Session V: Prognostic, Predictive and Response Markers in WM

Abstract 124

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International Waldenström Macroglobulinemia Prognostic Index Project.
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A prognostically meaningful staging system for survival of patients with Waldenström macroglobulinemia after first treatment initation (ISSWM) has been developed in a series of 587 patients (pts) diagnosed between September 1979 and December 2001 and treated mainly by single alkylating agent (369 pts) or fludarabine (195 pts) (Blood 2006 108: 127a). Using the combination of age >65 years, Hb $\leq$11.5 g/dL, platelet count $\leq$100 x10^9/L, B2M >3 mg/L, and M-protein >7.0 g/dL, low risk was defined by the presence of $\leq$1 adverse characteristic except age, high risk by the presence of >2 adverse characteristics; the remaining patients with 2 adverse characteristics or age >65yr had intermediate risk, with 5-yr survival rates of 87%, 36% and 68% respectively (p<0.0001). The prognostic system was effective in patients treated with alkylating agent or fludarabine (F). ISSWM has been validated in patients who received rituximab alone or in combination with dexamethasone and cyclophosphamide, as first line therapy (Blood, 2007; 110: 4730a). However, this system has not been evaluated yet in pts treated with F-based combination regimen or in more advanced phase of the disease. Therefore, we reviewed the prognostic value of ISSWM in a series of 81 pts (median age 63, range: 26 to 82, M/F ratio: 53/29) diagnosed between 11/1998 and 06/2007 and treated 1 to 217 months after diagnosis (median 39 months) with one of the following regimens, namely: F and rituximab (FR; Blood 2004; 104: 753a) or cyclophosphamide (FC; Leukemia. 2005; 10:1831-4) or both agents (RFC; Blood 2006; 108: 4727a) . FR, FC and RFC were given in 6, 47 and 28 subjects respectively. Treatment was given as first-line therapy in 14 pts, second line therapy in 41 pts or more advanced phase in 26 pts. At the time of the initiation of F-based therapy, baseline parameters included age >65 years in 47% of pts, Hb $\leq$11.5 g/dL in 80%, platelet count $\leq$100x10^9/L in 24%, B2M >3 mg/L in 53% and monoclonal protein >7.0g/dL in 2%. ISSWM was available in 58 pts (low-risk: 22% of pts, intermediate-risk: 38% and high-risk: 40%). With a median follow-up of 27 months (range, 3-104 months) in surviving pts, the 5-yrs survival after treatment initiation was 62% (95%CI 48-79) in the 81 pts. Time from first-line therapy to initiation of this regimen and the number of previous regimens had no prognostic value for subsequent survival. Three-year subsequent survival of high-risk pts was 51% (95CI: 30-88) years, whereas it was estimated 86% (95CI: 74-100) in remaining pts (p=0.05). This analysis confirms the usefulness of ISSWM for identifying high-risk pts in advanced phase of the disease.