

About this CME activity

Introduction and statement of needs

Despite the growth of our understanding of the biology and genetics associated with lymphoid neoplasms, there appears to be no real consensus among investigators as to the optimal therapy for follicular lymphoma (FL) and low-grade non-Hodgkin's lymphoma (NHL). Radiotherapy and chemotherapy remain standard treatment options, with combinations such as CVP (cyclophosphamide, vincristine, prednisone), CHOP (CVP with doxorubicin), and fludarabine-based regimens being used for indolent NHL. However, the well-documented side effects of some of these conventional options can severely reduce patients' quality of life and limit their ability to receive full doses of therapy, thereby hindering optimal treatment outcomes.

Moreover, patients with indolent NHL may experience multiple relapses over the natural course of their disease, since existing therapies are not curative. Resistance to current treatments also is a growing problem in this patient population. The new direction in therapy for NHL is toward more targeted and biologic approaches and away from the nonspecific cytotoxic agents. Used typically in combination with high-dose chemotherapy in patients with relapsed or refractory FL and low-grade NHL, rituximab (Rituxan) has been shown to improve responses to treatment. As a result of its efficacy and favorable side-effect profile, rituximab has been widely adopted in the treatment of NHL.

One of the most promising targeted agents presently under study in relapsed/refractory NHL appears to be bendamustine (Treanda), a hybrid alkylating agent that differs from conventional compounds in its apparently bifunctional mechanism of action. Used in Germany for many years for the treatment of patients with NHL, chronic lymphocytic leukemia (CLL), multiple myeloma, and other solid tumors, bendamustine reportedly has both alkylating and antimetabolic properties.

A phase II trial of bendamustine, performed in 17 sites in the United States and Canada, studied 77 patients with rituximab- and alkylator-refractory indolent NHL; approximately half of the patients had FL and the rest had more aggressive lymphomas. Bendamustine demonstrated significant activity, with objective responses achieved in 74% of patients (35% complete and 39% partial). Reversible myelosuppression was the primary toxicity observed with single-agent bendamustine in this study.

The use of bendamustine in combination with other agents has also yielded encouraging results. In a phase II study performed by the German Low Grade Lymphoma Study Group (GLSG), a regimen of bendamustine/mito-

xantrone (Novantrone)/rituximab appeared to be effective and well tolerated in 46 patients with relapsed or refractory indolent lymphomas. Similar positive findings were demonstrated in another phase II study of bendamustine in combination with rituximab in 66 patients with relapsed indolent and mantle cell NHL.

In conclusion, the challenge remains how best to combine these newer, targeted agents for patients with hematologic malignancies such as NHL and CLL, perhaps reducing dependence on the more nonspecific cytotoxic drugs. Selecting patients most likely to respond to a given therapy and developing multitargeted approaches to these cancers are the next steps to improve cure rates and, ultimately, patient outcomes.

Accreditation statement

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Ayalew Tefferi, MD, has nothing to disclose; Susan O'Brien, MD, has received grant and/or research support from Genentech, Inc., Berlex Laboratories, Biogen Idec, Eli Lilly and Company, Novartis Pharmaceuticals Corporation, Bristol-Myers Squibb, Gemin X Biotechnologies Inc., and Genta Incorporated; and Brad Kahl, MD, has received grant and/or research support from Genentech, Inc., Biogen Idec, Cephalon, Inc., and Millennium Pharmaceuticals, Inc. He has served as a consultant to Genentech, Inc., Biogen Idec, Cephalon, Inc., and Millennium Pharmaceuticals, Inc.

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Target audience

This activity has been developed for medical oncologists and other health professionals involved in the care of patients with indolent NHL and CLL.

Program goals

- Review the standard treatment options for FL and low-grade NHL.
- Identify options for first-line and subsequent treatments of FL/indolent NHL.
- Assess the new direction in therapy for NHL and evaluate the impact of recent research findings in upcoming agents for indolent NHL and CLL.

Educational objectives

After participating in this activity, participants should be able to:

- Discuss prognostic factors in CLL.
- Explore regimens and new agents used in first-line treatment or treatment of relapsing/refractory CLL.
- Recognize factors involved in patient and treatment selection for first-line treatment of FL.
- Determine options for first-line and subsequent treatments of FL/indolent NHL.
- Identify novel agents in the treatment of FL/indolent NHL.

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