



Submitted by:

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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 OPDIVO® (nivolumab) as neoadjuvant and adjuvant therapy in patients with non-small cell lung cancer (NSCLC) and as a treatment for patients with malignant pleural mesothelioma (MPM) to the NCCN® Non-Small Cell Lung Cancer/Malignant Pleural Mesothelioma Panel for your consideration.

A presentation at the World Conference on Lung Cancer (WCLC) presented results from the NADIM study, a phase II, single-arm, open-label, multicenter study which evaluated patients with resectable stage IIIA NSCLC who received neoadjuvant nivolumab + paclitaxel + carboplatin followed by adjuvant nivolumab.¹ These are updated results with additional patients to the clinical data presented at the American Society for Clinical Oncology (ASCO) 2018 Annual Meeting, which was previously submitted to this panel.

An additional presentation at the WCLC presented results from the MERIT study, 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.² These are updated results to the clinical data presented at the WCLC 2017, which was previously submitted to this panel.

A recent publication in the *Journal of Thoracic Oncology* reported results from the NivoMes study, 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 These are updated results to the clinical data presented at the WCLC 2016, which was previously submitted to this panel.

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.⁴

The use of OPDIVO® as a neoadjuvant or adjuvant therapy for patients with non-small cell lung cancer or as therapy for patients with malignant pleural mesothelioma is considered investigational.⁴

Rationale: These data are being submitted in response to a standing request from NCCN for new clinical data. Please note there were previous submissions to this panel on May 4, 2018 and June 3, 2018 that included the following data from the NADIM, MERIT, and NivoMes studies:

- Provencio M, Nadal- E, Cobo-Dols M, et al. Neo-adjuvant chemo/immunotherapy for the treatment of stages IIIA resectable non-small cell lung cancer (NSCLC): a phase II multicenter exploratory study-NADIM study-SLCG. Poster presentation at: The American Society for Clinical Oncology (ASCO) Annual Meeting; June 1-5, 2018; Chicago, IL.
- Goto Y, Okada M, Kijima T, et al. A phase II study of nivolumab: a multicenter open-label, single-arm study in malignant pleural mesothelioma (MPM); MERIT. Oral presentation at: the 18th International Association for the Study of Lung Cancer (IASLC) World Conference on Lung Cancer (WCLC); October 15-18, 2017; Yokohoma, Japan.
- 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.

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

1. Provencio M, Nadal-Alforja E, Insa Molla A, et al. Neo-adjuvant chemo/immunotherapy for the treatment of stages IIIA resectable non-small cell lung cancer (NSCLC): a phase II multicenter exploratory study-NADIM: Neo-Adjuvant Immunotherapy. Oral presentation at: International Association for the Study of Lung Cancer (IASLC) 19th World Conference on Lung Cancer (WCLC); September 23-26, 2018; Toronto, Ontario; Canada.
2. Nakano T, Okada M, Kijima T, et al. Long-term efficacy and safety of nivolumab in second- or third-line Japanese malignant pleural mesothelioma patients (phase II: MERIT study Oral presentation at: International Association for the Study of Lung Cancer (IASLC) 19th World Conference on Lung Cancer (WCLC); September 23-26, 2018; Toronto, Ontario; Canada.
3. Quispel-Janssen J, van der Noort V, de Vries JF, et al. Programmed death 1 blockade with nivolumab in patients with recurrent malignant pleural mesothelioma. [published online ahead of print June 13, 2018]. *J Thorac Oncol.* 2018; DOI: 10.1016/j.jtho.2018.05.038.
4. Product Information, OPDIVO[®] (nivolumab) injection for intravenous infusion. Bristol-Myers Squibb Company, Princeton, NJ. August 2018.

Thank you for your consideration.

Sincerely,



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