHYROXINE (C)  (8) DOCUSATE SODIUM\SENNOSIDE A+B (C)  (9) DIPHENHYDRAMINE\LIDOCAINE (C)  (10) HYDROCODONE BITARTRATE\PARACETAMOL (C)  (11) AMLODIPINE (C)	N/A N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(12) PREDNISONE (C)	
2753217 56 Female CHINA Clinical Study Healthcare professional	Pneumonia Grade 3	171	(1) PRALSETINIB (S)  (2) NIFEDIPINE (C)	Dose interrupted Positive Unknown Recovered/Resolved
2753743 37 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	COVID-19 Grade 3	390	(1) PRALSETINIB (S)  (2) MORPHINE SULFATE (C)  (3) ONDANSETRON (C)  (4) SENNA SPP. (C)  (5) ZOLEDRONIC ACID (C)  (6) SALBUTAMOL (C)  (7) MACROGOL 3350 (C)  (8) POTASSIUM CHLORIDE (C)  (9) MAGNESIUM OXIDE (C)  (10) AZITHROMYCIN (T)  (11) DOXYCYCLINE (T)  (12) DEXAMETHASONE (T)  (13) CEFTRIAXONE (T)	NR Unknown N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(14) AMOXICILLIN (T)	
2758001 72 Female KOREA, REPUBLIC OF Clinical Study Healthcare professional	Sepsis Grade 3	7	(1) PRALSETINIB (S)  (2) VALSARTAN (C)  (3) ATORVASTATIN CALCIUM (C)  (4) EDOXABAN TOSILATE (C)  (5) METOCLOPRAMIDE (C)  (6) MEGESTROL ACETATE (C)  (7) AMLODIPINE BESILATE (C)  (8) LEVOTHYROXINE SODIUM (C)  (9) ATENOLOL (C)  (10) PARACETAMOL\TRAMADOL HYDROCHLORIDE (C)  (11) AMINO ACIDS NOS\CALCIUM\GLUCOSE\MAGNESIUM\POTASSIUM\SODI UM (C)  (12) CHROMIC CHLORIDE\COPPER SULFATE\MANGANESE SULFATE\ZINC SULFATE (C)  (13) BENZYDAMINE HYDROCHLORIDE (C)  (14) SODIUM BICARBONATE (C)  (15) PARACETAMOL (C)	Dose interrupted Positive Unknown Recovered/Resolve d

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(16) URSODEOXYCHOLIC ACID (C) (17) MOXIFLOXACIN HYDROCHLORIDE (C) (18) ALMAGATE (C) (19) ACETYLSALICYLIC ACID (C) (20) LORAZEPAM (C) (21) MUPIROCIN (C) (22) CARVEDILOL (C) (23) FERROUS SULFATE (C) (24) ADENINE HYDROCHLORIDE\BIFENDATE\CARNITINE OROTATE\CYANOCOBALAMIN\LIVER\PYRIDOXINE HYDROCHLORIDE\RIBOFLAVIN (C) (25) LOPERAMIDE (C) (26) ACETYL CYSTEINE (C) (27) ALBUMIN HUMAN (C) (28) FAMOTIDINE (C) (29) HEPARIN (C) (30) POTASSIUM CHLORIDE (C) (31) FUROSEMIDE (C)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(32) ESOMEPRAZOLE (C) (33) CHLORPHENAMINE MALEATE (C) (34) SIMETICONE (C) (35) PARACETAMOL (C) (36) QUETIAPINE FUMARATE (C) (37) ALANINE\ARGININE\CALCIUM CHLORIDE DIHYDRATE\FISH OIL\GLUCOSE MONOHYDRATE\GLYCINE\GLYCINE MAX OIL\HISTIDINE\ISOLEUCINE\LEUCINE\LYSINE HYDROCHLORIDE\MAGNESIUM SULFATE HEPTAHYDRATE\MEDIUM-CHAIN TRIGLYCERIDES\METHIONINE\OLEA EUROPAEA OIL\PHENYLALANINE\POTASSIUM CHLORIDE\PROLINE\SERINE\SODIUM ACETATE TRIHYDRATE\SODIUM GLYCEROPHOSPHATE\THREONINE\TRYPTOPHANYRO SINE\VALINE\ZINC SULFATE HEPTAHYDRATE (C) (38) FLUCONAZOLE (T) (39) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)	
2758033 42 Female TAIWAN, PROVINCE OF CHINA Non-Interventional	Pneumonia aspiration Grade 3	27	(1) PRALSETINIB (S) (2) OSIMERTINIB (C) (3) GEFITINIB (C) (4) MEROPENEM (T)	Dose interrupted Positive Negative Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
Study/Program Healthcare professional			(5) LEVOFLOXACIN (T)	
2758483 62 Male FRANCE Non-Interventional Study/Program Healthcare professional	Pneumocystis jirovecii infection Grade 3	35	(1) PRALSETINIB (S)  (2) CALCIUM (C)  (3) PREDNISOLONE (C)	NR Unknown N/A Recovered/Resolved
2758803 69 Female GERMANY Clinical Study Healthcare professional	Urinary tract infection Grade 3	154	(1) PRALSETINIB (S)  (2) CEFTRIAXONE (T)	Dose interrupted Positive N/A Recovered/Resolved
2761086 70 Female GERMANY Clinical Study Healthcare professional	COVID-19 pneumonia Grade 3	254	(1) PRALSETINIB (S)  (2) RIVAROXABAN (C)  (3) HYDROCHLOROTHIAZIDE (C)  (4) POTASSIUM IODIDE (C)  (5) FOLIC ACID (C)	NR Unknown N/A Recovered/Resolved
2761624 79 Female GERMANY Non-Interventional Study/Program	Pneumonia Grade 3	32	(1) PRALSETINIB (S)  (2) DEXPANTHENOL (C)  (3) BISOPROLOL (C)  (4) LISINOPRIL (C)	NR Unknown N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
Healthcare professional			(5) ACETYLSALICYLIC ACID (C)  (6) ATORVASTATIN (C)  (7) LEVOTHYROXINE SODIUM (C)  (8) PANTOPRAZOLE (C)  (9) PIPERACILLIN\TAZOBACTAM (T)	
2777286 70 Female CHINA Clinical Study Healthcare professional	Bacteraemia Grade 3	146	(1) PRALSETINIB (S)  (2) CEFTRIAZONE SODIUM (T)	Dose interrupted Positive Negative Recovered/Resolved
2788575 53 Female GERMANY Clinical Study Healthcare professional	Herpes zoster Grade 3	261	(1) PRALSETINIB (S)  (2) ACICLOVIR (C)  (3) ACICLOVIR (T)  (4) PREGABALIN (T)	Dose not changed N/A N/A Recovered/Resolved With Sequelae
2791037 71 Female ITALY Clinical Study Healthcare professional	Urosepsis Grade 3	26	(1) PRALSETINIB (S)  (2) DENOSUMAB (C)  (3) NALOXONE HYDROCHLORIDE\OXYCODONE HYDROCHLORIDE (C)  (4) PARACETAMOL (C)  (5) PREGABALIN (C)	Drug withdrawn Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(6) RANITIDINE (C) (7) METOPROLOL (C) (8) ROSUVASTATIN (C) (9) CLOPIDOGREL (C) (10) EDOXABAN (C) (11) DOXAZOSIN MESILATE (C) (12) CALCIUM (C) (13) FERROUS SULFATE (C) (14) ALLOPURINOL (C) (15) COLECALCIFEROL (C) (16) BROMAZEPAM (C) (17) AMLODIPINE (C) (18) MICONAZOLE (C) (19) CLOTRIMAZOLE (C) (20) CEFTRIAXONE (T)	
2791289 71 Male UNITED STATES	Diverticulitis Grade 3	352	(1) PRALSETINIB (S)  (2) LEVOTHYROIDINE (C)	Dose interrupted Positive N/A

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
OF AMERICA Clinical Study Healthcare professional			(3) CALCITRIOL (C)  (4) ALFUZOSIN (C)  (5) CALCIUM CARBONATE\COLECALCIFEROL (C)  (6) MONTELUKAST SODIUM (C)  (7) PITAVASTATIN CALCIUM (C)  (8) ESOMEPRAZOLE (C)  (9) CIPROFLOXACIN (T)  (10) METRONIDAZOLE (T)  (11) SODIUM CHLORIDE (T)	Recovered/Resolved
2791328 69 Male UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Enterococcal bacteraemia Grade 3	6	(1) PRALSETINIB (S)  (2) GLUCOSE\SODIUM CHLORIDE (C)  (3) SODIUM CHLORIDE (C)  (4) DEXAMETHASONE (C)  (5) ENOXAPARIN (C)  (6) HYDROCHLOROTHIAZIDE\LISINOPRIL DIHYDRATE (C)  (7) PANTOPRAZOLE (C)  (8) PARACETAMOL (C)  (9) LORAZEPAM (C)	NR Unknown N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(10) SENNOSIDE A+B (C) (11) DALTEPARIN SODIUM (C) (12) HYDROCHLOROTHIAZIDE\LISINOPRIL (C) (13) OMEPRAZOLE (C) (14) OXYGEN (C) (15) PROCHLORPERAZINE EDISYLATE (C) (16) VANCOMYCIN (T) (17) CEFEPIME (T)	
2791662 60 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Skin infection Grade 3	672	(1) PRALSETINIB (S) (2) ACETYLSALICYLIC ACID (C) (3) COLECALCIFEROL (C) (4) FLUTICASONE (C) (5) OMEPRAZOLE (C) (6) LISINOPRIL (C) (7) BENZONATATE (C) (8) CODEINE PHOSPHATE\GUAIFENESIN (C) (9) HYDROCODONE BITARTRATE\PARACETAMOL (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(10) CEFALEXIN (T)  (11) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)	
2791862 72 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Diverticulitis intestinal perforated Grade 3	204	(1) PRALSETINIB (S)  (2) PARACETAMOL (C)  (3) ONDANSETRON (C)  (4) PANTOPRAZOLE (C)  (5) TADALAFIL (C)  (6) CETIRIZINE HYDROCHLORIDE (C)  (7) FEXOFENADINE HYDROCHLORIDE (C)  (8) TERBINAFINE (C)  (9) XYLITOL (C)  (10) TAMSULOSIN (C)  (11) AMLODIPINE (C)  (12) ROSUVASTATIN (C)  (13) ACETYLSALICYLIC ACID (C)  (14) MELOXICAM (C)  (15) OXYCODONE (C)  (16) METRONIDAZOLE (T)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(17) CEFTRIAXONE (T)  (18) ENOXAPARIN (T)  (19) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (20) AMOXICILLIN\CLAVULANATE POTASSIUM (T)	
2792158 60 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia Grade 3	20	(1) PRALSETINIB (S)  (2) ATENOLOL (C)  (3) CLONAZEPAM (C)  (4) ERGOCALCIFEROL (C)  (5) FAMOTIDINE (C)  (6) FUROSEMIDE (C)  (7) HYDROMORPHONE HYDROCHLORIDE (C)  (8) LEVOTHYROXINE SODIUM (C)  (9) METHADONE HYDROCHLORIDE (C)  (10) NYSTATIN (C)  (11) GLYCERYL TRINITRATE (C)  (12) ONDANSETRON (C)  (13) QUETIAPINE FUMARATE (C)	NR Unknown N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(14) HYDROCHLOROTHIAZIDE\TRIAMTERENE (C) (15) SALBUTAMOL SULFATE (C) (16) CEFEPIME (C) (17) DEXAMETHASONE (C) (18) DOCUSATE SODIUM (C) (19) HYDROMORPHONE HYDROCHLORIDE (C) (20) NALOXONE HYDROCHLORIDE (C) (21) SENNOSIDE A+B (C) (22) TRIAMCINOLONE ACETONIDE (C) (23) CEPPODOXIME PROXETIL (C) (24) LEVOFLOXACIN (C) (25) SODIUM CHLORIDE (T) (26) CEFEPIME HYDROCHLORIDE (T) (27) AMOXICILLIN\CLAVULANATE POTASSIUM (T)	
2792160 75 Male UNITED KINGDOM Clinical Study	Urinary tract infection Grade 3	16	(1) PRALSETINIB (S) (2) ZOPICLONE (C) (3) ALFACALCIDOL (C) (4) BISOPROLOL (C)	Drug withdrawn Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
Healthcare professional			(5) LEVOTHYROXINE (C)  (6) BICALUTAMIDE (C)  (7) TAMOXIFEN (C)  (8) LOPERAMIDE (C)  (9) NITROFURANTOIN (T)	
2792192 69 Male KOREA, REPUBLIC OF Clinical Study Healthcare professional	Pneumonia Grade 3	101	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) LORAZEPAM (C)  (4) BROMAZEPAM (C)  (5) LOPERAMIDE (C)  (6) RANITIDINE (C)  (7) TIROPRAMIDE HYDROCHLORIDE (C)  (8) CHLORPHENAMINE MALEATE (C)  (9) CIPROFLOXACIN (T)  (10) CEFOTAXIME (T)  (11) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (12) CEFIXIME (T)	N/A N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
2792250 69 Female CHINA Clinical Study Healthcare professional	Pneumonia Grade 3	290	(1) PRALSETINIB (S)  (2) ATORVASTATIN CALCIUM (C)  (3) BISOPROLOL FUMARATE (C)  (4) GLICLAZIDE (C)  (5) NIFEDIPINE (C)  (6) ZOLPIDEM TARTRATE (C)  (7) GLUTATHIONE SODIUM (C)  (8) POLYENE PHOSPHATIDYLCHOLINE (C)	Dose interrupted positive N/A Recovered/Resolved
2792290 70 Male SPAIN Clinical Study Healthcare professional	Sepsis Grade 3	103	(1) PRALSETINIB (S)  (2) VERAPAMIL HYDROCHLORIDE (C)  (3) PARACETAMOL (C)  (4) OMEPRAZOLE (C)  (5) METOCLOPRAMIDE (C)  (6) ENOXAPARIN (C)  (7) CEFTRIAXONE (T)  (8) MEROPENEM (T)  (9) VANCOMYCIN (T)	Dose not changed N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
2792649 51 Female KOREA, REPUBLIC OF Clinical Study Healthcare professional	Pyelonephritis acute Grade 3	142	(1) PRALSETINIB (S)  (2) ISOSORBIDE MONONITRATE (C)  (3) CILAZAPRIL (C)  (4) MAGNESIUM OXIDE (C)  (5) AMMONIUM CHLORIDE\CHLORPHENAMINE MALEATE\DIHYDROCODEINE BITARTRATE\METHYLEPHEDRINE HYDROCHLORIDE-DL (C)  (6) BISACODYL (C)  (7) LACTULOSE (C)  (8) TETRACOSACTIDE ACETATE (C)  (9) MEROPENEM TRIHYDRATE (T)  (10) CEFTRIAXONE SODIUM (T)  (11) CIPROFLOXACIN (T)	Dose interrupted Positive N/A  Recovered/Resolved With Sequelae
2792701 76 Male NETHERLANDS Clinical Study Healthcare professional	Pneumonia Grade 3	57	(1) PRALSETINIB (S)  (2) SIMVASTATIN (C)  (3) FOLIC ACID (C)  (4) DEXAMETHASONE (C)  (5) SULFAMETHOXAZOLE\TRIMETHOPRIM (C)	NR Unknown N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(6) CYANOCOBALAMIN (C)  (7) RISEDRONIC ACID (C)  (8) CEFUROXIME (T)	
2792727 60 Female FRANCE Clinical Study Healthcare professional	Bronchitis Grade 3	38	(1) PRALSETINIB (S)  (2) FUROSEMIDE (C)  (3) BISOPROLOL FUMARATE (C)  (4) ATORVASTATIN CALCIUM (C)  (5) ACETYLSALICYLATE LYSINE (C)  (6) POTASSIUM CHLORIDE (C)  (7) PARACETAMOL (C)  (8) METOCLOPRAMIDE HYDROCHLORIDE (C)  (9) AMOXICILLIN\CLAVULANATE POTASSIUM (T)	NR Unknown N/A Recovered/Resolved
2792736 82 Male SINGAPORE Clinical Study Healthcare professional	Pneumonia Grade 3	26	(1) PRALSETINIB (S)  (2) AMLODIPINE (C)  (3) SIMVASTATIN (C)  (4) LACTULOSE (C)  (5) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (6) OSELTAMIVIR PHOSPHATE (T)	Dose interrupted positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(7) AZITHROMYCIN (T)	
2793034 67 Female UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Pneumocystis jirovecii pneumonia Grade 3	306	(1) PRALSETINIB (S)  (2) RIVAROXABAN (C)  (3) LORAZEPAM (C)  (4) SALBUTAMOL SULFATE (C)  (5) CODEINE PHOSPHATE\GUAIFENESIN\PSEUDOEPHEDRINE HYDROCHLORIDE (C)  (6) FLUDROCORTISONE ACETATE (C)  (7) FLUTICASONE PROPIONATE (C)  (8) HYDROCORTISONE (C)  (9) FENOTEROL HYDROBROMIDE\IPRATROPIUM BROMIDE (C)  (10) FORMOTEROL FUMARATE\MOMETASONE FUROATE (C)  (11) MONTELUKAST SODIUM (C)  (12) PANTOPRAZOLE SODIUM SESQUIHYDRATE (C)  (13) RIVAROXABAN (C)  (14) LEVOTHYROXINE SODIUM (C)	Dose interrupted positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(15) TOPIRAMATE (C) (16) GUAIFENESIN\PSEUDOEPHEDRINE HYDROCHLORIDE (C) (17) GABAPENTIN (C) (18) MACROGOL 3350 (C) (19) HYDROCODONE BITARTRATE\PARACETAMOL (C) (20) MELATONIN (C) (21) MACROGOL\PROPYLENE GLYCOL\SIMETICONE\SORBIC ACID\SORBITOL\WHITE SOFT PARAFFIN (C)	
2793454 46 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Diverticulitis Grade 3	51	(1) PRALSETINIB (S) (2) ENOXAPARIN SODIUM (C) (3) AMLODIPINE BESILATE (C) (4) CETIRIZINE HYDROCHLORIDE (C) (5) FLUTICASONE PROPIONATE (C) (6) SILYBUM MARIANUM (C) (7) FISH OIL (C) (8) PLANTAGO OVATA (C) (9) POTASSIUM PHOSPHATE MONOBASIC\SODIUM PHOSPHATE DIBASIC\SODIUM PHOSPHATE MONOBASIC	Dose interrupted positive Negative Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(ANHYDROUS) (C)  (10) TRAZODONE HYDROCHLORIDE (C)  (11) METRONIDAZOLE (T)  (12) CEFTRIAXONE SODIUM (T)  (13) METRONIDAZOLE (T)  (14) MORPHINE (T)  (15) AMOXICILLIN/CLAVULANATE POTASSIUM (T)  (16) CEFEPIME (T)  (17) VANCOMYCIN (T)  (18) CEFTRIAXONE (T)  (19) CEFUROXIME AXETIL (T)	
2793490 46 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Scrotal cellulitis Grade 3	58	(1) PRALSETINIB (S)  (2) OMEPRAZOLE (C)  (3) ATORVASTATIN CALCIUM (C)  (4) VENLAFAXINE (C)  (5) WARFARIN (C)  (6) COLECALCIFEROL (C)  (7) BISOPROLOL FUMARATE (C)	Dose not changed N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(8) LEVOTHYROXINE (C) (9) MIRTAZAPINE (C) (10) ZOLEDRONIC ACID MONOHYDRATE (C) (11) LISINOPRIL (C) (12) SALBUTAMOL (C) (13) FUROSEMIDE (C) (14) MACROGOL 3350 (C) (15) HYDROCODONE BITARTRATE\PARACETAMOL (C) (16) CALCIUM\MAGNESIUM\ZINC (C) (17) PARACETAMOL (T) (18) CEFTRIAXONE SODIUM (T) (19) MORPHINE (T) (20) WARFARIN SODIUM (T) (21) METOCLOPRAMIDE HYDROCHLORIDE (T) (22) ALUMINIUM HYDROXIDE\MAGNESIUM HYDROXIDE\SIMETICONE (T) (23) NALOXONE HYDROCHLORIDE (T)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(24) ONDANSETRON (T)  (25) AMOXICILLIN\CLAVULANATE POTASSIUM (T)	
2793522 48 Female KOREA, REPUBLIC OF Clinical Study Healthcare professional	Pneumonia Grade 3	136	(1) PRALSETINIB (S)  (2) ACECLOFENAC (C)  (3) FAMOTIDINE (C)  (4) THEOBROMINE (C)  (5) AMBROXOL (C)  (6) MOXIFLOXACIN (C)  (7) OXYCODONE (C)  (8) MORPHINE (C)  (9) MAGNESIUM OXIDE (C)  (10) MEGESTROL (C)  (11) TRAMADOL (C)  (12) GEMCITABINE (C)  (13) CARBOPLATIN (C)  (14) SITRAVATINIB (C)  (15) METOCLOPRAMIDE HYDROCHLORIDE (T)  (16) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)	N/A N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(17) LEVOFLOXACIN (T)  (18) MEROPENEM TRIHYDRATE (T)	
2794773 58 Male SINGAPORE Clinical Study Healthcare professional	Pneumonia Grade 3	270	(1) PRALSETINIB (S)  (2) ACETYLSALICYLIC ACID (C)  (3) ATORVASTATIN (C)  (4) BISOPROLOL (C)  (5) NIFEDIPINE (C)  (6) FAMOTIDINE (C)  (7) LEVETIRACETAM (C)  (8) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (9) DEXAMETHASONE (T)  (10) VALPROATE SODIUM (T)  (11) AMOXICILLIN\CLAVULANATE POTASSIUM (T)  (12) DEXAMETHASONE PHOSPHATE (T)	NR Unknown N/A Recovered/Resolved
2794779 49 Male UNITED STATES OF AMERICA Clinical Study	Pneumonia Grade 3	117	(1) PRALSETINIB (S)  (2) TAMSULOSIN (C)  (3) LEVOTHYROXINE (C)  (4) MIDODRINE (C)	Dose interrupted positive Negative Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
Healthcare professional			(5) CALCIUM CITRATE\COLECALCIFEROL (C)  (6) FINASTERIDE (C)  (7) OXYCODONE (C)  (8) POTASSIUM CHLORIDE (C)  (9) PROCHLORPERAZINE (C)  (10) ONDANSETRON (C)  (11) FAMOTIDINE (C)  (12) CALCITRIOL (C)  (13) DILTIAZEM (C)	
2794784 70 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Urinary tract infection Grade 3	9	(1) PRALSETINIB (S)  (2) BACLOFEN (C)  (3) LEVETIRACETAM (C)  (4) LEVOTHYROXINE (C)  (5) DOCUSATE SODIUM (C)  (6) NITROFURANTOIN (C)  (7) BISACODYL (C)  (8) ERGOCALCIFEROL (C)	Dose interrupted positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(9) MAGNESIUM HYDROXIDE (C)  (10) IBUPROFEN (C)  (11) SENNA SPP. (C)  (12) OXYCODONE (C)  (13) MACROGOL (C)  (14) DOCUSATE SODIUM\SENNOSIDE A+B (C)  (15) ENOXAPARIN (C)  (16) PANTOPRAZOLE (C)  (17) CEFTRIAXONE (T)  (18) AZITHROMYCIN (T)  (19) PARACETAMOL (T)	
2794879 25 Female UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Osteomyelitis Grade 3	351	(1) PRALSETINIB (S)  (2) HYDROCHLOROTHIAZIDE (C)  (3) ONDANSETRON (C)  (4) CARVEDILOL (C)  (5) HYDRALAZINE HYDROCHLORIDE (C)  (6) AMLODIPINE BESILATE (C)  (7) CALCIUM CARBONATE (C)	NR Unknown N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(8) ESOMEPRAZOLE (C) (9) TRAMADOL (C) (10) CALCITRIOL (C) (11) SOLIFENACIN SUCCINATE (C) (12) OLANZAPINE (C) (13) MELATONIN (C) (14) LORAZEPAM (C) (15) ESCITALOPRAM OXALATE (C) (16) LEVOTHYROXINE SODIUM (C) (17) PREDNISONE (C) (18) PROMETHAZINE (C) (19) METHYLPREDNISOLONE (C) (20) LEVOFLOXACIN (C)	
2795146 51 Female ITALY Clinical Study Healthcare professional	Pneumonia Grade 3	77	(1) PRALSETINIB (S) (2) RANITIDINE (C) (3) DELORAZEPAM (C) (4) CALCIUM CARBONATE (C)	Dose interrupted positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(5) ARNICA MONTANA (C) (6) LACTOBACILLUS ACIDOPHILUS (C) (7) BUPRENORPHINE (C) (8) ZOLEDRONIC ACID (C) (9) DIHYDROCODEINE (C) (10) RAMIPRIL (C) (11) POTASSIUM CHLORIDE (C) (12) CALCIUM CARBONATE (C) (13) PARACETAMOL (C) (14) LEVOFLOXACIN (T) (15) OXYGEN (T) (16) CEFTRIAXONE (T) (17) PIPERACILLIN\TAZOBACTAM (T) (18) SULFAMETHOXAZOLE\TRIMETHOPRIM (T) (19) METHYLPREDNISOLONE (T)	
2795155 56 Male UNITED STATES OF AMERICA	Pneumonia Grade 3	77	(1) PRALSETINIB (S) (2) ATORVASTATIN CALCIUM (C) (3) FOLIC ACID (C)	NR Unknown N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
Clinical Study Healthcare professional			(4) ACETYLSALICYLIC ACID (C)  (5) CYANOCOBALAMIN (C)  (6) FLUDROCORTISONE ACETATE (C)  (7) GABAPENTIN (C)  (8) LEVOTHYROXINE SODIUM (C)  (9) SERTRALINE HYDROCHLORIDE (C)  (10) SILDENAFIL CITRATE (C)  (11) CALCIUM (C)  (12) ZINC (C)  (13) MAGNESIUM (C)  (14) CETIRIZINE HYDROCHLORIDE (C)	
2796670 64 Female FRANCE Clinical Study Healthcare professional	Clostridium difficile colitis Grade 3	156	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) AMLODIPINE (C)  (4) DENOSUMAB (C)  (5) AMOXICILLIN\CLAVULANATE POTASSIUM (C)  (6) CEFTRIAXONE SODIUM (T)	NR Unknown N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			(7) METRONIDAZOLE (T)  (8) OFLOXACIN (T)	
2797009 65 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Cellulitis Grade 3	208	(1) PRALSETINIB (S)  (2) APIXABAN (C)  (3) NIFEDIPINE (C)  (4) TAMSULOSIN HYDROCHLORIDE (C)  (5) VANCOMYCIN (T)  (6) SODIUM CHLORIDE (T)  (7) MINOCYCLINE (T)	Dose not changed N/A N/A Recovered/Resolved
2797651 44 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia Grade 3	130	(1) PRALSETINIB (S)  (2) AZITHROMYCIN (T)  (3) CEFTRIAXONE (T)  (4) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (5) DOXYCYCLINE (T)  (6) FILGRASTIM (T)  (7) AMOXICILLIN\CLAVULANATE POTASSIUM (T)	Dose interrupted positive Unknown Recovered/Resolved
2797985 53 Male KOREA, REPUBLIC OF	Epididymitis Grade 3	95	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (C)  (3) TRAMADOL (C)	Dose interrupted  Positive Negative

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
Clinical Study Healthcare professional			(4) CALCIUM\COLECALCIFEROL\MAGNESIUM (C)  (5) CODEINE (C)  (6) LACTULOSE (C)  (7) FAMOTIDINE (C)  (8) CHLORPHENAMINE MALEATE (C)  (9) CALCIUM CARBONATE\MAGNESIUM CARBONATE\MAGNESIUM HYDROXIDE\MAGNESIUM TRISILICATE (C)  (10) LEVOTHYROXINE (C)  (11) CEFTRIAZONE (C)  (12) CEFIXIME (C)  (13) ACECLOFENAC (C)  (14) PROPACETAMOL (C)  (15) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (16) AMOXICILLIN TRIHYDRATE\CLAVULANATE POTASSIUM (T)	Recovered/Resolu d With Sequelae
2798031 69 Female UNITED STATES OF AMERICA	Bacteraemia Grade 3	85	(1) PRALSETINIB (S)  (2) ATORVASTATIN CALCIUM (C)  (3) DULAGLUTIDE (C)	Dose interrupted  Positive Unknown

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
Clinical Study Healthcare professional			(4) INSULIN GLARGINE (C)  (5) INSULIN LISPRO (C)  (6) INSULIN GLARGINE (C)  (7) FISH OIL (C)  (8) HEPARIN (C)  (9) ALLOPURINOL (C)  (10) COLECALCIFEROL (C)  (11) ACETYLSALICYLIC ACID (C)  (12) ZOLPIDEM (C)  (13) ALPRAZOLAM (C)  (14) POTASSIUM PHOSPHATE (T)  (15) VANCOMYCIN (T)  (16) AMPICILLIN (T)  (17) PARACETAMOL (T)	Recovered/Resolv ed
2798108 68 Male UNITED STATES OF AMERICA Clinical Study	Bacteraemia  Sepsis Grade 3  Grade 3	923  923	(1) PRALSETINIB (S)  (2) DIPHENHYDRAMINE HYDROCHLORIDE (C)  (3) LEVOTHYROXINE SODIUM (C)	Dose interrupted  Dose interrupted  Positive

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
Healthcare professional			(4) LOPERAMIDE HYDROCHLORIDE (C)  (5) HYDROCODONE BITARTRATE\PARACETAMOL (C)  (6) PREDNISONE (C)  (7) SENNA SPP. (C)  (8) CEFAZOLIN (T)  (9) CEFEPIME (T)	Positive Negative  Negative Recovered/Resolved  Recovered/Resolved
2798334 46 Male UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Pneumonia staphylococcal Grade 3	29	(1) PRALSETINIB (S)  (2) OMEPRAZOLE (C)  (3) ATORVASTATIN CALCIUM (C)  (4) WARFARIN (C)  (5) COLECALCIFEROL (C)  (6) BISOPROLOL FUMARATE (C)  (7) LEVOTHYROXINE (C)  (8) MIRTAZAPINE (C)  (9) ZOLEDRONIC ACID MONOHYDRATE (C)  (10) LISINOPRIL (C)  (11) SALBUTAMOL (C)  (12) FUROSEMIDE (C)	Dose interrupted  Positive Negative Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(13) MACROGOL 3350 (C) (14) HYDROCODONE BITARTRATE\PARACETAMOL (C) (15) AMINOSALICYLATE CALCIUM (C) (16) ZINC (C) (17) POTASSIUM CHLORIDE (C) (18) ALUMINIUM HYDROXIDE\MAGNESIUM HYDROXIDE (C) (19) OXYGEN (C) (20) SUNITINIB MALATE (C) (21) ALUMINIUM HYDROXIDE\MAGNESIUM HYDROXIDE\SIMETICONE (C) (22) CEFTRIAXONE SODIUM (T) (23) VANCOMYCIN (T) (24) CEFEPIME HYDROCHLORIDE (T) (25) AZITHROMYCIN (T) (26) DOXYCYCLINE HYCLATE (T) (27) PARACETAMOL (T) (28) SODIUM CHLORIDE (T)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decchallenge Rechallenge Event Outcome
2798372 87 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Device related infection Grade 3	117	(1) PRALSETINIB (S)  (2) ASCORBIC ACID (C)  (3) COLECALCIFEROL (C)  (4) DILTIAZEM (C)  (5) DIGOXIN (C)  (6) SODIUM CHLORIDE (C)  (7) FINASTERIDE (C)  (8) PARACETAMOL (C)  (9) SENNA ALEXANDRINA (C)  (10) APIXABAN (C)  (11) MAGNESIUM HYDROXIDE (C)  (12) CYANOCOBALAMIN (C)  (13) CEFTRIAXONE (T)	Dose not changed N/A N/A Recovered/Resolved
2798495 81 Male KOREA, REPUBLIC OF Clinical Study Healthcare professional	Urinary tract infection Grade 3	124	(1) PRALSETINIB (S)  (2) BISACODYL (C)  (3) AMLODIPINE BESILATE (C)  (4) METFORMIN (C)  (5) CALCIUM CARBONATE\COLECALCIFEROL (C)	Dose interrupted positive Unknown Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Decalage Rechallenge Event Outcome
			(6) LEVOTHYROXINE SODIUM (C) (7) MAGNESIUM OXIDE (C) (8) MEGESTROL ACETATE (C) (9) DEXAMETHASONE (C) (10) URSODEOXYCHOLIC ACID (C) (11) DICLOFENAC DEANOL (T) (12) CEFTRIAXONE SODIUM SESQUATERHYDRATE (T) (13) CEPPIRAMIDE SODIUM (T) (14) PARACETAMOL (T)	

## Category C (N=40)

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
2800573 66 Female UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Pneumonia Grade 3	200	(1) PRALSETINIB (S)	Dose interrupted Positive Negative Recovered/Resolved
2802047 63 Male TAIWAN, PROVINCE OF CHINA Clinical Study Non-healthcare professional	Pneumonia klebsiella Grade 3	641	(1) PRALSETINIB (S)	Dose interrupted Positive Negative Recovered/Resolved
2974676 Not reported Not reported CHINA Spontaneous Non-healthcare professional	Pneumonia legionella Grade 3	NR	(1) PRALSETINIB (S)	NR Unknown N/A Recovering/Resolving
3029413 63 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia bacterial Grade 3	112	(1) PRALSETINIB (S)	NR Unknown N/A Unknown

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
2904495 60 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	COVID-19  Grade 3	1095	(1) PRALSETINIB (S)  (2) REMDESIVIR (T)  (3) TOCILIZUMAB (T)  (4) SALBUTAMOL (T)  (5) METHYLSPREDNISOLONE (T)  (6) HOMATROPINE METHYLBROMIDE\HYDROCO DONE BITARTRATE (T)  (7) COLECALCIFEROL (T)	Dose interrupted Positive N/A Recovered/Resolved With Sequelae
2932342 67 Male SPAIN Clinical Study Healthcare professional	Cholecystitis infective Grade 3	921	(1) PRALSETINIB (S)	Dose interrupted Positive Unknown Recovered/Resolved
2960716 53 Male CHINA Clinical Study Healthcare professional	Pneumonia Grade 3	725	(1) PRALSETINIB (S)  (2) CEFIXIME (T)  (3) MECAMYLAMINE (T)  (4) IBUPROFEN (T)  (5) CEFOTAXIME SODIUM (T)  (6) ASCORBIC ACID (T)	Dose interrupted Positive Negative Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(7) DEXAMETHASONE SODIUM PHOSPHATE (T)  (8) CEFOPERAZONE SODIUM\SULBACTAM SODIUM (T)  (9) MOXIFLOXACIN HYDROCHLORIDE (T)  (10) CEFOPERAZONE SODIUM\SULBACTAM SODIUM (T)	
2993277 69 Male KOREA, REPUBLIC OF Clinical Study Healthcare professional	Pneumonia influenzal Grade 3	24	(1) PRALSETINIB (S)  (2) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (3) LEVOFLOXACIN (T)	Dose interrupted Positive Unknown Recovered/Resolved
2998733 72 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Urinary tract infection Grade 3	149	(1) PRALSETINIB (S)  (2) VANCOMYCIN (T)	Dose interrupted Positive N/A Recovered/Resolved
3038243 74 Male IRELAND Non-Interventional Study/Program	COVID-19 pneumonia Grade 3	665	(1) PRALSETINIB (S)	Dose interrupted Positive Unknown Recovering/Resolving

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Non-healthcare professional				
3038751 32 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	COVID-19 Grade 3	1825	(1) PRALSETINIB (S)  (2) AMOXICILLIN (T)	Dose interrupted Positive Negative Recovered/Resolved
3094592 61 Male KOREA, REPUBLIC OF Clinical Study Healthcare professional	Pneumonia Grade 3	460	(1) PRALSETINIB (S)  (2) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (3) MOXIFLOXACIN HYDROCHLORIDE (T)  (4) LEVOFLOXACIN (T)	Dose interrupted Positive Negative Recovered/Resolved
3113090 74 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Bacteraemia Grade 3	1095	(1) PRALSETINIB (S)  (2) LINEZOLID (T)  (3) MEROPENEM (T)  (4) CEFAZOLIN (T)	Dose interrupted Positive N/A Recovered/Resolved
3145942 68 Female SWITZERLAND Clinical Study Healthcare professional	Herpes zoster Grade 3	31	(1) PRALSETINIB (S)  (2) METAMIZOLE (C)  (3) MACROGOL (C)  (4) ONDANSETRON (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(5) DOMPERIDONE (C)  (6) BUTYLCYCOPOLAMINE BROMIDE (C)  (7) AMLODIPINE (C)  (8) OXYCODONE HYDROCHLORIDE (T)  (9) PARACETAMOL (T)  (10) METAMIZOLE (T)  (11) LIDOCAINE (T)  (12) CAPSAICIN (T)	
3208469 64 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Pneumonia Grade 3	1825	(1) PRALSETINIB (S)	NR Unknown N/A Recovered/Resolved
3277606 54 Female CHINA Clinical Study Healthcare professional	COVID-19 Grade 3	1121	(1) PRALSETINIB (S)  (2) IBUPROFEN (C)	Dose interrupted Positive N/A Recovered/Resolved
3278393 71 Male ITALY	Q fever Grade 3	405	(1) PRALSETINIB (S)  (2) PIPERACILLIN SODIUM/TAZOBACTAM	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Clinical Study Healthcare professional			SODIUM (T)  (3) LINEZOLID (T)	
3300876 80 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Haemophilus infection Grade 3	1095	(1) PRALSETINIB (S)	Dose interrupted Positive N/A Recovered/Resolved With Sequelae
3323385 61 Female CHINA Clinical Study Healthcare professional	Gastroenteritis Grade 3	838	(1) PRALSETINIB (S)  (2) FUROSEMIDE (C)  (3) ESOMEPRAZOLE MAGNESIUM (T)  (4) PINAVERIUM BROMIDE (T)  (5) ESOMEPRAZOLE SODIUM (T)  (6) PHLOROGLUCINOL (T)	Dose not changed N/A N/A Recovered/Resolved
3330307 66 Male ITALY Clinical Study Healthcare professional	Pneumonia  Pneumonia legionella  COVID-19 pneumonia Grade 3  Grade 3  Grade 3	36  4  4	(1) PRALSETINIB (S)  (2) CEFTAROLINE FOSAMIL (C)  (3) LEVOFLOXACIN (T)  (4) REMDESIVIR (T)	Dose interrupted  Dose interrupted  Dose interrupted Negative  Positive  Positive N/A

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
				Unknown  Unknown Not Recovered/Not Resolved/Ongoing  Recovered/Resolved With Sequelae  Recovered/Resolved
3336773 67 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Bacteraemia Grade 3	1460	(1) PRALSETINIB (S)  (2) CEFTRIAXONE (C)	Dose interrupted Positive Unknown Recovered/Resolved
3365358 69 Male SPAIN Clinical Study Healthcare professional	Meningitis bacterial Grade 3	1825	(1) PRALSETINIB (S)	Dose interrupted Positive N/A Recovered/Resolved
3386191 49 Male UNITED STATES OF AMERICA Clinical Study Healthcare professional	Varicella Grade 3	1825	(1) PRALSETINIB (S)  (2) ACICLOVIR (C)	Dose interrupted Positive N/A Recovered/Resolved
3393152 60 Male	Urinary tract infection Grade 3	1095	(1) PRALSETINIB (S)  (2) CEFTRIAXONE (T)	NR Unknown

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
SPAIN Clinical Study Healthcare professional			(3) PARACETAMOL (T)	N/A Recovered/Resolved
3446811 54 Male ITALY Clinical Study Healthcare professional	Urinary tract infection Grade 3	567	(1) PRALSETINIB (S)  (2) ESOMEPRAZOLE (C)  (3) BISOPROLOL FUMARATE\PERINDOPRIL ARGININE (C)  (4) CEFTRIAXONE (T)  (5) AZITHROMYCIN (T)	Dose not changed N/A N/A Recovering/Resolving
3447222 61 Female CHINA Clinical Study Non-healthcare professional	Pneumonia Grade 3	1095	(1) PRALSETINIB (S)  (2) MOXIFLOXACIN HYDROCHLORIDE (C)  (3) DOXYCYCLINE HYCLATE (C)  (4) IBUPROFEN (C)	NR Unknown N/A Recovered/Resolved With Sequelae
3452720 72 Female GERMANY Clinical Study Healthcare professional	Infection Grade 3	1825	(1) PRALSETINIB (S)  (2) COLECALCIFEROL (C)  (3) VALSARTAN (C)  (4) AMLODIPINE (C)  (5) MOMETASONE FUROATE (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(6) AMPICILLIN SODIUM\SULBACTAM SODIUM (T)  (7) AZITHROMYCIN (T)	
3477682 54 Male GERMANY Clinical Study Non-healthcare professional	Respiratory tract infection Grade 3	1825	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (C)  (3) BISOPROLOL (C)  (4) LOPERAMIDE (C)  (5) RAMIPRIL (C)  (6) TAZOBACTAM (T)  (7) AMOXICILLIN TRIHYDRATE\CLAVULANIC ACID (T)	Dose not changed N/A N/A Recovered/Resolved
3489069 55 Male GERMANY Clinical Study Healthcare professional	Spontaneous bacterial peritonitis Grade 3	NR	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) BISOPROLOL (C)  (4) MEROPENEM (T)	Dose not changed N/A N/A Recovered/Resolved
3509451 67 Female KOREA, REPUBLIC OF Clinical Study Healthcare professional	Pneumonia  Pyelonephritis acute Grade 3  Grade 3	24  24	(1) PRALSETINIB (S)  (2) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)	Dose interrupted  Dose interrupted Positive  Positive

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(3) LEVOFLOXACIN (T)  (4) MEROPENEM (T)  (5) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)  (6) FUROSEMIDE (T)  (7) METHYL PREDNISOLONE SODIUM SUCCINATE (T)	N/A  N/A Recovered/Resolved  Recovered/Resolved
2717114 54 Male UNITED STATES OF AMERICA Non-Interventional Study/Program Healthcare professional	Pharyngeal abscess Grade 3	124	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (C)  (3) CALCITRIOL (C)  (4) OXYCODONE HYDROCHLORIDE (C)  (5) CODEINE PHOSPHATE\GUAIFENESIN (C)  (6) VANCOMYCIN (C)  (7) BENZONATATE (C)  (8) LEVOFLOXACIN (C)	Dose interrupted Negative N/A Not Recovered/Not Resolved/Ongoing
2721262 57 Female	Pneumonia Grade 3	27	(1) PRALSETINIB (S)	Dose interrupted

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
CHINA Clinical Study Healthcare professional			(2) OS ELTAMIVIR PHOSPHATE (T)	Positive Positive Recovered/Resolved
2721878 57 Female CHINA Clinical Study Healthcare professional	Pneumonia Grade 3	28	(1) PRALSETINIB (S)  (2) ACETYLCYSTEINE (T)  (3) AMBROXOL HYDROCHLORIDE (T)  (4) METHYL PREDNISOLONE SODIUM SUCCINATE (T)  (5) IMIPENEM (T)  (6) CILASTATIN SODIUM (T)  (7) SULFAMETHOXAZOLE\TRIME THOPRIM (T)	Dose interrupted Positive Unknown Recovered/Resolved
2724735 59 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Appendicitis Grade 3	71	(1) PRALSETINIB (S)  (2) ONDANSETRON (C)  (3) PROCHLORPERAZINE (C)  (4) POTASSIUM PHOSPHATE (C)  (5) AMOXICILLIN\CLAVULANATE POTASSIUM (C)  (6) VANCOMYCIN (T)	N/A N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(7) CEFEPIME (T)  (8) METRONIDAZOLE (T)	
2733259 62 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Diverticulitis Grade 3	450	(1) PRALSETINIB (S)  (2) PARACETAMOL (C)  (3) ASCORBIC ACID (C)  (4) CETIRIZINE HYDROCHLORIDE (C)  (5) LORAZEPAM (C)  (6) OMEPRAZOLE (C)  (7) CURCUMA LONGA (C)  (8) POTASSIUM GLUCONATE (C)	Dose interrupted Positive N/A Recovered/Resolved
2775469 53 Female UNITED KINGDOM Clinical Study Healthcare professional	Urinary tract infection Grade 3	766	(1) PRALSETINIB (S)	Dose not changed N/A N/A Recovered/Resolved
2791119 52 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Appendicitis Grade 3	25	(1) PRALSETINIB (S)  (2) SENNA SPP. (C)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
2794008 59 Male UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Sepsis Grade 3	266	(1) PRALSETINIB (S)  (2) KETOROLAC TROMETHAMINE (C)  (3) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)	NR Unknown N/A Recovered/Resolved
2794401 63 Female UNITED STATES OF AMERICA Clinical Study Healthcare professional	Sepsis  Pneumonia Grade 3  Grade 3	20  43	(1) PRALSETINIB (S)  (2) PARACETAMOL (C)  (3) ACETYLSALICYLIC ACID (C)  (4) ERGOCALCIFEROL (C)  (5) GABAPENTIN (C)  (6) LIDOCAINE (C)  (7) TIZANIDINE (C)  (8) ONDANSETRON (C)  (9) MACROGOL (C)  (10) OXYCODONE (C)  (11) PROCHLORPERAZINE (C)  (12) FLUTICASONE FUROATE\VILANTEROL TRIFENATATE (C)	NR  NR Unknown  Unknown N/A  N/A Recovered/Resolved  Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time To Onset (in Days)	Drug Type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(13) ATORVASTATIN (C) (14) ENOXAPARIN (C) (15) VANCOMYCIN (T) (16) PIPERACILLIN (T) (17) AZITHROMYCIN (T) (18) MEROPENEM (T) (19) BUDESONIDE (T) (20) AMPICILLIN SODIUM\SULBACTAM SODIUM (T) (21) LEVOFLOXACIN (T)	
2796571 63 Female CHINA Clinical Study Healthcare professional	Upper respiratory tract infection  Grade 3	229	(1) PRALSETINIB (S)	Dose interrupted positive Unknown Recovered/Resolved

**Appendix 7    Listings of Cases Lacking Information on Severity Grades  
for Infection Events from the Company Safety Database (N=249)**

**Category B (N=26)**

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Decchallenge Rechallenge Event Outcome
2767869 43 Female UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Post procedural infection NR	NR	(1) PRALSETINIB (S)	Dose not changed NA NA Not Resolved
2800655 68 Female UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Pneumonia NR	154	(1) PRALSETINIB (S)  (2) COLECALCIFEROL (C)  (3) FAMOTIDINE (C)  (4) LEVOTHYROXINE (C)  (5) MORPHINE (C)  (6) NAPROXEN (C)  (7) OXYCODONE (C)  (8) PROCHLORPERAZINE (C)  (9) SENNOSIDE A+B (C)  (10) SALBUTAMOL (C)  (11) CANNABIDIOL (C)  (12) LORATADINE (C)	Drug withdrawn NA NA Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(13) DOCUSATE SODIUM (C) (14) ROFLUMILAST (C) (15) CICLESONIDE (C) (16) TIOTROPIUM (C) (17) MACROGOL 3350 (C) (18) BENZOCAINE (C) (19) FUROSEMIDE (C) (20) POTASSIUM CHLORIDE (C) (21) PREDNISONE (C) (22) LOPERAMIDE (C) (23) IPRATROPIUM/SALBUTAMOL (C) (24) OXYGEN (C) (25) METHYLPREDNISOLONE SODIUM SUCCINATE (C) (26) BENZOCAINE (C)	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(27) PIPERACILLIN/TAZOBACTAM (C)  (28) VANCOMYCIN (C)  (29) BENZONATATE (C)  (30) ENOXAPARIN SODIUM (T)  (31) DOXYCYCLINE (T)  (32) LEVOFLOXACIN (T)  (33) CEFTRIAXONE (T)  (34) AZITHROMYCIN (T)  (35) PREDNISONE (T)  (36) METRONIDAZOLE (T)	
2817246 Not reported Female UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)  (2) PREDNISONE (C)	Dose not changed NA NA Resolved
2823365 34 Male	Oral infection NR	78	(1) PRALSETINIB (S)	Dose interrupted Negative N/A

<b>AER No</b> <b>Age in Years</b> <b>Sex</b> <b>Country</b> <b>Primary Source</b> <b>Reporter Type</b>	<b>Event Preferred Term of Interest*</b> <b>Severity Grade</b>	<b>Time to Onset (in days)</b>	<b>Drug type (All)</b>	<b>Action Taken</b> <b>Decchallenge</b> <b>Rechallenge</b> <b>Event Outcome</b>
UNITED STATES OF AMERICA Spontaneous Healthcare Professional				Not Recovered/Not Resolved/Ongoing
2826988 77 Male SWITZERLAND Non-Interventional Study/Program Healthcare Professional	Pneumonia NR	NR	(1) PRALSETINIB (S)  (2) TORASEMIDE (S)  (3) RIVAROXABAN (C)  (4) OLMESARTAN (C)  (5) AMLODIPINE (C)  (6) RIVAROXABAN (C)  (7) MOXIFLOXACIN (T)  (8) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (9) PREDNISOLONE (T)	Drug withdrawn NA NA NR
2869377 53 Male FRANCE Non-Interventional Study/Program Healthcare Professional	Pneumonia NR	NR	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) PREDNISOLONE (C)  (4) FOLIC ACID (C)  (5) ATORVASTATIN (C)  (6) CALCIUM	Drug withdrawn NA NA Recovering/Resolving

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			CARBONATE (C) (7) PARACETAMOL (C) (8) LACTULOSE (C) (9) ESCITALOPRAM (C) (10) GABAPENTIN (C) (11) GLICLAZIDE (C) (12) LEVOTHYROXINE (C) (13) MACROGOL 3350\POTASSIUM CHLORIDE\SODIUM BICARBONATE\SODIUM CHLORIDE (C) (14) OXYCODONE (C) (15) OXYCODONE HYDROCHLORIDE (C) (16) PANTOPRAZOLE (C) (17) QUETIAPINE (C) (18) OXAZEPAM (C) (19) ALFACALCIDOL (C) (20) COLECALCIFEROL	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			(C)  (21) CEFOTAXIME (C)  (22) INSULIN ASPART (C)  (23) ENOXAPARIN SODIUM (C)  (24) SODIUM CHLORIDE (C)  (25) HEPARIN (C)  (26) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (C)  (27) METHYLSPREDNISOLONE SODIUM SUCCINATE (C)  (28) ESOMEPRAZOLE (C)	
2901843 76 Male JAPAN Clinical Study Healthcare Professional	Bacteraemia NR	22	(1) PRALSETINIB (S)  (2) THYROID (C)  (3) CALCIUM CARBONATE (C)  (4) ENALAPRIL MALEATE (C)  (5) CLOBETASOL	Dose interrupted Positive NA Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
			PROPIONATE (C) (6) HYDROCORTISONE BUTYRATE (C) (7) WHITE SOFT PARAFFIN (C) (8) BETAMETHASONE BUTYRATE PROPIONATE (C) (9) LORATADINE (C) (10) GUAIAZULENE (C) (11) DICLOFENAC SODIUM (C) (12) HEPARINOID (C) (13) TRICHLORMETHIAZIDE (C) (14) NIFEDIPINE (C) (15) MAGNESIUM OXIDE (C) (16) PREDNISOLONE (T) (17) PIPERACILLIN SODIUM\TAZOBACTAM	

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Decalibrate Rechallenge Event Outcome
			SODIUM (T)  (18) CEFEPIME (T)	
2973364 57 Male ITALY Non-Interventional Study/Program Healthcare Professional	Infected skin ulcer NR	NR	(1) PRALSETINIB (S)	NR Unknown N/A Not Reported
3018332 64.2055 Female RUSSIAN FEDERATION Non-Interventional Study/Program Healthcare Professional	COVID-19 NR	NR	(1) PRALSETINIB (S)  (2) CALCITONIN (C)  (3) LEVOTHYROXINE SODIUM (C)  (4) CIPROFLOXACIN (T)	Dose interrupted Unknown Unknown Not Reported
3028727 57 Male ITALY Non-Interventional Study/Program Healthcare Professional	COVID-19 pneumonia NR	391	(1) PRALSETINIB (S)	Dose interrupted Pos NA Resolved
3059430 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	Drug withdrawn Negative NA Unknown

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3111943 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	123	(1) PRALSETINIB (S)	Dose interrupted  Positive N/A Recovering/Resolving
3176631 61 Female CHINA Non-Interventional Study/Program Healthcare Professional	Pneumonia NR	76	(1) PRALSETINIB (S)	Dose interrupted  Negative N/A Not Recovered/Not Resolved/Ongoing
3194144 84.3123 Male UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	Cellulitis NR	10	(1) PRALSETINIB (S)  (2) TAMSULOSIN (C)  (3) RIVAROXABAN (C)  (4) SPIRONOLACTONE (C)  (5) FUROSEMIDE (C)  (6) DEXAMETHASONE (C)  (7) IPRATROPIUM BROMIDE (C)  (8) PRAVASTATIN (C)  (9) METOPROLOL (C)	NR Unknown N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Decchallenge Rechallenge Event Outcome
			(10) AMOXICILLIN (C)	
3195341 55 Female FRANCE Spontaneous Non-healthcare professional	Pneumonia cytomegaloviral  Pneumocystis jirovecii pneumonia NR  NR	150  150	(1) PRALSETINIB (S)  (2) PREDNISONE (S)  (3) ZOLPIDEM TARTRATE (C)  (4) CALCIUM CARBONATE\COLECALCI FEROL (C)  (5) GABAPENTIN (C)  (6) OXAZEPAM (C)  (7) OMEPRAZOLE (C)  (8) LEVETIRACETAM (C)	Dose interrupted  Dose interrupted  Positive  Positive N/A  N/A Recovering/Resolving  Recovering/Resolving
3205949 60 Female NETHERLANDS Non-Interventional Study/Program Healthcare Professional	Pneumonia NR	NR	(1) PRALSETINIB (S)  (2) AMOXICILLINCLAVULAN ATE POTASSIUM (T)	NR Unkown N/A Not Reported
3219847 77 Male UNITED STATES OF AMERICA Spontaneous	Hepatitis B  Pneumonia NR  NR	NR  NR	(1) PRALSETINIB (S)  (2) TENOFOVIR ALAFENAMIDE FUMARATE (S)	Dose interrupted  NR Unkown  Unknown Unknown

<b>AER No</b> <b>Age in Years</b> <b>Sex</b> <b>Country</b> <b>Primary Source</b> <b>Reporter Type</b>	<b>Event Preferred Term of Interest*</b> <b>Severity Grade</b>	<b>Time to Onset (in days)</b>	<b>Drug type (All)</b>	<b>Action Taken</b> <b>Decchallenge</b> <b>Rechallenge</b> <b>Event Outcome</b>
Non-healthcare professional				Unknown Not Reported  Not reported
3255319 81 Male CHINA Literature Spontaneous Non-healthcare professional	Pneumonia cryptococcal  Lung abscess NR  NR	144  234	(1) PRALSETINIB (S)  (2) ALECTINIB (S)  (3) FLUCONAZOLE (T)  (4) VORICONAZOLE (T)  (5) BIAPENEM (T)  (6) CISPLATIN (T)  (7) BEVACIZUMAB (T)  (8) MITOMYCIN (T)	NR  NR  Unkown  Unknown N/A  N/A Recovering/Resolving  Recovering/Resolving
3337315 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	121	(1) PRALSETINIB (S)	Dose not changed N/A N/A Recovered/Resolved
3349170 61 Male CHINA Spontaneous	Infection NR	NR	(1) PRALSETINIB (S)	Dose interrupted  Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Non-healthcare professional				
3430100 44 Male CHINA Literature Spontaneous Non-healthcare professional	Pulmonary tuberculosis  Tuberculous pleurisy NR  NR	212  NR	(1) PRALSETINIB (S)  (2) ETHAMBUTOL DIHYDROCHLORIDE (T)  (3) PYRAZINAMIDE (T)  (4) MOXIFLOXACIN (T)	Dose interrupted  Dose interrupted  Positive  Positive Unknown  Unknown  Recovering/Resolving  Recovering/Resolving
3467781 Not reported Male IRELAND Spontaneous Healthcare Professional	Fungal foot infection NR	NR	(1) PRALSETINIB (S)	Dose interrupted Unknown N/A Not Reported
3517666 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Liver abscess NR	2	(1) PRALSETINIB (S)  (2) NIFEDIPINE (C)  (3) INSULIN NOS (C)	Dose interrupted Positive Unknown Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3528428 43 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pulmonary tuberculosis NR	173	(1) PRALSETINIB (S)  (2) VORICONAZOLE (T)	Dose not changed N/A N/A Recovering/Resolving
10000040960 Not reported Male CHINA Spontaneous Non-healthcare professional	Fungal infection  Bacterial infection NR  NR	37  7	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not Reported  Not Reported
3065813 64 Female ITALY Non-Interventional Study/Program Healthcare Professional	Sepsis  Abdominal abscess  Grade 5  NR	NR  NR  NR	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (S)  (3) BISOPROLOL (S)  (4) FUROSEMIDE (S)  (5) METHYLSPREDNISOLONE (S)  (6) APIXABAN (S)  (7) PANTOPRAZOLE SODIUM SESQUIHYDRATE (C)	N/A  N/A N/A  N/A N/A  N/A Fatal  Not Reported

**Category C (N=223)**

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
2727399 67 Female UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Cellulitis NR	12	(1) PRALSETINIB (S)	Dose interrupted Pos NA Resolved
2769291 67 Female UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Pneumonia NR	84	(1) PRALSETINIB (S)	Drug withdrawn Unknown N/A Not Recovered/Not Resolved/Ongoing
2775653 72 Male UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Infection susceptibility increased NR	85	(1) PRALSETINIB (S)	Dose not changed NA NA Not Resolved
2776893 37 Female UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Hepatic infection NR	16	(1) PRALSETINIB (S)	Dose interrupted Neg NA Not Resolved
2783639 Not reported Male UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Cellulitis NR	NR	(1) PRALSETINIB (S)	Dose interrupted Unk NA Unknown
2785349 85 Male UNITED STATES OF AMERICA	Enterococcal infection Urinary tract infection NR NR	26 26	(1) PRALSETINIB (S)	Dose interrupted  Dose interrupted Negative  Negative

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Spontaneous Non-healthcare professional				N/A  N/A Not Recovered/Not Resolved/Ongoing  Not Recovered/Not Resolved/Ongoing
2796604 36 Female UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Liver abscess NR	33	(1) PRALSETINIB (S)	Dose not changed NA NA Not Resolved
2802310 43 Male UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Pneumonia NR	0	(1) PRALSETINIB (S)	Dose interrupted Neg NA Not Resolved
2802446 43 Male UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Pneumonia NR	24	(1) PRALSETINIB (S)	Dose interrupted Unk NA Unknown
2802504 Not reported Male UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Prostate infection NR	NR	(1) PRALSETINIB (S)  (2) LEVOFLOXACIN (T)	NR Unknown N/A Not Resolved
2807851 43 Male UNITED STATES OF AMERICA	Pneumonia NR	53	(1) PRALSETINIB (S)	Dose interrupted Unk NA Unknown

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Spontaneous Healthcare Professional				
2812730 43 Female UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Infection NR	0	(1) PRALSETINIB (S)	Dose not changed NA NA Not Recovered/Not Resolved/Ongoing
2818321 84 Male UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Urosepsis  Urinary tract infection  Sepsis NR  NR  NR	98  98  98	(1) PRALSETINIB (S)	Drug withdrawn  Dose not changed  Dose not changed Negative  NA  NA NA  NA NA NA  NA Not Recovered/Not Resolved/Ongoing  Not Recovered/Not Resolved/Ongoing  Recovered/Resolved
2831537 67 Male UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Pneumonia NR	181	(1) PRALSETINIB (S)	Dose not changed NA NA Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
2832829 46 Female UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	COVID-19  Pneumonia NR  NR	25	(1) PRALSETINIB (S)  (2) CYCLOBENZAPRINE HYDROCHLORIDE (T)	Dose not changed  Dose not changed NA  NA NA  NA Unknown  Unknown
2842714 Not reported Male UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Staphylococcal infection NR	NR	(1) PRALSETINIB (S)  (2) TAMSULOSIN (C)  (3) METOPROLOL (C)  (4) AMLODIPINE (C)  (5) FAMOTIDINE (C)  (6) FISH OIL (C)	Dose not changed NA NA Not Reported
2844803 61	Herpes zoster NR	177	(1) PRALSETINIB (S)	Dose interrupted Neg

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Female UNITED STATES OF AMERICA Spontaneous Non-healthcare professional				NA Not Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
2849379 Not reported Female UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Infection NR	NR	(1) PRALSETINIB (S)  (2) AMLODIPINE (C)  (3) FUROSEMIDE (C)  (4) LEVOTHYROXINE (C)  (5) LISINOPRIL (C)  (6) MAGNESIUM (C)  (7) METOPROLOL (C)  (8) MIDODRINE (C)  (9) DOCOSAHEXAENOIC ACID\EICOSAPENTAENOIC ACID (C)  (10) OXYCODONE (C)  (11) PANTOPRAZOLE (C)  (12) MACROGOL 3350 (C)  (13) SENNA SPP. (C)  (14) WARFARIN (C)	Dose not changed NA NA Not reported

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
2866603 Not reported Female UNITED STATES OF AMERICA Spontaneous Healthcare Professional	Oral candidiasis NR	4	(1) PRALSETINIB (S)	Dose interrupted Pos NA Resolved
2881497 48 Male CHINA Spontaneous Healthcare Professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	Dose not changed NA NA Unknown
2882115 85 Female UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	Urinary tract infection bacterial NR	NR	(1) PRALSETINIB (S)  (2) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)	NR Unknown N/A Unknown
2888383 70 Male CHINA Spontaneous Healthcare Professional	Sepsis NR	24	(1) PRALSETINIB (S)	Drug withdrawn Positive NA Recovered/Resolved
2892868 79 Male INDIA Non-Interventional Study/Program Non-healthcare professional	Urinary tract infection NR	43	(1) PRALSETINIB (S)	Drug withdrawn NA NA NR
2902745 73 Male CHINA	Pneumonia NR	124	(1) PRALSETINIB (S)	Drug withdrawn NA NA Unknown

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Spontaneous Non-healthcare professional				
2904489 58 Female CHINA Spontaneous Non-healthcare professional	Pneumonia NR	60	(1) PRALSETINIB (S)	Drug withdrawn Unk NA Unknown
2908467 75 Female CHINA Spontaneous Non-healthcare professional	Nasopharyngitis NR	64	(1) PRALSETINIB (S)	Dose interrupted NA NA Unknown
2911785 Not reported Female PERU Non-Interventional Study/Program Healthcare Professional	Cellulitis NR	NR	(1) PRALSETINIB (S)  (2) GABAPENTIN (C)  (3) VITAMIN B COMPLEX (C)	modification of dose NA NA NR
2918762 70 Male CHINA Non-Interventional Study/Program Healthcare Professional	Sepsis NR	24	(1) PRALSETINIB (S)  (2) TISLELIZUMAB (C)	Drug withdrawn Positive NA Recovered/Resolved
2919095 52 Female	Pneumonia NR	150	(1) PRALSETINIB (S)	Drug withdrawn Unk

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
CHINA Non-Interventional Study/Program Non-healthcare professional				NA Unknown
2919955 46 Female CHINA Spontaneous Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	NR Unknown N/A Unknown
2920549 59 Female CHINA Spontaneous Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	Dose interrupted Unk NA Unknown
2920757 Not reported Not reported UNITED KINGDOM Non-Interventional Study/Program Non-healthcare professional	Bacterial sepsis NR	NR	(1) PRALSETINIB (S)	NR Unknown N/A Not Reported
2929798 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Nasopharyngitis NR	250	(1) PRALSETINIB (S)	Dose not changed NA NA Unknown

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
2941881 59 Female CHINA Spontaneous Non-healthcare professional	Nasopharyngitis  Infection NR  NR	NR	(1) PRALSETINIB (S)  (2) FLUTICASONE PROPIONATE\ SALMETEROL XINAFOATE (T)	Dose interrupted  Dose interrupted Positive  Positive NA  NA Recovering/Resolving  Recovering/Resolving
2946575 57 Female KOREA, REPUBLIC OF Non-Interventional Study/Program Non-healthcare professional	Pyelonephritis  Lymph node tuberculosis NR  NR	136  51	(1) PRALSETINIB (S)  (2) ISONIAZID (C)  (3) ETHAMBUTOL (C)	NR  NR Unknown  Unknown N/A  N/A Resolved  Resolved
2951571 Not reported Not reported CHINA Spontaneous Non-healthcare professional	Pneumocystis jirovecii pneumonia NR	31	(1) PRALSETINIB (S)  (2) AMOXICILLIN (T)	Dose reduced Unknown Unknown Unknown
2954830 Not reported Male	Pneumonia NR	24	(1) PRALSETINIB (S)	Dose not changed NA

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
CHINA Spontaneous Non-healthcare professional				NA Not Resolved
2955349 79 Female UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	NR Unknown N/A Resolving
2959905 60 Female CHINA Spontaneous Non-healthcare professional	Pneumocystis jirovecii pneumonia NR	82	(1) PRALSETINIB (S)	Drug withdrawn Negative NA Not Recovered/Not Resolved/Ongoing
2963526 56 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	29	(1) PRALSETINIB (S)	Dose not changed NA NA Unknown

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
2963946 59 Female NETHERLANDS Non-Interventional Study/Program Non-healthcare professional	Urinary tract infection NR	84	(1) PRALSETINIB (S)  (2) COLOSTRUM\HYETELLOSE\LACTOPER OXIDASE\MALTOSIDE\SODIUM FLUOROPHOSPHATE\SORBITOL\XYLIT OL (C)  (3) CAFFEINE\PARACETAMOL (C)  (4) ONDANSETRON (C)  (5) SULFAMETHOXAZOLE\TRIMETHOPRIM (C)  (6) PARACETAMOL (C)	N/A N/A N/A Recovering/Resolving

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
2968652 68 Female PERU Non-Interventional Study/Program Healthcare Professional	Pulmonary sepsis  Pneumonia NR  NR		(1) PRALSETINIB (S)	NR  NR Unknown  Unknown N/A  N/A Not Recovered/Not Resolved/Ongoing  Not Reported
2974208 75 Female ITALY Spontaneous Non-healthcare professional	Listeriosis  Bronchopulmonary aspergillosis  Enterococcal sepsis  Pneumonia cytomegaloviral  Escherichia sepsis NR  NR  NR  NR	18  18  18  18  18	(1) PRALSETINIB (S)	Drug withdrawn Neg NA Not Resolved  Not Resolved  Not Resolved  Not Resolved  Not Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
2974550 65 Female ITALY Non-Interventional Study/Program Healthcare Professional	Device related sepsis NR	NR	(1) PRALSETINIB (S)  (2) PANTOPRAZOLE (C)  (3) ATENOLOL (C)  (4) OXYCODONE (C)  (5) DULOXETINE (C)  (6) AMLODIPINE (C)  (7) NADROPARIN CALCIUM (C)  (8) LEVOSULPIRIDE (C)  (9) CYANOCOBALAMIN (C)  (10) THIAMAZOLE (C)	Drug interrupted NA NA Unknown

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
2974677 Not reported Not reported CHINA Spontaneous Non-healthcare professional	Pneumonia NR	14	(1) PRALSETINIB (S)	Dose interrupted NEg NA Not Resolved
2974851 65 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	182	(1) PRALSETINIB (S)	NR Unkown N/A Not Recovered/Not Resolved/Ongoing
2977940 78 Female CHINA Spontaneous Non-healthcare professional	Viral infection NR	34	(1) PRALSETINIB (S)	Dose not changed NA NA Resolving
2982419 72 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	12	(1) PRALSETINIB (S)	Drug withdrawn Positive NA Recovering/Resolving
2982421 45 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	61	(1) PRALSETINIB (S)	Dose interrupted Pos Neg Resolving
2987198 50 Male KOREA, REPUBLIC OF Non-Interventional Study/Program Non-healthcare professional	Chronic sinusitis NR	202	(1) PRALSETINIB (S)	NR Unkown N/A Recovered/Resolved
2988507 34 Female CHINA	Pneumonia NR	249	(1) PRALSETINIB (S)	NR Unknown N/A Not Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Non-Interventional Study/Program Non-healthcare professional				
2995238 54 Female KOREA, REPUBLIC OF Non-Interventional Study/Program Healthcare Professional	Pyelonephritis acute NR	691	(1) PRALSETINIB (S)	NR Unknown N/A Recovered/Resolved
2998059 82 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	330	(1) PRALSETINIB (S)	Dose not changed NA NA Resolving
2998101 Not reported Male ISRAEL Spontaneous Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	NR Unknown N/A Not Reported
2998731 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Lymph node tuberculosis NR	NR	(1) PRALSETINIB (S)	NR Unknown N/A Unknown
3006308 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	137	(1) PRALSETINIB (S)	Dose interrupted Pos NA Resolving
3008928 59 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	75	(1) PRALSETINIB (S)	Drug interrupted Negative NA Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3009926 77 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	Dose not changed NA NA Not Resolved
3028355 66 Male NEW ZEALAND Spontaneous Healthcare Professional	Lower respiratory tract infection  Herpes zoster NR NR	46 46	(1) PRALSETINIB (S)  (2) AMOXICILLIN(CLAVULANATE POTASSIUM (T)  (3) VALACICLOVIR (T)	NR  NR Unknown N/A Resolved  Resolved
3033200 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	29	(1) PRALSETINIB (S)	Dose interrupted Neg NA Not Resolved
3038753 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Appendicitis  Tuberculosis NR NR	122 168	(1) PRALSETINIB (S)	NR  NR Unknown  Unknown N/A  N/A Not Recovered/Not

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
				Resolved/Ongoing  Not Recovered/Not Resolved/Ongoing
3041704 Not reported Not reported SPAIN Non-Interventional Study/Program Non-healthcare professional	COVID-19 pneumonia NR	NR	(1) PRALSETINIB (S)	NR Unknown N/A Not Reported
3042661 Not reported Male CANADA Non-Interventional Study/Program Healthcare Professional	Pneumonia legionella NR	NR	(1) PRALSETINIB (S)	NR Unknown N/A Not Reported
3043347 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	52	(1) PRALSETINIB (S)	Dose interrupted Neg NA Not Resolved
3048742 Not reported Not reported INDIA Non-Interventional Study/Program Healthcare Professional	Tuberculosis NR	NR	(1) PRALSETINIB (S)	NR Unkown N/A Not Reported
3053470 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	63	(1) PRALSETINIB (S)	Drug withdrawn Positive NA Recovering/Resolving
3059596 Not reported Not reported CHINA Non-Interventional	Pneumonia NR	93	(1) PRALSETINIB (S)	Drug withdrawn Positive NA Recovering/Resolving

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Study/Program Non-healthcare professional				
3060681 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Herpes zoster NR	34	(1) PRALSETINIB (S)	Dose not changed NA NA Not Recovered/Not Resolved/Ongoing
3062048 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	42	(1) PRALSETINIB (S)	Dose not changed NA NA Not Recovered/Not Resolved/Ongoing
3063921 69 Male SPAIN Non-Interventional Study/Program Healthcare Professional	Spinal cord abscess NR	NR	(1) PRALSETINIB (S)	Drug interrupted NA NA Recovering/Resolving
3064070 42 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	120	(1) PRALSETINIB (S)  (2) GEFITINIB (C)	Dose not changed NA NA Not Recovered/Not Resolved/Ongoing
3076615 44 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia bacterial NR	0	(1) PRALSETINIB (S)	Dose not changed NA NA Unknown
3081192 Not reported Not reported CHINA	Pneumonia NR	276	(1) PRALSETINIB (S)	Dose not changed NA NA Recovering/Resolving

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Non-Interventional Study/Program Non-healthcare professional				
3082744 Not reported Male UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Arthritis bacterial NR	NR	(1) PRALSETINIB (S)	Drug withdrawn NA NA Unknown
3083018 56 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	270	(1) PRALSETINIB (S)	Drug withdrawn Negative NA Not Recovered/Not Resolved/Ongoing
3087488 64 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	213	(1) PRALSETINIB (S)	Dose not changed NA NA Recovering/Resolving
3092325 65 Male UNITED STATES OF AMERICA Non-Interventional Study/Program Healthcare Professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	NR Unkown N/A Not Reported
3093310 67 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	93	(1) PRALSETINIB (S)	Dose not changed NA NA Recovering/Resolving
3094935 56 Female CHINA Non-Interventional	Pneumonia NR	55	(1) PRALSETINIB (S)	N/A N/A N/A Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Study/Program Non-healthcare professional				
3096494 62 Male ITALY Non-Interventional Study/Program Healthcare Professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	Drug withdrawn NA NA NR
3097721 67 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	93	(1) PRALSETINIB (S)	Drug withdrawn NA NA Recovering/Resolving
3100285 66 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)  (2) OSIMERTINIB (C)	NR Unknown N/A Recovering/Resolving
3100527 42 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	206	(1) PRALSETINIB (S)	Dose not changed NA NA Not Recovered/Not Resolved/Ongoing
3105028 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	69	(1) PRALSETINIB (S)	Dose not changed NA NA Recovering/Resolving
3116576 Not reported Not reported	Pneumonia NR	328	(1) PRALSETINIB (S)	Dose not changed NA

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
CHINA Non-Interventional Study/Program Non-healthcare professional				NA Recovering/Resolving
3118408 55 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	51	(1) PRALSETINIB (S)	Dose not changed NA NA Not Recovered/Not Resolved/Ongoing
3120942 57 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	69	(1) PRALSETINIB (S)	NR Unkown N/A Not Recovered/Not Resolved/Ongoing
3121806 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	NR Unkown N/A Unknown
3122985 63 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	151	(1) PRALSETINIB (S)	Dose reduced Negative NA Not Recovered/Not Resolved/Ongoing
3126681 34 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	71	(1) PRALSETINIB (S)	Dose reduced Negative NA Not Recovered/Not Resolved/Ongoing
3126688 71 Female CHINA Non-Interventional	Abdominal infection  Pneumonia NR	118  118	(1) PRALSETINIB (S)	NR  NR

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Study/Program Non-healthcare professional	NR			Unknown  Unknown N/A  N/A Not Recovered/Not Resolved/Ongoing  Not Recovered/Not Resolved/Ongoing
3127587 50 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Paronychia  Pneumonia NR  NR	12  89	(1) PRALSETINIB (S)	Dose not changed  Dose not changed N/A  N/A  N/A  N/A  N/A  Not Recovered/Not Resolved/Ongoing  Not Recovered/Not Resolved/Ongoing
3127600 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	87	(1) PRALSETINIB (S)	Drug withdrawn Positive NA Recovering/Resolving
3132376 42 Male CHINA	Pneumonia NR	42	(1) PRALSETINIB (S)	Drug withdrawn Neg NA Not Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Non-Interventional Study/Program Non-healthcare professional				
3133126 73 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	38	(1) PRALSETINIB (S)	Drug withdrawn Neg NA Not Resolved
3134079 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	196	(1) PRALSETINIB (S)	Dose interrupted Pos Unk Resolving
3134811 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	66	(1) PRALSETINIB (S)	Dose interrupted Neg NA Not Resolved
3134819 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	88	(1) PRALSETINIB (S)	Dose not changed NA NA Resolving
3142009 47 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	36	(1) PRALSETINIB (S)	Dose interrupted Pos NA Resolving
3142878 60 Female NETHERLANDS Non-Interventional	Pneumonia NR	192	(1) PRALSETINIB (S)	NR Unknown N/A Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Study/Program Non-healthcare professional				
3146495 67 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	304	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not Recovered/Not Resolved/Ongoing
3146496 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	108	(1) PRALSETINIB (S)	Dose interrupted Pos NA Resolving
3148581 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Herpes zoster NR	30	(1) PRALSETINIB (S)	Dose interrupted Pos Unk Resolving
3151896 69 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	58	(1) PRALSETINIB (S)	Drug withdrawn Pos NA Resolving
3160540 67 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	61	(1) PRALSETINIB (S)	Drug withdrawn Neg NA Not Resolved
3165945 46 Female CHINA Non-Interventional Study/Program Healthcare Professional	Pneumonia NR	188	(1) PRALSETINIB (S)	Dose not changed nA NA Not Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3168019 Not reported Not reported CHINA Spontaneous Non-healthcare professional	Pneumonia fungal  Pneumonia viral NR  NR	NR  NR	(1) PRALSETINIB (S)	Drug withdrawn  Drug withdrawn Unk NA Unknown  Unknown
3168844 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	24	(1) PRALSETINIB (S)	Dose not changed NA NA Resolving
3171889 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	74	(1) PRALSETINIB (S)	Dose reduced Positive NA Resolving
3171993 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	69	(1) PRALSETINIB (S)	Dose interrupted Pos NA Resolving
3173154 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	76	(1) PRALSETINIB (S)	Drug withdrawn Pos NA Resolving
3173160 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	22	(1) PRALSETINIB (S)	DOse interrupted Pos NA Resolving

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3178664 60 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	352	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not Recovered/Not Resolved/Ongoing
3187200 Not reported Not reported CHINA Non-Interventional Study/Program Healthcare Professional	Pneumonia NR	49	(1) PRALSETINIB (S)	Dose interrupted Positive Negative Recovering/Resolving
3189683 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	NR Unknown N/A Not Reported
3193091 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	76	(1) PRALSETINIB (S)	Dose not changed N/A N/A Recovering/Resolving
3196805 Not reported Not reported CHINA Non-Interventional Study/Program Healthcare Professional	Pneumonia NR	30	(1) PRALSETINIB (S)	Dose interrupted  Negative N/A Not Recovered/Not Resolved/Ongoing
3200399 63 Female CHINA Spontaneous Non-healthcare professional	Pneumocystis jirovecii pneumonia NR	153	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not Recovered/Not Resolved/Ongoing
3208819 54 Male	Infection NR	NR	(1) PRALSETINIB (S)	Dose not changed N/A

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional				N/A Not Reported
3210287 45 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	100	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not Recovered/Not Resolved/Ongoing
3210415 79 Male CHILE Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	NR Unknown N/A Not Reported
3211239 Not reported Female UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Salmonellosis NR	NR	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not Reported
3213783 Not reported Not reported FINLAND Spontaneous Non-healthcare professional	Infection NR	NR	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not Reported
3221280 35 Female CHINA Non-Interventional Study/Program Healthcare Professional	Pneumonia NR	0	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not Recovered/Not Resolved/Ongoing
3224251 Not reported Not reported CHINA Non-Interventional	Pneumonia NR	NR	(1) PRALSETINIB (S)	NR Unknown N/A Not Reported

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Study/Program Non-healthcare professional				
3224437 68 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	Dose interrupted Negative N/A Not Recovered/Not Resolved/Ongoing
3224977 47 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	37	(1) PRALSETINIB (S)	Dose interrupted  Negative N/A Not Recovered/Not Resolved/Ongoing
3224992 61 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	308	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not Recovered/Not Resolved/Ongoing
3225565 62 Female UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Urinary tract infection NR	NR	(1) PRALSETINIB (S)	NR Unkown N/A Not Reported
3226435 83 Male CHINA Spontaneous Non-healthcare professional	Pneumonia NR	90	(1) PRALSETINIB (S)	Dose interrupted  Positive N/A Recovering/Resolving
3227527 39 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	440	(1) PRALSETINIB (S)	Dose interrupted Positive Negative Recovering/Resolving

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3230757 Not reported Female PERU Non-Interventional Study/Program Non-healthcare professional	Cystitis NR	NR	(1) PRALSETINIB (S)  (2) PIPERACILLIN\TAZOBACTAM (T)	NR Unknown N/A Not Reported
3243699 64 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	30	(1) PRALSETINIB (S)	NR Unknown N/A Not reported  Not reported
3251309 64 Male CHINA Non-Interventional Study/Program Healthcare Professional	Pneumonia fungal NR	495	(1) PRALSETINIB (S)	Dose interrupted Positive Unknown Recovered/Resolved
3274607 76 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	50	(1) PRALSETINIB (S)	Dose interrupted Positive Negative Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3281243 60 Female NETHERLANDS Non-Interventional Study/Program Healthcare Professional	Urinary tract infection  NR	340	(1) PRALSETINIB (S)  (2) CEFTRIAXONE (T)  (3) ONDANSETRON (T)	NR Unkown N/A Not Recovered/Not Resolved/Ongoing
3286439 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	COVID-19 pneumonia  Pneumonia NR  NR	49  129	(1) PRALSETINIB (S)	Dose interrupted  Dose interrupted  Positive  Positive Unknown  Unknown  Recovered/Resolved  Recovered/Resolved
3291325 76 Female UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	COVID-19 NR	NR	(1) PRALSETINIB (S)	NR Unknown N/A Not reported
3295286 Not reported Male CHINA	Pulmonary tuberculosis NR	211	(1) PRALSETINIB (S)	Dose not changed N/A N/A Recovering/Resolving

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Non-Interventional Study/Program Healthcare Professional				
3298501 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia viral NR	378	(1) PRALSETINIB (S)	Dose not changed N/A N/A Recovering/Resolving
3298840 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	498	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not Recovered/Not Resolved/Ongoing
3300012 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	131	(1) PRALSETINIB (S)	Dose not changed N/A N/A Recovered/Resolved
3300142 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	261	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not Recovered/Not Resolved/Ongoing
3300849 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	455	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not Recovered/Not Resolved/Ongoing
3301382 Not reported Female CHINA Non-Interventional	Pneumonia bacterial NR	594	(1) PRALSETINIB (S)	Dose interrupted Unknown N/A  Not reported

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Study/Program Non-healthcare professional				
3301413 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	730	(1) PRALSETINIB (S)  (2) ALBUMIN HUMAN (T)	Dose not changed N/A N/A Recovering/Resolving
3308634 49 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	60	(1) PRALSETINIB (S)	Dose interrupted  Positive N/A Recovering/Resolving
3311852 Not reported Male CHINA Non-Interventional Study/Program Healthcare Professional	Pneumonia NR	100	(1) PRALSETINIB (S)	Dose interrupted Positive N/A Recovering/Resolving
3311910 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pulmonary tuberculosis  NR	118	(1) PRALSETINIB (S)	Dose not changed N/A N/A Recovered/Resolved
3312005 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	354	(1) PRALSETINIB (S)	Dose not changed N/A N/A Recovering/Resolving
3314824 Not reported Male	Pneumonia NR	15	(1) PRALSETINIB (S)	Dose interrupted Positive

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
CHINA Non-Interventional Study/Program Non-healthcare professional				Positive Recovering/Resolving
3317450 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	32	(1) PRALSETINIB (S)	Dose interrupted Positive N/A Recovering/Resolving
3323925 Not reported Female SWITZERLAND Spontaneous Healthcare Professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	N/A N/A N/A NR
3329397 Not reported Male CHINA Non-Interventional Study/Program Healthcare Professional	Pneumonia fungal NR	94	(1) PRALSETINIB (S)	Dose interrupted  Unknown N/A Not reported  Unknown
3329888 70 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	90	(1) PRALSETINIB (S)	Dose interrupted Negative N/A Not Recovered/Not Resolved/Ongoing
3329907 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia viral NR	224	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not reported  Unknown
3332246 Not reported Male CHINA Non-Interventional	Pneumonia NR	825	(1) PRALSETINIB (S)	Dose interrupted  Positive

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Study/Program Non-healthcare professional				N/A Recovered/Resolved
3332358 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	0	(1) PRALSETINIB (S)	Dose not changed N/A N/A Recovering/Resolving
3333031 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	30	(1) PRALSETINIB (S)	Dose not changed N/A N/A Unknown
3335188 71 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	413	(1) PRALSETINIB (S)	Dose interrupted Negative N/A Not Recovered/Not Resolved/Ongoing
3339577 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	202	(1) PRALSETINIB (S)	Dose not changed N/A N/A Recovering/Resolving
3347633 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	117	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not Recovered/Not Resolved/Ongoing
3350871 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Bacterial infection NR	203	(1) PRALSETINIB (S)	Dose interrupted Positive N/A Recovering/Resolving

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3353260 48 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	NR Unknown Unknown Unknown
3363056 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	42	(1) PRALSETINIB (S)	Dose interrupted Negative N/A Not Recovered/Not Resolved/Ongoing
3363172 67 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pulmonary tuberculosis NR	NR	(1) PRALSETINIB (S)	Dose not changed N/A N/A Recovering/Resolving
3373829 75 Male CHINA Spontaneous Non-healthcare professional	Pneumonia NR	25	(1) PRALSETINIB (S)	Dose interrupted  Positive N/A Recovering/Resolving
3374161 57 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)  (2) METHYLPREDNISOLONE (T)	Dose interrupted Positive Negative Recovered/Resolved
3376141 Not reported Female CHINA Non-Interventional	Pneumonia bacterial NR	72	(1) PRALSETINIB (S)	Dose not changed N/A N/A Recovering/Resolving

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Study/Program Non-healthcare professional				
3376203 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	71	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not Recovered/Not Resolved/Ongoing
3376828 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia fungal NR	116	(1) PRALSETINIB (S)	Dose interrupted Positive N/A Recovered/Resolved
3379141 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	22	(1) PRALSETINIB (S)	Dose interrupted Positive N/A Recovered/Resolved
3381878 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	114	(1) PRALSETINIB (S)	Dose not changed N/A N/A Recovered/Resolved
3383991 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pulmonary tuberculosis NR	591	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not Recovered/Not Resolved/Ongoing
3386716 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	10	(1) PRALSETINIB (S)	Dose not changed N/A N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3387504 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia viral NR	53	(1) PRALSETINIB (S)	Dose interrupted Positive N/A Recovering/Resolving
3389346 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia bacterial NR	41	(1) PRALSETINIB (S)	Dose not changed N/A N/A Recovering/Resolving
3397054 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia viral NR	82	(1) PRALSETINIB (S)	Dose interrupted Positive N/A Recovering/Resolving
3398505 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	29	(1) PRALSETINIB (S)	Dose interrupted  Positive N/A Recovering/Resolving
3401655 71 Male CHINA Spontaneous Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	NR Unknown N/A Recovering/Resolving
3401824 80 Female UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	Cystitis NR	NR	(1) PRALSETINIB (S)	NR Unknown N/A Not Reported
3402300 Not reported	Pneumonia NR	180	(1) PRALSETINIB (S)	Dose interrupted Unknown

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
Female CHINA Non-Interventional Study/Program Non-healthcare professional				N/A Not Reported
3409827 65 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	395	(1) PRALSETINIB (S)	Dose interrupted Positive Unknown Recovered/Resolved
3411505 71 Female CHINA Spontaneous Non-healthcare professional	Renal abscess NR	NR	(1) PRALSETINIB (S)	Dose interrupted Positive N/A Recovering/Resolving
3412987 80 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	90	(1) PRALSETINIB (S)	Dose interrupted Positive Unknown Recovered/Resolved
3428310 76 Male CHINA Spontaneous Non-healthcare professional	Pneumonia NR	0	(1) PRALSETINIB (S)	Dose interrupted  Positive N/A Recovering/Resolving
3429005 59 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Herpes zoster NR	NR	(1) PRALSETINIB (S)	Dose interrupted  Dose interrupted  Positive  Positive Unknown  Unknown

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
				Recovering/Resolving
3442167 70 Male ECUADOR Non-Interventional Study/Program Non-healthcare professional	Pneumocystis jirovecii pneumonia  NR	NR	(1) PRALSETINIB (S)	NR Unknown N/A Recovering/Resolving
3446901 57 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	365	(1) PRALSETINIB (S)	Dose interrupted  Positive N/A  Recovered/Resolved
3447575 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia Pneumonia NR  NR	95  581	(1) PRALSETINIB (S)	Dose not changed  Dose not changed N/A  N/A  N/A  N/A  Recovered/Resolved  Unknown
3447586 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	Dose interrupted Negative N/A Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3448189 70 Female UNITED STATES OF AMERICA Non-Interventional Study/Program Healthcare Professional	Localised infection NR	1095	(1) PRALSETINIB (S)	NR Unknown N/A Recovered/Resolved
3449732 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	Dose interrupted Unknown N/A Not Reported
3449782 67 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	90	(1) PRALSETINIB (S)	Dose interrupted Positive N/A Recovered/Resolved
3451085 75 Female UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	NR Unknown N/A Not Reported
3455222 84 Male UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	30	(1) PRALSETINIB (S)	NR Unknown N/A Not Recovered/Not Resolved/Ongoing

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3456562 55 Male CHINA Literature - Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)  (2) CASPOFUNGIN (T)  (3) GANCICLOVIR (T)  (4) MEROPENEM (T)	Dose interrupted Positive N/A Recovered/Resolved
3457446 34 Female CHINA Literature - Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)  (2) GANCICLOVIR (T)  (3) MOXIFLOXACIN (T)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3457456 47 Female CHINA Literature - Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)  (2) CASPOFUNGIN (T)  (3) GANCICLOVIR (T)  (4) MOXIFLOXACIN (T)  (5) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3457457 44 Female CHINA Literature - Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)  (2) CEFTAZIDIME (T)  (3) MOXIFLOXACIN (T)  (4) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)	Dose interrupted Positive N/A Recovered/Resolved
3457458 64 Female CHINA Literature - Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)  (2) GANCICLOVIR (T)  (3) MEROPENEM (T)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3457459 81 Male CHINA Literature - Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)  (2) VORICONAZOLE (T)  (3) FLUCONAZOLE (T)  (4) VANCOMYCIN (T)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3457460 57 Female CHINA Literature - Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)  (2) GANCICLOVIR (T)  (3) MEROPENEM (T)  (4) VORICONAZOLE (T)  (5) MOXIFLOXACIN (T)	Dose interrupted Positive N/A Recovered/Resolved
3457461 57 Female CHINA Literature - Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)  (2) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)	Dose interrupted Positive N/A Recovered/Resolved

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3469324 61 Female CHINA Literature Spontaneous Healthcare Professional	Oral candidiasis NR	52	(1) PRALSETINIB (I)  (2) FLUCONAZOLE (I)	Dose interrupted Positive Negative Recovering/Resolving
3470875 82 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	365	(1) PRALSETINIB (S)	NR Unknown N/A Recovering/Resolving
3472483 80 Female UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	Diverticulitis intestinal perforated NR	NR	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not Recovered/Not Resolved/Ongoing
3474852 Not reported Male CHINA Non-Interventional Study/Program Healthcare Professional	Pneumonia NR	NR	(1) PRALSETINIB (S)	Dose interrupted Positive N/A Recovered/Resolved
3500767 71 Male UNITED STATES OF AMERICA Spontaneous Healthcare Professional	Pneumonia NR	NR	(1) PRALSETINIB (S)  (2) ERYTHROPOIETIN (C)	Dose interrupted Unknown N/A Not Reported

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3538667 61 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Fungal infection NR	66	(1) PRALSETINIB (S)	Dose interrupted Positive N/A Recovering/Resolving
3542163 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia fungal NR	91	(1) PRALSETINIB (S)	Dose interrupted Positive Positive Recovered/Resolved
3566427 65 Male CANADA Spontaneous Non-healthcare professional	Cellulitis NR	NR	(1) PRALSETINIB (S)  (2) SELPERCANTINIB (S)  (3) OCTREOTIDE (C)	NR Unknown N/A Not reported
3566459 78 Male NEW ZEALAND Spontaneous Healthcare Professional	Pneumocystis jirovecii pneumonia NR	58	(1) PRALSETINIB (S)	Dose not changed N/A N/A Recovered/Resolved
3573082 Not reported Not reported UNITED STATES OF AMERICA Literature - Non-Interventional Study/Program Non-healthcare professional	Pneumonia cytomegaloviral NR	NR	(1) PRALSETINIB (S)	NR Unknown N/A Not Reported

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
3573396 Not reported Not reported UNITED STATES OF AMERICA Literature - Non-Interventional Study/Program Non-healthcare professional	Bronchopulmonary aspergillosis NR	NR	(1) PRALSETINIB (S)	Dose interrupted Unknown Unknown Not Reported
3573997 Not reported Not reported UNITED STATES OF AMERICA Literature - Non-Interventional Study/Program Non-healthcare professional	Bronchopulmonary aspergillosis NR	NR	(1) PRALSETINIB (S)	Dose interrupted Unknown Unknown Not Reported
3574008 Not reported Not reported UNITED STATES OF AMERICA Literature - Non-Interventional Study/Program Non-healthcare professional	Bronchopulmonary aspergillosis NR	NR	(1) PRALSETINIB (S)	Dose interrupted Unknown Unknown Not Reported
10000022729 Not reported Female UNITED KINGDOM Spontaneous Non-healthcare professional	Gangrene NR	NR	(1) PRALSETINIB (S)	Dose not changed N/A N/A Not Reported
10000029822 73 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	30	(1) PRALSETINIB (S)	Dose interrupted Positive N/A Recovering/Resolving

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug type (All)	Action Taken Dechallenge Rechallenge Event Outcome
10000042220 45 Male UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Pneumonia NR	NR	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (C)	Dose interrupted Positive N/A Recovering/Resolving
2902724 83 Female CHILE Non-Interventional Study/Program Healthcare Professional	Pneumonia  Sepsis NR  Grade 5	0  0	(1) ALECTINIB (S)  (2) PRALSETINIB (S)	NR  NR Unknown  Unknown N/A  N/A Not Reported  Fatal
2941403 63 Female HUNGARY Non-Interventional Study/Program Healthcare Professional	Herpes virus infection  Peritonitis  NR  Grade 5	78  NR	(1) PRALSETINIB (S)	Dose interrupted  Dose interrupted N/A N/A NR  Fatal
3360718 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia  Pneumonia Grade 5  NR	24	(1) PRALSETINIB (S)	Dose not changed N/A N/A Fatal  Recovering/Resolving

**Appendix 8 Case Listings Reporting Grade 1 and 2 Infections from the Company Safety Database (N=73)**

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
2709793 58 Female FRANCE Clinical Study Healthcare Professional	Gastroenteritis Grade 2	17	(1) PRALSETINIB (S)  (2) MACROGOL 3350\POTASSIUM CHLORIDE\SODIUM BICARBONATE\SODIUM CHLORIDE (C)  (3) ALPRAZOLAM (C)  (4) OXYCODONE HYDROCHLORIDE (C)  (5) OXYCODONE HYDROCHLORIDE (C)  (6) OXYCODONE HYDROCHLORIDE (C)  (7) PREDNISONE (C)  (8) PARACETAMOL (C)  (9) OLODATEROL HYDROCHLORIDE\TIOTROPIUM BROMIDE MONOHYDRATE (C)  (10) GABAPENTIN (C)  (11) LEVOTHYROXINE (C)  (12) PANTOPRAZOLE (C)  (13) LOPERAMIDE (C)  (14) DIOSMECTITE (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
2709974 59 Female FRANCE Clinical Study Healthcare Professional	Urinary tract infection Grade 2	59	(1) PRALSETINIB (S)  (2) GABAPENTIN (C)  (3) LEVOTHYROXINE SODIUM (C)  (4) POTASSIUM CHLORIDE (C)  (5) OXYCODONE HYDROCHLORIDE (C)  (6) MAGNESIUM CARBONATE (C)  (7) AMOXICILLIN (C)  (8) OLODATEROL HYDROCHLORIDE\TIOTROPIUM BROMIDE MONOHYDRATE (C)  (9) HYDROCORTISONE (C)  (10) PREDNISOLONE METASULFOBENZOATE SODIUM (C)  (11) PARACETAMOL (C)  (12) PACLITAXEL (C)  (13) OXYCODONE HYDROCHLORIDE (C)  (14) BEVACIZUMAB (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(15) CEFOTAXIME SODIUM (T)
2716439 68 Male KOREA, REPUBLIC OF Clinical Study Healthcare Professional	Pneumocystis jirovecii pneumonia Grade 2	48	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) AMLODIPINE (C)  (4) CHLORPHENAMINE MALEATE (C)  (5) PARACETAMOL (C)  (6) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)  (7) METHYLREDNISOLONE SODIUM SUCCINATE (T)
2717157 56 Male CHINA Clinical Study Non- healthcare professional	Pneumonia Grade 2	25	(1) PRALSETINIB (S)  (2) ENTECAVIR (C)  (3) ZOLEDRONIC ACID (C)  (4) MOXIFLOXACIN (T)  (5) LINEZOLID (T)
2717924 50 Male CHINA	Febrile infection Grade 1	186	(1) PRALSETINIB (S)  (2) ERYTHROPOIETIN HUMAN (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
Clinical Study Healthcare Professional			(3) METOPROLOL (C)  (4) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (C)  (5) CEFOPERAZONE SODIUM\SULBACTAM SODIUM (C)  (6) ACETYL CYSTEINE (C)
2719510 68 Female CHINA Clinical Study Healthcare Professional	Skin infection Grade 2	34	(1) PRALSETINIB (S)  (2) LEUCOGEN (C)  (3) AMOXICILLIN TRIHYDRATE\CLAVULANATE POTASSIUM (C)  (4) DEXTROMETHORPHAN HYDROBROMIDE (C)  (5) FOLIC ACID (C)  (6) SPIRONOLACTONE (C)  (7) FUROSEMIDE (C)  (8) CEFOPERAZONE SODIUM\SULBACTAM SODIUM (C)  (9) ALBUMIN HUMAN (C)  (10) CILASTATIN SODIUM\IMIPENEM (C)  (11) VANCOMYCIN HYDROCHLORIDE (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(12) DESONIDE (C)  (13) LINEZOLID (C)  (14) INDOMETACIN (T)  (15) IBUPROFEN (T)
2724162 51 Female KOREA, REPUBLIC OF Non- Interventional Study/Progra m Healthcare Professional	Peritoneal tuberculosis Grade 2	(1) (1) 104  (1) (3) 183	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) ISONIAZID (T)  (4) RIFABUTIN (T)  (5) ETHAMBUTOL (T)  (6) PYRAZINAMIDE (T)  (7) PYRIDOXINE HYDROCHLORIDE (T)
2728333 66 Female FRANCE Clinical Study	Cellulitis Grade 2	603	(1) PRALSETINIB (S)  (2) HYDROCORTISONE (C)  (3) LEVOTHYROXINE (C)  (4) MACROGOL 3350\POTASSIUM CHLORIDE\SODIUM BICARBONATE\SODIUM CHLORIDE

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
Healthcare Professional			(C) (5) PARACETAMOL (C) (6) COLECALCIFEROL (C) (7) DICLOFENAC (C) (8) PARACETAMOL (C) (9) TRAMADOL HYDROCHLORIDE (C) (10) CLOXACILLIN (C) (11) OFLOXACIN (C) (12) RIFAMPICIN (C)
2729086 58 Female FRANCE Clinical Study Healthcare Professional	Escherichia urinary tract infection Grade 2	40	(1) PRALSETINIB (S) (2) OXYCODONE HYDROCHLORIDE (C) (3) LOPERAMIDE (C) (4) DIOSMECTITE (C) (5) GABAPENTIN (C)
2730635 83	Pneumonia pneumococc	45	(1) PRALSETINIB (S)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
Female ITALY Clinical Study Non-healthcare professional	al Grade 2		(2) RAMIPRIL (C)  (3) AMLODIPINE BESILATE (C)  (4) METHYLSPREDNISOLONE (C)  (5) PANTOPRAZOLE (C)  (6) CEFTRIAXONE (T)  (7) AZITHROMYCIN (T)  (8) HEPARIN (T)  (9) OXYGEN (T)
2735584 58 Male SPAIN Clinical Study Healthcare Professional	Atypical pneumonia  Pneumocystis jirovecii pneumonia Grade 2  Grade 2	148  47	(1) PRALSETINIB (S)  (2) METAMIZOLE (C)  (3) FILGRASTIM (C)  (4) OMEPRAZOLE (C)  (5) ANASTROZOLE (C)  (6) LEVOFLOXACIN (T)  (7) MEROPENEM (T)

AER Number Age in Years Sex Primary Source Country	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			<p>(8) PARACETAMOL (T)</p> <p>(9) LINEZOLID (T)</p> <p>(10) BEMIPARIN SODIUM (T)</p> <p>(11) OMEPRAZOLE (T)</p> <p>(12) IPRATROPIUM BROMIDE (T)</p> <p>(13) BUDESONIDE (T)</p> <p>(14) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)</p> <p>(15) GANCICLOVIR (T)</p> <p>(16) LINEZOLID (T)</p> <p>(17) METOCLOPRAMIDE (T)</p> <p>(18) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)</p> <p>(19) VORICONAZOLE (T)</p> <p>(20) PREDNISONE (T)</p> <p>(21) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)</p>

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
2744518 68 Male CHINA Clinical Study Healthcare Professional	Tuberculosis Grade 2	91	(1) PRALSETINIB (S)  (2) METOPROLOL (C)  (3) ATORVASTATIN CALCIUM (C)  (4) ACETYLSALICYLIC ACID (C)  (5) METHYLSPREDNISOLONE SODIUM SUCCINATE (C)  (6) UMIFENOVIR (C)  (7) ISONIAZID (C)  (8) ETHAMBUTOL DIHYDROCHLORIDE (C)  (9) MOXIFLOXACIN (C)  (10) MOXIFLOXACIN HYDROCHLORIDE (C)  (11) LINEZOLID (T)
2755070 54 Male UNITED STATES OF AMERICA Clinical	Atypical mycobacteria l pneumonia Grade 2	730	(1) PRALSETINIB (S)  (2) AZITHROMYCIN (C)  (3) ETHAMBUTOL (C)  (4) MOXIFLOXACIN (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
Study Non-healthcare professional			(5) RIFAMPICIN (C) (6) LEVETIRACETAM (C) (7) RIFABUTIN (C) (8) ACETYLSALICYLIC ACID (C) (9) COLECALCIFEROL (C) (10) ESOMEPRAZOLE (C) (11) PLANTAGO OVATA (C) (12) METFORMIN (C) (13) PYRIDOXINE (C) (14) ROSUVASTATIN (C)
2755509 59 Female FRANCE Clinical Study Healthcare Professional	Bronchopulmonary aspergillosis Grade 2	261	(1) PRALSETINIB (S) (2) FORMOTEROL FUMARATE (C) (3) ZOLMITRIPTAN (C) (4) CARBOMER (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(5) AMPHOTERICIN B (C) (6) PARACETAMOL (C) (7) TRAMADOL (C) (8) METOCLOPRAMIDE HYDROCHLORIDE (C) (9) FOSFOMYCIN TROMETAMOL (C) (10) FLUTICASONE PROPIONATE (C) (11) SODIUM BICARBONATE (C) (12) ENOXAPARIN SODIUM (T) (13) MIDAZOLAM HYDROCHLORIDE (T) (14) ALPRAZOLAM (T) (15) ISAVUCONAZONIUM SULFATE (T)
2758736 27 Female UNITED STATES OF AMERICA Clinical	Upper respiratory tract infection Grade 2		(1) PRALSETINIB (S) (2) PARACETAMOL (C) (3) CYCLOBENZAPRINE HYDROCHLORIDE (C) (4) GABAPENTIN (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
Study Non-healthcare professional			<p>(5) HYDROCODONE BITARTRATE\PARACETAMOL (C)</p> <p>(6) LEVOTHYROXINE SODIUM (C)</p> <p>(7) MORPHINE SULFATE (C)</p> <p>(8) SUMATRIPTAN (C)</p> <p>(9) ZOLPIDEM TARTRATE (C)</p> <p>(10) DIAZEPAM (C)</p> <p>(11) DOXAZOSIN MESILATE (C)</p> <p>(12) ENOXAPARIN (C)</p> <p>(13) SODIUM CHLORIDE (T)</p> <p>(14) KETOROLAC TROMETHAMINE (T)</p> <p>(15) MORPHINE (T)</p> <p>(16) GABAPENTIN (T)</p> <p>(17) LEVOTHYROXINE (T)</p> <p>(18) IPRATROPIUM BROMIDE\SALBUTAMOL SULFATE (T)</p>

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(19) OSELTAMIVIR (T) (20) ZOLPIDEM (T) (21) CYCLOBENZAPRINE (T) (22) DIPHENHYDRAMINE (T) (23) HYDROCODONE BITARTRATE\PARACETAMOL (T) (24) ONDANSETRON (T)
2772612 57 Female KOREA, REPUBLIC OF Non- Interventional Study/Program Non- healthcare professional	Lymph node tuberculosis Grade 2	(1) (1) 51	(1) PRALSETINIB (S) (2) METOCLOPRAMIDE (C)
2788572 67 Female	Lymph node tuberculosis	131 165	(1) PRALSETINIB (S) (2) RAMIPRIL (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
GERMANY Clinical Study Healthcare Professional	Lymph node tuberculosis Grade 1  Grade 1		(3) AMLODIPINE (C)  (4) DEXPANTHENOL (C)  (5) SODIUM CHLORIDE (C)  (6) PANTOPRAZOLE (C)  (7) ACETYLSALICYLIC ACID (C)  (8) TICAGRELOR (C)  (9) FONDAPARINUX SODIUM (C)  (10) METOPROLOL (C)  (11) NITRENDIPINE (C)  (12) ETHAMBUTOL DIHYDROCHLORIDE (T)  (13) RIFAMPICIN (T)  (14) PYRAZINAMIDE (T)
2788593 65 Male SPAIN	Urinary tract infection Grade 2	41	(1) PRALSETINIB (S)  (2) ENALAPRIL (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
Clinical Study Non-healthcare professional			(3) ACETYLSALICYLIC ACID (C)  (4) TICAGRELOR (C)  (5) BISOPROLOL (C)  (6) LEVOTHYROXINE (C)  (7) ROSUVASTATIN (C)  (8) ESOMEPRAZOLE (C)  (9) PREGABALIN (C)
2788685 36 Male CHINA Clinical Study Non-healthcare professional	Gastroenteritis Grade 2	167	(1) PRALSETINIB (S)  (2) OSELTAMIVIR PHOSPHATE (C)  (3) POTASSIUM CHLORIDE (C)  (4) PYRIDOXINE HYDROCHLORIDE (C)  (5) ASCORBIC ACID (C)  (6) ZINC GLUCONATE (C)  (7) IRON DEXTRAN (C)  (8) LOXOPROFEN SODIUM (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(9) BACILLUS SUBTILIS\ENTEROCOCCUS FAECALIS\LACTOBACILLUS ACIDOPHILUS (C)  (10) CYSTEINE HYDROCHLORIDE\GLYCINE\GLYCRRHIZIC ACID, AMMONIUM SALT (C)
2793669 57 Female ITALY Clinical Study Healthcare Professional	Pneumonia Grade 2	139	(1) PRALSETINIB (S)  (2) PARACETAMOL (C)  (3) MAGNESIUM SULFATE (C)  (4) PANTOPRAZOLE (C)  (5) FERROUS SULFATE (C)  (6) PREDNISONE (C)  (7) FLUCONAZOLE (C)  (8) NYSTATIN (C)  (9) FOLINIC ACID (C)
2797075 71 Female ITALY Clinical Study	Pneumonia Grade 2	21	(1) PRALSETINIB (S)  (2) TRIAZOLAM (C)  (3) PREDNISONE (C)  (4) OMEPRAZOLE (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
Healthcare Professional			<p>(5) BUDESONIDE\FORMOTEROL FUMARATE (C)</p> <p>(6) COLECALCIFEROL (C)</p> <p>(7) BECLOMETASONE DIPROPIONATE (C)</p> <p>(8) FONDAPARINUX (C)</p> <p>(9) TRAMADOL (C)</p> <p>(10) SODIUM ALGINATE (C)</p> <p>(11) SODIUM BICARBONATE (C)</p> <p>(12) LORAZEPAM (C)</p> <p>(13) FOLIC ACID (C)</p> <p>(14) GLUCOSE (C)</p> <p>(15) SODIUM CHLORIDE (C)</p> <p>(16) GLUTATHIONE (C)</p> <p>(17) DEXAMETHASONE (C)</p> <p>(18) POTASSIUM CHLORIDE (C)</p>

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(19) BECLOMETASONE DIPROPIONATE (C) (20) MICONAZOLE (C) (21) THIAMPHENICOL (C) (22) LEVOFLOXACIN (C) (23) PARACETAMOL (C) (24) CODEINE PHOSPHATE\PARACETAMOL (C) (25) AMOXICILLIN (C) (26) TRIAZOLAM (C) (27) OMEPRAZOLE (C) (28) COLECALCIFEROL (C) (29) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T) (30) METHYL PREDNISOLONE SODIUM SUCCINATE (T) (31) OXYGEN (T)
2797540 57	Pneumonia Grade 2	63	(1) PRALSETINIB (S)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
Male KOREA, REPUBLIC OF Clinical Study Healthcare Professional			(2) ISOSORBIDE MONONITRATE (C)  (3) CILAZAPRIL (C)  (4) AMMONIUM CHLORIDE\CHLORPHENAMINE MALEATE\DIHYDROCODEINE BITARTRATE\METHYLEPHEDRINE HYDROCHLORIDE-DL (C)  (5) DEXAMETHASONE (C)  (6) FENTANYL CITRATE (C)  (7) SODIUM BICARBONATE (C)  (8) NYSTATIN (C)  (9) LIDOCAINE (C)  (10) POVIDONE-IODINE (C)  (11) CLONAZEPAM (C)  (12) LACTULOSE (C)  (13) ESOMEPRAZOLE MAGNESIUM\NAPROXEN (C)  (14) ALANINE\ARGININE\ASPARTIC ACID\CYSTEINE\GLUTAMIC ACID\GLYCINE\HISTIDINE\ISOLEUCINE\LEUCINE\LYSINE ACETATE\METHIONINE\PHENYLALANINE\PROLINE\SERINE\THREONINE\TRYPTOPHAN\TY

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			ROSINE\VALINE (C) (15) SODIUM SELENITE PENTAHYDRATE (C) (16) MORPHINE HYDROCHLORIDE (T) (17) AMPICILLIN SODIUM\SULBACTAM SODIUM (T) (18) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T) (19) LEVOFLOXACIN (T) (20) PROPACETAMOL HYDROCHLORIDE (T) (21) MORPHINE (T) (22) TIROPRAMIDE HYDROCHLORIDE (T)
2797904 57 Female UNITED STATES OF AMERICA Clinical Study Healthcare Professional	Pneumonia Grade 2	28	(1) PRALSETINIB (S) (2) ALPRAZOLAM (C) (3) AMLODIPINE (C) (4) COLECALCIFEROL (C) (5) LEVOTHYROXINE (C) (6) VANCOMYCIN (T)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(7) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)
2798534 61 Male UNITED STATES OF AMERICA Clinical Study Non- healthcare professional	Viral infection Grade 2	289	(1) PRALSETINIB (S)  (2) BENZONATATE (C)  (3) CALCIUM CITRATE\COLECALCIFEROL (C)  (4) BETAMETHASONE DIPROPIONATE\CLOTRIMAZOLE (C)  (5) MELATONIN (C)  (6) TRAMADOL (C)  (7) DIPHENHYDRAMINE (C)  (8) DENOSUMAB (C)  (9) TAMSULOSIN (C)  (10) RIBOFLAVIN (C)  (11) LOPERAMIDE (C)  (12) OMEPRAZOLE (C)  (13) MAGNESIUM OXIDE (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			<p>(14) SILDENAFIL (C)</p> <p>(15) PANTOPRAZOLE (C)</p> <p>(16) METHYL PREDNISOLONE (C)</p> <p>(17) MORPHINE (C)</p> <p>(18) ONDANSETRON (C)</p> <p>(19) CALCIUM CHLORIDE DIHYDRATE\GLUCOSE\POTASSIUM CHLORIDE\SODIUM CHLORIDE\SODIUM LACTATE (C)</p> <p>(20) HYDROMORPHONE (C)</p> <p>(21) ENOXAPARIN (C)</p> <p>(22) SODIUM PHOSPHATE DIBASIC\SODIUM PHOSPHATE MONOBASIC (ANHYDROUS) (C)</p> <p>(23) BACLOFEN (C)</p> <p>(24) GABAPENTIN (C)</p> <p>(25) OXYCODONE (C)</p> <p>(26) PROCHLORPERAZINE EDISYLATE (C)</p> <p>(27) PARACETAMOL (C)</p>

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(28) ONDANSETRON (C)
2799334 74 Male SPAIN Non- Interventional Study/Progra m Healthcare Professional	Cytomegalov irus infection Grade 2	(1) (3) 28	(1) PRALSETINIB (S)  (2) ATENOLOL (C)  (3) CHLORTALIDONE (C)  (4) ENOXAPARIN (C)  (5) DEXAMETHASONE (C)  (6) CISPLATIN (C)  (7) VINORELBINE (C)  (8) OMEPRAZOLE (T)  (9) GANCICLOVIR (T)  (10) FOSCARNET (T)
2799583 58 Female UNITED STATES OF AMERICA Clinical	Pneumonia Grade 2	553	(1) PRALSETINIB (S)  (2) BENZONATATE (C)  (3) PARACETAMOL (C)  (4) NAPROXEN (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
Study Healthcare Professional			(5) LIDOCAINE (C)  (6) METFORMIN (C)
2800555 65 Male SPAIN Clinical Study Non-healthcare professional	Urinary tract infection Grade 2	154	(1) PRALSETINIB (S)  (2) ACETYLSALICYLIC ACID (C)  (3) LEVOTHYROXINE (C)  (4) TAMSULOSIN HYDROCHLORIDE (C)  (5) BISOPROLOL (C)  (6) ESOMEPRAZOLE (C)  (7) FOSFOMYCIN (C)  (8) COLECALCIFEROL (C)  (9) TICAGRELOR (C)  (10) PYRIDOSTIGMINE (C)  (11) PIPERACILLIN (T)
2800581 59 Female	Bacteraemia COVID-19	77 82	(1) PRALSETINIB (S)  (2) ZOLPIDEM (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
SPAIN Clinical Study Healthcare Professional	pneumonia Grade 2  Grade 2		(3) MELATONIN (C)  (4) ESCITALOPRAM (C)  (5) PARACETAMOL (C)  (6) LIDOCAINE (C)  (7) NYSTATIN (C)  (8) SODIUM BICARBONATE (C)  (9) DEXAMETHASONE (C)  (10) CEFTRIAXONE (T)  (11) CLOXA CILLIN (T)  (12) CIPROFLOXACIN (T)  (13) DAPTO MYCIN (T)  (14) AZITHROMYCIN (T)  (15) HYDROXYCHLOROQUINE SULFATE (T)  (16) TEICOPLANIN (T)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(17) ANAKINRA (T)  (18) TOCILIZUMAB (T)
2800611 67 Male KOREA, REPUBLIC OF Clinical Study Non- healthcare professional	Sepsis Grade 2	50	(1) PRALSETINIB (S)  (2) ARGININE HYDROCHLORIDE\IBUPROFEN (C)  (3) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (4) AZITHROMYCIN (T)  (5) CIPROFLOXACIN (T)
2800633 64 Male GERMANY Non- Interventional Study/Program Healthcare Professional	Pneumonia bacterial  Spontaneous bacterial peritonitis Grade 1  Grade 1	(1) (1) 531  (1) (2) 531	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE (C)  (3) FUROSEMIDE (C)  (4) SITAGLIPTIN (C)  (5) COLECALCIFEROL (C)
2800727 68 Male	Escherichia urinary tract	859	(1) PRALSETINIB (S)  (2) ERGOCALCIFEROL (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
UNITED STATES OF AMERICA Clinical Study Healthcare Professional	infection Grade 2		(3) KETOCONAZOLE (C) (4) MUPIROCIN (C) (5) NAPROXEN SODIUM (C) (6) OXYCODONE HYDROCHLORIDE\PARACETAMOL (C) (7) PHENAZOPYRIDINE (C) (8) PREGABALIN (C) (9) SENNA SPP. (C) (10) LEVOTHYROXINE SODIUM (C) (11) TAMSULOSIN (C) (12) CEFEPIME (T) (13) LEVOFLOXACIN (T) (14) VANCOMYCIN (T)
2800846 60 Male UNITED	Pneumonia Grade 2	315	(1) PRALSETINIB (S) (2) LEVETIRACETAM (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
STATES OF AMERICA Clinical Study Non-healthcare professional			(3) FUROSEMIDE (T)  (4) AZITHROMYCIN (T)  (5) CHLORHEXIDINE (T)
2801034 Not reported Female UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Upper respiratory tract infection Grade 2	Not reported	(1) PRALSETINIB (S)  (2) PARACETAMOL (C)  (3) CYCLOBENZAPRINE HYDROCHLORIDE (C)  (4) GABAPENTIN (C)  (5) HYDROCODONE BITARTRATE\PARACETAMOL (C)  (6) LEVOTHYROXINE SODIUM (C)  (7) MORPHINE SULFATE (C)  (8) SUMATRIPTAN (C)  (9) ZOLPIDEM TARTRATE (C)  (10) DIAZEPAM (C)  (11) DOXAZOSIN MESILATE (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(12) MORPHINE (C) (13) ENOXAPARIN (C) (14) KETOROLAC TROMETHAMINE (T) (15) GABAPENTIN (T) (16) IPRATROPIUM BROMIDE\SALBUTAMOL SULFATE (T) (17) LEVOTHYROXINE (T) (18) OSELTAMIVIR (T) (19) ZOLPIDEM (T) (20) CYCLOBENZAPRINE (T) (21) DIPHENHYDRAMINE (T) (22) HYDROCODONE BITARTRATE\PARACETAMOL (T) (23) ONDANSETRON (T)
2801426 32 Male CHINA	Pneumonia influenzal Grade 2	42	(1) PRALSETINIB (S) (2) GEMCITABINE (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
Clinical Study Healthcare Professional			(3) NEDAPLATIN (C) (4) MOXIFLOXACIN HYDROCHLORIDE (C) (5) POTASSIUM CHLORIDE (C) (6) OMEPRAZOLE SODIUM (C) (7) GLUTATHIONE (C) (8) IMMUNOGLOBULIN HUMAN NORMAL (C) (9) OSELTAMIVIR PHOSPHATE (T) (10) METHYL PREDNISOLONE SODIUM SUCCINATE (T) (11) THYMALFASIN (T)
2802306 71 Female ITALY Clinical Study Healthcare Professional	Pneumonia Grade 2	54	(1) PRALSETINIB (S) (2) DENOSUMAB (C) (3) METOPROLOL (C) (4) ROSUVASTATIN (C) (5) EDOXABAN (C) (6) DOXAZOSIN MESILATE (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(7) CALCIUM (C) (8) ALLOPURINOL (C) (9) COLECALCIFEROL (C) (10) BROMAZEPAM (C) (11) RANITIDINE (C) (12) CLOPIDOGREL (C) (13) AMLODIPINE (C) (14) MICONAZOLE (C) (15) CLOTRIMAZOLE (C) (16) CEFTRIAXONE (C) (17) DEXAMETHASONE (C) (18) RANITIDINE HYDROCHLORIDE (C) (19) METOCLOPRAMIDE (C) (20) MORPHINE (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(21) TRAMADOL (C) (22) ENOXAPARIN (C) (23) MACROGOL 3350\POTASSIUM CHLORIDE\SODIUM BICARBONATE\SODIUM CHLORIDE (C) (24) PIPERACILLIN (T) (25) AZITHROMYCIN (T)
2802338 60 Male FRANCE Clinical Study Non-healthcare professional	Pneumonia Grade 2	29	(1) PRALSETINIB (S) (2) LEVOTHYROXINE SODIUM (C) (3) LOPERAMIDE HYDROCHLORIDE (C) (4) MORPHINE SULFATE (C) (5) ALPRAZOLAM (C) (6) FENTANYL (C) (7) FLUDROCORTISONE ACETATE (C) (8) HYDROCORTISONE (C) (9) GABAPENTIN (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(10) LORMETAZEPAM (C) (11) CODEINE PHOSPHATE\PARACETAMOL (C) (12) OXYCODONE HYDROCHLORIDE (C) (13) SALBUTAMOL (C) (14) RACECADOTRIL (C) (15) TERBUTALINE SULFATE (T) (16) IPRATROPIUM BROMIDE (T) (17) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T) (18) SPIRAMYCIN (T) (19) SULFAMETHOXAZOLE\TRIMETHOPRIM (T) (20) PREDNISOLONE METASULFOBENZOATE SODIUM (T)
2802341 68 Female UNITED STATES OF AMERICA	Pneumonia influenzal Grade 2	241	(1) PRALSETINIB (S) (2) LEVOTHYROXINE SODIUM (C) (3) ALPRAZOLAM (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
Clinical Study Healthcare Professional			(4) AMLODIPINE BESILATE (C) (5) CALCIUM CITRATE (C) (6) COLECALCIFEROL (C) (7) LOPERAMIDE HYDROCHLORIDE (C) (8) METOPROLOL SUCCINATE (C) (9) HYDROCHLOROTHIAZIDE\VALSARTAN (C) (10) CYANOCOBALAMIN (C) (11) OMEPRAZOLE (C) (12) TRAMADOL HYDROCHLORIDE (C) (13) IBUPROFEN (C) (14) VANCOMYCIN (T) (15) MEROPENEM (T) (16) OSELTAMIVIR PHOSPHATE (T)
2810237 71 Female	Pneumonia Grade 2	89	(1) PRALSETINIB (S) (2) FERROUS SULFATE (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
KOREA, REPUBLIC OF Clinical Study Healthcare Professional			(3) AMPHOTERICIN B (C) (4) MOXIFLOXACIN HYDROCHLORIDE (C) (5) CARVEDILOL (C) (6) HEPARIN (C) (7) METOCLOPRAMIDE (C) (8) AMLODIPINE BESILATE (C) (9) PARACETAMOL\TRAMADOL HYDROCHLORIDE (C) (10) AMINO ACIDS NOS\CALCIUM\GLUCOSE\MAGNESIUM\POTASSIUM\SODIUM (C) (11) CHROMIC CHLORIDE\COPPER SULFATE\MANGANESE SULFATE\ZINC SULFATE (C) (12) LOPERAMIDE (C) (13) SODIUM CHLORIDE (C) (14) DIOSMECTITE (C) (15) PANTOPRAZOLE SODIUM SESQUIHYDRATE (C)
2830445 59	Pharyngitis Grade 2	56	(1) PRALSETINIB (S)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
Male ITALY Clinical Study Healthcare Professional			(2) ACETYLSALICYLIC ACID (C)  (3) ROSUVASTATIN (C)  (4) CEFTRIAXONE (T)
2867439 69 Female ITALY Non-Interventional Study/Program Healthcare Professional	Herpes zoster reactivation  Grade 2	(1) (2) 135	(1) PRALSETINIB (S)  (2) FOLIC ACID (C)  (3) FONDAPARINUX SODIUM (C)  (4) PREDNISONE (C)  (5) FUROSEMIDE (C)  (6) ALPRAZOLAM (C)  (7) FENTANYL (C)  (8) BENZERAZIDE HYDROCHLORIDE\LEVODOPA (C)  (9) DOXYCYCLINE (C)  (10) PREDNISONE (T)
2920551 29 Female	Pneumonia viral	(1) (1) 58 (1) (2)	(1) PRALSETINIB (S)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia bacterial Grade 2  Grade 2		
2967126 78 Male ITALY Non-Interventional Study/Program Healthcare Professional	Bronchiolitis Grade 2	(1) (12) 933  (1) (13) 943	(1) PRALSETINIB (S)  (2) CEFTRIAXONE (T)  (3) METHYLSPREDNISOLONE (T)  (4) LEVOFLOXACIN (T)  (5) FLUTICASONE FUROATE\ILANTELOR TRIFENATATE (T)  (6) VALACICLOVIR (T)
3015784 37 Male GERMANY Clinical Study Healthcare Professional	Psoas abscess Grade 1	1095	(1) PRALSETINIB (S)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
3051628 61 Male KOREA, REPUBLIC OF Clinical Study Healthcare Professional	Pneumonia Grade 2	361	(1) PRALSETINIB (S)  (2) MAGNESIUM OXIDE (C)  (3) REMDESIVIR (T)  (4) DEXAMETHASONE (T)
3081178 37 Male GERMANY Clinical Study Healthcare Professional	COVID-19 Grade 2	1095	(1) PRALSETINIB (S)
3102238 73 Female UNITED STATES OF AMERICA Clinical Study Healthcare Professional	COVID-19 Grade 1	1095	(1) PRALSETINIB (S)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
3143024 72 Male KOREA, REPUBLIC OF Clinical Study Healthcare Professional	Postoperative wound infection Grade 2	58	(1) PRALSETINIB (S)  (2) VALSARTAN (C)  (3) CODEINE PHOSPHATE\IBUPROFEN\PARACETAMOL (C)  (4) AZELASTINE (C)  (5) CHLORPHENAMINE (C)  (6) MAGNESIUM OXIDE (C)  (7) PANTOPRAZOLE (C)  (8) INSULIN HUMAN (C)  (9) AMBROXOL (C)  (10) CALCIUM GLUCONATE (C)  (11) SODIUM BICARBONATE (C)  (12) ALBUMIN HUMAN (C)  (13) FUROSEMIDE (C)  (14) PARACETAMOL (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			<p>(15) HYDROMORPHONE (C)</p> <p>(16) CHLORHEXIDINE (C)</p> <p>(17) GLUCONATE SODIUM MAGNESIUM CHLORIDE\POTASSIUM CHLORIDE\SODIUM ACETATE\SODIUM CHLORIDE (C)</p> <p>(18) POTASSIUM PHOSPHATE (C)</p> <p>(19) ACETYLSALICYLIC ACID (C)</p> <p>(20) AMLODIPINE (C)</p> <p>(21) ESCITALOPRAM (C)</p> <p>(22) DONEPEZIL (C)</p> <p>(23) MIRABEGRON (C)</p> <p>(24) TAMSULOSIN (C)</p> <p>(25) MEGESTROL (C)</p> <p>(26) ATORVASTATIN (C)</p> <p>(27) ESOMEPRAZOLE (C)</p> <p>(28) CEFIXIME (C)</p>

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			<p>(29) AMLODIPINE BESILATE\VALSARTAN (C)</p> <p>(30) MEROPENEM (T)</p> <p>(31) PIPERACILLIN\TAZOBACTAM (T)</p> <p>(32) CEFACLOR (T)</p> <p>(33) METRONIDAZOLE (T)</p> <p>(34) OXYCODONE HYDROCHLORIDE (T)</p> <p>(35) PARACETAMOL (T)</p> <p>(36) VANCOMYCIN (T)</p> <p>(37) MEROPENEM (T)</p> <p>(38) PETHIDINE (T)</p> <p>(39) IBUPROFEN (T)</p> <p>(40) CIPROFLOXACIN (T)</p>
3143754 64 Female CHINA	Febrile infection Grade 1	721	<p>(1) PRALSETINIB (S)</p> <p>(2) ASCORBIC ACID (C)</p>

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
Clinical Study Healthcare Professional			(3) POTASSIUM CHLORIDE (C) (4) PYRIDOXINE HYDROCHLORIDE (C) (5) MOSAPRIDE CITRATE (C) (6) MOXIFLOXACIN HYDROCHLORIDE (C) (7) PANTOPRAZOLE (C) (8) CEFTAZIDIME (C) (9) LORATADINE (C) (10) SPIRONOLACTONE (C) (11) FUROSEMIDE (C) (12) LOW MOLECULAR WEIGHT HEPARIN, CALCIUM SALT (C) (13) PARACETAMOL (C) (14) DIMETICON (C) (15) ALL OTHER THERAPEUTIC PRODUCTS (C)
3200448 51 Male	Nasopharyngitis Grade 1	1095	(1) PRALSETINIB (S) (2) PARACETAMOL (T)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
KOREA, REPUBLIC OF Clinical Study Healthcare Professional			(3) AMOXICILLIN TRIHYDRATE\CLAVULANATE POTASSIUM (T)  (4) PARACETAMOL (T)
3207348 68 Male ITALY Clinical Study Healthcare Professional	Pneumonia Grade 2	28	(1) PRALSETINIB (S)  (2) CEFDITOREN PIVOXIL (T)  (3) OMEPRAZOLE (T)  (4) METHYLSPREDNISOLONE (T)  (5) PARACETAMOL (T)
3211148 34 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pneumonia Grade 1	(1) (1)	(1) PRALSETINIB (S)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
3214831 52 Male FRANCE Clinical Study Healthcare Professional	Pseudomonas infection Grade 2	38	(1) PRALSETINIB (S)  (2) TESTOSTERONE ENANTHATE (C)  (3) OXYCODONE HYDROCHLORIDE (C)  (4) PREDNISOLONE METASULFOBENZOATE SODIUM (C)  (5) AMITRIPTYLINE HYDROCHLORIDE (C)  (6) POTASSIUM CHLORIDE (C)  (7) CALCIUM CARBONATE (C)  (8) METHADONE (C)  (9) HYDROCORTISONE (C)  (10) ENOXAPARIN SODIUM (C)  (11) ONDANSETRON (C)  (12) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (13) AMIKACIN (T)  (14) CIPROFLOXACIN (T)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(15) CALCIUM CHLORIDE\MAGNESIUM CHLORIDE\MALIC ACID\POTASSIUM CHLORIDE\SODIUM ACETATE\SODIUM CHLORIDE (T)
3220250 35 Male UNITED STATES OF AMERICA Clinical Study Healthcare Professional	Postoperative wound infection Grade 2	1460	(1) PRALSETINIB (S)  (2) ENOXAPARIN (C)  (3) KETOROLAC TROMETHAMINE (C)  (4) MAGNESIUM SULFATE (C)  (5) POTASSIUM CHLORIDE (C)  (6) PARACETAMOL (C)  (7) BUPROPION (C)  (8) HYDROMORPHONE (C)  (9) LAMOTRIGINE (C)  (10) LORAZEPAM (C)  (11) ONDANSETRON (C)  (12) OXYCODONE (C)  (13) MACROGOL 3350 (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			<p>(14) PROCHLORPERAZINE (C)</p> <p>(15) PROMETHAZINE (C)</p> <p>(16) RIVAROXABAN (C)</p> <p>(17) DOCUSATE SODIUM\SENNOSIDE A+B (C)</p> <p>(18) SIMETICONE (C)</p> <p>(19) BUPROPION (C)</p> <p>(20) COLECALCIFEROL (C)</p> <p>(21) LAMOTRIGINE (C)</p> <p>(22) MENTHOL (C)</p> <p>(23) RIVAROXABAN (C)</p> <p>(24) ATENOLOL (C)</p> <p>(25) AZITHROMYCIN (C)</p> <p>(26) CEFALEXIN (C)</p> <p>(27) PREDNISONE (C)</p>

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			<p>(28) ASCORBIC ACID (C)</p> <p>(29) DIPHENHYDRAMINE (C)</p> <p>(30) TOZINAMERAN (C)</p> <p>(31) DRONABINOL (C)</p> <p>(32) GRAMICIDIN\NEOMYCIN SULFATE\POLYMYXIN B SULFATE (C)</p> <p>(33) FENTANYL (C)</p> <p>(34) POTASSIUM PHOSPHATE MONOBASIC\SODIUM PHOSPHATE DIBASIC\SODIUM PHOSPHATE MONOBASIC (ANHYDROUS) (T)</p> <p>(35) GLUCOSE (T)</p> <p>(36) GABAPENTIN (T)</p> <p>(37) LIDOCAINE (T)</p> <p>(38) TIZANIDINE (T)</p> <p>(39) CALCIUM CHLORIDE\POTASSIUM CHLORIDE\SODIUM LACTATE (T)</p> <p>(40) EPINEPHRINE\LIDOCAINE HYDROCHLORIDE (T)</p> <p>(41) PIPERACILLIN\TAZOBACTAM (T)</p>

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(42) SODIUM CHLORIDE (T) (43) CIPROFLOXACIN (T) (44) METRONIDAZOLE (T)
3255124 73 Female FRANCE Clinical Study Healthcare Professional	Pneumonia  Grade 2	85	(1) PRALSETINIB (S) (2) ALLOPURINOL (C) (3) HYDROCHLOROTHIAZIDE\VALSARTAN (C) (4) NEBIVOLOL (C) (5) ACETYLSALICYLATE LYSINE (C) (6) PARACETAMOL (C) (7) LANSOPRAZOLE (C) (8) PRAVASTATIN (C) (9) BUDESONIDE (C) (10) SALMETEROL XINAFOATE (C) (11) MONTELUKAST SODIUM (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			<p>(12) METFORMIN (C)</p> <p>(13) LOPERAMIDE (C)</p> <p>(14) LEVOFLOXACIN (C)</p> <p>(15) DEXAMETHASONE\TOBRAMYCIN (C)</p> <p>(16) HYALURONATE SODIUM (C)</p> <p>(17) BRIMONIDINE TARTRATE\BRINZOLAMIDE (C)</p> <p>(18) LATANOPROST (C)</p> <p>(19) DEXAMETHASONE\OXYTETRACYCLINE (C)</p> <p>(20) ATROPINE (C)</p> <p>(21) CAFFEINE\PAPAVER SOMNIFERUM LATEX\PARACETAMOL (C)</p> <p>(22) PARACETAMOL (C)</p> <p>(23) TINZAPARIN SODIUM (C)</p> <p>(24) AMOXICILLIN\CLAVULANATE POTASSIUM (T)</p> <p>(25) HEPARIN (T)</p>

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(26) TINZAPARIN SODIUM (T)  (27) SODIUM CHLORIDE (T)
3256323 59 Female CHINA Clinical Study Healthcare Professional	Pneumonia viral Grade 2	904	(1) PRALSETINIB (S)  (2) ALLICIN (C)  (3) NADROPARIN CALCIUM (C)  (4) MAGNESIUM ISOGLYCYRRHIZINATE (C)  (5) INDOMETACIN (C)  (6) ACETYLCYSTEINE (C)  (7) ZOLEDRONIC ACID (C)  (8) ACETYLSALICYLATE LYSINE (C)  (9) DIAMMONIUM GLYCYRRHIZINATE (C)
3285099 64 Female UNITED STATES OF AMERICA Clinical Study	COVID-19 Grade 1	870	(1) PRALSETINIB (S)  (2) ASCORBIC ACID (C)  (3) RANITIDINE HYDROCHLORIDE (C)  (4) POTASSIUM CHLORIDE (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
Healthcare Professional			
3296579 48 Female CHINA Clinical Study Healthcare Professional	Pneumonia Grade 2	1095	(1) PRALSETINIB (S)  (2) CALCIUM CARBONATE\COLECALCIFEROL (C)  (3) ALBUMIN HUMAN (C)  (4) ESOMEPRAZOLE MAGNESIUM (C)  (5) LATAMOXEF SODIUM (T)  (6) IPRATROPIUM BROMIDE\SALBUTAMOL SULFATE (T)  (7) ACETYL CYSTEINE (T)  (8) LEVOFLOXACIN (T)  (9) BUDESONIDE (T)  (10) METHYL PREDNISOLONE (T)  (11) ACETYL CYSTEINE (T)  (12) METHYL PREDNISOLONE (T)
3301305 30 Female	Pneumonia Grade 2	1094	(1) PRALSETINIB (S)  (2) LEVOTHYROXINE SODIUM (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
CHINA Clinical Study Healthcare Professional			(3) AMOXICILLIN (C) (4) CEFRADINE (T) (5) FRITILLARIA SPP. BULB (T) (6) LORATADINE (T) (7) CEFOPERAZONE SODIUM\SULBACTAM SODIUM (T) (8) RIBAVIRIN (T) (9) BUDESONIDE (T) (10) ALBUMIN HUMAN (T)
3383099 53 Male FRANCE Clinical Study Healthcare Professional	Pneumocystis jirovecii pneumonia Grade 2	272	(1) PRALSETINIB (S) (2) TESTOSTERONE ENANTHATE (C) (3) PREDNISOLONE (C) (4) AMITRIPTYLINE HYDROCHLORIDE (C) (5) POTASSIUM CHLORIDE (C) (6) CALCIUM CARBONATE (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(7) METHADONE (C)  (8) HYDROCORTISONE (C)  (9) SULFAMETHOXAZOLE\TRIMETHOPRIM (T)
3430268 77 Male ROMANIA Clinical Study Healthcare Professional	COVID-19 Grade 1	4	(1) PRALSETINIB (S)  (2) DEXAMETHASONE (C)  (3) KETOPROFEN (C)  (4) METAMIZOLE (C)  (5) OXYGEN (T)
3479467 38 Male GERMANY Clinical Study Non-healthcare professional	Influenza Grade 2	1825	(1) PRALSETINIB (S)
3484843 47 Male ITALY Clinical	Pneumonia Grade 2	90	(1) PRALSETINIB (S)  (2) PIPERACILLIN SODIUM\TAZOBACTAM SODIUM (T)  (3) PREDNISONE (T)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
Study Healthcare Professional			(4) PARACETAMOL (T)  (5) MEROPENEM (T)  (6) ENOXAPARIN SODIUM (T)
3491936 49 Female CHINA Clinical Study Healthcare Professional	Pneumonia Grade 2	1460	(1) PRALSETINIB (S)  (2) LEVOFLOXACIN (S)  (3) SODIUM CHLORIDE (S)  (4) CEFOPERAZONE SODIUM (S)  (5) SULBACTAM SODIUM (S)  (6) CALCIUM CARBONATE (C)  (7) COLECALCIFEROL (C)
3498224 65 Male KOREA, REPUBLIC OF Clinical Study	Pneumonia Grade 2	1825	(1) PRALSETINIB (S)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
Healthcare Professional			
3509447 81 Female JAPAN Clinical Study Healthcare Professional	Pneumonia Grade 2	11	(1) PRALSETINIB (S)  (2) ATORVASTATIN (C)  (3) SITAGLIPTIN PHOSPHATE (C)  (4) BAZEDOXIFENE ACETATE (C)  (5) NIFEDIPINE (C)  (6) PREGABALIN (C)  (7) ELOBIXIBAT (C)  (8) SENNOSIDE A+B (C)  (9) FLUTICASONE FUROATE (C)  (10) LEVOFLOXACIN (T)
3520638 74 Male ITALY Clinical Study	Bronchitis Grade 2	189	(1) PRALSETINIB (S)  (2) LAMIVUDINE (C)  (3) DENOSUMAB (C)  (4) CALCIUM CARBONATE (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
Healthcare Professional			(5) COLECALCIFEROL (C) (6) METHYLREDNISOLONE (T) (7) CLARITHROMYCIN (T) (8) CEFTRIAXONE SODIUM (T) (9) CEFIXIME (T) (10) PREDNISONE (T) (11) BECLOMETASONE DIPROPIONATE (T) (12) CEFEPIME (T)
3528114 26 Female TURKIYE Clinical Study Healthcare Professional	COVID-19 Grade 2	8	(1) PRALSETINIB (S) (2) TRAMADOL HYDROCHLORIDE (C) (3) ONDANSETRON HYDROCHLORIDE (C) (4) PARACETAMOL (C) (5) PANTOPRAZOLE SODIUM SESQUIHYDRATE (C)
3528460 60 Male	Gastroenteritis Grade 2	1095	(1) PRALSETINIB (S) (2) PANTOPRAZOLE SODIUM SESQUIHYDRATE (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
ITALY Clinical Study Non-healthcare professional			(3) ONDANSETRON (C)  (4) FENTANYL (C)  (5) PREGABALIN (C)  (6) MORPHINE SULFATE PENTAHYDRATE (C)  (7) CEFTRIAXONE (T)  (8) FENTANYL (T)  (9) PREGABALIN (T)
3528527 60 Male ITALY Clinical Study Non-healthcare professional	Gastroenteritis Grade 2	1095	(1) PRALSETINIB (S)  (2) ALL OTHER THERAPEUTIC PRODUCTS (T)  (3) CIPROFLOXACIN (T)  (4) PROBIOTICS NOS (T)
2934155 55 Male UNITED STATES OF	Sepsis  Pneumonia Grade 4	884  884	(1) PRALSETINIB (S)  (2) IPRATROPIUM BROMIDE\SALBUTAMOL SULFATE (C)  (3) NAPROXEN (C)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
AMERICA Clinical Study Healthcare Professional	Grade 2		
2802164 87 Male UNITED STATES OF AMERICA Clinical Study Non-healthcare professional	Sepsis Urinary tract infection Grade 5 Grade 2	10	(1) PRALSETINIB (S)  (2) AMLODIPINE (C)  (3) LISINOPRIL (C)  (4) SILODOSIN (C)  (5) DUTASTERIDE (C)  (6) LEVOTHYROXINE (C)  (7) FINASTERIDE (C)  (8) FAMOTIDINE (C)  (9) CEFEPIME HYDROCHLORIDE (T)  (10) ACICLOVIR (T)  (11) HALOPERIDOL (T)  (12) VANCOMYCIN (T)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(13) MORPHINE (T)
2796030 59 Male UNITED STATES OF AMERICA Clinical Study Healthcare Professional	Sepsis  Bacteraemia Grade 4  Grade 2	7  10	(1) PRALSETINIB (S)  (2) CALCIUM CARBONATE (C)  (3) OXYGEN (C)  (4) LEVOTHYROXINE (C)  (5) RANITIDINE (C)  (6) ROSUVASTATIN (C)  (7) LACOSAMIDE (C)  (8) LEVETIRACETAM (C)  (9) LORAZEPAM (C)  (10) ONDANSETRON (C)  (11) PANTOPRAZOLE (C)  (12) MACROGOL (C)  (13) CEFEPIME HYDROCHLORIDE (T)

AER Number Age in Years Sex Primary Source Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to Onset (in days)	Drug Type (All)
			(14) VANCOMYCIN HYDROCHLORIDE (T)
2797521 66 Male UNITED STATES OF AMERICA Clinical Study Healthcare Professional	Escherichia sepsis  Escherichia bacteraemia Grade 4  Grade 2	212  212	(1) PRALSETINIB (S)  (2) MORPHINE SULFATE (C)  (3) MACROGOL 3350 (C)  (4) SENNOSIDE A+B (C)  (5) SALBUTAMOL (C)  (6) SODIUM CHLORIDE (C)  (7) SERTRALINE HYDROCHLORIDE (C)  (8) PARACETAMOL (C)  (9) ONDANSETRON (C)  (10) MEROPENEM (T)  (11) SALBUTAMOL (T)  (12) SALBUTAMOL (T)  (13) ACETYLSALICYLIC ACID (T)

AER Number	Event Preferred Term of Interest*	Time to Onset (in days)	Drug Type (All)
			(14) MUPIROCIN (T)  (15) CEFTRIAXONE (T)

**Appendix 9    Listings of Non-serious Cases Reporting Events of  
Infections from Safety Database (N=66)**

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to onset (in days)	Drug Type (All)
2712220 Not reported Male UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Herpes zoster NR	Not reported	(1) PRALSETINIB (S)  (2) MACROGOL 3350 (T)
2760057 Not reported Male UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Herpes zoster NR	Not reported	(1) PRALSETINIB (S)  (2) AMLODIPINE (C)  (3) ALPRAZOLAM (C)
2786698 72 Male UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Bacterial infection NR	(1) (1) 104	(1) PRALSETINIB (S)
2809616 84 Female UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Oral fungal infection  Urinary tract infection NR	(1) (1) 120  (1) (2) 120	(1) PRALSETINIB (S)
2845240 Not reported Female UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Urinary tract infection NR	Not reported	(1) PRALSETINIB (S)  (2) LEVOFLOXACIN (S)  (3) HYDROCODONE BITARTRATE\PARACETAMOL (T)
2850007 84 Female UNITED STATES OF AMERICA	Infection NR	(1) (1) 0	(1) PRALSETINIB (S)

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to onset (in days)	Drug Type (All)
Spontaneous Non-healthcare professional			
2851557 Not reported Male UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Nasopharyngitis NR	Not reported	(1) PRALSETINIB (S)
2852909 59 Male KOREA, REPUBLIC OF Non-Interventional Study/Program Non-healthcare professional	Oral candidiasis NR	(1) (1) 14	(1) PRALSETINIB (S)
2858278 Not reported Female UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Oral fungal infection NR	Not reported	(1) PRALSETINIB (S)
2881194 66 Female CHINA Spontaneous Healthcare professional	Cystitis NR	(1) (4) 13	(1) PRALSETINIB (S)  (2) CAMRELIZUMAB (C)  (3) NITROFURANTOIN (T)  (4) ALOE VERA (T)
2894543 65 Male CHINA Spontaneous Non-healthcare professional	Abscess limb NR	Not reported	(1) PRALSETINIB (S)

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to onset (in days)	Drug Type (All)
2907361 34 Female CHINA Spontaneous Non-healthcare professional	Laryngopharyngitis NR	Not reported	(1) PRALSETINIB (S)
2910947 77 Female CHINA Spontaneous Non-healthcare professional	Paronychia NR	Not reported	(1) PRALSETINIB (S)
2949447 48 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Fungal infection Fungal skin infection NR	(1) (3) 83 (1) (9) 120	(1) PRALSETINIB (S) (2) LEUCOGEN (T)
2965786 47 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Paronychia NR	(1) (1) 210	(1) PRALSETINIB (S)
2989008 51 Male TURKIYE Non-Interventional Study/Program Healthcare professional	COVID-19 NR	(1) (2) 106	(1) PRALSETINIB (S)
2994720 Not reported Male CHINA	Tinea infection NR	(1) (1) 124	(1) PRALSETINIB (S)

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to onset (in days)	Drug Type (All)
Non-Interventional Study/Program Non-healthcare professional			
3001092 51 Female KOREA, REPUBLIC OF Non-Interventional Study/Program Healthcare professional	Coronavirus infection NR	(1) (2) 498	(1) PRALSETINIB (S)
3080808 67 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Paronychia NR	(1) (2) 30	(1) PRALSETINIB (S)
3090360 55 Male UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	Nasopharyngitis NR	Not reported	(1) PRALSETINIB (S)
3100273 63 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Urinary tract infection NR	(1) (3) 330	(1) PRALSETINIB (S)
3103964 56 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Paronychia NR	Not reported	(1) PRALSETINIB (S)
3116502 Not reported	Herpes zoster NR	Not reported	(1) PRALSETINIB (S)

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to onset (in days)	Drug Type (All)
Not reported CHINA Non-Interventional Study/Program Non-healthcare professional			
3122710 62 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Urinary tract infection NR	Not reported	(1) PRALSETINIB (S)
3122711 52 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Urinary tract infection NR	(1) (1) 224	(1) PRALSETINIB (S)
3147568 41 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Urinary tract infection NR	(1) (11) 145	(1) PRALSETINIB (S)
3169172 42 Female ITALY Non-Interventional Study/Program Healthcare professional	COVID-19 NR	(1) (1) 365	(1) PRALSETINIB (S)  (2) OTHER MONOCLONAL ANTIBODIES AND ANTIBODY DRUG CONJUGATES (T)
3202186 85 Male UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	Infection NR	Not reported	(1) PRALSETINIB (S)

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to onset (in days)	Drug Type (All)
3215171 64 Female CHINA Non-Interventional Study/Program Healthcare professional	Urinary tract infection NR	(1) (4) 60	(1) PRALSETINIB (S)
3218767 Not reported Female ISRAEL Spontaneous Non-healthcare professional	Genital herpes NR	Not reported	(1) PRALSETINIB (S)
3222453 22 Female CHINA Non-Interventional Study/Program Healthcare professional	Paronychia NR	(1) (1) 204	(1) PRALSETINIB (S)
3225065 85 Male UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	Tongue fungal infection NR	Not reported	(1) PRALSETINIB (S)
3229307 80 Female UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	Nasopharyngitis NR	Not reported	(1) PRALSETINIB (S)
3230719 80 Male UNITED STATES OF AMERICA	COVID-19 NR	Not reported	(1) PRALSETINIB (S)

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to onset (in days)	Drug Type (All)
Non-Interventional Study/Program Non-healthcare professional			
3264550 48 Male CHINA Spontaneous Non-healthcare professional	COVID-19 NR	(1) (1) 10	(1) PRALSETINIB (S)
3268157 65 Female GERMANY Spontaneous Healthcare professional	Urinary tract infection NR	Not reported	(1) PRALSETINIB (S)  (2) CIPROFLOXACIN (T)
3276717 63 Female UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	COVID-19 Sinusitis NR	Not reported	(1) PRALSETINIB (S)
3291127 Not reported Female ISRAEL Non-Interventional Study/Program Non-healthcare professional	Sinusitis fungal NR	Not reported	(1) PRALSETINIB (S)
3298850 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	COVID-19 NR	(1) (1) 349	(1) PRALSETINIB (S)
3300832 Not reported	COVID-19	(1) (1) 349	(1) PRALSETINIB (S)

<b>AER No</b> <b>Age in Years</b> <b>Sex</b> <b>Country</b> <b>Primary Source</b> <b>Reporter Type</b>	<b>Event Preferred Term of Interest*</b> <b>Severity Grade</b>	<b>Time to onset (in days)</b>	<b>Drug Type (All)</b>
Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	NR		
3303724 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	COVID-19 NR	Not reported	(1) PRALSETINIB (S)
3310244 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Herpes virus infection NR	(1) (1) 321	(1) PRALSETINIB (S)
3330176 52 Female UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	Nasopharyngitis NR	Not reported	(1) PRALSETINIB (S)
3334423 Not reported Female FRANCE Spontaneous Non-healthcare professional	Infection NR	Not reported	(1) PRALSETINIB (S)
3340335 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Paronychia NR	Not reported	(1) PRALSETINIB (S)

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to onset (in days)	Drug Type (All)
3356437 Not reported Female CHINA Non-Interventional Study/Program Non-healthcare professional	Pulpitis dental NR	(1) (1) 365	(1) PRALSETINIB (S)
3360987 83 Female SPAIN Non-Interventional Study/Program Healthcare professional	Respiratory tract infection NR	Not reported	(1) PRALSETINIB (S)
3366826 61 Female CHINA Non-Interventional Study/Program Non-healthcare professional	Oral herpes NR	(1) (1) 60	(1) PRALSETINIB (S)
3382569 Not reported Female UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	Fungal foot infection NR	Not reported	(1) PRALSETINIB (S)
3386201 Not reported Not reported CHINA Non-Interventional Study/Program Non-healthcare professional	Laryngopharyngitis NR	(1) (1) 94	(1) PRALSETINIB (S)
3387498 59 Female CHINA	Urinary tract infection NR	(1) (1) 180	(1) PRALSETINIB (S)

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to onset (in days)	Drug Type (All)
Non-Interventional Study/Program Non-healthcare professional			
3399349 68 Male UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	Cellulitis NR	Not reported	(1) PRALSETINIB (S)
3410099 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Paronychia NR	(1) (2) 211	(1) PRALSETINIB (S)
3416674 Not reported Male CHINA Non-Interventional Study/Program Non-healthcare professional	Herpes zoster NR	(1) (1) 594	(1) PRALSETINIB (S)
3429265 75 Female UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	COVID-19 NR	Not reported	(1) PRALSETINIB (S)
3438102 62 Male UNITED STATES OF AMERICA Literature Spontaneous Non-healthcare professional	Pulmonary tuberculosis NR	Not reported	(1) PRALSETINIB (S)
3457463 Not reported	Bacterial infection NR	Not reported	(1) PRALSETINIB (S)

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to onset (in days)	Drug Type (All)
Not reported UNITED STATES OF AMERICA Literature Spontaneous Non-healthcare professional			
3471116 46 Male UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	Not reported	(1) PRALSETINIB (S)
3477159 70 Female UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	Laryngitis NR	Not reported	(1) PRALSETINIB (S)
3479890 73 Male CHINA Non-Interventional Study/Program Non-healthcare professional	Herpes zoster NR	Not reported	(1) PRALSETINIB (S)
3489984 73 Female UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	Nasopharyngitis NR	Not reported	(1) PRALSETINIB (S)
3500721 59 Male ITALY Non-Interventional Study/Program Non-healthcare professional	Pneumonia NR	Not reported	(1) PRALSETINIB (S)

AER No Age in Years Sex Country Primary Source Reporter Type	Event Preferred Term of Interest* Severity Grade	Time to onset (in days)	Drug Type (All)
3528080 Not reported Female CHINA Non-Interventional Study/Program Healthcare professional	Abscess NR	Not reported	(1) PRALSETINIB (S)  (2) OSIMERTINIB (S)
3551014 57 Female UNITED STATES OF AMERICA Non-Interventional Study/Program Non-healthcare professional	Ear infection NR	Not reported	(1) PRALSETINIB (S)
10000018795 Not reported Not reported FRANCE Spontaneous Healthcare professional	Infection NR	Not reported	(1) PRALSETINIB (S)
10000034956 Not reported Not reported UNITED STATES OF AMERICA Spontaneous Non-healthcare professional	COVID-19 NR	Not reported	(1) PRALSETINIB (S)