Vitrakvi Shows Good Results for Gastrointestinal Cancers

TRK inhibitor larotrectinib led to durable responses in people with colon, pancreatic, appendix, bile duct and liver cancers.

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The pancancer drug Vitrakvi (larotrectinib), which targets cancer with a specific genetic characteristic, works well against a variety of gastrointestinal (GI) cancers that carry the mutation, according to an analysis presented at the American Society of Clinical Oncology (ASCO) Gastrointestinal Cancers Symposium last week in San Francisco.

In November 2018, the Food and Drug Administration approved Vitrakvi as the first site-agnostic therapy developed to treat cancer with neurotrophic receptor tyrosine kinase (NTRK) gene fusions regardless of its location in the body. These gene fusions act as an ignition switch to accelerate tumor growth. Vitrakvi was approved for adults and children with metastatic solid tumors that cannot be surgically removed.

At the 2017 ASCO annual meeting, researchers reported combined results from the Phase II NAVIGATE trial and two other studies. According to a report in The New England Journal of Medicine, among 55 adults and children with 17 cancer types, the overall response rate—meaning complete or partial tumor shrinkage—was 75%. At the European Society for Medical Oncology Congress the same year, researchers reported follow-up data showing an overall response rate of 80%, including 18% with complete responses.

The analysis presented last week looked specifically at trial participants who had gastrointestinal cancers harboring NTRK fusions. These included eight people with colon cancer, two each with bile duct cancer (cholangiocarcinoma) and pancreatic cancer and one each with appendix cancer and liver cancer.

Eight of these 14 participants were women, and the median age was 68. Eight had Stage IV metastatic cancer at diagnosis, and nine had tried two or more prior treatments. Of note, all but one of the colon cancer patients had microsatellite instability-high (MSI-H) tumors, making them also eligible for the checkpoint immunotherapies Keytruda (pembrolizumab) or Opdivo (nivolumab).

The overall response rate was 43% for this subgroup of participants, rising to 50% for those with

colon cancer. The duration of response was quite variable, ranging from 3.5 to more than 14.7 months.

Among the colon cancer patients, four had a partial response, and the other four had stable disease without further progression. One pancreatic cancer patient had a partial response, and one had stable disease. Of the two people with cholangiocarcinoma, one had a partial response, while the other experienced disease progression. The appendix cancer patient had a partial response, and response could not be determined for the person with liver cancer.

After a median follow-up period of 19 months, the median overall survival time was 33.4 months, or nearly three years. At one year, the overall survival rate was 69%. At the time of the data cutoff, four colon cancer patients and one pancreatic cancer patient were still alive without worsening of their disease. The median progression-free survival time was 5.3 months, but one colon cancer patient still had not progressed after more than 16.7 months.

Vitrakvi was generally safe and well tolerated. One person was deemed to have a severe (Grade 3 or 4) treatment-related adverse event (nausea). No one needed to reduce their medication doses due to side effects, but one participant stopped treatment.

“Although the sample size is limited, there is evidence of clinical activity with larotrectinib in TRK fusion GI cancer, with a manageable safety profile,” the researchers concluded. “TRK fusion GI cancer may represent an underdiagnosed subset of patients with viable treatment options.”

Click here to ready the study abstract.

Click here for full prescribing information for Vitrakvi.
