

Submitted by:

Joseph Leveque, MD
Vice President, US Medical Oncology
Bristol-Myers Squibb Company
777 Scudders Mill Road
Plainsboro, NJ 08536
(609) 897 3945; Joseph.Leveque@bms.com
June 25, 2015

NCCN Guidelines® Panel: Hodgkin Lymphoma

Dear Panel Members:

On behalf of Bristol-Myers Squibb Company, I respectfully request the National Comprehensive Cancer Network (NCCN) Hodgkin Lymphoma Panel to review the enclosed data to consider the use of OPDIVO® (nivolumab) in patients with Classical Hodgkin Lymphoma (HL), after failure of autologous stem cell transplant and brentuximab.

Specific Changes: Please consider adding nivolumab to the list of regimens in “Additional Therapy Option (only for CHL)”, for relapsed or refractory HL patients, after failure of autologous stem cell transplant and brentuximab (page HODG-E).

FDA Clearance: The FDA has granted Breakthrough Therapy Designation for nivolumab in treatment of patients with HL after failure of autologous stem cell transplant and brentuximab.¹ Currently, nivolumab monotherapy has been approved in two solid tumor types: unresectable or metastatic melanoma (accelerated approval) and squamous non-small cell lung cancer (complete indications provided in the enclosed prescribing information).²

Background on Rationale:

High-dose therapy with autologous stem cell rescue (ASCR) appears to significantly improve outcome relative to treatment with conventional chemotherapy alone for patients with refractory disease or high-risk relapses. However, approximately 50% of patients relapse following ASCR, with lack of CR to second-line therapy prior to ASCR portending a worse prognosis for this patient population. [J Natl Compr Canc Netw. 2011 September 1; 9(9): 1060–1071.] Brentuximab is a treatment option for these patients; however, subsequent failures are left with no standard of care. Therefore, it is critically important to identify a retrieval regimen for patients with relapsed or refractory HL following ASCR and brentuximab.

Nivolumab

Data from an ongoing Phase 1b study of relapsed and refractory hematological malignancies showed clinical activity of nivolumab in heavily pre-treated patient population with HL.³ These findings were published in New England Journal of Medicine and updated data were presented at the 2015 congress of the European Hematology Association (EHA).⁴

BMS Study CA209-039:^{3,4} This Phase 1 dose escalation and expansion study enrolled patients with relapsed or refractory hematologic malignancies (105 patients overall, 23 patients with HL), ECOG PS of 0 to 1, previous treatment with at least one chemotherapy regimen and no autologous stem-cell transplantation within 100 days. The study was initiated at nivolumab 1 mg/kg with escalation to 3 mg/kg. Maximum tolerated dose was not reached at 3 mg/kg and the cohort was expanded. Patients received nivolumab every 2 weeks until disease progression or complete response or up to 2 years. Safety was the primary endpoint; secondary endpoints were investigator assessed best overall response (BORR), objective response (OR), duration of response (DoR), progression free survival (PFS), and biomarker studies.

All patients were heavily pre-treated; 78% had received brentuximab and 78% had undergone autologous stem-cell transplantation.

Efficacy findings, highlights:

- Objective response was reported in 20 patients (87%); 6 patients (26%) had a complete response and 14 patients (61%) had a partial response; the remaining 3 patients (13%) had stable disease.
- At median follow-up of 86 weeks (range: 32, 107+), 50% of the responses were ongoing and median duration of response was not reached (range: 2, 91+)

Safety findings, highlights:

- Drug-related adverse events (AEs), any grade, were reported in 19 patients (83%).
- Drug related Grade 3 AEs were reported in 5 patients (22%); there were no reports of Grade 4 or 5 AEs.
- Three patients discontinued treatment due to drug-related AEs

The following resources are included for your review. We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of some of these publications/ presentations.

- ¹ Investigational PD-1 Immune Checkpoint Inhibitor Nivolumab Receives U.S. FDA Breakthrough Therapy Designation for Hodgkin Lymphoma. Bristol-Myers Squibb press release. 14 May 2014.
- ² OPDIVO Prescribing Information
- ³ Ansell SM, Lesokhin AM, Borrello I, et al. PD-1 Blockade with Nivolumab in Relapsed or Refractory Hodgkin's Lymphoma. NEJM 2015;372:311-9.
- ⁴ Armand P, Timmerman J, Lesokhin AM, et al. Nivolumab in Relapsed or Refractory Lymphoid Malignancies and Classical Hodgkin Lymphoma: Updated Results of a Phase 1 Study. Presented at 20th Congress of the European Hematology Association. June 2015; Vienna, Austria.

Thank you for your consideration of this request.

Sincerely,

A handwritten signature in black ink, consisting of a large, stylized 'J' followed by a horizontal line.

Joseph Leveque, MD
Vice President, US Medical Oncology
Bristol-Myers Squibb Company