

[Abstract 34]

MANAGEMENT OF WALDENSTROM'S MACROGLOBULINEMIA (WM) IN THE PRE-RITUXIMAB ERA: UPDATE ON US INTERGROUP TRIAL S 9003 & THE ARKANSAS AUTOTRANSPLANT EXPERIENCE

Athanasios Fassas, Madhav Dhodapkar, Jason McCoy, Erik Rasmussen, John Crowley and Bart Barlogie. Myeloma Institute for Research & Therapy University of Arkansas for Medical Sciences, Little Rock, AR (AF, BB); Rockefeller University, New York, NY (MD); Cancer Research & Biostatistics, Seattle, WA (JM, ER, JC), USA.

S 9003 enrolled 231 patients with WM between 1992 and through 1997, one-third of whom had been diagnosed more than 12 mos earlier and 36% were older than 70 yr old. Upon disease progression or development of symptoms, 182 were re-registered to receive Fludarabine (F) 30 mg/sqm/d x 5 d every 28d for 4 to 8 cycles; 35% had received prior therapy; most started F within 6 mos from initial study entry. With a median follow-up of 9 yrs, the median overall survival (OS) from enrollment is 99 mos. Upon initiation of F therapy, 36 % achieved PR including only 3% CR's, resulting in median post-F event-free survival (EFS) of 28 mos and OS of 84 mos. B2M and IgM levels pre-F were confirmed as independently significant prognostic features affecting both OS and EFS: with B2M < 3 mg/L, 5 yr estimates of OS / EFS were 69% / 33% compared with only 28% / 8% with B2M > 3 mg/L and IgM < 4 g/dL; those with B2M > 3 mg/L and IgM > 4 g/dL had intermediate OS / EFS of 59% / 15% (p < .0001 / p < .0001). Median OS has not been reached for the two-thirds without prior therapy at 10 yrs, whereas the 64 previously treated patients had a median OS of 50 mos.

At Arkansas, 32 patients with WM in various disease stages were subjected to peripheral blood stem cell collection (PBSC) using either growth factor stimulation alone or chemotherapy plus growth factors (CTX +/- VP 16 or DT-PACE with DEX, Thalidomide plus 4 day continuous infusions of DDP 10 mg/sqm/d, ADR 10 mg/sqm/d, CTX 400 mg/sqm/d and VP 16 40 mg/sqm/d. PBSC collection was significantly impaired in case of prior F exposure, so that the CD34 target of at least 10 million/kg was obtained in 3 out of 10 with prior F exposure; 1 had received only 1 course of F more than 6 years prior to attempted collection. The remaining 2 patients had collected pre and post F exposure. In both patients, the time interval between F-collection exceeded 2 years. Of the 10 patients with prior F exposure, 2 had 1 collection, 6 had 2 collections, 1 had 3 collections and 1 had 1 PBSC and 1 bone marrow collection attempt. Twenty-one patients received high dose alkylator therapy mainly with melphalan 140 -200 mg/sqm or BEAM. Of the 11 patients mobilized with DT-PACE, all achieved PR including 3/11 achieving CR; all patients achieved PR post-transplant with 10/21 achieving CR. No patient suffered mobilization or transplant-related mortality. With a median follow-up of 30.4 mos, 18 patients remain alive. These pilot data attest to the remarkable efficacy and PBSC-mobilizing potential of DT-PACE as a prelude to further cytoreduction with well-tolerated high dose melphalan or BEAM. Prior F therapy significantly impairs PBSC collection (due to unknown mechanisms and recovery from F damage is slow) and should be avoided when highly effective autotransplants are considered for the management of patients with high-risk WM.