Genentech
A Member of the Roche Group

Submitted by:
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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 enclosed data for Gazyva™ (obinutuzumab) for the first-line treatment of patients with chronic lymphocytic leukemia (CLL).

Specific Changes: Consider the recently presented data on Gazyva monotherapy for the first-line treatment of CLL for your updating purposes.

FDA Clearance: Gazyva is not FDA approved as monotherapy for the first-line treatment of CLL. Gazyva is FDA approved in combination with chlorambucil, for the treatment of patients with previously untreated CLL.[1]

Rationale: Results from the GAGE study were recently presented at the 2014 American Society of Clinical Oncology (ASCO) Annual Meeting.[2,3] GAGE is a multicenter, randomized Phase II study that was conducted to evaluate Gazyva in the first-line treatment of patients with CLL. Eighty patients were randomized to receive either Gazyva 1000 mg or 2000 mg. The primary endpoint was overall response rate (ORR), and the secondary endpoints included progression-free survival (PFS), overall survival (OS), and safety.

Gazya showed single-agent activity in both arms.[2,3] The ORR was 49% in the Gazyva 1000 mg arm and 67% in the 2000 mg arm (2-sided p-value=0.08). At a median follow-up of 20.3 months, the median PFS was 21 months in the 1000 mg arm and 20 months in the 2000 mg arm. The 18-month PFS was 59% and 83%, respectively. At the time of the report, median OS was not reached in both arms. No new safety signals were identified. The most frequent adverse event (AE) was infusion-related reactions (IRRs). The incidence of Grade 3/4 AEs was similar between the 2 arms, except for IRRs (23% in the 1000 mg arm and 11% in the 2000 mg arm).

Currently, we are not aware of any additional clinical trials (completed, ongoing, or planned) for single-agent Gazyva in first-line CLL.

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

- Flynn JM, Byrd JC, Kipps TJ, et al. Obinutuzumab (GA101) 1000 mg vs 2000 mg in Patients with Chronic Lymphocytic Leukemia (CLL): Results of the Phase 2 GAGE (GAO4768g) Trial. Presented at the American Society of Clinical Oncology 2014 Annual Meeting in Chicago, Illinois; May 30 - June 3, 2014. ASCO Poster #7083.

- Gazyva Prescribing Information

Respectfully submitted,

Jihwon Im

Cited References

1. Gazyva Prescribing Information

2. Flynn JM, Byrd JC, Kipps TJ, et al. Obinutuzumab (GA101) 1000 mg vs 2000 mg in Patients with Chronic Lymphocytic Leukemia (CLL): Results of the Phase 2 GAGE (GAO4768g) Trial. Presented at the American Society of Clinical Oncology 2014 Annual Meeting in Chicago, Illinois; May 30 - June 3, 2014. ASCO Poster #7083.

3. Flynn JM, Byrd JC, Kipps TJ, et al. Obinutuzumab (GA101) 1000 mg vs 2000 mg in Patients with Chronic Lymphocytic Leukemia (CLL): Results of the Phase 2 GAGE (GAO4768g) Trial. Presented at the American Society of Clinical Oncology 2014 Annual Meeting in Chicago, Illinois; May 30 - June 3, 2014. ASCO Abstract #7083. http://www.asco.org.