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Date of request: June 22, 2011

NCCN Guidelines Panel: Non-Hodgkin's Lymphoma

On behalf of Genentech, I respectfully request the NCCN Non-Hodgkin's Lymphoma (NHL) Guideline Panel to review the enclosed data for Rituxan[®] (Rituximab) plus lenalidomide for the treatment of NHL.

Specific Changes: Consider the recently presented data on Rituxan plus lenalidomide for the treatment of NHL for your updating purposes.

FDA Clearance: The FDA has not approved Rituxan plus lenalidomide for the treatment of NHL. Please refer to the enclosed prescribing information (PI) for the full FDA-approved indications and safety information.

Rationale: Results from three Phase II studies evaluating Rituxan plus lenalidomide for the treatment of NHL were recently presented at the 11th International Conference on Malignant Lymphoma (ICML) on June 15-18 in Lugano, Switzerland.¹⁻³ In a Phase II study by Fowler and colleagues, the overall response rate (ORR) was 90% (n=70) for patients with untreated indolent NHL who received Rituxan plus lenalidomide. In a Phase I/II study by Wang and colleagues, patients with relapsed/refractory mantle cell lymphoma who received Rituxan plus lenalidomide had an ORR of 57.8% (n=52). In another Phase I/II study, Nowakowski and colleagues reported an ORR of 100% (n=30) in patients with aggressive B-cell lymphomas who were treated with Rituxan plus lenalidomide. The most frequently reported Grade 3/4 adverse events in the three studies were thrombocytopenia, lymphopenia, neutropenia, febrile neutropenia, fatigue, rash, muscle pain, thrombosis, and dehydration.

Additional data on Rituxan plus lenalidomide for the treatment of NHL has been previously reported.⁴⁻¹³

The following enclosures are included for your review (copyright-paid where applicable):

- Fowler N, Hagemester F, Mclaughlin P, et al. Lenalidomide plus rituximab is a highly effective and well-tolerated biologic therapy in untreated indolent B cell non-hodgkin's lymphoma. Ann Oncol 2011;22(suppl 4):iv128-iv129. ICML Abstract #137.
- Wang M, Fayad L, Wagner-Bartak N, et al. Oral lenalidomide plus 4 doses of rituximab induced prolonged remissions in relapsed/refractory mantle cell lymphoma: a completed phase I/II clinical trial. Ann Oncol 2011;22(suppl 4):iv119-iv120. ICML Abstract #109.
- Nowakowski G, Reeder CB, Laplant B, et al. Combination of lenalidomide with R-CHOP (R2CHOP) is safe and effective as initial therapy for aggressive B-cell lymphomas – a phase I/II study. Ann Oncol 2011;22(suppl 4):iv119-iv120. ICML Abstract #110.
- Rituxan Prescribing Information

Cited References

1. Fowler N, Hagemester F, McLaughlin P, et al. Lenalidomide plus rituximab is a highly effective and well-tolerated biologic therapy in untreated indolent B cell non-hodgkin's lymphoma. *Ann Oncol* 2011;22(suppl 4):iv128-iv129. ICML Abstract #137.
2. Wang M, Fayad L, Wagner-Bartak N, et al. Oral lenalidomide plus 4 doses of rituximab induced prolonged remissions in relapsed/refractory mantle cell lymphoma: a completed phase I/II clinical trial. *Ann Oncol* 2011;22(suppl 4):iv119-iv120. ICML Abstract #109.
3. Nowakowski G, Reeder CB, Laplant B, et al. Combination of lenalidomide with R-CHOP (R2CHOP) is safe and effective as initial therapy for aggressive B-cell lymphomas – a phase I/II study. *Ann Oncol* 2011;22(suppl 4):iv119-iv120. ICML Abstract #110.
4. Ahmadi T, Chong EA, Gordon A, et al. Phase II trial of lenalidomide - dexamethasone - rituximab in relapsed or refractory indolent B cell or mantle cell lymphomas resistant to rituximab. *Blood* 2010;116:ASH Abstract #3962.
5. DeRook I, Odonnell RT, Noble B, et al. R(2): Preliminary results of a phase II study of lenalidomide and rituximab in relapsed/refractory indolent non-Hodgkin's lymphoma (NHL). *Blood* 2008;112:ASH Abstract #3060.
6. Dutia M, DeRoock I, Reed-Pease C, et al. Lenalidomide overcomes Fc γ R3-mediated resistance to rituximab in patients with relapsed/refractory indolent non-Hodgkin's lymphoma (NHL): A correlative analysis of a phase 2 study. *Blood* 2010;116:ASH Abstract #3967.
7. Dutia M, DeRoock I, Chee K, et al. Analysis of a phase 2 study of lenalidomide and rituximab in relapsed or refractory non-Hodgkin's lymphoma. *Haematologica* 2010;95(suppl 2):EHA Abstract #0295.
8. Fowler N, McLaughlin P, Hagemester FB, et al. A biologic combination of lenalidomide and rituximab for front-line therapy of indolent B-cell non-Hodgkin's lymphoma. *Blood* 2009;114:ASH Abstract #1714.
9. Ivanov V, Tabouret E, Chuto G, et al. Rituximab-lenalidomide-dexamethasone induces complete and durable remission in relapsed refractory diffuse large B-cell non-Hodgkin lymphoma. *Leuk Lymphoma* 2010;51:1758-1760.
10. Tempescul A, Ianotto JC, Guillermin G, et al. Lenalidomide in elderly patients with mantle cell lymphoma. *Haematologica* 2009;94(suppl 2):EHA Abstract #0187.
11. Veliz M, Santana R, Lancet JE, et al. Phase II study of lenalidomide in combination with rituximab for patients with CD5+/CD20+ hematologic malignancies who relapse or progress after rituximab. Interim analysis. *Blood* 2009;114:ASH Abstract #2376.
12. Nowakowski GS, LaPlant B, Habermann T, et al. A phase I/II trial of lenalidomide and RCHOP (R2CHOP) in patients with newly diagnosed diffuse large B-cell (DLBCL) and follicular grade 3 lymphoma. *Blood* 2009;114:ASH Abstract #1669.
13. Vitolo U, Chiappella A, Carella AM, et al. Prospective, multicenter phase I-II pilot trial to evaluate efficacy and safety of lenalidomide plus rituximab CHOP21 (LR CHOP21) for elderly patients with untreated diffuse large B cell lymphoma (DLBCL) interim analysis of the Intergruppo Italiano Linfomi (IIL) REAL07 study. *Blood* 2010;116:ASH Abstract #2871.