Keytruda® (pembrolizumab) – New and Updated Indications

- On October 24, 2016, the FDA announced the approval of Merck's Keytruda (pembrolizumab) for the first line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression [(tumor proportion score (TPS) ≥ 50%)] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.

- Keytruda is indicated for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥ 1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda.

    - Previously, this indication was approved by accelerated approval. Now the indication is confirmed.

- Keytruda is also indicated for patients with unresectable or metastatic melanoma and patients with recurrent or metastatic head and neck squamous cell carcinoma with disease progression on or after platinum-containing chemotherapy.

- Keytruda is the first anti-PD-1 (programmed death receptor-1) therapy to be approved for first-line treatment of NSCLC.

- The efficacy of Keytruda for the new indication was based on KEYNOTE-024, an open-label trial of 305 patients who had not received prior systemic chemotherapy for their metastatic NSCLC and whose tumors had high PD-L1 expression (TPS ≥ 50%) with no EGFR or ALK aberrations. Patients were randomized to Keytruda or platinum-containing chemotherapy. The primary endpoint was progression-free survival (PFS); additional efficacy outcome measures were overall survival (OS) and objective response rate (ORR).

    - Keytruda demonstrated a significant improvement in PFS (HR 0.50; 95% CI: 0.37, 0.68; $p < 0.001$) with a median PFS of 10.3 months vs. 6.0 months for those receiving chemotherapy.
    - A statistically significant improvement in OS was shown for patients randomized to Keytruda vs. chemotherapy (HR 0.60; 95% CI: 0.41, 0.89; $p < 0.005$).
    - The ORR was statistically significantly greater with Keytruda vs. chemotherapy (45% vs. 28%, respectively; $p < 0.001$).

- The efficacy of Keytruda for the updated indication was based on KEYNOTE-010, an open-label trial enrolling 1,033 patients with metastatic NSCLC with all levels of PD-L1 expression (TPS ≥ 1%) who had progressed following platinum-containing chemotherapy and, if appropriate, targeted therapy for EGFR or ALK genomic tumor aberrations. Patients were randomized to Keytruda or docetaxel. The primary endpoints were OS and PFS.

    - Patients in the Keytruda arms had improved OS (Keytruda 2 mg/kg: HR 0.71; 95% CI: 0.58, 0.88; $p < 0.001$ and Keytruda 10 mg/kg: HR 0.61; 95% CI: 0.49, 0.75; $p < 0.001$) vs. patients receiving docetaxel. The median survival was 10.4 months in the 2 mg/kg arm, 12.7 months in the 10 mg/kg arm, and 8.5 months in the docetaxel arm.

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- Patients in the Keytruda 10 mg/kg arm had improved PFS vs. docetaxel (Keytruda 2 mg/kg: HR 0.88; 95% CI 0.73, 1.04; p = 0.068; Keytruda 10 mg/kg: HR 0.79; 95% CI 0.66, 0.94; p = 0.005).

- The recommended dose of Keytruda for NSCLC and HNSCC is 200 mg administered intravenously (IV) every 3 weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression.

- The dose for melanoma is 2 mg/kg IV every 3 weeks until disease progression or unacceptable toxicity.