

Recent Advances in the Treatment of Lymphoma

A Review of Selected Presentations

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3419 Durable Complete Responses Following Therapy With Epratuzumab Plus Rituximab: Final Efficacy Results of a Multicenter Study in Recurrent Indolent Non-Hodgkin's Lymphoma¹

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Targeting NHL cells with monoclonal antibody therapies offers a potentially potent and active lymphoma treatment, often with a safety profile which is more favorable than standard chemotherapy regimens.² Epratuzumab is a novel monoclonal antibody directed against CD22, a molecule commonly expressed on the surface of NHL cells. Phase I and II clinical studies in NHL patients have shown that epratuzumab is active both as a single agent and in combination with rituximab.³⁻⁷ Additionally, the results of a pilot study evaluating the addition of epratuzumab and rituximab to CHOP therapy were recently published, showing an overall response (OR) rate of 87%.⁸ Here, Leonard and colleagues report a final analysis of a clinical study evaluating the safety and activity of the combination of epratuzumab and rituximab in patients with indolent NHL.¹

This was an international, multicenter, open-label trial which followed patients for long-term responses over 4 years. All patients (N=49) had low-grade CD20-positive B-cell lymphoma, with measurable disease by CT scan and an Eastern Cooperative Oncology Group (ECOG) performance status of 1 or less. A total of 41 patients had low-grade FL and 7 patients had SLL or CLL. Patients were classified as having either recurrent or refractory NHL, and had failed at least one prior regimen of standard chemotherapy. Additionally, patients were either rituximab-naïve or had demonstrated a partial response (PR) or complete response (CR) to rituximab as a single-agent or in combination with chemotherapy,

with a time to progression (TTP) of greater than or equal to 12 months. All patients received intravenous infusions of epratuzumab (360 mg/m²) followed by rituximab (375 mg/m²) weekly for 4 consecutive weeks.

Of the 49 enrolled patients, 48 completed the entire 4-week treatment regimen, with only 1 patient declining rituximab therapy after an infusion reaction. A safety analysis found that 88% of patients experienced at least one adverse effect.⁹ The most frequently reported adverse effects included rigors, nausea, pyrexia, fatigue, vomiting, headache, cough, and dyspnea. All of the adverse events associated with epratuzumab therapy were grade 1 or 2, and usually occurred with the first infusion. Only 4 patients experienced a severe adverse event, 2 of which were considered to be related to the study treatment.

A total of 54.2% (95% confidence interval [CI], 39.2–68.6%) of patients had an objective response to the combination therapy, with 27.1% having a CR or unconfirmed CR (CRu). The epratuzumab plus rituximab combination was active in both FL (objective response: 53.7%) and SLL/CLL (objective response: 57.1%) histologies. FL patients with Follicular Lymphoma International Prognostic Index (FLIPI) scores of 0 or 1 responded better to the combination regimen than patients with FLIPI scores of 2 or more (objective response: 84.6% vs 39.3%, respectively). Prior exposure to rituximab did not significantly affect response to the epratuzumab plus rituximab combination, as individuals with a prior response to rituximab had an objective response rate of 64.3% compared to 50.0% of rituximab-naïve patients.

The median progression-free survival (PFS) for all patients was 11.1 months. The response in FL patients who achieved a CR or CRu was especially long-lived, with a median PFS of 35.1 months (range: 12.8–52.3 months). Importantly, 5 FL patients who experienced a CR remained in remission at the final study evaluation (median follow-up 44.3 months; range: 18.2–52.4 months). Future studies to evaluate this combination as first-line therapy for indolent NHL are both ongoing and planned.^{10,11}