



Sample Information

Patient Name: 姜仁佩  
Gender: Male  
ID No.: A110225967  
History No.: 13528682  
Age: 90  
  
Ordering Doctor: DOC3153J 黃煦晴  
Ordering REQ.: C2GH2B8  
Signing in Date: 2022/11/18

Path No.: M111-00012  
MP No.: F22128  
Assay: Oncomine Focus Assay  
Sample Type: FFPE  
Block No.: S111-45474A+B  
Percentage of tumor cells: 30%

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

Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

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Relevant Non-Small Cell Lung Cancer Variants

| Gene  | Finding       | Gene  | Finding                    |
|-------|---------------|-------|----------------------------|
| ALK   | None detected | NTRK1 | None detected              |
| BRAF  | None detected | NTRK2 | <b>SQSTM1-NTRK2 fusion</b> |
| EGFR  | None detected | NTRK3 | None detected              |
| ERBB2 | None detected | RET   | None detected              |
| KRAS  | None detected | ROS1  | None detected              |
| MET   | None detected |       |                            |

## Relevant Biomarkers

| Tier | Genomic Alteration   | Relevant Therapies<br>(In this cancer type)                             | Relevant Therapies<br>(In other cancer type) | Clinical Trials |
|------|--|---|--|-----------------|
| IA   | <b>SQSTM1-NTRK2 fusion</b><br>sequestosome 1 - neurotrophic receptor tyrosine kinase 2 | <b>entrectinib</b> <sup>1, 2</sup><br><b>larotrectinib</b> <sup>1</sup> | entrectinib<br>larotrectinib                 | 4               |

Public data sources included in relevant therapies: FDA1, NCCN, EMA2, 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)

### DNA Sequence Variants

| Gene   | Amino Acid Change | Coding    | Variant ID | Locus           | Allele Frequency | Transcript     | Variant Effect | Coverage |
|--------|-------------------|-----------|------------|-----------------|------------------|----------------|----------------|----------|
| FGFR3  | p.(H101=)         | c.303C>T  | .          | chr4:1801174    | 5.56%            | NM_000142.4    | synonymous     | 1097     |
| FGFR3  | p.(G382C)         | c.1144G>T | .          | chr4:1806125    | 7.52%            | NM_000142.4    | missense       | 479      |
| APC    | p.(W685*)         | c.2055G>A | .          | chr5:112173346  | 4.61%            | NM_000038.6    | nonsense       | 738      |
| SMO    | p.(V411L)         | c.1231G>C | .          | chr7:128846395  | 4.75%            | NM_005631.5    | missense       | 1998     |
| BRAF   | p.(G474E)         | c.1421G>A | .          | chr7:140481387  | 11.17%           | NM_004333.6    | missense       | 1997     |
| BRAF   | p.(S335F)         | c.1004C>T | .          | chr7:140494244  | 5.72%            | NM_004333.6    | missense       | 1818     |
| FGFR1  | p.(T726=)         | c.2178T>G | .          | chr8:38271771   | 5.17%            | NM_001174067.1 | synonymous     | 677      |
| MYC    | p.(G123R)         | c.367G>A  | .          | chr8:128750830  | 5.30%            | NM_002467.6    | missense       | 2000     |
| FGFR2  | p.(I383L)         | c.1147A>T | .          | chr10:123274771 | 8.01%            | NM_000141.5    | missense       | 1549     |
| FGFR2  | p.(P256L)         | c.767C>T  | .          | chr10:123279665 | 4.56%            | NM_000141.5    | missense       | 1996     |
| ERBB3  | p.(S346=)         | c.1038C>T | .          | chr12:56482581  | 9.55%            | NM_001982.4    | synonymous     | 2000     |
| CDK4   | p.(A205=)         | c.615A>G  | .          | chr12:58144456  | 5.75%            | NM_000075.4    | synonymous     | 1999     |
| MAP2K1 | p.(K64R)          | c.191A>G  | .          | chr15:66727475  | 13.75%           | NM_002755.4    | missense       | 2000     |
| MAP2K1 | p.(Y134F)         | c.401A>T  | .          | chr15:66729193  | 4.80%            | NM_002755.4    | missense       | 2000     |
| MAP2K1 | p.(G210=)         | c.630G>T  | .          | chr15:66774154  | 11.36%           | NM_002755.4    | synonymous     | 1999     |
| ERBB2  | p.(D307A)         | c.920A>C  | .          | chr17:37868199  | 4.50%            | NM_004448.3    | missense       | 1999     |
| BRCA1  | p.(N1774Y)        | c.5320A>T | .          | chr17:41203092  | 5.46%            | NM_007294.4    | missense       | 952      |
| JAK3   | p.(E547*)         | c.1639G>T | .          | chr19:17948803  | 6.10%            | NM_000215.4    | nonsense       | 2000     |

### Gene Fusions (RNA)

| Genes        | Variant ID                      | Locus                          | Read Count |
|--------------|---------------------------------|--------------------------------|------------|
| SQSTM1-NTRK2 | SQSTM1-NTRK2.S5N16.Non-Targeted | chr5:179252226 - chr9:87482158 | 975        |

## Biomarker Descriptions

### NTRK2 (neurotrophic receptor tyrosine kinase 2)

**Background:** The NTRK genes encode a family of neurotrophic receptor tyrosine kinases that function as receptors for nerve growth factors. NTRKs are activated by different neurotrophins and are important for the development of the nervous system<sup>1</sup>. The NTRK1,2,3 proteins are also known as tropomyosin related kinases (TrkA,B,C) because NTRK1 was originally discovered as part of a chimeric fusion gene with tropomyosin-3 isolated from a human colon carcinoma cell line<sup>2</sup>. NTRKs are the target of recurrent chromosomal rearrangements that generate fusion proteins containing the intact tyrosine kinase domain combined with numerous fusion partner genes<sup>3,4</sup>. NTRK fusion kinases are constitutively active and lead to increased RAS/RAF/MEK/ERK, PI3K/AKT/MTOR, or PLCγ/PKC pathway signaling and can promote cell growth and proliferation<sup>3,5</sup>.

**Alterations and prevalence:** NTRK fusions are infrequently observed in diverse cancer types including glioma, glioblastoma, lung adenocarcinoma, colorectal carcinoma, thyroid cancer, and sarcoma<sup>3,6,7,8,9</sup>. In certain cancer subtypes, including infantile fibrosarcoma, papillary thyroid carcinoma, and secretory carcinoma of the breast or salivary gland, NTRK fusions are more prevalent<sup>3,10,11,12</sup>.

**Potential relevance:** The first-generation selective tropomyosin receptor kinase (TRK) inhibitor, larotrectinib<sup>13</sup>, is approved (2018) for the treatment of patients with any solid tumors harboring NTRK gene fusions and is the first approved small molecule inhibitor with tissue agnostic indication. Entrectinib<sup>14</sup> is another first-generation TRK inhibitor approved (2019) for NTRK fusion-positive solid tumors as well as ROS1-positive non-small cell lung cancer (NSCLC). However, acquired resistance to first-generation NTRK inhibition is often mediated by the acquisition of solvent-front and gatekeeper mutations in the kinase domain<sup>15</sup>. Consequently, the second generation TRK inhibitor, repotrectinib<sup>16</sup>, was granted fast-track designation by the FDA (2020) for the treatment of patients with advanced solid tumors and an NTRK gene fusion that have progressed following treatment with at least one prior line of chemotherapy and prior TRK inhibitor treatment.

## Relevant Therapy Summary

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ☒ No evidence

### SQSTM1-NTRK2 fusion

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|------------------|-----|------|-----|------|------------------|
| entrectinib      | ●   | ◐    | ●   | ○    | ● (II)           |
| larotrectinib    | ●   | ◐    | ×   | ○    | ● (II)           |
| repotrectinib    | ×   | ×    | ×   | ×    | ● (I/II)         |

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

## Relevant Therapy Details

### Current FDA Information

☒ In this cancer type    ☐ In other cancer type    ☒ In this cancer type and other cancer types

FDA information is current as of 2022-09-14. For the most up-to-date information, search [www.fda.gov](https://www.fda.gov).

#### SQSTM1-NTRK2 fusion

##### ☒ entrectinib

Cancer type: Solid Tumor

Label as of: 2022-07-18

Variant class: NTRK fusion

##### Indications and usage:

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

- Adult patients with ROS1-positive metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test.
- Adult and pediatric patients 12 years of age and older with solid tumors that:
  - have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion as detected by an FDA-approved test 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/2022/212725s006lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/212725s006lbl.pdf)

##### ☒ larotrectinib

Cancer type: Solid Tumor

Label as of: 2021-03-25

Variant class: NTRK fusion

##### Indications and usage:

VITRAKVI® is a kinase inhibitor indicated for the treatment of adult and pediatric patients with solid tumors that:

- have a neurotrophic receptor tyrosine 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 no satisfactory alternative treatments or that have progressed following treatment.

Select patients for therapy based on an FDA-approved test.

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

##### Reference:

[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2021/210861s006lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/210861s006lbl.pdf)

## Current NCCN Information

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types

NCCN information is current as of 2022-09-01. For the most up-to-date information, search [www.nccn.org](http://www.nccn.org).  
For NCCN International Adaptations & Translations, search [www.nccn.org/global/international\\_adaptations.aspx](http://www.nccn.org/global/international_adaptations.aspx).

### SQSTM1-NTRK2 fusion

#### ● entrectinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: NTRK2 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

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

#### ● larotrectinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: NTRK2 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

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

#### ● entrectinib

Cancer type: Solid Tumor

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Brain Metastases (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2022]

## SQSTM1-NTRK2 fusion (continued)

### ● larotrectinib

Cancer type: Solid Tumor

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Brain Metastases (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2022]

### ○ entrectinib

Cancer type: Colon Cancer

Variant class: NTRK2 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 1.2022]

### ○ entrectinib

Cancer type: Cutaneous Melanoma

Variant class: NTRK2 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic, Unresectable, Progression (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Cutaneous Melanoma [Version 3.2022]

### ○ entrectinib

Cancer type: Esophageal Cancer,  
Gastroesophageal Junction Adenocarcinoma

Variant class: NTRK2 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Squamous Cell; Unresectable, Locally Advanced, Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2022]

## SQSTM1-NTRK2 fusion (continued)

### ○ entrectinib

Cancer type: Gastric Cancer

Variant class: NTRK2 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Unresectable, Locally Advanced, Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2022]

### ○ entrectinib

Cancer type: Hepatocellular Carcinoma

Variant class: NTRK2 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Hepatobiliary Cancers [Version 2.2022]

### ○ entrectinib

Cancer type: Extrahepatic Cholangiocarcinoma, Gallbladder Carcinoma, Intrahepatic Cholangiocarcinoma

Variant class: NTRK2 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Unresectable, Metastatic (First-line therapy); Useful in certain circumstances
- Unresectable, Metastatic, Progression (Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Hepatobiliary Cancers [Version 2.2022]

### ○ entrectinib

Cancer type: Rectal Cancer

Variant class: NTRK2 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 1.2022]

## SQSTM1-NTRK2 fusion (continued)

### ○ entrectinib

Cancer type: Soft Tissue Sarcoma

Variant class: NTRK2 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Unspecified histology; Advanced, Metastatic (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Soft Tissue Sarcoma [Version 2.2022]

### ○ entrectinib

Cancer type: Thyroid Gland Anaplastic Carcinoma Variant class: NTRK2 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Stage IVC; Metastatic (Second-line therapy); Preferred intervention, Consider
- Stage IVA, Stage IVB; Local, Unresectable, Regional (Neoadjuvant therapy); Consider

Reference: NCCN Guidelines® - NCCN-Thyroid Carcinoma [Version 2.2022]

### ○ larotrectinib

Cancer type: Colon Cancer

Variant class: NTRK2 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Colon Cancer [Version 1.2022]

### ○ larotrectinib

Cancer type: Cutaneous Melanoma

Variant class: NTRK2 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic, Unresectable, Progression (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Cutaneous Melanoma [Version 3.2022]



## SQSTM1-NTRK2 fusion (continued)

### ○ larotrectinib

**Cancer type:** Esophageal Cancer,  
Gastroesophageal Junction Adenocarcinoma

**Variant class:** NTRK2 fusion

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Adenocarcinoma, Squamous Cell; Unresectable, Locally Advanced, Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Esophageal and Esophagogastric Junction Cancers [Version 3.2022]

### ○ larotrectinib

**Cancer type:** Gastric Cancer

**Variant class:** NTRK2 fusion

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Unresectable, Locally Advanced, Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Gastric Cancer [Version 2.2022]

### ○ larotrectinib

**Cancer type:** Hepatocellular Carcinoma

**Variant class:** NTRK2 fusion

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Hepatobiliary Cancers [Version 2.2022]

### ○ larotrectinib

**Cancer type:** Extrahepatic Cholangiocarcinoma,  
Gallbladder Carcinoma, Intrahepatic  
Cholangiocarcinoma

**Variant class:** NTRK2 fusion

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Unresectable, Metastatic (First-line therapy); Useful in certain circumstances
- Unresectable, Metastatic, Progression (Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Hepatobiliary Cancers [Version 2.2022]

## SQSTM1-NTRK2 fusion (continued)

### ○ larotrectinib

Cancer type: Rectal Cancer

Variant class: NTRK2 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Rectal Cancer [Version 1.2022]

### ○ larotrectinib

Cancer type: Soft Tissue Sarcoma

Variant class: NTRK2 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Unspecified histology; Advanced, Metastatic (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Soft Tissue Sarcoma [Version 2.2022]

### ○ larotrectinib

Cancer type: Thyroid Gland Anaplastic Carcinoma

Variant class: NTRK2 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Stage IVC; Metastatic (Second-line therapy); Preferred intervention, Consider
- Stage IVA, Stage IVB; Local, Unresectable, Regional (Neoadjuvant therapy); Consider

Reference: NCCN Guidelines® - NCCN-Thyroid Carcinoma [Version 2.2022]

### ○ entrectinib

Cancer type: Breast Cancer

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Stage IV; Invasive, Recurrent, Unresectable, Local, Regional (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 4.2022]

## SQSTM1-NTRK2 fusion (continued)

### ○ entrectinib

**Cancer type:** Glioblastoma IDH-wild type

**Variant class:** NTRK fusion

**Other criteria:** IDH wild type

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Recurrent (Recurrence therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2022]

### ○ entrectinib

**Cancer type:** Ganglioglioma, Pilocytic Astrocytoma, **Variant class:** NTRK fusion

Pleomorphic Xanthoastrocytoma, Subependymal

Giant Cell Astrocytoma

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- WHO CNS Tumor Grade I; Recurrent, Progression (Line of therapy not specified); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2022]

### ○ entrectinib

**Cancer type:** Gastrointestinal Stromal Tumor

**Variant class:** NTRK fusion

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Unresectable, Progression, Metastatic (First-line therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Gastrointestinal Stromal Tumor [Version 1.2022]

### ○ entrectinib

**Cancer type:** Head and Neck Cancer

**Variant class:** NTRK fusion

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Salivary Gland Neoplasm; Recurrent, Unresectable, Distant Metastases (Line of therapy not specified); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 2.2022]

## SQSTM1-NTRK2 fusion (continued)

### ○ entrectinib

Cancer type: Ovarian Cancer

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Epithelial, Less Common Ovarian Cancers, Fallopian Tube, Primary Peritoneal; Recurrent (Recurrence therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 4.2022]

### ○ entrectinib

Cancer type: Pancreatic Cancer

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma; Locally Advanced, Metastatic, Recurrent (Subsequent therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Pancreatic Adenocarcinoma [Version 1.2022]

### ○ entrectinib

Cancer type: Thyroid Gland Follicular Carcinoma, Thyroid Gland Hurthle Cell Carcinoma, Thyroid Gland Papillary Carcinoma

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Locally Recurrent, Advanced, Metastatic (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Thyroid Carcinoma [Version 2.2022]

### ○ larotrectinib

Cancer type: Breast Cancer

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Stage IV; Invasive, Recurrent, Unresectable, Local, Regional (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 4.2022]

## SQSTM1-NTRK2 fusion (continued)

### ○ larotrectinib

**Cancer type:** Glioblastoma IDH-wild type

**Variant class:** NTRK fusion

**Other criteria:** IDH wild type

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Recurrent (Recurrence therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2022]

### ○ larotrectinib

**Cancer type:** Ganglioglioma, Pilocytic Astrocytoma, **Variant class:** NTRK fusion

Pleomorphic Xanthoastrocytoma, Subependymal

Giant Cell Astrocytoma

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- WHO CNS Tumor Grade I; Recurrent, Progression (Line of therapy not specified); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2022]

### ○ larotrectinib

**Cancer type:** Gastrointestinal Stromal Tumor

**Variant class:** NTRK fusion

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Unresectable, Progression, Metastatic (First-line therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Gastrointestinal Stromal Tumor [Version 1.2022]

### ○ larotrectinib

**Cancer type:** Head and Neck Cancer

**Variant class:** NTRK fusion

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Salivary Gland Neoplasm; Recurrent, Unresectable, Distant Metastases (Line of therapy not specified); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 2.2022]

## SQSTM1-NTRK2 fusion (continued)

### ○ larotrectinib

Cancer type: Ovarian Cancer

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Epithelial, Less Common Ovarian Cancers, Fallopian Tube, Primary Peritoneal; Recurrent (Recurrence therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Ovarian Cancer [Version 4.2022]

### ○ larotrectinib

Cancer type: Pancreatic Cancer

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma; Metastatic (First-line therapy); Useful in certain circumstances
- Adenocarcinoma; Locally Advanced, Metastatic, Recurrent (Subsequent therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Pancreatic Adenocarcinoma [Version 1.2022]

### ○ larotrectinib

Cancer type: Thyroid Gland Follicular Carcinoma, Thyroid Gland Hurthle Cell Carcinoma, Thyroid Gland Papillary Carcinoma

Variant class: NTRK fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Locally Recurrent, Advanced, Metastatic (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Thyroid Carcinoma [Version 2.2022]

### ○ entrectinib

Cancer type: Cervical Small Cell Neuroendocrine Carcinoma

Variant class: NTRK fusion

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Cervical Cancer [Version 1.2022]

## SQSTM1-NTRK2 fusion (continued)

### ○ entrectinib

Cancer type: Cervical Cancer

Variant class: NTRK fusion

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Squamous Cell, Adenocarcinoma, Adenosquamous; Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Cervical Cancer [Version 1.2022]

### ○ entrectinib

Cancer type: Pancreatic Cancer

Variant class: NTRK fusion

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Adenocarcinoma; Metastatic (First-line therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Pancreatic Adenocarcinoma [Version 1.2022]

### ○ entrectinib

Cancer type: Endometrial Carcinoma, Endometrial

Clear Cell Adenocarcinoma, Endometrial

Serous Adenocarcinoma, Undifferentiated and

Dedifferentiated Carcinomas of the Uterine Corpus,

Uterine Corpus Carcinosarcoma

Variant class: NTRK fusion

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Advanced, Recurrent (Second-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 1.2022]

### ○ entrectinib

Cancer type: Uterine Sarcoma

Variant class: NTRK fusion

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Recurrent, Metastatic, Progression (Second-line therapy); Consider, Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 1.2022]

## SQSTM1-NTRK2 fusion (continued)

### ○ larotrectinib

**Cancer type:** Cervical Small Cell Neuroendocrine Carcinoma      **Variant class:** NTRK fusion

**NCCN Recommendation category:** 2B

**Population segment (Line of therapy):**

- Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Cervical Cancer [Version 1.2022]

### ○ larotrectinib

**Cancer type:** Cervical Cancer      **Variant class:** NTRK fusion

**NCCN Recommendation category:** 2B

**Population segment (Line of therapy):**

- Squamous Cell, Adenocarcinoma, Adenosquamous; Recurrent, Metastatic (Second-line therapy, Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Cervical Cancer [Version 1.2022]

### ○ larotrectinib

**Cancer type:** Endometrial Carcinoma, Endometrial Clear Cell Adenocarcinoma, Endometrial Serous Adenocarcinoma, Undifferentiated and Dedifferentiated Carcinomas of the Uterine Corpus, Uterine Corpus Carcinosarcoma      **Variant class:** NTRK fusion

**NCCN Recommendation category:** 2B

**Population segment (Line of therapy):**

- Advanced, Recurrent (Second-line therapy); Other recommended intervention

**Reference:** NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 1.2022]

### ○ larotrectinib

**Cancer type:** Uterine Sarcoma      **Variant class:** NTRK fusion

**NCCN Recommendation category:** 2B

**Population segment (Line of therapy):**

- Recurrent, Metastatic, Progression (Second-line therapy); Consider, Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Uterine Neoplasms [Version 1.2022]



## Current EMA Information

☒ In this cancer type    ☐ In other cancer type    ☐ In this cancer type and other cancer types

EMA information is current as of 2022-09-14. For the most up-to-date information, search [www.ema.europa.eu/ema](https://www.ema.europa.eu/ema).

### SQSTM1-NTRK2 fusion

#### ☒ entrectinib

Cancer type: Solid Tumor

Label as of: 2022-06-27

Variant class: NTRK fusion

Reference:

[https://www.ema.europa.eu/en/documents/product-information/rozlytrek-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/rozlytrek-epar-product-information_en.pdf)

## Current ESMO Information

☒ In this cancer type    ☐ In other cancer type    ☒ In this cancer type and other cancer types

ESMO information is current as of 2022-09-01. For the most up-to-date information, search [www.esmo.org](http://www.esmo.org).

### SQSTM1-NTRK2 fusion

#### ☐ entrectinib

Cancer type: Gastrointestinal Stromal Tumor    Variant class: NTRK2 fusion

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

Population segment (Line of therapy):

- Advanced, Metastatic (Line of therapy not specified); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-EUROCAN-Gastrointestinal Stromal Tumours [Annals of Oncology (2021), doi: <https://doi.org/10.1016/j.annonc.2021.09.005>.]

#### ☐ larotrectinib

Cancer type: Gastrointestinal Stromal Tumor    Variant class: NTRK2 fusion

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

Population segment (Line of therapy):

- Advanced, Metastatic (Line of therapy not specified); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-EUROCAN-Gastrointestinal Stromal Tumours [Annals of Oncology (2021), doi: <https://doi.org/10.1016/j.annonc.2021.09.005>.]

#### ☐ entrectinib

Cancer type: Soft Tissue Sarcoma    Variant class: NTRK fusion

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

Population segment (Line of therapy):

- Locally Advanced, Metastatic (Line of therapy not specified); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-EUROCAN-Soft Tissue and Visceral Sarcomas [Ann Oncol (2021), <https://doi.org/10.1016/j.annonc.2021.07.006>]

#### ☐ larotrectinib

Cancer type: Soft Tissue Sarcoma    Variant class: NTRK fusion

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

Population segment (Line of therapy):

- Locally Advanced, Metastatic (Line of therapy not specified); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-EUROCAN-Soft Tissue and Visceral Sarcomas [Ann Oncol (2021), <https://doi.org/10.1016/j.annonc.2021.07.006>]

## SQSTM1-NTRK2 fusion (continued)

### ○ entrectinib

**Cancer type:** Differentiated Thyroid Gland Carcinoma, Poorly Differentiated Thyroid Gland Carcinoma

**Variant class:** NTRK fusion

**ESMO Level of Evidence/Grade of Recommendation:** V / B

**Population segment (Line of therapy):**

- Metastatic, Unresectable, Progression (Line of therapy not specified); ESMO-MCBS v1.1 score: 3

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Thyroid Cancer [Ann Oncol. 2022; <https://doi.org/10.1016/j.annonc.2022.04.009>]

### ○ larotrectinib

**Cancer type:** Differentiated Thyroid Gland Carcinoma, Poorly Differentiated Thyroid Gland Carcinoma

**Variant class:** NTRK fusion

**ESMO Level of Evidence/Grade of Recommendation:** V / B

**Population segment (Line of therapy):**

- Metastatic, Progression (Line of therapy not specified); ESMO-MCBS v1.1 score: 3

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Thyroid Cancer [Ann Oncol. 2022; <https://doi.org/10.1016/j.annonc.2022.04.009>]

## Clinical Trials in Taiwan region:

### Clinical Trials Summary

#### SQSTM1-NTRK2 fusion

| NCT ID      | Title   | Phase |
|-------------|---|-------|
| NCT04589845 | Tumor-Agnostic Precision Immunooncology and Somatic Targeting Rational for You (TAPISTRY) Phase II Platform Trial   | II    |
| NCT02576431 | A Phase II Basket Study of the Oral TRK Inhibitor Larotrectinib in Subjects With NTRK Fusion-positive Tumors.   | II    |
| NCT03093116 | A Phase I/II, Open-Label, Multi-Center, First-in-Human Study of the Safety, Tolerability, Pharmacokinetics, and Anti-Tumor Activity of TPX-0005 in Patients With Advanced Solid Tumors Harboring ALK, ROS1, or NTRK1-3 Rearrangements (TRIDENT-1) | I/II  |
| NCT04094610 | A Phase I/II, Open-Label, Safety, Tolerability, Pharmacokinetics, and Anti-Tumor Activity Study of Repotrectinib in Pediatric and Young Adult Subjects With Advanced or Metastatic Malignancies Harboring ALK, ROS1, NTRK1-3 Alterations          | I/II  |

### Alerts Informed By Public Data Sources

#### Current FDA Information

 Contraindicated
  Not recommended
  Resistance
  Breakthrough
  Fast Track

FDA information is current as of 2022-09-14. For the most up-to-date information, search [www.fda.gov](https://www.fda.gov).

#### SQSTM1-NTRK2 fusion

#### repotrectinib

Cancer type: Solid Tumor

Variant class: NTRK fusion

#### Supporting Statement:

The FDA has granted Fast Track Designation to the ALK/ROS1/TRK inhibitor, repotrectinib, for:

- ROS1-positive advanced non-small cell lung cancer (NSCLC) previously treated with one prior platinum chemotherapy and one prior ROS1 TKI.
- ROS1-positive advanced non-small cell lung cancer (NSCLC) without prior ROS1 TKI treatment.
- NTRK fusion positive advanced solid tumors that have progressed following treatment with at least one prior line of chemotherapy and one or two prior TRK TKIs.

#### Reference:

<https://ir.tptherapeutics.com/news-releases/news-release-details/turning-point-therapeutics-granted-fast-track-designation>

## Current NCCN Information

 Contraindicated    Not recommended    Resistance    Breakthrough    Fast Track

NCCN information is current as of 2022-09-01. For the most up-to-date information, search [www.nccn.org](http://www.nccn.org).  
For NCCN International Adaptations & Translations, search [www.nccn.org/global/international\\_adaptations.aspx](http://www.nccn.org/global/international_adaptations.aspx).

### SQSTM1-NTRK2 fusion

#### **larotrectinib**

**Cancer type:** Angiosarcoma, Pleomorphic  
Rhabdomyosarcoma

**Variant class:** NTRK2 fusion

##### Summary:

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

- "Not recommended for angiosarcoma or pleomorphic rhabdomyosarcoma."

**Reference:** NCCN Guidelines® - NCCN-Soft Tissue Sarcoma [Version 2.2022]

## Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:

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