FDA Approves Keytruda for Solid Tumors With High Mutation Burden

A retrospective analysis showed that 29% of people with previously treated tumors responded to treatment.

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FDA approves pembrolizumab for adults and children with TMB-H solid tumors

On June 16, 2020, the Food and Drug Administration granted accelerated approval to pembrolizumab (KEYTRUDA, Merck & Co., Inc.) for the treatment of adult and pediatric patients with unresectable or metastatic tumor mutational burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options.

Today, the FDA also approved the FoundationOneCDx assay (Foundation Medicine, Inc.) as a companion diagnostic for pembrolizumab.

Efficacy was investigated in a prospectively-planned retrospective analysis of 10 cohorts of patients with various previously treated unresectable or metastatic TMB-H solid tumors enrolled in a multicenter, non-randomized, open-label trial, KEYNOTE-158 (NCT02628067). Patients received pembrolizumab 200 mg intravenously every 3 weeks until unacceptable toxicity or documented disease progression.

The main efficacy outcome measures were overall response rate (ORR) and duration of response (DoR) in patients who have received at least one dose of pembrolizumab as assessed by blinded independent central review according to RECIST v1.1, modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ.

A total of 102 patients (13%) had tumors identified as TMB-H, defined as TMB ≥10 mut/Mb. The ORR for these patients was 29% (95% CI: 21,39), with a 4% complete response rate and 25% partial response rate. The median DoR was not reached, with 57% of patients having response durations ≥12 months and 50% of patients having response durations ≥24 months.

Adverse reactions occurring in patients with TMB-H cancer enrolled in KEYNOTE-158 were similar to those occurring in patients with other solid tumors who received pembrolizumab as a single agent. The most common adverse reactions to pembrolizumab are fatigue, musculoskeletal pain,

decreased appetite, pruritus, diarrhea, nausea, rash, pyrexia, cough, dyspnea, constipation, pain, and abdominal pain. Pembrolizumab is associated with immune-mediated side effects, including pneumonitis, colitis, hepatitis, endocrinopathies, nephritis, and skin adverse reactions.

The prescribing information for pembrolizumab includes a “Limitation of Use” stating that the safety and effectiveness of pembrolizumab in pediatric patients with TMB-H central nervous system cancers have not been established.

The recommended pembrolizumab dosage regimen for TMB-H solid tumors is 200 mg every 3 weeks or 400 mg every 6 weeks for adults; 2 mg/kg (up to a maximum of 200 mg) every 3 weeks for pediatric patients.

View full prescribing information for KEYTRUDA.

This review used the Assessment Aid, a voluntary submission from the applicant to facilitate the FDA’s assessment. This application was granted 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.

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