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POSTER ABSTRACTS

732.ALLOGENEIC TRANSPLANTATION: DISEASE RESPONSE AND COMPARATIVE TREATMENT STUDIES

Post-Transplant Cyclophosphamide-Based Graft-Versus-Host Disease Prophylaxis in HLA-Matched and Haploidentical Donor Transplants for Patients with Hodgkin disease: A Comparative Study of the LWP EBMT

Juan Montoro[1], Ariane Boumendil[2], Hervé Finel[3], Stefania Bramanti[4], Luca Castagna Sr.[5], Didier Blaise, MD PhD[6], Alida Dominietto, MD[7], Aleksandr Kulagin Sr.[8], Ibrahim Yakoub-Agha, MD PhD[9], Abdelghani Tbakhi, MD[10], Carlos Solano, MDPhD[11], Sebastian Giebel[12], Zafer Gulbas, MD[13], Dolores Caballero[14], Jose A. Perez-Simon, MD PhD[15], Jose Luis Diez Martin[16], Paolo Corradini, MD[17], Yener Koc, MD[18], Gerard Socié[19], Mutlu Arat[20], Manuel Jurado, MD PhD[21], Arancha Bermudez[22], Hélène Labussière-Wallet[23], Marta Villalba[24], Fabio Ciceri[25], Montserrat Rovira, MD[26], Arnon Nagler, MD[27], Anna Maria Sureda Balari, MD PhD[28], Bertram Glass, MD[29]

[1] Hematology Department, Hospital La Fe, Valencia, Spain
[2] EBMT Lymphoma Working Party, Paris Office, Paris, FRA
[3] European Society for Blood and Marrow Transplantation, Paris, France
[4] Humanitas Clinical and Research Center, IRCCS, Rozzano, Italy
[5] Istituto Clinico Humanitas, Rozzano Milano, Italy, Palermo, ITA
[6] Program of Transplant and cellular immunotherapy, Department of Hematology, Institut Paoli Calmettes, Marseille, France
[7] IRCCS Ospedale Policlinico San Martino, Genoa, Italy
[8] b. First State Pavlov Medical University of St. Petersburg, Raisa Gorbacheva Memorial Research Institute for Paediatric Oncology, Hematology, and Transplantation, St-Petersburg, Russia, St. Petersburg, RUS
[9] CHU de Lille, Université de Lille, INSERM U1286, Infinite, 59000, Lille, France
[10] King Hussein Cancer Centre, Amman, JOR
[11] Hematology Department, Hematology Department, Hospital Clínico Universitario-INCLIVA, Valencia, Spain
[12] Department of Bone Marrow Transplantation and Onco-Hematology, Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice Branch, Gliwice, Poland
[13] Anadolu Health Center Affiliated John Hopkins, Kocaeli, TUR
[14] Hematology Department, Hospital Universitario de Salamanca, IBSAL, CIBERONC, University of Salamanca, Salamanca, Spain
[15] Department of Hematology, University Hospital Virgen del Rocio-IBIS. Universidad de Sevilla., Sevilla, Spain
[16] Hospital Gregorio Marañon, Madrid, ESP
[17] University of Milan and Fondazione IRCCS Istituto Nazionale Tumori, Milano, Italy
[18] MEDICAL PARK HOSPITALS, Beylikduzu, TUR
[19] Hopital St. Louis, Department of Hematology - BMT, Paris, France
[20] İstanbul Florence Nightingale Hospital, Hematology Department, İstanbul, Turkey
[21] Hospital Virgen De Las Nieves, Granada, ESP
[22] Hospital Universitario Marqués de Valdecilla (IDIVAL), Santander, Spain
[23] Centre Hospitalier Lyon Sud, Lyon, France
[24] Hospital Universitario y Politecnico La Fe, Valencia, ESP
[25] University Vita-Salute, IRCCS Ospedale San Raffaele, Haematology and BMT, Milan, Italy
[26] Hematopoietic Cell Transplantation Unit, Hospital Clínic de Barcelona, ICHMO, Barcelona, Spain
[27] Division of Hematology and Bone Marrow Transplantation, Chaim Sheba Medical Center, Tel Hashomer, Israel
[28] Institut Catala D'Oncologia, Barcelona, Spain
[29] Department of Hematology, Oncology and Stem Cell Transplantation, Asklepios Klinik St. Georg, Hamburg, Germany

INTRODUCTION

Post-transplant cyclophosphamide (PTCy) has proven to be a highly effective strategy in preventing graft-versus-host disease (GVHD) in haploidentical (haplo) hematopoietic stem cell transplantation (HSCT), but it is being increasingly used in HLA-matched transplants.

The outcomes of haplo HSCT with PTCY in various hematologic malignancies, particularly in relapsed/refractory Hodgkin disease (HD), have shown promising results, challenging those obtained in transplant patients from HLA-matched donors without PTCy. However, there is limited information on the impact of donor types on the outcomes of patients with HD undergoing allogenic HSCT when using homogeneous GVHD prophylaxis with PTCy. To address this knowledge gap, we have conducted an extensive study using the Lymphoma Working Party of the European Society for Blood and Marrow Transplantation (LWP-EBMT) registry.

The aim of this study was to compare the outcomes of patients with HD undergoing HSCT from both HLA-matched donors, which include matched sibling donors (MSD) and matched unrelated donors (MUD), and haplo donors, using PTCy as GVHD prophylaxis approach in all cohorts.

PATIENTS AND METHODS

Inclusion criteria All adults (≥ 18 years) patients diagnosed with HD who underwent their first HSCT between January 2010 and December 2020 from either a MSD, MUD or haplo, and whose data were reported to the EBMT registry were included. For the purposes of this study, only transplants who received PTCy-based as GVHD prophylaxis were considered.

Statistical Analysis

The study utilized statistical methods such as Kaplan-Meier estimation, Log-Rank test, competing risks analysis, and Cox proportional hazards regression. The analyses included OS, PFS, NRM, aGVHD, cGVHD, and graft failure. The statistical software R and packages were used.

RESULTS

Patient and Transplantation Characteristics

Patient, disease and transplant-related characteristics of the 860 patients are summarized in Table 1.

Engraftment

The cumulative incidence (Cum Inc) of neutrophil recovery at day 30 was 95% (95% CI, 93-96) in the HLA-matched group and 96% (95% CI, 91-98) in the haplo cohort (p=0.18). The 60-day Cum Inc of platelet recovery in similar order was 94% (95% CI, 88-97) and 86% (95% CI, 83-88) (p<0.001).

GVHD

The Cum Inc of acute GVHD grade II-IV at 100 days in the HLA-matched and the haplo cohorts was 24% (95% CI, 17-31) and 34% (95% CI, 30-37), respectively (p=0.01), whereas for grade III-IV it was 8% (95% CI, 4-13) and 10% (95% CI, 8-13), (p=0.44). In multivariable analysis (table 2), haplo was associated with an increased risk of acute GVHD grades II-IV, when compared with HLA-matched (HR 0.65; 95% CI, 0.46-0.93; p=0.01). Other variables are shown in table 2.

The 2-year Cum Inc of chronic GVHD in the HLA-matched and haplo cohorts was 26% (95% CI, 19-33) and 27% (95% CI, 24-31), respectively (p=0.75). Other variables are shown in table 2.

NRM and relapse

The Cum Inc of NRM at 2 years was 10% (95% CI; 6-16) for HLA-matched and 18% (95% CI; 15-21) for haplo (p=0.02). In multivariable analysis (table 2), haplo was associated with an increased risk of NRM, when compared to HLA-matched (HR 0.5; 95% CI, 0.28-0.89; p=0.01). Other variables are shown in table 2.

The Cum Inc of relapse at 2 years was 22% (95% CI; 15-29) for HLA-matched and 24% (95% CI; 20-27) for haplo (p=0.81). Other variables are shown in table 2.

Survival

The 2-year OS for the HLA-matched and haplo cohorts was 82% (95% CI; 75-88) and 70% (95% CI; 67-74), respectively (p=0.002). In multivariable analysis (table 2), compared to HLA-matched, haplo (HR, 0.51; 95% CI, 0.34-0.77; p=0.001) was associated with worse survival. Other variables are shown in table 2.

The 2-year PFS was similar between HLA-matched and haplo (66%; 95% CI, 58-74; and 58%; 95% CI, 54-62, respectively; p=0.17). Other variables are shown in table 2.

Comparison of outcomes for MSD and MUD

With regards to the donor type, most posttransplant outcomes did not exhibit significant differences, except for a higher incidence of grades II-IV acute GVHD in the MUD group (33%; 95% CI, 32-44) compared to the MSD group (17%; 95% CI, 10-25) (p=0.01).

CONCLUSION

Our study shows that in patients with HD undergoing HSCT with PTCy for GVHD prophylaxis, no significant differences in 2-year PFS were observed between HLA-matched and haplo. A higher risk of acute GVHD and NRM is associated with haplo, leading to lower OS compared to HLA-matched transplantation.

Disclosures Yakoub-Agha: *Novartis:* Consultancy, Honoraria; *Kite, a Gilead Company:* Consultancy, Honoraria, Other: Travel Support; *Bristol-Myers Squibb:* Honoraria; *Janssen:* Honoraria. **Giebel:** *Pfizer:* Consultancy, Honoraria, Speakers Bureau; *Janssen:* Consultancy, Honoraria, Speakers Bureau; *Gilead:* Consultancy, Honoraria, Speakers Bureau; *Abbvie:* Consultancy, Honoraria, Speakers Bureau; *AstraZeneca:* Consultancy, Honoraria, Speakers Bureau; *Amgen:* Consultancy, Honoraria, Speakers Bureau; *Roche:* Consultancy, Honoraria, Speakers Bureau; *Novartis:* Consultancy, Honoraria, Speakers Bureau; *Servier:* Honoraria, Speakers Bureau; *Swixx:* Honoraria, Speakers Bureau; *Angelini:* Honoraria, Speakers Bureau; *BMS:* Honoraria, Speakers Bureau; *Zentiva:* Consultancy, Honoraria. **Corradini:** *Celgene:* Other: Honoraria (Consulting, advisory role, or lecturer), Travel and accomodations; *Gilead/Kite:* Other: Honoraria (Consulting, advisory role, or lecturer), Travel and accomodations; *AbbVie:* Other: Honoraria (Consulting, advisory role, or lecturer), Travel and accomodations; *Pfizer:* Other: Honoraria

(Consulting, advisory role, or lecturer); *Incyte:* Other: Honoraria (Consulting, advisory role, or lecturer); *Sanofi:* Other: Honoraria (Consulting, advisory role, or lecturer); *Novartis:* Other: Honoraria (Consulting, advisory role, or lecturer), Travel and accomodations; *Roche:* Other: Honoraria (Consulting, advisory role, or lecturer), Travel and accomodations; *Kyowa Kirin:* Other: Honoraria (Consulting, advisory role, or lecturer); *Daiichi Sankyo:* Other: Honoraria (Consulting, advisory role, or lecturer); *Janssen:* Other: Honoraria (Consulting, advisory role, or lecturer), Travel and accomodations; *SOBI:* Other: Honoraria (Consulting, advisory role, or lecturer); *Nerviano Medical Science:* Other: Honoraria (Consulting, advisory role, or lecturer); *Amgen:* Other: Honoraria (Consulting, advisory role, or lecturer), Travel and accomodations; *ADC Theraputics (DSMB):* Other: Honoraria (Consulting, advisory role, or lecturer); *Takeda:* Other: Honoraria (Consulting, advisory role, or lecturer), Travel and accomodations; *GlaxoSmithKline:* Other: Honoraria (Consulting, advisory role, or lecturer); *BeiGene:* Honoraria; *Bristol Myers Squibb:* Other: Travel and accomodations. **Bermudez:** *NEOVII:* Speakers Bureau; *Janssen:* Speakers Bureau; *Pfizer:* Speakers Bureau; *Amgen:* Speakers Bureau; *Sanofi:* Speakers Bureau; *GSK:* Speakers Bureau; *BMS:* Speakers Bureau. **Ciceri:** *ExCellThera:* Other: Scientific Advisory Board . **Sureda Balari:** *Astra Zeneca:* Consultancy, Honoraria; *Sanofi:* Consultancy, Honoraria; *MSD:* Consultancy, Honoraria; *BMS/Celgene:* Consultancy, Honoraria, Research Funding; *Takeda:* Consultancy, Honoraria, Research Funding, Speakers Bureau; *Novartis:* Consultancy, Honoraria; *Jannsen:* Consultancy, Honoraria; *Pierre Fabre:* Consultancy, Honoraria; *GenMab:* Consultancy, Honoraria; *Kite:* Consultancy, Honoraria. **Glass:** *Gilead, BMS, Novartis, Milteneyi, Roche, Jazz:* Honoraria, Other: Advisory board.

Table 1 Patient, disease and transplant-related characteristics

PATIENT CHARACTERISTICS	HLA-MATCHED N = 166	HAPLO N = 694	p
Median age, years (range)	32 (18-71)	32 (18-72)	0.5
Gender, n (%)			0.5
Male	99 (60)	430 (62)	
Female	67 (40)	263 (38)	
Karnofsky performance status, n (%)			
≥ 90	132 (83)	564 (83)	0.8
< 90	28 (17)	113 (17)	
Missing	6	17	
HCT-CI, n (%)			0.68
Low	84 (64)	340 (68)	
Intermediate	23 (18)	82 (17)	
High	23 (18)	75 (15)	
Missing	36	197	
HL status			
Chemosensitive	133 (80)	580 (83)	0.3
Refractory	33 (20)	114 (17)	
Prior auto-SCT	106 (64)	520 (75)	0.004
Median time from diagnosis to HSCT, months (range)	38 (10-366)	34 (4-342)	0.01
Donors, n (%)			NA
MSD	96 (58)	-	
MUD	70 (42)	-	
Haplo	-	694 (100)	
Stem cell source, n (%)			<0.001
Bone marrow	25 (15)	273 (39)	
Peripheral blood	141 (85)	421 (61)	
Female donor to male recipient, n (%)	36 (22)	185 (26)	0.19
Reduced intensity conditioning regimen, n (%)	124 (75)	544 (80)	0.24
TBI in conditioning, n (%)	39 (23)	401 (58)	<0.001
Conditioning regimen, n (%)			
Flu + Cy + TBI	31 (19)	378 (54)	<0.001
Flu + Cy + Bu	18 (11)	144 (21)	
Flu + Bu	56 (34)	99 (14)	
Other Flu-based regimen	40 (24)	34 (5)	
Other	21 (12)	39 (6)	
GVHD prophylaxis, n (%)			<0.001
PTCy + 2 drugs	108 (65)	654 (94)	
PTCy + 1 drug	42 (25)	33 (5)	
PTCy alone	16 (10)	7 (1)	

Table 2. Multivariate analysis of transplant outcomes

VARIABLE	aGVHD II-IV	aGVHD III-IV	cGVHD	Ext cGVHD	NRM	Relapse	OS	PFS
	HR (95% CI) p	HR (95% CI) p	HR (95% CI) p	HR (95% CI) p	HR (95% CI) p	HR (95% CI) p	HR (95% CI) p	HR (95% CI) p
Donor type								
Haplo	1	1	1	1	1	1	1	1
HLA-matched	0.65 (0.46-0.93) 0.01	0.76 (0.42-1.37) 0.35	0.95 (0.66-1.36) 0.78	0.98 (0.56-1.71) 0.93	0.5 (0.28-0.89) 0.01	0.9 (0.61-1.32) 0.59	0.51 (0.34-0.77) 0.001	0.78 (0.58-1.06) 0.11
Patient age (five years increase)	1.07 (1.01-1.12) 0.01	1.01 (0.92-1.11) 0.83	0.98 (0.92-1.04) 0.53	1.04 (0.95-1.15) 0.38	1.18 (1.1-1.25) <0.001	0.99 (0.93-1.06) 0.8	1.11 (1.05-1.16) <0.001	1.07 (1.03-1.12) 0.001
Karnofsky performance status								
≥ 90	1	1	1	1	1	1	1	1
< 90	0.87 (0.61-1.23) 0.42	1.01 (0.56-1.83) 0.96	1.12 (0.77-1.63) 0.55	0.89 (0.74-2.02) 0.42	1.82 (1.23-2.69) 0.002	1.32 (0.91-1.93) 0.14	1.87 (1.39-2.51) <0.001	1.54 (1.18 -2.01) 0.001
Disease status at allo-SCT								
Nonrefractory	1	1	1	1	1	1	1	1
Refractory	1.02 (0.72-1.44) 0.91	1.19 (0.64-2.01) 0.68	1.33 (0.92-1.92) 0.13	1.81 (1.07-3.08) 0.02	1.6 (1.05-2.45) 0.02	2.46 (1.77-3.41) <0.001	2.32 (1.74-3.1) <0.001	2.07 (1.61-2.66) <0.001
Gender								
Male	1	1	1	1	1	1	1	1
Female	1.05 (0.81-1.36) 0.7	1.05 (0.67-1.64) 0.83	0.94 (0.72-1.24) 0.66	0.96 (0.62-1.48) 0.85	1.41 (0.98-2.03) 0.06	1.05 (0.78-1.42) 0.74	1.16 (0.89-1.51) 0.26	1.15 (0.92-1.44) 0.22
Conditioning intensity								
MAC	1	1	1	1	1	1	1	1
RIC	1.03 (0.76-1.39) 0.84	1.2 (0.72-1.99) 0.48	1 (0.72-1.4) 0.97	1.22 (0.74-2.02) 0.42	0.89 (0.58-1.39) 0.61	0.9 (0.63-1.29) 0.56	1.07 (0.79-1.45) 0.67	0.92 (0.7-1.2) 0.54

Figure 1

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