Phase I study of Zevalin (Ibritumomab Tiuxetan) in Waldenstrom's Macroglobulinemia (Lymphoplasmacytic Lymphoma) C. Emmanouilides, P. Multani, S.Treon. UCLA Medical Center, Los Angeles, CA; IDEC Pharmaceuticals, Sna Diego, CA, Dana-Farber Cancer Institute, Boston, MA.

Radioimmunothery targeting CD20 against B-cell NHL has been associated with response rates higher than those achieved with rituximab. Prior trials have established the safe dose of Zevalin (^{90}Y-Ibritumomab tiuxetan, Y2B8) for patients with B-cell NHL with no more than 25% involvement of the bone marrow by disease. However, this exclusion eliminates many WM patients who have primarily BM involvement. Anecdotal experience suggests a high response rate of Zevalin in WM patients. A phase I clinical trial has been designed aiming at defining the safe dose of Zevalin in patients with WM and BM involvement up to 50% with disease and to assess feasibility of repeated administrations of small doses of Zevalin in such patients. Eligible patients need to have adequate hematologic indices (ANC>1500/mm3, Platelets>100k/mm3) organ function, no prior autologous stem cell transplant and recent BM biopsy with involvement up to 50%. Starting dose of Zevalin will be 0.08 mCi/kg in a cohort of 3 patients. Zevalin will be administered according to current standards. Dose escalation of the starting dose by 0.04 mCi/kg in cohorts of 3-6 patients will be performed if dose limiting toxicity is not noted in more than 1 out of 6 patients. Dose limiting toxicity is defined as either of the following: grade IV cytopenia or other Zevalin-related grade IV toxicity lasting more than 3 weeks; grade III cytopenia lasting over 8 weeks; failure to achieve hematologic recovery (ANC > 1500/mm3, platelets > 100000/mm3) at week 12 post treatment; serious unexpected Zevalin-related toxicity. At the end of the 12 week period, patients will be assessed with a BM aspirate and biopsy. Retreatment will be provided for as any times as applicable if there is no complete response and no progression. If the degree of bone marrow involvement remains in the 25-50% range, retreatment will involve a similar dose of Zevalin; if it is <20%, patients will receive such an amount of Zevalin to reach the maximum allowed cumulative dose of 0.4 mCi/kg (or 0.3 mCi/kg for mild thrombocytopenia). Despite the phase I design, the retreatment provision is expected to result in significant clinical benefit, especially given the fact that antibody-based treatments seem to be particularly effective in the blood and bone marrow compartment. Thus, even patients who enroll in the early stages of the trial are expected to improve. The protocol has been reviewed by FDA and has been approved for implementation. Patient enrollment is expected to start in the autumn of 2002.