



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) clinical data to the NCCN® Non-Small Cell Lung Cancer Panel for your consideration.

An oral presentation at the American Association for Cancer Research (AACR) 2018 Annual Meeting and *New England Journal of Medicine* publication presented results from CheckMate 227, an open-label, randomized phase 3 trial that included a co-primary endpoint of progression-free survival (PFS) for nivolumab plus ipilimumab versus platinum doublet chemotherapy as first-line therapy in patients with stage IV or recurrent non-small cell lung cancer (NSCLC) whose tumors have a tumor mutational burden (TMB) of  $\geq 10$  mutations/Megabase, regardless of PD-L1 expression.<sup>1-3</sup>

An additional oral presentation at the AACR 2018 Annual Meeting presented results from CheckMate 568, an open-label, non-randomized, phase 2 trial evaluating nivolumab plus ipilimumab as first-line therapy in patients with stage IV NSCLC.<sup>4</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>5</sup>

The use of OPDIVO® in combination with YERVOY® as a first-line therapy for patients with non-small cell lung cancer is considered investigational.<sup>5-6</sup>

**Rationale:** This data is being submitted in response to a standing request from NCCN for new clinical data. The following resources are included for your review:

1. 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.
2. 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

3. 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
4. Ramalingam SS, Hellmann MD, Awad MM, et al. Tumor mutation burden (TMB) as a biomarker for clinical benefit from dual immune checkpoint blockade with nivolumab + ipilimumab in first-line non-small cell lung cancer (NSCLC): identification of TMB cutoff from CheckMate 568. Oral presentation at: the American Association for Cancer Research (AACR) Annual Meeting; April 14-18, 2018; Chicago, IL.
5. Product Information, OPDIVO® (nivolumab) injection for intravenous infusion. Bristol-Myers Squibb Company, Princeton, NJ. April 2018.
6. 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 flourish at the end.

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