Prospective molecular monitoring of minimal residual disease after nonmyeloablative allografting in newly diagnosed multiple myeloma

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Data on minimal residual disease (MRD) after tandem autologous-nonmyeloablative allografting (auto-allo) are lacking

Aim of the study. To carry out MRD analyses by nested qualitative PCR and real time quantitative (RQ) PCR on newly diagnosed MM patients treated with auto-allo

Methods. Twenty-six patients with a diagnostic bone marrow (BM) specimen suitable for immunoglobulin heavy-chain gene rearrangement (IGH) sequencing were evaluated for MRD by PCR methods. Auto-allo consisted of an autograft followed by 200 cGy TBI and an allograft. BM samples were collected at diagnosis, after the autograft, at month 1, 3, 6 after the allograft and then every 6 months. Nested-PCR and RQ-PCR analyses were carried out using patient-specific primers. FullMR and StandardMR indicated MRD negativity on two consecutive samples by nested-PCR or RQ-PCR respectively

Results. In 19/26 patients had a molecular marker. At a median follow-up of 10 years (4.4-12) from diagnosis and 8.9 years (3.5-11) from the allograft, overall survival (OS) was 61% and median time-to-progression (TTP) 5.6 years. TRM was 16%. MRD studies showed that after the autograft 3/19 patients (16%) were negative by nested-PCR. After the allograft PCR-negativity rates gradually increased to 4/18 (22%) at 1 and 3 months, 7/17 (41%) at 6 months and 8/15 (53%) at 1 year post-transplant. Overall, 8 patients achieved FullMR at a median time from allograft of 6 months (1-12) and for a median duration of 33 months (6-102). Overall, 8 relapses occurred, 6 in the 11 patients who never achieved FullMR and 2 in patients who reached FullMR: one showed molecular relapse, with persistent CCR, after 3 years and the other after 6 months from the last PCR-negative sample. Patients in FullMR had better median TTP (not reached vs 1.6 years, p=0.043) and OS (not reached vs 3.3 years, p=0.008) than patients who did not achieve FullMR. StandardMR occurred in 12/19 patients (63%) during the first 24 months post-transplant, at a median time of 2 months (1-18) and for a median duration of 27 months (3-102). Patients in StandardMR showed better median TTP (not reached vs 1 year, p=0.005) and OS (not reached vs 3.3 years, p=0.031) as compared to patients with positive PCR. There was no correlation with chronic graft-vs-host disease suggesting specific graft-vs-myeloma

Conclusions. Auto-allo induces high molecular remission rates, significantly associated with better TTP and OS, that indicate potentially curative graft-vs-myeloma