



Submitted by:

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NCCN Guidelines® Panel: Non-Small Cell Lung Cancer Panel

Dear Panel Members,

On behalf of Bristol-Myers Squibb Company, I respectfully submit the enclosed OPDIVO® (nivolumab) in combination with YERVOY® (ipilimumab), OPDIVO® (nivolumab) in combination with platinum-doublet chemotherapy vs platinum-doublet chemotherapy clinical data to the NCCN® Non-Small Cell Lung Cancer Panel for your consideration.

Two presentations at the American Society for Clinical Oncology (ASCO) presented results from CheckMate 227, an open-label, randomized a phase 3 study of first-line nivolumab + ipilimumab, nivolumab monotherapy, or nivolumab + chemotherapy vs chemotherapy in patients with stage IV or recurrent non-small cell lung cancer (NSCLC).¹⁻²

- Borghaei et al presented efficacy and safety results for nivolumab + ipilimumab, nivolumab + platinum-doublet chemotherapy, or platinum-doublet chemotherapy in patients with <1% tumor PD-L1 expression.¹
- Reck et al presented safety analysis and patient-reported outcomes for patients receiving nivolumab + ipilimumab vs platinum-doublet chemotherapy.²

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.³

The use of OPDIVO® in combination with YERVOY® or platinum-doublet chemotherapy as a first-line therapy for patients with non-small cell lung cancer is considered investigational.³⁻⁴

Rationale: These data are being submitted in response to a standing request from NCCN for new clinical data. Please note there was a previous submission to the NCCN NSCLC Panel on April 16, 2018 that included the following data from CheckMate 227 evaluating nivolumab plus ipilimumab as first-line therapy in patients with stage IV NSCLC:

- Hellmann MD, Ciuleanu TE, Pluzanski A, et al. Nivolumab + ipilimumab vs platinum-doublet chemotherapy as first-line treatment for advanced non-small cell lung cancer (NSCLC): initial results from CheckMate 227. Oral presentation at: the American Association for Cancer Research (AACR) Annual Meeting; April 14-18, 2018; Chicago, IL.
- Hellmann MD, Ciuleanu T-E, Pluzanski A, et al. Nivolumab plus ipilimumab in lung cancer with a high tumor mutational burden [published online April 16, 2018]. *N Engl J Med*. DOI: 10.1056/NEJMoa1801946

- Hellmann MD, Ciuleanu T-E, Pluzanski A, et al. Nivolumab plus ipilimumab in lung cancer with a high tumor mutational burden [Supplementary Appendix] [published online April 16, 2018]. *N Engl J Med*. DOI: 10.1056/NEJMoa1801946

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

1. Borghaei H, Hellmann MD, Paz-Ares L, et al. Nivolumab + ipilimumab, nivolumab + chemotherapy, and chemotherapy in chemo-naïve patients with advanced non-small cell lung cancer and <1% tumor PD-L1 expression: results from CheckMate 227. Oral presentation at: the American Society for Clinical Oncology (ASCO) Annual Meeting; June 1-5, 2018; Chicago, IL.
2. Reck M, Hellmann MD, Paz-Ares L, et al. Nivolumab + ipilimumab vs platinum-doublet chemotherapy as first-line treatment for advanced non-small cell lung cancer: safety analysis and patient-reported outcomes (PROs) from CheckMate 227. Poster presentation at: the American Society for Clinical Oncology (ASCO) Annual Meeting; June 1-5, 2018; Chicago, IL.
3. Product Information, OPDIVO® (nivolumab) injection for intravenous infusion. Bristol-Myers Squibb Company, Princeton, NJ. April 2018.
4. Product Information, YERVOY® (ipilimumab) injection for intravenous infusion. Bristol-Myers Squibb Company, Princeton, NJ. April 2018.

Thank you for your consideration.

Sincerely,

A handwritten signature in black ink, appearing to read 'Awny Farajallah', with a stylized, flowing script.

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