FDA Approves Gavreto for RET-Altered Thyroid Cancers

Targeted therapy demonstrated high response rates for thyroid tumors with RET mutations or fusions.

December 1, 2020 By Food and Drug Administration (FDA)

On December 1, 2020, the Food and Drug Administration approved pralsetinib (GAVRETO, Blueprint Medicines Corporation) for adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy or RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).

Efficacy was investigated in a multicenter, open label, multi-cohort clinical trial (ARROW, NCT03037385) in patients whose tumors had RET gene alterations. Identification of RET gene alterations was prospectively determined in local laboratories using either next generation sequencing, fluorescence in situ hybridization, or other tests.

The main efficacy outcome measures were overall response rate (ORR) and response duration determined by a blinded independent review committee using RECIST 1.1. Efficacy for advanced or metastatic RET-mutant MTC was evaluated in 55 patients who received prior cabozantinib or vandetanib. The ORR for these patients was 60% (95% CI: 46%, 73%); 79% of responding patients had responses lasting 6 months or longer. Efficacy was also evaluated in 29 patients with RET-mutant MTC who did not receive prior cabozantinib or vandetanib. The ORR was 66% (95% CI: 46%, 82%); 84% of patients had responses lasting 6 months or longer.

Efficacy for patients with RET fusion-positive thyroid cancer was evaluated in 9 patients who were radioactive iodine-refractory. The ORR was 89% (95% CI: 52%, 100%); all responding patients had responses lasting 6 months or longer.

The most common adverse reactions (≥25%) were constipation, hypertension, fatigue, musculoskeletal pain, and diarrhea. The most common Grade 3-4 laboratory abnormalities (≥2%) were decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased phosphate, decreased calcium (corrected), decreased sodium, increased aspartate aminotransferase (AST), increased alanine aminotransferase (ALT), decreased platelets, and increased alkaline phosphatase.

The recommended pralsetinib dose in adults and pediatric patients 12 years and older is 400 mg

orally once daily on an empty stomach with no food intake for at least 2 hours before and at least 1 hour after taking pralsetinib.

View full prescribing information for Gavreto.

This review used the Real-Time Oncology Review (RTOR) pilot program and Assessment Aid, a voluntary submission from the applicant to facilitate the FDA's assessment. The FDA approved this application 3 months ahead of the FDA goal date.

This application was granted accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

This application was granted priority review, breakthrough therapy, and orphan drug designation. A description of FDA expedited programs is in the Guidance for Industry: Expedited Programs for Serious Conditions-Drugs and Biologics.

Healthcare professionals should report all serious adverse events suspected to be associated with the use of any medicine and device to FDA's MedWatch Reporting System or by calling 1-800-FDA-1088.

For assistance with single-patient INDs for investigational oncology products, healthcare professionals may contact OCE's Project Facilitate at 240-402-0004 or email OncProjectFacilitate@fda.hhs.gov.

This announcement was originally published on the Food and Drug Administration website on December 1, 2020.
