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Rituximab

A Viewpoint by Myron S. Czuczman

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In the US, the prevalence of non-Hodgkin's lymphoma (NHL) has increased approximately 4 to 7% a year for 20 years. Similar trends are reported in many other parts of the world. It is estimated that 56 800 new cases of NHL and 25 700 deaths related to this disease will occur in the US in 1999.[1] Most NHL is of B-cell origin; >90% of NHL express the CD20 antigen. Indolent lymphomas are typically associated with high initial response rates but have a relapsing, incurable nature following treatment with standard chemotherapy or radiation therapy.[2,3]

Monoclonal antibody technology was developed by Kohler and Milstein in 1975. Nadler et al. published the first report of a patient being treated with a murine monoclonal antibody in 1980.[4] Approximately 2 decades later, a chimaeric (mouse-human) anti-CD20 monoclonal antibody, rituximab, is available. Rituximab exhibits complement- or antibody-dependent cytotoxicity and has direct antiproliferative and apoptotic effects on CD20-positive cells. In addition, rituximab has been shown to sensitise a drug-resistant cell line to killing by cytotoxic drugs.[5] Theoretically, chimaeric unconjugated antibodies (mAbs) are less antigenic than their murine or toxin-conjugated counterparts.

Rituximab has demonstrated significant efficacy as a single agent in the treatment of recurrent or refractory indolent (in particular, follicular) NHL. After it achieved an overall response rate of 48% in a pivotal study of monotherapy, rituximab became the first mAb approved in the US for treatment of cancer when it was approved for previously treated indolent B-cell NHL in November 1997. Because of its toxicity profile and unique mechanism(s) of action, rituximab may also be effective in combination with chemotherapy or with other immunomodulatory agents in the treatment of B-cell neoplasms, and a number of clinical trials investigating these possibilities are in progress.[6] These trials, and ongoing basic research into ways of augmenting the antitumour activity of rituximab, should make it possible to optimise the dosage of this drug. Rituximab represents a major advance in the treatment of B-cell NHL and marks the beginning of a promising new era in the field of cancer immunotherapy. ▲

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