Taipei Veterans General Hospital

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Sample Information

Patient Name: 張丁水菊
Gender: Female
ID No.: P202039335
History No.: 46436822
Age: 68

Ordering Doctor: DOC3109L 邱昭華
Ordering REQ.: D5C6K1C
Signing in Date: 2020/09/03

Path No.: S109-99967
MP No.: F20067
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S109-27876A
Percentage of tumor cells: 50%
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	Not detected	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	***CD74-ROS1 fusion***
MET	Not detected		

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*CD74-ROS1 fusion* CD74 molecule - ROS proto-oncogene 1, receptor tyrosine kinase	**crizotinib** [1, 2] **entrectinib** [1] ceritinib lorlatinib	None	32

Public data sources included in relevant therapies: FDA[1], 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.

Variants (Exclude variant in Taiwan BioBank with >1% allele frequency)

Gene Fusions (RNA)

Genes	Variant ID	Locus
CD74-ROS1	CD74-ROS1.C6R34.COSF1200	chr5:149784243 - chr6:117645578
CD74-ROS1	CD74-ROS1.C6R35	chr5:149784243 - chr6:117642557

Biomarker Descriptions

ROS1 (ROS proto-oncogene 1, receptor tyrosine kinase)

Background: The ROS1 gene encodes the ROS proto-oncogene receptor tyrosine kinase 1 which exhibits structural similarity to anaplastic lymphoma kinase (ALK)[1,2]. Like ALK, ROS1 is the target of recurrent chromosomal rearrangements that generate fusion proteins containing the intact ROS1 tyrosine kinase domain combined with numerous fusion partner genes[3]. ROS1 fusion kinases are constitutively activated and drive oncogenic transformation[4].

Alterations and prevalence: ROS1 fusions occur in approximately 1-2% of patients with non-small cell lung cancer (NSCLC) and are also observed in cholangiocarcinoma, gastric cancer, ovarian cancer, and glioblastoma[1,5,6,7,8,9].

Potential relevance: The tyrosine kinase inhibitor, entrectinib[10], is approved (2019) for the treatment of ROS1 fusion positive metastatic NSCLC. Crizotinib[11], originally approved for the treatment of ALK positive NSCLC (2011), is also approved (2016) for the treatment of ROS1 positive NSCLC[12]. Acquired resistance to crizotinib in ROS1 positive NSCLC is associated with kinase domain mutations S1986F/Y, G2032R, D2033N, and L2155S[13,14,15]. The ROS1 tyrosine kinase inhibitor, repotrectinib[16], was grated fast-track designation (2020) for ROS1 positive NSCLC. Ceritinib is a second generation ALK inhibitor approved (2017) for ALK positive NSCLC that has also shown efficacy in ROS1 positive NSCLC. In a phase II study, ceritinib demonstrated systemic and intra-cranial activity with an objective response rate (ORR) of 62% in patients with advanced ROS1 positive NSCLC[17]. In addition to crizotinib and ceritinib, entrectinib is recommended for first-line treatment of ROS1-positive NSCLC[18]. Lorlatinib is a CNS-penetrant third-generation ALK and ROS1 inhibitor with preclinical activity against almost all known ALK and ROS1 resistance mutations[19,20]. Lorlatinib is currently FDA approved (2018) for ALK positive metastatic NSCLC. In a phase I study testing lorlatinib in advanced ROS1-positive NSCLC, objective response was observed in 6/12 (50%) of patients[21]. Lorlatinib is recommended for subsequent therapy in ROS1 fusion-positive NSCLC in patients who have progressed after treatment with crizotinib, entrectinib, or ceritinib[18].

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

CD74-ROS1 fusion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
crizotinib	●	●	●	●	● (IV)
entrectinib	●	●	✖	✖	● (II/III)
ceritinib	✖	●	✖	●	● (II)
lorlatinib	✖	●	✖	✖	● (II)
ipilimumab, nivolumab, radiation therapy, surgical intervention	✖	✖	✖	✖	● (III)
bevacizumab + crizotinib	✖	✖	✖	✖	● (II)
bevacizumab, atezolizumab, chemotherapy	✖	✖	✖	✖	● (II)
bintrafusp alfa, chemoradiation therapy, durvalumab	✖	✖	✖	✖	● (II)
brigatinib	✖	✖	✖	✖	● (II)
cabozantinib	✖	✖	✖	✖	● (II)
ensartinib	✖	✖	✖	✖	● (II)
targeted therapy, chemotherapy	✖	✖	✖	✖	● (II)
WX-0593	✖	✖	✖	✖	● (II)
CBT-502, anlotinib hydrochloride	✖	✖	✖	✖	● (I/II)
ceritinib, trametinib	✖	✖	✖	✖	● (I/II)
foritinib	✖	✖	✖	✖	● (I/II)
repotrectinib	✖	✖	✖	✖	● (I/II)
U3-1402	✖	✖	✖	✖	● (I/II)
APG-2449	✖	✖	✖	✖	● (I)
binimetinib, brigatinib	✖	✖	✖	✖	● (I)
ceritinib, everolimus	✖	✖	✖	✖	● (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 2020-05-26. For the most up-to-date information, search www.fda.gov.

CD74-ROS1 fusion

● crizotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2019-06-25 **Variant class:** ROS1 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

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● entrectinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2019-08-15 **Variant class:** ROS1 fusion

Indications and usage:

ROZLYTREK® is a kinase inhibitor indicated for the treatment of:

- Adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are ROS1-positive.
- Adult and pediatric patients 12 years of age and older with solid tumors that:
  - have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion without a known acquired resistance mutation,
  - are metastatic or where surgical resection is likely to result in severe morbidity, and
  - have progressed following treatment or have no satisfactory alternative therapy

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212726s000lbl.pdf

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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 2020-05-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

CD74-ROS1 fusion

ceritinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; ROS1 rearrangement discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; ROS1 rearrangement discovered during first-line systemic therapy; Complete planned systemic therapy, including maintenance therapy, or interrupt (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

crizotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease;ROS1 rearrangement discovered prior to during first-line systemic therapy (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

entrectinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease;ROS1 rearrangement discovered prior to during first-line systemic therapy (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

CD74-ROS1 fusion (continued)

lorlatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Becomes resistant to crizotinib, ceritinib, or entrectinib (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

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crizotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Non-Small Cell Lung Cancer; Brain metastases; Use agents active against primary tumor (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 2.2020]

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afatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Specific targeted therapy for RET rearrangements, BRAF mutations, METex14 skipping mutations, and sensitizing EGFR mutations is not recommended as subsequent therapy in patients with ALK or ROS1 fusions who relapse on alectinib, brigatinib, crizotinib, ceritinib, or lorlatinib"

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

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alectinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

Summary:

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

- "Alectinib, brigatinib, and ceritinib are not recommended in patients with ROS1 fusions whose disease becomes resistant to crizotinib."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

CD74-ROS1 fusion (continued)

brigatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

Summary:

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

- "Alectinib, brigatinib, and ceritinib are not recommended in patients with ROS1 fusions whose disease becomes resistant to crizotinib."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

cabozantinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

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

- "Specific targeted therapy for RET rearrangements, BRAF mutations, METex14 skipping mutations, and sensitizing EGFR mutations is not recommended as subsequent therapy in patients with ALK or ROS1 fusions who relapse on alectinib, brigatinib, crizotinib, ceritinib, or lorlatinib"

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

capmatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

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

- "Specific targeted therapy for RET rearrangements, BRAF mutations, METex14 skipping mutations, and sensitizing EGFR mutations is not recommended as subsequent therapy in patients with ALK or ROS1 fusions who relapse on alectinib, brigatinib, crizotinib, ceritinib, or lorlatinib"

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

ceritinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

Summary:

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

- "Alectinib, brigatinib, and ceritinib are not recommended in patients with ROS1 fusions whose disease becomes resistant to crizotinib."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

CD74-ROS1 fusion (continued)

cetuximab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Specific targeted therapy for RET rearrangements, BRAF mutations, METex14 skipping mutations, and sensitizing EGFR mutations is not recommended as subsequent therapy in patients with ALK or ROS1 fusions who relapse on alectinib, brigatinib, crizotinib, ceritinib, or lorlatinib"

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

dabrafenib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Specific targeted therapy for RET rearrangements, BRAF mutations, METex14 skipping mutations, and sensitizing EGFR mutations is not recommended as subsequent therapy in patients with ALK or ROS1 fusions who relapse on alectinib, brigatinib, crizotinib, ceritinib, or lorlatinib"

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

dacomitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Specific targeted therapy for RET rearrangements, BRAF mutations, METex14 skipping mutations, and sensitizing EGFR mutations is not recommended as subsequent therapy in patients with ALK or ROS1 fusions who relapse on alectinib, brigatinib, crizotinib, ceritinib, or lorlatinib"

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Specific targeted therapy for RET rearrangements, BRAF mutations, METex14 skipping mutations, and sensitizing EGFR mutations is not recommended as subsequent therapy in patients with ALK or ROS1 fusions who relapse on alectinib, brigatinib, crizotinib, ceritinib, or lorlatinib"

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

CD74-ROS1 fusion (continued)

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Specific targeted therapy for RET rearrangements, BRAF mutations, METex14 skipping mutations, and sensitizing EGFR mutations is not recommended as subsequent therapy in patients with ALK or ROS1 fusions who relapse on alectinib, brigatinib, crizotinib, ceritinib, or lorlatinib"

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Specific targeted therapy for RET rearrangements, BRAF mutations, METex14 skipping mutations, and sensitizing EGFR mutations is not recommended as subsequent therapy in patients with ALK or ROS1 fusions who relapse on alectinib, brigatinib, crizotinib, ceritinib, or lorlatinib"

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

selpercatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Specific targeted therapy for RET rearrangements, BRAF mutations, METex14 skipping mutations, and sensitizing EGFR mutations is not recommended as subsequent therapy in patients with ALK or ROS1 fusions who relapse on alectinib, brigatinib, crizotinib, ceritinib, or lorlatinib"

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

trametinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Specific targeted therapy for RET rearrangements, BRAF mutations, METex14 skipping mutations, and sensitizing EGFR mutations is not recommended as subsequent therapy in patients with ALK or ROS1 fusions who relapse on alectinib, brigatinib, crizotinib, ceritinib, or lorlatinib"

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

CD74-ROS1 fusion (continued)

vandetanib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

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

- "Specific targeted therapy for RET rearrangements, BRAF mutations, METex14 skipping mutations, and sensitizing EGFR mutations is not recommended as subsequent therapy in patients with ALK or ROS1 fusions who relapse on alectinib, brigatinib, crizotinib, ceritinib, or lorlatinib"

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

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 2020-05-26. For the most up-to-date information, search www.ema.europa.eu/ema.

CD74-ROS1 fusion

● crizotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-01-22 **Variant class:** ROS1 fusion

Reference:

https://www.ema.europa.eu/en/documents/product-information/xalkori-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 2020-05-01. For the most up-to-date information, search www.esmo.org.

CD74-ROS1 fusion

● crizotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

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

Population segment (Line of therapy):
- Stage IV; ESMO-Magnitude of Clinical Benefit Scale Version v1.1 Score: 3 (First-line therapy)
- Stage IV; Have not received crizotinib in the first-line setting (Second 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:** ROS1 fusion

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

Population segment (Line of therapy):
- Crizotinib-naive (Not specified)

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]

Signatures

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References

1. Bergethon et al. ROS1 rearrangements define a unique molecular class of lung cancers. J Clin Oncol. 2012 Mar 10;30(8):863-70. doi: 10.1200/JCO.2011.35.6345. Epub 2012 Jan 3. PMID: 22215748
2. Davare et al. Structural insight into selectivity and resistance profiles of ROS1 tyrosine kinase inhibitors. Proc Natl Acad Sci U S A. 2015 Sep 29;112(39):E5381-90. doi: 10.1073/pnas.1515281112. Epub 2015 Sep 8. PMID: 26372962
3. Kohno et al. Beyond ALK-RET, ROS1 and other oncogene fusions in lung cancer. Transl Lung Cancer Res. 2015 Apr;4(2):156-64. PMID: 25870798
4. Lin et al. Recent Advances in Targeting ROS1 in Lung Cancer. J Thorac Oncol. 2017 Nov;12(11):1611-1625. PMID: 28818606
5. Shaw et al. Crizotinib in ROS1-rearranged non-small-cell lung cancer. N Engl J Med. 2014 Nov 20;371(21):1963-71. doi: 10.1056/NEJMoa1406766. Epub 2014 Sep 27. PMID: 25264305
6. Gu et al. Survey of tyrosine kinase signaling reveals ROS kinase fusions in human cholangiocarcinoma. PLoS ONE. 2011 Jan 6;6(1):e15640. PMID: 21253578
7. Charest et al. Fusion of FIG to the receptor tyrosine kinase ROS in a glioblastoma with an interstitial del(6)(q21q21). Genes Chromosomes Cancer. 2003 May;37(1):58-71. PMID: 12661006
8. Birch et al. Chromosome 3 anomalies investigated by genome wide SNP analysis of benign, low malignant potential and low grade ovarian serous tumours. PLoS ONE. 2011;6(12):e28250. PMID: 22163003
9. Lee et al. Identification of ROS1 rearrangement in gastric adenocarcinoma. Cancer. 2013 May 1;119(9):1627-35. PMID: 23400546
10. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212726s000lbl.pdf
11. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/202570s028lbl.pdf
12. Kazandjian et al. Benefit-Risk Summary of Crizotinib for the Treatment of Patients With ROS1 Alteration-Positive, Metastatic Non-Small Cell Lung Cancer. Oncologist. 2016 Aug;21(8):974-80. doi: 10.1634/theoncologist.2016-0101. Epub 2016 Jun 21. PMID: 27328934
13. Song et al. Molecular Changes Associated with Acquired Resistance to Crizotinib in ROS1-Rearranged Non-Small Cell Lung Cancer. Clin Cancer Res. 2015 May 15;21(10):2379-87. doi: 10.1158/1078-0432.CCR-14-1350. Epub 2015 Feb 16. PMID: 25688157
14. Drilon et al. A Novel Crizotinib-Resistant Solvent-Front Mutation Responsive to Cabozantinib Therapy in a Patient with ROS1-Rearranged Lung Cancer. Clin Cancer Res. 2016 May 15;22(10):2351-8. doi: 10.1158/1078-0432.CCR-15-2013. Epub 2015 Dec 16. PMID: 26673800
15. Facchinetti et al. Crizotinib-Resistant ROS1 Mutations Reveal a Predictive Kinase Inhibitor Sensitivity Model for ROS1- and ALK-Rearranged Lung Cancers. Clin Cancer Res. 2016 Dec 15;22(24):5983-5991. Epub 2016 Jul 11. PMID: 27401242
16. https://www.nasdaq.com/press-release/turning-point-therapeutics-announces-program-updates-and-milestones-for-2020-2020-01
17. Lim et al. Open-Label, Multicenter, Phase II Study of Ceritinib in Patients With Non-Small-Cell Lung Cancer Harboring ROS1 Rearrangement. J Clin Oncol. 2017 Aug 10;35(23):2613-2618. doi: 10.1200/JCO.2016.71.3701. Epub 2017 May 18. PMID: 28520527
18. NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]
19. Zou et al. PF-06463922, an ALK/ROS1 Inhibitor, Overcomes Resistance to First and Second Generation ALK Inhibitors in Preclinical Models. Cancer Cell. 2015 Jul 13;28(1):70-81. PMID: 26144315
20. Zou et al. PF-06463922 is a potent and selective next-generation ROS1/ALK inhibitor capable of blocking crizotinib-resistant ROS1 mutations. Proc. Natl. Acad. Sci. U.S.A. 2015 Mar 17;112(11):3493-8. PMID: 25733882
21. Shaw et al. Lorlatinib in non-small-cell lung cancer with ALK or ROS1 rearrangement: an international, multicentre, open-label, single-arm first-in-man phase 1 trial. Lancet Oncol. 2017 Dec;18(12):1590-1599. PMID: 29074098