Taipei Veterans General Hospital

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Sample Information

Patient Name: 崔健偉
Gender: Male
ID No.: F103966752
History No.: 14567089
Age: 67

Ordering Doctor: DOC6285K 王亭雅
Ordering REQ.: 0ALXBJF
Signing in Date: 2019/11/01

Path No.: S108-98773
MP No.: F1903
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S108-48574A
Percentage of tumor cells: 70%
Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

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Report Highlights

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Clinically Significant Biomarkers

Indicated Contraindicated

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
EML4-ALK fusion 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 [1, 2] atezolizumab + bevacizumab + chemotherapy	ceritinib crizotinib	41

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
ALK	p.(I1461V)	c.4381A>G	.	chr2:29416572	99.80%	NM_004304.4	missense	1998
FGFR3	p.(=)	c.1953G>A	.	chr4:1807894	99.90%	NM_000142.4	synonymous	1996
PDGFRA	p.(=)	c.1701A>G	.	chr4:55141055	99.70%	NM_006206.5	synonymous	1999
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.15%	NM_213647.2	missense	1999
FGFR4	p.(=)	c.483A>G	.	chr5:176517985	11.60%	NM_213647.2	synonymous	2000
EGFR	p.(=)	c.2361G>A	.	chr7:55249063	49.27%	NM_005228.4	synonymous	1999
RET	p.(=)	c.2307G>T	.	chr10:43613843	99.95%	NM_020975.4	synonymous	1994

Gene Fusions (RNA)

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

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)

* 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*
ceritinib	●	◑	●	●	● (IV)
alectinib	●	●	●	●	● (IV)
brigatinib	●	●	●	●	● (II)
lorlatinib	●	●	●	●	● (II)
atezolizumab + bevacizumab + carboplatin + paclitaxel	✖	✖	✖	●	✖
alectinib, brigatinib	✖	✖	✖	✖	● (III)
alectinib, crizotinib	✖	✖	✖	✖	● (III)
crizotinib, lorlatinib	✖	✖	✖	✖	● (III)
alectinib, brigatinib, ceritinib, chemotherapy, ensartinib, lorlatinib	✖	✖	✖	✖	● (II)
bevacizumab + crizotinib	✖	✖	✖	✖	● (II)
ensartinib	✖	✖	✖	✖	● (II)
entrectinib	✖	✖	✖	✖	● (II)
ipilimumab + nivolumab, nivolumab + chemotherapy	✖	✖	✖	✖	● (II)
pembrolizumab + chemotherapy	✖	✖	✖	✖	● (II)
alectinib + bevacizumab	✖	✖	✖	✖	● (I/II)
alectinib + cobimetinib	✖	✖	✖	✖	● (I/II)
ceritinib + trametinib	✖	✖	✖	✖	● (I/II)
repotrectinib	✖	✖	✖	✖	● (I/II)
SAF-189s	✖	✖	✖	✖	● (I/II)
U3-1402	✖	✖	✖	✖	● (I/II)
WX-0593	✖	✖	✖	✖	● (I/II)
brigatinib, radiation therapy, surgical intervention	✖	✖	✖	✖	● (I)
ceritinib, ceritinib + everolimus	✖	✖	✖	✖	● (I)
CT-707	✖	✖	✖	✖	● (I)

* 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*
GSK3326595	✖	✖	✖	✖	● (I)
PLB1003	✖	✖	✖	✖	● (I)
RF-A089	✖	✖	✖	✖	● (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 2019-08-23. 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 2019-05-15. 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 5.2019]

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 5.2019]

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 5.2019]

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 5.2019]

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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):
- 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]

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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, 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 with crizotinib or are intolerant to crizotinib (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2019]

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 with crizotinib or are intolerant to crizotinib (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2019]

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 with crizotinib or are intolerant to crizotinib (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2019]

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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):
- 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]

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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, 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 5.2019]

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 5.2019]

● 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 2.2019]

○ 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 2.2019]

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 5.2019]

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 5.2019]

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 2019-08-23. 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:** 2018-07-12 **Variant class:** ALK positive

Reference:

https://www.ema.europa.eu/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 2019-05-15. 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: