



Positive Quality Intervention: Larotrectinib Genomic Testing Management

Description:

This PQI is developed to provide guidance to genomic testing with respect to larotrectinib (Vitrakvi).

Background:

Larotrectinib is 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.

This indication is approved under accelerated approval based on overall response rate and duration of response.¹

As a key oncogenic driver, *NTRK* gene fusions are found in many types of solid tumors. Note that *NTRK* gene fusion is separate from general *NTRK* gene mutation. Within adult patients *NTRK* gene fusion frequency displays in estimated amounts such as the select tumors below³:

Lung: 0.2%-3.3%

GI Cancers: 0.7%-3.6%

Thyroid: 2.4%-12%

Sarcoma: 1%

Glioblastoma: 1.2%

Mammary Analogue Secretory Carcinoma: up to 100%

In October 2020, the FDA approved the next generation sequencing based FoundationONE CDx test (F1CDx) as a companion diagnostic for *NTRK1*, *NTRK2*, and *NTRK3* in DNA isolated from tumor tissue from eligible patients. F1CDx is a next generation sequencing (NGS) based in-vitro diagnostic device capable detecting several mutations along with *NTRK* gene fusions.²

PQI Process:

- Consider the following preferred testing methods when planning for *NTRK* genomic testing:
 - NGS (Next generation sequencing)
 - Utilize FoundationONE CDx test as available
 - Confirm the NGS assay used has the capacity to detect *NTRK* gene fusions (See *Supplemental Information*)
 - Ensure gene fusion testing of *NTRK1*, *NTRK2*, and *NTRK3* are included in the panel order
 - IHC (Immunohistochemistry)
 - Can be used as a screening diagnostic
 - Following TRK IHC positive result, confirmation of *NTRK* gen fusion would be required for initiation of larotrectinib
 - FISH (fluorescence in situ hybridization)
 - Note that multiple tests would need to be run in order to detect *NTRK* gene fusions at multiple locations
 - Suited for tumor histologies that are pathognomonic for the *NTRK3*-ETV6 fusion such as Infantile Fibrosarcoma, secretory breast cancer, and MASC

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Patient Centered Activities:

- Provide education to patients regarding genetic testing and what to expect
- Prepare care team for timely turnaround time of testing results
- Refer to **Positive Quality Intervention: Larotrectinib Overview** for more information on medication management

Supplemental Information:

The following NGS testing laboratories are confirmed to detect all 3 *NTRK gene fusions*

- Caris Life Sciences
- Foundation Medicine
- Integrated Oncology (LabCorp)/OmniSeq
- NAVICAN
- NeoGenomics Laboratories
- Paradigm Diagnostics
- PathGroup
- Tempus

References:

1. VITRAKVI [package insert]. Bayer HealthCare Pharmaceuticals Inc., Whippany, NJ; July 2019
2. Food and Drug Administration. FDA Approves Companion Diagnostic to identify NTRK fusions in solid tumors for Vitrakvi. October 2020. <https://www.fda.gov/drugs/fda-approves-companion-diagnostic-identify-ntrk-fusions-solid-tumors-vitrakvi>
3. Vitrakvi. Testing For Oncologists. <https://www.hcp.vitrakvi-us.com/testing-for-oncologists/#oncolog-ngs-testing>. October 2020

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