FDA grants nivolumab accelerated approval for MSI-H or dMMR colorectal cancer

On July 31, 2017, the U.S. Food and Drug Administration granted accelerated approval to nivolumab (OPDIVO, Bristol-Myers Squibb Company) for the treatment of patients 12 years and older with mismatch repair deficient (dMMR) and microsatellite instability high (MSI-H) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

The approval was based on data from Study CA209142 (CHECKMATE 142; NCT 02060188), a multicenter, open-label, single arm study conducted in 53 patients with locally determined dMMR or MSI-H metastatic colorectal cancer (CRC) who had disease progression during, after, or were intolerant to prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy. This was a subset of the 74 patients who received at least one prior regimen for treatment of metastatic disease containing a fluoropyrimidine with oxaliplatin or irinotecan for treatment of metastatic disease. All patients received nivolumab 3 mg/kg by intravenous infusion every 2 weeks until unacceptable toxicity or radiographic progression.

The objective response rate (ORR) as assessed by independent radiographic review committee using RECIST 1.1 was 28% (n=15) (95% CI: 17, 42) in the 53 patients who received prior fluoropyrimidine, oxaliplatin, and irinotecan. Responses lasted 6 or more months for 67% (95% CI: 38, 88) of patients. There was 1 complete response and 14 partial responses. The ORR was 32% (n=24) (95% CI: 22, 44) among the 74 patients in the overall population.

Trials of nivolumab have not been conducted in pediatric patients. Efficacy for adolescent patients (12 years and older) with MSI-H or dMMR metastatic CRC is extrapolated from the results in the respective adult population.

The most common adverse reactions (≥20%) to nivolumab as a single agent include fatigue, rash, musculoskeletal pain, pruritus, diarrhea, nausea, asthenia, cough, dyspnea, constipation, decreased appetite, back pain, arthralgia, upper respiratory tract infection, pyrexia.

The recommended nivolumab dose for this indication is 240 mg every 2 weeks.

Full prescribing information is available at:
https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/125554s034lbl.pdf
(https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/125554s034lbl.pdf)

FDA granted this application priority review status. As a condition of accelerated approval, further studies are required to confirm clinical benefit of nivolumab for this indication. A description of FDA expedited programs is in the Guidance for Industry: Expedited Programs for Serious Conditions-

MERCK EX1120
Merck Sharp & Dohme LLC v. The Johns Hopkins University
IPR2024-00650

Drugs and Biologics, available at: http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm358301.pdf (/media/86377/download).

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 by completing a form online at http://www.fda.gov/medwatch/report.htm (http://www.fda.gov/medwatch/report.htm), by faxing (1-800-FDA-0178) or mailing the postage-paid address form provided online, or by telephone (1-800-FDA-1088).

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