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Alemtuzumab

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Alemtuzumab is a humanised anti-CD52 monoclonal antibody that binds to almost all malignant and normal B- and T-lymphocytes.

It has demonstrated significant clinical activity in numerous phase II trials, primarily in patients with B-cell chronic lymphocytic leukaemia (B-CLL) or T-cell prolymphocytic leukaemia (T-PLL). Promising results have also been reported in mycosis fungoides/Sézary syndrome.

In patients with fludarabine-refractory B-CLL, alemtuzumab induced an overall response rate (OR) of 33–43%, with a median response duration of 9 months. Promising results were obtained when alemtuzumab was used as first-line therapy in B-CLL (OR rate >80%), although these preliminary findings require confirmation in further studies. Initial data from ongoing trials indicate that the antitumour effects may be enhanced when alemtuzumab is combined with purine analogue-based chemotherapy or used to eradicate minimal residual disease (MRD).

For as yet unknown reasons, the response to alemtuzumab depends on the tumour location; major activity has been observed against tumour cells in the blood, bone marrow, and skin, whereas lymph nodes are less responsive. Prolonged therapy (up to 12 weeks) may be critically important in achieving high-quality remissions, particularly in bone marrow (the primary site of disease in CLL).

Like many other monoclonal antibodies, intravenous infusion of alemtuzumab may induce transient, flu-like, 'first-dose' adverse effects, such as fever, rigor and nausea. These reactions may be managed by (pre)medication and appear to be minimised by subcutaneous administration, although the latter may induce transient skin reactions, especially when used in previously untreated CLL patients.

Alemtuzumab also induces a profound T-cell lymphopenia, which (in combination with advanced disease and prior therapy) results in an increased risk of opportunistic and other infections. Cotrimoxazole and valaciclovir prophylaxis is mandatory in all patients. Cytomegalovirus (CMV) reactivation, causing fever, may occur in 10–20% of patients; early detection and treatment is important. Most patients respond promptly to intravenous ganciclovir therapy, and preliminary data indicate that alemtuzumab may, under close supervision, be reinstituted following resolution of a CMV reactivation episode, provided there is a great need to continue with treatment.

Transient grade 4 neutropenia may occur in approximately 20% of patients, but febrile episodes are uncommon and these complications typically normalise spontaneously or respond rapidly to colony-stimulating factor therapy.

In conclusion, alemtuzumab is an important new agent for the treatment of patients with chronic B- and T-cell malignancies. It has unique properties that are not shared by chemotherapeutic agents or other monoclonal antibodies. Its potent T-lympholytic properties require careful management and monitoring of patients during and after treatment. Further studies are warranted on the use of alemtuzumab in combination with other agents and for MRD eradication, as well as to clarify its emerging role in allogeneic bone marrow/stem cell transplantation. The subcutaneous route of administration also needs further evaluation, as it may lead to improved quality of life and reduced healthcare costs. ▲