Bristol-Myers Squibb

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NCCN Guidelines® Panel: B-Cell Lymphoma

Dear Panel Members:

On behalf of Bristol-Myers Squibb Company, I respectfully submit the enclosed OPDIVO® (nivolumab) clinical data that has been recently published in *Journal of Clinical Oncology* on August 9, 2019.[1] Additionally, we have also attached the study results that have been presented as a poster presentation at both the American Society of Hematology (ASH) 2018 and European Hematology Association (EHA) 2019 Annual Meeting for review by the NCCN® B-Cell Lymphoma Panel.[2,3]

CheckMate 436 is a phase 1/2 open-label, single-arm, dose-finding, and cohort-expansion study which evaluated the use of nivolumab in combination with brentuximab vedotin for the treatment of patients with non-Hodgkin lymphoma. The study results are from the cohort of patients with relapsed or refractory primary mediastinal b-cell lymphoma (PMBL) who previously received either high dose chemotherapy and autologous hematopoietic cell transplant (auto-HCT) or 2 or more multi-agent chemotherapy regimens if auto-HCT ineligible.[1-3]

FDA Clearance of OPDIVO® (nivolumab) (indications in lymphoma)[4]:

- Adult patients with classical Hodgkin lymphoma that has relapsed or progressed after[a]
  - Autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin, or
  - 3 or more lines of systemic therapy that includes autologous HSCT

The use of nivolumab with or without brentuximab vedotin for patients with primary mediastinal b-cell lymphoma is considered investigational.[4,5]

Rationale: These data are being submitted in response to a standing request from NCCN for new clinical data.

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

1. Zinzani P, Santoro A, Gritti G, et al. Nivolumab combined with brentuximab vedotin for relapsed/refractory primary mediastinal large b-cell lymphoma: efficacy and safety from the phase II Checkmate 436 study. *JCO* 2019. DOI: https://doi.org/10.1200/JCO.19.01492.

[a] 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

2. Moskowitz A., Santoro A, Gritti G, et al. Nivolumab combined with brentuximab vedotin for relapsed/refractory primary mediastinal large b-cell lymphoma: preliminary results from the phase 2 CheckMate 436 trial. Poster presentation at the 60th American Society of Hematology Annual Meeting; December 1-4, 2018; San Diego, C.A., USA.
3. Zinzani PL, Santoro A, Gritti G, et al. Nivolumab combined with brentuximab vedotin for relapsed/refractory primary mediastinal large b-cell lymphoma: efficacy and safety results from the phase 2 CheckMate 436 study. Oral presentation at the 24th Congress of the European Hematology Association (EHA); June 13–16, 2019; Amsterdam, The Netherlands. S1601.
4. Product Information, Opdivo® (nivolumab) injection, for intravenous use. Bristol-Myers Squibb Company, Princeton NJ. May 2019.
5. Product information for Adcetris® (brentuximab vedotin) for injection, for intravenous use. Seattle Genetics, Bothell, WA. November 2018.

Thank you for your consideration.

Sincerely,

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