

25 May 2010

To Whom It May Concern:

On behalf of Millennium: the Takeda Oncology Company, I respectfully request that the NCCN Non-Hodgkin's Lymphoma Panel review the attached application which is summarized below. The application consists of a word document summarizing data supporting the requested indication along with the relevant references.

Bortezomib in Marginal Zone Lymphoma (MZL)

- The data demonstrate the efficacy of bortezomib in MZL.
- The purpose of this submission is to request that bortezomib be listed as a treatment option for newly diagnosed and relapsed MZL with a Category 2A recommendation. As there are no recommended treatment regimens specific for MZL, this request is for the addition of a footnote to the recommendations on the MZL pages noting bortezomib as a treatment option.
- MZL is not part of the FDA approved label for bortezomib; bortezomib is approved for multiple myeloma and for mantle cell lymphoma after at least 1 prior therapy.

The following references are being submitted in support of this proposed change. We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of some of these publications.

1. Conconi A, Martinelli G, Lopez-Guillermo A, et al. Single agent bortezomib is active in relapsed/refractory MALT lymphomas. Final results of an international extranodal lymphoma study group (IELSG) phase II study [abstract 1044]. *Haematologica*. 2009;94:419.
2. Di Bella N, Taetle R, Kolibaba K, et al. Results of a phase 2 study of bortezomib in patients with relapsed or refractory indolent lymphoma. *Blood*. 2010;115(3):475-480.
3. O'Connor OA, Portlock C, Moskowitz C, et al. Time to treatment response in patients with follicular lymphoma treated with bortezomib is longer compared with other histologic subtypes. *Clin Cancer Res*. 2010;16(2):719-726.
4. Spadaro P, Pitini V, Toscano G, et al. Clinical activity of bortezomib in relapsed or refractory gastric marginal zone b-cell lymphoma of malt type [abstract 8567]. *J Clin Oncol*. 2008;26:470s
5. Troch M, Jonak C, Mullauer L, et al. A phase II study of bortezomib in patients with MALT lymphoma. *Haematologica*. 2009;94(5):738-742
6. Ribrag V, Gisselbrecht C, Haioun C, et al. Efficacy and toxicity of 2 schedules of frontline rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone plus bortezomib in patients with B-cell lymphoma: a randomized phase 2 trial from the French Adult Lymphoma Study Group (GELA). *Cancer*. 2009;115(19):4540-4546.
7. Gerecitano J, Portlock CS, Hamlin PA, et al. Rituximab, cyclophosphamide, bortezomib and prednisone (R-CBorP): final results of a phase I trial evaluating two dosing schedules and the safety of overlapping pegfilgrastim in patients with relapsed/refractory indolent and mantle cell lymphomas [abstract 3708]. *Blood*. 2009;114:1428a
8. Chiappella A, Pregno P, Zinzani PL, et al. The combination of bortezomib and rituximab is effective and safe in relapsed/refractory indolent non follicular and mantle-cell non Hodgkin lymphoma: a phase II multicenter study by Intergruppo Italiano Linfomi [abstract 3758]. *Blood*. 2009;114:1446a-1447a.
9. De Vos S, Goy A, Dakhil SR, et al. Multicenter randomized phase II study of weekly or twice-weekly bortezomib plus rituximab in patients with relapsed or refractory follicular or marginal-zone B-cell lymphoma. *J Clin Oncol*. 2009;27(30):5023-5030.

We are looking forward to your decision. Please do not hesitate to contact us if you need any additional information or if you have any questions.

Thank you.

Yours sincerely,

Dixie

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