

Submitted by:  
Emily Costerison, Pharm.D., Scientist  
Medical Communications, Medical Affairs  
Genentech, Inc.  
1 DNA Way  
South San Francisco, CA 94080  
Phone: (650) 225-8084  
Email: [mc-mc-d@gene.com](mailto:mc-mc-d@gene.com)  
Date of request: January 11, 2011  
NCCN Guidelines Panel: Non-Hodgkin's Lymphomas

On behalf of Genentech, I respectfully request the NCCN Non-Hodgkin's Lymphomas Guideline Panel to review the enclosed data for Rituxan<sup>®</sup> (rituximab) maintenance for the treatment of non-Hodgkin's lymphoma (NHL).

Specific Changes: Consider the recently published and presented data on the use of Rituxan maintenance for the treatment of NHL for your updating purposes.

FDA Clearance: The FDA has not approved Rituxan maintenance for the treatment of follicular NHL. Please refer to the enclosed prescribing information for the full FDA-approved indications and safety information.

Rationale: Results from the Phase III, international, multicenter, randomized PRIMA (Primary Rituximab and MAintenance) study were recently published in *The Lancet* and presented at the 52<sup>nd</sup> American Society of Hematology (ASH) meeting and exposition on December 4-7, 2010.<sup>1-3</sup> The PRIMA study evaluated Rituxan maintenance every 8 weeks for 2 years in patients with previously untreated advanced follicular NHL who responded to initial treatment with Rituxan plus chemotherapy. At a median follow-up of 36 months, the primary endpoint, progression free survival (PFS), was 74.9% (95% CI: 70.9-78.9) in the Rituxan maintenance group compared with 57.6% (95% CI: 53.2-62.0) in the observation group (hazard ratio [HR]=0.55; 95% CI: 0.44-0.68, p<0.0001). Grade 3 and 4 adverse events were reported in 24% of patients in the Rituxan maintenance group and 17% of patients in the observation group.

Results from additional studies on Rituxan maintenance were also presented at the 2010 ASH meeting.<sup>4-11</sup>

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

- Ardeschna KM, Smith P, Qian W, et al. An intergroup randomized trial of rituximab versus a watch and wait strategy in patients with stage II, III, IV, asymptomatic, non-bulky follicular lymphoma (grades 1, 2 and 3a). A preliminary analysis. *Blood* 2010;116:5. ASH Abstract #6.
- Ardeschna KM, Smith P, Qian W, et al. An intergroup randomized trial of rituximab vs a watch & wait approach in patients with advanced stage, asymptomatic, non-bulky follicular lymphoma. Presented at the 52<sup>nd</sup> American Society of Hematology Annual Meeting and Exposition in Orlando, Florida; December 4-7, 2010. ASH Presentation #6.
- Foá R, Di Rocco A, van Hazel G, et al. Maintenance rituximab every 2 months for 2 years is effective and well tolerated in patients with follicular lymphoma with both standard or rapid infusion: updated results from the phase IIb MAXIMA study. *Blood* 2010;116:1608. ASH Abstract #3945.

- Foá R, Di Rocco A, van Hazel G, et al. Maintenance rituximab every 2 months for 2 years is effective and well tolerated in patients with follicular lymphoma with both standard or rapid infusion: updated results from the phase IIIb MAXIMA study. Presented at the 52<sup>nd</sup> American Society of Hematology Annual Meeting and Exposition in Orlando, Florida; December 4-7, 2010. ASH Poster #3945
- Salles GA, Catalano J, Feugier P, et al. Updated results of the PRIMA study confirms the benefit of 2-years rituximab maintenance in follicular lymphoma patients responding to immunochemotherapy. Blood 2010;116:746. ASH Abstract #1788
- Salles GA, Catalano J, Feugier P, et al. Updated results of the PRIMA study confirms the benefit of 2-years rituximab maintenance in follicular lymphoma patients responding to immunochemotherapy. Presented at the 52<sup>nd</sup> American Society of Hematology Annual Meeting and Exposition in Orlando, Florida; December 4-7, 2010. ASH Poster #1788.
- Salles G, Seymour JF, Offner F, et al. Rituximab maintenance for 2 years in patients with high tumour burden follicular lymphoma responding to rituximab plus chemotherapy (PRIMA): a phase 3, randomized controlled trial. Lancet 2010;377:42-51.
- Taverna CJ, Bassi S, Hitz F, et al. Rituximab maintenance treatment for a maximum of 5 years in follicular lymphoma: safety analysis of the randomized phase III trial SAKK 35/03. Blood 2010;116:752. ASH Abstract #1802.
- Taverna CJ, Bassi S, Hitz F, et al. Rituximab maintenance treatment for a maximum of 5 years in follicular lymphoma: safety analysis of the randomized phase III trial SAKK 35/03. Presented at the 52<sup>nd</sup> American Society of Hematology Annual Meeting and Exposition in Orlando, Florida; December 4-7, 2010. ASH Poster #1802.
- Vidal L, Gafter-Gvili A, Salles G, et al. Rituximab maintenance for the treatment of patients with follicular lymphoma: systematic review and meta-analysis of randomized trials – 2010 update. Blood 2010;116:751. ASH Abstract #1798.
- Vidal L, Gafter-Gvili A, Salles G, et al. Rituximab as maintenance therapy (MR) for patients with follicular lymphoma – meta-analysis update. Presented at the 52<sup>nd</sup> American Society of Hematology Annual Meeting and Exposition in Orlando, Florida; December 4-7, 2010. ASH Poster #1798.
- Rituxan Prescribing Information

### **Cited References**

1. Salles GA, Catalano J, Feugier P, et al. Updated results of the PRIMA study confirms the benefit of 2-years rituximab maintenance in follicular lymphoma patients responding to immunochemotherapy. Blood 2010;116:746. ASH Abstract #1788.
2. Salles GA, Catalano J, Feugier P, et al. Updated results of the PRIMA study confirms the benefit of 2-years rituximab maintenance in follicular lymphoma patients responding to immunochemotherapy. Presented at the 52<sup>nd</sup> American Society of Hematology Annual Meeting and Exposition in Orlando, Florida; December 4-7, 2010. ASH Poster #1788.
3. Salles G, Seymour JF, Offner F, et al. Rituximab maintenance for 2 years in patients with high tumour burden follicular lymphoma responding to rituximab plus chemotherapy (PRIMA): a phase 3, randomized controlled trial. Lancet 2010;377:42-51.
4. Foá R, Di Rocco A, van Hazel G, et al. Maintenance rituximab every 2 months for 2 years is effective and well tolerated in patients with follicular lymphoma with both standard or rapid infusion: updated results from the phase IIIb MAXIMA study. Blood 2010;116:1608. ASH Abstract #3945.
5. Foá R, Di Rocco A, van Hazel G, et al. Maintenance rituximab every 2 months for 2 years is effective and well tolerated in patients with follicular lymphoma with both standard or rapid infusion: updated results from the phase IIIb MAXIMA study. Presented at the 52<sup>nd</sup> American Society of Hematology Annual Meeting and Exposition in Orlando, Florida; December 4-7, 2010. ASH Poster #3945.
6. Taverna CJ, Bassi S, Hitz F, et al. Rituximab maintenance treatment for a maximum of 5 years in follicular lymphoma: safety analysis of the randomized phase III trial SAKK 35/03. Blood 2010;116:752. ASH Abstract #1802.
7. Taverna CJ, Bassi S, Hitz F, et al. Rituximab maintenance treatment for a maximum of 5 years in follicular lymphoma: safety analysis of the randomized phase III trial SAKK 35/03. Presented at the

- 52<sup>nd</sup> American Society of Hematology Annual Meeting and Exposition in Orlando, Florida; December 4-7, 2010. ASH Poster #1802.
8. Ardeschna KM, Smith P, Qian W, et al. An intergroup randomized trial of rituximab versus a watch and wait strategy in patients with stage II, III, IV, asymptomatic, non-bulky follicular lymphoma (grades 1, 2 and 3a). A preliminary analysis. *Blood* 2010;116:5. ASH Abstract #6.
  9. Ardeschna KM, Smith P, Qian W, et al. An intergroup randomized trial of rituximab vs a watch & wait approach in patients with advanced stage, asymptomatic, non-bulky follicular lymphoma. Presented at the 52<sup>nd</sup> American Society of Hematology Annual Meeting and Exposition in Orlando, Florida; December 4-7, 2010. ASH Presentation #6.
  10. Vidal L, Gafter-Gvili A, Salles G, et al. Rituximab maintenance for the treatment of patients with follicular lymphoma: systematic review and meta-analysis of randomized trials – 2010 update. *Blood* 2010;116:751. ASH Abstract #1798.
  11. Vidal L, Gafter-Gvili A, Salles G, et al. Rituximab as maintenance therapy (MR) for patients with follicular lymphoma – meta-analysis update. Presented at the 52<sup>nd</sup> American Society of Hematology Annual Meeting and Exposition in Orlando, Florida; December 4-7, 2010. ASH Poster #1798.