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Alemtuzumab

A Viewpoint by Geoff Hale

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Alemtuzumab is a humanised monoclonal antibody that recognises the CD52 antigen, a small lipid-anchored glycoprotein abundantly expressed on virtually all human lymphocytes. It is the most powerful lympholytic agent known – a single dose of 10mg can cause long-term depletion of blood T-cell levels.

Originally developed for the prevention of graft-versus-host disease and transplant rejection, alemtuzumab is approved (in Europe and the US) for the treatment of B-cell chronic lymphocytic leukemia (B-CLL) after the failure of alkylating agents and fludarabine. It can destroy a large proportion of tumour cells in many of these patients. Combined with other drugs, or used earlier, it reportedly gives a quality of remission that is otherwise difficult to obtain.

Clinical results come from small open-label studies, and there are few data to justify the recommended dosage regimen (3mg escalating to 30mg three times weekly for up to 12 weeks) or the empirical treatments used to prevent 'first-dose' flu-like reactions.

The most important complication is the long-term reduction in blood T cells; patients are susceptible to viral reactivation and infection for several months or more post-treatment. Antiglobulin responses are rare in the licensed indication, but may be more frequent when alemtuzumab is used in less heavily pretreated patients.

Besides its use in B-CLL, alemtuzumab is being tested as an immunosuppressant in transplantation and autoimmune diseases, including multiple sclerosis (MS). Early results provide some insights into its effects on the immune system. For example, in previously untreated patients with MS, there were very few infections, but approximately 30% developed autoimmune thyroid disease. When alemtuzumab is used for the first-line treatment of B-CLL, perhaps the profile of complications might change in a similar fashion.

The pharmacokinetics of alemtuzumab have only been described briefly. More information is needed about the relationship between drug levels and tumour burden, since the dose required for full lymphodepletion in CLL can be much greater than in transplantion or autoimmunity.

In conclusion, alemtuzumab is a valuable new agent for the treatment of B-CLL. It offers a completely different mode of action from chemotherapeutics, and may be synergistic with them. It has exciting possibilities as an immunosuppressive, but should be used with caution. In particular, the high doses and relatively lengthy treatment period approved for third-line B-CLL treatment may be excessive in other situations. ▲