

**FLUDARABINE FOR WALDENSTROM'S MACROGLOBULINEMIA: UPDATE OF
SOUTHWEST ONCOLOGY GROUP S9003 TRIAL**

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An update is provided of a prospective observational multi-center clinical trial that enrolled 231 patients with Waldenstrom's Macroglobulinemia (WM) between 1992 and 1998. Of these, 184 patients with symptomatic or progressive disease were treated with 4 to 8 cycles of fludarabine (30 mg/m² daily for 5 days every 28 days). The median age was 66 (range, 38 – 88 years), 59% were male. The median survival from study enrollment has now been reached at 88 months with 97 deaths, with a 10 year projected survival of 43% (\pm 12%). One hundred eighty-four patients went on to treatment registration, 64 were previously treated and 120 were untreated. More than 90% of patients were re-registered for treatment within 1 month of initial registration. Their progression-free survival is 48 months overall and 59 months in those without prior therapy compared to 30 months in the pretreated group (p=.07), which reached statistical significance for survival (84 versus 46 months, p=.01). The 54 patients not requiring therapy had a lower incidence of anemia, thrombocytopenia, lymphadenopathy, hepatosplenomegaly and hypoalbuminemia (all p<.05). Likewise, their IgM, CRP and B2M levels were significantly lower than among those requiring treatment. Factors predicting requirement for eventual treatment included B2M, hemoglobin and IgM level. Response was measured as complete remission (CR), remission (R; 75% reduction in IgM together with at least 50% reduction in tumor mass lesions and decrease in marrow lymphocytosis to below 25%) and partial remission (PR > 50% reduction in IgM and tumor mass lesions). Altogether, 6 achieved CR, 21 had R and 33 had PR for an overall response rate of 33%. Responses were more frequent in patients <65 years (44% versus 27%) and not affected by prior therapy. On multivariate analysis, factors associated with overall survival included B2M, IgM, hemoglobin and prior therapy whereas analysis of progression-free and overall survival of those 184 patients requiring treatment revealed B2M \geq 3 mg/L and IgM \geq 4000 mg/dL as predictors of poor outcome.