ADVANCES IN LLM

Current Developments in the Management of Leukemia, Lymphoma, and Myeloma

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Galiximab in Relapsed Hodgkin Lymphoma

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H&O What is the standard of care in relapsed Hodgkin lymphoma?

SS In general, patients with relapsed Hodgkin lymphoma are divided between those who can undergo an autologous stem cell transplant and those who cannot. Patients who can undergo an autologous stem cell transplant tend to be younger and have had a relapse of disease. The unmet need that persists in this disease is management of relapsed patients who are either not eligible for a transplant or who have already had an autologous stem cell transplant and relapsed. For that patient population, there is no standard of care, and essentially all treatment is palliative. Most patients in that situation do not survive more than a year.

H&O What was the trial design for Cancer and Leukemia Group B (CALGB) 50602?

SS CALGB 50602 was a single-arm, phase II study of single-agent galiximab (Biogen Idec) for patients with relapsed Hodgkin lymphoma who had received at least 2 prior therapies.

H&O Could you provide some background on galiximab?

SS Galiximab is a primatized monoclonal antibody against CD80. *Primatized* means that the agent includes some genetic material from primates, which distinguishes it from most other monoclonal antibodies, which are often humanized or murine. CD80 is a protein that is normally expressed on activated cells of the immune system, but it is abnormally expressed in between 80% and 100% of patients with Hodgkin lymphoma. The Reed-Sternberg cell, which is the malignant cell in Hodgkin lymphoma, expresses CD80. Galiximab is given intravenously, and it attaches only to its target—CD80—and destroys that cell.

There is another possible mechanism of action for galiximab. CD80 is increased on some cells in the immune system, and it is possible that by targeting CD80, galiximab also affects some of the background cells in Hodgkin lymphoma. This hypothesis remains to be proven.

H&O What were the results of CALGB 50602?

SS We enrolled 30 patients, but 1 patient never started treatment. The treatment schedule began with 500 mg/m^2 administered once weekly for 4 weeks, which we called the induction phase. Treatment continued with 500 mg/m^2 of galiximab administered every 4 weeks. Patients could continue to receive treatment as long as they were still responding.

Among the 29 evaluable patients, there was only 1 complete response and 1 partial response. The patient who achieved a complete response progressed at 7.5 months, and the patient who achieved a partial response progressed at 3 months. Unfortunately, most patients progressed, and 24 patients discontinued treatment because of progressive disease.

H&O What toxicities were observed in the study?

SS There were very few toxicities. Because galiximab is a monoclonal antibody, it will not cause many of the

side effects usually associated with chemotherapy. The infrequent grade 3/4 side effects included 2 patients with abnormal liver function tests, 2 patients with infections, and 3 patients with low phosphate levels. Overall, galiximab was well tolerated.

H&O What did you conclude from the study?

SS There are 2 general conclusions. The first is that galiximab had limited activity but was well tolerated. The second is that we were able to accrue 30 patients in only 6 months, and Hodgkin lymphoma is a rare disease. There are only about 7,500 new cases of Hodgkin lymphoma diagnosed per year, and most patients are cured with frontline therapy. The subset that cannot undergo autologous transplant or who have relapsed after an autologous transplant includes approximately 1,000–1,500 patients annually. The fact that we were able to accrue patients so quickly suggests that there is a very strong continued unmet medical need for nonchemotherapy approaches in relapsed Hodgkin lymphoma.

H&O Do you believe that galiximab has a role in therapy for relapsed Hodgkin lymphoma?

SS Single-agent galiximab is not appropriate for relapsed Hodgkin lymphoma. I think the only possibility for the use of galiximab in these patients would be in combination with chemotherapy. Galiximab is well tolerated, so combination studies could be promising, although this approach has not yet been studied.

H&O What is the future direction of therapy for patients with relapsed Hodgkin lymphoma?

SS There are many other drugs in development. One of the more promising ones is brentuximab vedotin (SGN-35, Seattle Genetics, Inc/Millennium), a monoclonal antibody that is linked to a toxic molecule released inside the cell. The future for this population is in trying to identify targeted therapies. The CALGB has looked at bortezomib (Velcade, Millennium), which did not work. Now, we have looked at galiximab, which also had limited activity. We need nonchemotherapy agents. We must continue to test new agents and encourage patients to participate in clinical trials whenever possible.

Acknowledgment: *All CALGB 50602 trial data discussed in this interview were published in the* Journal of Clinical Oncology, *2010 ASCO Annual Meeting Proceedings.*

Suggested Readings

Smith SM, Bartlett N, Johnson JL, et al. Galiximab, an anti-CD80 primatized monoclonal antibody, in relapsed Hodgkin lymphoma: final results of CALGB 50602. *J Clin Oncol* (ASCO Meeting Abstracts). 2010;28(15s). Abstract 8039.

Blum KA, Johnson JL, Niedzwiecki D, et al. A phase II study of bortezomib in relapsed Hodgkin lymphoma: preliminary results of CALGB 50206. *J Clin Oncol* (ASCO Meeting Abstracts). 2006;24(18s). Abstract 7576.