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Radioimmunotherapy in the treatment of lymphoma

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Background

Conventional treatment for haematological malignancies achieves high remission rates but 75% of patients with non Hodgkin's lymphoma [NHL] remain incurable.and eventually die from their disease. The monoclonal antibody rituximab directed against the CD20 surface antigen prolongs time to progression but has not yet been shown to prolong survival in low grade NHL. Targeted radiotherapy using radiolabelled antibodies exploits the inherent radiosensitivity of haematological malignancies and, acting systemically, can be used to treat multi-site disease. The cross fire effect of long range beta radiation helps to overcome variable CD20 antigen expression so that, unlike rituximab, radiolabelled antibodies do not need to bind to every single tumour cell to achieve cell kill.

Indications

Radioimmunotherapy [RIT] using ^{90}Y ibritumomab tiuxetan or ^{131}I tositumomab is used to treat relapsed or refractory low grade B cell non Hodgkin's lymphoma. Patient selection criteria include relapsed CD20 positive B cell NHL and reasonable bone marrow reserve [peripheral platelet count > 100 x10^9/l]. RIT is contraindicated for patients who have greater than 25% bone marrow involvement by lymphoma.

Treatment regimen

Treatment is administered in 2 stages. First, patients receive an infusion of unlabelled rituximab to block non target antigen sites on circulating B cells and in the spleen. This step may be combined with a diagnostic imaging/dosimetry study. Stage 2 takes place 1 week later and comprises a 2nd rituximab infusion followed by therapeutic radiolabelled antibody administered intravenously. The administered activity is calculated by body weight or by individual dosimetry, depending on the radiopharmaceutical used. The prescribed activity is reduced for patients who have a low peripheral platelet count [100 – 149 x 10^9/l.]

Efficacy & tolerability

Clinical trials consistently report overall and complete response rates in the order of approximately 80% and 30% respectively following single agent RIT in relapsed/ refractory low grade NHL [1,2]. RIT is effective even in the growing population of patients who develop rituximab resistance. Optimal responses are reported in patients treated early in the natural history of their disease [3,4]. The main toxicity of treatment is temporary myelosuppression 4-6 weeks post treatment with slow recovery over the next 8 weeks . Close haematological monitoring is essential following RIT, particularly in patients who have been heavily pretreated with combination chemotherapy.

Conclusion

RIT is an effective treatment for patients with refractory/relapsed low grade NHL. Toxicity is modest and manageable. The optimal timing of RIT in relation to other treatment options remains unclear. Clinical trials are in progress to assess the feasibility of integrating RIT with chemotherapy as first line treatment, within a myeloablative setting prior to autologous stem cell transplantation and in aggressive NHL.

References

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