Taipei Veterans General Hospital

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Sample Information

Patient Name: 張仁佑
Gender: Male
ID No.: A103594126
History No.: 16179967
Age: 76

Ordering Doctor: DOC3109L 邱昭華
Ordering REQ.: D595DEN
Signing in Date: 2020/07/23

Path No.: S109-99750
MP No.: F20048
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S109-21063A
Percentage of tumor cells: 30%
Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

Report Highlights

1 Relevant Biomarkers
7 Therapies Available
45 Clinical Trials

Relevant Non-Small Cell Lung Cancer Findings

Gene	Finding	Gene	Finding
ALK	***EML4-ALK fusion***	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		

Relevant 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] next-generation ALK inhibitor atezolizumab + bevacizumab + chemotherapy	ceritinib crizotinib	45

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.

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	55.30%	NM_002227.3	synonymous	1991
ALK	p.(D1529E)	c.4587C>G	.	chr2:29416366	100.00%	NM_004304.4	missense	1995
ALK	p.(I1461V)	c.4381A>G	.	chr2:29416572	99.70%	NM_004304.4	missense	1998
ALK	p.(=)	c.3600G>C	.	chr2:29443617	50.51%	NM_004304.4	synonymous	1970
ALK	p.(=)	c.3375C>A	.	chr2:29445458	100.00%	NM_004304.4	synonymous	1995
FGFR3	p.(=)	c.1953G>A	.	chr4:1807894	99.66%	NM_000142.4	synonymous	1782
PDGFRA	p.(=)	c.939T>G	.	chr4:55133726	51.08%	NM_006206.5	synonymous	1997
PDGFRA	p.(=)	c.1701A>G	.	chr4:55141055	99.90%	NM_006206.5	synonymous	1997
PDGFRA	p.(=)	c.2472C>T	.	chr4:55152040	48.90%	NM_006206.5	synonymous	1998
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.55%	NM_213647.2	missense	2000
RET	p.(=)	c.2307G>T	.	chr10:43613843	99.90%	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

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[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. 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 the preferred first-line treatment of ALK positive NSCLC[22].

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	✖	✖	✖	●	✖
next-generation ALK inhibitor	✖	✖	✖	●	✖
alectinib, crizotinib	✖	✖	✖	✖	● (III)
brigatinib, alectinib	✖	✖	✖	✖	● (III)

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

Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

EML4-ALK fusion (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
toripalimab, chemotherapy	✖	✖	✖	✖	● (III)
TQ-B3139, crizotinib	✖	✖	✖	✖	● (III)
bevacizumab + crizotinib	✖	✖	✖	✖	● (II)
bevacizumab, atezolizumab, chemotherapy	✖	✖	✖	✖	● (II)
bintrafusp alfa, chemoradiation therapy, durvalumab	✖	✖	✖	✖	● (II)
crizotinib, lorlatinib, alectinib, brigatinib, ceritinib, ensartinib, chemotherapy	✖	✖	✖	✖	● (II)
ensartinib	✖	✖	✖	✖	● (II)
entrectinib	✖	✖	✖	✖	● (II)
pembrolizumab + chemotherapy	✖	✖	✖	✖	● (II)
TQ-B3139	✖	✖	✖	✖	● (II)
alectinib + cobimetinib	✖	✖	✖	✖	● (I/II)
alectinib, bevacizumab	✖	✖	✖	✖	● (I/II)
CBT-502, anlotinib hydrochloride	✖	✖	✖	✖	● (I/II)
ceritinib + trametinib	✖	✖	✖	✖	● (I/II)
foritinib	✖	✖	✖	✖	● (I/II)
repotrectinib	✖	✖	✖	✖	● (I/II)
U3-1402	✖	✖	✖	✖	● (I/II)
APG-2449	✖	✖	✖	✖	● (I)
brigatinib, radiation therapy, surgical intervention	✖	✖	✖	✖	● (I)
ceritinib, everolimus	✖	✖	✖	✖	● (I)
CT-707	✖	✖	✖	✖	● (I)
GSK3326595	✖	✖	✖	✖	● (I)
nivolumab, ipilimumab, radiation therapy	✖	✖	✖	✖	● (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 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*
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 2020-02-28. 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 2019-11-01. 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, 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 2.2020]

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) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

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) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

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) (Useful in Certain Circumstances)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

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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 3.2019]

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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 or intolerant to crizotinib (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

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 3.2019]

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 2.2020]

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 3.2019]

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 2.2020]

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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 3.2019]

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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 2.2020]

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 2.2020]

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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 3.2019]

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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 4.2019]

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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 4.2019]

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 2.2020]

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 2.2020]

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 2020-02-28. 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:** 2020-01-22 **Variant class:** ALK fusion

Reference:

https://www.ema.europa.eu/en/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:** 2020-02-12 **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:** 2020-01-13 **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 2019-11-01. 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)
- Advanced stage; Progression on or intolerant to crizotinib; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 4 (Second-line or greater)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

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 stage; Progression on or intolerant to crizotinib; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 4 (Second-line or greater)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

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; ESMO-Magnitude of Clinical Benefit Scale Score version 1.1 score: 4 (First-line therapy)
- 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; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

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; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

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; 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; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

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 stage; 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; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

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):
- 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; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

EML4-ALK fusion (continued)

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 stage; Crizotinib resistance; Progression on crizotinib; Magnitude of Clinical Benefit Scale Version v1.1 Score: 3 (Second-line or greater)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

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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):
- Advanced stage; Progression on crizotinib (Second-line or greater)
- Stage IV; Progression after next-generation ALK TKI; Magnitude of Clinical Benefit Scale Version v1.1 Score: 3 (Second-line or greater)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

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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; Magnitude of Clinical Benefit Scale Score version 1.1 score: 3 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

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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 stage; 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; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

EML4-ALK fusion (continued)

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):
- 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; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

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:

Shin-Ying Lin 2020.07.24 08:20:49 +08'00'

Laboratory Supervisor:

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Pathologist:

Yi-Chu Yeh 2020.07.24 08:21:23 +08'00'

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