Krazati® (adagrasib) – New indication

- On June 21, 2024, the FDA approved Bristol Myers Squibb's Krazati (adagrasib), in combination with cetuximab, for the treatment of adult patients with *KRAS* G12C-mutated locally advanced or metastatic colorectal cancer (CRC), as determined by an FDA-approved test, who have received prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy.
    - This indication is approved under accelerated approval based on objective response rate (ORR) and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of a clinical benefit in a confirmatory trial.
- Krazati is also approved as a single-agent, for the treatment of adult patients with *KRAS* G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), as determined by an FDA-approved test, who have received at least one prior systemic therapy.
- The approval of Krazati for the new indication was based on KRYSTAL-1, a multicenter, single-arm, open-label expansion cohort study. Eligible patients (N = 94) were required to have locally advanced or metastatic *KRAS* G12C-mutated CRC. Patients were treated with Krazati in combination with cetuximab. The major outcome measures were confirmed ORR and DOR.
    - The ORR was 34% (95% CI: 25, 45).
    - The median DOR was 5.8 months (95% CI: 4.2, 7.6).
- The most common adverse reactions (≥ 25%) with Krazati use in combination with cetuximab in CRC were rash, nausea, diarrhea, vomiting, fatigue, musculoskeletal pain, hepatotoxicity, headache, dry skin, abdominal pain, decreased appetite, edema, anemia, and cough. The most common (≥ 2%) grade 3 or 4 laboratory abnormalities were decreased lymphocytes, decreased potassium, decreased magnesium, decreased hemoglobin, increased aspartate aminotransferase, increased lipase, decreased albumin, and increased alanine aminotransferase.
- The recommended dosage of Krazati as a single agent or in combination with cetuximab is 600 mg orally twice daily until disease progression or unacceptable toxicity.
    - Patients should be selected for treatment of locally advanced or metastatic CRC based on the presence of *KRAS* G12C mutation in tumor specimens. Information on FDA-approved tests for the detection of a *KRAS* G12C mutation is available at: https://www.fda.gov/CompanionDiagnostics.