

Targeted therapy pralsetinib achieves high response rates in advanced cancers with RET gene fusions

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Cancer cell during cell division. Credit: National Institutes of Health

The targeted therapy pralsetinib appears to have high response rates and durable activity in patients with a broad variety of tumors harboring RET

gene fusions, according to results from the international Phase I/II ARROW trial, led by researchers at The University of Texas MD Anderson Cancer Center.

In [patients](#) with RET fusion-positive thyroid cancers, pralsetinib achieved an overall response rate (ORR), indicating tumor shrinkage, of 91% and disease control rate (DCR), indicating [tumor shrinkage](#) or stable disease, of 100%. For all other tumor types included in the cohort, pralsetinib resulted in a 50% ORR and 92% DCR.

Trial data were shared in an oral presentation at the 2020 American Society of Clinical Oncology Annual Meeting by principal investigator Vivek Subbiah, M.D., associate professor of Investigational Cancer Therapeutics.

"This trial shows that pralsetinib has broad and durable anti-tumor activity across multiple advanced solid tumor types, giving it the potential to address an unmet medical need for patients with RET fusion-positive cancers," said Subbiah. "The recent tumor-agnostic drug approvals have resulted in a paradigm shift in [cancer treatment](#), away from organ-histology specific indications to a biomarker-guided, tumor-agnostic approach. However, until recently, we haven't had any effective targeted therapies targeting RET alterations."

RET fusions occur when a portion of the chromosome containing the RET gene breaks off and joins with a gene on another chromosome, creating a fusion protein capable of fueling [cancer](#) development. RET alterations are most common in medullary thyroid cancers (approximately 90% of advanced cases), papillary thyroid cancers (approximately 10-20% of cases) and non-small cell lung cancers (approximately 1-2% of cases).

The presentation included data for 13 patients with RET fusion-positive

thyroid cancers and 14 patients with other RET fusion-positive cancers, including pancreatic cancer, cholangiocarcinoma, ovarian cancer, colon cancer and others. Nearly all patients had stage IV disease and had progressed or relapsed on available standard therapies.

Among those patients with RET fusion-positive thyroid cancers, the duration of treatment ranged from three to 22 months, and 70% of responding patients remain on therapy

In other RET fusion-positive cancers, all patients with [pancreatic cancer](#) (3) and cholangiocarcinoma (2) in the trial had a partial response from treatment. The duration of treatment ranged from two to 21 months, and 67% of responding patients remain on therapy.

Further, treatment with pralsetinib was well-tolerated across all patients in the cohort, explained Subbiah. "Pralsetinib was consistently safe across the overall population, and the majority of adverse events were low-grade. None of the patients in the basket cohort discontinued therapy due to treatment-related adverse events."

Additional cohorts of the ARROW trial focus on patients with RET fusion-positive non-small cell lung cancers and RET-mutant medullary thyroid cancer. Data from the non-small cell lung cancer cohort, indicating an ORR of 65% and DCR of 93%, also were presented in a poster discussion at the ASCO Annual Meeting. Results from the non-small cell lung cancer cohorts have been submitted to the U.S. Food and Drug Administration for approval of pralsetinib in these patients

"This study stresses the importance of considering genomic testing for all patients regardless of tumor histology, so we can identify those that may benefit from targeted therapies such as pralsetinib," said Subbiah. "It's encouraging to be able to offer effective options to these patients and give them the gift of time."

Provided by University of Texas M. D. Anderson Cancer Center

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