REDUCED INTENSITY HSCT FOR CHRONIC GRANULOMATOUS DISEASE

Reinhard Seger and Tayfun Güngör,
Univ.Children`s Hospital Zürich, CH

HSCT is now offered early to patients with X-CGD and severe a/r CGD with evidence of absent O2- production or one life-threatening infection/ severe inflammatory disease. This lecture compares two reduced toxicity conditioning regimens (full dose treosulfan/fludarabin versus low dose/targeted busulfan/fludarabin) with balanced in vivo T-cell depletion (by serotherapy) and double immunosuppressive therapy for prophylaxis of GVHD and graft rejection/failure.

Both regimens can completely cure CGD patients of their disease, even if suffering from ongoing therapy–refractory infection or steroid-dependent granulomatous disease, provided an HLA-matched donor (sibling/family or unrelated 9-10/10 HLA compatible) can be found. Using the myelo-suppressive low busulfan regimen a 2 year probability of overall survival of 96%, an event-free survival of 90%, equivalent outcomes between matched siblings and unrelated donors and low incidence of acute/ chronic GVHD are achieved. To prevent underdosing low busulfan conditioning requires real-time drug monitoring and dose adjustment. If unavailable, a fixed submyeloablative busulfan dose (e.g. 14 mg/kg iv < 10 yrs and 12 mg/kg > 12 years) or the treosulfan regimen (dosed according to age) can be used instead.

Mismatched (haploidentical) donor HSCT is still experimental. A new strategy for patients lacking a conventional donor with first promising results in CGD, the posttransplant cyclophosphamide technique, will be discussed.