Larotrectinib

A targeted therapy for solid tumors

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BACKGROUND: Although neurotrophic tyrosine receptor kinase (*NTRK*) gene fusions are not common in most cancers, they are present in more than 90% of some rare tumors. The U.S. Food and Drug Administration has approved larotrectinib for patients with *NTRK* gene fusion–positive cancers that meet certain criteria. With ongoing advancements in tumor sequencing, it is anticipated that cancer treatment will be determined by genetic variants rather than by cancer type in the future.

OBJECTIVES: This article provides an overview of larotrectinib, a targeted therapy.

METHODS: This article reviews clinical trial results and highlights implications for oncology nurses caring for patients taking larotrectinib.

FINDINGS: Larotrectinib is an effective treatment option for some patients with *NTRK* gene fusion–positive cancers. Oncology nurses are key to educating patients on dosing, administration, side effects, and precautions.

KEYWORDS
larotrectinib; targeted therapy; gene fusion; solid tumor; genetic variants

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NEUROTROPHIC TYROSINE RECEPTOR KINASE (*NTRK*) GENES are responsible for coding tropomycin receptor kinase (TRK) proteins (U.S. Food and Drug Administration [FDA], 2018b). TRK proteins are normally found on neuronal cells and assist with cell signaling processes that influence cell proliferation and survival (National Cancer Institute [NCI], n.d.). A genetic alteration can arise if the *NTRK* gene incorrectly fuses with an unrelated gene (FDA, 2018b). *NTRK* gene fusions occur in less than 1% of pediatric and adult cancers. Although rare, this gene alteration occurs in a variety of cancer diagnoses, including thyroid cancers, colon adenocarcinomas, low-grade gliomas, sarcomas, lung cancers, melanomas, and leukemias (Cocco et al., 2018; Okamura et al., 2018). In addition, it is estimated that almost 100% of patients with certain rare tumors, such as infantile fibrosarcomas and salivary gland cancers, have an *NTRK* gene fusion (NCI, 2019).

In tumors with an *NTRK* gene fusion, malignant cells have an abundance of TRK proteins or have TRK proteins that are overactive (Federman & McDermott, 2019). *NTRK* gene fusions promote cancer development. The downstream signaling caused by the fusion allows for cancer cell growth and survival. Targeting *NTRK* gene fusions may be an effective treatment strategy in preventing tumor growth in cancers with this genetic feature (Okamura et al., 2018).

Larotrectinib, a targeted therapy, binds to the TRK proteins on the malignant cells and blocks downstream signaling for cancer cell growth. Through this action, the medication interferes with cancer cell survival (Bayer, 2019). This kinase inhibitor drug is indicated for certain patients with *NTRK* gene fusion–positive cancers (Loxo Oncology, 2018). Based on clinical trial results, the FDA granted accelerated approval of larotrectinib in 2018. Larotrectinib received FDA approval for multiple cancer diagnoses based on a shared genetic variant, rather than for a specific cancer (FDA, 2018b).

NTRK Testing

Because of ongoing developments in tumor sequencing, it is anticipated that cancer treatment will soon be determined by genetic variants rather than by tumor type (NCI, 2019). With this approach, patients will receive more specific and effective cancer treatments (FDA, 2018b). As more targeted treatments become available, some have advocated screening for *NTRK* gene fusions in the initial diagnostic process (Penault-Llorca et al., 2019). Others recommend testing primarily in patients who are young, are diagnosed with cancers known to have a high incidence of *NTRK* gene fusions, are negative for other commonly seen genetic alterations, or have advanced disease (Marchiò et al., 2019).