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NCCN Guidelines® Panel: Non-Hodgkin's 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 expanding the use of ADCETRIS® (brentuximab vedotin) to include mycosis fungoides.

Specific Changes: Recommend brentuximab vedotin as a treatment option for relapsed or refractory mycosis fungoides.

FDA Clearance: Brentuximab vedotin is approved 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.
- The treatment of patients with systemic anaplastic large cell lymphoma after failure of at least one prior multi-agent chemotherapy regimen.

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

Rationale:

Mycosis fungoides is the most common type of cutaneous T-cell lymphoma. The acceptable treatment of mycosis fungoides includes topical and systemic therapies, alone or in combination. The decision on which therapy to use mainly depends on the clinical stage, TMNB classification, and major prognostic factors.

Data supporting the use of brentuximab vedotin for mycosis fungoides are derived from two phase 2 studies. In the first study, Krathen et al reported results of a phase 2 investigator-sponsored trial to evaluate the response rate of brentuximab vedotin in patients (N = 20) with stages IB-IVB mycosis fungoides who failed at least one prior systemic therapy. Data were presented in an oral session at the 2012 American Society of Hematology meeting. The overall response rate (ORR) was 70% (n = 14). There was a statistically significant correlation between clinical response and stage. The ORR for patients who were stage IB (n=2), stage IIB (n=11), and IVA/B (n=7) was 100%, 91%, and 29%, respectively. The median event-free survival was 31 weeks (range, 4-61+).

Grade 3-5 AEs reported were skin eruption (n=3), neutropenia (n=2), and peripheral neuropathy, pain, thrombocytopenia, respiratory failure, acute renal failure, decreased white blood cell count, febrile neutropenia, hyperglycemia, lymphocytosis, pneumonia, pruritis, and sepsis, which occurred in one patient each.

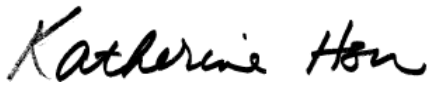
In a second study, Duvic et al evaluated the safety and efficacy of brentuximab vedotin in patients with cutaneous CD30+ lymphoproliferative disorders and CD30+ mycosis fungoides in a phase 2 investigator-initiated study. Data were presented at the 2012 American Society of Hematology meeting and updated at a plenary session of the 2013 Society of Investigative Dermatology.

A total of 64 patients have been enrolled on study, of whom 50 were evaluable for toxicity (received ≥1 dose) and 46 were evaluable for efficacy (received ≥2 doses). Eligible patients had histologically confirmed CD30+ disease within 12 months of treatment and progression after radiation or systemic therapy. The ORR was 72%. The median duration of response in mycosis fungoides patients was 22 weeks (range, 3-56). Grade 3 adverse events included neutropenia (n=3), elevated liver function tests (n=1), nausea (n=2), hypoglycemia (n=1), unstable angina (n=2), infection (n=2), deep vein thrombosis (n=1), pulmonary embolism (n=1), fatigue (n=1), arthralgia (n=2) and dehydration (n=1).

In addition to the two phase 2 trials, other investigators have described in case reports successful use of brentuximab vedotin for cutaneous T-cell lymphoma. (Mody et al.)

These phase II studies evaluating the use of brentuximab vedotin as a single agent in patients with relapsed mycosis fungoides demonstrate efficacy and manageable toxicity. We respectfully request that NCCN NHL panel members consider adding brentuximab vedotin as a treatment option for patients with mycosis fungoides.

Sincerely,



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References:

ADCETRIS® (brentuximab vedotin) prescribing information. Seattle Genetics, Inc. January 2012.

Duvic M, Tetzlaff M, Gangar P, Clos AL, Talpur R. Phase II trial of brentuximab vedotin (SGN-35) for CD30+ cutaneous T-cell lymphomas and lymphoproliferative disorders. J Invest Dermatol 2013;133: Abstract 1058.

Duvic M, Tetzlaff M, Clos AL, et al. Results of a phase II trial of brentuximab vedotin (SGN-35) for CD30+ cutaneous T-cell lymphomas and lymphoproliferative disorders. Blood 2012;120: Abstract 3688.

Krathen M, Bashey S, Sutherland K, et al. Brentuximab vedotin demonstrates clinical activities in mycosis fungoides/Sézary syndrome. Blood 2012:120: Abstract 797.

Mody K, Wallace JS, Stearns DM, et al. CD30-positive cutaneous T-cell lymphoma and response to brentuximab vedotin: 2 illustrative cases. Clin Lymphoma Myeloma Leuk. 2013;13:319-23.

Additional Data Enclosures

ASH 2012 Oral Presentation for abstract 797

ASH 2012 Poster presentation for abstract 3688

SID 2013 Poster presentation for abstract 1058