

## 《Invited Special Lecture》

High Dose Radioimmunotherapy of Non-Hodgkin's Lymphoma:  
Update and Future Studies

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We have been conducting high dose  $^{131}\text{I}$  radioimmunotherapy trials for non-Hodgkin's lymphoma with bone marrow transplantation since 1986. The hypothesis was that pre-transplant conditioning with high dose  $^{131}\text{I}$  attached to anti-B cell antibodies would deliver an effective therapy dose with reduced toxicity compared to standard whole body radiation transplant. Our treatment approach is based on pre-treatment estimation of radiation absorbed doses to normal organs from trace labeled infusion of  $^{131}\text{I}$  B1 antibody. Quantitative imaging studies with whole body counting and organ volume determination are obtained as MIRD calculation input for each patient. MIRD dose output rad/mCi values per organ are adjusted for the actual organ volumes in each patient. In the Phase I and Phase II clinical trials conducted with high dose  $^{131}\text{I}$  antibody alone followed by bone marrow transplant, pulmonary toxicity was achieved at the maximally tolerated dose limit of 27 Gy (approximately 600–800 mCi). Patients in these groups experienced nausea and limited anorexia, but no mucositis or major GI complications normally associated with bone marrow transplant conditioning regimens. In this group, there was an overall 95% complete response rate, with approximately 65% long term survival.

Current experimental treatment protocols are aimed at increasing long term response. They employ a modified dose escalation protocol using  $^{131}\text{I}$  anti-B1 antibody combined with high dose etoposide (60 mg/kg) and cyclophosphamide (100 mg/kg) combined with autologous stem cell or bone marrow transplantation. Since January 1995, 40 patients have been enrolled in this  $^{131}\text{I}$  radiation dose escalation (groups of 4 patients) to the current dose of 25 Gy. Of 37 evaluable patients, 92% are alive, and 78% are progression free after median follow-up of 1.5 years. Toxicities include grade 4 myelosuppression, grade II–III nausea, pulmonary infiltrates, and veno-occlusive disease of the liver. Pulmonary and gastrointestinal toxicities are dose-limiting. This trial is ongoing to define the maximally tolerated dose limited.

In the next year we will begin testing  $^{90}\text{Y}$  DOTA labeled antibodies for use in non-Hodgkin's lymphoma treatment. These studies will be aided with the use of  $^{86}\text{Y}$  PET imaging for dosimetry estimation in pre-treatment biodistribution studies. We will exploit the capabilities of PET imaging to determine tissue trace isotope concentrations and high resolution imaging to contribute to successful high dose  $^{90}\text{Y}$  antibody therapy.