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Oral Sessions

722. *Clinical Allogeneic Transplantation - Acute and Chronic GVHD, Immune Reconstitution: Chronic Graft-versus-Host Disease - Modulation and Impact on Outcome*

Impact of Chronic Graft-Versus-Host disease (GVHD) After Reduced Intensity Conditioning (RIC) Allogeneic Stem Cell Transplantation (allo-SCT) As Treatment for Acute Myeloid Leukemia (AML): A Survey From the Acute Leukemia Working Party of the EBMT

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The goal of RIC allo-SCT is to harness the graft-versus-leukemia (GVL) effect, while minimizing toxicities and the risk of GVHD. However, prior studies have shown a lower risk of relapse in AML patients (pts) who experienced chronic GVHD after RIC allo-SCT versus in those who did not. Here, we investigated the impact of occurrence of GVHD on transplantation outcomes in a large cohort of AML pts given allogeneic PBSC after RIC conditioning. Data from 1859 AML pts in first (n=1439) or second (n=420) CR transplanted between 2000 and 2009 following a RIC regimen at EBMT affiliated centres were analyzed. Pts were given PBSC from HLA-identical sibling (MRD, n=1208), or from HLA-matched unrelated donors (MUD, n=651). Median pt age at transplantation was 56 y (range, 18–77). 338 male pts were given grafts from female donors. RIC was based on low-dose TBI in 520 (28%) pts, while the remaining pts received chemotherapy-based RIC. ATG was given in 269 (22%) MRD and in 267 (41%) MUD recipients, respectively, while 151 (13%) MRD and 165 (25%) MUD recipients received in-vivo T cell depletion with alemtuzumab. The impact of chronic GVHD on relapse risk, non-relapse mortality (NRM), leukemia-free survival (LFS), and overall survival (OS) was assessed using time-dependent multivariate Cox models and in a landmark analysis at 18 months after transplant. Three-year incidences of relapse, NRM, LFS and OS were 34±1%, 15±1%, 51±2% and 60±2% in MRD recipients, respectively, and 34±2% (p=NS), 24±2% (P<0.001), 42±2% (P=0.001) and 47±2% (P=0.001) in MUD recipients, respectively. Grade II, III and IV acute GVHD were observed in 133 (11%), 61 (5%) and 30 (2%) MRD recipients and in 119 (18%), 41 (6%) and 24 (4%) MUD recipients, respectively. The 3-y cumulative incidence of chronic GVHD was 47%. Fifty-three percent of patients with chronic GVHD had extensive chronic GVHD, while the remaining 47% had limited chronic GVHD. In multivariate analyses, occurrence of grade II-IV acute GVHD was associated with a lower risk of

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relapse (HR=0.8; $P=0.04$), a higher risk of chronic (HR=2.2; $P<0.001$) and extensive chronic GVHD (HR=2.8; $P<0.001$), a higher risk of NRM (HR=2.4 $P<0.001$), a worsened LFS (HR=1.3; $P=0.01$), and a worsened OS (HR=1.5; $P<0.001$). In multivariate time-dependent analyses, occurrence of limited chronic GVHD was associated with a lower risk of relapse (HR=0.7; $P=0.05$), comparable NRM (HR=1.4; $P=0.16$), comparable LFS (HR=0.9; $P=0.29$) and better OS (HR=0.5; $P<0.001$), while occurrence of extensive chronic GVHD was associated with a lower risk of relapse (HR=0.6; $P=0.01$), higher NRM (HR=3.2; $P<0.001$), a trend for worsened LFS (HR=1.3; $P=0.06$) and comparable OS (HR=0.9; $P=0.34$). The median interval from transplantation to occurrence of chronic GVHD was 163 (range, 100–1545) days. To further assess the graft-versus-leukemia effect of chronic GVHD, we performed a landmark analysis in patients who were leukemia-free at 18 months after transplantation ($n=776$). Median follow-up from this landmark time-point was 24 (range, 0.1–112) months. Two-year relapse, NRM, LFS and OS were $16\pm 2\%$, $2.5\pm 1\%$, $82\pm 2\%$, and $89\pm 2\%$, respectively, in patients without chronic GVHD before the landmark time-point, versus $9\pm 1\%$ ($P=0.001$), $8\pm 1\%$ ($P<0.001$), $83\pm 2\%$ ($P=0.65$), and $86\pm 2\%$ ($P=0.38$), respectively, in patients with chronic GVHD before the landmark time-point. In conclusion, in this cohort of AML patients transplanted in remission, occurrence of chronic GVHD was associated with a lower risk of relapse that translated to better OS in patients with limited chronic GVHD but not in those with extensive chronic GVHD who experienced higher long term NRM, highlighting the need for long term prospective assessment of long term effects and quality of life in patients receiving RIC allo-SCT.

Disclosures: No relevant conflicts of interest to declare.

Footnotes

* Asterisk with author names denotes non-ASH members.



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