



**Submitted by:**

Awny Farajallah, MD, FACP  
Vice President, Head US Medical Oncology  
Bristol-Myers Squibb Company  
777 Scudders Mill Road  
Plainsboro, NJ 08536  
609-897-3945; awny.farajallah@bms.com

June 28, 2016

**NCCN Guideline® Panel: Non-Small Cell Lung Cancer (NSCLC)**

Dear Panel Members,

On behalf of Bristol-Myers Squibb Company, I respectfully submit the enclosed published clinical data from the *Journal of Clinical Oncology* for OPDIVO® (nivolumab) for the Panel's consideration. This phase 1 study evaluated the use of nivolumab monotherapy as first-line treatment of patients with advanced NSCLC.

This data is being submitted in response to a standing request from NCCN for new clinical data.

**FDA Clearance (NSCLC indications):** Currently nivolumab is approved for the treatment of patients with metastatic NSCLC, who have progressed on or after platinum-based chemotherapy. Patients with EGFR or ALK aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving nivolumab.<sup>1</sup>

**Rationale:** We are here in providing recently published data from a cohort in a phase 1 trial (CA209-012), that evaluated the safety and efficacy of nivolumab monotherapy for the treatment of patients with stage IIIB/IV NSCLC who had no prior chemotherapy for advanced disease.

**Study CA209-012, monotherapy cohort (N = 52):**<sup>2</sup> This phase 1 multi-cohort study evaluated patients with Stage IIIB/IV NSCLC who have not received prior chemotherapy for advanced NSCLC. Patients received nivolumab monotherapy 3 mg/kg intravenously every 2 weeks until unacceptable toxicity or disease progression. Patients may have received prior radiotherapy or EGFR tyrosine kinase inhibitor therapy if completed at least two weeks prior to study administration. Patients were eligible regardless of their PD-L1 status.

The primary objective of the study was to assess the safety and tolerability of nivolumab monotherapy. Secondary endpoints included objective response rate (ORR), and 24-week progression free survival (PFS) rate. Overall survival (OS) was an exploratory endpoint.

Of the patient population, 94% had stage IV disease, 75% had tumors of non-squamous (NSQ) histology, 15% had EGFR-mutant tumors, 79% were former/current smokers, and 21% and 4% had received prior adjuvant and neoadjuvant systemic platinum-based therapy, respectively. Median follow-up was 14.3 months (range 0.2-30.1). Of the 88% patients (46/52) with available tumor specimens, 70% (32/46) and 30% (14/46) had PD-L1 expression  $\geq 1\%$  and  $< 1\%$ , respectively; and 57% (26/46) and 43% (20/46) had PD-L1 expression  $\geq 5\%$  and  $< 5\%$ , respectively.

## **Safety findings, highlights<sup>2</sup>**

- Any grade treatment-related adverse events (AEs) were reported in 71% of patients. The most commonly reported AEs ( $\geq 10\%$ ) were fatigue (29%), rash (19%), nausea (14%), diarrhea (12%), pruritus (12%), and arthralgia (10%).
- Grade 3 or 4 treatment-related AEs were reported in 19% of patients. The most common event was rash (4%).
- Discontinuation due to treatment-related AEs occurred in 12% of patients.
- No treatment-related deaths were reported.

## **Efficacy findings, highlights<sup>2</sup>**

- Confirmed ORR was 23% (12/52 patients)
  - Ongoing complete response achieved in 4/52 patients (8%)
  - Partial response achieved in 8/52 patients (15%)
  - Stable disease was achieved in 14/52 patients (27%) for a disease control rate of 50%
- Median duration of response was not reached (range: 4.2 months, 25.8+ months)
- Median PFS was 3.6 months (range:  $<0.1+$ , 28+ months)
  - PFS rate at 24 weeks was 41% (95% CI: 27, 54)
- Median OS was 19.4 months (range: 0.2, 35.8+ months)
  - OS rate at 12 months was 73% (95% CI: 59, 83)
  - OS rate at 18 months was 57% (95% CI: 42, 70)
- Efficacy by PD-L1 expression:
  - Confirmed ORR was 28% (9/32) and 14% (2/14) with PDL1-expression of  $\geq 1\%$  and  $<1\%$ , respectively. Confirmed ORR was 31% (8/26) and 15% (3/20) of patients with PD-L1 expression of  $\geq 5\%$  and  $<5\%$ , respectively.

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. Opdivo Prescribing Information.
2. Gettinger S, Rizvi NA, Chow LQ, et al. Nivolumab monotherapy for first-line treatment of advanced non-small cell lung cancer. *J Clin Oncol*. Published Online: June 27, 2016 (doi: 10.1200/JCO.2016.66.9929).

Sincerely,



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