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Effect of graft source on safety and efficacy in patients undergoing hematopoietic stem cell transplantation

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Introduction: Donor availability remains a major challenge in allogeneic stem cell transplantations (HSCT). For patients who cannot find an HLA-matched sibling donor, current standard of care is a fully matched unrelated donor (MUD). However, not for all a MUD can be found and additional alternatives such as single loci mismatched unrelated donors, umbilical cord blood or haploidentical donors are used.

Material (or patients) and methods: In this retrospective, multicenter study (CR-AIR-006; NCT02188290) data was collected on outcome of HSCT in patients with AML or ALL (both in remission) or MDS, using either a fully matched (8/8 or 10/10) unrelated donor (MUD), a single-locus mismatched (9/10) unrelated donor (MMUD), umbilical cord blood (UCB) or a haploidentical (3/6, 4/6, 5/10, 6/10) donor (HAPLO). Data from transplantations performed between January 2010 and January 2013 (MUD, MMUD, UCB) or between January 2006 and July 2013 (HAPLO) was collected from centers participating in ATIR101 studies (CR-AIR-007; NCT01794299) and will serve as historic control group in the development of post-HSCT donor lymphocyte infusion (ATIR101). Haploidentical donor transplantations were conducted using myeloablative conditioning and a CD34+ cell selected graft. Transplant-related mortality (TRM), nonrelapse mortality (NRM), and overall survival (OS) up to 12 months post HSCT were compared between the four groups. In addition, incidence and severity of acute and chronic graft-versus-host disease (GvHD) up to 12 months was compared between groups. To determine clinical benefit the composite end-point of GVHD-free, Relapse-Free Survival (GRFS) was used.

Results: Data on 158 subjects was collected: HAPLO =35; MUD=64; MMUD=37; UCB (double cord)=22. Relapse occurred in 15% of the 158 patients with 12 months cumulative incidences of
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20% in the HAPLO group, 14% in the MUD group, 16% in the MMUD group and 9% in the UCB group. NRM was lower for the MUD group (9%) compared to the other groups (HAPLO: 66%; MMUD: 25%; UCB: 36%). Acute GvHD grade III-IV was less frequent in the HAPLO group (6%) compared with other groups (MUD: 11%; MMUD: 16%; UCB: 27%), and there was also less chronic GvHD in the HAPLO groups (11%) compared to the other groups (MUD: 39%; MMUD: 30%; UCB: 32%). Twelve month OS was lower for the HAPLO treatment group (20%) compared to all other treatment groups (MUD: 86%; MMUD: 64%; UCB: 55%). However, when looking at the GRFS it is clear that MUD transplantations have the best outcome, and that all other alternative donor sources have a low GRFS at 1-year post-HSCT.

**Conclusion:** Our data show that the current alternatives (HAPLO, MMUD or UCB) have a worse outcome compared to standard of care (MUD). Use of MMUD or UCB donors shows high rates of GVHD and TRM. Use of T-cell depleted haploidentical donors has substantially less GVHD, but more infections and thus higher rates of TRM. Adding additional donor lymphocytes (ATIR101) post-HSCT could overcome limitation of this CD34+ selected HAPLO regimen.

**Figure 1:**