

Submitted by:
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November 30, 2015

NCCN Guidelines[®] Panel: Melanoma

Dear Panel Members,

On behalf of Bristol-Myers Squibb Company, I submit to the melanoma panel the prescribing information for OPDIVO[®] (nivolumab) with updated indication. Single agent OPDIVO is now approved for the first line treatment of patients with BRAF V600 wild-type unresectable or metastatic melanoma.

Specific Changes: No specific changes are requested at this time to the current NCCN Guidelines[®] for melanoma.

FDA Clearance: The FDA approved single agent OPDIVO[®] (nivolumab) on November 23, 2015 for the first line treatment of patients with BRAF V600 wild-type unresectable or metastatic melanoma. This is full approval based on overall survival data.

Other currently approved indications for nivolumab are¹:

- Unresectable or metastatic melanoma:
 - as a single agent in patients with BRAF V600 mutation-positive melanoma and disease progression following ipilimumab and a BRAF inhibitor. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.
 - in combination with ipilimumab in patients with BRAF V600 wild-type melanoma. This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.
- Metastatic non-small cell lung cancer in patients with 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.
- Advanced renal cell carcinoma in patients who have received prior antiangiogenic therapy.

Rationale: This submission to NCCN does not summarize the data from the registrational Phase 3 trial for first line use in patients with BRAF wild-type unresectable or metastatic melanoma because the publication from this trial was submitted to NCCN on December 22, 2014.²

The following resources are included for your reference. We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of the publication.

1. Product Information, OPDIVO[®] (nivolumab) injection for intravenous infusion. Bristol-Myers Squibb Company, Princeton, NJ. November 2015.

2. Robert C, Long G, Brady B et. al. Nivolumab in previously untreated melanoma without BRAF mutation. *N Engl J Med*. 2015; 372(4):320-30.

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 Oncology
Bristol-Myers Squibb Company