



February 13, 2019

Awny Farajallah, MD, FACP  
Vice President, Head US Medical  
Bristol-Myers Squibb Company  
3401 Princeton Pike  
Lawrence NJ, 08648  
609-302-3927; awny.farajallah@bms.com

**NCCN Guidelines® Panel: Non-Small Cell Lung Cancer/Malignant Pleural Mesothelioma Panel**

Dear Panel Members,

On behalf of Bristol-Myers Squibb Company, I respectfully submit the enclosed clinical data which evaluated the use of nivolumab with or without ipilimumab in patients with relapsed malignant pleural mesothelioma (MPM) that have now been published in peer-reviewed journals, to the NCCN® Non-Small Cell Lung Cancer/Malignant Pleural Mesothelioma Panel for your consideration.

MAPS2 is a randomized, non-comparative, phase 2 trial that investigated nivolumab with or without ipilimumab in patients with unresectable MPM who progressed after a maximum of 1 or 2 lines of chemotherapy, including pemetrexed/platinum doublet.<sup>1</sup> The clinical data were previously presented at the 2018 International Conference of the International Mesothelioma Interest Group (iMiG) and are now published in *Lancet Oncology* on January 16, 2019.<sup>1</sup>

INITIATE is a single arm phase 2 study of nivolumab plus ipilimumab in patients with MPM who experienced disease progression on recurrence after at least 1 line of platinum-containing chemotherapy. The clinical data were previously presented at the 2018 International Conference of the International Mesothelioma Interest Group (iMiG) and are now published in *Lancet Respiratory Medicine* on January 16, 2019.<sup>2</sup>

**FDA Clearance of OPDIVO® (nivolumab) (indication in non-small cell lung cancer):**

- Patients with metastatic non-small cell lung cancer and progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving OPDIVO.<sup>3</sup>

The use of nivolumab with or without ipilimumab for patients with relapsed malignant pleural mesothelioma is considered investigational.<sup>3,4</sup>

**Rationale:** These data are being submitted in response to a standing request from NCCN for new clinical data. Please note that there were previous submissions to this panel on May 4, 2018 that included the following data from the MAPS2 and INITIATE studies:

- Scherpereel A. Second- or third-line nivolumab vs. nivo + ipilimumab in mesothelioma: final results of IFCT-1501 MAPS2 randomized phase 2 trial. Oral presentation at: the 14<sup>th</sup> International Conference of the International Mesothelioma Interest Group (iMiG); May 2-5, 2018; Ottawa, Canada.
- Baas P. Ipilimumab and nivolumab in the treatment of malignant pleural mesothelioma: final results of a phase II study (INITIATE). Oral presentation at: the 14<sup>th</sup> International Conference of the International Mesothelioma Interest Group (iMiG); May 2-5, 2018; Ottawa, Canada.

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

1. Scherpereel A, Mazieres L, Greiller L, et al. Nivolumab or nivolumab plus ipilimumab in patients with relapsed malignant pleural mesothelioma (IFCT-1501 MAPS2): a multicentre, open-label, randomised, non-comparative, phase 2 trial. [published online ahead of print January 16, 2019]. *Lancet Oncol.* 2019; DOI: 10.1016/S1470-2045(18)30765-4.
2. Disselhorst MJ, Quispel-Janssen J, Lalezari F, et al. Ipilimumab and nivolumab in the treatment of recurrent malignant pleural mesothelioma (INITIATE): results of a prospective, single-arm, phase 2 trial. [published online ahead of print January 16, 2019]. *Lancet Resp Med.* 2019; DOI: 10.1016/S2213-2600(18)30420-X.
3. Product Information, OPDIVO® (nivolumab) injection for intravenous infusion. Bristol-Myers Squibb Company, Princeton, NJ. February 2019.
4. Product Information, YERVOY® (ipilimumab) injection for intravenous infusion. Bristol-Myers Squibb Company, Princeton, NJ. July 2018.

Thank you for your consideration.

Sincerely,

A handwritten signature in black ink, appearing to read 'Awny Farajallah', with a stylized flourish at the end.

Awany Farajallah, MD, FACP  
Vice President, Head US Medical  
Bristol-Myers Squibb Company