



Sample Information

Patient Name: 龔雅慈
Gender: Female
ID No.: A224763052
History No.: 27437305
Age: 42

Ordering Doctor: DOC5310D 曾彥寒
Ordering REQ.: D792369
Signing in Date: 2023/11/23

Path No.: M112-00299
MP No.: F23086
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S112-35789F
Percentage of tumor cells: 40%

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	EML4::ALK fusion	NTRK1	None detected
BRAF	None detected	NTRK2	None detected
EGFR	None detected	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	EML4::ALK fusion EMAP like 4 - ALK receptor tyrosine kinase	alectinib ^{1,2} brigatinib ^{1,2} ceritinib ^{1,2} crizotinib ^{1,2} lorlatinib ^{1,2} atezolizumab + bevacizumab + chemotherapy	crizotinib ¹ alectinib brigatinib ceritinib lorlatinib	4

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.

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
JAK1	p.(P733=)	c.2199A>G	.	chr1:65310489	50.90%	NM_002227.4	synonymous	1996
PDGFRA	p.(V824=)	c.2472C>T	.	chr4:55152040	49.47%	NM_006206.6	synonymous	1999
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.55%	NM_213647.3	missense	2000
RET	p.(L769=)	c.2307G>T	.	chr10:43613843	100.00%	NM_020975.6	synonymous	1998

Gene Fusions (RNA)

Genes	Variant ID	Locus	Read Count
EML4-ALK	EML4-ALK.E6aA20.AB374361	chr2:42491871 - chr2:29446394	1735
EML4-ALK	EML4-ALK.E6bA20.AB374362	chr2:42492091 - chr2:29446394	2673

Biomarker Descriptions

ALK (ALK receptor tyrosine kinase)

Background: The ALK gene encodes the ALK receptor tyrosine kinase (RTK) with sequence similarity to the insulin receptor subfamily of kinases¹. ALK is the target of recurrent alterations in cancer, the most common being chromosomal rearrangements that generate fusion genes containing the intact ALK tyrosine kinase domain combined with multiple partner genes². ALK fusion kinases are constitutively activated and drive oncogenic transformation via activation of downstream STAT3, PI3K/AKT/MTOR, and RAS/RAF/MEK/ERK pathways^{2,3,4,5}.

Alterations and prevalence: ALK was discovered by positional cloning of translocations involving nucleophosmin (NPM) on 5q35 with a previously unidentified RTK on 2p23 (ALK), which occur in over 50% of anaplastic large cell lymphoma cases (ALCL)^{1,6}. In contrast, about 5% of non-small cell lung cancer (NSCLC) cases generate recurrent ALK fusions with EML4, KIF5B, and HIP1^{7,8,9}.

Potential relevance: The first generation small molecule tyrosine kinase inhibitor (TKI), crizotinib¹⁰, was FDA approved (2011) for the treatment of ALK positive advanced NSCLC as well as ALK positive ALCL or inflammatory myofibroblastic tumor (IMT). Kinase domain mutations including L1196M, G1269A, F1174L, G1202R, as well as other variants have been shown to confer acquired resistance to crizotinib in ALK positive NSCLC^{11,12,13,14}. Other mechanisms of acquired resistance involve amplification of the ALK fusion gene and activation of alternate or bypass signaling pathways involving EGFR, KIT, MET, and IGF1R¹⁵. In order to overcome acquired resistance, second and third-generation ALK inhibitors including ceritinib¹⁶ (2014), alectinib¹⁷ (2015), brigatinib¹⁸ (2017), and lorlatinib¹⁹ (2018) were developed and approved by the FDA. Two phase III trials evaluating crizotinib and alectinib as first line therapy in NSCLC, including patients with asymptomatic central nervous system (CNS) disease, were conducted and both studies showed consistent

Biomarker Descriptions (continued)

higher objective response rates (ORR) with alectinib relative to crizotinib^{20,21}. For this reason, alectinib is a preferred first-line treatment of ALK positive NSCLC²².

Relevant Therapy Summary

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

EML4::ALK fusion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
crizotinib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	✕
lorlatinib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/> (IV)
alectinib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	✕
brigatinib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	✕
ceritinib	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input checked="" type="radio"/>	✕
atezolizumab + bevacizumab + carboplatin + paclitaxel	✕	✕	✕	<input checked="" type="radio"/>	✕
alectinib, durvalumab	✕	✕	✕	✕	<input checked="" type="radio"/> (III)
repotrectinib	✕	✕	✕	✕	<input checked="" type="radio"/> (I/II)

* 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 2023-09-13. For the most up-to-date information, search www.fda.gov.

EML4::ALK fusion

☒ crizotinib

Cancer type: Inflammatory Myofibroblastic Tumor, Non-Small Cell Lung Cancer

Label as of: 2023-09-07

Variant class: ALK fusion

Indications and usage:

XALKORI® is a kinase inhibitor indicated for the treatment of

- adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK) or ROS1-positive as detected by an FDA-approved test.
- pediatric patients 1 year of age and older and young adults with relapsed or refractory, systemic anaplastic large cell lymphoma (ALCL) that is ALK-positive.
 - Limitations of Use: The safety and efficacy of XALKORI® have not been established in older adults with relapsed or refractory, systemic ALK-positive ALCL.
- adult and pediatric patients 1 year of age and older with unresectable, recurrent, or refractory inflammatory myofibroblastic tumor (IMT) that is ALK-positive.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/202570s036lbl.pdf

☐ alectinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-09-03

Variant class: ALK fusion or ALK overexpression

Indications and usage:

ALECENSA® is a kinase inhibitor indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/208434s012lbl.pdf

☐ brigatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-02-28

Variant class: ALK fusion

Indications and usage:

ALUNBRIG® is a kinase inhibitor indicated for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208772s013lbl.pdf

EML4::ALK fusion (continued)

● ceritinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-10-07

Variant class: ALK fusion or ALK overexpression

Indications and usage:

ZYKADIA® is a kinase inhibitor indicated for the treatment of adults with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/211225s004lbl.pdf

● lorlatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-03-03

Variant class: ALK fusion or ALK overexpression

Indications and usage:

LORBRENA® is a kinase inhibitor indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/210868s004lbl.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 2023-09-01. 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.

EML4::ALK fusion

☒ alectinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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]

☒ brigatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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]

☒ ceritinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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]

☒ crizotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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); Useful in certain circumstances

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

EML4::ALK fusion (continued)

● lorlatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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]

● alectinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK 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]

● alectinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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); Preferred intervention
- 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]

● brigatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK 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]

EML4::ALK fusion (continued)

● brigatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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); Preferred intervention
- 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]

● ceritinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK 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]

● ceritinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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)
- 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]

● crizotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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)
- 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]

EML4::ALK fusion (continued)

● lorlatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK 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]

● lorlatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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); Preferred intervention
- 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]

● crizotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Brain Metastases (Line of therapy not specified)

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

● alectinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Brain Metastases (Line of therapy not specified)

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

EML4::ALK fusion (continued)

● lorlatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK overexpression

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Brain Metastases (Line of therapy not specified)

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

○ alectinib

Cancer type: Inflammatory Myofibroblastic Tumor Variant class: ALK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Line of therapy not specified); Preferred intervention

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

○ alectinib

Cancer type: Inflammatory Myofibroblastic Tumor Variant class: ALK 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]

○ brigatinib

Cancer type: Inflammatory Myofibroblastic Tumor Variant class: ALK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Line of therapy not specified); Preferred intervention

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

○ brigatinib

Cancer type: Inflammatory Myofibroblastic Tumor Variant class: ALK 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]

EML4::ALK fusion (continued)

○ ceritinib

Cancer type: Inflammatory Myofibroblastic Tumor **Variant class:** ALK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Line of therapy not specified); Preferred intervention

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

○ ceritinib

Cancer type: Inflammatory Myofibroblastic Tumor **Variant class:** ALK 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]

○ crizotinib

Cancer type: Inflammatory Myofibroblastic Tumor **Variant class:** ALK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Line of therapy not specified); Preferred intervention

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

○ crizotinib

Cancer type: Inflammatory Myofibroblastic Tumor **Variant class:** ALK 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]

○ lorlatinib

Cancer type: Inflammatory Myofibroblastic Tumor **Variant class:** ALK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Line of therapy not specified); Preferred intervention

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

EML4::ALK fusion (continued)

○ lorlatinib

Cancer type: Inflammatory Myofibroblastic Tumor Variant class: ALK 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]

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 2023-09-13. For the most up-to-date information, search www.ema.europa.eu/ema.

EML4::ALK fusion

☒ alectinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-03-29

Variant class: ALK fusion or ALK overexpression

Reference:

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

☒ brigatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-05-18

Variant class: ALK fusion

Reference:

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

☒ crizotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-12-02

Variant class: ALK fusion

Reference:

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

☒ ceritinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-02-25

Variant class: ALK positive

Reference:

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

☒ lorlatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-04-18

Variant class: ALK positive

Reference:

https://www.ema.europa.eu/en/documents/product-information/lorviqua-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 2023-09-01. For the most up-to-date information, search www.esmo.org.

EML4::ALK fusion

● alectinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic, Progression (Subsequent therapy); ESMO-MCBS v1.1 score: 4
- 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)]

● brigatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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)]

● ceritinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic, Progression (Subsequent 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)]

● lorlatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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)]

EML4::ALK fusion (continued)

● ceritinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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)]

● crizotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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)]

● brigatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic, Progression (Subsequent 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)]

● lorlatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic, Progression (Subsequent 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)]

EML4::ALK fusion (continued)

● atezolizumab + bevacizumab + carboplatin + paclitaxel

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

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

EML4::ALK fusion

NCT ID	Title	Phase
NCT05170204	A Phase I-III, Multicenter Study Evaluating the Efficacy and Safety of Multiple Therapies in Cohorts of Patients Selected According to Biomarker Status, With Locally Advanced, Unresectable, Stage III Non-Small Cell Lung Cancer	III
NCT05144997	Lorlatinib (PF-06463922) Continuation Protocol: An Open-Label, Single-Arm Continuation Study For Participants With ALK-Positive or ROS1-Positive Non-Small Cell Lung Cancer (NSCLC) Continuing From Pfizer Sponsored Lorlatinib Clinical Studies	IV
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

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