IMMUNOPHENOTYPIC RESPONSE AFTER ALLOGRAFTING IN MULTIPLE MYELOMA

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RISPOSTA IMMUNOFENOTIPICA DOPO TRAPIANTO ALLOGENICO NEL MIELOMA MULTIPLO

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In myeloma, data on immunophenotypic remission (IR) after an allograft are lacking. Our study compared the impact of IR to that of complete clinical remission (CR) in 66 consecutive patients, median age 54 years (35-66), transplanted between 2000 and 2011, and with at least a follow-up of 3 months. Disease response was evaluated by serum/urine electrophoresis and bone marrow aspirate at scheduled time-points. Skeletal survey or MRI were performed yearly or as clinically indicated (overt relapse or complaints of bone pain). IR was defined as absence of monoclonal marrow plasma-cells detected by 4 or 6-colour staining flow cytometry using CD38, CD138, CD56, CD19, CD45, cyKappa, cyLambda. CCR was defined according to standard criteria. Conditioning regimen was non-myeloablative in 55 patients, reduced-intensity in 10 and myeloablative in 1. Donors were HLA identical siblings in 58 patients and unrelated in 8. Thirty-five/66 (53%) received an allograft up-front. In patients surviving at least 3 months, treatment related mortality was 10.6% at 3 years. After a median follow-up of 69 months (19-147), incidence of acute and chronic graft-versus-host disease was 45% and 49%, with no significant difference between responsive and refractory patients. At follow-up, 24/66 (36%) patients achieved CR and IR (CR/IR), 22/66 (33%) achieved IR but not CR because of persistence of the M-component (noCR/IR), and 20/66 (31%) did not achieve either CR or IR (noCR/noIR). Median overall (OS) and event-free survivals (EFS) were not reached and 59 months in the CR/IR group, 77 and 15 months in the noCR/IR, and 30 and 5 months in the noCR/noIR respectively ($p<0.001$ for both OS and EFS). Belonging to the CR/IR group was the only statistically significant predictor for prolonged OS and EFS ($p<0.001$). Of note, cumulative incidence of extramedullary disease at first relapse post-trasnsplant was 4.4% in the CR/IR, 31.8% in the noCR/IR and 15.0% in the noCR/noIR groups respectively ($p<0.001$). In conclusion**, t**he achievement of IR showed a significant impact on clinical outcomes including patients who did not clear the M-component. Discrepancies between IR and CR, and a higher incidence of extramedullary relapse in the noCR/IR group suggest that myeloma cells may escape immune control outside the bone marrow. In this group, positron emission tomography may be indicated to detect early relapse.