Lumakras™ (sotorasib) – New orphan drug approval

- On May 28, 2021, the FDA announced the approval of Amgen's Lumakras (sotorasib), 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.
    - This indication is approved under accelerated approval based on overall response rate (ORR) and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).
- Lumakras is the first approved targeted therapy for tumors with any KRAS mutation, which accounts for approximately 25% of mutations in NSCLC. KRAS G12C mutations represent about 13% of mutations in NSCLC.
- The efficacy of Lumakras was established in a subset of patients (N= 124) with locally advanced or metastatic *KRAS G12C*-mutated NSCLC enrolled in a single-arm, open-label study (CodeBreaK 100). Patients were treated with Lumakras until disease progression or unacceptable toxicity. The major efficacy outcome measures were ORR and DOR.
    - The ORR was 36% (95% CI: 28, 45).
    - The median DOR was 10.0 months (range: 1.3+, 11.1).
- Warnings and precautions for Lumakras include hepatotoxicity and interstitial lung disease/pneumonitis.
- The most common adverse reactions (≥ 20%) with Lumakras use were diarrhea, musculoskeletal pain, nausea, fatigue, hepatotoxicity, and cough.
- The most common laboratory abnormalities (≥ 25%) with Lumakras use were decreased lymphocytes, decreased hemoglobin, increased aspartate aminotransferase, increased alanine aminotransferase, decreased calcium, increased alkaline phosphatase, increased urine protein, and decreased sodium.
- The recommended dosage of Lumakras is 960 mg (eight 120 mg tablets) orally once daily until disease progression or unacceptable toxicity.
    - Patients should be selected for treatment of locally advanced or metastatic NSCLC with Lumakras based on the presence of *KRAS G12C* mutation in tumor or plasma specimens. If no mutation is detected in a plasma specimen, test tumor tissue.
    - Information on FDA-approved tests for the detection of *KRAS G12C* mutations is available at: http://www.fda.gov/CompanionDiagnostics.
- Amgen's launch plans for Lumakras are pending. Lumakras will be available as a 120 mg tablet.