Lumakras® (sotorasib) plus Vectibix® (panitumumab) – New indication

- On January 17, 2025, Amgen announced the FDA approval of **Lumakras (sotorasib)**, **in combination with Vectibix (panitumumab), for the treatment of adult patients with *KRAS G12C*-mutated metastatic colorectal cancer (mCRC),** as determined by an FDA-approved test, who have received prior fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy.

- Lumakras is also approved via accelerated approval 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.

- Vectibix is also approved for the treatment of adult patients with wild-type RAS (defined as wild-type in both *KRAS* and *NRAS* as determined by an FDA-approved test) mCRC: as first-line therapy in combination with FOLFOX and as monotherapy following disease progression after prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy.

- The approval of Lumakras plus Vectibix for the new indication was based on CodeBreaK 300, a randomized, open-label, active-controlled study in 160 previously treated patients with *KRAS G12C*-mutated mCRC. Patients received either Lumakras 960 mg and Vectibix, or Lumakras 240 mg orally once daily and Vectibix, or investigator's choice of standard of care (SOC) trifluridine/tipiracil or regorafenib. The major outcome measure was progression-free survival (PFS). Additional efficacy outcome measures included overall survival (OS), objective response rate (ORR), and duration of response (DOR). Only the results of the approved dosing regimen Lumakras 960 mg in combination with Vectibix are described below.

    - The median PFS was 5.6 months in the Lumakras plus Vectibix arm vs. 2 months in the SOC arm (hazard ratio [HR] 0.48, 95% CI: 0.3, 0.78; p = 0.005).
    - Median OS was not reached in the Lumakras plus Vectibix arm vs. 10.3 months in the SOC arm (HR 0.7, 95% CI: 0.41, 1.18).
    - ORR was 26% (95% CI: 15, 40) in the Lumakras plus Vectibix arm vs. 0% (95% CI: 0, 7) in the SOC arm.
    - Median DOR was 4.4 months (range: 1.9+, 6+) in the Lumakras plus Vectibix arm.

- The most common adverse reactions (≥ 20%) with Lumakras plus Vectibix use for mCRC were rash, dry skin, diarrhea, stomatitis, fatigue and musculoskeletal pain. The most common grade 3 or 4 laboratory abnormalities in ≥ 2 patients (4.3%) were decreased magnesium, decreased potassium, decreased corrected calcium, and increased potassium.

- The recommended dose of Lumakras for the treatment of mCRC is 960 mg (three 320 mg tablets or four 240 mg tablets or eight 120 mg tablets) orally once daily in combination with Vectibix until disease progression or unacceptable toxicity. The first dose of Lumakras should be administered prior to first Vectibix infusion.

    - Refer to the Lumakras drug label for dosing for NSCLC.

- The recommended dosage for Vectibix in combination with Lumakras is 6 mg/kg, administered as an intravenous infusion every 14 days until disease progression, unacceptable toxicity, or until Lumakras is withheld or discontinued.

    - Refer to the Vectibix drug label for dosing for its other indications.

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- Patients should be selected for treatment with Lumakras plus Vectibix based on the presence of *KRAS G12C* mutation in tumor specimens. Information on FDA-approved tests for the detection of *KRAS G12C* mutations is available at: http://www.fda.gov/CompanionDiagnostics.