Genentech
A Member of the Roche Group

Submitted by:
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Dear NCCN B-Cell Lymphomas Panel:

We respectfully request the B-Cell Lymphomas Panel to consider the enclosed Phase II GO29365 study on the use of Polivy™ (polatuzumab vedotin) in combination with bendamustine and rituximab (BR) for the treatment of patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL).

Request:
For your updating purposes, please consider the recent JCO publication and updated results from the Phase II GO29365 study presented at the American Society of Hematology (ASH) 2019 meeting.

Rationale:
This submission is an update to the previous submission dated June 10th, 2019, as the pivotal study was recently published in the *Journal of Clinical Oncology* on November 6, 2019.[1] We have also enclosed updated results from the study that were recently presented at the 2019 American Society of Hematology (ASH) Meeting.[2]

American Society of Hematology (ASH) 2019 Data:[2]
Data with a longer median follow-up of 30 months from the GO29365 study was recently presented at the 2019 ASH Conference. Results of the longer follow up were consistent with previous data readout conclusions, as Polivy-BR demonstrated improved efficacy outcomes vs BR.

- mPFS by INV= 7.5 months vs 2.0 months (HR: 0.33; 95% CI: 0.2-0.56; p<0.0001)
- mOS= 12.4 months vs 4.7 months (HR: 0.41; 95% CI: 0.24-0.71; p=0.0011)
- mDOR by INV for all responding patients in Polivy-BR (n=28) vs BR (n=13) was 12.7 months vs 4.1 months (HR:0.42; 95% CI: 0.19-0.91; p=0.0245)
- Durability of response outcomes from the combined Phase Ib/II studies (n=45) showed that 38% (17/45) patients had response durations ≥12 months (INV) and 29% (13/45) patients had long-term duration responses lasting ≥24 months (INV).

No new safety signals were identified with longer follow-up. The safety-evaluable population included all patients in the Phase Ib/II randomized arms that received at least one dose of any study drug (Polivy-BR, n=45). Peripheral neuropathy (PN) occurred in 40% (18/45) of Polivy-BR patients and were all Grade 1-2 events. 56% of patients experienced complete resolution of peripheral neuropathy. Second malignancies occurred in 4% (2/45) of Polivy-BR and 5% (2/39) of BR patients. No new viral or *Pneumocystis jirovecii* pneumonia (PJP) infections were observed with additional follow up.

FDA Clearance:

- Polivy is FDA approved in combination with bendamustine and a rituximab product, for the treatment of adult patients with R/R DLBCL, not otherwise specified, after at least two prior therapies.
- Accelerated approval was granted for this indication based on complete response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- Please refer to the product prescribing information for the full FDA-approved indication and safety information of Polivy, available at: https://www.gene.com/download/pdf/polivy_prescribing.pdf

- Rituxan ® (rituximab) is FDA-approved for the treatment of adult patients with Non-Hodgkin's Lymphoma (NHL), Chronic Lymphocytic Lymphoma (CLL), Rheumatoid Arthritis (RA), Granulomatosis with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA), and moderate to severe Pemphigus Vulgaris (PV). Please refer to the product prescribing information for the full FDA-approved indications and safety information of Rituxan, available at: https://www.gene.com/download/pdf/rituxan_prescribing.pdf

Thank you for your consideration and I hope this information is helpful to you. If you have any questions, please contact us at the phone number and email provided above.

Respectfully submitted,
Hannah Lee, PharmD

References:

1. Sehn LH, Herrera AF, Flowers CR, et al. Polatuzumab vedotin in relapsed or refractory diffuse large b-cell lymphoma (epub ahead of print). J Clin Oncol. 2019:JCO1900172. DOI: 10.1200/JCO.19.00172. https://www.ncbi.nlm.nih.gov/pubmed/31693429
2. Sehn LH, Matasar MJ, Flowers CR, et al. Polatuzumab vedotin plus bendamustine with rituximab in relapsed/refractory diffuse large b-cell lymphoma: updated results of a phase Ib/II randomized study. Presented at the American Society of Hematology (ASH) 2019 Congress in Orlando, Florida; December 7-10, 2019. ASH Abstract #4081.