

## Positive Quality Intervention: Larotrectinib (Vitrakvi®) Genomic Testing Management

**Description:** This PQI is developed to provide guidance to genomic testing with respect to larotrectinib.

**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.<sup>1</sup> 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 below:<sup>2</sup>

**Lung:** 0.2%-3.3%

**Sarcoma:** 1%

**GI Cancers:** 0.7%-3.6%

**Glioblastoma:** 1.2%

**Thyroid:** 2.4%-12%

**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 or RNA 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.<sup>3</sup>

### PQI Process:

- Consider the following testing methods when planning for *NTRK* genomic testing:
  - NGS (Next generation sequencing)<sup>4</sup> \*preferred\*
    - 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
    - It is important to note that if DNA does not detect *NTRK*, then the sample should be re-sequenced using RNA to ensure proper detection of *NTRK*
  - IHC (Immunohistochemistry)
    - Can be used as a screening diagnostic, however, sensitivity/specificity has been questioned
    - Following TRK IHC positive result, confirmation of *NTRK* gene 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 ETV6-*NTRK3* fusion such as Infantile Fibrosarcoma, secretory breast cancer, and MASC

### 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 [Larotrectinib \(Vitrakvi®\) Overview](#) PQI for more information on medication management

**Important Notice:** NCODA has developed this Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional. Updated 3.3.22



and provide [Oral Chemotherapy Education \(OCE\)](#) sheet

### 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.](#)
2. Sigal, D. S., Bhangoo, M. S., Hermel, J. A., Pavlick, D. C., Frampton, G., Miller, V. A., Ross, J. S., & Ali, S. M. Comprehensive genomic profiling identifies novel NTRK fusions in neuroendocrine tumors. Retrieved September 23, 2021, from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC6254675/>.
3. Food and Drug Administration. FDA Approves Companion Diagnostic to identify NTRK fusions in solid tumors for Vitrakvi®. <https://www.fda.gov/drugs/fda-approves-companion-diagnostic-identify-ntk-fusions-solid-tumors-vitakvi>.
4. Vitrakvi®. Testing For Oncologists. <https://www.hcp.vitakvi-us.com/testing-for-oncologists/#oncolog-ngs-testing>.

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