EFS was significantly longer in the Dex/Thal arm (median, 44 vs. 12 months; $P = .0021$).Complete response on serum electrophoresis was achieved in 4/13 patients. Two presented a TE (0/30 in the control arm). Otherwise, tolerability of maintenance Dex/Thal (median duration 17 months) was acceptable. Within a median follow-up of 39 months, 3-year OS were 73% and 72% ($P = .66$) since first randomization and estimated at 64% and 74% ($P = .52$) after maintenance randomization. In combination with alkylating agents, oral Dex/Thal is an effective induction regimen in elderly MM patients. When administered as an intermittent maintenance treatment, it has a good safety profile and significantly prolongs EFS, but does not significantly improve OS.

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Role of Soluble Syndecan-1 in FLC Hypersecretion in MM

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Baseline free light chain (FLC) values and their ratio (FLCR) were shown valuable for the prognostication of survival in MM. The underlying biologic mechanisms of FLC hypersecretion by malignant plasma cells are unknown and it could be assumed that molecular or microenvironmental factors are involved. Numerous cytokines secreted mostly by the bone marrow microenvironmental cells participate in MM pathogeny. The purpose of the present study was to determine the baseline serum levels of such cytokines, namely IL-6 and its soluble receptor (sIL-6R), syndecan-1 and its cleaved soluble form (s-synd-1), VEGF and BLyS, and to investigate any possible correlation of their levels with FLC values. 152 MM patients were studied (derived from a series of 245 patients with FLCs measured at diagnosis). 50% of patients were males, 25% were in Durie-Salmon stage I, 33% stage II, and 42% stage III respectively. 33% were ISS stage I, 25% stage II and 42% stage III respectively. 15% of the patients had impaired renal function, 32% presented anemia and 4% thrombocytopenia. LDH and CRP were abnormal in 15% and 48% respectively. FLCs were measured by nephelometry (FREELITE, The Binding Site Ltd. Birmingham, UK). The light chain ratio (sFLCR) κ/λ or λ/κ was built with the uninvolved LC as denominator and values over the median were defined as high. Statistical analysis was performed by standard methods. S-synd-1, VEGF, IL-6, sIL-6R and BLyS were measured in 98, 80, 81, 92, and 79 patients respectively with available frozen serum aliquots at diagnosis. Measurements were performed by ELISA, in duplicate (Diaclone Research's kit for s-synd-1 and R&D Systems' for the rest). The median sFLCR was 8 for κ-MM patients and 50.5 for λ-MM. High sFLCR values correlated with s-synd-1 ($P = .012$) while no correlation was found with VEGF ($P = .08$), IL-6 ($P = .61$), sIL-6R ($P = .9$) and BLyS ($P = .83$). Prognostic impact with regard to patients' survival was observed for baseline sFLCR, serum s-synd-1, sIL-6R and BLyS. The prognostic implication of sFLCR was independent of sIL-6R and BLyS by multivariate analysis. In conclusion, the correlation between sFLCR and serum s-syndecan may suggest that the last could play a role in the inappropriate FLC secretion.

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Frequent Amplification of IL-6 Receptor Gene in Patients with Multiple Myeloma

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Multiple myeloma (MM) is characterized by proliferation of plasma cell, and IL-6 is essential growth factor of myeloma cell. IL-6 play a key role through IL-6 receptor, which is located in the long arm of chromosome 1 (1q). Gain of 1q is one of the most frequent cytogenetic changes in myeloma. We hypothesized increased expression of IL-6R in myeloma cells gives a growth previlage to myeloma cells among bone marrow hematopoietic cells. We investigated the frequency of the amplification of IL-6 receptor gene among 144 newly diagnosed MM patients. Amplification of IL-6R was assessed by interphase FICTION method using IL-6R probe and anti-light chain antibody with bone marrow nucleated cells. In context with IL-6R, interphase FISH for 1q (1q21), Rb1 (13q14) deletion, IGH translocation and numerical changes of chromosome (chromosome 9,17,20) was performed. We detected IL-6R amplification in 65% (66/102) of the multiple myeloma patients using IL-6R FISH. Using Rb1 (13q14) FISH probes, 93% (28/30) of patients were identified as having genetic changes. Similarly, using IgH (14q32), 1q25 and TP53 (17p13.1) FISH probes, 48% (49/102), 43% (31/72) and 18% (9/50) of patients were found to have genetic changes. Several poor-risk genetic features, such as low albulin level, positive IGH FISH result and positive TP53 FISH results were significantly associated with IL-6R amplification. We suggest that amplification of IL-6R in myeloma cells may contribute to the proliferation of myeloma cells and is associated with poor prognosis in myeloma patients.