May 4, 2018

NCCN Guidelines® Panel: Malignant Pleural Mesothelioma Panel

Dear Panel Members,

On behalf of Bristol-Myers Squibb Company, I respectfully submit the enclosed clinical data which evaluated OPDIVO® (nivolumab) with or without YERVOY® (ipilimumab) as a treatment option for patients with malignant pleural mesothelioma to the NCCN® Malignant Pleural Mesothelioma Panel for your consideration.

MAPS-2 is a randomized, non-comparative, phase 2 trial of 2nd or 3rd-line nivolumab as monotherapy or in combination with ipilimumab in patients with unresectable malignant pleural mesothelioma (MPM) who progressed after a maximum of 1 or 2 previous lines of chemotherapy, including pemetrexed/platinum doublet.1

INITIATE is a single-arm, phase 2 study of nivolumab plus ipilimumab in patients MPM who experienced disease progression or recurrence after at least one previous line of platinum-based chemotherapy.2

NivoMes is a single-arm, phase 2 study that investigated nivolumab monotherapy as 2nd-line treatment in patients with recurrent MPM who progressed after at least 1 prior line of chemotherapy.3

MERIT is a multicenter, open-label, single-arm, phase 2 study that investigated the use of nivolumab monotherapy in patients with 2nd or 3rd line advanced or metastatic MPM, resistant or intolerant to platinum-based combination therapy with pemetrexed.4

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.5

OPDIVO® with or without YERVOY® is not FDA-approved for the treatment of patients with malignant pleural mesothelioma.5-6

**Rationale**: Clinical evidence from a phase 2 trial of patients with second or third line malignant pleural mesothelioma who were treated with nivolumab monotherapy or nivolumab plus ipilimumab combination therapy was previously submitted to this panel:

- Scherpereel A, Mazieres J, Greiller L, et al. Second or 3rd line nivolumab (nivo) versus nivo plus ipilimumab (ipi) in malignant pleural mesothelioma (MPM) patients: results of the IFCT-1501 MAPS-2 randomized phase 2 trial. Oral presentation at: the Annual Meeting of the American Society for Clinical Oncology (ASCO); June 1-5, 2017; Chicago, IL, USA.
As part of this submission, we are submitting final results\(^1\) to the previously submitted MAPS-2 study and additional available data\(^2-4\) investigating the use of nivolumab with or without ipilimumab for the treatment of patients with malignant pleural mesothelioma that were presented at the 2018 International Conference of the International Mesothelioma Interest Group (iMiG) and the 2017 and 2016 IASCL World Conferences on Lung Cancer (WCLC).

The following resources are included for your review.

1. 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\(^{th}\) International Conference of the International Mesothelioma Interest Group (iMiG); May 2-5, 2018; Ottawa, Canada.
2. 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\(^{th}\) International Conference of the International Mesothelioma Interest Group (iMiG); May 2-5, 2018; Ottawa, Canada.
3. Baas P. NivoMes: nivolumab in mesothelioma. Oral presentation at: the 17th International Association for the Study of Lung Cancer (IASLC) World Conference on Lung Cancer (WCLC); December 4-7, 2016; Vienna, Austria.

Thank you for your consideration.

Sincerely,

\[\text{Signature}\]

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Vice President, Head US Medical
Bristol-Myers Squibb Company