

Submitted by:  
Jihwon Im, Pharm.D.  
Managed Care Medical Communications, Medical Affairs  
Genentech, Inc.  
1 DNA Way  
South San Francisco, CA 94080  
Phone: (650) 467-0427  
Email: [genentechmedinfo-d@gene.com](mailto:genentechmedinfo-d@gene.com)  
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NCCN Guidelines Panel: Non-Hodgkin's Lymphomas

On behalf of Genentech, I respectfully request the NCCN Non-Hodgkin's Lymphomas (NHL) Guideline Panel to review the following enclosed Gazyva® (obinutuzumab) Phase III trial data for the treatment of patients with indolent NHL.

Sehn LH, Chua N, Mayer J, et al. GADOLIN: primary results from a Phase III study of obinutuzumab plus bendamustine compared with bendamustine alone in patients with rituximab-refractory indolent non-hodgkin lymphoma. Presented at the American Society of Clinical Oncology 2015 Annual Meeting in Chicago, IL; 2015 May 29 - June 2. ASCO Oral presentation.

**Specific Changes:**

Consider Gazyva + bendamustine as a treatment option for second-line and subsequent therapy of indolent NHL based on the results of the Phase III GADOLIN trial.

**FDA Clearance:**

Gazyva is not FDA-approved for the treatment of indolent NHL. Please refer to the product prescribing information for the full FDA-approved indication and safety information.

- Full Gazyva® prescribing information available at:  
[http://www.gene.com/download/pdf/gazyva\\_prescribing.pdf](http://www.gene.com/download/pdf/gazyva_prescribing.pdf)

**Rationale:**

Results from the GADOLIN trial were recently presented at the 2015 American Society of Clinical Oncology (ASCO) Annual Meeting. GADOLIN is a Phase III, multicenter, open-label, randomized trial that was conducted to compare bendamustine monotherapy with Gazyva + bendamustine followed by Gazyva maintenance in patients with indolent NHL whose disease did not respond or progressed within 6 months after Rituxan-based therapy (either monotherapy or in combination with chemotherapy). The primary endpoint was progression-free survival (PFS) assessed by an independent radiology facility (IRF).

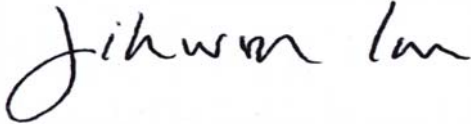
A total of 396 patients were analyzed at the time of the pre-planned interim analysis, and approximately 80% of patients had follicular lymphoma. After a median follow up of 21 months, the IRF-assessed PFS was significantly prolonged in patients treated with Gazyva + bendamustine compared with those treated with bendamustine alone (median PFS=not reached and 14.9 months, respectively; stratified hazard ratio [HR]=0.55, 95% CI 0.4-0.74; p=0.0001). The investigator-assessed median PFS, a secondary endpoint, was 29.2 months for patients treated with Gazyva + bendamustine and 14 months for patients treated with bendamustine alone (stratified HR=0.52, 95% CI 0.39-0.70; p<0.0001). At the time of the report, median overall survival was not reached in either arm, and no significant differences in overall response rates were observed. No new safety signals were identified. Grade 3-4 adverse events that occurred in >5% of patients treated with either Gazyva + bendamustine or bendamustine alone included neutropenia (33% vs 26.3%), infusion-related reactions (10.8% vs 5.6%), thrombocytopenia (10.8% vs 16.2%), and anemia (7.7% vs 10.1%).

Additional studies have been conducted to evaluate Gazyva + bendamustine in chronic lymphocytic leukemia (CLL) and indolent NHL.<sup>1-4</sup>

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I hope this information is helpful to you. If you have any questions, please contact me directly at (650) 467-0427 or by email at [jchang@gene.com](mailto:jchang@gene.com).

Respectfully submitted,



Jihwon Im, Pharm.D.

Supplemental References

1. Brown JR, O'Brien S, Kingsley CD, et al. Obinutuzumab plus fludarabine/cyclophosphamide or bendamustine in the initial therapy of CLL patients: the Phase 1b GALTON trial. *Blood* 2015;125:2779-2785. <http://www.ncbi.nlm.nih.gov/pubmed/25769620>.
2. Dyer MJS, Grigg A, González-Díaz M, et al. Obinutuzumab (GA101) in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or bendamustine in patients with previously untreated follicular lymphoma: results of the Phase 1b GAUDI study (BO21000). Presented at the 54th American Society of Hematology Annual Meeting and Exposition in Atlanta, GA; December 8–11, 2012. ASH Poster.
3. Dyer MJS, Grigg A, Diaz MG, et al. Obinutuzumab (GA101) in combination with CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) or bendamustine for the first-line treatment of follicular non-Hodgkin lymphoma: final results from the maintenance phase of the Phase 1b GAUDI study. Presented at the 56th ASH Annual Meeting and Exposition in San Francisco, CA; December 6–9, 2014. ASH Poster #1743.
4. Bosch F, Illmer T, Turgut M, et al. Preliminary Safety Results from the Phase IIIb GREEN Study of Obinutuzumab (GA101) Alone or in Combination with Chemotherapy for Previously Untreated or Relapsed/Refractory Chronic Lymphocytic Leukemia (CLL). Presented at the 56<sup>th</sup> American Society of Hematology Annual Meeting and Exposition in San Francisco, CA; December 6-9, 2014, ASH Poster #3345.

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