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POSTER ABSTRACTS

721.ALLOGENEIC TRANSPLANTATION: CONDITIONING REGIMENS, ENGRAFTMENT AND ACUTE TOXICITIES

Trends in Allogeneic Stem Cell Transplantation for Good Risk Acute Myelogenous Leukemia in First Complete Remission: A Longitudinal Study of > 15 Years from the ALWP/EBMT

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Background:
Favorable acute myelogenous leukemia (AML) includes AML with t (8:21), inv (16), and those with *NPM1* without *FLT3- ITD* without adverse cytogenetics (ELN 2022). The incidence of relapse (RI) in favorable-risk AML with chemotherapy is 35%-40%. Although RI is ~20% lower with allogeneic transplantation (HSCT), transplantation is usually not indicated in favorable risk AML at first complete remission (CR1) due to transplant-related mortality. However, in recent years, HSCTs have been associated with significantly lower non relapse mortality (NRM) and better outcomes.
Methods: Our aim was to assess outcomes of HSCT in favorable risk AML (t (8:21), inv (16), and NPM1 ^{mut}FLT3 ^{WT}) in CR1, comparing 3 time periods: 2005-2009, 2010-2014, and 2015-2021. Statistical tests included a multivariate analysis (MVA) adjusting for potential confounding factors performed using a Cox proportional-hazards regression model for main outcomes.
Results: 1850 patients (pts) were included, 526 with t (8:21), 625 with inv (16), and 699 with NPM1 ^{mut}FLT3 ^{WT} (normal karyotype). 222 pts were transplanted in 2005-2009, 392 in 2010-2014, and 1236 in 2015-2021. As the follow-up period differed, being 103.1 (IQR, 92.1-114.0), 78.3 (IQR, 69.4-86.3), and 32.0 (IQR, 29.5-34.5) months, respectively ($p<0.0001$), all survival events were censored at 3 y. Pts undergoing HSCT in 2015-2021 were older, with a median age of 50.9 (range 18.2-76.4) *vs*40.4 (range 18.3-67.7) and 42.4 (range 18.4-71) y, in those transplanted in 2005-2009 and 2010-2014, respectively ($p<0.0001$). More pts >50 y of

age were transplanted in the latest period with 52.7% *vs* the 2 earlier periods 27.9% and 32.1% (p<0.0001) and figures for >60 y were 25.4% *vs* 8.1% and 11% (p<0.0001), respectively. In 2005-2009 the most frequent diagnosis was t (8:21) at 44.6%, while in 2015-2021, it was NPM1 ^{mut}FLT3 ^{WT} at 45.6% (p<0001). In 2005-2009, the most frequent donors were matched siblings (MSD) (63.1%), while in 2015-2021 they were unrelated (UD) (50.7%). Haploidentical (haplo) transplants increased from 5.9% to 14.5% (p<0.0001). Bone marrow grafts decreased from 24.8% to 13.2%, while peripheral blood (PB) grafts increased from 75.2% to 86.8% (p<0.0001). Conditioning was myeloablative in 69.8%, 64.8%, and 60.2% and was reduced intensity in 30.2%, 35.2%, and 39.8% in pts transplanted in 2005-2009, 2010-2014, and 2015-2021 (p=0.014). Graft-versus-host disease (GVHD) prophylaxis with *in vivo* T cell depletion or post-transplant cyclophosphamide (PTCy) was more frequent in 2015-2021 compared to the other two periods (p<0.0001).

Day 60 engraftment (ANC >0.5 x 10 ^{9}/L) was 98.2 % vs 98.4% vs 98.5% (p=0.17). Day 180 incidence of acute (a) GVHD grade II-IV was 18.2%, 21.1%, and 21.6%; grade III-IV was 5.1% 5.7%, and 7.3% while the incidence of 3-y chronic (c) GVHD was 49.3%, 50.4% and 39.2%.

On MVA the incidence of total cGVHD was reduced in HSCTs performed >2015 compared to those performed in 2005-2009, hazard ratio (HR) =0.74 (95% CI 0.56-0.99, p=0.046) and GVHD-free, relapse-free survival (GRFS) improved for pts transplanted from 2010-2014 *vs* those transplanted in 2005-2009, HR=0.74 (95% CI 0.56-0.98, p=0.037) (Figure 1). All other HSCT outcome parameters including NRM, RI, leukemia-free survival (LFS), and overall survival (OS) did not differ (Figure 1) with no improvement >2015 compared to 2010-2014 (Figure-1 A). LFS, OS, and GRFS were superior in pts with t (8:21) with HR=1.32 (95% CI 1.03-1.68, p=0.026), HR=1.38 (95% CI 1.04-1.83, p=0.027) and HR=01.25 (95% CI 1.02-1.53, p=0.035), respectively. Other poor prognostic factors were older pt age (by 10 y) for NRM and OS; 10/10 and 9/10 UD vs MSD for aGVHD II-IV (9/10 also for III-IV aGVHD) and haplo vs MSD for NRM, OS, aGVHD II-IV, and total cGVHD. The combination of female donor to male pt was a poor prognostic factor for NRM, OS, GRFS, and cGVHD. *In vivo* T cell depletion was a positive prognostic factor for GRFS and reduced incidence of aGVHD and cGVHD. PTCy was associated with a lower incidence of cGVHD and PB grafts with an increased risk of total cGVHD.

Conclusions: In this retrospective analysis of HSCT in pts with favorable risk AML in CR1, transplanted over 16 years, we observed an increased number of transplants in pts >60y, from UD and haplo with PB grafts and *in vivo* T cell depletion or PTCy as GVHD prophylaxis. Most importantly, 3-y GRFS improved >2010 and total cGVHD reduced >2015, while other HSCT outcome parameters have not changed.

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Figure: HSCT in pts with favorable de novo AML in CR1, transplanted over 16 comparing three periods 2005-2009, 2010-2014, and 2015-2021: (A)-Multivariable analysis; (B) non-relapse mortality (NRM)(a), relapse incidence (RI)(b), leukemia-free survival (LFS)(c), overall survival (OS)(d); (C) Graft versus host disease (GVHD) -free, relapse-free survival (GRFS), acute (GVHD), chronic GVHD

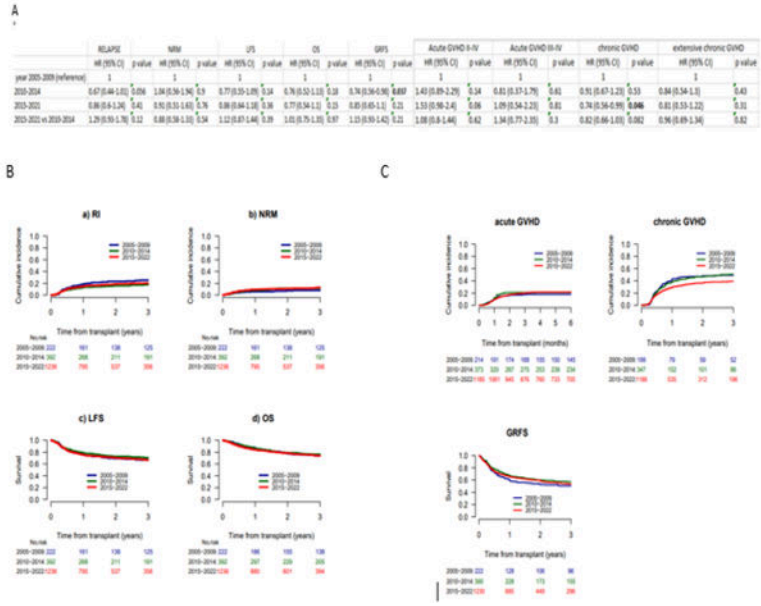

Figure 1

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