[haematologica reports]
2006;2(7):8

Impact of radioimmumotherapy on aggressive non-Hodgkin's lymphoma

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Unconjugated monoclonal antibodies, particularly rituximab, are now an important part of the treatment of B-cell lymphoma. The use of radiolabeled antibodies offers a different way to deliver radiotherapy and take advantage of the well known radiosensibility of lymphoma. Radio-immunotherapy (RIT) is defined as a treatment modality in which cytotoxic radiation is delivered to tumour cells via antibodies binding to tumour-specific or tumour-associated antigen. The antibody serves as transporter for the radioisotope and participates on its own in the tumour killing. The advantage of conjugated radiolabeled antibody over unconjugated antibody is that there is no need to target every to achieve an antitumour effect. Tumour with low or heterogeneous antigen expression, as poorly vascularised and bulky tumour can also be killed by the cross-fire of neighbourhood targeted cells.

Studies of Zevalin in relapsed mantel cell lymphoma

Limited numbers of patients with relapsed mantle cell NHL have been treated with Zevalin. Although the malignant cells in mantle cell lymphoma (MCL) strongly express CD20, the disease often heavily infiltrates the marrow making these patients ineligible for RIT studies. Oki and colleagues reported on 15 patients with relapsed MCL that received treatment with Zevalin. There were 5 objective responses (33%) with all responses being CR/CRu. The median TTP was 4.9 months for all patients and the median DR was 5.7 months. Thus it appears that in relapsed MCL patients, the ORR to single-agent Zevalin is lower than observed for low-grade NHL or large cell NHL. Current trials are using Zevalin after R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) induction for patients with previously untreated MCL. This approach uses the RIT at a time of minimal residual disease. It will be several years before it will be known whether this strategy can improve the otherwise relentless relapses that typically occur in the MCL patient group.

Zevalin in relapsed diffuse large cell lymphoma

Patients with relapsed large cell lymphoma who are in good health, less than 75 years of age, and with chemosensitive disease are usually treated with high-dose therapy with stem cell rescue. However, elderly patients, or those who are not candidates for transplant do not have good therapeutic options and can be considered candidates for trials of RIT. In the phase I trial of Zevalin there were 14 patients with relapsed large cell NHL and 43% responded. A recent trial in Europe treated 104 patients with relapsed or refractory diffuse large cell NHL with a single dose of Zevalin 0.4 mCi/kg (maximum of 32 mCi). They found an ORR of 44% for the entire group with 55% of rituximab-naive patients responding compared to 19% of patients with prior treatment with rituximab-containing regimens. Further follow-up of the patients and full publication of the results are needed before conclusions on the use of Zevalin RIT in this setting can be made. Current trials in the Eastern Cooperative Oncology Group for diffuse large cell NHL are focusing on using Zevalin as adjuvant therapy after completion of R-CHOP induction. The aim is to increase the rate of CR and TTP.