Keytruda® (pembrolizumab) – Expanded indications

- On June 11, 2019, Merck announced the FDA approval of Keytruda (pembrolizumab), in combination with platinum and fluorouracil (FU), for the first-line treatment of patients with metastatic or with unresectable, recurrent head and neck squamous cell carcinoma (HNSCC); and as a single agent, for the first line treatment of patients with metastatic or with unresectable, recurrent HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test.

    - Keytruda was previously approved for the treatment of patients with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy under the FDA's accelerated approval process. In accordance with the accelerated approval process, continued approval was contingent upon verification and description of clinical benefit, which has now been demonstrated and has resulted in the FDA converting the accelerated approval to a full (regular) approval.

- Keytruda is also indicated for melanoma, non-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 expanded indications for Keytruda were based on data from KEYNOTE-048, an open-label study in 882 patients with metastatic HNSCC. Patients were randomized to one of the following arms: (1) Keytruda, (2) Keytruda + carboplatin or cisplatin + FU, or (3) Erbitux® (cetuximab) + carboplatin or cisplatin + FU. The main efficacy outcome measures were overall survival (OS) and progression-free survival (PFS).

    - Overall, median OS was 13.0 months for Keytruda + chemotherapy vs. 10.7 months for cetuximab + chemotherapy (Hazard Ratio [HR] 0.77; 95% CI: 0.63, 0.93; p = 0.0067). There was no significant difference in PFS between the two groups at the pre-specified interim analysis.
    - There was also a statistically significant improvement in OS for the subgroup of patients with PD-L1 CPS ≥ 1 randomized to Keytruda as a single agent vs. cetuximab + chemotherapy. Median OS was 12.3 months vs. 10.3 months, respectively (HR 0.78; 95% CI: 0.64, 0.96; p = 0.0171). There was no significant difference in PFS between the two groups at the pre-specific interim analysis.
    - At the time of the interim analysis, there was no significant difference in OS between Keytruda as a single agent vs. cetuximab + chemotherapy for the overall population.

- 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 most common adverse reactions (≥ 20%) with Keytruda use in combination with chemotherapy include fatigue/asthenia, nausea, constipation, diarrhea, decreased appetite, rash, vomiting, cough, dyspnea, pyrexia, alopecia, peripheral neuropathy, mucosal inflammation, and stomatitis.

- The recommended dose of Keytruda for HNSCC 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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- When administering Keytruda in combination with chemotherapy, administer Keytruda prior to chemotherapy when given on the same day. Refer to the drug labels for the chemotherapy agents administered in combination with Keytruda for recommended dosing information, as appropriate.
- Refer to the Keytruda drug label for dosing for all its other indications.