Ayvakit™ (avapritinib) – New orphan drug approval

- On January 9, 2020, the FDA announced the approval of Blueprint Medicines' Ayvakit (avapritinib), for the treatment of adults with unresectable or metastatic gastrointestinal stromal tumor (GIST) harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations.

- GIST is a sarcoma of bone or connective tissue of the gastrointestinal (GI) tract. Tumors arise from cells in the wall of the GI tract and occur most often in the stomach or small intestine. Most patients are diagnosed between the ages of 50 to 80.

    — The activating mutations in PDGFRA have been linked to the development of GISTs, and up to approximately 10% of GIST cases involve mutations of this gene.

- Ayvakit is a selective and potent inhibitor of KIT and PDGFRA mutant kinases.

- The efficacy of Ayvakit was established in NAVIGATOR, a single-arm, open-label study in 43 patients with GIST harboring a PDGFRA exon 18 mutation, including 38 patients with PDGFRA D842V mutation. The major efficacy outcome measure was overall response rate (ORR). An additional efficacy outcome measure was duration of response (DOR).

    — The ORR was 84% (95% CI: 69, 93) in PDGFRA exon 18 patients. The ORR was 89% (95% CI: 75, 97) in PDGFRA D842V patients.
    — The median DOR in both groups was not reached (range: 1.9+ months, 20.3+ months).

- Warnings and precautions for Ayvakit include intracranial hemorrhage, central nervous system effects, and embryo-fetal toxicity.

- The most common adverse reactions (≥ 20%) with Ayvakit use were edema, nausea, fatigue/asthenia, cognitive impairment, vomiting, decreased appetite, diarrhea, hair color changes, increased lacrimation, abdominal pain, constipation, rash, and dizziness.

- The recommended dose of Ayvakit is 300 mg orally once daily on an empty stomach, at least 1 hour before and 2 hours after a meal. Treatment should be continued until disease progression or unacceptable toxicity.

    — Patients should be selected for treatment with Ayvakit based on the presence of a PDGFRA exon 18 mutation. An FDA-approved test for the detection of exon 18 mutations is not currently available.

- Blueprint Medicines plans to launch Ayvakit within a week. Ayvakit will be available as 100 mg, 200 mg, and 300 mg tablets.