FDA approves pembrolizumab for first-line treatment of MSI-H/dMMR colorectal cancer

On June 29, 2020, the Food and Drug Administration approved pembrolizumab (KEYTRUDA, Merck & Co.) for the first-line treatment of patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer.

Approval was based on KEYNOTE-177 (NCT02563002), a multicenter, international, open-label, active-controlled, randomized trial that enrolled 307 patients with previously untreated unresectable or metastatic MSI-H or dMMR colorectal cancer. Determination of MSI or MMR tumor status was made locally using polymerase chain reaction (PCR) or immunohistochemistry (IHC), respectively. Patients were randomized (1:1) to receive pembrolizumab 200 mg intravenously every 3 weeks or investigator's choice of mFOLFOX6/FOLFIRI ± bevacizumab or cetuximab given intravenously every 2 weeks. Patients randomized to chemotherapy were offered pembrolizumab at the time of disease progression.

The main efficacy outcome measures were progression-free survival (PFS) and overall survival (OS). Median PFS was 16.5 months (95% Confidence Interval [CI]: 5.4, 32.4) in the pembrolizumab arm and 8.2 months (95% CI: 6.1, 10.2) in the chemotherapy arm (HR 0.60, 95% CI 0.45, 0.80; two-sided p-value=0.0004). At the time of the PFS analysis, the OS data were not mature.

The most common adverse reactions reported in ≥20% of patients receiving pembrolizumab as a single agent are fatigue, musculoskeletal pain, decreased appetite, pruritus, diarrhea, nausea, rash, pyrexia, cough, dyspnea, constipation, pain, and abdominal pain.

The recommended pembrolizumab dose for MSI-H/dMMR colorectal cancer is 200 mg every 3 weeks or 400 mg every 6 weeks.

View full prescribing information for KEYTRUDA (https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125514s084lbl.pdf).

This review was conducted under Project Orbis (/about-fda/oncology-center-excellence/project-orbis), an initiative of the FDA Oncology Center of Excellence. Project Orbis provides a framework for concurrent submission and review of oncology drugs among international partners. For this application, a modified Project Orbis was undertaken because of the timing of

MERCK EX1279
Merck Sharp & Dohme LLC v. The Johns Hopkins University
IPR2024-00625

submission to other regulatory agencies. FDA is collaborating with the Australian Therapeutic Goods Administration, Health Canada, and Swissmedic. The review is ongoing for these three agencies.

This review used the Real-Time Oncology Review (/about-fda/oncology-center-excellence/real-time-oncology-review-pilot-program) (RTOR) pilot program, the Assessment Aid (/about-fda/oncology-center-excellence/assessment-aid), a voluntary submission from the applicant to facilitate the FDA's assessment, and Summary Level Review (https://www.fda.gov/files/Proposed-FDA-Work-Plan-for-21st-Century-Cures-Act-Innovation-Account-Activities-as-Submitted-to-Science-Board.pdf), which relied on qualified data summaries to support approval of a supplemental application. The FDA approved this application approximately 5 months ahead of the FDA goal date.

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 (/regulatory-information/search-fda-guidance-documents/expedited-programs-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 (https://www.accessdata.fda.gov/scripts/medwatch/index.cfm) or by calling 1-800-FDA-1088.

For assistance with single-patient INDs for investigational oncology products, healthcare professionals may contact OCE's Project Facilitate (/about-fda/oncology-center-excellence/project-facilitate) at 240-402-0004 or email OncProjectFacilitate@fda.hhs.gov (mailto:OncProjectFacilitate@fda.hhs.gov).

For information on the COVID-19 pandemic, see the following resources:

- FDA: Coronavirus Disease 2019 (COVID-19) (/emergency-preparedness-and-response/mcm-issues/coronavirus-disease-2019-covid-19)
- NCI: Coronavirus: What People With Cancer Should Know (https://www.cancer.gov/contact/emergency-preparedness/coronavirus)
- CDC: Coronavirus (COVID-19) (https://www.cdc.gov/coronavirus/2019-ncov/index.html)

Follow the Oncology Center of Excellence (/OCE) on Twitter @FDAOncology (http://www.twitter.com/@fdaoncology) (http://www.fda.gov/about-fda/website-policies/website-disclaimer).