Taipei Veterans General Hospital

Department of Pathology and Laboratory Medicine
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Sample Information

Patient Name: 藍簡沐
Gender: Male
ID No.: H121189808
History No.: 48226842
Age: 48

Ordering Doctor: DOC8158D 張正暘
Ordering REQ.: 0CAFLDU
Signing in Date: 2022/09/28

Path No.: S111-97911
MP No.: F22100
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S111-77479A
Percentage of tumor cells: 70%

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

Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

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Report Highlights

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Relevant Non-Small Cell Lung Cancer Variants

Gene	Finding	Gene	Finding
ALK	***EML4-ALK fusion, ALK p.([L1195_L1196delinsIM]) c.3583_3586delCTGCinsATAA***	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] next-generation ALK inhibitor	**crizotinib** [1] brigatinib ceritinib lorlatinib	5
IIC	*ALK p.([L1195_L1196delinsIM]) c.3583_3586delCTGCinsATAA* ALK receptor tyrosine kinase Allele Frequency: 12.61%	None	None	1

Public data sources included in relevant therapies: FDA1, NCCN, **EMA**2, ESMO
Tier Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.

Prevalent cancer biomarkers without relevant evidence based on included data sources

MYC amplification

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
ALK	p.([L1195_L1196delinsIM])	c.3583_3586delCTGCinsATAA	.	chr2:29443631	12.61%	NM_004304.5	missense, missense	1990
ALK	p.(F1193=)	c.3579C>T	.	chr2:29443638	12.80%	NM_004304.5	synonymous	2000
ALK	p.(G1125=)	c.3375C>A	.	chr2:29445458	59.09%	NM_004304.5	synonymous	1755
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.35%	NM_213647.3	missense	2000
RET	p.(L769=)	c.2307G>T	.	chr10:43613843	100.00%	NM_020975.6	synonymous	1998
RET	p.(S904=)	c.2712C>G	.	chr10:43615633	99.90%	NM_020975.6	synonymous	1995

Gene Fusions (RNA)

Genes	Variant ID	Locus	Read Count
EML4-ALK	EML4-ALK.E6aA20.AB374361	chr2:42491871 - chr2:29446394	7196
EML4-ALK	EML4-ALK.E6bA20.AB374362	chr2:42492091 - chr2:29446394	2496

Copy Number Variations

Gene	Locus	Copy Number
MYC	chr8:128748885	22.57

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 kinases[1]. 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 genes[2]. 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), crizotinib[10], 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 IGF1R[15]. In order to overcome acquired resistance, second and third-generation ALK inhibitors including ceritinib[16] (2014), alectinib[17] (2015), brigatinib[18] (2017), and lorlatinib[19] (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 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 NSCLC[22].

MYC (MYC proto-oncogene, bHLH transcription factor)

Background: The MYC gene encodes the MYC proto-oncogene (c-MYC), a basic helix-loop-helix transcription factor that regulates the expression of numerous genes that control cell cycle progression, apoptosis, metabolic pathways, and cellular transformation[23,24,25,26]. MYC is part of the MYC oncogene family that includes related transcription factors MYCN and MYCL that regulate transcription in 10-15% of promoter regions[27]. MYC functions as a heterodimer in complex with the transcription factor MAX[24,28].

Alterations and prevalence: Recurrent somatic alterations are observed in both solid and hematological cancers. Recurrent somatic mutations in MYC, including codon T58, are infrequent and hypothesized to increase the stability of the MYC protein[29,30]. MYC gene amplification is particularly common in diverse solid tumors. MYC amplification is observed in 30% of serous ovarian cancer, 20% of uterine serous carcinoma, 15% of esophageal and breast cancers, and is common (1-10%) in numerous other cancer types[31,32,33]. MYC is the target of the t(8;14)(q24;32) chromosomal translocation in Burkitt's lymphoma that places MYC coding sequences adjacent to immunoglobulin region regulatory sequences, which results in increased MYC expression[34,35].

Potential relevance: Currently, no therapies are approved for MYC aberrations. Due to the high frequency of somatic MYC alterations in cancer, many approaches are being investigated in clinical trials including strategies to disrupt complex formation with MAX, including inhibition of MYC expression and synthetic lethality associated with MYC overexpression[23,36,37,38].

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	◑	◑	●	●	✖
ceritinib	●	◑	●	●	● (IV)
lorlatinib	●	◑	●	●	● (IV)
brigatinib	●	◑	●	●	✖

* 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

EML4-ALK fusion (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
alectinib	●	●	●	●	✖
next-generation ALK inhibitor	✖	✖	✖	●	✖
brigatinib, alectinib	✖	✖	✖	✖	● (III)
repotrectinib	✖	✖	✖	✖	● (I/II)

ALK p.([L1195_L1196delinsIM]) c.3583_3586delCTGCinsATAA

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
repotrectinib	✖	✖	✖	✖	● (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 2022-08-17. 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:** 2022-07-14 **Variant class:** ALK fusion

Indications and usage:

XALKORI® is a kinase inhibitor indicated for the treatment of

- 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/2022/202570s033lbl.pdf

EML4-ALK fusion (continued)

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

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 2022-08-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

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 (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

● 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 (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

● 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 (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

● 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 (First-line therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

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 (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

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alectinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ALK fusion or 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 2.2021]

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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); Metastatic, Advanced (Subsequent therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

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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)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 2.2021]

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); Metastatic, Advanced (Subsequent therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

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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)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 2.2021]

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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 (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

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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 (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

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lorlatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ALK fusion or 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 2.2021]

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

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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 2.2021]

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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 2.2022]

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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 2.2022]

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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 2.2022]

EML4-ALK fusion (continued)

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 2.2022]

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 2022-08-17. 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:** 2022-08-11 **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:** 2022-06-27 **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:** 2022-04-07 **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 2022-08-01. 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 (First-line therapy); ESMO-MCBS v1.1 score: 4
- Advanced, Progression (Second-line therapy, Subsequent therapy); ESMO-MCBS v1.1 score: 4

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

● 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 (First-line therapy)

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

● 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):
- Advanced, Progression (Second-line therapy, Subsequent therapy); ESMO-MCBS v1.1 score: 4

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

EML4-ALK fusion (continued)

crizotinib

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 (First-line therapy); ESMO-MCBS v1.1 score: 4
- (Second-line therapy, Subsequent therapy)

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

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next-generation ALK inhibitor

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):
- Advanced (Second-line therapy, Subsequent therapy)

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

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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 (First-line therapy); ESMO-MCBS v1.1 score: 4

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

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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 (First-line therapy); ESMO-MCBS v1.1 score: 4

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

EML4-ALK fusion (continued)

next-generation ALK inhibitor

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ALK fusion

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

Population segment (Line of therapy):
- Advanced, Progression (Second-line therapy, Subsequent therapy)

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

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alectinib

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):
- (First-line therapy)

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

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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):
- Advanced (Second-line therapy, Subsequent therapy); ESMO-MCBS v1.1 score: 3

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

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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, Progression (Second-line therapy, Subsequent therapy); ESMO-MCBS v1.1 score: 3

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

EML4-ALK fusion (continued)

brigatinib

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):
- Advanced (First-line therapy)

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

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ceritinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ALK fusion

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

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

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

Clinical Trials in Taiwan region:

Clinical Trials Summary

EML4-ALK fusion

NCT ID	Title	Phase
NCT03596866	A Phase III Randomized Open-label Study of Brigatinib (Alunbrig) Versus Alectinib (Alecensa) in Advanced Anaplastic Lymphoma Kinase-Positive Non Small-Cell Lung Cancer Patients Who Have Progressed on Crizotinib (Xalkori)	III
NCT02584933	An Open-label, Multi-center, Phase IV Roll-over Study in Patients With ALK Positive Malignancies Who Have Completed a Novartis-sponsored Ceritinib (LDK378) Study and Are Judged by the Investigator to Benefit From Continued Treatment With Ceritinib	IV
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

ALK p.([L1195_L1196delinsIM]) c.3583_3586delCTGCinsATAA

NCT ID	Title	Phase
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

Alerts Informed By Public Data Sources

Current NCCN Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

NCCN information is current as of 2022-08-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

EML4-ALK fusion

atezolizumab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ALK fusion

Summary:

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

- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK rearrangements."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

nivolumab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ALK fusion

Summary:

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

- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK rearrangements."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

pembrolizumab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ALK fusion

Summary:

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

- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK rearrangements."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

Signatures

Testing Personnel:

2022.09.30
15:26:25 +08'00'

Laboratory Supervisor:

2022.09.30
15:26:39 +08'00'

Pathologist:

2022.09.30
15:26:53 +08'00'

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