Early Clinical Investigations of Idiotype Vaccines in the Treatment of Follicular and Mantle Cell Lymphoma

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By Julie M. Vose, MD [1]

This special supplement to Oncology News International includes updated results of studies with anti-CD20 therapy and other targeted therapies in the treatment of lymphomas, chronic lymphocytic leukemia, and immune thrombocytopenic purpura. The results were presented at the American Society of Hematology 44th Annual Meeting in Philadelphia, December 6 to 10, 2002. City Hall in Philadelphia, Pennsylvania

PHILADELPHIA-Studies of aggressive or treatment-refractory lymphoma in patients who undergo stem cell transplantation suggest that graft-vs-lymphoma effects improve the complete response rate. Therefore, investigators have postulated that lymphoma may also be responsive to other immunomodulatory therapies. Idiotype vaccines (autologous tumor-derived immunoglobulin idiotype conjugated to keyhole limpet hemocyanin [KLH]) may be an effective immunomodulatory technique to eliminate minimal residual disease in patients with an intact immune system. Studies of immunomodulatory idiotype vaccines are currently in phase III development, and the optimal vaccine and vaccination schedule have yet to be identified. Novel antilymphoma strategies are under investigation. Two studies of vaccine therapy for the treatment of follicular and mantle cell lymphoma were reported at the American Society of Hematology 2002 Annual Meeting (ASH abstracts 608 and 609).[1-3] Depleting B But Not T Cells Animal models suggest that B-cell depletion may enhance cellular immune responses while reducing humoral immune responses. Rituximab (Rituxan) is an anti-CD20 antibody that specifically depletes B cells and is used to treat lymphoma. Investigators at the Center for Cancer Research, National Cancer Institute, Bethesda, Maryland, initiated a study of dose-adjusted etoposide, vincristine (Oncovin), doxorubicin, bolus cyclophosphamide (Cytoxan, Neosar), and prednisone, plus rituximab (EPOCH-R) (ASH abstract 608).[2] Wyndham Wilson, MD, PhD, Chief, Lymphoma Section, explained that Dose-adjusted EPOCH-R was selected for the initial therapy because this novel combination regimen may achieve a higher cell kill than cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP)-based regimens and may be more likely to achieve molecular remission.[1] The regimen was administered every 3 weeks for six cycles, followed by five cycles of idiotype vaccine beginning at least 12 weeks later. The 26 patients enrolled in this study had a median age of 57 years, performance status of 0 to 2, and 96% had stage IV mantle cell lymphoma.[2] Approximately one-third of patients had elevated lactate dehydrogenase levels, and 15% exhibited blastic disease histology. Among the 25 patients who completed EPOCH-R, 92% achieved a complete response and 8% achieved a partial response. The majority (92%) of the 12 patients with peripheral blood mantle cell lymphoma achieved a complete response as assessed by flow cytometry. At the time of the report, 13 patients had completed all five anti-idiotype vaccinations and six patients had completed one to four vaccinations. After a median of 14 months of follow-up, the overall survival is 100%, and the event-free survival is 87% at 18 months. Humoral responses to KLH occurred in 9 of 13 patients. Responses to KLH were achieved 5 to 10 months after the last vaccine in three patients, suggesting that B-cell depletion may delay the humoral immune response. These early results suggest that EPOCH-R therapy achieves a high response rate without depleting T cells, and that idiotype vaccines may have efficacy in combination with EPOCH-R despite a delay in the humoral immune response.

Plant-Derived Vaccine Sunil Reddy, MD, of Stanford Medical Center in California presented the first report of a plant-derived, single-chain Fv idiotype vaccine in development for patients with follicular lymphoma (ASH abstract 609).[3] This idiotype vaccine was produced in the plant Nicotiana benthamiana using recombinant technology developed by Large Scale Biology. The phase I study involved patients with follicular lymphoma who were in first chemotherapy-induced remission. The patients received six monthly doses of high-dose (2.0 mg) or low-dose (0.2 mg) single-chain Fv vaccine administered with or without growth-factor support. Among 15 patients who successfully completed the vaccine series, there were no significant toxicities or serious adverse events. Ten patients developed humoral and/or cellular immune responses to the vaccine. Specific cellular
immune responses were documented in four patients treated with growth factors and in two patients who did not receive growth factors, independent of high vs lowdose vaccine. This novel approach to vaccine therapy for lymphoma may increase the speed of producing idiotype vaccines and does not require conjugation to KLH. Further studies in the phase II setting are planned.


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