



Sample Information

Patient Name: 郭瑋笛**Gender:** Female**ID No.:** G221522957**History No.:** 44282215**Age:** 35**Ordering Doctor:** DOC3109L 邱昭華**Ordering REQ.:** 0AQJVDL**Signing in Date:** 2020/03/23**Path No.:** S109-99265**MP No.:** F2005**Assay:** Oncomine Focus Assay**Sample Type:** FFPE**Block No.:** C109-07888**Percentage of tumor cells:** 90%**Note:**

Sample Cancer Type: Non-Small Cell Lung Cancer

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Relevant Non-Small Cell Lung Cancer Findings

Gene	Finding	Gene	Finding
ALK	<i>EML4-ALK fusion</i>	NTRK1	Not detected
BRAF	Not detected	NTRK2	Not detected
EGFR	Not detected	NTRK3	Not detected
ERBB2	Not detected	RET	Not detected
KRAS	Not detected	ROS1	Not detected
MET	Not detected		

Clinically Significant Biomarkers

■ Indicated ■ Contraindicated

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
<i>EML4-ALK fusion</i> echinoderm microtubule associated protein like 4 - ALK receptor tyrosine kinase Tier: IA	■ brigatinib ^{1, 2} ■ crizotinib ^{1, 2} ■ lorlatinib ^{1, 2} ■ alectinib ^{1, 2}	■ ceritinib ■ crizotinib	42

Sources included in relevant therapies: FDA1, NCCN, EMA2, ESMO



Clinically Significant Biomarkers (continued)

■ Indicated ■ Contraindicated

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
	<div style="background-color: green; width: 10px; height: 10px; display: inline-block; margin-right: 5px;"></div> ceritinib ^{1, 2} atezolizumab + bevacizumab + chemotherapy		

Sources included in relevant therapies: FDA1, NCCN, EMA2, ESMO

Tier Criteria Met

Genomic Alteration	Tier Classification for Non-Small Cell Lung Cancer
EML4-ALK fusion Tier: IA	IA: Biomarker predicts response or resistance to FDA or EMA approved therapies in this cancer type IA: Biomarker is included in NCCN or ESMO guidelines that predict response or resistance to therapies in this cancer type IIC: Biomarker is included in NCCN or ESMO guidelines that predict response or resistance to therapies in other cancer types IIC: Biomarker is an inclusion criteria for clinical trials

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.(=)	c.2199A>G	.	chr1:65310489	99.44%	NM_002227.3	synonymous	1976
ALK	p.(D1529E)	c.4587C>G	.	chr2:29416366	49.82%	NM_004304.4	missense	1999
ALK	p.(I1461V)	c.4381A>G	.	chr2:29416572	99.85%	NM_004304.4	missense	1998
ALK	p.(=)	c.3375C>A	.	chr2:29445458	51.08%	NM_004304.4	synonymous	1995
FGFR3	p.(=)	c.1953G>A	.	chr4:1807894	99.87%	NM_000142.4	synonymous	1550
PDGFRA	p.(=)	c.1701A>G	.	chr4:55141055	99.90%	NM_006206.5	synonymous	1998
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.25%	NM_213647.2	missense	2000
FGFR4	p.(=)	c.483A>G	.	chr5:176517985	5.77%	NM_213647.2	synonymous	1873
FGFR4	p.(T179A)	c.535A>G	.	chr5:176518037	35.89%	NM_213647.2	missense	1959

Gene Fusions (RNA)		
Genes	Variant ID	Locus
EML4-ALK	EML4-ALK.E13A20.COSF408.1	chr2:42522656 - chr2:29446394



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^{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 clinical relevance: The first generation small molecule tyrosine kinase inhibitor (TKI), crizotinib¹⁰, was FDA approved (2011) for the treatment of ALK positive advanced NSCLC. 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 higher objective response rates (ORR) with alectinib relative to crizotinib^{20,21}. For this reason, alectinib is the 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
 ⛔ Contraindicated
 ⚠ Both for use and contraindicated
 ✕ No evidence

EML4-ALK fusion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
crizotinib	●	◐	●	◐	● (IV)
ceritinib	●	◐	●	●	● (IV)
alectinib	●	●	●	●	● (IV)
brigatinib	●	●	●	●	● (II)
lorlatinib	●	●	●	●	● (II)
atezolizumab + bevacizumab + carboplatin + paclitaxel	✕	✕	✕	●	✕
alectinib, brigatinib	✕	✕	✕	✕	● (III)
alectinib, crizotinib	✕	✕	✕	✕	● (III)
alectinib, brigatinib, ceritinib, chemotherapy, ensartinib, lorlatinib	✕	✕	✕	✕	● (II)

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



Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ● In this cancer type and other cancer types ⛔ Contraindicated ⚠ Both for use and contraindicated ✕ No evidence

EML4-ALK fusion (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
bevacizumab + crizotinib	✕	✕	✕	✕	● (II)
bintrafusp alfa, chemoradiation therapy, durvalumab	✕	✕	✕	✕	● (II)
ensartinib	✕	✕	✕	✕	● (II)
entrectinib	✕	✕	✕	✕	● (II)
ipilimumab + nivolumab, nivolumab + chemotherapy	✕	✕	✕	✕	● (II)
pembrolizumab + chemotherapy	✕	✕	✕	✕	● (II)
alectinib + cobimetinib	✕	✕	✕	✕	● (I/II)
alectinib, bevacizumab	✕	✕	✕	✕	● (I/II)
anlotinib hydrochloride, CBT-502	✕	✕	✕	✕	● (I/II)
ceritinib + trametinib	✕	✕	✕	✕	● (I/II)
repotrectinib	✕	✕	✕	✕	● (I/II)
SAF-189s	✕	✕	✕	✕	● (I/II)
U3-1402	✕	✕	✕	✕	● (I/II)
APG-2449	✕	✕	✕	✕	● (I)
brigatinib, radiation therapy, surgical intervention	✕	✕	✕	✕	● (I)
ceritinib, everolimus	✕	✕	✕	✕	● (I)
CT-707	✕	✕	✕	✕	● (I)
GSK3326595	✕	✕	✕	✕	● (I)
PLB1003	✕	✕	✕	✕	● (I)
RF-A089	✕	✕	✕	✕	● (I)
XZP-3621	✕	✕	✕	✕	● (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 ☒ Contraindicated ☒ Not recommended ☒ Resistance

FDA information is current as of 2019-11-25. For the most up-to-date information, search www.fda.gov.

EML4-ALK fusion

● brigatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2018-12-21

Variant class: ALK fusion

Indications and usage:

ALUNBRIG™ a kinase inhibitor indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/208772s004lbl.pdf

● crizotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2019-06-25

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.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/202570s028lbl.pdf



EML4-ALK fusion (continued)

● lorlatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2018-11-02

Variant class: ALK fusion or ALK overexpression

Indications and usage:

LORBRENA® is a kinase inhibitor indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) whose disease has progressed on

- crizotinib and at least one other ALK inhibitor for metastatic disease; or
- alectinib as the first ALK inhibitor therapy for metastatic disease; or
- ceritinib as the first ALK inhibitor therapy for metastatic disease.

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210868s000lbl.pdf

● alectinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2018-06-05

Variant class: ALK positive

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/2018/208434s004lbl.pdf

● ceritinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2019-03-05

Variant class: ALK positive

Indications and usage:

ZYKADIA® 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)-positive as detected by an FDA-approved test.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/205755s016lbl.pdf



Current NCCN Information

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ☒ Contraindicated
 ☒ Not recommended
 ☒ Resistance

NCCN information is current as of 2019-08-15. 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, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; ALK rearrangement discovered prior to first-line systemic therapy (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2019]

● brigatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; ALK rearrangement discovered prior to first-line systemic therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2019]

● ceritinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; ALK rearrangement discovered prior to first-line systemic therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2019]



EML4-ALK fusion (continued)

● crizotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; ALK rearrangement discovered prior to first-line systemic therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2019]

● alectinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2019]

● alectinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; ALK rearrangement discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy) (Preferred)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression on first-line therapy or intolerant to crizotinib (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2019]



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):

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2019]

● brigatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; ALK rearrangement discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression on first-line therapy or intolerant to crizotinib (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2019]

● ceritinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2019]



EML4-ALK fusion (continued)

● ceritinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; ALK rearrangement discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression on first-line therapy or intolerant to crizotinib (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2019]

● crizotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2019]

● crizotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; ALK rearrangement discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression after first-line therapy (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2019]



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, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression on first-line therapy with alectinib, brigatinib, or ceritinib (Subsequent therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression on subsequent therapy with crizotinib and alectinib, brigatinib, or ceritinib (Not Specified)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2019]

● ceritinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Non-Small Cell Lung Cancer; Brain metastases; Newly diagnosed (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2019]

○ ceritinib

Cancer type: Soft Tissue Sarcoma

Variant class: ALK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Inflammatory Myofibroblastic Tumor (Systemic therapy)

Reference: NCCN Guidelines® - NCCN-Soft Tissue Sarcoma [Version 3.2019]

○ crizotinib

Cancer type: Soft Tissue Sarcoma

Variant class: ALK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Inflammatory Myofibroblastic Tumor (Systemic therapy)

Reference: NCCN Guidelines® - NCCN-Soft Tissue Sarcoma [Version 3.2019]



EML4-ALK fusion (continued)

EGFR tyrosine kinase inhibitor

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

Summary:

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

- "EGFR TKI therapy is not effective in patients with KRAS mutations, BRAF V600E mutations, ALK gene rearrangements, or ROS1 rearrangements."
- "Thus, EGFR TKI therapy is not recommended as subsequent therapy in patients with ALK or ROS1 rearrangements who relapse on alectinib, brigatinib, crizotinib, ceritinib, or lorlatinib."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2019]

pembrolizumab

Cancer type: Non-Small Cell Lung Cancer

Variant class: ALK fusion

Other criteria: CD274 overexpression

Summary:

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

- "Patients with ALK-positive NSCLC and very high PD-L1 expression do not respond to pembrolizumab."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2019]



Current EMA Information

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ☒ Contraindicated
 ☒ Not recommended
 ☒ Resistance

EMA information is current as of 2019-11-25. For the most up-to-date information, search www.ema.europa.eu/ema.

EML4-ALK fusion

● brigatinib

Cancer type: Non-Small Cell Lung Cancer Label as of: 2019-02-18 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: 2019-04-03 Variant class: ALK fusion

Reference:

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

● alectinib

Cancer type: Non-Small Cell Lung Cancer Label as of: 2018-09-14 Variant class: ALK overexpression

Reference:

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

● ceritinib

Cancer type: Non-Small Cell Lung Cancer Label as of: 2019-08-26 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: 2019-06-17 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
 ☒ Contraindicated
 ☒ Not recommended
 ☒ Resistance

ESMO information is current as of 2019-08-15. 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):

- Non-Small Cell Lung Cancer (First-line therapy)
- Advanced Non-Small Cell Lung Cancer; Progression on or intolerant to crizotinib; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 4 (Second-line or greater)
- Non-Small Cell Lung Cancer; Progressing on crizotinib; Central nervous system progression (Second-line or greater)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237. (Corrigendum: 30 January 2019)]

● 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 Non-Small Cell Lung Cancer; Progression on or intolerant to crizotinib; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 4 (Second-line or greater)
- Non-Small Cell Lung Cancer; Progressing on crizotinib; Central nervous system progression (Second-line or greater)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237. (Corrigendum: 30 January 2019)]

● 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 Non-Small Cell Lung Cancer; ESMO-Magnitude of Clinical Benefit Scale Score version 1.1 score: 4 (First-line therapy)
- Non-Small Cell Lung Cancer; If crizotinib not previously used (Second-line or greater)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237. (Corrigendum: 30 January 2019)]



EML4-ALK fusion (continued)

● brigatinib

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 Non-Small Cell Lung Cancer (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237. (Corrigendum: 30 January 2019)]

● 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 Non-Small Cell Lung Cancer; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 4 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237. (Corrigendum: 30 January 2019)]

● 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):

- Non-Small Cell Lung Cancer; Central nervous system involvement (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237. (Corrigendum: 30 January 2019)]

● 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):

- Metastatic Non-Squamous Non-Small Cell Lung Cancer (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237. (Corrigendum: 30 January 2019)]



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):

- Non-Small Cell Lung Cancer; Central nervous system involvement (First-line therapy)
- Stage IV Non-Small Cell Lung Cancer; Progression after second-generation ALK TKI (Second-line or greater)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237. (Corrigendum: 30 January 2019)]

● lorlatinib

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 Non-Small Cell Lung Cancer; Progression after second-generation ALK TKI (Second-line or greater)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237. (Corrigendum: 30 January 2019)]

● 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):

- Non-Small Cell Lung Cancer; Central nervous system involvement (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237. (Corrigendum: 30 January 2019)]

○ crizotinib

Cancer type: Soft Tissue Sarcoma

Variant class: ALK fusion

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

Population segment (Line of therapy):

- Advanced or Metastatic Inflammatory Myofibroblastic Tumor (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-EUROCAN-Soft Tissue and Visceral Sarcomas [Ann Oncol (2018) 29 (Suppl 4): iv51–iv67. (eUpdate: 22 March 2019; 22 March 2019; Corrigendum: 03 OCT 2018)]

Signatures



Testing Personnel:

Laboratory Supervisor:

Pathologist:



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