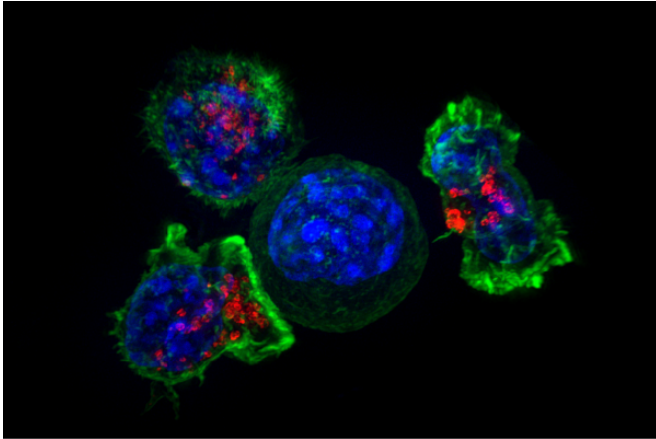


# Strong, durable responses to selpercatinib in RET-driven medullary thyroid cancer

26 August 2020



Killer T cells surround a cancer cell. Credit: NIH

Selpercatinib (Retevmo), a drug targeted precisely against cancers driven by mutations or alterations in the gene RET, was effective in a clinical trial at shrinking tumors in patients with medullary thyroid cancer, with a majority of patients living for more than a year without disease progression.

The drug was effective both in patients with no prior treatment with targeted [anti-cancer drugs](#) and in those who had disease progression following treatment with other multitargeted agents, report Lori J. Wirth, MD, investigator in the Massachusetts General Hospital (MGH) Cancer Center, and colleagues.

"What we're seeing is a combination of very good efficacy and also very good tolerability with selpercatinib," says Wirth. "The response rates are high, responses are very durable, and overall the drug does not cause a lot of toxicity."

Wirth is the lead author of a study published in the *New England Journal of Medicine* reporting results of the phase 1/2 trial. The trial formed the basis for the approval of selpercatinib by the US Food and

Drug Administration in May 2020 for adults and children 12 and older with advanced or metastatic RET-mutated medullary [thyroid cancer](#) who require systemic therapy, adults with metastatic RET-driven non-[small cell lung cancer](#), and patients 12 and older with advanced or metastatic RET-fusion positive thyroid cancer resistant to radioactive iodine who require systemic therapy.

Selpercatinib is the first approved drug of its kind targeted specifically to cancers driven by mutations or alterations in the gene RET. Mutations in RET are responsible for up to 70 percent of medullary thyroid cancers (MTC), while RET gene fusions (abnormal combinations of parts of two different genes) account for one-to-two percent of all non-small cell lung cancers and ten-to-twenty percent of other thyroid cancers.

Physicians typically treat patients with RET-associated cancers with drugs that target RET and multiple other enzymes (kinases) commonly found in many different types of cancer. But the two multi-[kinase inhibitors](#) currently approved for treatment of medullary thyroid cancer, vandetanib and cabozantinib, have substantial off-target side effects that limit their use in patients with RET-driven cancers.

"If you have a clean, RET-specific inhibitor such as selpercatinib, then you can really pound down RET very strongly and hit the driver alteration much harder, with a better side effect profile," Wirth explains.

In the trial objective response rates, a measure of significant and clinically important tumor shrinkage, were 69 percent for patients with RET-mutated medullary thyroid cancers treated with selpercatinib who had previously received vandetanib, cabozantinib, or both; 73 percent in similar patients who had not received either of the other drugs; and 79 percent for patients with previously treated RET fusion-positive thyroid cancers.

In all, 82 percent of previously treated patients with medullary thyroid cancer, and 92 percent of patients who had not received either vandetanib or cabozantinib lived for at least one year without further [disease progression](#).

The most common side effects with selpercatinib were [high blood pressure](#), increased liver enzyme levels, decrease in sodium levels, and diarrhea, all of which were manageable. Only four of 162 patients had to stop selpercatinib because of side effects.

Wirth and colleagues have launched an international phase-three trial comparing selpercatinib with either vandetanib or cabozantinib as first-line therapy for RET-mutated medullary thyroid cancer.

**More information:** *New England Journal of Medicine* (2020). [DOI: 10.1056/NEJMoa2005651](https://doi.org/10.1056/NEJMoa2005651)

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