December 4, 2019

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NCCN Guidelines® Panel: Small Cell Lung Cancer (SCLC) Panel

Dear Panel Members,

On behalf of Bristol-Myers Squibb Company, I respectfully submit the enclosed clinical data from CheckMate 032 which was recently published as a manuscript on December 04, 2019 in the *Journal of Thoracic Oncology*.

CheckMate 032, is a Phase 1/2 multicenter, open-label, trial that evaluated the safety and efficacy of nivolumab monotherapy or in combination with ipilimumab for the treatment of patients with recurrent SCLC, who had received at least one prior platinum-containing regimen. With a database lock date of November 6, 2017 and a minimum follow-up of 11.2 months for nivolumab in combination with ipilimumab and 11.9 months for nivolumab monotherapy, the primary endpoint of overall response rate (ORR) was 21.9% with nivolumab in combination with ipilimumab (n=96) versus 11.6% with nivolumab monotherapy (n=147); odds ratio: 2.12 [95% CI: 1.06–4.26]; p=0.03. With a database lock date of April 12, 2019 and a minimum follow-up for overall survival (OS) of 28.4 months for nivolumab in combination with ipilimumab and 29.0 months for nivolumab monotherapy, median (95% CI) OS was 4.7 months (3.1–8.3) versus 5.7 months (3.8–7.6), respectively. Twenty-four-month OS rates were 16.9% for nivolumab in combination with ipilimumab and 17.9% for nivolumab monotherapy. Grade 3–4 treatment-related adverse event rates were 37.5% for nivolumab in combination with ipilimumab and 12.9% for nivolumab monotherapy. Treatment-related deaths occurred in 3 patients receiving nivolumab in combination with ipilimumab and in 1 patient receiving nivolumab monotherapy.[1]

Specific Changes: We request the Panel to modify the recommendation of nivolumab with or without ipilimumab as subsequent systemic therapy for the treatment of SCLC to only include nivolumab monotherapy (SCL-E, 2 OF 4).

FDA Clearance of OPDIVO® (nivolumab) (indication in small cell lung cancer):
• Patients with metastatic small cell lung cancer with progression after platinum-based chemotherapy and at least one other line of therapy.

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

All other uses of nivolumab for patients with small cell lung cancer are considered investigational.[2]

FDA Clearance of YERVOY® (ipilimumab):
The use of ipilimumab for patients with small cell lung cancer is considered investigational.[3]

Rationale: This data is being submitted in response to a standing request from NCCN for new clinical data. Please note that there was a previous submission to NCCN regarding data from CheckMate 032 with database lock dates of

March 24, 2016 (for OS) and November 6, 2015 (for all other efficacy and safety) which was submitted on June 4, 2016.

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

1. Ready NE, Ott PA, Hellmann MD, et al. Nivolumab monotherapy and nivolumab plus ipilimumab in recurrent small cell lung cancer: results from the CheckMate 032 randomized cohort [Epub ahead of print]. *Journal of Thoracic Oncology*; 2019. doi: https://doi.org/10.1016/j.jtho.2019.10.004.
2. Product Information, OPDIVO® (nivolumab) injection for intravenous infusion. Bristol-Myers Squibb Company, Princeton, NJ. September 2019.
3. Product Information, YERVOY® (ipilimumab) injection for intravenous infusion. Bristol-Myers Squibb Company, Princeton, NJ. September 2019.

Thank you for your consideration.
Sincerely,

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