



Sample Information

Patient Name: 林金鳳
Gender: Female
ID No.: U220699192
History No.: 37120357
Age: 67

Ordering Doctor: DOC1878G 沈佳儀
Ordering REQ.: OCPXYPA
Signing in Date: 2023/08/24

Path No.: M112-00232
MP No.: F23066
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S112-32636A
Percentage of tumor cells: 60%

Reporting Doctor: DOC5466K 葉奕成 (Phone: 8#5466)

Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

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Relevant Non-Small Cell Lung Cancer Variants

| Gene | Finding | Gene | Finding |
|-------|--|-------|---------------------------|
| ALK | None detected | NTRK1 | TPM3::NTRK1 fusion |
| BRAF | None detected | NTRK2 | None detected |
| EGFR | EGFR exon 19 deletion, EGFR amplification | NTRK3 | None detected |
| ERBB2 | None detected | RET | None detected |
| KRAS | None detected | ROS1 | None detected |
| MET | None detected | | |

Relevant Biomarkers

| Tier | Genomic Alteration | Relevant Therapies (In this cancer type) | Relevant Therapies (In other cancer type) | Clinical Trials |
|------|--|---|--|-----------------|
| IA | TPM3::NTRK1 fusion tropomyosin 3 - neurotrophic receptor tyrosine kinase 1 | entrectinib ^{1, 2} larotrectinib ¹ | entrectinib larotrectinib | 4 |
| IA | EGFR exon 19 deletion epidermal growth factor receptor Allele Frequency: 81.97% | afatinib ^{1, 2} bevacizumab* + erlotinib ² dacomitinib ^{1, 2} erlotinib ^{1, 2} erlotinib + ramucirumab ^{1, 2} gefitinib ^{1, 2} osimertinib ^{1, 2} atezolizumab + bevacizumab + chemotherapy gefitinib + chemotherapy | None | 14 |

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/generics

Prevalent cancer biomarkers without relevant evidence based on included data sources

EGFR amplification

Variants (Exclude variant in Taiwan BioBank with >1% allele frequency)

DNA Sequence Variants

| Gene | Amino Acid Change | Coding | Variant ID | Locus | Allele Frequency | Transcript | Variant Effect | Coverage |
|------|-------------------|-----------------------------------|------------|---------------|------------------|-------------|---------------------------|----------|
| EGFR | p.(E746_A750del) | c.2235_2249delGGAA TTAAGAGAAGC | COSM6223 | chr7:55242464 | 81.97% | NM_005228.5 | nonframeshift Deletion | 1969 |

Gene Fusions (RNA)

| Genes | Variant ID | Locus | Read Count |
|------------|-------------------------------|---------------------------------|------------|
| TPM3-NTRK1 | TPM3-NTRK1.T7N12 | chr1:154142876 - chr1:156845312 | 18129 |
| TPM3-NTRK1 | TPM3-NTRK1.T7N12.Non-Targeted | chr1:154142876 - chr1:156845358 | 404 |

Copy Number Variations

| Gene | Locus | Copy Number |
|------|---------------|-------------|
| EGFR | chr7:55198956 | 5.67 |

Biomarker Descriptions

EGFR (epidermal growth factor receptor)

Background: The EGFR gene encodes the epidermal growth factor receptor (EGFR) tyrosine kinase, a member of the ERBB/human epidermal growth factor receptor (HER) family. In addition to EGFR/ERBB1/HER1, other members of the ERBB/HER family include ERBB2/HER2, ERBB3/HER3, and ERBB4/HER4¹. EGFR ligand induced dimerization results in kinase activation and leads to stimulation of oncogenic signaling pathways including the PI3K/AKT/MTOR and RAS/RAF/MEK/ERK pathways. Activation of these pathways promote cell proliferation, differentiation, and survival^{2,3}.

Biomarker Descriptions (continued)

Alterations and prevalence: Recurrent somatic mutations in the tyrosine kinase domain (TKD) of EGFR are observed in approximately 10-20% of lung adenocarcinoma, and at higher frequencies in never-smoker, female, and Asian populations^{4,5,6,7}. The most common mutations occur near the ATP-binding pocket of the TKD and include short in-frame deletions in exon 19 (EGFR exon 19 deletion) and the L858R amino acid substitution in exon 21⁸. These mutations constitutively activate EGFR resulting in downstream signaling, and represent 80% of the EGFR mutations observed in lung cancer. A second group of less prevalent activating mutations include E709K, G719X, S768I, L861Q, and short in-frame insertion mutations in exon 20^{9,10,11,12}. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations¹³. In contrast, a different set of recurrent activating EGFR mutations in the extracellular domain include R108K, A289V and G598V and are primarily observed in glioblastoma^{8,14}. Amplification of EGFR is observed in several cancer types including 30% of glioblastoma, 12% of esophageal cancer, 10% of head and neck cancer, 5% of bladder cancer, and 5% of lung squamous cell carcinoma^{5,6,7,14,15}. Deletion of exons 2-7, encoding the extracellular domain of EGFR (EGFRvIII), results in overexpression of a ligand-independent constitutively active protein and is observed in approximately 30% of glioblastoma^{16,17,18}.

Potential relevance: Approved first-generation EGFR tyrosine kinase inhibitors (TKIs) include 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 most EGFR exon 20 insertions, except p.A763_Y764insFQEA, confer resistance to the same therapies^{23,24,25,26}. However, in 2021, the irreversible tyrosine kinase inhibitor, mobocertinib²⁷ was FDA approved for the treatment of NSCLC with EGFR exon 20 insertion mutations. Additionally, in 2022, the FDA granted breakthrough therapy designation to the irreversible EGFR inhibitors, CLN-081 (TPC-064)²⁸ and sunvozertinib²⁹, for locally advanced or metastatic non-small cell lung cancer harboring EGFR exon 20 insertion mutations. In lung cancer containing EGFR exon 19 or 21 activating mutations, treatment with TKIs is eventually associated with the emergence of drug resistance³⁰. 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. Osimertinib³¹ (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 cases³⁰. 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 versa³². T790M and C797S can occur in either cis or trans allelic orientation³². 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 TKIs³². 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^{32,33}. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs³². 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, amivantamab³⁴, targeting EGFR and MET was approved (2021) NSCLC tumors harboring EGFR exon 20 insertion mutations. The Oncoprex immunogene therapy quaratusugene ozeplasmid³⁵ 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-189³⁶ was granted a fast track designation (2020) for the treatment of solid tumors harboring an EGFR exon 20 insertion mutation.

NTRK1 (neurotrophic receptor tyrosine kinase 1)

Background: The NTRK genes encode a family of neurotrophic receptor tyrosine kinases that function as receptors for nerve growth factors. NTRKs are activated by different neurotrophins and are important for the development of the nervous system³⁷. The NTRK1,2,3 proteins are also known as tropomyosin related kinases (TrkA,B,C) because NTRK1 was originally discovered as part of a chimeric fusion gene with tropomyosin-3 isolated from a human colon carcinoma cell line³⁸. NTRKs are the target of recurrent chromosomal rearrangements that generate fusion proteins containing the intact tyrosine kinase domain combined with numerous fusion partner genes^{39,40}. NTRK fusion kinases are constitutively active and lead to increased RAS/RAF/MEK/ERK, PI3K/AKT/MTOR, or PLCγ/PKC pathway signaling and can promote cell growth and proliferation^{39,41}.

Alterations and prevalence: NTRK fusions are infrequently observed in diverse cancer types including glioma, glioblastoma, lung adenocarcinoma, colorectal carcinoma, thyroid cancer, and sarcoma^{6,39,42,43,44}. In certain cancer subtypes, including infantile fibrosarcoma, papillary thyroid carcinoma, and secretory carcinoma of the breast or salivary gland, NTRK fusions are more prevalent^{39,45,46,47}.

Potential relevance: The first-generation selective tropomyosin receptor kinase (TRK) inhibitor, larotrectinib⁴⁸, is approved (2018) for the treatment of patients with any solid tumors harboring NTRK gene fusions and is the first approved small molecule inhibitor with tissue agnostic indication. Entrectinib⁴⁹ is another first-generation TRK inhibitor approved (2019) for NTRK fusion-positive solid tumors

Biomarker Descriptions (continued)

as well as ROS1-positive non-small cell lung cancer (NSCLC). However, acquired resistance to first-generation NTRK inhibition is often mediated by the acquisition of solvent-front and gatekeeper mutations in the kinase domain⁵⁰. Consequently, the second generation TRK inhibitor, repotrectinib⁵¹, was granted fast-track designation by the FDA (2020) for the treatment of patients with advanced solid tumors and an NTRK gene fusion that have progressed following treatment with at least one prior line of chemotherapy and prior TRK inhibitor treatment.

Relevant Therapy Summary

● In this cancer type
 ○ In other cancer type
 ◐ In this cancer type and other cancer types
 ✕ No evidence

TPM3::NTRK1 fusion

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|------------------|-----|------|-----|------|------------------|
| entrectinib | ● | ◐ | ● | ◐ | ● (II) |
| larotrectinib | ● | ◐ | ✕ | ◐ | ● (II) |
| repotrectinib | ✕ | ✕ | ✕ | ✕ | ● (I/II) |

EGFR exon 19 deletion

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|-----|------|-----|------|------------------|
| osimertinib | ● | ● | ● | ● | ● (III) |
| afatinib | ● | ● | ● | ● | ● (II) |
| dacomitinib | ● | ● | ● | ● | ✕ |
| erlotinib | ● | ● | ● | ● | ✕ |
| erlotinib + ramucirumab | ● | ● | ● | ● | ✕ |
| gefitinib | ● | ● | ● | ● | ✕ |
| bevacizumab + erlotinib | ✕ | ● | ● | ● | ✕ |
| bevacizumab (Allergan) + erlotinib | ✕ | ✕ | ● | ✕ | ✕ |
| bevacizumab (Celltrion) + erlotinib | ✕ | ✕ | ● | ✕ | ✕ |
| bevacizumab (Mabxience) + erlotinib | ✕ | ✕ | ● | ✕ | ✕ |
| bevacizumab (Pfizer) + erlotinib | ✕ | ✕ | ● | ✕ | ✕ |
| bevacizumab (Samsung Bioepis) + erlotinib | ✕ | ✕ | ● | ✕ | ✕ |
| bevacizumab (Stada) + erlotinib | ✕ | ✕ | ● | ✕ | ✕ |
| atezolizumab + bevacizumab + carboplatin + paclitaxel | ✕ | ✕ | ✕ | ● | ✕ |
| gefitinib + carboplatin + pemetrexed | ✕ | ✕ | ✕ | ● | ✕ |
| amivantamab, lazertinib, chemotherapy | ✕ | ✕ | ✕ | ✕ | ● (III) |
| osimertinib, chemotherapy | ✕ | ✕ | ✕ | ✕ | ● (III) |

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

Relevant Therapy Summary (continued)

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ☒ No evidence

EGFR exon 19 deletion (continued)

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|--------------------------|-----|------|-----|------|------------------|
| patritumab deruxtecan | × | × | × | × | ● (III) |
| savolitinib, osimertinib | × | × | × | × | ● (III) |
| erlotinib, OBI-833 | × | × | × | × | ● (II) |
| osimertinib, savolitinib | × | × | × | × | ● (II) |
| BLU-451, chemotherapy | × | × | × | × | ● (I/II) |
| sunvozertinib | × | × | × | × | ● (I/II) |
| ABBV 400 | × | × | × | × | ● (I) |
| BAY-2927088 | × | × | × | × | ● (I) |
| lazertinib, amivantamab | × | × | × | × | ● (I) |
| TNO-155, nazartinib | × | × | × | × | ● (I) |

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

Relevant Therapy Details

Current FDA Information

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types

FDA information is current as of 2023-06-14. For the most up-to-date information, search www.fda.gov.

TPM3::NTRK1 fusion

● entrectinib

Cancer type: Solid Tumor

Label as of: 2022-07-18

Variant class: NTRK fusion

Indications and usage:

ROZLYTREK® is a kinase inhibitor indicated for the treatment of:

- Adult patients with ROS1-positive metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test.
- Adult and pediatric patients 12 years of age and older with solid tumors that:
 - have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion as detected by an FDA-approved test without a known acquired resistance mutation,
 - are metastatic or where surgical resection is likely to result in severe morbidity, and
 - have progressed following treatment or have no satisfactory alternative therapy.

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/212725s006lbl.pdf

TPM3::NTRK1 fusion (continued)

● larotrectinib

Cancer type: Solid Tumor

Label as of: 2022-11-23

Variant class: NTRK fusion

Indications and usage:

VITRAKVI® is a kinase inhibitor indicated for the treatment of adult and pediatric patients with solid tumors that:

- have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known acquired resistance mutation,
- are metastatic or where surgical resection is likely to result in severe morbidity, and
- have no satisfactory alternative treatments or that have progressed following treatment.

Select patients for therapy based on an FDA-approved test.

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/210861s008lbl.pdf

EGFR exon 19 deletion

● afatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-04-07

Variant class: EGFR exon 19 deletion

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.

Limitations 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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/201292s017lbl.pdf

● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2020-12-18

Variant class: EGFR exon 19 deletion

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/2020/211288s003lbl.pdf

EGFR exon 19 deletion (continued)

● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2016-10-18

Variant class: EGFR exon 19 deletion

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: 2022-03-22

Variant class: EGFR exon 19 deletion

Indications and usage:

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

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125477s042lbl.pdf

EGFR exon 19 deletion (continued)

● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-05-05

Variant class: EGFR exon 19 deletion

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/2021/206995s004lbl.pdf

● osimertinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-10-21

Variant class: EGFR exon 19 deletion

Indications and usage:

TAGRISSO® is a kinase inhibitor indicated for:

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208065s027lbl.pdf

Current NCCN Information

☒ In this cancer type ☐ In other cancer type ☒ In this cancer type and other cancer types

NCCN information is current as of 2023-06-01. For the most up-to-date information, search www.nccn.org. For NCCN International Adaptations & Translations, search www.nccn.org/global/what-we-do/international-adaptations.

Some variant specific evidence in this report may be associated with a broader set of alterations from the NCCN Guidelines. Specific variants listed in this report were sourced from approved therapies or scientific literature. These therapeutic options are appropriate for certain population segments with cancer. Refer to the NCCN Guidelines® for full recommendation.

TPM3::NTRK1 fusion

● entrectinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered prior to first line therapy (First-line therapy); Preferred intervention
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered during first line therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Progression (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

● larotrectinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered prior to first line therapy (First-line therapy); Preferred intervention
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered during first line therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Progression (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

● entrectinib

Cancer type: Solid Tumor

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Brain Metastases (Line of therapy not specified); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2023]

TPM3::NTRK1 fusion (continued)

● larotrectinib

Cancer type: Solid Tumor

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Brain Metastases (Line of therapy not specified); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2023]

○ entrectinib

Cancer type: Extrahepatic Cholangiocarcinoma,
Gallbladder Carcinoma, Intrahepatic
Cholangiocarcinoma

Variant class: NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Progression (Subsequent therapy); Useful in certain circumstances
- Unresectable, Metastatic (Primary therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Biliary Tract Cancers [Version 2.2023]

○ entrectinib

Cancer type: Colon Cancer

Variant class: NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 2.2023]

○ entrectinib

Cancer type: Cutaneous Melanoma

Variant class: NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic, Unresectable, Progression (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Cutaneous Melanoma [Version 2.2023]

TPM3::NTRK1 fusion (continued)**○ entrectinib**

Cancer type: Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma

Variant class: NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Squamous Cell; Unresectable, Locally Advanced, Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2023]

○ entrectinib

Cancer type: Gastric Cancer

Variant class: NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Unresectable, Locally Advanced, Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 1.2023]

○ entrectinib

Cancer type: Gastrointestinal Stromal Tumor

Variant class: NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Resectable (Neoadjuvant therapy); Useful in certain circumstances
- Unresectable, Progression, Metastatic (First-line therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Gastrointestinal Stromal Tumor [Version 1.2023]

○ entrectinib

Cancer type: Hepatocellular Carcinoma

Variant class: NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Progression (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Hepatocellular Carcinoma [Version 1.2023]

TPM3::NTRK1 fusion (continued)

○ entrectinib

Cancer type: Rectal Cancer

Variant class: NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 3.2023]

○ entrectinib

Cancer type: Soft Tissue Sarcoma

Variant class: NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Advanced, Metastatic (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Soft Tissue Sarcoma [Version 2.2023]

○ entrectinib

Cancer type: Thyroid Gland Anaplastic Carcinoma Variant class: NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Stage IVC; Metastatic (Line of therapy not specified); Preferred intervention
- Stage IVA, Stage IVB; Local, Unresectable, Regional (Neoadjuvant therapy); Consider

Reference: NCCN Guidelines® - NCCN-Thyroid Carcinoma [Version 2.2023]

○ larotrectinib

Cancer type: Extrahepatic Cholangiocarcinoma, Gallbladder Carcinoma, Intrahepatic Cholangiocarcinoma Variant class: NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Progression (Subsequent therapy); Useful in certain circumstances
- Unresectable, Metastatic (Primary therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Biliary Tract Cancers [Version 2.2023]

TPM3::NTRK1 fusion (continued)**○ larotrectinib****Cancer type:** Colon Cancer**Variant class:** NTRK1 fusion**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 2.2023]**○ larotrectinib****Cancer type:** Cutaneous Melanoma**Variant class:** NTRK1 fusion**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Metastatic, Unresectable, Progression (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Cutaneous Melanoma [Version 2.2023]**○ larotrectinib****Cancer type:** Esophageal Cancer,
Gastroesophageal Junction Adenocarcinoma**Variant class:** NTRK1 fusion**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Adenocarcinoma, Squamous Cell; Unresectable, Locally Advanced, Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 2.2023]**○ larotrectinib****Cancer type:** Gastric Cancer**Variant class:** NTRK1 fusion**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Unresectable, Locally Advanced, Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 1.2023]

TPM3::NTRK1 fusion (continued)**○ larotrectinib**

Cancer type: Gastrointestinal Stromal Tumor **Variant class:** NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Resectable (Neoadjuvant therapy); Useful in certain circumstances
- Unresectable, Progression, Metastatic (First-line therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Gastrointestinal Stromal Tumor [Version 1.2023]

○ larotrectinib

Cancer type: Hepatocellular Carcinoma **Variant class:** NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Progression (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Hepatocellular Carcinoma [Version 1.2023]

○ larotrectinib

Cancer type: Rectal Cancer **Variant class:** NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 3.2023]

○ larotrectinib

Cancer type: Soft Tissue Sarcoma **Variant class:** NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Advanced, Metastatic (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Soft Tissue Sarcoma [Version 2.2023]

○ larotrectinib

Cancer type: Thyroid Gland Anaplastic Carcinoma **Variant class:** NTRK1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Stage IVC; Metastatic (Line of therapy not specified); Preferred intervention
- Stage IVA, Stage IVB; Local, Unresectable, Regional (Neoadjuvant therapy); Consider

Reference: NCCN Guidelines® - NCCN-Thyroid Carcinoma [Version 2.2023]

TPM3::NTRK1 fusion (continued)

○ entrectinib

Cancer type: Breast Cancer

Variant class: NTRK fusion

Other criteria: ERBB2 negative, Hormone receptor positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Stage IV; Invasive, Recurrent, Unresectable, Local, Regional, Progression (Third-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 4.2023]

○ entrectinib

Cancer type: Triple Negative Breast Cancer

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Stage IV; Regional, Progression, Invasive, Recurrent, Unresectable, Local (Third-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 4.2023]

○ entrectinib

Cancer type: Circumscribed Astrocytic Gliomas

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Recurrent, Progression (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2023]

○ entrectinib

Cancer type: Glioblastoma IDH-wildtype (Grade 4)

Variant class: NTRK fusion

Other criteria: IDH wild type

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- WHO CNS Tumor Grade IV; Recurrent, Progression (Recurrence therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2023]

TPM3::NTRK1 fusion (continued)

○ entrectinib

Cancer type: Head and Neck Cancer

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Salivary Gland Neoplasm; Recurrent, Unresectable, Metastatic (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 2.2023]

○ entrectinib

Cancer type: Large Cell Neuroendocrine Carcinoma, Mixed Neuroendocrine Non-Neuroendocrine Neoplasm

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Extrapulmonary, Poorly Differentiated; Progression, Unresectable, Metastatic (Line of therapy not specified); Consider

Reference: NCCN Guidelines® - NCCN-Neuroendocrine and Adrenal Tumors [Version 2.2022]

○ entrectinib

Cancer type: Extrapulmonary Small Cell Neuroendocrine Carcinoma

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Poorly Differentiated; Progression, Unresectable, Metastatic (Line of therapy not specified); Consider

Reference: NCCN Guidelines® - NCCN-Neuroendocrine and Adrenal Tumors [Version 2.2022]

○ entrectinib

Cancer type: Ovarian Cancer

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Epithelial, Less Common Ovarian Cancers, Fallopian Tube, Primary Peritoneal; Recurrent (Recurrence therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2023]

TPM3::NTRK1 fusion (continued)**○ entrectinib****Cancer type:** Pancreatic Cancer**Variant class:** NTRK fusion**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Adenocarcinoma; Locally Advanced, Metastatic, Recurrent (Subsequent therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Pancreatic Adenocarcinoma [Version 1.2023]**○ entrectinib****Cancer type:** Thyroid Gland Follicular Carcinoma, Thyroid Gland Hurthle Cell Carcinoma, Thyroid Gland Papillary Carcinoma**Variant class:** NTRK fusion**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Locally Recurrent, Advanced, Metastatic, Radioactive Iodine Ablation refractory, Unresectable, Persistent (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Thyroid Carcinoma [Version 2.2023]**○ entrectinib****Cancer type:** Uterine Sarcoma**Variant class:** NTRK fusion**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Advanced, Recurrent, Metastatic (First-line therapy, Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 2.2023]**○ larotrectinib****Cancer type:** Breast Cancer**Variant class:** NTRK fusion**Other criteria:** ERBB2 negative, Hormone receptor positive**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Stage IV; Invasive, Recurrent, Unresectable, Local, Regional, Progression (Third-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 4.2023]

TPM3::NTRK1 fusion (continued)**○ larotrectinib****Cancer type:** Triple Negative Breast Cancer**Variant class:** NTRK fusion**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Stage IV; Regional, Progression, Invasive, Recurrent, Unresectable, Local (Third-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 4.2023]**○ larotrectinib****Cancer type:** Circumscribed Astrocytic Gliomas**Variant class:** NTRK fusion**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Recurrent, Progression (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2023]**○ larotrectinib****Cancer type:** Glioblastoma IDH-wildtype (Grade 4)**Variant class:** NTRK fusion**Other criteria:** IDH wild type**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- WHO CNS Tumor Grade IV; Recurrent, Progression (Recurrence therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2023]**○ larotrectinib****Cancer type:** Head and Neck Cancer**Variant class:** NTRK fusion**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Salivary Gland Neoplasm; Recurrent, Unresectable, Metastatic (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 2.2023]

TPM3::NTRK1 fusion (continued)

○ larotrectinib

Cancer type: Large Cell Neuroendocrine Carcinoma, Mixed Neuroendocrine Non-Neuroendocrine Neoplasm

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Extrapulmonary, Poorly Differentiated; Progression, Unresectable, Metastatic (Line of therapy not specified); Consider

Reference: NCCN Guidelines® - NCCN-Neuroendocrine and Adrenal Tumors [Version 2.2022]

○ larotrectinib

Cancer type: Extrapulmonary Small Cell Neuroendocrine Carcinoma

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Poorly Differentiated; Progression, Unresectable, Metastatic (Line of therapy not specified); Consider

Reference: NCCN Guidelines® - NCCN-Neuroendocrine and Adrenal Tumors [Version 2.2022]

○ larotrectinib

Cancer type: Ovarian Cancer

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Epithelial, Less Common Ovarian Cancers, Fallopian Tube, Primary Peritoneal; Recurrent (Recurrence therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 1.2023]

○ larotrectinib

Cancer type: Pancreatic Cancer

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma; Metastatic (First-line therapy); Useful in certain circumstances
- Adenocarcinoma; Locally Advanced, Metastatic, Recurrent (Subsequent therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Pancreatic Adenocarcinoma [Version 1.2023]

TPM3::NTRK1 fusion (continued)

○ larotrectinib

Cancer type: Thyroid Gland Follicular Carcinoma, Thyroid Gland Hurthle Cell Carcinoma, Thyroid Gland Papillary Carcinoma

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Locally Recurrent, Advanced, Metastatic, Radioactive Iodine Ablation refractory, Unresectable, Persistent (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Thyroid Carcinoma [Version 2.2023]

○ larotrectinib

Cancer type: Uterine Sarcoma

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Advanced, Recurrent, Metastatic (First-line therapy, Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 2.2023]

○ entrectinib

Cancer type: Cervical Cancer

Variant class: NTRK fusion

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Squamous Cell, Adenocarcinoma, Adenosquamous; Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Cervical Cancer [Version 1.2023]

○ entrectinib

Cancer type: Pancreatic Cancer

Variant class: NTRK fusion

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Adenocarcinoma; Metastatic (First-line therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Pancreatic Adenocarcinoma [Version 1.2023]

TPM3::NTRK1 fusion (continued)

○ entrectinib

Cancer type: Endometrial Carcinoma, Endometrial Clear Cell Adenocarcinoma, Endometrial Serous Adenocarcinoma, Undifferentiated and Dedifferentiated Carcinomas of the Uterine Corpus, Uterine Corpus Carcinosarcoma

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Recurrent (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 2.2023]

○ larotrectinib

Cancer type: Cervical Cancer

Variant class: NTRK fusion

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Squamous Cell, Adenocarcinoma, Adenosquamous; Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Cervical Cancer [Version 1.2023]

○ larotrectinib

Cancer type: Endometrial Carcinoma, Endometrial Clear Cell Adenocarcinoma, Endometrial Serous Adenocarcinoma, Undifferentiated and Dedifferentiated Carcinomas of the Uterine Corpus, Uterine Corpus Carcinosarcoma

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Recurrent (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 2.2023]

EGFR exon 19 deletion

● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered prior to first line therapy (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

EGFR exon 19 deletion (continued)

● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered prior to first line therapy (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered prior to first line therapy (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered prior to first line therapy (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

● osimertinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered prior to first line therapy (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

EGFR exon 19 deletion (continued)

● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered during first line therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

Other criteria: EGFR T790M mutation negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Progression, Symptomatic, Asymptomatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Non-squamous Cell; Advanced, Metastatic, Biomarker discovered prior to first line therapy (First-line therapy); Other recommended intervention
- Non-squamous Cell; Advanced, Metastatic, Biomarker discovered during first line therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

Other criteria: EGFR T790M mutation negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Non-squamous Cell; Advanced, Metastatic, Progression, Symptomatic, Asymptomatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

EGFR exon 19 deletion (continued)

● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered during first line therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

Other criteria: EGFR T790M mutation negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Progression, Symptomatic, Asymptomatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Brain Metastases (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2023]

● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered during first line therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

EGFR exon 19 deletion (continued)

● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

Other criteria: EGFR T790M mutation negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Progression, Symptomatic, Asymptomatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

● erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered prior to first line therapy (First-line therapy); Other recommended intervention
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered during first line therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

● erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

Other criteria: EGFR T790M mutation negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Progression, Symptomatic, Asymptomatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered during first line therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

EGFR exon 19 deletion (continued)

● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

Other criteria: EGFR T790M mutation negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Progression, Symptomatic, Asymptomatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

● osimertinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Brain Metastases, Leptomeningeal Metastases (Line of therapy not specified); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2023]

● osimertinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Stage IB , Stage IIA, Stage IIB, Stage IIIA, Stage IIIB; Resected (Adjuvant therapy)
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered during first line therapy (First-line therapy); Preferred intervention
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Progression, Symptomatic, Asymptomatic (Subsequent therapy)
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Leptomeningeal Metastases, Progression (Subsequent therapy); Consider

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Brain Metastases (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2023]

EGFR exon 19 deletion (continued)

● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Leptomeningeal Metastases (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2023]

● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Brain Metastases (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2023]

Current EMA Information

☒ In this cancer type ☐ In other cancer type ☒ In this cancer type and other cancer types

EMA information is current as of 2023-06-14. For the most up-to-date information, search www.ema.europa.eu/ema.

TPM3::NTRK1 fusion

☒ entrectinib

Cancer type: Solid Tumor

Label as of: 2023-05-15

Variant class: NTRK fusion

Reference:

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

EGFR exon 19 deletion

☒ afatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-04-21

Variant class: EGFR exon 19 deletion

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: 2023-01-05

Variant class: EGFR exon 19 deletion

Reference:

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

☒ bevacizumab (Celltrion) + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-05-10

Variant class: EGFR exon 19 deletion

Reference:

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

☒ bevacizumab (Mabxience) + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-04-18

Variant class: EGFR exon 19 deletion

Reference:

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

☒ bevacizumab (Pfizer) + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-01-05

Variant class: EGFR exon 19 deletion

Reference:

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

EGFR exon 19 deletion (continued)

● bevacizumab (Samsung Bioepis) + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-04-11

Variant class: EGFR exon 19 deletion

Reference:

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

● bevacizumab (Samsung Bioepis) + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-04-11

Variant class: EGFR exon 19 deletion

Reference:

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

● bevacizumab (Stada) + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-01-05

Variant class: EGFR exon 19 deletion

Reference:

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

● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-12-15

Variant class: EGFR exon 19 deletion

Reference:

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

● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-03-17

Variant class: EGFR exon 19 deletion

Reference:

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

● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-07-21

Variant class: EGFR exon 19 deletion

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: 2023-05-16

Variant class: EGFR exon 19 deletion

Reference:

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

EGFR exon 19 deletion (continued)

● erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-12-13

Variant class: EGFR exon 19 deletion

Other criteria: EGFR T790M mutation negative

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: 2022-06-16

Variant class: EGFR exon 19 deletion

Reference:

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

● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-07-05

Variant class: EGFR exon 19 deletion

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: 2022-11-29

Variant class: EGFR exon 19 deletion

Reference:

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

Current ESMO Information

☒ In this cancer type ☐ In other cancer type ☒ In this cancer type and other cancer types

ESMO information is current as of 2023-06-01. For the most up-to-date information, search www.esmo.org.

TPM3::NTRK1 fusion

☒ entrectinib

Cancer type: Non-Small Cell Lung Cancer Variant class: NTRK fusion

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic (Subsequent therapy); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

☒ larotrectinib

Cancer type: Non-Small Cell Lung Cancer Variant class: NTRK fusion

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic (Subsequent therapy); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

☐ entrectinib

Cancer type: Gastrointestinal Stromal Tumor Variant class: NTRK1 fusion

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

Population segment (Line of therapy):

- Advanced, Metastatic (Line of therapy not specified); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-EUROCAN-Gastrointestinal Stromal Tumours [Ann Oncol (2021), doi: <https://doi.org/10.1016/j.annonc.2021.09.005>.]

☐ larotrectinib

Cancer type: Gastrointestinal Stromal Tumor Variant class: NTRK1 fusion

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

Population segment (Line of therapy):

- Advanced, Metastatic (Line of therapy not specified); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-EUROCAN-Gastrointestinal Stromal Tumours [Ann Oncol (2021), doi: <https://doi.org/10.1016/j.annonc.2021.09.005>.]

TPM3::NTRK1 fusion (continued)**○ entrectinib****Cancer type:** Biliary Tract Carcinoma**Variant class:** NTRK fusion**ESMO Level of Evidence/Grade of Recommendation:** III / A**Population segment (Line of therapy):**

- Progression (Second-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Biliary Cancer [Ann Oncol (2023), doi: <https://doi.org/10.1016/j.annonc.2022.10.506>]**○ entrectinib****Cancer type:** Soft Tissue Sarcoma**Variant class:** NTRK fusion**ESMO Level of Evidence/Grade of Recommendation:** III / A**Population segment (Line of therapy):**

- Locally Advanced, Metastatic (Line of therapy not specified); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-EUROCAN-Soft Tissue and Visceral Sarcomas [Ann Oncol (2021), <https://doi.org/10.1016/j.annonc.2021.07.006> (Published)]**○ entrectinib****Cancer type:** Colorectal Cancer**Variant class:** NTRK fusion**ESMO Level of Evidence/Grade of Recommendation:** III / A**Population segment (Line of therapy):**

- (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Colorectal Cancer [Ann Oncol (2023); <https://doi.org/10.1016/j.annonc.2022.10.003> (published)]**○ entrectinib****Cancer type:** Head and Neck Cancer**Variant class:** NTRK fusion**ESMO Level of Evidence/Grade of Recommendation:** III / A**Population segment (Line of therapy):**

- Secretory carcinoma; Locally Recurrent, Metastatic (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Salivary Gland Cancer [Annals of Oncology (2022); <https://doi.org/10.1016/j.esmoop.2022.100602> (Published)]

TPM3::NTRK1 fusion (continued)**○ larotrectinib****Cancer type:** Biliary Tract Carcinoma**Variant class:** NTRK fusion**ESMO Level of Evidence/Grade of Recommendation:** III / A**Population segment (Line of therapy):**

- Progression (Second-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Biliary Cancer [Ann Oncol (2023), doi: <https://doi.org/10.1016/j.annonc.2022.10.506>]**○ larotrectinib****Cancer type:** Soft Tissue Sarcoma**Variant class:** NTRK fusion**ESMO Level of Evidence/Grade of Recommendation:** III / A**Population segment (Line of therapy):**

- Locally Advanced, Metastatic (Line of therapy not specified); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-EUROCAN-Soft Tissue and Visceral Sarcomas [Ann Oncol (2021), <https://doi.org/10.1016/j.annonc.2021.07.006> (Published)]**○ larotrectinib****Cancer type:** Colorectal Cancer**Variant class:** NTRK fusion**ESMO Level of Evidence/Grade of Recommendation:** III / A**Population segment (Line of therapy):**

- (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Colorectal Cancer [Ann Oncol (2023); <https://doi.org/10.1016/j.annonc.2022.10.003> (published)]**○ larotrectinib****Cancer type:** Head and Neck Cancer**Variant class:** NTRK fusion**ESMO Level of Evidence/Grade of Recommendation:** III / A**Population segment (Line of therapy):**

- Secretory carcinoma; Locally Recurrent, Metastatic (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Salivary Gland Cancer [Annals of Oncology (2022); <https://doi.org/10.1016/j.esmoop.2022.100602> (Published)]

TPM3::NTRK1 fusion (continued)

○ entrectinib

Cancer type: Differentiated Thyroid Gland Carcinoma, Poorly Differentiated Thyroid Gland Carcinoma

Variant class: NTRK fusion

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

Population segment (Line of therapy):

- Metastatic, Unresectable, Progression (Line of therapy not specified); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Thyroid Cancer [Ann Oncol. 2022; <https://doi.org/10.1016/j.annonc.2022.04.009>]

○ larotrectinib

Cancer type: Differentiated Thyroid Gland Carcinoma, Poorly Differentiated Thyroid Gland Carcinoma

Variant class: NTRK fusion

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

Population segment (Line of therapy):

- Metastatic, Progression (Line of therapy not specified); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Thyroid Cancer [Ann Oncol. 2022; <https://doi.org/10.1016/j.annonc.2022.04.009>]

EGFR exon 19 deletion

● osimertinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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

Population segment (Line of therapy):

- Stage IB, Stage IIA, Stage IIB, Stage IIIA; Resected (Adjuvant therapy); ESMO-MCBS v1.1 score: A

Reference: ESMO Clinical Practice Guidelines - ESMO-Early-Stage and Locally Advanced (non-metastatic) Non-Small-Cell Lung Cancer [Ann Oncol (2017) 28 (suppl 4): iv1–iv21. (eUpdate: 01 September 2021, 04 May 2020)]

● osimertinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic (First-line therapy); ESMO-MCBS v1.1 score: 4

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

EGFR exon 19 deletion (continued)

● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic (First-line therapy); ESMO-MCBS v1.1 score: 5

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic (First-line therapy); ESMO-MCBS v1.1 score: 2

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic (First-line therapy); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic (First-line therapy); ESMO-MCBS v1.1 score: 4

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

EGFR exon 19 deletion (continued)

● erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic (First-line therapy); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic (First-line therapy); ESMO-MCBS v1.1 score: 4

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

● gefitinib + carboplatin + pemetrexed

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

● atezolizumab + bevacizumab + carboplatin + paclitaxel

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic, Progression (Subsequent therapy); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

Clinical Trials in Taiwan region:

Clinical Trials Summary

TPM3::NTRK1 fusion

| NCT ID | Title | Phase |
|-------------|---|-------|
| NCT02576431 | A Phase II Basket Study of the Oral TRK Inhibitor Larotrectinib in Subjects With NTRK Fusion-positive Tumors. | II |
| NCT04589845 | Tumor-Agnostic Precision Immunooncology and Somatic Targeting Rational for You (TAPISTRY) Phase II Platform Trial | II |
| NCT03093116 | A Phase I/II, Open-Label, Multi-Center, First-in-Human Study of the Safety, Tolerability, Pharmacokinetics, and Anti-Tumor Activity of TPX-0005 in Patients With Advanced Solid Tumors Harboring ALK, ROS1, or NTRK1-3 Rearrangements (TRIDENT-1) | I/II |
| NCT04094610 | A Phase I/II, Open-Label, Safety, Tolerability, Pharmacokinetics, and Anti-Tumor Activity Study of Repotrectinib in Pediatric and Young Adult Subjects With Advanced or Metastatic Malignancies Harboring ALK, ROS1, NTRK1-3 Alterations | I/II |

EGFR exon 19 deletion

| NCT ID | Title | Phase |
|-------------|--|-------|
| NCT04988295 | A Phase III, Open-Label, Randomized Study of Amivantamab and Lazertinib in Combination With Platinum-Based Chemotherapy Compared With Platinum-Based Chemotherapy in Patients With EGFR-Mutated Locally Advanced or Metastatic Non-Small Cell Lung Cancer After Osimertinib Failure | III |
| NCT05120349 | A Phase III, Double-blind, Randomised, Placebo-Controlled, International Study to Assess the Efficacy and Safety of Adjuvant Osimertinib Versus Placebo in Participants With EGFR Mutation-positive Stage IA2-IA3 Non-small Cell Lung Cancer, Following Complete Tumour Resection | III |
| NCT04351555 | A Phase III, Randomised, Controlled, Multi-center, 3-Arm Study of Neoadjuvant Osimertinib as Monotherapy or in Combination With Chemotherapy Versus Standard of Care Chemotherapy Alone for the Treatment of Patients With Epidermal Growth Factor Receptor Mutation Positive, Resectable Non-small Cell Lung Cancer | III |
| NCT05338970 | HERTHENA–Lung02: Phase III, Randomized, Open-label Study of Patritumab Deruxtecan Versus Platinum-Based Chemotherapy in Metastatic or Locally Advanced Non-Small Cell Lung Cancer (NSCLC) With Epidermal Growth Factor Receptor (EGFRm) Mutation After Failure treatment with epidermal growth factor (EGFR) tyrosine kinase inhibitors (TKIs) | III |
| NCT05261399 | A Phase III, Randomised, Open-Label Study of Savolitinib in Combination With Osimertinib Versus Platinum-Based Doublet Chemotherapy in Participants With EGFR Mutated, MET-Overexpressed and/or Amplified, Locally Advanced or Metastatic Non-Small Cell Lung Cancer Who Have Progressed on Treatment With Osimertinib (SAFFRON). | III |
| NCT05215548 | A Phase II Study of Primary Tumor Resection for Stage IV Non-small-cell Lung Cancer Without Progression After First-line Epidermal Growth Factor Receptor-tyrosine Kinase Inhibitor | II |
| NCT05442060 | A Randomized, Open-Label, Phase 2 Study to Evaluate OBI-833/OBI-821 in Combination With First-Line Erlotinib in Patients With EGFR-Mutated, Globo H-Positive, Locally Advanced or Metastatic Non-Small Cell Lung Cancer | II |
| NCT03778229 | A Phase II Study Assessing the Efficacy of Osimertinib in Combination With Savolitinib in Patients With EGFRm+ and MET+, Locally Advanced or Metastatic Non Small Cell Lung Cancer Who Have Progressed Following Treatment With Osimertinib. | II |
| NCT04077463 | An Open-label Phase I/Ib 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 |

Clinical Trials Summary (continued)

EGFR exon 19 deletion (continued)

| NCT ID | Title | Phase |
|-----------------------------|---|-------|
| NCT05099172 | An Open Label, First-in-human Study of BAY 2927088 in Participants With Advanced Non-small Cell Lung Cancer (NSCLC) Harboring an EGFR and/or HER2 Mutation | I |
| NCT03114319 | An Open-label, Multi-center, Phase I, Dose Finding Study of Oral TNO155 in Adult Patients With Advanced Solid Tumors. | I |
| NCT05241873 | Phase I/II Study of BLU-451 in Advanced Cancers With EGFR Exon 20 Insertion Mutations | I/II |
| NCT03974022 | A Phase I/II, Open-Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics and Anti-tumor Efficacy of DZD9008 in Patients With Advanced Non-Small Cell Lung Cancer (NSCLC) with EGFR or HER2 Mutation | I/II |
| NCT05029882 | A Phase I First in Human Study Evaluating Safety, Pharmacokinetics and Efficacy of ABBV-400 in Adult Subjects With Advanced Solid Tumors | I |

Alerts Informed By Public Data Sources

Current FDA Information

 Contraindicated
  Not recommended
  Resistance
  Breakthrough
  Fast Track

FDA information is current as of 2023-06-14. For the most up-to-date information, search www.fda.gov.

TPM3::NTRK1 fusion

repotrectinib

Cancer type: Solid Tumor

Variant class: NTRK fusion

Supporting Statement:

The FDA has granted Fast Track Designation to the ALK/ROS1/TRK inhibitor, repotrectinib, for:

- ROS1-positive advanced non-small cell lung cancer (NSCLC) previously treated with one prior platinum chemotherapy and one prior ROS1 TKI.
- ROS1-positive advanced non-small cell lung cancer (NSCLC) without prior ROS1 TKI treatment.
- NTRK fusion positive advanced solid tumors that have progressed following treatment with at least one prior line of chemotherapy and one or two prior TRK TKIs.

Reference:

<https://ir.tptherapeutics.com/news-releases/news-release-details/turning-point-therapeutics-granted-fast-track-designation>

EGFR exon 19 deletion

patritumab deruxtecan

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation or EGFR exon 19 deletion

Supporting Statement:

The FDA has granted Breakthrough Therapy Designation to a potential first-in-class HER3 directed antibody-drug conjugate, patritumab deruxtecan, for metastatic or locally advanced, EGFR-mutant non-small cell lung cancer.

Reference:

<https://www.cancernetwork.com/view/fda-grants-breakthrough-therapy-status-to-patritumab-deruxtecan-for-egfr-metastatic-nslc>

CPO-301

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR mutation

Supporting Statement:

The FDA has granted Fast Track Designation to a first-in-class antibody drug conjugate, CPO301, for EGFR mutations in patients with metastatic non-small cell lung cancer (NSCLC) who are relapsed/refractory to or ineligible for EGFR targeting therapy such as 3rd-generation EGFR inhibitors including Osimertinib.

Reference:

<http://iis.aastocks.com/20230612/10770455-0.PDF>

osimertinib + quaratusugene ozeplasmid

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR mutation

Supporting Statement:

The FDA has granted Fast Track Designation to the immunogene therapy, quaratusugene ozeplasmid, in combination with EGFR inhibitor osimertinib for the treatment of non-small cell lung cancer (NSCLC) with EFGR mutations that progressed after treatment with osimertinib alone.

Reference:

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

Current NCCN Information

 Contraindicated  Not recommended  Resistance  Breakthrough  Fast Track

NCCN information is current as of 2023-06-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/what-we-do/international-adaptations.

Some variant specific evidence in this report may be associated with a broader set of alterations from the NCCN Guidelines. Specific variants listed in this report were sourced from approved therapies or scientific literature. These therapeutic options are appropriate for certain population segments with cancer. Refer to the NCCN Guidelines® for full recommendation.

TPM3::NTRK1 fusion

larotrectinib

Cancer type: Angiosarcoma, Pleomorphic
Rhabdomyosarcoma

Variant class: NTRK1 fusion

Summary:

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

- "Not recommended for angiosarcoma or pleomorphic rhabdomyosarcoma."

Reference: NCCN Guidelines® - NCCN-Soft Tissue Sarcoma [Version 2.2023]

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