Gavreto™ (pralsetinib) – New orphan indications

- On December 1, 2020, Blueprint Medicines announced the FDA approval of Gavreto (pralsetinib), for the treatment of (1) adult and pediatric patients 12 years of age and older with advanced or metastatic *rearranged during transfection* (*RET)*-mutant medullary thyroid cancer (MTC) who require systemic therapy and (2) adult and pediatric patients 12 years of age and older with advanced or metastatic *RET* fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).
    - These indications were approved under accelerated approval based on overall response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trial(s).
- Gavreto is also approved for the treatment of adult patients with metastatic *RET* fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA approved test.
- *RET* activating fusions and mutations are key disease drivers in many cancer types, including NSCLC and multiple types of thyroid cancer. *RET* fusions are implicated in approximately 10 to 20% of patients with papillary thyroid cancer, while *RET* mutations are implicated in approximately 90% of patients with advanced MTC.
- The approval of Gavreto for the new indications was based on the open-label ARROW study. The study included 55 patients with *RET*-mutant metastatic MTC previously treated with Cometriq® (cabozantinib) or Caprelsa® (vandetanib) (or both) and 29 patients with *RET*-mutant advanced MTC who were Cometriq and Caprelsa treatment-naïve. The primary endpoints were overall response rate (ORR) and duration of response (DOR)
    - The ORR in the previously Cometriq or Caprelsa treated group was 60% (95% CI: 46, 73) and the median DOR was not reached (95% CI: 15.1, not estimable).
    - The ORR in the Cometriq and Caprelsa treatment-naive group was 66% (95% CI: 46, 82) and the median DOR was not reached (95% CI: not estimable, not estimable).
- ARROW also included 9 patients with *RET* fusion-positive thyroid with disease progression following standard therapy.
    - The ORR was 89% (95% CI: 52, 100) and the median DOR was not reached (95% CI: not estimable, not estimable).
- The recommended dose of Gavreto for all its uses is 400 mg orally once daily on an empty stomach. Treatment should be continued until disease progression or until unacceptable toxicity.
    - Patients should be selected for treatment with Gavreto based on the presence of a *RET* gene fusion or *RET* gene mutation.

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— Information on FDA-approved tests for *RET* gene fusion (NSCLC) is available at http://www.fda.gov/CompanionDiagnostics. An FDA-approved test for the detection of *RET* gene fusion (thyroid cancer) and *RET* gene mutations is not currently available.

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