YOUNGER PATIENTS WITH MULTIPLE MYELOMA.

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BACKGROUND: While the majority of patients with multiple myeloma (MM) are diagnosed during their 7th decade of life, a small percentage of them belong to a much younger age group. With current treatment modalities, survival has been prolonged to 8 years or even longer. However, despite considerable progress in the pathophysiology and treatment of MM, eradication of the disease remains most of the times not feasible. It is still uncertain whether younger patients with MM have a better outcome and a superior response to therapy.

PATIENTS AND METHODS: We conducted a retrospective descriptive study of relatively young patients diagnosed with MM. Between 2003 and 2012, 275 patients were diagnosed with MM at our Center, 10 (3.6%) of which were at most 40 years old. Our primary objective was to evaluate the quality and duration of response to treatment, as well as overall survival.

RESULTS: Seven patients were men and 3 were women. The patients' age ranged from 30 to 40 years old, with a median age at diagnosis of 35 years. Medical history was unremarkable for most of our patients (6/10), while 1 had a thyroid gland nodule, 1 had had multiple surgeries due to car accident and ruptured cruciate ligaments, and in 2 patients medical history was unknown.

Median percentage of bone marrow infiltration by plasma cells at diagnosis was 50%. Extramedullary disease (brain plasmacytomas, resulting in left facial, sublingual and lower laryngeal nerve palsy) was present in only 1 patient. In 7 patients a chromosome analysis by karyotyping was conducted while fluorescence in situ hybridization (FISH) was performed in 6 patients. Karyotype abnormalities were detected in only 1 patient (complex, non hyperdiploid). However, by FISH, chromosomal abnormalities were detected in 5 patients, 3 of whom had normal karyotype. The most frequent karyotype abnormalities revealed by FISH were del(13) (in 3 patients) and t(4;14) (in 2 patients).

Five patients were diagnosed with stage IIA disease, 4 with IIIA and 1 with IIIB according to Durie-Salmon staging system. Regarding IPS staging, 6 patients were diagnosed with stage I disease, 2 with stage III disease and for the remaining patients data was not available.

First-line chemotherapy consisted of various combinations including proteasome inhibitor (bortezomib), anthracycline and/or alkylating agent (doxorubicin and/or cyclophosphamide) in addition to corticosteroids (dexamethasone). Specifically, first-line treatment was VDPACE (bortezomib, dexamethasone, doxorubicin, cyclophosphamide, etoposide and cisplatin) in 3 patients, VCD (bortezomib, cyclophosphamide, dexamethasone) and PAD (bortezomib, doxorubicin, dexamethasone) were equally administered in 2 patients, and VAD (vincristine, doxorubicin, dexamethasone), a combination of VAD with liposomal doxorubicin, and thalidomide and dexamethasone, were each one given to 1 patient. Eight out of 10 patients underwent autologous hematopoietic stem cell transplantation (ASCT) while 2 of them received tandem transplantation. One patient could not be submitted to ASCT due to rapid disease progression and death, and 1 patient proceeded directly to allogeneic hematopoietic stem cell transplantation (alloSCT), after completion of 8 cycles of PAD and 4 cycles of lenalidomide/dexamethasone. The patient is still alive seven years from diagnosis and six years after allogeneic transplantation. In another patient alloSCT was performed after late 2nd ASCT, due to disease relapse, but the patient died because of progressive disease 8 months after alloSCT.

The median duration of response to first-line therapy is 25.3 months and overall survival is 50% at 5 years. Three patients are in complete remission 57 to 135 months after diagnosis (2 of which have received a tandem ASCT), 2 in near complete remission and 1 in partial remission. Four patients have died due to progressive disease.

CONCLUSION: Younger (less than or equal to 40 years old) patients with MM may have long-term survival, should they be offered hematopoietic stem cell transplantation, since their performance status usually allows even for alloSCT which remains the only true curative option. These patients require vigorous treatment with the aim of complete remission and hematopoietic stem cell transplantation in order to achieve the optimal outcome. In this age group, it seems reasonable to pursue even the cure of MM by appropriate therapy.