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POSTER ABSTRACTS

722.ALLOGENEIC TRANSPLANTATION: ACUTE AND CHRONIC GVHD, IMMUNE RECONSTITUTION

Graft-Versus-Host Disease after Anti-CD19 Chimeric Antigen Receptor T-Cell Infusion Post Allogeneic Hematopoietic Cell Transplantation: A Transplant Complications and Paediatric Disease Working Parties EBMT Joint Study

Guillermo Orti, MDPhD[1], Christophe Peczynski, MSc[2], Christian Koenecke, MD[3], William Boreland[4], Maeve O'Reilly[5], Martin Bornhäuser, MD[6], Adriana Balduzzi[7], Caroline Besley, MD[8], Krzysztof Kalwak[9], Samppa Ryhanen Sr., MD PhD[10], Tayfun Güngör, MD[11], Robert F. Wynn, MRCP,MDFRCPath[12], Peter Bader, MD PhD[13], Stephan Mielke, MD[14], Didier Blaise, MD PhD[15], Persis Amrolia, FRCP, FRCPath, PhD[16], Ibrahim Yakoub-Agha, MD PhD[17], Friso G. J. Calkoen, MD[18], Maria-Luisa Schubert, MD[19], Victoria Potter[20], Wolfgang Holter, MD[21], Nicolaus Kröger, MD[22], Mi Kwon[23], Henrik Sengeloev[24], Helene Schoemans, MD[25], Ivan Sergeevich Moiseev, MD[26], Olaf Penack, MD[27], Zinaida Peric, MDPhD[28]

[1] Vall D' Hebron University Hospital, Barcelona, Spain
[2] EBMT Paris study office / CEREST-TC, Hôpital Saint Antoine, Sorbonne University, Paris, France
[3] Department of Hematology, Hemostasis, Oncology, and Stem Cell Transplantation, Hannover Medical School, Hannover, Germany
[4] EBMT Paris Study Unit, Paris, France
[5] Department of Haematology, University College London Hospitals, London, United Kingdom
[6] Department of Internal Medicine 1, University Hospital Carl Gustav Carus, Technical University Dresden, Dresden, Germany
[7] Pediatric Hematopoietic Transplant Unit, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy, School of Medicine and Surgery, Milano-Bicocca University, Milan, Italy
[8] Department of Haematology, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, United Kingdom
[9] Department of Pediatric Hematology Oncology and BMT, Wroclaw Medical University, Wroclaw, Poland
[10] Hospital For Children and Adolescent, Helsinki University Central Hospital, Helsinki, FIN
[11] University Children's Hospital, Zürich, Switzerland, Zürich, Switzerland
[12] Royal Manchester Children's Hospital, Manchester, GBR
[13] Division for Stem Cell Transplantation and Immunology, University Children's Hospital Frankfurt, Frankfurt, Germany
[14] Department of Cellular Therapy and Allogeneic Stem Cell Transplantation, Karolinska Institute & University Hospital, Stockholm, Sweden
[15] Program of Transplant and cellular immunotherapy, Department of Hematology, Institut Paoli Calmettes, Marseille, France
[16] Great Ormond Street Children's Hospital, London, United Kingdom
[17] CHU de Lille, Université de Lille, INSERM U1286, Infinite, 59000, Lille, France
[18] Princess Maxima Center for Pediatric Oncology, Utrecht, Netherlands
[19] University of Heidelberg, Heidelberg, Heidelberg, DEU
[20] Department of Haematological Medicine, King's College Hospital NHS, London, United Kingdom
[21] St.Anna Children's Hospital, Vienna, AUT
[22] University Hospital Eppendorf, Bone Marrow Transplantation Centre, Hamburg, Germany
[23] General University Hospital Gregorio Marañón, Madrid, Spain
[24] Rigshospitalet, Copenhagen, Denmark
[25] Department of Hematology,Department of Public Health and Primary Care, ACCENT VV, University Hospitals Leuven, KU Leuven - University of Leuven, Leuven, Belgium
[26] St Petersburg University, St Petersburg, Russian Federation
[27] Department of Hematology, Oncology, and Cancer Immunology, Charité Universitätsmedizin Berlin, Campus Virchow Klinik, Berlin, Germany
[28] University Hospital Center Rebro, Zagreb, Croatia

Background

Anti-CD19 chimeric antigen receptor T-cells (CART) have been incorporated into the therapeutic landscape of B-acute lymphoblastic leukemia (B-ALL) and B-non-Hodgkin's lymphoma (B-NHL). The manufacturing process of commercially available autologous CART in patients relapsing after allogeneic hematopoietic cell transplant (allo-HCT) might include T-cells of donor origin. In this setting, there is limited data on graft-versus-host disease (GvHD) as an off-target effect in patients treated with CART after allo-HCT. We hereby report on a large, retrospective, EBMT registry-based study on GvHD in patients treated with CART therapy after allo-HCT.

Methods

Inclusion criteria were B-ALL and B-NHL adult and pediatric allo-HCT patients, treated with a first anti-CD19 CART (axicabtagene ciloleucel [axi-cel] and tisagenlecleucel [tisa-cel]) from 2018 to August 2022. The primary study endpoints were the cumulative incidences (CI) of new acute GvHD (aGvHD) and chronic GvHD (cGvHD). Secondary endpoints were the 1-year GvHD relapse-free survival (GRFS), non-relapse mortality (NRM), and overall survival (OS). Overall data was analyzed in a descriptive manner.

Results

A total of 257 allo-HCT patients treated with anti-CD19 CART were included. One hundred seventy-two patients (66.9%) were ≥18 years old. Tisa-cel was the therapy of choice in 184 patients (71.6%), whereas axi-cel was used in 73 patients (28.4%). More than half of the cohort (57.6%) underwent allo-HCT from unrelated donors. Notably, 109 patients (46.6%) and 38 patients (15%) had previously develop aGvHD and cGvHD between allo-HCT and CART infusion. Table 1 describes data on baseline patient, allo-HCT and CART characteristics of the whole cohort and of patients developing aGvHD and cGvHD.

In total, 3 patients developed new aGvHD and 6 patients developed new cGvHD after CART therapy. The 100-day CI of new aGvHD was 1.6% (95% CI, 0.4-4.2) and the 12-month CI of new cGvHD was 2.8% (95% CI, 1.1-5.7). No GvHD was observed in the pediatric cohort. The median time from allo-HCT to CART infusion was 15.8 months (range, 3.8-220.3) and the median times from CART to the development of aGvHD and cGvHD were respectively 44 days (range, 8-81) and 144 days (range, 5-182).

The 1-year GRFS and NRM were 52.1% (95% CI 45.6-59.4) and 4.7% (95% CI 2.5-8.1) respectively (Figure 1). With a median follow up of 18.8 months (95% CI, 16.2-23.7), the 1-year OS was 76.8% (95% CI 71.5-82.4). The most frequent cause of death was disease-related in 56 patients (74.6%).

Conclusion

Together, in this large cohort including adult and pediatric allo-HCT patients treated with tisa-cel and axi-cel after allo-HCT, these data show that the incidence of both aGvHD and cGvHD is very low. Of note, GvHD was not observed in the pediatric cohort. Furthermore, no excessive NRM was observed compared to previously published methods of treating relapse post allo-HCT, being disease progression a major hurdle to optimal outcomes in this cohort of patients.

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Table 1

Variable		Whole Cohort, n (%)	aGvHD Patients, n (%)	cGvHD Patients, n (%)
Total		257 (100)	3	6
Age at CART	<18 years	85 (33.1)	0 (0)	0 (0)
	≥18 years	172 (66.9)	3 (100)	6 (100)
Disease Diagnosis	B-ALL	181 (70.4)	2 (66.7)	4 (66.7)
	B-NHL	76 (29.6)	1 (33.3)	2 (33.3)
CART Lymphodepletion	FluCy	242 (95.7)	3 (100)	6 (100)
	Other	11 (4.3)	0 (0)	0 (0)
	Missing	4	0 (0)	0 (0)
Disease status at CART	CR	62 (24.7)	2 (66.7)	0 (0)
	Not in CR	189 (75.3)	1 (33.3)	6 (100)
	Missing	6	0	0
ECOG at CART	0-1	208 (90)	3 (100)	5 (100)
	≥2	23 (10)	0 (0)	0 (0)
	Missing	26	0	1
CART	Tisa-cel	184 (71.6)	2 (66.7)	5 (83.3)
	Axi-cel	73 (28.4)	1 (33.3)	1 (16.7)
HCT Conditioning Regimen	MAC	173 (73)	1 (50)	4 (66.7)
	RIC	65 (27)	1 (50)	2 (33.3)
	Missing	19	1	0
In vivo T-cell Depletion	Yes	141 (56)	0 (0)	1 (16.7)
	No	111 (44)	3 (100)	5 (83.3)
	Missing	5	0	0
Ex vivo T-cell Depletion	Yes	7 (2.9)	0 (0)	0 (100)
	No	234 (97.1)	2 (100)	6 (0)
	Missing	16	1	0
Number of prior allo-HCT	First allo-HCT	239 (93)	3 (100)	6 (100)
	Second allo-HCT	18 (7)	0 (0)	0 (0)
Graft Source	Bone Marrow	76 (30.3)[Table 1]	1 (50)	5 (83.3)
	Peripheral Blood	166 (66.1)	1 (50)	1 (16.7)
	Cord Blood	9 (3.6)	0	0 (0)
	Missing	6	1	0
Donor Type	Matched Sibling Donor	70 (28.3)	2 (100)	2 (33.3)
	Unrelated Donor	142 (57.6)	0 (0)	1 (16.7)
	Mismatched Related Donor	30 (12.1)	0 (0)	2 (33.3)
	Other	5 (2)	0 (0)	1 (16.7)
	Missing	10	1	0
Previous aGvHD before CART	Yes	109 (46.6)	2 (100)	4 (80)
	No	125 (53.4)	0 (0)	1 (20)
	Missing	23	1	1
Previous cGvHD before CART	Yes	38 (15)	1 (33.3)	3 (50)
	No	215 (85)	2 (66.7)	3 (50)
	Missing	4	0	0
Female Donor / Male Recipient	Yes	43 (17.7)	1 (50.0)	1 (16.7)
	No	200 (82.3)	1 (50.0)	5 (83.3)
	Missing	14	1	0
Time between Allo-HCT and CART, months.	Median (range)	15.8 (3.8-220.3)	15.4 (10.3-32.9)	15.7 (5.7-99.6)

Figure 1. GvHD Relapse-Free Survival

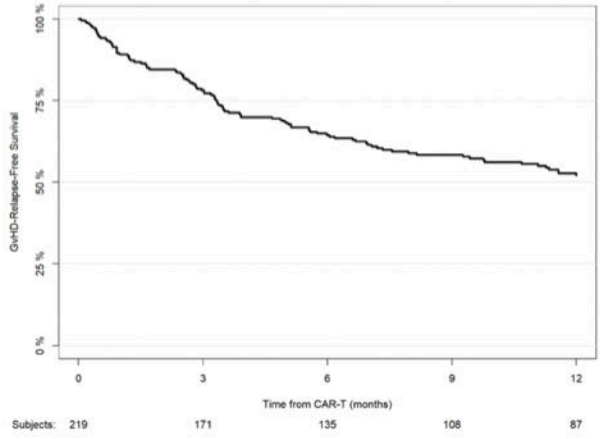

Figure 1

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