[ABSTRACT WM1.7]

INTERNATIONAL PROGNOSTIC SCORING SYSTEM FOR WALDENSTRÖM'S MACROGLOBULINEMIA

P. Morel, A. Duhamel, P. Gobbi, M. Dimopoulos, M. Dhodapkar, J. McCoy, E. Ocio, R. Garcia-Sanz, V. Leblond, R. Kyle, B. Barlogie, G. Merlini
Hematology. Hôpital Schaffner, Lens, France

Waldenström macroglobulinemia (WM) patients (pts) may require treatment in order to control symptoms caused by anemia, organomegaly or hyperviscosity. Median survival has ranged between 60 and 120 mo. In retrospective analyses, several characteristics were constantly associated with a poor clinical outcome such as an advanced age, a low hemoglobin concentration (Hb), a low platelet count, a low albumin concentration and an elevated serum β2-microglobulin (B2M). Few prognostic indices have been proposed, but none of them have been widely accepted and used. Therefore, 9 cooperative groups or institutions decided to join their records in order to design a prognostically meaningful staging system for symptomatic WM patients, requiring therapy. We performed multivariate analyses with bootstrap validation in a series of 587 pts (median age 67, range: 28 to 95, M/F ratio: 1.7) diagnosed between September 1979 and December 2001. Diagnostic and treatment criteria fulfilled recommendations of the 2nd international WM workshop. Front-line treatment was initiated at diagnosis in 69% and 4 to 164 mo later in the remaining pts. Criteria for initiation of therapyincluded cytopenia, constitutional symptoms, organomegaly, hyperviscosity, IgM-related disorders, which pertained to 51%, 44%, 35%, 31% and 13%, respectively. Treatment regimens comprised alkylating agents, fludarabine and rituximab in 369, 195 and 23 subjects, respectively. Baseline parameters included age>65 yr in 57%, Hb≤11.5 g/dL in 65%, platelet count ≤100·109/L in 9%, granulocyte count ≤1.5·109/L in 9%, B2M >3 mg/L in 56%, albumin ≤3.5 g/dL in 36% and monoclonal protein >7.0 g/dL in 7%. With a median follow-up of 64 mo (range, 6-182 mo), the median survival after treatment initiation was 87 mo (95%CI 79-103) regardless of the type of therapy applied (p=0.3). Using results of univariate survival analyses, recursive partitioning and martingale residuals analyses, 7 adverse characteristics for inclusion in multivariate analyses were identified during an expert meeting: age >65 yr, platelet count ≤100·109/L, B2M >3 mg/L, M-protein >7.0 g/dL, granulocytes ≤1.5 ·109/L, Hb ≤11.5 g/dL and albumin ≤3.5 g/dL. The Cox proportional hazard model with stepwise selection selected the first 6 covariates. Bootstrap resampling (500 replicates) validated the selection of the first 4 covariates in at least 80% of the replicates. Selection of at least one of the last 2 covariates in more than 80% of the replicates indicated a correlation between these 2 covariates, and validated the inclusion of Hb only. Using the combination of age, Hb, platelet count, B2M and M-protein, low risk was defined by the presence of ≤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, comprising 27%, 35% and 38% of patients with 5-yr survival rates of 87%, 36% and 68% (p<0.0001), independent of treatment and age. IPSS split each subgroup identified by previous scoring systems (Morel, Merlini, Ghobrial and Dhodapkar). Conversely, log-rank test was significant only when the latter prognostic system was assessed in low IPSS-risk pts. Thus the combination of age, B2M, M-protein and blood counts provides simple prognostic model for survival in WM, hopefully serving as an objective basis for initiation of therapy and comparison of treatment results.