Keytruda® (pembrolizumab) – New indication

- On July 31, 2019, Merck announced the FDA approval of Keytruda (pembrolizumab), for the treatment of patients with recurrent locally advanced or metastatic squamous cell carcinoma of the esophagus whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 10] as determined by an FDA-approved test, with disease progression after one or more prior lines of systemic therapy.

- Keytruda is also indicated for melanoma, non-small cell lung cancer, head and neck squamous cell cancer, small cell lung cancer, classical Hodgkin lymphoma, primary mediastinal large B-cell lymphoma, urothelial carcinoma, microsatellite instability-high or mismatch repair deficient solid tumors or colorectal cancer, gastric cancer, cervical cancer, hepatocellular cancer, Merkel cell carcinoma, and renal cell carcinoma.

- The new indication for Keytruda was based on data from KEYNOTE-181, an open-label study enrolling 628 patients with recurrent locally advanced or metastatic esophageal cancer who progressed on or after one prior line of systemic treatment for advanced disease. Patients received Keytruda or investigator's choice of chemotherapy. Treatment with Keytruda or chemotherapy continued until unacceptable toxicity or disease progression. The major efficacy outcome measure was overall survival (OS).

    - The median OS for patients with esophageal squamous cell carcinoma (ESCC) with CPS ≥ 10 was 10.3 months for the Keytruda-treated patients vs. 6.7 months for the chemotherapy-treated patients (Hazard ratio [HR] 0.64; 95% CI: 0.46, 0.90).
    - In addition, the progression free survival was 3.2 months in the Keytruda group vs. 2.3 months in the chemotherapy group (HR 0.66; 95% CI: 0.48, 0.92).
    - The objective response rate (ORR) for Keytruda patients was 22% (95% CI: 14, 33) vs. 7% (95% CI: 3, 15) for the chemotherapy group.
    - The duration of response (DOR) for the Keytruda and chemotherapy groups was 9.3 months (range: 2.1+, 18.8+) and 7.7 months (range: 4.3, 16.8+), respectively.

- The new indication was also supported by data from KEYNOTE-180, an open-label study enrolling 121 patients with locally advanced or metastatic esophageal cancer who progressed on or after at least 2 prior systemic treatments for advanced disease. Patients received the same treatments as in KEYNOTE-181. The major efficacy outcome measures were ORR and DOR.

    - The ORR in the 35 patients with ESCC expressing PD-L1 was 20% (95% CI: 8, 37).
    - Among the 7 responding patients, the DOR ranged from 4.2 to 25.1+ months, with 5 patients (71%) having responses of 6 months or longer and 3 patients (57%) having responses of 12 months or longer.

- The most common adverse reactions (≥ 20%) with Keytruda use as a single agent include fatigue, musculoskeletal pain, decreased appetite, pruritus, diarrhea, nausea, rash, pyrexia, cough, dyspnea, constipation, pain, and abdominal pain.

- The recommended dose of Keytruda for esophageal cancer is 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.

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