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POSTER ABSTRACTS

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

Allogeneic Hematopoietic Stem Cell Transplantation in Elderly Patients: The Experience of the Spanish Group of Hematopoietic Transplantation and Cell Therapy (GETH-TC)

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Introduction

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is associated with significant toxicity and high risk of related mortality in older patients, especially when myeloablative conditioning is used. However, the upper limit of age for this procedure is not clearly defined.

The aim of the study is to evaluate the safety and effectiveness of allo-HSCT in a cohort of elderly patients transplanted in Spain, considering non-relapse mortality (NRM), cumulative incidence (CI) of relapse, overall survival (OS) and progression-free survival (PFS).

As secondary objectives, we evaluate the potential toxicity of allo-HSCT analyzing the days from infusion to hospital discharge, the number of readmissions within the first year, the CI of graft-versus-host disease (GvHD) and GVHD-free/relapse-free survival (GRFS). Finally, we also looked for prognostic factors significantly impacting OS.

Methods

We retrospectively analyzed 529 patients ≥65 years of age undergoing a first allo-HSCT between 2011 and 2020 in 17 Spanish centres, regardless of the indication and characteristics of transplantation.

Subanalyses were performed according to chronological age (65-69 vs ≥70 years of age) and conditioning intensity (myeloablative vs non-myeloablative).

Results

Median age was 67.2 years (range 65.0-82.5) and 54 patients were ≥70 years. The most frequent indication was acute leukemia in 260 patients (49.1%). Clinical characteristics are shown in Table 1. Patients ≥70 years were more frequently male and had a lower HCT-CI than patients <70, without any other differences in patients' or transplant characteristics.

The median follow-up was 51.2 months (range 9.3-139.6). At 1- and 4-years post-transplant, NRM were 24.3% (95%CI 21-28) and 32.0% (95%CI 28-36), CI of relapse were 21.4% (95%CI 18-25) and 29.1% (95%CI 25-33), OS were 61.2% (95%CI 57-65) and 43.4% (95%CI 39-48) and PFS were 54.3% (95%CI 50-58) and 38.9% (95%CI 35-43), respectively (Figure 1). No differences were found according to age group 65-69 vs ≥70 (p=0.822, p=0.835, p=0.648 and p=0.743, respectively). Patients who had received myeloablative conditioning had lower CI of relapse (at 4 years post-transplant 19.3% vs. 30.7%, p=0.030), with no differences in NRM (p=0.308), OS (p=0.440) or PFS (p=0.261).

Regarding the duration of allo-HSCT admission, 486 patients were discharged alive, with a median number of hospital days from infusion to discharge of 22 (range 8-142). There were no differences based on age group (p=0.635) or conditioning intensity (p=0.606). Among 486 patients who were primary discharged, 320 (66.0%) needed a new readmission during the first-year post-transplant, with a median of 1 (range 0-6) up to day +100 and 2 (range 1-10) up to day +365. There were also no differences according to age (p=0.789 and p=0.779, respectively) or conditioning intensity (p=0.264 and p=0.818, espectively).

Acute GvHD occurred in 265 patients (58.2%), 205 (45.1%) grades I-II and 60 (13.2%) grades III-IV. The CI of acute GvHD grades II-IV and grades III-IV at day +100 was 43.5% and 16.9%, respectively. A total of 174 patients (38.2%) developed chronic GvHD, 66 (14.6%) mild, 49 (10.8%) moderate and 56 (12.4%) severe. The CI of moderate-severe chronic GvHD at 1 and 2 years was 18.2% and 22.4%, respectively. According to age group, there were no differences in the CI of acute GvHD grades II-IV (p=0.920), acute GvHD grades III-IV (p=0.853) or chronic moderate-severe GvHD (p=0.798).

At 1- and 4-years after allo-HSCT, GRFS were 37.6% (95%CI 33-42) and 23.7% (95%CI 20-28), with no differences by age group (p=0.569) or conditioning intensity (p=0.707).

In multivariate analysis, ECOG pretransplant ≥1 (HR 1.32, 95%CI 1-1.7; p=0.028), HCT-CI ≥3 (HR 1.34, 95%CI 1.1-1.7; p=0.016), high/very high DRI (HR 1.62, 95%CI 1.3-2.1; p<0.001) and no development of chronic GvHD (HR 2.99, 95%CI 2.3-3.9; p<0.001) were associated with worse OS. Age, gender, previous lines of treatment or autologous HSCT, donor type, stem cell source, conditioning intensity and development of acute GvHD did not influence OS.

Conclusions

Allo-HSCT is effective and safe at ages over 65 years, or even 70 years old. Myeloablative conditioning regimen may offer a lower risk of relapse without increasing toxicity.

In our experience, ECOG, HCT-CI, DRI and chronic GvHD are more relevant parameters for post-transplant survival than chronological age.

Disclosures Bermudez: *GSK:* Speakers Bureau; *Janssen:* Speakers Bureau; *Amgen:* Speakers Bureau; *Pfizer:* Speakers Bureau; *NEOVII:* Speakers Bureau; *Sanofi:* Speakers Bureau; *BMS:* Speakers Bureau. **Yanez San Segundo:** *Novartis:* Speakers Bureau; *MSD:* Other: Advisory board, Speakers Bureau; *Gilead-Kite:* Other: Advisory board, Speakers Bureau; *Beigene:* Other: Advisory board, Speakers Bureau; *Abbvie:* Other: Advisory board, Speakers Bureau; *AstraZeneca:* Other: Advisory board, Speakers Bureau; *Janssen:* Other: advisory board, Research Funding, Speakers Bureau; *Pierre Fabré:* Speakers Bureau; *Pfizer:* Speakers Bureau. **Gonzalez:** *Astra Zeneca:* Consultancy, Speakers Bureau; *SOBI, Roche:* Honoraria; *Alexion:* Consultancy, Honoraria, Speakers Bureau; *Janssen:* Consultancy, Honoraria; *BMS/Celgene:* Honoraria; *Takeda:* Honoraria, Speakers Bureau; *Jazz Pharma:* Consultancy. **Bailen:** *Kite:* Speakers Bureau; *Pfizer:* Speakers Bureau. **Sureda Balari:** *Kite:* Consultancy, Honoraria; *GenMab:* Consultancy, Honoraria; *Takeda:* Consultancy, Honoraria, Research Funding, Speakers Bureau; *BMS/Celgene:* Consultancy, Honoraria, Research Funding; *Sanofi:* Consultancy, Honoraria; *Astra Zeneca:* Consultancy, Honoraria; *MSD:* Consultancy, Honoraria; *Novartis:* Consultancy, Honoraria; *Jannsen:* Consultancy, Honoraria; *Pierre Fabre:* Consultancy, Honoraria.

Table 1. Patient characteristics		All patients (n 529)	65-69 years (n 475)	≥70 years (n 54)	*p value*
Sex, n (%)	Male	342 (64.7)	296 (62.3)	46 (85.2)	**<0.001**
	Female	187 (35.3)	179 (37.7)	8 (14.8)	
Diagnose, n (%)	Acute leukemia	260 (49.1)	226 (47.6)	34 (63.0)	0.169
	MDS / MPD	199 (37.6)	185 (38.9)	14 (25.9)	
	Lymphoproliferative disease / lymphoma	51 (9.6)	46 (9.7)	5 (9.3)	
	Other	19 (3.6)	18 (3.8)	1 (1.9)	
Disease status, n (%)	Complete remission	315 (59.5)	277 (58.3)	38 (70.4)	0.395
	Partial remission	74 (14.0)	68 (14.3)	6 (11.1)	
	Progression disease	29 (5.5)	27 (5.7)	2 (3.7)	
	Stable disease/ no previous treatment	111 (21.0)	103 (21.7)	8 (14.8)	
Previous lines of treatment, median (range)		1 (0-6)	1 (0-6)	1 (0-6)	0.933
Previous auto-HSCT, n (%)		24 (4.5)	23 (4.8)	1 (1.9)	0.274
ECOG, median (range)		0 (0-3)	0 (0-3)	0 (0-1)	0.151
Karnofsky, median (range)		90 (50-100)	90 (50-100)	90 (70-100)	0.452
HCT-CI, n (%)	<3	310 (60.2)	272 (58.7)	38 (73.1)	**0.045**
	≥3	205 (39.8)	191 (41.3)	14 (26.9)	
DRI, n (%)	Low	24 (4.9)	22 (5.1)	2 (3.8)	0.529
	Intermediate	312 (64.1)	275 (63.2)	37 (71.2)	
	High / Very high	151 (31.0)	138 (31.7)	13 (25.0)	
Donor, n (%)	HLA-identical related	164 (31.0)	148 (31.2)	16 (29.6)	0.188
	HLA-haploidentical related	180 (34.0)	156 (32.8)	24 (44.4)	
	HLA-matched unrelated	145 (27.4)	132 (27.8)	13 (24.1)	
	HLA-mismatched unrelated	40 (7.6)	39 (8.2)	1 (1.9)	
Stem cell source, n (%)	Peripheral blood	450 (85.1)	405 (85.3)	45 (83.3)	0.805
	Bone marrow	77 (14.6)	68 (14.3)	9 (16.7)	
	Umbilical cord	2 (0.4)	2 (0.4)	0	
Myeloablative conditioning regimen, n (%)		74 (14.0)	65 (13.7)	9 (16.7)	0.549

Abbreviations: auto-HSCT: autologous hematopoietic stem cell transplantation; DRI: Disease Risk Index; HCT-CI: Hematopoietic Cell Transplantation-specific Comorbidity Index; MDS/MPD: myelodysplastic syndrome / myeloproliferative disease.

Figure 1. Survival and cumulative incidence curves.

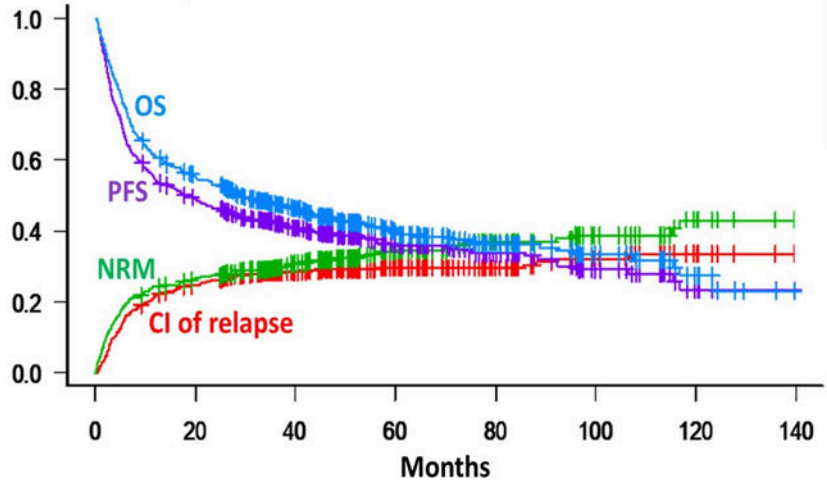

Figure 1

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