Retevmo Is Active Against Multiple Types of Advanced Cancer

The response rate was nearly 50% for people with breast, colon, pancreatic and other cancers.

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The targeted therapy Retevmo (selpercatinib), which is approved for the treatment of non-small-cell lung cancer (NSCLC) and thyroid cancer, also works against other types of advanced cancer with RET fusions, according to a report this week at the American Association for Cancer Research (AACR) virtual annual meeting.

"Selpercatinib demonstrates promising activity across a variety of non-lung and non-thyroid RET fusion-positive advanced solid tumors, including treatment-refractory gastrointestinal malignancies," presenter Vivek Subbiah, MD, of MD Anderson Cancer Center in Houston, said in a press release. "Although RET fusions are rare, this undoubtedly has conferred clinical benefit and the gift of time to these patients."

Retevmo (formerly known as LOXO-292), from Eli Lilly and company, inhibits a tyrosine kinase known as RET. This enzyme plays a role in cell proliferation, and mutations or fusions in the RET gene can drive cancer development. RET alterations are rare overall, occurring in less than 1% of all cancers, but they are more common in certain cancer types.

The Food and Drug Administration approved Retevmo for advanced NSCLC and thyroid cancer with RET alterations in May 2020. These new findings could make the drug eligible for an expanded indication as a pancancer, or site-agnostic, therapy that works against cancers with specific genetic changes regardless of where they occur in the body.

The results come from the Phase I/II LIBRETTO-001 trial (NCT03157128), which enrolled people in 16 countries with advanced NSCLC, thyroid cancer and a variety of other solid tumors with RET fusions. Both previously treated patients and those starting systemic treatment for the first time were eligible. All participants were treated with Retevmo taken as a pill twice daily; there was no placebo group.

Subbiah presented results from 32 study participants with 12 types of advanced cancer. Nearly two thirds had gastrointestinal cancers, including nine with pancreatic cancer and nine with colon cancer. Other cancer types represented in smaller numbers included breast, small intestine, ovarian and salivary cancers, sarcoma, xanthogranuloma and metastatic cancer with an unknown

primary site. All but three had previously received systemic therapy.

The overall response rate for this group—meaning complete or partial tumor shrinkage—was 47%. Confirmed responses were observed in people with nine different cancer types. Eleven of the 15 responders had ongoing responses after about a year of follow-up.

Retevmo was generally safe and well tolerated. The most common adverse events were elevated ALT and AST liver enzymes, dry mouth, hypertension, diarrhea, fatigue, nausea and abdominal pain. No one in this group stopped therapy due to treatment-related adverse events.

Researchers previously reported that Retevmo led to an overall response rate of 64% for the 105 treatment-experienced people with NSCLC, rising to 85% for the 39 patients new to treatment; 10 of the 11 lung cancer patients with brain metastasis experienced cancer shrinkage in the brain. The overall response rate was 69% for previously treated and 73% for treatment-naive people with medullary thyroid cancer with RET mutations, and 79% and 100%, respectively, for those with RET-fusion-positive thyroid cancer.

The availability of novel targeted therapies like Retevmo underscores the need for tumor genomic testing to determine which patients have gene mutations, fusions or other alterations that could make them eligible for these new treatments.

“While uncommon, RET fusions occur in a ’long tail’ of solid tumors beyond lung and thyroid cancers, and these patients do not yet have an approved targeted therapy option to address the underlying genomic driver of their cancer,” Subbiah said in another press release from Lilly. “These results demonstrate selpercatinib’s potential for this patients population and reiterate the importance of broad-based genomic profiling to identify actionable oncogenic drivers, including RET fusions.”

Click here to read the study abstract.
Click here for more coverage from the AACR annual meeting.
Click here for full prescribing information for Retevmo.
