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**Date**: 04 Feb 2021 1 of 40

## **Sample Information**

Patient Name: 黃璿樺 Gender: Female ID No.: S222510263 History No.: 46575886

**Age:** 44

Ordering Doctor: DOC3109L 邱昭華

Ordering REQ.: 0BBSQEC Signing in Date: 2021/02/04

**Path No.:** S110-98185 **MP No.:** F21009

Assay: Oncomine Focus Assay

Sample Type: FFPE Block No.: S110-03072A+B Percentage of tumor cells: 40%

Note:

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

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Report Highlights
1 Relevant Biomarkers
13 Therapies Available
185 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.(L858R) c.2573T>G | 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<br>(In this cancer type)                                                                                                                                                                                                     | Relevant Therapies<br>(In other cancer type) | Clinical Trials |
|------|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|-----------------|
| IA   | EGFR p.(L858R) c.2573T>G epidermal growth factor receptor Allele Frequency: 15.61% | afatinib 1,2 bevacizumab* + erlotinib 2 dacomitinib 1,2 erlotinib 1,2 erlotinib + ramucirumab 1,2 gefitinib 1,2 osimertinib 1,2 afatinib + cetuximab atezolizumab + bevacizumab + chemotherapy bevacizumab + gefitinib gefitinib + chemotherapy | None                                         | 185             |

Public data sources included in relevant therapies: FDA1, NCCN, EMA2, 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

### **Variant Details**

| DNA    | Sequence Vari     | ants      |            |                |                     |             |                |          |
|--------|-------------------|-----------|------------|----------------|---------------------|-------------|----------------|----------|
| Gene   | Amino Acid Change | Coding    | Variant ID | Locus          | Allele<br>Frequency | Transcript  | Variant Effect | Coverage |
| EGFR   | p.(L858R)         | c.2573T>G | COSM6224   | chr7:55259515  | 15.61%              | NM_005228.4 | missense       | 1986     |
| JAK1   | p.(=)             | c.2199A>G |            | chr1:65310489  | 44.68%              | NM_002227.3 | synonymous     | 1992     |
| ALK    | p.(D1529E)        | c.4587C>G |            | chr2:29416366  | 51.85%              | NM_004304.4 | missense       | 2000     |
| ALK    | p.(I1461V)        | c.4381A>G |            | chr2:29416572  | 99.80%              | NM_004304.4 | missense       | 1997     |
| ALK    | p.(=)             | c.3375C>A |            | chr2:29445458  | 49.67%              | NM_004304.4 | synonymous     | 1993     |
| FGFR3  | p.(=)             | c.1953G>A |            | chr4:1807894   | 99.74%              | NM_000142.4 | synonymous     | 1935     |
| PDGFRA | p.(=)             | c.939T>G  |            | chr4:55133726  | 48.59%              | NM_006206.5 | synonymous     | 1990     |
| PDGFRA | p.(=)             | c.1701A>G |            | chr4:55141055  | 99.80%              | NM_006206.5 | synonymous     | 1995     |
| FGFR4  | p.(P136L)         | c.407C>T  |            | chr5:176517797 | 99.15%              | NM_213647.2 | missense       | 2000     |
| EGFR   | p.(=)             | c.2361G>A |            | chr7:55249063  | 57.03%              | NM_005228.4 | synonymous     | 1999     |
| RET    | p.(=)             | c.2307G>T |            | chr10:43613843 | 52.38%              | NM_020975.4 | synonymous     | 1993     |
|        |                   |           |            |                |                     |             |                |          |

## **Biomarker Descriptions**

#### EGFR (epidermal growth factor receptor)

<u>Background:</u> 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<sup>1</sup>. 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<sup>2,3</sup>.

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<sup>4,5,6,7</sup>. 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)

## **Biomarker Descriptions (continued)**

and the L858R amino acid substitution in exon 21<sup>8</sup>. 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<sup>9,10,11,12</sup>. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations<sup>13</sup>. 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<sup>8,14</sup>. 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<sup>5,6,7,14,15</sup>. 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<sup>16,17,18</sup>.

Potential relevance: Approved first-generation EGFR tyrosine kinase inhibitors (TKIs) include erlotinib19 (2004) and gefitinib20 (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 afatinib21 (2013) and dacomitinib22 (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 EGFR exon 20 insertions confer resistance to the same therapies<sup>23</sup>. In lung cancer containing EGFR exon 19 or 21 activating mutations, treatment with TKIs is eventually associated with the emergence of drug resistance<sup>24</sup>. The primary resistance mutation that emerges following treatment with first-generation TKI is T790M, accounting for 50-60% of resistant cases8. Third generation TKIs were developed to maintain sensitivity in the presence of T790M. Osimertinib25 (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<sup>24</sup>. 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<sup>26</sup>. T790M and C797S can occur in either cis or trans allelic orientation<sup>26</sup>. 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<sup>26</sup>. 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<sup>26,27</sup>. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs<sup>26</sup>. 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-6118637228, targeting EGFR and MET, and the TKI mobocertinib<sup>29</sup>, each received a breakthrough designation from the FDA (2020) for NSCLC tumors harboring EGFR exon 20 insertion mutations. The Oncoprex immunogene therapy CNVN-20230 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-18931 was granted a fast track designation (2020) for the treatment of solid tumors harboring an EGFR exon 20 insertion mutation.

## Relevant Therapy Summary

| In this cancer type | O In other cancer type | In this cancer type and other cancer types |      |     | X No evidence |                  |  |
|---------------------|------------------------|--------------------------------------------|------|-----|---------------|------------------|--|
| EGFR p.(L858R       | ) c.2573T>G            |                                            |      |     |               |                  |  |
| Relevant Therapy    |                        | FDA                                        | NCCN | EMA | ESMO          | Clinical Trials* |  |
| afatinib            |                        | •                                          |      |     |               | (IV)             |  |
| dacomitinib         |                        | •                                          |      |     |               | (IV)             |  |
| gefitinib           |                        | •                                          | •    | •   | •             | (IV)             |  |
| erlotinib           |                        | •                                          |      | •   | •             | <b>(III)</b>     |  |
| osimertinib         |                        | •                                          | •    | •   | •             | <b>(III)</b>     |  |

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

■ In this cancer type
O In other cancer type
In this cancer type and other cancer types
X No evidence

| Relevant Therapy                                            | FDA | NCCN | EMA | ESMO | Clinical Trials |
|-------------------------------------------------------------|-----|------|-----|------|-----------------|
| erlotinib + ramucirumab                                     |     |      |     |      | ×               |
| bevacizumab + erlotinib                                     | ×   |      |     |      | ×               |
| afatinib + cetuximab                                        | ×   | •    | ×   | ×    | ×               |
| bevacizumab (Allergan) + erlotinib                          | ×   | ×    | •   | ×    | ×               |
| bevacizumab (Fujifilm Kyowa Kirin Biologics) +<br>erlotinib | ×   | ×    | •   | ×    | ×               |
| bevacizumab (Pfizer) + erlotinib                            | ×   | ×    | •   | ×    | ×               |
| bevacizumab (Samsung Bioepis) + erlotinib                   | ×   | ×    | •   | ×    | ×               |
| atezolizumab + bevacizumab + carboplatin +<br>paclitaxel    | ×   | ×    | ×   | •    | ×               |
| bevacizumab + gefitinib                                     | ×   | ×    | ×   | •    | ×               |
| gefitinib + carboplatin + pemetrexed                        | ×   | ×    | ×   | •    | ×               |
| afatinib, osimertinib                                       | ×   | ×    | ×   | ×    | (IV)            |
| anlotinib hydrochloride, toripalimab                        | ×   | ×    | ×   | ×    | (IV)            |
| apatinib + EGFR tyrosine kinase inhibitor                   | ×   | ×    | ×   | ×    | (IV)            |
| apatinib, gefitinib                                         | ×   | ×    | ×   | ×    | (IV)            |
| bevacizumab + osimertinib, osimertinib                      | ×   | ×    | ×   | ×    | (IV)            |
| EGFR tyrosine kinase inhibitor                              | ×   | ×    | ×   | ×    | (IV)            |
| gefitinib, chemotherapy                                     | ×   | ×    | ×   | ×    | (IV)            |
| gefitinib, radiation therapy                                | ×   | ×    | ×   | ×    | (IV)            |
| icotinib hydrochloride                                      | ×   | ×    | ×   | ×    | (IV)            |
| icotinib hydrochloride, chemotherapy                        | ×   | ×    | ×   | ×    | (IV)            |
| icotinib hydrochloride, radiation therapy                   | ×   | ×    | ×   | ×    | (IV)            |
| almonertinib, gefitinib                                     | ×   | ×    | ×   | ×    | <b>(III)</b>    |
| amivantamab, lazertinib, osimertinib                        | ×   | ×    | ×   | ×    | <b>(III)</b>    |
| ASK120067, gefitinib                                        | ×   | ×    | ×   | ×    | <b>(III)</b>    |
| atezolizumab, bevacizumab, chemotherapy                     | ×   | ×    | ×   | ×    | <b>(III)</b>    |
| bevacizumab, erlotinib                                      | ×   | ×    | ×   | ×    | <b>(III)</b>    |
| BPI-7711, gefitinib                                         | ×   | ×    | ×   | ×    | <b>(III)</b>    |
| durvalumab, chemotherapy                                    | ×   | ×    | ×   | ×    | (III)           |

 $<sup>^{\</sup>star}$  Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

In this cancer type

O In other cancer type

• In this cancer type and other cancer types

× No evidence

| Relevant Therapy                                                         | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|--------------------------------------------------------------------------|-----|------|-----|------|------------------|
| erlotinib, chemotherapy                                                  | ×   | ×    | ×   | ×    | <b>(III)</b>     |
| erlotinib, erlotinib + chemotherapy                                      | ×   | ×    | ×   | ×    | <b>(III)</b>     |
| gefitinib + chemotherapy                                                 | ×   | ×    | ×   | ×    | <b>(III)</b>     |
| gefitinib, anlotinib hydrochloride                                       | ×   | ×    | ×   | ×    | <b>(III)</b>     |
| gefitinib, erlotinib                                                     | ×   | ×    | ×   | ×    | <b>(III)</b>     |
| gefitinib, icotinib hydrochloride, erlotinib, radiation therapy          | ×   | ×    | ×   | ×    | <b>(III)</b>     |
| lazertinib, gefitinib                                                    | ×   | ×    | ×   | ×    | <b>(III)</b>     |
| maihuatinib, gefitinib                                                   | ×   | ×    | ×   | ×    | <b>(III)</b>     |
| osimertinib, chemotherapy                                                | ×   | ×    | ×   | ×    | <b>(III)</b>     |
| SH-1028, gefitinib                                                       | ×   | ×    | ×   | ×    | <b>(III)</b>     |
| AZD-3759, erlotinib, gefitinib                                           | ×   | ×    | ×   | ×    | (II/III)         |
| D-0316, icotinib hydrochloride                                           | ×   | ×    | ×   | ×    | <b>(</b>   /   ) |
| afatinib, bevacizumab                                                    | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| afatinib, chemotherapy, radiation therapy                                | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| anlotinib hydrochloride                                                  | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| anlotinib hydrochloride, erlotinib, icotinib<br>hydrochloride, gefitinib | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| anlotinib hydrochloride, gefitinib                                       | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| anlotinib hydrochloride, icotinib hydrochloride                          | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| atezolizumab, bevacizumab                                                | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| atezolizumab, chemotherapy                                               | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| avitinib, AZD-3759                                                       | ×   | ×    | ×   | ×    | (II)             |
| bevacizumab, atezolizumab                                                | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| bevacizumab, atezolizumab, chemotherapy                                  | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| bevacizumab, erlotinib, chemotherapy                                     | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| bevacizumab, gefitinib                                                   | ×   | ×    | ×   | ×    | (II)             |
| bevacizumab, osimertinib                                                 | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| bintrafusp alfa, chemoradiation therapy, durvalumab                      | ×   | ×    | ×   | ×    | <b>●</b> (II)    |
| chemotherapy, atezolizumab, bevacizumab                                  | ×   | ×    | ×   | ×    | (II)             |

 $<sup>^{\</sup>star}$  Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

■ In this cancer type
O In other cancer type
O In this cancer type and other cancer types
X No evidence

| Relevant Therapy                                                                                                                              | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|-----------------------------------------------------------------------------------------------------------------------------------------------|-----|------|-----|------|------------------|
| chemotherapy, durvalumab                                                                                                                      | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| crizotinib + chemotherapy                                                                                                                     | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| durvalumab, tremelimumab, chemotherapy                                                                                                        | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| EGFR tyrosine kinase inhibitor + chemotherapy, EGFR tyrosine kinase inhibitor                                                                 | ×   | ×    | ×   | ×    | <b>●</b> (II)    |
| EGFR tyrosine kinase inhibitor, apatinib                                                                                                      | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| EGFR tyrosine kinase inhibitor, radiation therapy                                                                                             | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| erlotinib, anlotinib hydrochloride                                                                                                            | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| erlotinib, bevacizumab                                                                                                                        | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| erlotinib, gefitinib                                                                                                                          | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| erlotinib, gefitinib, icotinib hydrochloride, erlotinib<br>+ chemotherapy, gefitinib + chemotherapy, icotinib<br>hydrochloride + chemotherapy | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| erlotinib, radiation therapy                                                                                                                  | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| famitinib, almonertinib                                                                                                                       | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| gefitinib, erlotinib, afatinib                                                                                                                | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| gefitinib, surgical intervention                                                                                                              | ×   | ×    | ×   | ×    | (II)             |
| gefitinib, thalidomide                                                                                                                        | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| nazartinib, gefitinib                                                                                                                         | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| nivolumab, ipilimumab                                                                                                                         | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| olaparib, durvalumab                                                                                                                          | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| osimertinib, afatinib                                                                                                                         | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| osimertinib, bevacizumab                                                                                                                      | ×   | ×    | ×   | ×    | (II)             |
| osimertinib, gefitinib + osimertinib                                                                                                          | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| osimertinib, radiation therapy                                                                                                                | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| osimertinib, ramucirumab                                                                                                                      | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| osimertinib, savolitinib                                                                                                                      | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| osimertinib, selumetinib                                                                                                                      | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| pembrolizumab, chemotherapy                                                                                                                   | ×   | ×    | ×   | ×    | <b>(II)</b>      |
| poziotinib                                                                                                                                    | ×   | ×    | ×   | ×    | (II)             |

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

■ In this cancer type
O In other cancer type
O In this cancer type and other cancer types
X No evidence

| Relevant Therapy                                                                                                             | FDA | NCCN | EMA | ESMO | Clinical Trials <sup>3</sup> |
|------------------------------------------------------------------------------------------------------------------------------|-----|------|-----|------|------------------------------|
| ramucirumab, chemotherapy, cytokine                                                                                          | ×   | ×    | ×   | ×    | <b>(II)</b>                  |
| ramucirumab, pembrolizumab                                                                                                   | ×   | ×    | ×   | ×    | <b>(II)</b>                  |
| SH-1028                                                                                                                      | ×   | ×    | ×   | ×    | <b>(II)</b>                  |
| tyrosine kinase inhibitors, radiation therapy                                                                                | ×   | ×    | ×   | ×    | <b>(II)</b>                  |
| zoledronic acid, gefitinib                                                                                                   | ×   | ×    | ×   | ×    | <b>(II)</b>                  |
| anlotinib hydrochloride, chemotherapy                                                                                        | ×   | ×    | ×   | ×    | <b>(</b> 1/11)               |
| BDTX-189                                                                                                                     | ×   | ×    | ×   | ×    | <b>(</b> I/II)               |
| CBT-502, anlotinib hydrochloride                                                                                             | ×   | ×    | ×   | ×    | <b>(</b> 1/11)               |
| DZD-9008                                                                                                                     | ×   | ×    | ×   | ×    | <b>(</b> 1/11)               |
| EMB01                                                                                                                        | ×   | ×    | ×   | ×    | <b>(</b> I/II)               |
| erlotinib, chemotherapy, bevacizumab                                                                                         | ×   | ×    | ×   | ×    | (I/II)                       |
| KP-673                                                                                                                       | ×   | ×    | ×   | ×    | <b>(</b> I/II)               |
| ningetinib, gefitinib                                                                                                        | ×   | ×    | ×   | ×    | <b>(</b> 1/11)               |
| telaglenastat, osimertinib                                                                                                   | ×   | ×    | ×   | ×    | <b>(</b> 1/11)               |
| afatinib, chemotherapy                                                                                                       | ×   | ×    | ×   | ×    | (I)                          |
| alisertib, osimertinib                                                                                                       | ×   | ×    | ×   | ×    | (I)                          |
| alisertib, sapanisertib, osimertinib                                                                                         | ×   | ×    | ×   | ×    | (I)                          |
| amivantamab, lazertinib                                                                                                      | ×   | ×    | ×   | ×    | (I)                          |
| BCA101                                                                                                                       | ×   | ×    | ×   | ×    | (I)                          |
| bevacizumab + erlotinib + chemotherapy                                                                                       | ×   | ×    | ×   | ×    | (I)                          |
| C-005                                                                                                                        | ×   | ×    | ×   | ×    | (I)                          |
| CK-101                                                                                                                       | ×   | ×    | ×   | ×    | (I)                          |
| EGFR tyrosine kinase inhibitor, anlotinib hydrochloride                                                                      | ×   | ×    | ×   | ×    | (I)                          |
| etrumadenant, zimberelimab, chemotherapy                                                                                     | ×   | ×    | ×   | ×    | (I)                          |
| genolimzumab, fruquintinib                                                                                                   | ×   | ×    | ×   | ×    | (I)                          |
| lazertinib, amivantamab                                                                                                      | ×   | ×    | ×   | ×    | (I)                          |
| nazartinib + trametinib, nazartinib + ribociclib,<br>LXH254 + nazartinib, capmatinib + nazartinib,<br>gefitinib + nazartinib | ×   | ×    | ×   | ×    | <b>(</b> I)                  |
| neratinib, palbociclib, everolimus, trametinib                                                                               | ×   | ×    | ×   | ×    | (I)                          |

 $<sup>^{\</sup>star}$  Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

In this cancer type O In other cancer type In this cancer type and other cancer types X No evidence

| Relevant Therapy                    | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|-------------------------------------|-----|------|-----|------|------------------|
| niraparib, osimertinib              | ×   | ×    | ×   | ×    | <b>(</b> I)      |
| osimertinib, ipilimumab             | ×   | ×    | ×   | ×    | <b>(</b> I)      |
| osimertinib, necitumumab            | ×   | ×    | ×   | ×    | <b>(</b> I)      |
| pirotinib                           | ×   | ×    | ×   | ×    | <b>●</b> (I)     |
| ramucirumab, erlotinib, osimertinib | ×   | ×    | ×   | ×    | <b>(</b> I)      |
| telaglenastat, sapanisertib         | ×   | ×    | ×   | ×    | <b>(</b> I)      |
| telisotuzumab vedotin, osimertinib  | ×   | ×    | ×   | ×    | <b>(</b> I)      |
| TNO-155, nazartinib                 | ×   | ×    | ×   | ×    | <b>(</b> I)      |
| TQB 3804                            | ×   | ×    | ×   | ×    | <b>(</b> l)      |
| U3-1402                             | ×   | ×    | ×   | ×    | <b>(</b> l)      |
| WSD-0922                            | ×   | ×    | ×   | ×    | <b>(</b> I)      |
|                                     |     |      |     |      |                  |

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

## **Relevant Therapy Details**

### **Current FDA Information**

In this cancer type O In other cancer type In this cancer type and other cancer types

FDA information is current as of 2020-11-18. For the most up-to-date information, search www.fda.gov.

## EGFR p.(L858R) c.2573T>G

#### afatinib

Cancer type: Non-Small Cell Lung Cancer Label as of: 2019-10-11 Variant class: EGFR L858R mutation

### Indications and usage:

GILOTRIF® is a kinase inhibitor indicated for:

 First-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test.

Limitation of Use: Safety and efficacy of GILOTRIF® were not established in patients whose tumors have resistant EGFR mutations

Treatment of patients with metastatic, squamous NSCLC progressing after platinum-based chemotherapy

https://www.accessdata.fda.gov/drugsatfda\_docs/label/2019/201292s015lbl.pdf

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## EGFR p.(L858R) c.2573T>G (continued)

### dacomitinib

Cancer type: Non-Small Cell Lung Cancer Label as of: 2018-09-27 Variant class: EGFR L858R mutation

#### Indications and usage:

VIZIMPRO® is a kinase inhibitor indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutations as detected by an FDA-approved test.

#### Reference:

https://www.accessdata.fda.gov/drugsatfda\_docs/label/2018/211288s000lbl.pdf

#### erlotinib

Cancer type: Non-Small Cell Lung Cancer Label as of: 2016-10-18 Variant class: EGFR L858R mutation

#### Indications and usage:

TARCEVA® is a kinase inhibitor indicated for:

- The treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test receiving first-line, maintenance, or second or greater line treatment after progression following at least one prior chemotherapy regimen.
- First-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer, in combination with gemcitabine.

#### Limitations of Use:

- Safety and efficacy of TARCEVA® have not been established in patients with NSCLC whose tumors have other EGFR
  mutations.
- TARCEVA® is not recommended for use in combination with platinum-based chemotherapy.

### Reference:

https://www.accessdata.fda.gov/drugsatfda\_docs/label/2016/021743s025lbl.pdf

#### erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer Label as of: 2020-07-06 Variant class: EGFR L858R mutation

#### 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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## EGFR p.(L858R) c.2573T>G (continued)

## gefitinib

Cancer type: Non-Small Cell Lung Cancer Label as of: 2018-08-22 Variant class: EGFR L858R mutation

### Indications and usage:

IRESSA® is a tyrosine kinase inhibitor indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.

Limitation of Use: Safety and efficacy of IRESSA® have not been established in patients whose tumors have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution mutations.

#### Reference:

https://www.accessdata.fda.gov/drugsatfda\_docs/label/2018/206995s003lbl.pdf

### osimertinib

Cancer type: Non-Small Cell Lung Cancer Label as of: 2020-05-23 Variant class: EGFR L858R mutation

### Indications and usage:

TAGRISSO® is a kinase inhibitor indicated for

- the first-line treatment of patients with metastatic 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 treatment of 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/2020/208065s016lbl.pdf

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#### **Current NCCN Information**

In this cancer type

O In other cancer type

In this cancer type and other cancer types

NCCN information is current as of 2020-11-02. 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.(L858R) c.2573T>G

#### afatinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

NCCN Recommendation category: 1

#### Population segment (Line of therapy):

Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease;
 Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

### dacomitinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

NCCN Recommendation category: 1

#### Population segment (Line of therapy):

Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease;
 Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

### erlotinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

NCCN Recommendation category: 1

#### Population segment (Line of therapy):

Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease;
 Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

### gefitinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

NCCN Recommendation category: 1

#### Population segment (Line of therapy):

Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease;
 Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

## osimertinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

NCCN Recommendation category: 1

#### Population segment (Line of therapy):

Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease;
 EGFR sensitizing mutation discovered prior to first-line systemic therapy (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

#### afatinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

NCCN Recommendation category: 2A

### Population segment (Line of therapy):

 Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

#### afatinib + cetuximab

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

NCCN Recommendation category: 2A

#### Population segment (Line of therapy):

 Non-Small Cell Lung Cancer; Progression on erlotinib, afatinib, dacomitinib, gefitinib, chemotherapy, or osimertinib; Systemic multiple lesions (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

#### dacomitinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

NCCN Recommendation category: 2A

## Population segment (Line of therapy):

 Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)

**Date**: 04 Feb 2021 13 of 40

## EGFR p.(L858R) c.2573T>G (continued)

### erlotinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

NCCN Recommendation category: 2A

#### Population segment (Line of therapy):

Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease;
 Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy,
 including maintenance therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

### erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

NCCN Recommendation category: 2A

#### Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease;
   Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease;
   Sensitizing EGFR mutation discovered during first-line systemic therapy (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

### gefitinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

NCCN Recommendation category: 2A

### Population segment (Line of therapy):

 Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

#### osimertinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

NCCN Recommendation category: 2A

### Population segment (Line of therapy):

 Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (Subsequent therapy) (Preferred)

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## EGFR p.(L858R) c.2573T>G (continued)

### bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

Non-Squamous Non-Small Cell Lung Cancer; Advanced or metastatic disease; No recent history of hemoptysis; Sensitizing EGFR mutation discovered prior to or during first-line systemic therapy (First-line therapy) (Useful in Certain Circumstances)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

#### erlotinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

Non-Small Cell Lung Cancer; Leptomeningeal and spine metastases; Pulsatile erlotinib (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2020]

#### erlotinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

Non-Small Cell Lung Cancer; Brain metastases; Use active agents against primary tumor; Pulsatile erlotinib (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2020]

#### afatinib

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

NCCN Recommendation category: 2B

Population segment (Line of therapy):

Non-Small Cell Lung Cancer; Brain metastases; Use active agents against primary tumor (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2020]

### gefitinib

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

NCCN Recommendation category: 2B

Population segment (Line of therapy):

Non-Small Cell Lung Cancer; Brain metastases; Use active agents against primary tumor (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2020]

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## EGFR p.(L858R) c.2573T>G (continued)

## osimertinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

■ Non-Small Cell Lung Cancer; Leptomeningeal and spine metastases (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2020]

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#### **Current EMA Information**

In this cancer type

O In other cancer type

In this cancer type and other cancer types

EMA information is current as of 2020-11-18. For the most up-to-date information, search www.ema.europa.eu/ema.

## EGFR p.(L858R) c.2573T>G

#### afatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2020-11-04

Variant class: EGFR L858R mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/giotrif-epar-product-information\_en.pdf

## bevacizumab (Allergan) + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2020-11-03

Variant class: EGFR L858R mutation

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 L858R mutation

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: 2020-11-16

Variant class: EGFR L858R mutation

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: 2020-09-02

Variant class: EGFR L858R mutation

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: 2020-03-11

Variant class: EGFR L858R mutation

Reference:

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

**Date**: 04 Feb 2021 17 of 40

## EGFR p.(L858R) c.2573T>G (continued)

### dacomitinib

Cancer type: Non-Small Cell Lung Cancer Label as of: 2019-06-05 Variant class: EGFR L858R mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/vizimpro-epar-product-information\_en.pdf

### erlotinib

Cancer type: Non-Small Cell Lung Cancer Label as of: 2019-04-24 Variant class: EGFR L858R mutation

Reference:

https://www.ema.europa.eu/documents/product-information/tarceva-epar-product-information\_en.pdf

### erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer Label as of: 2020-07-02 Variant class: EGFR L858R mutation

Reference:

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

### gefitinib

Cancer type: Non-Small Cell Lung Cancer Label as of: 2019-05-28 Variant class: EGFR L858R mutation

Reference:

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

### osimertinib

Cancer type: Non-Small Cell Lung Cancer Label as of: 2020-10-16 Variant class: EGFR L858R mutation

Reference:

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

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#### **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 2020-11-02. For the most up-to-date information, search www.esmo.org.

## EGFR p.(L858R) c.2573T>G

## atezolizumab + bevacizumab + carboplatin + paclitaxel

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

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

#### Population segment (Line of therapy):

- Metastatic Non-Squamous; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 3 (First-line therapy)
- Metastatic; PS 0-1; Without contraindications to immunotherapy after targeted therapies have been exploited (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.]

#### afatinib

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 stage; Regardless of PS (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

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 stage; Regardless of PS (First-line therapy)

## gefitinib

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 stage; Regardless of PS (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.]

### 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 stage; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 4 (First-line therapy) (Preferred)

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.]

#### dacomitinib

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

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

Population segment (Line of therapy):

 Advanced stage; Regardless of PS; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 3 (First-line therapy) (Preferred)

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

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

ESMO Level of Evidence/Grade of Recommendation: III / B

Population segment (Line of therapy):

■ Non-Squamous (Maintenance therapy)

#### afatinib

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; PS 0-2 (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.]

### 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; PS 0-2 (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.]

### 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; PS 0-2 (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.]

#### dacomitinib

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; PS 0-2 (First-line therapy)

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## EGFR p.(L858R) c.2573T>G (continued)

### 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; PS 0-2 (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: I / A

Population segment (Line of therapy):

■ Stage IV; PS 0-2 (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

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; PS 0-2 (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: I / A

Population segment (Line of therapy):

■ Stage IV; PS 0-2 (First-line therapy)

#### 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; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 3 (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.]

### 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; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 3 (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: I / B

Population segment (Line of therapy):

Stage IV; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 3 (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: I / B

Population segment (Line of therapy):

Advanced stage (First-line therapy)

### afatinib

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; PS 3-4 (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.]

### 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; PS 3-4 (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.]

## 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; PS 3-4 (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.]

#### dacomitinib

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; PS 3-4 (First-line therapy)

### 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; PS 3-4 (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; PS 3-4 (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

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; PS 3-4 (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; PS 3-4 (First-line therapy)

## **Clinical Trials Summary**

## EGFR p.(L858R) c.2573T>G

| 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    |
| NCT03264794 | Evaluation of the Efficacy of Domestic Gefitinib Tablets in the Treatment of Locally Advanced or Metastatic Non-small Cell Lung Cancer Patients Using a Multicenter, Randomized, Positive Drug Gefitinib Pharmacodynamics and Pharmacodynamics                                            | 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    |
| 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    |
| NCT03849768 | A Randomized, Open-Label, Multi Center, Phase III Study to Assess the Efficacy and Safety of HS-10296 Versus Gefitinib as First-Line Treatment in Patients With EGFR Mutation Positive, Locally Advanced or Metastatic NSCLC                                                              | III   |
| 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   |
| NCT04143607 | A Phase III,Double-Blind, Randomised Study to Assess the Efficacy and Safety of ASK120067 Versus Gefitinib as First-Line Treatment in Patients With Epidermal Growth Factor Receptor Mutation Positive, Locally Advanced or Metastatic Non-Small Cell Lung Cancer                         | III   |
| NCT02633189 | A Randomized Open-label Phase III Trial Comparing Bevacizumab + Erlotinib vs Erlotinib Alone as First Line Treatment of Patients With EGFR Mutated Advanced Non Squamous Non Small Cell Lung Cancer                                                                                       | III   |
| NCT02193282 | Randomized Study of Erlotinib vs Observation in Patients With Completely Resected Epidermal Growth Factor Receptor (EGFR) Mutant Non-small Cell Lung Cancer (NSCLC)                                                                                                                       | III   |
| NCT02886195 | EGFR-TKIs Combine Chemotherapy as First-line Therapy for Patients With Advanced EGFR Mutation-positive NSCLC                                                                                                                                                                              | III   |
| NCT02518802 | Pemetrexed Disodium and Cisplatin Chemotherapy Combined With Synchronous Gefitinib vs<br>Chemotherapy Alone as Adjuvant Therapy in Patient With Stage II-IIIA, Epidermal Growth Factor<br>Receptor Mutant Expressing Lung Adenocarcinoma                                                  | III   |
| NCT04028778 | A Multicenter, Randomized, Double-Blind Study of Gefitinib in Combination With Anlotinib or Placebo in Previously Untreated Patients With EGFR Mutation-Positive Advanced Non-Small-Cell Lung Cancer                                                                                      | III   |
| No NCT ID   | A Phase III Study Comparing Gefitinib And Inserted Cisplatin And Pemetrexed With Gefitinib As A First-<br>Line Treatment For Patients With Advanced Non-Squamous Non-Small-Cell Lung Cancer Harboring<br>EGFR Activating Mutation (JCOG1404/WJOG8214L, AGAIN study)                       | III   |
| NCT03381066 | A Phase III, Randomized, Multi-center Study to Determine the Efficacy of the Intercalating Combination Treatment of Chemotherapy and Gefitinib or Chemotherapy as Adjuvant Treatment in NSCLC With Common EGFR 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   |
| NCT04248829 | A Phase III, Randomized, Double-blind Study to Assess the Efficacy and Safety of Lazertinib Versus<br>Gefitinib as the First-line Treatment in Patients With Epidermal Growth Factor Receptor Sensitizing<br>Mutation Positive, Locally Advanced or Metastatic Non-Small Cell Lung Cancer | III   |
| No NCT ID   | A Phase III Trial for Mefatinib (MET-306) Versus Gefitinib in the Treatment of 1st Line EGFR Mutation of Patients with Advanced Non-Small Cell Lung Cancer                                                                                                                                | III   |

| 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    |
| 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    |
| NCT04239833 | A Phase III, Double-blind, Randomised Study of SH-1028 Tablets Versus Gefiitinib as First Line<br>Treatment in Patients With Epidermal Growth Factor Receptor Mutation Positive, Locally Advanced or<br>Metastatic Non Small Cell Lung Cancer                                                                                                       | III    |
| NCT03653546 | A Randomized, Open-label, Controlled, Multi-Center Phase II/III Study to Assess the Efficacy and Safety of AZD3759 vs. a Standard of Care EGFR TKI, as First Line Treatment to EGFR Mutation Positive Advanced NSCLC With CNS Metastases                                                                                                            | 11/111 |
| 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                                                                                                                                   | 11/111 |
| NCT02338011 | Gefitinib Alone or With Concomitant Whole Brain Radiotherapy for Patients Harboring an EGFR<br>Mutation With Multiple Brain Metastases From Non-Small-cell Lung Cancer: a Phase II/III Randomized<br>Controlled Trial                                                                                                                               | 11/111 |
| No NCT ID   | Phase II Study Of Low-Dose Afatinib For Elderly Patients With Non-Small Cell Lung Cancer Harboring EGFR Mutation                                                                                                                                                                                                                                    | II     |
| No NCT ID   | Multicenter, Prospective Interventional Study To Evaluate Therapeutic Effect of Afatinib in Patients With Advanced Non-Small Cell Lung Cancer, EGFR Mutation Positive And Brain Metastasis.                                                                                                                                                         | II     |
| No NCT ID   | The feasibility study and biomarker research of afatinib in patients with previously treated advanced NSCLC harboring EGFR mutation.                                                                                                                                                                                                                | II     |
| NCT03720873 | An Multicenter,Phase II Trial of EGFR-TKIs Combine With Anlotinib as First-line Treatment for Patients With Advanced EGFR Mutation-positive NSCLC                                                                                                                                                                                                   | II     |
| NCT03736837 | A Multi-center, One-arm Clinical Study of Anlotinib Combined With Icotinib as the First-line Treatment in Patients With EGFR Mutation-positive Advanced NSCLC. The Trial Aims to Evaluate the Efficacy and Safety of This Treatment.                                                                                                                | 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     |
| NCT02655536 | A Phase II, Open Label, Multicenter Study of Bevacizumab in Combination With Erlotinib Versus<br>Erlotinib Alone in Patients With EGFR Mutant Non-small Cell Lung Cancer Who Have Brain Metastases                                                                                                                                                  | II     |
| No NCT ID   | Phase II Study Of Combination Chemotherapy Of Carboplatin, Pemetrexed, Bevacizumab And Erlotinib In Patients With Advanced Non-Squamous Non-Small Cell Lung Cancer Harboring EGFR Active Mutation.                                                                                                                                                  | II     |
| NCT04425187 | Bevacizumab Combined With Gefitinib in the Treatment of Advanced NSCLC Clinical Study of L858R Positive Mutation Patients                                                                                                                                                                                                                           | II     |

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## **Clinical Trials Summary (continued)**

| NCT ID      | Title                                                                                                                                                                                                                                                         | Phase |
|-------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|
| No NCT ID   | Low-dose Decitabine plus Crizotinib in EGFR-Mutation-Positive Advanced Non-Small Cell Lung Cancer<br>Patients :A Open-Label,Single-Arm Phase II Study                                                                                                         | II    |
| NCT04027647 | A Single-arm, Open-label, Phase II Study of Dacomitinib With or Without Dose Titration for the First-line Treatment of Locally Advanced or Metastatic Non-small Cell Lung Cancer in Subjects With Epidermal Growth Factor Receptor (EGFR) Activation Mutation | 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 Trial of Induction Erlotinib Followed by Surgical Resection in Patients with Pathologically Confirmed Stage IIIA-N2 EGFR Mutated Non-small cell lung cancer                                                                                        | II    |
| NCT03628521 | Anlotinib-based Combination as First-line Treatment in Advanced Non-small Cell Lung Cancer: a Single Center, Three Arms and Exploratory Study                                                                                                                 | II    |
| NCT03126799 | A Randomized Phase II Study of Erlotinib Alone Versus Erlotinib Plus Bevacizumab for Advanced Nonsmall Cell Lung Cancer With Epidermal Growth Factor Receptor Activating Mutations                                                                            | II    |
| NCT02098954 | Second Line Erlitinib Combination With Gemcitabine Cisplatinum in Non-small Cell Lung Cancer<br>Patients Who Harbored EGFR Sensitive Mutation Developed Resistance After First Line TKI Treatment                                                             | II    |
| No NCT ID   | Phase II study of EGFR-TKI in Elderly Patients With Lung Cancer Harboring EGFR Gene Mutation in Liquid Biopsy                                                                                                                                                 | II    |
| NCT03267654 | Gefitinib Versus Combination of Gefitinib With Chemotherapy or Anti-angiogenesis as 1st Line<br>Treatment in Advanced NSCLC Patients Detected With Bim Deletion or Low EGFR Activating Mutation<br>Abundance:A Randomized, Multicentre, Phase II Study        | II    |
| No NCT ID   | A randomized phase II trial of docetaxel or pemetrexed with or without gefitinib in elderly advanced non-small cell lung cancer patients harboring activating EGFR mutation after failure of the therapy as first-line treatment.                             | II    |
| NCT03457337 | A Randomized, Controlled, Open-label, Prospective Trial of S-1 Plus Gefitinib Versus Gefitinib Monotherapy for First-line Treatment of Advanced Non-squamous Non-small Cell Lung Cancer With EGFR-sensitive Mutation                                          | II    |
| NCT03382795 | Retreatment With 1st Generation EGFR TKIs in Sensitizing EGFR Mutation Positive Non-Squamous Cell Carcinoma Patients Who Previously Treated With EGFR TKI and Cytotoxic Chemotherapy                                                                          | II    |
| NCT03341494 | A Randomized Phase II Study of Gefitinib Alone Versus Gefitinib Plus Thalidomide for Advanced Non-<br>small Cell Lung Cancer With Epidermal Growth Factor Receptor Activating Mutations                                                                       | 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    |
| 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    |
| NCT03292133 | A Phase II Study of EGF816 and Gefitinib in TKI-naive EGFR-mutant Non-Small Cell Lung Cancer                                                                                                                                                                  | II    |

| NCT ID      | Title                                                                                                                                                                                                                                                                                     | Phase |
|-------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|
| No NCT ID   | A Phase II trial of Osimertinib for Elderly patients with Advanced or Postoperative Recurrent Non-Small-Cell Lung Cancer (SPIRAL-0 Study)                                                                                                                                                 | II    |
| No NCT ID   | A Phase II, Noncomparative, Open Label, Multicentre, Study Of AZD9291 In Patients With Locally Advanced Or Metastatic EGFR Mutated "T790M Undetectable Or Unknown" Non-Small Cell Lung Cancer (Stage IIIb-IV) After No Immediate Prior EGFR TKI (OSIRIS Study)                            | II    |
| NCT02736513 | Pilot, Phase II Study Assessing Intracranial Activity of AZD9291 (TAGRISSO) in Advanced EGFRm(EGFR Mutation) NSCLC Patients With Asymptomatic 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    |
| NCT03586453 | A Phase II Study of Osimertinib With On-study and Post-progression Biopsy in the First Line Treatment of EGFR Inhibitor naive Advanced EGFR Mutant Lung Cancer                                                                                                                            | II    |
| NCT03969823 | Whole Genomic Landscape of EGFR Mutation-Positive Advanced Non-Small Cell Lung Cancer Treated With First-Line Osimertinib (WARRIOR)                                                                                                                                                       | 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    |
| No NCT ID   | Phase 2 clinical trial of the alternative therapy with osimertinib and afatinib for treatment-naive advanced NSCLC with EGFR mutation. (Alt trial) (WJOG10818L)                                                                                                                           | II    |
| No NCT ID   | A Phase II Study of osimertinib plus cisplatin/carboplatin+pemetrexed for previously-untreated patients with NSCLC harboring EGFR sensitizing mutations. (NEJ032C/LOGIK1801)                                                                                                              | II    |
| NCT02856893 | APPLE Trial: Feasibility and Activity of AZD9291 (Osimertinib) Treatment on Positive PLasma T790M in EGFR Mutant NSCLC Patients                                                                                                                                                           | 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    |
| 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    |
| NCT03392246 | A Phase II Study of Osimertinib in Combination With Selumetinib in EGFR Inhibitor naive Advanced EGFR Mutant Lung Cancer                                                                                                                                                                  | II    |
| NCT03242915 | Phase II Multi-center Study of Pembrolizumab in Combination With Platinum-based Doublet Chemotherapy in NSCLC (Non-small Cell Lung Cancer) Patients With Targetable Genetic Alterations in Their Tumor Previously Treated With Appropriate Targeted Agents With Progressive Disease       | 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    |
| No NCT ID   | Afatinib Translational Study in Patients with EGFR Mutation-Positive Non-Squamous Non-small Cell Lung Cancer Acquired Resistance to Osimertinib (ASPEC)                                                                                                                                   | I/II  |

| NCT ID      | Title                                                                                                                                                                                                                                                            | Phase |
|-------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|
| NCT03706287 | Efficacy and Safety of Anlotinib Combined With Platinum Plus Pemetrexed in T790M Mutation<br>Negative Metastastic Non-squamous Non-small-cell Lung Cancer After Progression on First-line EGFR<br>TKI: a Phase II, Muti-center, Single Arm Study                 | 1/11  |
| 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 | 1/11  |
| NCT03831932 | A Phase I/II Study of AZD9291 (Osimertinib) and CB-839 HCl in Patients With EGFR Mutant Non-Small Cell Lung Cancer                                                                                                                                               | 1/11  |
| No NCT ID   | A Non-interventional, Single-arm, Prospective Clinical Study for the Efficacy and Safety of Low-dose Alfaatinib Combined with Pemetrexed and Carboplatin in First-line Treatment of Advanced EGFR Mutant Non-squamous Non-small Cell Lung Cancer                 | I     |
| NCT04085315 | A Phase I/Ib Study of Alisertib in Combination With Osimertinib in Metastatic EGFR-mutant Lung Cancer                                                                                                                                                            | 1     |
| NCT04479306 | A Ph Ib Study of Osimertinib + Alisertib or Sapanisertib for Osimertinib-Resistant EGFR Mutant Non-<br>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                                                                                                                                                                   | 1     |
| 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     |
| No NCT ID   | The Clinical Observational Study of Neoadjuvant Target Therapy in Stage IIIB and IV Non-small Cell Lung Cancer Patients                                                                                                                                          | I     |
| No NCT ID   | Study for Efficacy and Safety of Continuing to Treat with TKI Combined with Anlotinib Monotherapy in Advanced NSCLC Patients with T790M Mutation-negative after Tki Treatment Failure                                                                            | 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     |
| NCT03333343 | A Phase Ib, Open Label, Multi-center Study to Characterize the Safety, Tolerability and Preliminary Efficacy of EGF816 in Combination With Selected Targeted Agents in EGFR Mutant 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     |
| NCT02496663 | A Phase I Trial of AZD9291 and Necitumumab in EGFR-Mutant Non-small Cell Lung Cancer After Progression on a Previous EGFR Tyrosine Kinase Inhibitor                                                                                                              | I     |
| No NCT ID   | Single-arm Phase I Study of Erlotinib or Osmeltinib plus Ramcilmab in Patients with Untreated EGFR Gene Mutation-Positive Non-Small Cell Lung Cancer with Brain Metastases                                                                                       | 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                                                                                                                     | 1     |
| NCT03260491 | A Multicenter, Open-Label Phase I Study of U3-1402 in Subjects With Metastatic or Unresectable Non-small Cell Lung Cancer.                                                                                                                                       | I     |
| NCT04197934 | Phase I Study to Evaluate Safety, Tolerability, Pharmacokinetics and Anti-Tumor Activity of WSD0922-FUFU                                                                                                                                                         | I     |

| NCT ID      | Title                                                                                                                                                                                                                                                                                     | Phase |
|-------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|
| NCT04132102 | An Open-label, Single-arm Clinical Study to Evaluate the Efficacy of Afatinib in Advanced Lung Squamous Cell Carcinoma With EGFR Sensitive Mutation                                                                                                                                       | IV    |
| NCT04116918 | Efficacy and Safety of the Combination of Anlotinib and JS001 in EGFR-TKI Resistant T790M-Negative NSCLC                                                                                                                                                                                  | IV    |
| No NCT ID   | Gefitinib Combined with Vinorelbine Soft Capsules vs Gefitinib Monotherapy in the Treatment of Stage IIIB-IV NSCLC Patients with EGFR-sensitive Mutation                                                                                                                                  | IV    |
| No NCT ID   | Phase III Study of Afatinib or Chemotherapy in Patients with Non-small Cell Lung Cancer Harboring Sensitizing Uncommon Epidermal Growth Factor Receptor Mutations (ACHILLES study/TORG1834)                                                                                               | III   |
| NCT03866499 | A Randomized, Double-blind, Positive Controlled Phase III Study to Evaluate the Efficacy and Safety of BPI-7711 Capsule in Locally Advanced or Recurrent/Metastatic Treatment-naive Non-small Cell Lung Cancer Patients With EGFR Mutation                                                | III   |
| No NCT ID   | A Randomized Phase III Study Of Erlotinib Compared To Intercalated Erlotinib With Cisplatinum Pemetrexed As First-Line Therapy For Advanced EGFR Mutated Non-Small-Cell Lung Cancer. The NVALT-17 Study                                                                                   | III   |
| No NCT ID   | Randomized Phase III Trial Of Icotinib Combined With Thoracic Radiotherapy Vs. Icotinib Alone In Treatment Of Advanced NSCLC Patients With EGFR Mutation                                                                                                                                  | III   |
| 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   |
| NCT02183883 | Deciphering Afatinib Response and Resistance With INtratumour Heterogeneity                                                                                                                                                                                                               | II    |
| NCT04201756 | Neoadjuvant Afatinib Therapy for Resectable Stage III EGFR Mutation-Positive Lung Adenocarcinoma: A Single-Arm, Open-Label, Phase II Clinical Trial                                                                                                                                       | II    |
| No NCT ID   | Hypothesis generative H2H study comparing the efficacy between afatinib and osimertinib based on the immunological biomarker in the NSCLC patients with EGFR mutations (HeaT ON BeaT)                                                                                                     | 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    |
| 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    |
| No NCT ID   | The Clinical Effect of EGFR-TKI Combined with Chemotherapy on Patients with EGFR Multiple Gene Mutations                                                                                                                                                                                  | II    |

| NCT ID      | Title                                                                                                                                                                                                                                                                                                                                                                | Phase |
|-------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|
| NCT02347839 | A Multicenter Phase II Trial of Neoadjuvant Gefitinib Followed by Surgery, Followed by Adjuvant Gefitinib in Patients With Unresectable Stage III Non-Small Cell Lung Cancer Harboring Activating Epidermal Growth Factor Receptor Mutations NEoadjuvant Gefitinib fOllowed by Surgery and gefiTinib In unresectAble sTage III NSCLC With EGFR Mutations (NEGOTIATE) | II    |
| NCT02264210 | A Randomized, Phase II Trial of Icotinib Versus Observation as Adjuvant Treatment in Stage IB Non-<br>Small Cell Lung Cancer Harboring Activating Epidermal Growth Factor Receptor Mutation                                                                                                                                                                          | 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    |
| NCT02824952 | Neo-adjuvant Trial With AZD9291 in EGFRm+ Stage IIIA/B NSCLC - a Phase II Open-label Study                                                                                                                                                                                                                                                                           | II    |
| NCT04120454 | An Investigator-Sponsored Phase II Single Arm Trial of Ramucirumab and Pembrolizumab in Patients With EGFR Mutant Non-Small Cell Lung Cancer                                                                                                                                                                                                                         | II    |
| NCT03983928 | A Phase Ib, Open-label, Single Center, Non-randomized Study for Safety and Efficacy of TQB2450<br>Combined With Anlotinib in Subjects With Advanced Mutation Positive Non-Small Cell Lung Cancer                                                                                                                                                                     | 1/11  |
| NCT03846310 | A Phase I/lb 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                                                                                                                                                                                                   | 1     |
| NCT04511533 | Single Arm Study to Evaluate the Safety of Dacomitinib for the First-Line Treatment of Participants in India With Metastatic Non-Small Cell Lung Cancer With Epidermal Growth Factor Receptor (EGFR)-Activating Mutations                                                                                                                                            | IV    |
| No NCT ID   | The Continuous Evaluation of EGFR Mutation in EGFR-mutation Positive Lung Cancer Patients During EGFR TKI Treatment.                                                                                                                                                                                                                                                 | IV    |
| NCT02404675 | High Dose Icotinib in Advanced Non-small Cell Lung Cancer With EGFR 21 Exon Mutation (INCREASE): a Randomized, Open-label Study                                                                                                                                                                                                                                      | 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   |
| NCT02714010 | Whole Brain Radiotherapy Concurrent With EGFR-TKI Versus EGFR-TKI Alone in the Treatment of Non-small Cell Lung Cancer Patients With Brain Metastasis                                                                                                                                                                                                                | III   |
| NCT02448797 | Icotinib as Adjuvant Therapy Compared With Standard Chemotherapy in Stage II-IIIA Non-small Cell Lung Cancer With EGFR-mutation: a Randomized, Positive-controlled, Phase 3 Study (EVIDENCE, CCTC-1501)                                                                                                                                                              | 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    |
| NCT01470716 | A Phase II Study of Neo-adjuvant Erlotinib for Operable Stage IIB or IIIA Non-small Cell Lunc Cancer<br>With Epidermal Growth Factor Receptor Activation Mutations                                                                                                                                                                                                   | II    |
| No NCT ID   | ITAC 2 TRIAL: Intermittent TKI and Chemotherapy for Patients with Advanced Non-Small Cell Lung Cancer                                                                                                                                                                                                                                                                | II    |
| NCT01951469 | Multicenter Phase II Study of Gefitinib Mono-therapy or Gefitinib Combined With Pemetrexed/Cisplatin in Patients With Brain Metastases From Non-small Cell Lung Cancer Harboring EGFR Mutation                                                                                                                                                                       | II    |

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| NCT ID      | Title                                                                                                                                                                                                                                                                                    | Phase |
|-------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|
| 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    |
| 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    |
| NCT03667820 | Phase II Trial of Osimertinib in Combination With Stereotactic Ablative Radiation (SABR) in EGFR Mutant Advanced Non-Small Cell Lung Cancer (NSCLC)                                                                                                                                      | II    |
| NCT03318939 | A Phase II Study of Poziotinib in Patients With Non-Small Cell Lung Cancer (NSCLC), Locally Advanced or Metastatic, With EGFR or HER2 Exon 20 Insertion Mutation (ZENITH20).                                                                                                             | II    |
| No NCT ID   | Zoledronate combinate with gefitinib in advanced non-small cell lung cancer with EGFR activation mutation: a multicenter, randomised controlled, phase II trial                                                                                                                          | II    |
| No NCT ID   | A Phase I Study Afatinib In Combination Of Osimertinib In Patients With Relapsed Non-Small Cell Lung<br>Cancer After Failure of Prior Osimertinib                                                                                                                                        | I     |
| NCT03755102 | A Pilot Study of Dacomitinib for Patients With Metastatic EGFR Mutant Lung Cancers With Disease Progression on Osimertinib                                                                                                                                                               | I     |
| NCT03891615 | Phase I Study of Niraparib in Combination With Osimertinib in EGFR-Mutated Advanced Lung Cancer                                                                                                                                                                                          | 1     |
| NCT04250545 | A Phase I Trial of MLN0128 (Sapanisertib) and CB-839 HCI (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     |
| NCT04413201 | AFAMOSI: Prospective, Randomized, Multicenter Phase IV Study to Evaluate the Efficacy and Safety of Afatinib Followed by Osimertinib Compared to Osimertinib in Patients With EGFRmutated/T790M Mutation Negative Non-squamous NSCLC in the First-line Setting                           | IV    |
| 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 Gefitinib And Brain Radiotherapy On EGFR-Mutated Non-Small-Cell Lung Cancer Patients With Brain Metastasis                                                                                                                                          | 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   |
| NCT03656393 | Observational Clinical Trial of Adjuvant Chemotherapy for Non-squamous Cell Carcinoma of Non-small Cell Lung Cancer                                                                                                                                                                      | 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   |
| No NCT ID   | A Phase II Study Of Afatinib For Advanced Non-Small Cell Lung Cancer With Uncommon Epidermal<br>Growth Factor Receptor (EGFR) Mutation Including Compound Mutation Detected By Next Generation<br>Sequencing                                                                             | II    |

| NCT ID      | Title                                                                                                                                                                                                                                 | Phase |
|-------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|
| No NCT ID   | Afatinib plus Bevacizumab Combination after osimertinib failure for advanced EGFR-mutant non-small cell lung cancer: a multicenter prospective single arm phase II study (ABCD-study)                                                 | II    |
| NCT01553942 | Afatinib Sequenced With Concurrent Chemotherapy and Radiation in EGFR-Mutant Non-Small Cell Lung Tumors: The ASCENT Trial                                                                                                             | II    |
| No NCT ID   | A Single-center, Open Label, Phase II Study of Anlotinib as Second/Third-line Treatment for Advanced Non-small Cell Lung Cancer                                                                                                       | II    |
| No NCT ID   | Clinical Study And Safety Analysis On The Treatment Of Advanced Non-Small Cell Lung Cancer With Anlotinib And Gefitinib                                                                                                               | II    |
| No NCT ID   | Osimertinib Combined Bevacizumab in Untreated Epidermal Growth Factor Receptor Mutated Non-<br>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    |
| No NCT ID   | To Evaluate the Relationships Between the Serum Concentration of Erlotinib and the Effects and Toxicities of Them                                                                                                                     | II    |
| No NCT ID   | Efficacy and safety of erlotinib in elderly patients with non-small-cell lung cancer harboring epidermal growth factor receptor mutations.                                                                                            | II    |
| NCT01763385 | Erlotinib With Concurrent Brain Radiotherapy and Secondary Brain Radiotherapy After Recurrence With Erlotinib in NSCLC Non-increased-intracranial-pressure Symptomatic Brain Metastases: A Prospective Multicenter Trial (TRACTS)     | 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    |
| NCT01784549 | A Multi-center Phase II Randomized Study of Customized Neoadjuvant Therapy Versus Standard Chemotherapy in Non-small Cell Lung Cancer (NSLC) Patients With Resectable Stage IIIA (N2) Disease                                         | 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    |
| NCT03091491 | Randomised Phase II Study of Nivolumab Versus Nivolumab and Ipilimumab Combination in EGFR Mutant Non-small Cell Lung Cancer                                                                                                          | 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    |
| NCT04425681 | Phase II Study of Osimertinib With Bevacizumab for Leptomeningeal Metastasis From EGFR-mutation<br>Non-Small Cell Lung Cancer                                                                                                         | 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    |

| NCT ID      | Title                                                                                                                                                                                                                                                                                         | Phase |
|-------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|
| No NCT ID   | Clinical Study of Combined Action of the First Generation of TKIs and Brain Radiotherapy on EGFR-<br>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                                                                   | 1/11  |
| NCT03797391 | First-in-human, Phase I/II, Multicenter, Open-Label Study of EMB-01 in Patients With Advanced/<br>Metastatic Solid Tumors                                                                                                                                                                     | 1/11  |
| No NCT ID   | A phase I/II study of erlotinib/carboplatin/pemetrexed/bevacizumab in chemotherapy-naive patients with EGFR mutation positive advanced non-squamous non-small-cell lung cancer                                                                                                                | 1/11  |
| NCT03758287 | A Phase Ib, Multi-center, Open Label Study of Ningetinib (CT053PTSA) in Combination With Gefitinib in Stage IIIB or IV NSCLC Patients With EGFR Mutation and T790M Negative Who Have Progressed After EGFR TKI Therapy                                                                        | 1/11  |
| NCT03711422 | A Dose Finding Study of Continuous and Intermittent High-dose (HDI) Afatinib (EGFR TKI) on CNS Metastases and Leptomeningeal Disease (LMD) in Patients With Advanced Refractory EGFR Mutation Positive Non-small Cell Lung Cancer                                                             | I     |
| No NCT ID   | Feasibility Study of Pemetrexed / Bevacizumab / Erlotinib in Chemotherapy Naive Patients With Non-<br>Small Cell Lung Cancer Harboring EGFR Mutation                                                                                                                                          | 1     |
| 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     |
| No NCT ID   | Pharmacokinetic and dose finding study of osimertinib in patients with impaired renal function and low body weight                                                                                                                                                                            | 1     |
| NCT03535363 | Phase I Trial of Osimertinib With Stereotactic Radiosurgery (SRS) in Patients With Brain Metastases From EGFR Positive Non-Small-Cell Lung Cancer (NSCLC)                                                                                                                                     | I     |
| No NCT ID   | Phase I Clinical Study With Advanced Solid Tumors KBP-5209 Treatment                                                                                                                                                                                                                          | I     |
| No NCT ID   | A Pilot Study for Apatinib Mesylate Combined with Gefitinib in First-line Treatment of Lung<br>Adenocarcinoma with Malignant Pleural Effusion or Pericardial Effusion                                                                                                                         | IV    |
| NCT03346811 | Efficiency of Icotinib in Plasma ctDNA EGFR Mutation-positive Patients Diagnosed With Lung Cancer:a Single Arm,Multi-center,Open-label Study                                                                                                                                                  | II    |
| NCT04209465 | MasterKey-01: A Phase I/II, Open-label, Two-part, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics & Antitumor Activity of BDTX-189, an Inhibitor of Allosteric ErbB Mutations, in Patients w/ Advanced Solid Malignancies                                              | 1/11  |
| No NCT ID   | Observational Research To Decide Optimal Dose Of Afatinib In Patients With Primary Lung<br>Adenocarcinoma Harbouring The Sensitive Mutation Of Epidermal Growth Factor Receptor (EGFR) By<br>Pharmacokinetic Analyses                                                                         | I     |
| NCT03618043 | A Phase I, Open-label Study to Assess the Safety and Tolerability of Ascending Doses of SH-1028<br>Tablets in Patients With Advanced Solid Cancer                                                                                                                                             | I     |
| No NCT ID   | Additional analysis of PFS and OS in a randomized phase III trial of gefitinib and erlotinib for advanced lung and lung adenocarcinoma (WJOG5108LFS)                                                                                                                                          | III   |
| NCT03810872 | An Open Explorative Phase II, Open Label Study of Afatinib in the Treatment of Advanced Cancer Carrying an EGFR, a HER2 or a HER3 Mutation                                                                                                                                                    | II    |

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## **Clinical Trials Summary (continued)**

## EGFR p.(L858R) c.2573T>G (continued)

| NCT ID      | Title                                                                                                                                                                                                                                             | Phase |
|-------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|
| NCT03239015 | Efficacy and Safety of Targeted Precision Therapy in Refractory Tumor With Druggable Molecular Event                                                                                                                                              | 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     |
| 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     |
| NCT03297606 | Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial                                                                                                                                                         | II    |
| 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     |

## **Alerts Informed By Public Data Sources**

#### **Current NCCN Information**







NCCN information is current as of 2020-11-02. 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.(L858R) c.2573T>G

### alectinib

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

#### Summary:

NCCN Guidelines® include the following supporting statement(s):

■ "Thus, 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 8.2020]

## brigatinib

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

#### Summary:

NCCN Guidelines® include the following supporting statement(s):

■ "Thus, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

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## EGFR p.(L858R) c.2573T>G (continued)

## ceritinib

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

Summary:

NCCN Guidelines® include the following supporting statement(s):

■ "Thus, 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 8.2020]

### crizotinib

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

Summary:

NCCN Guidelines® include the following supporting statement(s):

■ "Thus, 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 8.2020]

### lorlatinib

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

Summary:

NCCN Guidelines® include the following supporting statement(s):

"Thus, 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 8.2020]

### 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 8.2020]

### 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."

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## EGFR p.(L858R) c.2573T>G (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."

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## **Signatures**

Testing Personnel:

Laboratory Supervisor:

Pathologist:

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