# Clinical Trials Data KIT - Document 37

# A Phase 2 Trial of Ponatinib in Participants With Metastatic and/or Unresectable Gastrointestinal Stromal Tumor

## Clinical Trial: https://clinicaltrials.gov/study/NCT01874665

"eligibilityCriteria": "Inclusion Criteria:\n\n1. Male or female participants \\>=18 years old.\n2. GIST with failure of prior TKI therapy defined as:\n\n 1. Histologically confirmed metastatic and/or unresectable GIST after experiencing failure of prior treatment with imatinib, sunitinib, and regorafenib. If prior TKI treatment was neoadjuvant therapy, then relapse must have occurred during the neoadjuvant therapy in order to consider it failed therapy.\n 2. Participants in Cohort A must have evidence of activation mutations in exon 11 of KIT in their tumors. Demonstration of an exon 11 mutation may be based on prior assessment or on evaluation of a tumor sample after enrollment in this study. Participants in Cohort B must have GIST that lacks activating mutations in KIT exon 11, but may have evidence of another activating mutation such as in KIT exon 9 or in PDGFR-\u03b1. Participants may be enrolled in the study prior to determination of the appropriate cohort (as long as both cohorts are open for enrollment).\n3. Measurable disease per modified RECIST 1.1. A lesion in a previously irradiated area is eligible to be considered as measurable disease as long as there is objective evidence of progression of the lesion prior to study enrollment.\n4. Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2.\n5. Adequate hepatic function as defined by the following criteria:\n\n 1. Total serum bilirubin less than or equal to (\\<=) 1.5\\\*Upper Limit of Normal (ULN), unless due to Gilbert's syndrome.\n 2. ALT \\<=2.5\\\*ULN or \\<=5.0\\\*ULN if liver metastases are present.\n 3. AST \\<=2.5\\\*ULN or \\<=5.0\\\*ULN if liver metastases are present.\n6. Adequate renal function as defined by the following criterion:\n\n a. Serum creatinine \\<1.5\\\*ULN.\n7. Adequate pancreatic function as defined by the following criterion:\n\n a. Serum lipase and amylase \\<=1.5\\\*ULN.\n8. For participants of childbearing potential, a negative pregnancy test must be documented prior to enrollment.\n9. Female and male participants who are fertile must agree to use an effective form of contraception with their sexual partners from signing of the informed consent form for this study through 4 months after the end of treatment.\n10. Provision of written informed consent.\n11. Willingness and ability to comply with scheduled visits and study procedures\n12. Fully recovered (\\<= Grade 1 or returned to baseline or deemed irreversible) from the acute effects of prior cancer therapy before initiation of study drug.\n\nExclusion Criteria:\n\n1. Major surgery within 28 days prior to initiating therapy\n2. History of bleeding disorder\n3. History of acute pancreatitis within 1 year of study or history of chronic pancreatitis\n4. History of alcohol abuse\n5. Uncontrolled hypertriglyceridemia (triglycerides \\>450 milligram per deciliter \\[mg/dL\\])\n6. Clinically significant, uncontrolled, or active cardiovascular disease, specifically including, but not restricted to:\n\n 1. Any history of myocardial infarction (MI).\n 2. Any history of unstable angina.\n 3. Congestive heart failure within 6 months prior to enrollment, or left ventricular ejection fraction (LVEF) less than lower limit of normal per local institutional standards within 6 months prior to enrollment.\n 4. History of clinically significant (as determined by the treating physician) atrial arrhythmia.\n 5. Any history of ventricular arrhythmia.\n 6. Any history of cerebrovascular accident or transient ischemic attack (TIA).\n 7. Any history of peripheral vascular infarction, including visceral infarction; or any revascularization procedure of any vasculature, including the placement of a stent.\n 8. Venous thromboembolism including deep venous thrombosis (DVT) or pulmonary embolism within 6 months prior to enrollment.\n7. Uncontrolled hypertension (diastolic blood pressure greater than (\\>) 90 millimeter of mercury \\[mmHg\\]; systolic \\>150 mmHg). Participants with hypertension should be under treatment on study entry to effect blood pressure control.\n8. Taking medications with a known risk of Torsades de Pointes.\n9. Taking any medications or herbal supplements that are known to be strong inhibitors of cytochrome P3A4 (CYP3A4) within at least 14 days before the first dose of ponatinib.\n10. Ongoing or active infection. This includes but is not limited to the requirement for intravenous antibiotics.\n11. Known history of human immunodeficiency virus (HIV). Testing is not required in the absence of prior documentation or known history.\n12. Pregnant or breastfeeding.\n13. Malabsorption syndrome or other gastrointestinal illness that could affect oral absorption of study drugs.\n14. Individuals with a history of a different malignancy, other than cervical cancer in situ, basal cell or squamous cell carcinoma of the skin, are ineligible, except if they have been disease-free for at least 5 years, and are deemed by the investigator to be at low risk for recurrence of that malignancy OR if the other primary malignancy is neither currently clinically significant nor requiring active intervention.\n15. Use of any approved TKIs or investigational agents within 2 weeks or 6 half-lives of the agent, whichever is longer, prior to receiving study drug.\n16. Any condition or illness that, in the opinion of the investigator, would compromise participant safety or interfere with the evaluation of the drug.",  
 "healthyVolunteers": false,  
 "sex": "ALL",  
 "minimumAge": "18 Years",  
"stdAges": [  
"ADULT",  
"OLDER\_ADULT"  
]

Question:  
Based on the following clinical trial information, would a patient with a KIT gene mutation be eligible for the clinical trial?

Answer:  
To determine whether a patient with a KIT gene mutation is eligible for this clinical trial, let's review the relevant inclusion criteria:  
  
1. \*\*General Inclusion Criteria:\*\*  
 - The patient must be at least 18 years old and have histologically confirmed metastatic and/or unresectable GIST after the failure of prior treatment with imatinib, sunitinib, and regorafenib.  
  
2. \*\*Mutation-Specific Inclusion Criteria:\*\*  
 - The trial includes two cohorts:  
 - \*\*Cohort A\*\*: Requires participants to have activating mutations in exon 11 of the KIT gene.  
 - \*\*Cohort B\*\*: Specifically for participants lacking KIT exon 11 mutations but may have other activating mutations, such as in KIT exon 9 or PDGFR-α.  
  
If the patient has a KIT exon 11 mutation, they would potentially be eligible for Cohort A. If they lack the exon 11 mutation but have another KIT mutation (such as in exon 9), they might be eligible for Cohort B.  
  
Given that the patient has a KIT gene mutation, further clarification on which exon this mutation affects is necessary to determine the appropriate cohort:  
- If it's an activating mutation in exon 11, the patient is eligible for Cohort A.  
- If the mutation is elsewhere in the KIT gene, such as exon 9, and there is no exon 11 mutation, the patient is eligible for Cohort B.  
  
Therefore, the eligibility depends on the specific exon affected by the KIT mutation.