



Submitted by:  
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Dear NCCN Non-Hodgkin's Lymphoma Guidelines Panel Members:

On behalf of Celgene Corporation, we respectfully request that the NCCN Guidelines Panel for Non-Hodgkin's Lymphomas (NHL) review recent updated data regarding the use of REVLIMID® (lenalidomide) in combination with rituximab as first line therapy in patients with follicular lymphoma (FL). This is in follow-up to earlier data that had been submitted to the panel the previous year (refer to the attached document *FL Celgene Submission 27June2013*).

Specific Changes: Recommend the use of lenalidomide in combination with rituximab as a suggested treatment regimen for FL (grade 1-2) as first line therapy. In addition, we respectfully request an update to the discussion surrounding first-line therapies for FL to reflect the recently presented results.

FDA Clearance: The FDA has not approved lenalidomide for the treatment of FL. Please refer to the attached Prescribing Information for the FDA approved indications.

Rationale: A multi-center, single-arm, Phase II Alliance/Cancer and Leukemia Group B (CALGB) study of lenalidomide in combination with rituximab in 65 previously untreated patients with grade 1-3a FL was recently presented at the 50th Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago, Illinois (Martin et al. 2014). Patients had stage III-IV or bulky stage II ( $\geq 7$  cm) disease and a Follicular Lymphoma International Prognostic Index (FLIPI) score of 0-2. Lenalidomide was initiated at a dose of 20 mg/day, and was able to be escalated to a target dose of 25 mg/day in 54 (84%) patients. Treatment was administered on Days 1-21 of each 28-day cycle for 12 planned cycles. Rituximab 375 mg/m<sup>2</sup> was administered weekly for 4 weeks during Cycle 1 and then on Day 1 of Cycles 4, 6, 8 and 10. Overall response was observed in 96% of evaluable patients, with 71% complete response (CR) and 25% partial response (PR), without association between FLIPI score, bulk, or grade and CR. At a median follow-up of 2.3 years, 2-year progression-free survival (PFS) was 89%. Grade 3/4 hematologic adverse events (AEs) included neutropenia (19%), lymphopenia (8%), and thrombocytopenia (2%). Febrile neutropenia occurred in 1 patient. Grade 3/4 non-hematologic AEs occurring in at least 2 patients included rash (8%), infection (8%), pain (6%), fatigue (6%), and tumor lysis (3%).

The results from this Alliance/CALGB study expand on and corroborate the findings of the single-center, single-arm, Phase II study of lenalidomide in combination with rituximab in patients with previously untreated, stage III or IV indolent NHL, already described within the guidelines (Fowler et al. 2012).

A copy of the Martin et al. poster from ASCO 2014 is attached for your review.

Your consideration of this submission is greatly appreciated.

Sincerely,



Carole Zuckerman, RPh  
Senior Therapeutic Manager, Global Medical Information



Kenneth Foon, MD  
Vice President, Medical Affairs Global Disease Lead – Lymphoma and CLL

Cited References:

1. Fowler NH, Neelapu SS, Hagemeister FB, et al. Lenalidomide and Rituximab for Untreated Indolent Lymphoma: Final Results of a Phase II Study [oral]. *Oral presented at: 54th Annual Meeting of the American Society of Hematology (ASH) 2012; December 8-11; Atlanta, GA; USA.*
2. Martin P, Jung SH, Johnson JL, et al. CALGB 50803 (Alliance): A phase II trial of lenalidomide plus rituximab in patients with previously untreated follicular lymphoma [poster]. *Poster presented at: 50th Annual Meeting of the American Society of Clinical Oncology (ASCO) 2014; May 30-June 3; Chicago, IL USA*