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NCCN Guidelines® Panel: Non-Hodgkin Lymphoma

On behalf of Seattle Genetics, Inc., I respectfully request the *National Comprehensive Cancer Network (NCCN) Non-Hodgkin's Lymphoma Panel* to review the enclosed data for inclusion of the use of ADCETRIS® (brentuximab vedotin) for the treatment of patients with relapsed/refractory (R/R) CD30-positive diffuse large B-cell lymphoma (DLBCL).

Specific Changes:
Recommend ADCETRIS (brentuximab vedotin) as a treatment option for CD30-positive R/R DLBCL.

FDA Clearance:
ADCETRIS (brentuximab vedotin) is a CD30-directed antibody-drug conjugate indicated for:

- The treatment of patients with Hodgkin lymphoma after failure of autologous stem cell transplant (ASCT) or after failure of at least two prior multi-agent chemotherapy regimens in patients who are not ASCT candidates.[1]
- The treatment of patients with systemic anaplastic large cell lymphoma after failure of at least one prior multi-agent chemotherapy regimen.[1]

These indications are based on response rate. There are no data available demonstrating improvements in patient reported outcomes or survival with ADCETRIS.[1]

Rationale:
Brentuximab vedotin offers a viable treatment option for a group of patients who have very poor outcomes after failing prior therapies. The administration of single agent brentuximab vedotin resulted in an overall response rate of 42% and a complete response rate of 16% in patients with R/R CD30-positive DLBCL who had received a median of 2 prior systemic therapies. The safety profile was consistent with the labeled indications.[2]

Data Summary:
Current standard of care for DLBCL salvage therapy is high-dose chemotherapy followed by autologous stem cell transplantation (ASCT); however a large proportion of patients relapse post ASCT[3]. Additionally, some patients may not be able to tolerate high-dose chemotherapy. Hence, there is an unmet need for further treatment options for patients with R/R DLBCL.

The safety and efficacy of brentuximab vedotin in patients with R/R CD30-positive (per local pathology laboratory immunohistochemistry assessment) DLBCL (n=50) was evaluated in an open-label, phase 2 trial. The majority (92%) of patients had an ECOG performance status of 0 or 1. Advanced stage disease (III-IV) was seen in 72% of the patients. Other notable patient characteristics include: 74% of patients were refractory to front-line therapy, 82% of patients were refractory to the most recent prior therapy, and the median number of prior systemic therapy received was 2 (range 1-6)[2].

Treatment with brentuximab vedotin produced an overall response rate of 42% with 16% complete remission (CR) rate. Although all patients were determined to be CD30-positive at the local pathology lab, some patients had very low or undetectable CD30 upon central pathology lab review. Responses were seen in patients with all levels of CD30 expression levels, including undectable by standard immunohistochemistry. The median duration of response was 5.8 months, and the median response duration for CR was 11.5 months. The median progression-free survival for all patients was 4.0 months (95% CI, 1.6-5.0). The median number of brentuximab vedotin cycles received was 4 (range, 1-19).[2]

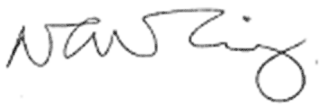
Treatment related serious adverse events were pneumonia (n=3), anemia, febrile neutropenia, neutropenia, thrombocytopenia (n=2 each). Five patients died within 30 days of therapy; all of these deaths were disease related.[2] A manuscript of this phase 2 clinical trial is currently in preparation and will be submitted for publication shortly.

In addition, an ongoing clinical trial of R/R DLBCL patients will evaluate single-agent brentuximab vedotin in the treatment of 50 patients with undetectable CD30 expression as well as a cohort of 15 CD30-positive patients in combination with rituximab (NCT01421667).[4]

Finally, a Phase 2 trial to evaluate brentuximab vedotin plus R-CHOP in the frontline treatment of patients with DLBCL is ongoing.

As brentuximab vedotin has demonstrated promising antitumor activity in R/R CD30-positive DLBCL, we respectfully request that panel members consider adding brentuximab vedotin as a treatment option in the NCCN Guidelines for NHL.

Sincerely,



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References:

1. ADCETRIS® (brentuximab vedotin) for Injection U.S. Prescribing Information. Seattle Genetics, Inc. September 2013.
2. Bartlett NL, Sharman JP, Oki Y, et al. A phase 2 study of brentuximab vedotin in patients with relapsed or refractory CD30-positive non-Hodgkin lymphomas: Interim results in patients with DLBCL and other B-cell lymphomas. Poster presentation at the American Society of Hematology Annual Meeting. December 7-10, 2013; New Orleans, LA. Abstract #848. (Enclosed)
3. Gisselbrecht C, Glass B, Mounier N, et al. Salvage regimens with autologous transplantation for relapsed large B-cell lymphoma in the rituximab era. J Clin Oncol. 2010;28(27):4184-90.
4. A Study of Brentuximab Vedotin in Relapsed or Refractory Non-Hodgkin Lymphoma. ClinicalTrials.gov website. https://clinicaltrials.gov/ct2/show/NCT01421667?term=NCT01421667&rank=1 Updated April 30, 2014. Accessed May 16, 2014.