FDA Approves Keytruda for Advanced Esophageal Squamous Cell Cancer

Keytruda (pembrolizumab)'s efficacy was investigated in two clinical trials of people with recurrent, locally advanced or metastatic disease.

July 31, 2019 By Food and Drug Administration (FDA)

On July 30, 2019, the Food and Drug Administration approved pembrolizumab (KEYTRUDA, Merck) for patients with recurrent, locally advanced or metastatic, squamous cell carcinoma of the esophagus (ESCC) 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.

FDA also approved a new use for the PD-L1 IHC 22C3 pharmDx kit as a companion diagnostic device for selecting patients for the above indication.

Efficacy was investigated in two clinical trials, KEYNOTE-181 (NCT02564263) and KEYNOTE-180 (NCT02559687). KEYNOTE-181 was a randomized, open-label, active-controlled trial that enrolled 628 patients with recurrent, locally advanced or metastatic esophageal cancer who progressed on or after one prior line of systemic treatment for advanced or metastatic disease. Patients were randomized (1:1) to receive either KEYTRUDA 200 mg intravenously (IV) every 3 weeks or the investigator's choice of the following regimens: paclitaxel 80-100 mg/m2 IV on days 1, 8, and 15 of every 4-week cycle; docetaxel 75 mg/m2 IV every 3 weeks; or irinotecan 180 mg/m2 IV every 2 weeks (control arm). Randomization was stratified by geographic region and histologic subtype (squamous versus adenocarcinoma). PD-L1 status was determined using the PD-L1 IHC 22C3 pharmDx kit.

The primary efficacy outcome measure of KEYNOTE-181 was overall survival (OS) in patients with ESCC, patients with tumors expressing PD-L1 CPS ≥10, and all randomized patients. Additional efficacy outcome measures were progression-free survival (PFS), overall response rate (ORR), and response duration. The hazard ratio for OS in patients with ESCC whose tumors expressed PD-L1 CPS ≥10 was 0.64 (95% CI: 0.46, 0.90). Median OS was 10.3 months (95% CI: 7.0, 13.5) and 6.7 months (95% CI: 4.8, 8.6) in the pembrolizumab and control arms, respectively.

KEYNOTE-180 was a single arm, open-label trial that enrolled 121 patients with locally advanced or metastatic esophageal cancer who progressed on or after at least 2 prior systemic treatments for advanced disease. With the exception of the number of prior lines of treatment, the eligibility

criteria were similar to and the dosage regimen identical to KEYNOTE-181.

The major efficacy outcome measures of KEYNOTE-180 were ORR and response duration. In the 35 patients with ESCC expressing PD-L1 CPS ≥10, ORR was 20% (95% CI: 8, 37) and response durations ranged from 4.2 to 25.1+ months, with 71% (5 patients) having responses of 6 months or longer and 57% (3 patients) having responses of 12 months or longer.

Adverse reactions in patients with esophageal cancer were similar to those in 2,799 patients with melanoma or NSCLC treated with single-agent pembrolizumab. Common adverse reactions reported in at least 20% of patients receiving pembrolizumab include fatigue, musculoskeletal pain, decreased appetite, pruritus, diarrhea, nausea, rash, pyrexia, cough, dyspnea, constipation, pain, and abdominal pain.

The recommended pembrolizumab dose for esophageal cancer is 200 mg every 3 weeks.

View full prescribing information for KEYTRUDA.

FDA granted these applications priority review. A description of FDA expedited programs is in the Guidance for Industry: Expedited Programs for Serious Conditions—Drugs and Biologics.

Healthcare professionals should report all serious adverse events suspected to be associated with the use of any medicine and device to FDA's MedWatch Reporting System or by calling 1-800-FDA-1088.

Check out recent approvals at the OCE's podcast, Drug Information Soundcast in Clinical Oncology (D.I.S.C.O.).

For assistance with single-patient INDs for investigational oncology products, healthcare professionals may contact OCE's Project Facilitate at 240-402-0004 or email OncProjectFacilitate@fda.hhs.gov.

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