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PROLONGED MOLECULAR REMISSIONS AFTER TANDEM AUTOLOGOUS-NONMYELOABLATIVE ALLOGRAFTING IN NEWLY DIAGNOSED MYELOMA

Benedetto Bruno 1,* , Simone Ferrero 1, Daniela Drandi 1, , Moreno Festuccia 1, Francesca Patriarca 3, Nicola Mordini 4, Silvia Cena 1, Luigia Monitillo 1, Luisa Giaccone 1, Federica Ferrando 1, Daniela Barbero 1, Alberto Rocci 1, Sara Barbiero 1, Andrea Gallamini 4, Renato Fanin 3, Roberto Passera 5, Antonio Palumbo 1, Mario Boccadoro 1, Paola Omedè 2, Marco Ladetto 1

1Department of Molecular Biotechnology and Health Science, 2Division of Hematology, A.O. San Giovanni Battista, Torino Italy, University of Torino, Torino, 3A.O. U. Haematological Clinic, University of Udine, Udine, 4Hematology, A.O. S. Croce Carle, Cuneo, 5Division of Nuclear Medicine, Statistical Consultant, University of Torino, Torino, Italy

Allografting induces persistent molecular remissions (MR) in multiple myeloma (MM). We here present the results of minimal residual disease (MRD) analyses by nested qualitative PCR (Nested-PCR) and real time quantitative (RQ)-PCR in 26 patients (pts) with stage II-III MM treated with a tandem auto-allo approach. Transplants consisted of an autograft followed by non-myeloablative 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 as previously described (Voena, Leuk 1997; Ladetto, BBMT 2000). For outcome analysis pts were grouped according to reported criteria (Ladetto, ASH 2011): FullMR and StandardMR indicated MRD negativity on two consecutive samples by nested-PCR or by RQ-PCR respectively. Nineteen/26 pts had a molecular marker. At a median follow-up of 10,5 years (5,2-13,9) from diagnosis and 9,9 years (4,2-12,9) from the allograft, overall survival (OS) was 61% and median progression-free survival was 5,2 years. Transplant-related mortality occurred in 3/19 pts (16%), while 5/19 pts (26%) died of disease progression. Overall, cumulative incidence of non-relapse mortality (NRM) was 16%. MRD analysis showed that after the autograft 3/19 pts (16%) were negative by nested-PCR. After the allograft, the rate of PCR negativity remained low at month 1 (3/19, 16%) and 3 (5/19, 26%). However, PCR negativity went up to 44% (8/18) at 6 months and 47% (7/15) at one year post-transplant. Overall, 8 pts 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 among 11 pts who never achieved FullMR and 2 in 8 pts who reached FullMR. Of these one has incomplete follow up and in the other one clinical relapse was heralded by a molecular relapse. Pts in FullMR had lower relapse incidence (27% vs 55% p=0,189) and better median OS (not reached vs p=0,027) than pts who did not achieve FullMR. StandardMR occurred in 12/19 pts (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). Pts in StandardMR showed lower relapse incidence (RI) (27% vs 71% p=0,016) and better median OS (not reached vs p=0,05) as compared to pts with positive PCR.