[Abstract 29]

THE WM1 TRIAL, AN INTERNATIONAL COLLABORATIVE PHASE III STUDY OF CHLORAMBUCIL VERSUS FLUDARABINE AS INITIAL THERAPY FOR WALDENSTROM'S MACROGLOBULINAEMIA AND RELATED DISORDERS.

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The WM1 study is a prospective randomized open-label study which includes patients with previously untreated Waldenstrom's Macroglobulinaemia (WM), splenic lymphoma with villous lymphocytes (SLVL) and non-IgM lymphoplasmacytic lymphoma (LPL) who have an indication for treatment. Patients who have received plasmapheresis for control of clinically significant hyperviscocity or splenectomy are still eligible for subsequent randomization. At registration, patients are categorized as WM, SLVL or LPL and these cohorts are planned to be analysed separately.

The aim of this study is to compare the efficacy of oral chlorambucil at a dose of 8 mg/m^2 (6 mg/m^2 for those over the age of 75 years) for 10 days every 28 days to a maximum of 12 cycles with oral or iv fludarabine at a dose of 40 mg/m^2 po or 25 mg/m^2 iv (30mg/m^2 po or 20 mg/m^2 iv for those over the age of 75 years) for 5 days every 28 days to a maximum of 6 cycles. Primary end-points are response to therapy and duration of response; secondary end-points are improvement in haematological parameters, toxicity of therapy, quality of life and survival.

To detect a difference in response rate of patients with WM of 15%, assuming that the overall response rate to chlorambucil will be 50% and to fludarabine will be 65% with a power of 80%, requires the sample size of each group to be 183; this indicates the need for collaboration of a number of national investigator groups. Accrual to the study stands at 75 patients at April 2004. Registration, randomization and data collection is entirely internet based (www.waldenstroms.org) and the study is organized by an international collaboration with planned central interim analysis to assess adequacy of accrual and data capture. An external data monitoring committee has been convened to monitor the study.