Submitted by:
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NCCN Guidelines® Panel: Central Nervous System Cancers

Dear Panel Members,

On behalf of Bristol-Myers Squibb Company, I respectfully submit the enclosed OPDIVO® (nivolumab) and YERVOY® (ipilimumab) clinical data that has been presented at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting to the NCCN® Central Nervous System Cancers Panel for your consideration.

The first study is a phase 2 open-label study that evaluated the safety and efficacy in subjects with melanoma metastatic to the brain treated with nivolumab in combination with ipilimumab followed by nivolumab monotherapy.[1]

The second study is a randomized phase 2 study that evaluated nivolumab combined with ipilimumab or nivolumab alone in patients with melanoma brain metastases.[2]

FDA Clearance OPDIVO® (nivolumab) (indications in melanoma): On January 23, 2016, the FDA approved first-line use of nivolumab in combination with ipilimumab for the treatment of patients with unresectable or metastatic melanoma. This indication is approved under accelerated approval based on progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials. [3]
Additionally, nivolumab is indicated in melanoma:[3]

- As a single agent for the treatment of patients with BRAF V600 wild-type unresectable or metastatic melanoma.
- As a single-agent for the treatment of BRAF V600 mutation-positive unresectable or metastatic melanoma. This indication is approved under accelerated approval based on progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

FDA Clearance YERVOY® (ipilimumab) (indications in melanoma): The FDA-approved ipilimumab on October 28, 2015 for the adjuvant treatment of patients with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy.[4]
Ipilimumab was also approved on March 25, 2011 for the treatment of unresectable or metastatic melanoma.[4]

Rationale: This data is being submitted in response to a standing request from NCCN for new clinical data. These two studies are cited in the current Melanoma NCCN Guideline as ongoing trials designed specifically to address the safety and efficacy of anti-PD-1 in patients with melanoma brain metastases (reference 522 and 523, respectively).

The following resources are included for your review.

1. Tawbi H, Forsyth P, Algazi A et al. Efficacy and Safety of Nivolumab Plus Ipilimumab in Patients with Melanoma Metastatic to the Brain: Results of the Phase II Study CheckMate 204. Oral Presentation at the 2017 American Society for Clinical Oncology (ASCO) Annual Meeting June 2-6, 2017; Chicago, IL
2. Long GV, Atkinson V, Menzies AM et al. A Randomized Phase 2 Study of Nivolumab or Nivolumab plus Ipilimumab in Patients with Melanoma Brain Metastases: The Anti-PD1 Brain Collaboration (ABC). Oral Presentation at the 2017 American Society for Clinical Oncology (ASCO) Annual Meeting June 2-6, 2017; Chicago, IL
3. Product Information, OPDIVO® (nivolumab) injection for intravenous infusion. Bristol-Myers Squibb Company, Princeton, NJ. April 2017
4. Product Information, YERVOY® (ipilimumab) injection for intravenous infusion. Bristol-Myers Squibb Company, Princeton, NJ. March 2017

Thank you for your consideration.

Sincerely,

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Vice President, Head US Medical Oncology
Bristol-Myers Squibb Company