Bristol-Myers Squibb

July 9, 2019

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NCCN Guidelines® Panel: Bladder Cancer

Dear Panel Members:

On behalf of Bristol-Myers Squibb Company, I respectfully submit the enclosed clinical data regarding nivolumab in combination with ipilimumab and nivolumab monotherapy that has been recently published on Journal of Clinical Oncology to the NCCN® Bladder Cancer Panel for your consideration. CheckMate--032 is an open-label, Phase 1/2 multi-cohort study. The enclosed manuscript reports safety and efficacy data with extended follow up for patients with platinum-pretreated unresectable locally advanced or metastatic urothelial carcinoma (mUC) treated with nivolumab monotherapy 3 mg/kg every 2 weeks (NIVO3), nivolumab 3 mg/kg plus ipilimumab 1 mg/kg every 3 weeks for four doses followed by nivolumab monotherapy 3 mg/kg every 2 weeks (NIVO3 + IPI1), and the expanded cohort of nivolumab 1 mg/kg plus ipilimumab 3 mg/kg every 3 weeks for four doses followed by nivolumab monotherapy 3 mg/kg every 2 weeks (NIVO1 + IPI3).[1]

FDA Clearance of OPDIVO® (nivolumab) (indications in bladder cancer): The FDA approved OPDIVO® (nivolumab) on February 2, 2017 for the treatment of locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.[2]

The use of nivolumab in combination with ipilimumab for the treatment of bladder cancer is considered investigational.[2,3]

Rationale: This data is being submitted in response to a standing request from NCCN for new clinical data. Please note that there was a previous submission to this Panel on October 21, 2018 that included Checkmate 032 data that was presented at the 2018 ESMO Annual Meeting.

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As part of this submission, the following resources are included for your review:

1. Sharma P, Siefker-Radtke A, de Braud F, et al. Nivolumab alone and with ipilimumab in previously treated metastatic urothelial carcinoma: Checkmate 032 nivolumab 1 mg/kg plus ipilimumab 3 mg/kg expansion cohort results. *J Clin Oncol*. 2019.
2. Product Information, OPDIVO® (nivolumab) injection for intravenous infusion [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; May 2019.
3. Product Information, YERVOY® (ipilimumab) injection for intravenous infusion [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; May 2019

Thank you for your consideration of this request.

Sincerely,
Awny Farajallah, MD, FACP
Vice-President, Head of US Medical
Bristol-Myers Squibb Company