Taipei Veterans General Hospital

Department of Pathology and Laboratory Medicine
No.201, Sec. 2, Shipai Rd., Beitou District, Taipei City, Taiwan
11217, R.O.C.
Tel: 02-2875-7449



## Sample Information

**Patient Name:** 薛耀淵
**Gender:** Male
**ID No.:** Y120137802
**History No.:** 37798713
**Age:** 60

**Ordering Doctor:** DOC3016D 江起陸
**Ordering REQ.:** 0BGCTPA
**Signing in Date:** 2021/05/20

**Path No.:** S110-98842
**MP No.:** F21041
**Assay:** Oncomine Focus Assay
**Sample Type:** FFPE
**Block No.:** S110-16420A
**Percentage of tumor cells:** 50%
**Note:**

## Sample Cancer Type: Non-Small Cell Lung Cancer

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### Report Highlights

3 Relevant Biomarkers
10 Therapies Available
143 Clinical Trials

## Relevant Non-Small Cell Lung Cancer Variants

| Gene | Finding | Gene | Finding |
|---|---|---|---|
| ALK | Not detected | NTRK1 | Not detected |
| BRAF | Not detected | NTRK2 | Not detected |
| EGFR | ***EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC (EGFR exon 19 deletion), EGFR p.(T790M) c.2369C>T*** | NTRK3 | Not detected |
| ERBB2 | Not detected | RET | Not detected |
| KRAS | Not detected | ROS1 | Not detected |
| MET | Not detected | | |

## Relevant Biomarkers

| Tier | Genomic Alteration | Relevant Therapies (In this cancer type) | Relevant Therapies (In other cancer type) | Clinical Trials |
|---|---|---|---|---|
| IA | *EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC*<br>EGFR exon 19 deletion<br>epidermal growth factor receptor<br>Allele Frequency: 15.61% | **bevacizumab* + erlotinib** [2]<br>**erlotinib + ramucirumab** [1, 2]<br>**osimertinib** [1, 2]<br>afatinib + cetuximab<br>atezolizumab + bevacizumab + chemotherapy<br>bevacizumab + gefitinib<br>gefitinib + chemotherapy<br>osimertinib + chemotherapy | None | 116 |
| IA | *EGFR p.(T790M) c.2369C>T*<br>epidermal growth factor receptor<br>Allele Frequency: 8.65% | **osimertinib** [1, 2]<br>osimertinib + chemotherapy | None | 78 |
| IIC | *PIK3CA p.(E726K) c.2176G>A*<br>phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha<br>Allele Frequency: 9.31% | None | None | 15 |

**Public data sources included in relevant therapies: FDA**[1], NCCN, **EMA**[2], ESMO
**Tier Reference:** Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.
*** Includes biosimilars**

**Alerts informed by public data sources:** ⊘ Contraindicated, 🛡 Resistance

| | |
|---|---|
| *EGFR p.(T790M) c.2369C>T* | ⊘ **gefitinib** [2]<br>🛡 afatinib, dacomitinib, erlotinib, gefitinib |

**Public data sources included in alerts: FDA**[1], NCCN, **EMA**[2], ESMO

## Variant Details

### DNA Sequence Variants

| Gene | Amino Acid Change | Coding | Variant ID | Locus | Allele Frequency | Transcript | Variant Effect | Coverage |
|---|---|---|---|---|---|---|---|---|
| PIK3CA | p.(E726K) | c.2176G>A | COSM87306 | chr3:178938934 | 9.31% | NM_006218.3 | missense | 1997 |
| EGFR | p.(E746_A750del) | c.2235_2249delGGAATTAAGAGAAGC | COSM6223 | chr7:55242464 | 15.61% | NM_005228.4 | nonframeshift Deletion | 1947 |
| EGFR | p.(T790M) | c.2369C>T | COSM6240 | chr7:55249071 | 8.65% | NM_005228.4 | missense | 1999 |
| FGFR4 | p.(P136L) | c.407C>T | . | chr5:176517797 | 98.95% | NM_213647.2 | missense | 2000 |
| MET | p.(N375S) | c.1124A>G | . | chr7:116340262 | 46.05% | NM_001127500.2 | missense | 2000 |

## Biomarker Descriptions

**EGFR (epidermal growth factor receptor)**

Background: The EGFR gene encodes the epidermal growth factor receptor (EGFR) tyrosine kinase, a member of the ERBB/human epidermal growth factor receptor (HER) family. In addition to EGFR/ERBB1/HER1, other members of the ERBB/HER family include ERBB2/HER2, ERBB3/HER3, and ERBB4/HER4[1]. EGFR ligand induced dimerization results in kinase activation and leads to stimulation of oncogenic signaling pathways including the PI3K/AKT/MTOR and RAS/RAF/MEK/ERK pathways. Activation of these pathways promote cell proliferation, differentiation, and survival[2,3].

## Biomarker Descriptions (continued)

Alterations and prevalence: Recurrent somatic mutations in the tyrosine kinase domain (TKD) of EGFR are observed in approximately 10-20% of lung adenocarcinoma, and at higher frequencies in never-smoker, female, and Asian populations[4,5,6,7]. The most common mutations occur near the ATP-binding pocket of the TKD and include short in-frame deletions in exon 19 (EGFR exon 19 deletion) and the L858R amino acid substitution in exon 21[8]. These mutations constitutively activate EGFR resulting in downstream signaling, and represent 80% of the EGFR mutations observed in lung cancer. A second group of less prevalent activating mutations include E709K, G719X, S768I, L861Q, and short in-frame insertion mutations in exon 20[9,10,11,12]. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations[13]. In contrast, a different set of recurrent activating EGFR mutations in the extracellular domain include R108K, A289V and G598V and are primarily observed in glioblastoma[8,14]. Amplification of EGFR is observed in several cancer types including 30% of glioblastoma, 12% of esophageal cancer, 10% of head and neck cancer, 5% of bladder cancer, and 5% of lung squamous cell carcinoma[5,6,7,14,15]. Deletion of exons 2-7, encoding the extracellular domain of EGFR (EGFRvIII), results in overexpression of a ligand-independent constitutively active protein and is observed in approximately 30% of glioblastoma[16,17,18].

Potential relevance: Approved first-generation EGFR tyrosine kinase inhibitors (TKIs) include erlotinib[19] (2004) and gefitinib[20] (2015), which block the activation of downstream signaling by reversible interaction with the ATP-binding site. Although initially approved for advanced lung cancer, the discovery that drug sensitivity was associated with exon 19 and exon 21 activating mutations allowed first-generation TKIs to become subsequently approved for front-line therapy in lung cancer tumors containing exon 19 or exon 21 activating mutations. Second-generation TKIs afatinib[21] (2013) and dacomitinib[22] (2018) bind EGFR and other ERBB/HER gene family members irreversibly and were subsequently approved. First- and second-generation TKIs afatinib, dacomitinib, erlotinib, and gefitinib are recommended for the treatment NSCLC harboring EGFR exon 19 insertions, exon 19 deletions, point mutations L861Q, L858R, S768I, and codon 719 mutations, whereas most EGFR exon 20 insertions, except p.A763_Y764insFQEA, confer resistance to the same therapies[23,24,25,26]. In lung cancer containing EGFR exon 19 or 21 activating mutations, treatment with TKIs is eventually associated with the emergence of drug resistance[27]. The primary resistance mutation that emerges following treatment with first-generation TKI is T790M, accounting for 50-60% of resistant cases[8]. Third generation TKIs were developed to maintain sensitivity in the presence of T790M. Osimertinib[28] (2015) is an irreversible inhibitor indicated for metastatic EGFR T790M positive lung cancer and for the first-line treatment of metastatic NSCLC containing EGFR exon 19 deletions or exon 21 L858R mutations. Like first-generation TKIs, treatment with osimertinib is associated with acquired resistance. In this case, resistance is associated with the C797S mutation, and occurs in 22-44% of cases[27]. The T790M and C797S mutations may be each selected following sequential treatment with a first-generation TKI followed by a third-generation TKI or vice versa[29]. T790M and C797S can occur in either cis or trans allelic orientation[29]. If C797S is observed following progression after treatment with a third-generation TKI in the first-line setting, sensitivity may be retained to first-generation TKIs[29]. If C797S co-occurs in trans with T790M following sequential treatment with first- and third-generation TKIs, patients may exhibit sensitivity to combination first- and third-generation TKIs, but resistance to third-generation TKIs alone[29,30]. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs[29]. Fourth-generation TKIs are in development to overcome acquired C797S and T790M resistance mutations after osimertinib treatment. EGFR targeting antibodies including cetuximab (2004), panitumumab (2006), and necitumumab (2016) are under investigation in combination with EGFR-targeting TKIs for efficacy against EGFR mutations. The bispecific antibody, JNJ-61186372[31], targeting EGFR and MET, and the TKI mobocertinib[32], each received a breakthrough designation from the FDA (2020) for NSCLC tumors harboring EGFR exon 20 insertion mutations. The Oncoprex immunogene therapy CNVN-202[33] in combination with osimertinib received a fast track designation from the FDA (2020) for NSCLC tumors harboring EGFR mutations that progressed on osimertinib alone. BDTX-189[34] was granted a fast track designation (2020) for the treatment of solid tumors harboring an EGFR exon 20 insertion mutation.

**PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha)**

Background: The PIK3CA gene encodes the phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha of the class I phosphatidylinositol 3-kinase (PI3K) enzyme[35]. PI3K is a heterodimer that contains a p85 regulatory subunit, which couples one of four p110 catalytic subunits to activated tyrosine protein kinases[36,37]. The p110 catalytic subunits include p110α, β, δ, γ and are encoded by genes PIK3CA, PIK3CB, PIK3CD, and PIK3CG, respectively[36]. PI3K catalyzes the conversion of phosphatidylinositol (4,5)-bisphosphate (PI(4,5)P2) into phosphatidylinositol (3,4,5)-trisphosphate (PI(3,4,5)P3) while the phosphatase and tensin homolog (PTEN) catalyzes the reverse reaction[38,39]. The reversible phosphorylation of inositol lipids regulates diverse aspects of cell growth and metabolism[38,39,40,41]. Recurrent somatic alterations in PIK3CA are frequent in cancer and result in the activation of PI3K/AKT/MTOR pathway, which can influence several hallmarks of cancer including cell proliferation, apoptosis, cancer cell metabolism and invasion, and genetic instability[42,43,44].

Alterations and prevalence: Recurrent somatic activating mutations in PIK3CA are common in diverse cancers and are observed in 20-30% of breast, cervical, and uterine cancers and 10-20% of bladder, gastric, head and neck, and colorectal cancers[6,7]. Activating mutations in PIK3CA commonly cluster in two regions corresponding to the exon 9 helical (codons E542/E545) and exon 20 kinase (codon H1047) domains, each having distinct mechanisms of activation[45,46,47]. PIK3CA resides in the 3q26 cytoband, a region frequently amplified (10-30%) in diverse cancers including squamous carcinomas of the lung, cervix, head and neck, and esophagus, and in serous ovarian and uterine cancers[6,7].

## Biomarker Descriptions (continued)

Potential relevance: The PI3K inhibitor, alpelisib[48], is FDA approved (2019) in combination with fulvestrant for the treatment of patients with PIK3CA-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, advanced or metastatic breast cancer. Additionally, a phase Ib study of alpelisib with letrozole in patients with metastatic estrogen receptor (ER)-positive breast cancer, the clinical benefit rate, defined as lack of disease progression ≥ 6 months, was 44% (7/16) in PIK3CA-mutated tumors and 20% (2/20) in PIK3CA wild-type tumors[49]. Specifically, exon 20 H1047R mutations were associated with more durable clinical responses in comparison to exon 9 E545K mutations[49]. However, alpelisib did not improve response when administered with letrozole in patients with ER+ early breast cancer with PIK3CA mutations[50]. Case studies with MTOR inhibitors sirolimus and temsirolimus report isolated cases of clinical response in PIK3CA mutated refractory cancers[51,52].

## Relevant Therapy Summary

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

### EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| osimertinib | ● | ● | ● | ● | ● (III) |
| erlotinib + ramucirumab | ● | ● | ● | ● | ✖ |
| bevacizumab + erlotinib | ✖ | ● | ● | ● | ✖ |
| afatinib + cetuximab | ✖ | ● | ✖ | ✖ | ✖ |
| osimertinib + chemotherapy | ✖ | ● | ✖ | ✖ | ✖ |
| osimertinib + chemotherapy + surgical intervention | ✖ | ● | ✖ | ✖ | ✖ |
| bevacizumab (Allergan) + erlotinib | ✖ | ✖ | ● | ✖ | ✖ |
| bevacizumab (Fujifilm Kyowa Kirin Biologics) + erlotinib | ✖ | ✖ | ● | ✖ | ✖ |
| bevacizumab (Pfizer) + erlotinib | ✖ | ✖ | ● | ✖ | ✖ |
| bevacizumab (Samsung Bioepis) + erlotinib | ✖ | ✖ | ● | ✖ | ✖ |
| atezolizumab + bevacizumab + carboplatin + paclitaxel | ✖ | ✖ | ✖ | ● | ✖ |
| bevacizumab + gefitinib | ✖ | ✖ | ✖ | ● | ✖ |
| gefitinib + carboplatin + pemetrexed | ✖ | ✖ | ✖ | ● | ✖ |
| apatinib + EGFR tyrosine kinase inhibitor | ✖ | ✖ | ✖ | ✖ | ● (IV) |
| bevacizumab + osimertinib, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (IV) |
| EGFR tyrosine kinase inhibitor | ✖ | ✖ | ✖ | ✖ | ● (IV) |
| icotinib hydrochloride | ✖ | ✖ | ✖ | ✖ | ● (IV) |
| icotinib hydrochloride, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (IV) |
| icotinib hydrochloride, radiation therapy | ✖ | ✖ | ✖ | ✖ | ● (IV) |
| almonertinib | ✖ | ✖ | ✖ | ✖ | ● (III) |

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

## Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

### EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC (continued)

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| amivantamab, lazertinib, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (III) |
| atezolizumab, bevacizumab, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (III) |
| atezolizumab, PF-06744547 | ✖ | ✖ | ✖ | ✖ | ● (III) |
| durvalumab, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (III) |
| EGFR tyrosine kinase inhibitor, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (III) |
| icotinib hydrochloride, anlotinib hydrochloride | ✖ | ✖ | ✖ | ✖ | ● (III) |
| osimertinib, bevacizumab | ✖ | ✖ | ✖ | ✖ | ● (III) |
| osimertinib, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (III) |
| D-0316, icotinib hydrochloride | ✖ | ✖ | ✖ | ✖ | ● (II/III) |
| almonertinib, radiation therapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| anlotinib hydrochloride, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| anlotinib hydrochloride, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| atezolizumab, bevacizumab | ✖ | ✖ | ✖ | ✖ | ● (II) |
| atezolizumab, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| avitinib, zorifertinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| bevacizumab, atezolizumab | ✖ | ✖ | ✖ | ✖ | ● (II) |
| bevacizumab, atezolizumab, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| bevacizumab, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| bintrafusp alfa, chemoradiation therapy, durvalumab | ✖ | ✖ | ✖ | ✖ | ● (II) |
| camrelizumab, apatinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| chemotherapy, atezolizumab, bevacizumab | ✖ | ✖ | ✖ | ✖ | ● (II) |
| chemotherapy, durvalumab | ✖ | ✖ | ✖ | ✖ | ● (II) |
| crizotinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| datopotamab deruxtecan | ✖ | ✖ | ✖ | ✖ | ● (II) |
| durvalumab, tremelimumab, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| EGFR tyrosine kinase inhibitor + chemotherapy, EGFR tyrosine kinase inhibitor | ✖ | ✖ | ✖ | ✖ | ● (II) |
| EGFR tyrosine kinase inhibitor, apatinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| EGFR tyrosine kinase inhibitor, radiation therapy | ✖ | ✖ | ✖ | ✖ | ● (II) |

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

## Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

### EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC (continued)

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| famitinib, almonertinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| olaparib, durvalumab | ✖ | ✖ | ✖ | ✖ | ● (II) |
| osimertinib, abemaciclib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| osimertinib, radiation therapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| osimertinib, ramucirumab | ✖ | ✖ | ✖ | ✖ | ● (II) |
| osimertinib, savolitinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| patritumab deruxtecan | ✖ | ✖ | ✖ | ✖ | ● (II) |
| ramucirumab, chemotherapy, cytokine | ✖ | ✖ | ✖ | ✖ | ● (II) |
| SH-1028 | ✖ | ✖ | ✖ | ✖ | ● (II) |
| tyrosine kinase inhibitors, radiation therapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| ASK120067 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| BBT-176, cetuximab | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| CBT-502, anlotinib hydrochloride | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| DZD-9008 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| EMB01 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| KP-673 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| mobocertinib | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| necitumumab, trastuzumab, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| osimertinib, anlotinib hydrochloride | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| alisertib, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| alisertib, sapanisertib, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| amivantamab, lazertinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| BBP-398 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| BCA101 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| C-005 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| chemotherapy, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| CK-101 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| etrumadenant, zimberelimab, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (I) |
| FCN-411 | ✖ | ✖ | ✖ | ✖ | ● (I) |

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

## Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

### EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC (continued)

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| FT500, nivolumab, pembrolizumab, atezolizumab | ✖ | ✖ | ✖ | ✖ | ● (I) |
| genolimzumab, fruquintinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| lazertinib, amivantamab | ✖ | ✖ | ✖ | ✖ | ● (I) |
| MRX-2843, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| nazartinib, trametinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| neratinib, palbociclib, everolimus, trametinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| niraparib, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| nivolumab, ipilimumab, radiation therapy | ✖ | ✖ | ✖ | ✖ | ● (I) |
| osimertinib, ipilimumab | ✖ | ✖ | ✖ | ✖ | ● (I) |
| pirotinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| PLB-1004 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| telaglenastat, sapanisertib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| telisotuzumab vedotin, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| TNO-155, nazartinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| TQB 3804 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| TY-9591 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| XZP-5809 | ✖ | ✖ | ✖ | ✖ | ● (I) |

### EGFR p.(T790M) c.2369C>T

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| osimertinib | ● | ● | ● | ● | ● (II) |
| osimertinib + chemotherapy | ✖ | ● | ✖ | ✖ | ✖ |
| osimertinib + chemotherapy + surgical intervention | ✖ | ● | ✖ | ✖ | ✖ |
| anlotinib hydrochloride, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (IV) |
| apatinib + EGFR tyrosine kinase inhibitor | ✖ | ✖ | ✖ | ✖ | ● (IV) |
| icotinib hydrochloride, radiation therapy | ✖ | ✖ | ✖ | ✖ | ● (IV) |
| almonertinib | ✖ | ✖ | ✖ | ✖ | ● (III) |
| durvalumab, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (III) |
| EGFR tyrosine kinase inhibitor, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (III) |

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

## Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

### EGFR p.(T790M) c.2369C>T (continued)

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| icotinib hydrochloride, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (III) |
| osimertinib, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (III) |
| sintilimab, bevacizumab (Innovent Biologics), chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (III) |
| toripalimab, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (III) |
| abivertinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| anlotinib hydrochloride, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| apatinib, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| atezolizumab, bevacizumab | ✖ | ✖ | ✖ | ✖ | ● (II) |
| atezolizumab, bevacizumab, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| avitinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| bevacizumab, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| crizotinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| durvalumab, tremelimumab, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| EGFR tyrosine kinase inhibitor + chemotherapy, EGFR tyrosine kinase inhibitor | ✖ | ✖ | ✖ | ✖ | ● (II) |
| EGFR tyrosine kinase inhibitor, apatinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| EGFR tyrosine kinase inhibitor, radiation therapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| famitinib, almonertinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| icotinib hydrochloride | ✖ | ✖ | ✖ | ✖ | ● (II) |
| KN046 | ✖ | ✖ | ✖ | ✖ | ● (II) |
| olaparib, durvalumab | ✖ | ✖ | ✖ | ✖ | ● (II) |
| osimertinib, radiation therapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| ramucirumab, chemotherapy, cytokine | ✖ | ✖ | ✖ | ✖ | ● (II) |
| SH-1028 | ✖ | ✖ | ✖ | ✖ | ● (II) |
| toripalimab, anlotinib hydrochloride, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| tyrosine kinase inhibitors, radiation therapy | ✖ | ✖ | ✖ | ✖ | ● (II) |
| ASK120067 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| DZD-9008 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| EMB01 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

## Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

### EGFR p.(T790M) c.2369C>T (continued)

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| KP-673 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| mobocertinib | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| alisertib, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| alisertib, sapanisertib, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| amivantamab | ✖ | ✖ | ✖ | ✖ | ● (I) |
| BBP-398 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| BCA101 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| BEBT-109 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| C-005 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| chemotherapy, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| CK-101 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| FCN-411 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| FT500, nivolumab, pembrolizumab, atezolizumab | ✖ | ✖ | ✖ | ✖ | ● (I) |
| lazertinib, amivantamab | ✖ | ✖ | ✖ | ✖ | ● (I) |
| nazartinib, trametinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| neratinib, palbociclib, everolimus, trametinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| nivolumab, ipilimumab, radiation therapy | ✖ | ✖ | ✖ | ✖ | ● (I) |
| Palcitoclax, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| pirotinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| PLB-1004 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| SPH3348, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| telisotuzumab vedotin, osimertinib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| TQB 3804 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| TQB3456 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| TY-9591 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| XZP-5809 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| YK-029A | ✖ | ✖ | ✖ | ✖ | ● (I) |
| YZJ-0318 | ✖ | ✖ | ✖ | ✖ | ● (I) |

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

## Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

### PIK3CA p.(E726K) c.2176G>A

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| EGFR tyrosine kinase inhibitor, chemotherapy | ✖ | ✖ | ✖ | ✖ | ● (III) |
| everolimus | ✖ | ✖ | ✖ | ✖ | ● (II) |
| inavolisib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| ipatasertib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| paxalisib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| samotolisib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| sirolimus | ✖ | ✖ | ✖ | ✖ | ● (II) |
| temsirolimus | ✖ | ✖ | ✖ | ✖ | ● (II) |
| ipatasertib, atezolizumab | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| TAS-117, futibatinib | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| copanlisib, olaparib, durvalumab | ✖ | ✖ | ✖ | ✖ | ● (I) |
| palbociclib, gedatolisib | ✖ | ✖ | ✖ | ✖ | ● (I) |
| paxalisib, radiation therapy | ✖ | ✖ | ✖ | ✖ | ● (I) |

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

# Relevant Therapy Details

## Current FDA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

FDA information is current as of 2021-04-14. For the most up-to-date information, search www.fda.gov.

## EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC

### ● erlotinib + ramucirumab

**Cancer type:** Non-Small Cell Lung Cancer **Label as of:** 2020-07-06 **Variant class:** EGFR exon 19 deletion

**Indications and usage:**

CYRAMZA® is a human vascular endothelial growth factor receptor 2 (VEGFR2) antagonist indicated:

- as a single agent or in combination with paclitaxel, for treatment of advanced or metastatic gastric or gastro-esophageal junction adenocarcinoma with disease progression on or after prior fluoropyrimidine- or platinum-containing chemotherapy.
- in combination with erlotinib, for first-line treatment of metastatic non-small cell lung cancer with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) mutations.
- in combination with docetaxel, for treatment of metastatic non-small cell lung cancer with disease progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving CYRAMZA®.
- in combination with FOLFIRI, for the treatment of metastatic colorectal cancer with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine.
- as a single agent, for the treatment of hepatocellular carcinoma in patients who have an alpha fetoprotein of ≥400 ng/mL and have been treated with sorafenib.

**Reference:**

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125477s037lbl.pdf

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### ● osimertinib

**Cancer type:** Non-Small Cell Lung Cancer **Label as of:** 2020-12-18 **Variant class:** EGFR exon 19 deletion

**Indications and usage:**

TAGRISSO® is a kinase inhibitor indicated for:

- as adjuvant therapy after tumor resection in adult patients with non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
- the first-line treatment of adult patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
- the treatment of adult patients with metastatic EGFR T790M mutation positive NSCLC, as detected by an FDA-approved test, whose disease has progressed on or after EGFR TKI therapy.

**Reference:**

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/208065s021lbl.pdf

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## EGFR p.(T790M) c.2369C>T

### osimertinib

**Cancer type:** Non-Small Cell Lung Cancer **Label as of:** 2020-12-18 **Variant class:** EGFR T790M mutation

**Indications and usage:**

TAGRISSO® is a kinase inhibitor indicated for:

- as adjuvant therapy after tumor resection in adult patients with non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
- the first-line treatment of adult patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
- the treatment of adult patients with metastatic EGFR T790M mutation positive NSCLC, as detected by an FDA-approved test, whose disease has progressed on or after EGFR TKI therapy.

**Reference:**

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/208065s021lbl.pdf

## Current NCCN Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

NCCN information is current as of 2021-04-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

## EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC

### ● osimertinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

**NCCN Recommendation category:** 1

**Population segment (Line of therapy):**
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Preferred intervention

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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### ● afatinib + cetuximab

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Progression (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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### ● bevacizumab + erlotinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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### ● erlotinib + ramucirumab

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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## EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC (continued)

### osimertinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy); Preferred intervention

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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### osimertinib + chemotherapy

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Stage IIB, Stage IIIA, Stage IIIB (Adjuvant therapy)
- Stage IIIA; Resectable (Adjuvant therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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### osimertinib + chemotherapy + surgical intervention

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Stage IIB (Adjuvant therapy)
- Stage IIIA; Resectable (Adjuvant therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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## EGFR p.(T790M) c.2369C>T

### osimertinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

**NCCN Recommendation category:** 1

**Population segment (Line of therapy):**
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Progression, Asymptomatic, Symptomatic (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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## EGFR p.(T790M) c.2369C>T (continued)

### osimertinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Brain Metastases, Leptomeningeal Metastases, Spine Metastases (Line of therapy not specified)

**Reference:** NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 4.2020]

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### osimertinib + chemotherapy

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Stage IIB, Stage IIIA, Stage IIIB (Adjuvant therapy)
- Stage IIIA; Resectable (Adjuvant therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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### osimertinib + chemotherapy + surgical intervention

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Stage IIB (Adjuvant therapy)
- Stage IIIA; Resectable (Adjuvant therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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## Current EMA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

EMA information is current as of 2021-04-14. For the most up-to-date information, search www.ema.europa.eu/ema.

## EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC

### ● bevacizumab (Allergan) + erlotinib

**Cancer type:** Non-Small Cell Lung Cancer **Label as of:** 2020-11-03 **Variant class:** EGFR exon 19 deletion

**Reference:**

https://www.ema.europa.eu/en/documents/product-information/mvasi-epar-product-information_en.pdf

### ● bevacizumab (Fujifilm Kyowa Kirin Biologics) + erlotinib

**Cancer type:** Non-Small Cell Lung Cancer **Label as of:** 2020-11-16 **Variant class:** EGFR exon 19 deletion

**Reference:**

https://www.ema.europa.eu/en/documents/product-information/equidacent-epar-product-information_en.pdf

### ● bevacizumab (Pfizer) + erlotinib

**Cancer type:** Non-Small Cell Lung Cancer **Label as of:** 2021-01-07 **Variant class:** EGFR exon 19 deletion

**Reference:**

https://www.ema.europa.eu/en/documents/product-information/zirabev-epar-product-information_en.pdf

### ● bevacizumab (Samsung Bioepis) + erlotinib

**Cancer type:** Non-Small Cell Lung Cancer **Label as of:** 2021-04-06 **Variant class:** EGFR exon 19 deletion

**Reference:**

https://www.ema.europa.eu/en/documents/product-information/aybintio-epar-product-information_en.pdf

### ● bevacizumab + erlotinib

**Cancer type:** Non-Small Cell Lung Cancer **Label as of:** 2021-01-28 **Variant class:** EGFR exon 19 deletion

**Reference:**

https://www.ema.europa.eu/en/documents/product-information/avastin-epar-product-information_en.pdf

### ● erlotinib + ramucirumab

**Cancer type:** Non-Small Cell Lung Cancer **Label as of:** 2020-07-02 **Variant class:** EGFR exon 19 deletion

**Reference:**

https://www.ema.europa.eu/en/documents/product-information/cyramza-epar-product-information_en.pdf

## EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC (continued)

### osimertinib

**Cancer type:** Non-Small Cell Lung Cancer **Label as of:** 2020-10-16 **Variant class:** EGFR exon 19 deletion

**Reference:**

https://www.ema.europa.eu/en/documents/product-information/tagrisso-epar-product-information_en.pdf

## EGFR p.(T790M) c.2369C>T

### osimertinib

**Cancer type:** Non-Small Cell Lung Cancer **Label as of:** 2020-10-16 **Variant class:** EGFR T790M mutation

**Reference:**

https://www.ema.europa.eu/en/documents/product-information/tagrisso-epar-product-information_en.pdf

## Current ESMO Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

ESMO information is current as of 2021-04-01. For the most up-to-date information, search www.esmo.org.

## EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC

### ● atezolizumab + bevacizumab + carboplatin + paclitaxel

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

**ESMO Level of Evidence/Grade of Recommendation:** III / A

**Population segment (Line of therapy):**
- Non-squamous Cell; Metastatic (First-line therapy); ESMO-MCBS v1.1 score: 3
- Metastatic (Second-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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### ● osimertinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**
- Advanced (First-line therapy); ESMO-MCBS v1.1 score: 4

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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### ● bevacizumab + erlotinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**
- Stage IV (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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## EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC (continued)

### bevacizumab + gefitinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**
- Stage IV (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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### erlotinib + ramucirumab

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**
- Stage IV (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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### gefitinib + carboplatin + pemetrexed

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**
- Stage IV (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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### bevacizumab + erlotinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / B

**Population segment (Line of therapy):**
- Stage IV (First-line therapy); ESMO-MCBS v1.1 score: 3

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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## EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC (continued)

### bevacizumab + gefitinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / B

**Population segment (Line of therapy):**
- Stage IV (First-line therapy); ESMO-MCBS v1.1 score: 3

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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### erlotinib + ramucirumab

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / B

**Population segment (Line of therapy):**
- Stage IV (First-line therapy); ESMO-MCBS v1.1 score: 3

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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### gefitinib + carboplatin + pemetrexed

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / B

**Population segment (Line of therapy):**
- Advanced (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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### bevacizumab + erlotinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

**ESMO Level of Evidence/Grade of Recommendation:** III / A

**Population segment (Line of therapy):**
- Stage IV (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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## EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC (continued)

### bevacizumab + gefitinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

**ESMO Level of Evidence/Grade of Recommendation:** III / A

**Population segment (Line of therapy):**
- Stage IV (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### erlotinib + ramucirumab

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

**ESMO Level of Evidence/Grade of Recommendation:** III / A

**Population segment (Line of therapy):**
- Stage IV (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### gefitinib + carboplatin + pemetrexed

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR activating mutation

**ESMO Level of Evidence/Grade of Recommendation:** III / A

**Population segment (Line of therapy):**
- Stage IV (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

## EGFR p.(T790M) c.2369C>T

### osimertinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**
- Stage IV (Second-line therapy); ESMO-MCBS v1.1 score: 4

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

## Clinical Trials Summary

### EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC + EGFR p.(T790M) c.2369C>T + PIK3CA p.(E726K) c.2176G>A

| NCT ID | Title | Phase |
|---|---|---|
| NCT04552613 | Efficacy of Targeted Therapy Combined Chemotherapy in Advanced EGFR Positive NSCLC Patients With Concurrent Driver Gene Mutations | III |

### EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC + EGFR p.(T790M) c.2369C>T

| NCT ID | Title | Phase |
|---|---|---|
| NCT04687241 | Efficacy and Safety of Almonertinib Versus Placebo as Adjuvant Therapy for Subjects With Resected Stage II-IIIB NSCLC Harboring EGFR-sensitive Mutations: A Randomized, Controlled, Double-blind, Phase III and Multicenter Clinical Study | III |
| NCT04035486 | A Phase III, Open-label, Randomized Study of Osimertinib With or Without Platinum Plus Pemetrexed Chemo, as First-line Treatment in Patients With Epidermal Growth Factor Receptor (EGFR) Mutation Positive, Locally Advanced or Metastatic Non-small Cell Lung Cancer (FLAURA2) | III |
| NCT04351555 | A Phase III, Randomised, Controlled, Multi-center, 3-Arm Study of Neoadjuvant Osimertinib as Monotherapy or in Combination With Chemotherapy Versus Standard of Care Chemotherapy Alone for the Treatment of Patients With Epidermal Growth Factor Receptor Mutation Positive, Resectable Non-small Cell Lung Cancer | III |
| NCT04029350 | A Multi-center, One-arm, Phase II Trial of Anlotinib Combined With Osimertinib as the Second-line Treatment in Stage IIIb-IV NSCLC With Confirmed EGFRm and T790M. | II |
| NCT04426825 | A Single Arm, Phase II Study of Atezolizumab (MPDL3280A, Anti-PD-L1 Antibody) in Combination With Bevacizumab in Patients With EGFR Mutation Positive Stage IIIB/IV Non-Squamous Non-Small Cell Lung Cancer Pretreated With Epidermal Growth Factor Receptor Tyrosine-Kinase Inhibitors | II |
| NCT03994393 | A Phase II Trial of Durvalumab (MEDI4736) and Tremelimumab With Chemotherapy in Metastatic EGFR Mutant Non-squamous Non-small Cell Lung Cancer (NSCLC) Following Progression on EGFR Tyrosine Kinase Inhibitors (TKIs) | II |
| No NCT ID | A Phase II Study Of Osimertinib For Untreated CNS Metastasis, EGFR T790M-Positive Non-Small Cell Lung Cancer(LOGIK1603/ WJOG9116L). | II |
| NCT02811354 | Phase II Study of AZD9291 in Patients With Advanced Stage Non-small Cell Lung Cancer Following Prior EGFR TKI Therapy With EGFR and T790M Mutations Detected in Plasma Circulating Tumor DNA (PLASMA) | II |
| NCT02824952 | Neo-adjuvant Trial With AZD9291 in EGFRm+ Stage IIIA/B NSCLC - a Phase II Open-label Study | II |
| NCT04233021 | A Phase II, Multi-centre Study, to Evaluate the Efficacy and Safety of Osimertinib Treatment for Patients With EGFR-mutated Non-small Cell Lung Cancer (NSCLC) With Brain or Leptomeningeal Metastases | II |
| NCT04563871 | A Phase II, Open-label, Single-arm, Multicenter, Efficacy and Safety of 80mg Osimertinib in Patients With Leptomeningeal Metastases(LM) Associated With EGFR Mutation-positive Non-small Cell Lung Cancer(NSCLC) | II |
| NCT03823807 | A Multicenter, Open-label, Phase II Study to Evaluate the Safety and Efficacy of SH-1028 in Locally Advanced or Metastatic NSCLC | II |
| NCT03502850 | A Phase I/II Study to Assess the Safety,Tolerability, Pharmacokinetics and Anti-tumour Activity of ASK120067 in Patients With Locally Advanced or Metastatic T790M Mutation-positive Non-Small Cell Lung Cancer Who Have Progressed Following Prior Therapy With an Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor Agent | I/II |
| NCT02716116 | A Phase I/II Study of the Safety, Pharmacokinetics, and Anti-Tumor Activity of the Oral EGFR/HER2 Inhibitor TAK-788 (AP32788) in Non-Small Cell Lung Cancer | I/II |

## Clinical Trials Summary (continued)

### EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC + EGFR p.(T790M) c.2369C>T (continued)

| NCT ID | Title | Phase |
|---|---|---|
| NCT04541407 | A Phase I Study of Temozolomide in Combination with Targeted Therapy for NSCLC Patients With CNS Progression on Either Osimertinib or Lorlatinib | I |
| NCT03420079 | A Phase I, Multi-center, Open-label, Single-arm, Dose-escalation and Dose-expansion Clinical Study to Evaluate the Safety, Tolerability, Pharmacokinetics (PK) and Anti-tumor Activities of FCN-411 Monotherapy in Advanced Non-small Cell Lung Cancer | I |
| NCT03516214 | An Open-label, Multicenter, Phase I Dose-escalation Trial of EGF816 and Trametinib in Patients With Non-small Cell Lung Cancer and Acquired EGFR p.T790M-positive Resistance to 1st or 2nd Generation EGFR TKI Therapy | I |
| No NCT ID | To Evaluate the Safety and Effectiveness of PLB1004 in the Treatment of Advanced Non-Small Cell Lung Cancer | I |
| NCT03603262 | A Phase I, Open-label Study to Assess the Safety, Tolerability and Pharmacokinetics of Ascending Doses of SH-1028 Tablets in Patients With Advanced Non-small Cell Lung Cancer | I |
| NCT03618043 | A Phase I, Open-label Study to Assess the Safety and Tolerability of Ascending Doses of SH-1028 Tablets in Patients With Advanced Solid Cancer. | I |
| NCT02099058 | A Multicenter, Phase I/Ib, Open-Label, Dose-Escalation Study of ABBV-399, an Antibody Drug Conjugate, in Subjects With Advanced Solid Tumors | I |
| NCT04204473 | Phase I, Open-label, Single-arm Study to Evaluate the Safety, Tolerance, Pharmacokinetics and Preliminary Efficacy of TY-9591 Tablets in Advanced NSCLC Patients With Epidermal Growth Factor Receptor( EGFR) Positive Mutation | I |
| NCT04622072 | A Single-arm, Open, Multi-center Phase I/II Clinical Trial to Evaluate the Safety, Tolerability, Pharmacokinetic Characteristics and Effectiveness of XZP-5809-TT1 Tablets in Patients With T790M Mutation-positive Locally Advanced or Metastatic Non-small Cell Lung Cancer Who Have Progressed After Treatment With Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor (EGFR-TKI). | I |

### EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC

| NCT ID | Title | Phase |
|---|---|---|
| No NCT ID | The Efficacy and Safety of Osimertinib Combined with Bevacizumab in the Treatment of SD Patients with Non-Squamous Cell Lung Cancer | IV |
| NCT01665417 | Randomized, Open Label, Positive Controlled, Multicenter Trial to Evaluate Icotinib as First-line and Maintenance Treatment in EGFR Mutated Patients With Lung Adenocarcinoma | IV |
| NCT02404675 | High Dose Icotinib in Advanced Non-small Cell Lung Cancer With EGFR 21 Exon Mutation (INCREASE): a Randomized, Open-label Study | IV |
| NCT02103257 | Sequential Icotinib Plus Chemotherapy Versus Icotinib Alone as First-line Treatment in Stage IIIB/IV Lung Adenocarcinoma: a Randomized, Open-label, Multicenter Study | IV |
| NCT04487080 | A Phase III, Randomized Study of Amivantamab and Lazertinib Combination Therapy Versus Osimertinib Versus Lazertinib as First-Line Treatment in Patients With EGFR-Mutated Locally Advanced or Metastatic Non-Small Cell Lung Cancer. | III |
| NCT04797806 | Phase III Study Comparing Anlotinib Plus Icotinib to Icotinib in Patients With Untreated Non-squmous NSCLC Harboring EGFR Concomitant Mutations | III |
| NCT04058704 | A Multi-center, Prospective Study to Determine the Efficiency of Icotinib Combined With Radiation Therapy Early Intervention or Late Intervention For NSCLC Patients With Brain Metastases and EGFR(Epidermal Growth Factor Receptor) Mutation | III |

## Clinical Trials Summary (continued)

### EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC (continued)

| NCT ID | Title | Phase |
|---|---|---|
| NCT03521154 | A Phase III, Randomized, Double-blind, Placebo-controlled, Multicenter, International Study of Osimertinib as Maintenance Therapy in Patients With Locally Advanced, Unresectable EGFR Mutation-positive Non-Small Cell Lung Cancer (Stage III) Whose Disease Has Not Progressed Following Definitive Platinum-based Chemoradiation Therapy (LAURA) | III |
| NCT04181060 | Randomized Phase III Study of Combination AZD9291 (Osimertinib) and Bevacizumab Versus AZD9291 (Osimertinib) Alone as First-Line Treatment for Patients With Metastatic EGFR-Mutant Non-Small Cell Lung Cancer (NSCLC) | III |
| NCT04206072 | A Phase II/III, Open-Label, Randomised Study to Assess the Safety and Efficacy of D-0316 Versus Icotinib as First Line Treatment in Patients With EGFR Sensitising Mutation, Locally Advanced or Metastatic NSCLC | II/III |
| NCT04636593 | Almonertinib With Concurrent Radiotherapy in The Treatment of Unresectable, Stage III Non-small-cell Lung Cancer Harboring EGFR Mutations: A Phase II Cohort Study | II |
| NCT04245085 | A Randomised Non-comparative Open Label Phase II Trial of Atezolizumab Plus Bevacizumab, With Carboplatin-paclitaxel or Pemetrexed, in EGFR-mutant Non-small Cell Lung Carcinoma With Acquired Resistance | II |
| No NCT ID | Phase II Study of Platinum-Based Doublet Chemotherapy Plus Atezolizumab, In Completely Resected, P-Stage II-IIIA NSCLC Patients Harboring EGFR Mutation. (WJOG11719L Investigator-Initiated Clinical Trial) | II |
| NCT04099836 | Single Arm Phase II Trial of Atezolizumab and Bevacizumab in Epidermal Growth Factor Receptor (EGFR) Mutant Non-Small Cell Lung Cancer in Patients With Progressive Disease After Receiving Osimertinib (TOP 1901). | II |
| No NCT ID | Clinical Study of Camrelizumab Combined With Apatinib in the Treatment of EGFR-TKI Resistance in NSCLC | II |
| No NCT ID | A Phase IIa Clinical Study of crizotinib in the Treatment of Advanced Non-small Cell Lung Cancer | II |
| NCT02820116 | An Open-label, Multicenter,Single-arm, Phase II Clinical Study of Icotinib for IIIA - IIIB NSCLC Patients with Epidermal Growth Factor Receptor Mutation | II |
| NCT03349203 | Icotinib as Neoadjuvant and Adjuvant Therapy in EGFR-mutant Stage IIIB or Oligometastasis Non-small Cell Lung Cancer: a Single Arm, Phase II Clinical Study | II |
| NCT03396185 | Icotinib as Consolidation Therapy After Synchronous or Sequential Chemoradiotherapy in Stage IIIA-IIIB Non-small Cell Lung Cancer With EGFR Sensitive Mutation: A Single Center, Single Arm, Open Label and Prospective Clinical Study | II |
| NCT03749213 | Icotinib as Neoadjuvant Therapy in EGFR-mutant Stage IIIA-N2 Non-small Cell Lung Cancer: a Single Arm, Phase II Clinical Study | II |
| NCT03151161 | A Prospective,Multi-center, Open-labeled Phase II Randomized and Comparative Clinical Study of First Line Intermittent and Maintenance of Icotinib in Combination With Pemetrexed/Carboplatin Compared With Icotinib Single Drug in IIIB/IV Non Small Cell Lung Cancer With Epidermal Growth Factor Receptor (EGFR) Mutation | II |
| NCT02726568 | A Phase II Study to Determine the Efficacy and Safety of High Dose Icotinib Combined With Stereotatic Radiosurgery for NSCLC Patients Harboring EGFR Mutation With Brain Metastases | II |
| NCT03433469 | A Phase II Study to Evaluate Neoadjuvant Osimertinib Therapy in Patients with Surgically Resectable, EGFR-Mutant Non-Small Cell Lung Cancer | II |
| NCT04545710 | A Phase II Trial of Osimertinib and Abemaciclib With a Focus on Non-Small Cell Lung Cancer Patients With EGFR Activating Mutations With Osimertinib Resistance | II |

## Clinical Trials Summary (continued)

### EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC (continued)

| NCT ID | Title | Phase |
|---|---|---|
| NCT03497767 | A Randomised Phase II Trial of Osimertinib With or Without Stereotactic Radiosurgery for EGFR Mutated Non-Small Cell Lung Cancer (NSCLC) With Brain Metastases | II |
| NCT03769103 | Open Label, Multicenter, Phase II Study of Patients With Treatment Naive Metastatic Epidermal Growth Factor Receptor (EGFR) Mutation-Positive Non-Small Cell Lung Cancer (NSCLC) With Brain Metastases Randomized to Stereotactic Radiosurgery (SRS) and Osimertinib or Osimertinib Alone | II |
| NCT03909334 | An Open-Label Randomized Phase II Study of Combining Osimertinib With and Without Ramucirumab in Tyrosine Kinase Inhibitor (TKI)-naïve Epidermal Growth Factor Receptor (EGFR)-Mutant Locally Advanced or Metastatic NSCLC | II |
| NCT03778229 | A Phase II, Single Arm Study Assessing Efficacy of Osimertinib With Savolitinib in Patients With EGFRm + MET+, Locally Advanced or Metastatic Non Small Cell Lung Cancer Who Have Progressed Following Osimertinib Treatment (SAVANNAH Study) | II |
| NCT04619004 | HERTHENA-Lung01: A Phase II Randomized Open-Label Study of Patritumab Deruxtecan (U3-1402) in Subjects With Previously Treated Metastatic or Locally Advanced EGFR-mutated Non-Small Cell Lung Cancer (NSCLC) | II |
| NCT04820023 | A Phase I/II, Open-Label Study to Assess the Safety, Tolerability, Pharmacokinetics, and Anti-tumor Activity of BBT-176 in Patients With Advanced Non-Small Cell Lung Cancer (NSCLC) Who Progressed Following Prior Therapy With an Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor (EGFR TKI) Agent | I/II |
| NCT03446417 | A Phase 1/2 Open Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics, and Anti-tumor Activity of ZN-e4 (KP-673) in Patients With Advanced Non-Small Cell Lung Cancer with Activating Epidermal Growth Factor Receptor (EGFR) Mutations | I/II |
| NCT04285671 | UCLA L-08: A Phase Ib/II Study of Combined HER Inhibition Adding Necitumumab and Trastuzumab to Osimertinib in Patients With Refractory EGFR-Mutated Lung Cancer | I/II |
| NCT04770688 | Safety and Efficacy of Osimertinib Combined With Anlotinib in EGFRm+, Treatment-naive IIIb/IV NSCLC Patients: a Prospective, Single Arm, Phase Ib/IIa Study | I/II |
| NCT04085315 | A Phase I/Ib Study of Alisertib in Combination With Osimertinib in Metastatic EGFR-mutant Lung Cancer | I |
| NCT04479306 | A Ph Ib Study of Osimertinib + Alisertib or Sapanisertib for Osimertinib-Resistant EGFR Mutant Non-Small Cell Lung Cancer (NSCLC) (Crossover Study) | I |
| NCT02609776 | A Phase I, First-in-Human, Open-Label, Dose Escalation Study of JNJ-61186372, a Human Bispecific EGFR and cMet Antibody, in Subjects With Advanced Non-Small Cell Lung Cancer. | I |
| No NCT ID | Phase I Clinical Study of C-005 Tablet In The Treatment Of Advanced Non-Small Cell Lung Cancer | I |
| No NCT ID | Phase I Clinical Study of Safety, Tolerability, Pharmacokinetics and Initial Efficacy of RX518 in Patients with Advanced Non-small Cell Lung Cancer | I |
| NCT03976856 | A Phase Ib Clinical Study With Extension Phase to Evaluate Safety and Efficacy of Genolimzumab (GB226) in Combination With Fruquintinib in the Treatment of Relapsed or Metastatic NSCLC Patients | I |
| No NCT ID | Study Of Immunologic Factor In Re-Biopsy Specimen, Peritumoral BALF, And The Peripheral Blood For Predicting Response To Osimertinib In NSCLC Patients | I |
| NCT03735121 | A Randomized, Multicenter, Phase Ib/II Study to Investigate the Pharmacokinetics, Efficacy, and Safety of Atezolizumab Subcutaneous Compared With Atezolizumab Intravenous in Patients With Previously Treated Locally Advanced or Metastatic Non-Small Cell Lung Cancer | III |

## Clinical Trials Summary (continued)

### EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC (continued)

| NCT ID | Title | Phase |
|---|---|---|
| NCT01996098 | A Multicenter, Randomized, Phase III Trial of Chemotherapy Followed by 6-month or 12-month Icotinib Versus Chemotherapy as Adjuvant Therapy in Stage IIA-IIIA Non-small Cell Lung Cancer Harboring Epidermal Growth Factor Receptor Mutation | III |
| NCT03574402 | An Open-label, Multi-center, Phase II Umbrella Study to Assess Efficacy of Targeted Therapy or Immunotherapy Directed by Next Generation Sequencing (NGS) in Chinese Patients With Advanced NSCLC (TRUMP) | II |
| NCT04042558 | A Multicentre Phase II, Open-label, Non-randomized Study Evaluating Platinum-Pemetrexed-Atezolizumab (+/- Bevacizumab) for Patients With Stage IIIB/IV Non-squamous Non-small Cell Lung Cancer With EGFR Mutations, ALK Rearrangement or ROS1 Fusion Progressing After Targeted Therapies | II |
| NCT03840902 | A Multicenter, Double Blind, Randomized, Controlled Study of M7824 With Concurrent Chemoradiation Followed by M7824 Versus Concurrent Chemoradiation Plus Placebo Followed by Durvalumab in Participants With Unresectable Stage III Non-small Cell Lung Cancer | II |
| NCT03944772 | A Biomarker-directed Phase II Platform Study in Patients With Advanced Non-Small Lung Cancer Whose Disease Has Progressed on First-Line Osimertinib Therapy | II |
| NCT02264210 | A Randomized, Phase II Trial of Icotinib Versus Observation as Adjuvant Treatment in Stage IB Non-Small Cell Lung Cancer Harboring Activating Epidermal Growth Factor Receptor Mutation | II |
| NCT03983928 | A Phase Ib, Open-label, Single Center, Non-randomized Study for Safety and Efficacy of TQB2450 Combined With Anlotinib in Subjects With Advanced Mutation Positive Non-Small Cell Lung Cancer | I/II |
| NCT03846310 | A Phase I/Ib Study to Evaluate the Safety and Tolerability of Immunotherapy Combinations in Participants With Lung Cancer | I |
| NCT04141644 | A Phase Ib Study to Evaluate the Safety and Efficacy of Osimertinib in Combination With Ipilimumab in Patients With EGFR Mutated Non-Small-Cell Lung Cancer Tumors | I |
| No NCT ID | The Continuous Evaluation of EGFR Mutation in EGFR-mutation Positive Lung Cancer Patients During EGFR TKI Treatment. | IV |
| NCT03991403 | Study of Atezolizumab in Combination With Carboplatin + Paclitaxel +Bevacizumab vs With Pemetrexed + Cisplatin or Carboplatin With Stage IV Non-Squamous Non-Small Cell Lung Cancer with EGFR (+) or ALK (+) | III |
| NCT03786692 | TH-138: Phase II Randomized Trial of Carboplatin + Pemetrexed + Bevacizumab, With or Without Atezolizumab in Stage IV Non-squamous NSCLC Patients Who Harbor a Sensitizing EGFR Mutation or Have Never Smoked | II |
| NCT04484142 | Phase II, Single-arm, Open-label Study of DS-1062a in Advanced or Metastatic Non-small Cell Lung Cancer With Actionable Genomic Alterations and Progressed on or After Kinase Inhibitor Therapy and Platinum Based Chemotherapy (TROPION-Lung05) | II |
| NCT02044328 | Icotinib as an Adjuvant Therapy for Patients With Stage IIA-IIIA Adenocarcinoma With EGFR Mutation: a Prospective, Exploratory Study | II |
| NCT03804580 | First-Line Treatment With Osimertinib In EGFR-Mutated Non-Small Cell Lung Cancer, Coupled To Extensive Translational Studies | II |
| NCT04335292 | Osimertinib Then Chemotherapy in EGFR-mutated Lung Cancer With Osimertinib Third-line Rechallenge | II |
| NCT04410796 | A Phase 2 Randomized Study of Osimertinib Versus Osimertinib Plus Chemotherapy for Patients With Metastatic EGFR-Mutant Lung Cancers That Have Detectable EGFR-Mutant cfDNA in Plasma After Initiation of Osimertinib | II |

## Clinical Trials Summary (continued)

### EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC (continued)

| NCT ID | Title | Phase |
|---|---|---|
| NCT03667820 | Phase II Trial of Osimertinib in Combination With Stereotactic Ablative Radiation (SABR) in EGFR Mutant Advanced Non-Small Cell Lung Cancer (NSCLC) | II |
| NCT04762199 | A Phase Ib Safety and Pharmacodynamic Study of MER Tyrosine Kinase Inhibitor, MRX-2843, in Combination With Osimertinib in Advanced EGFR Mutant Non-Small Cell Lung Cancer | I |
| NCT03891615 | Phase I Study of Niraparib in Combination With Osimertinib in EGFR-Mutated Advanced Lung Cancer | I |
| NCT04250545 | A Phase I Trial of MLN0128 (Sapanisertib) and CB-839 HCl (Telaglenastat) in Advanced NSCLC Patients | I |
| NCT03114319 | An Open-label, Multi-center, Phase I, Dose Finding Study of Oral TNO155 in Adult Patients With Advanced Solid Tumors | I |
| No NCT ID | Apatinib Combined With EGFR-TKI For Patients With EGFR Mutation Who Failed EGFR-TKI: A Prospective Study | IV |
| No NCT ID | Clinical Study Of Combined Action Of Icotinib And Brain Radiotherapy On EGFR-Mutated Non-Small-Cell Lung Cancer Patients With Brain Metastasis | IV |
| NCT03800134 | A Phase III, Double-blind, Placebo-controlled, Multi-center International Study of Neoadjuvant/Adjuvant Durvalumab for the Treatment of Patients With Resectable Stages II and III Non-small Cell Lung Cancer (AEGEAN) | III |
| NCT03992885 | Combination Therapy With Icotinib, Pemetrexed and Platinum in Patients With Metastatic Non-squamous Non-small Cell Lung Cancer With EGFR Mutations Who Did Not Progress After Pemetrexed in Combination With Platinum-based Chemotherapy:a Single-arm, Open, Multicenter Clinical Study. | III |
| NCT04619563 | A Single-arm Exploratory Clinical Study of Anlotinib Hydrochloride Combined With Docetaxel in EGFR Mutations Advanced Non Small Cell Lung Cancer Patients Who Have Progressed After Targeted Therapy and Chemotherapy | II |
| No NCT ID | Osimertinib Combined Bevacizumab in Untreated Epidermal Growth Factor Receptor Mutated Non-small-cell Lung Cancer Patients with Malignant Pleural And/Or Pericardial Effusion -phase II Trial | II |
| No NCT ID | Randomized Controlled Trial for EGFR-TKIs Plus S-1 or EGFR-TKIs as the First-Line Therapy for Patients with Advanced Non-small Cell Lung Cancer Harboring EGFR Mutations | II |
| No NCT ID | Single arm, Exploratory Study for Apatinib mesylate Combined with EGFR-TKI in Patients with EGFR Mutation-positive Advanced Non-squamous Non–small-cell Lung Cancer | II |
| No NCT ID | EGFR-TKI Combined With Stereotactic Body Radiation Therapy Versus TKI alone for Stage IV Oncogene-Driven Non-Small Cell Lung Cancer. | II |
| NCT03904823 | An Open, Single-arm, Multi-center, Phase II Clinical Trial of Famitinib Combined With Epidermal Growth Factor Receptor (EGFR) Inhibitor HS-10296 in Patients With Advanced EGFR-mutant Non-Small Cell Lung Cancer (NSCLC) | II |
| NCT02960607 | A Phase II Study of High-dose Icotinib in Previously Treated Non-small Cell Lung Cancer Patients With Epidermal Growth Factor Receptor Mutation | II |
| NCT04538378 | Phase II Trial of Olaparib (LYNPARZA) Plus Durvalumab (IMFINZI) in EGFR-Mutated Adenocarcinomas That Transform to Small Cell Lung Cancer (SCLC) and Other Neuroendocrine Tumors. | II |
| NCT03460275 | Osimertinib as First-line Therapy for Patients With EGFR Mutation-positive Locally Advanced or Metastatic Non-squamous Non-Small Cell Lung Cancer(NSCLC), a Single-Arm, Open-Label, Prospective, Multicenter, Phase II Clinical Trial | II |

# Clinical Trials Summary (continued)

## EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC (continued)

| NCT ID | Title | Phase |
|---|---|---|
| No NCT ID | Efficacy Of Osimertinib With Platinum And Pemetrexed In EGFR Mutant Non-Small Cell Lung Cancer Patients Bearing CNS Metastasis, And Have Systemic Progression But Stable Intracranial Disease On Osimertinib Resistance. (EPONA) | II |
| No NCT ID | Phase II Trial Of Docetaxel Plus Ramucirumab Combination Therapy In Patients With Advanced EGFR Gene Mutation Positive Advanced Stage Non-Squamous Cell Non small Cell Lung Cancer | II |
| No NCT ID | Clinical Study of Combined Action of the First Generation of TKIs and Brain Radiotherapy on EGFR-Mutated Non-Small-Cell Lung Cancer Patients with Brain Metastasis | II |
| NCT03974022 | A Phase I/II, Open-Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics and Anti-tumor Efficacy of DZD9008 in Patients With Advanced Non-Small Cell Lung Cancer (NSCLC) With EGFR or HER2 Mutation | I/II |
| NCT03797391 | First-in-human, Phase I/II, Multicenter, Open-Label Study of EMB-01 in Patients With Advanced/ Metastatic Solid Tumors | I/II |
| NCT04528836 | A Phase I/IB First-in-Human Study of the SHP2 Inhibitor BBP-398 (Formerly Known as IACS-15509) in Patients With Advanced Solid Tumors | I |
| No NCT ID | Phase I Study of DZD9008 in EGFR or HER2 Mutant NSCLC Chinese Patients | I |
| NCT04077463 | An Open-label Phase 1/1b Study to Evaluate the Safety and Pharmacokinetics of JNJ-73841937 (Lazertinib), a Third Generation EGFR-TKI, as Monotherapy or in Combinations With JNJ-61186372, a Human Bispecific EGFR and cMet Antibody in Participants With Advanced Non-Small Cell Lung Cancer | I |
| NCT04013542 | A Pilot Trial of Ipilimumab-Nivolumab in Local-Regionally Advanced Non Small Cell Lung Cancer (NSCLC) | I |
| No NCT ID | Pharmacokinetic and dose finding study of osimertinib in patients with impaired renal function and low body weight | I |
| NCT03346811 | Efficiency of Icotinib in Plasma ctDNA EGFR Mutation-positive Patients Diagnosed With Lung Cancer:a Single Arm,Multi-center,Open-label Study | II |
| NCT03065387 | Phase I Study of the Pan-ERBB Inhibitor Neratinib Given in Combination With Everolimus, Palbociclib, or Trametinib in Advanced Cancer Subjects With EGFR Mutation/Amplification, HER2 Mutation/ Amplification, or HER3/4 Mutation or KRAS Mutation | I |
| No NCT ID | Phase I Clinical Study With Advanced Solid Tumors KBP-5209 Treatment | I |
| NCT04128085 | A Phase I, Open-label, Multicenter, Dose Escalation and Expansion Study to Evaluate the Tolerance and Pharmacokinetics of TQB3804 in Subjects With Advanced Malignant Tumors | I |
| NCT03841110 | FT500 as Monotherapy and in Combination With Immune Checkpoint Inhibitors in Subjects With Advanced Solid Tumors (Phase I) | I |
| NCT04429542 | First-in-Human, Phase I/Ib, Open-label, Multicenter Study of Bifunctional EGFR/TGFß Fusion Protein BCA101 Alone and in Combination With Pembrolizumab in Patients With EGFR-Driven Advanced Solid Tumors | I |

## EGFR p.(T790M) c.2369C>T

| NCT ID | Title | Phase |
|---|---|---|
| No NCT ID | Clinical Study Anlotinib Combined with Osimertinib in the Treatment of Advanced Non-Squamous Non-Small Cell Lung Cancer with 1st Generation and 2nd Generation EGFR-TKI Resistance with T790M Mutation. | IV |

# Clinical Trials Summary (continued)

## EGFR p.(T790M) c.2369C>T (continued)

| NCT ID | Title | Phase |
|---|---|---|
| NCT03300115 | Single-arm,Multi-center,Phase II Clinical Trial of the Efficacy and Safety of AC0010 in the Treatment of EGFR T790M Mutation-positive Patients With Advanded NSCLC | II |
| NCT03574402 | An Open-label, Multi-center, Phase II Umbrella Study to Assess Efficacy of Targeted Therapy or Immunotherapy Directed by Next Generation Sequencing (NGS) in Chinese Patients With Advanced NSCLC (TRUMP) | II |
| NCT03433469 | A Phase II Study to Evaluate Neoadjuvant Osimertinib Therapy in Patients with Surgically Resectable, EGFR-Mutant Non-Small Cell Lung Cancer | II |
| NCT03497767 | A Randomised Phase II Trial of Osimertinib With or Without Stereotactic Radiosurgery for EGFR Mutated Non-Small Cell Lung Cancer (NSCLC) With Brain Metastases | II |
| NCT04316351 | Efficacy and Safety of Toripalimab (JS001) Combined With Pemetrexed and Anlotinib for Patients With T790M Positive Non-Small Cell Lung Cancer After Osimertinib Resistance: a Phase II, Muti-center, Single Arm Study | II |
| NCT03446417 | A Phase 1/2 Open Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics, and Anti-tumor Activity of ZN-e4 (KP-673) in Patients With Advanced Non-Small Cell Lung Cancer with Activating Epidermal Growth Factor Receptor (EGFR) Mutations | I/II |
| NCT04085315 | A Phase I/Ib Study of Alisertib in Combination With Osimertinib in Metastatic EGFR-mutant Lung Cancer | I |
| NCT04479306 | A Ph Ib Study of Osimertinib + Alisertib or Sapanisertib for Osimertinib-Resistant EGFR Mutant Non-Small Cell Lung Cancer (NSCLC) (Crossover Study) | I |
| No NCT ID | Evaluation of Phase I Clinical Trial of BEBT-109 in Patients with Advanced Non-small Cell Lung Cancer | I |
| No NCT ID | Phase I Clinical Study of C-005 Tablet In The Treatment Of Advanced Non-Small Cell Lung Cancer | I |
| No NCT ID | Phase I Clinical Study of Safety, Tolerability, Pharmacokinetics and Initial Efficacy of RX518 in Patients with Advanced Non-small Cell Lung Cancer | I |
| NCT03754244 | A Phase I Study of TQ-B3456 on Tolerance and Pharmacokinetics | I |
| No NCT ID | Evaluation Of The Phase I Clinical Trial Of Safety, Tolerability, Pharmacokinetic Characteristics, And Preliminary Efficacy Of YK-029A Tablets In Patients With Advanced Non-Small Cell Lung Cancer (NSCLC) | I |
| No NCT ID | A Multicenter, Open and Dose Escalation Phase I Study of YZJ-0318 Maleate Tablets in Patients with Advanced Non-Small Cell Lung Cancer with Positive Epidermal Growth Factor Receptor T790M Mutation | I |
| NCT03802240 | A Randomized, Double-blind, Multi-center, Phase III Clinical Study Assessing the Efficacy and Safety of Sintilimab ± IBI305 Combined With Pemetrexed and Cisplatin in Patients With EGFR-mutant Locally Advanced or Metastatic Non-squamous Non-small Cell Lung Cancer Who Have Failed Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor (EGFR-TKI) Treatment (ORIENT-31) | III |
| NCT03924050 | A Randomized, Double-Blind, Placebo-Controlled, Multicenter, Phase III Study of Pemetrexed + Platinum Chemotherapy With or Without Toripalimab (JS001) in Advanced Non-small Cell Lung Cancer (NSCLC) Participants With TKI-resistant EGFR-mutated Tumors | III |
| NCT03376737 | A Single-Arm Phase II Clinical Trial of Apatinib as the Maintenance Therapy in Advanced Lung Adenocarcinoma | II |
| NCT03838848 | A Phase II Study to Evaluate the Efficacy, Safety, and Tolerability of KN046 in Patients With Advanced Non-small Cell Lung Cancer | II |

# Clinical Trials Summary (continued)

## EGFR p.(T790M) c.2369C>T (continued)

| NCT ID | Title | Phase |
|---|---|---|
| NCT03804580 | First-Line Treatment With Osimertinib In EGFR-Mutated Non-Small Cell Lung Cancer, Coupled To Extensive Translational Studies | II |
| NCT02609776 | A Phase I, First-in-Human, Open-Label, Dose Escalation Study of JNJ-61186372, a Human Bispecific EGFR and cMet Antibody, in Subjects With Advanced Non-Small Cell Lung Cancer. | I |
| NCT04001777 | A Phase Ib Study of Safety and Efficacy of APG-1252 in Combination With Osimertinib (AZD9291) in EGFR TKI Resistant NSCLC Patients | I |
| No NCT ID | Phase I Clinical Trial of SPH3348 Single-agent Combined with Oxitinib in Patients with Advanced Solid Tumors with Abnormal c-Met in China. | I |
| No NCT ID | Apatinib Combined With EGFR-TKI For Patients With EGFR Mutation Who Failed EGFR-TKI: A Prospective Study | IV |
| No NCT ID | Clinical Study Of Combined Action Of Icotinib And Brain Radiotherapy On EGFR-Mutated Non-Small-Cell Lung Cancer Patients With Brain Metastasis | IV |
| NCT03800134 | A Phase III, Double-blind, Placebo-controlled, Multi-center International Study of Neoadjuvant/Adjuvant Durvalumab for the Treatment of Patients With Resectable Stages II and III Non-small Cell Lung Cancer (AEGEAN) | III |
| NCT03992885 | Combination Therapy With Icotinib, Pemetrexed and Platinum in Patients With Metastatic Non-squamous Non-small Cell Lung Cancer With EGFR Mutations Who Did Not Progress After Pemetrexed in Combination With Platinum-based Chemotherapy:a Single-arm, Open, Multicenter Clinical Study. | III |
| NCT04619563 | A Single-arm Exploratory Clinical Study of Anlotinib Hydrochloride Combined With Docetaxel in EGFR Mutations Advanced Non Small Cell Lung Cancer Patients Who Have Progressed After Targeted Therapy and Chemotherapy | II |
| NCT04245085 | A Randomised Non-comparative Open Label Phase II Trial of Atezolizumab Plus Bevacizumab, With Carboplatin-paclitaxel or Pemetrexed, in EGFR-mutant Non-small Cell Lung Carcinoma With Acquired Resistance | II |
| No NCT ID | Osimertinib Combined Bevacizumab in Untreated Epidermal Growth Factor Receptor Mutated Non-small-cell Lung Cancer Patients with Malignant Pleural And/Or Pericardial Effusion -phase II Trial | II |
| No NCT ID | Randomized Controlled Trial for EGFR-TKIs Plus S-1 or EGFR-TKIs as the First-Line Therapy for Patients with Advanced Non-small Cell Lung Cancer Harboring EGFR Mutations | II |
| No NCT ID | Single arm, Exploratory Study for Apatinib mesylate Combined with EGFR-TKI in Patients with EGFR Mutation-positive Advanced Non-squamous Non–small-cell Lung Cancer | II |
| No NCT ID | EGFR-TKI Combined With Stereotactic Body Radiation Therapy Versus TKI alone for Stage IV Oncogene-Driven Non-Small Cell Lung Cancer. | II |
| NCT03904823 | An Open, Single-arm, Multi-center, Phase II Clinical Trial of Famitinib Combined With Epidermal Growth Factor Receptor (EGFR) Inhibitor HS-10296 in Patients With Advanced EGFR-mutant Non-Small Cell Lung Cancer (NSCLC) | II |
| NCT02960607 | A Phase II Study of High-dose Icotinib in Previously Treated Non-small Cell Lung Cancer Patients With Epidermal Growth Factor Receptor Mutation | II |
| NCT04538378 | Phase II Trial of Olaparib (LYNPARZA) Plus Durvalumab (IMFINZI) in EGFR-Mutated Adenocarcinomas That Transform to Small Cell Lung Cancer (SCLC) and Other Neuroendocrine Tumors. | II |
| NCT03460275 | Osimertinib as First-line Therapy for Patients With EGFR Mutation-positive Locally Advanced or Metastatic Non-squamous Non-Small Cell Lung Cancer(NSCLC), a Single-Arm, Open-Label, Prospective, Multicenter, Phase II Clinical Trial | II |

# Clinical Trials Summary (continued)

## EGFR p.(T790M) c.2369C>T (continued)

| NCT ID | Title | Phase |
|---|---|---|
| No NCT ID | Efficacy Of Osimertinib With Platinum And Pemetrexed In EGFR Mutant Non-Small Cell Lung Cancer Patients Bearing CNS Metastasis, And Have Systemic Progression But Stable Intracranial Disease On Osimertinib Resistance. (EPONA) | II |
| No NCT ID | Phase II Trial Of Docetaxel Plus Ramucirumab Combination Therapy In Patients With Advanced EGFR Gene Mutation Positive Advanced Stage Non-Squamous Cell Non small Cell Lung Cancer | II |
| No NCT ID | Clinical Study of Combined Action of the First Generation of TKIs and Brain Radiotherapy on EGFR-Mutated Non-Small-Cell Lung Cancer Patients with Brain Metastasis | II |
| NCT03974022 | A Phase I/II, Open-Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics and Anti-tumor Efficacy of DZD9008 in Patients With Advanced Non-Small Cell Lung Cancer (NSCLC) With EGFR or HER2 Mutation | I/II |
| NCT03797391 | First-in-human, Phase I/II, Multicenter, Open-Label Study of EMB-01 in Patients With Advanced/ Metastatic Solid Tumors | I/II |
| NCT04528836 | A Phase I/IB First-in-Human Study of the SHP2 Inhibitor BBP-398 (Formerly Known as IACS-15509) in Patients With Advanced Solid Tumors | I |
| No NCT ID | Phase I Study of DZD9008 in EGFR or HER2 Mutant NSCLC Chinese Patients | I |
| NCT04077463 | An Open-label Phase 1/1b Study to Evaluate the Safety and Pharmacokinetics of JNJ-73841937 (Lazertinib), a Third Generation EGFR-TKI, as Monotherapy or in Combinations With JNJ-61186372, a Human Bispecific EGFR and cMet Antibody in Participants With Advanced Non-Small Cell Lung Cancer | I |
| NCT04013542 | A Pilot Trial of Ipilimumab-Nivolumab in Local-Regionally Advanced Non Small Cell Lung Cancer (NSCLC) | I |
| No NCT ID | Study Of Immunologic Factor In Re-Biopsy Specimen, Peritumoral BALF, And The Peripheral Blood For Predicting Response To Osimertinib In NSCLC Patients | I |
| No NCT ID | Pharmacokinetic and dose finding study of osimertinib in patients with impaired renal function and low body weight | I |
| No NCT ID | A Phase IIa Clinical Study of crizotinib in the Treatment of Advanced Non-small Cell Lung Cancer | II |
| NCT03065387 | Phase I Study of the Pan-ERBB Inhibitor Neratinib Given in Combination With Everolimus, Palbociclib, or Trametinib in Advanced Cancer Subjects With EGFR Mutation/Amplification, HER2 Mutation/ Amplification, or HER3/4 Mutation or KRAS Mutation | I |
| No NCT ID | Phase I Clinical Study With Advanced Solid Tumors KBP-5209 Treatment | I |
| NCT04128085 | A Phase I, Open-label, Multicenter, Dose Escalation and Expansion Study to Evaluate the Tolerance and Pharmacokinetics of TQB3804 in Subjects With Advanced Malignant Tumors | I |
| NCT03841110 | FT500 as Monotherapy and in Combination With Immune Checkpoint Inhibitors in Subjects With Advanced Solid Tumors (Phase I) | I |
| NCT04429542 | First-in-Human, Phase I/Ib, Open-label, Multicenter Study of Bifunctional EGFR/TGFß Fusion Protein BCA101 Alone and in Combination With Pembrolizumab in Patients With EGFR-Driven Advanced Solid Tumors | I |

## Clinical Trials Summary (continued)

### PIK3CA p.(E726K) c.2176G>A

| NCT ID | Title | Phase |
|---|---|---|
| NCT03065062 | Phase I Study of the CDK4/6 Inhibitor Palbociclib (PD-0332991) in Combination With the PI3K/mTOR Inhibitor Gedatolisib (PF-05212384) for Patients With Advanced Squamous Cell Lung, Pancreatic, Head & Neck and Other Solid Tumors | I |
| NCT04591431 | The Rome Trial From Histology to Target: the Road to Personalize Target Therapy and Immunotherapy | II |
| NCT03994796 | Genomically-Guided Treatment Trial in Brain Metastases | II |
| NCT03239015 | Efficacy and Safety of Targeted Precision Therapy in Refractory Tumor With Druggable Molecular Event | II |
| NCT04589845 | Tumor-Agnostic Precision Immunooncology and Somatic Targeting Rational for You (TAPISTRY) Phase II Platform Trial | II |
| NCT02688881 | Study to Evaluate the Safety and Efficacy of Sirolimus, in Subject With Refractory Solid Tumors | II |
| NCT03842228 | A Phase Ib Biomarker-Driven Combination Trial of Copanlisib, Olaparib, and Durvalumab (MEDI4736) in Patients With Advanced Solid Tumors | I |
| NCT03006172 | A Phase I, Open-Label, Dose-Escalation Study Evaluating the Safety, Tolerability, and Pharmacokinetics of GDC-0077 as a Single Agent in Patients With Locally Advanced or Metastatic PIK3CA-Mutant Solid Tumors and in Combination With Endocrine and Targeted Therapies in Patients With Locally Advanced or Metastatic PIK3CA-Mutant Breast Cancer | I |
| NCT04192981 | A Phase I Study With Expansion Cohort of Concurrent GDC-0084 With Radiation Therapy for Patients With Solid Tumor Brain Metastases or Leptomeningeal Metastases Harboring PI3K Pathway Mutations | I |
| NCT03297606 | Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial | II |
| No NCT ID | Phase I/II Study of TAS-117 In Combination With TAS-120 In Patients With Advanced Solid Tumors | I/II |
| NCT03155620 | NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice) Screening Protocol | II |
| NCT03213678 | NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice)- Phase II Subprotocol of LY3023414 in Patients With Solid Tumors | II |
| NCT03673787 | Ice-CAP: A Phase I Trial of Ipatasertib in Combination With Atezolizumab in Patients With Advanced Solid Tumours With PI3K Pathway Hyperactivation | I/II |

# Alerts Informed By Public Data Sources

## Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2021-04-14. For the most up-to-date information, search www.fda.gov.

### EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC

#### osimertinib + quaratusugene ozeplasmid

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR mutation

**Supporting Statement:**
The FDA has granted Fast Track Designation to the immunogene therapy, quaratusugene ozeplasmid, in combination with the EGFR inhibitor osimertinib, for EGFR mutated non-small cell lung cancer after progression on osimertinib alone.

**Reference:**

https://www.genprex.com/news/genprex-receives-u-s-fda-fast-track-designation-for-gene-therapy-that-targets-lung-cancer/

### EGFR p.(T790M) c.2369C>T

#### osimertinib + quaratusugene ozeplasmid

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR mutation

**Supporting Statement:**
The FDA has granted Fast Track Designation to the immunogene therapy, quaratusugene ozeplasmid, in combination with the EGFR inhibitor osimertinib, for EGFR mutated non-small cell lung cancer after progression on osimertinib alone.

**Reference:**

https://www.genprex.com/news/genprex-receives-u-s-fda-fast-track-designation-for-gene-therapy-that-targets-lung-cancer/

## Current NCCN Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

NCCN information is current as of 2021-04-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

### EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC

#### alectinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

**Summary:**
NCCN Guidelines® include the following supporting statement(s):
- "Crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

## EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC (continued)

### brigatinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

**Summary:**
NCCN Guidelines® include the following supporting statement(s):
- "Crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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### ceritinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

**Summary:**
NCCN Guidelines® include the following supporting statement(s):
- "Crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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### crizotinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

**Summary:**
NCCN Guidelines® include the following supporting statement(s):
- "Crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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### lorlatinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFRi sensitizing mutation

**Summary:**
NCCN Guidelines® include the following supporting statement(s):
- "Crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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### atezolizumab

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR mutation

**Summary:**
NCCN Guidelines® include the following supporting statement(s):
- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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## EGFR p.(E746_A750del) c.2235_2249delGGAATTAAGAGAAGC (continued)

### nivolumab

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR mutation

**Summary:**
NCCN Guidelines® include the following supporting statement(s):
- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

### pembrolizumab

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR mutation

**Summary:**
NCCN Guidelines® include the following supporting statement(s):
- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

## EGFR p.(T790M) c.2369C>T

### atezolizumab

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR mutation

**Summary:**
NCCN Guidelines® include the following supporting statement(s):
- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

### nivolumab

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR mutation

**Summary:**
NCCN Guidelines® include the following supporting statement(s):
- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

## EGFR p.(T790M) c.2369C>T (continued)

### pembrolizumab

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR mutation

**Summary:**
NCCN Guidelines® include the following supporting statement(s):
- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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### afatinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

**Summary:**
NCCN Guidelines® include the following supporting statement(s):
- "The most common known mechanism is the acquisition of T790M (which is a secondary mutation in EGFR), which renders the kinase resistant to erlotinib, gefitinib, dacomitinib, or afatinib."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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### dacomitinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

**Summary:**
NCCN Guidelines® include the following supporting statement(s):
- "The most common known mechanism is the acquisition of T790M (which is a secondary mutation in EGFR), which renders the kinase resistant to erlotinib, gefitinib, dacomitinib, or afatinib."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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### erlotinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

**Summary:**
NCCN Guidelines® include the following supporting statement(s):
- "The most common known mechanism is the acquisition of T790M (which is a secondary mutation in EGFR), which renders the kinase resistant to erlotinib, gefitinib, dacomitinib, or afatinib."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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### gefitinib

**Cancer type:** Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

**Summary:**
NCCN Guidelines® include the following supporting statement(s):
- "The most common known mechanism is the acquisition of T790M (which is a secondary mutation in EGFR), which renders the kinase resistant to erlotinib, gefitinib, dacomitinib, or afatinib."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

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## Current EMA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

EMA information is current as of 2021-04-14. For the most up-to-date information, search www.ema.europa.eu/ema.

## EGFR p.(T790M) c.2369C>T

### gefitinib

**Cancer type:** Non-Small Cell Lung Cancer **Label as of:** 2021-03-05 **Variant class:** EGFR T790M mutation

**Reference:**

https://www.ema.europa.eu/en/documents/product-information/iressa-epar-product-information_en.pdf

## Signatures

**Testing Personnel:**

2021.05.20
12:06:46 +08'00'

**Laboratory Supervisor:**

2021.05.20
12:07:29 +08'00'

**Pathologist:**

2021.05.20
12:07:39 +08'00'

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