ELSEVIER

Blood 142 (2023) 4867–4869

The 65th ASH Annual Meeting Abstracts

# POSTER ABSTRACTS

## 705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

### High Body Mass Index Is Associated with Favorable Outcome in Younger Patients Receiving CD19 CAR T-Cell Therapy for B-Cell Lymphoma: A Retrospective Study from the EBMT Transplant Complications Working Party

*Christian R. Schultze-Florey, MD*[1], *Christophe Peczynski, MSc*[2], *William Boreland*[2], *Michael Daskalakis, MD*[3], *Anne Sirvent, MD*[4], *Ibrahim Yakoub-Agha, MD PhD*[5], *Maria-Luisa Schubert, MD*[6], *Christof Scheid, MD*[7], *Anne Huynh, MD*[8], *Victoria Potter*[9], *Didier Blaise*[10], *Matthew P. Collin Sr., MD PhD*[11], *Rafael Hernani*[12], *Gerald G. Wulf, MD*[13], *Francis A. Ayuk, MD*[14], *Caroline Besley, MD*[15], *Lucia Lopez Corral, PhD MD*[16], *Edouard Forcade, MD PhD*[17], *Peter Vandenberghe, MD PhD*[18], *Dominik Schneidawind, MD PhD*[19], *Matthias Stelljes, MD*[20], *Friedrich Stölzel, MD*[21], *Bertram Glass, MD*[22], *Ivan Sergeevich Moiseev, MD*[23], *Helene Schoemans, MD*[24], *Olaf Penack, MD*[25], *Christian Koenecke, MD*[26], *Zinaida Peric, MD PhD*[27]

[1] Department of Hematology, Hemostasis, Oncology, and Stem Cell Transplantation, Hannover Medical School, Hannover, Germany
[2] EBMT Paris study office / CEREST-TC, Hôpital Saint Antoine, Sorbonne University, Paris, France
[3] University Hospital Bern, Inselspital, Bern, Switzerland
[4] CHU Montpellier, Montpellier, France
[5] CHU de Lille, Université de Lille, INSERM U1286, Infinite, 59000, Lille, France
[6] University of Heidelberg, Heidelberg, Heidelberg, DEU
[7] Department of Internal Medicine I, University Hospital Cologne, Cologne, Germany, Cologne, Germany
[8] Institut Universitaire du Cancer Toulouse - Oncopole, Toulouse, France
[9] Department of Haematological Medicine, King's College Hospital NHS, London, United Kingdom
[10] Programme de Transplantation & Thérapie Cellulaire, Centre de Recherche en Cancérologie de Marseille, Marseille, France
[11] Northern Centre for Bone Marrow Transplantation, Newcastle University, Newcastle Upon Tyne, GBR
[12] Clinical Univesity Hospital of Valencia, Valencia, Spain
[13] Universitaetsklinikum Goettingen, Goettingen, Germany
[14] Department of Stem Cell Transplantation with Research Department Cell and Gene Therapy, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
[15] Department of Haematology, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, United Kingdom
[16] Instituto de Investigacion Biomedica de Salamanca (IBSAL), Centro de Investigación del Cáncer-IBMCC (USAL-CSIC), Hospital Universitario de Salamanca, SALAMANCA, Spain
[17] Service d'Hématologie Clinique et Thérapie Cellulaire, CHU Bordeaux, Hopital Haut-Leveque, Pessac, France
[18] Department of Hematology, Department of Human Genetics, University Hospitals Leuven, KU Leuven, Leuven, Belgium
[19] Department of Medical Oncology and Hematology, University Hospital of Zurich, Zurich, Switzerland
[20] Department of Internal Medicine A, University of Muenster, Muenster, Germany
[21] Department of Internal Medicine II, University Hospital Schleswig-Holstein, Kiel, Germany
[22] Department of Hematology, Oncology and Tumor Immunology, Helios Klinik Berlin-Buch, Berlin, Germany
[23] RM Gorbacheva Research Institute, Pavlov University, Saint-Petersburg, Russian Federation
[24] Department of Hematology,Department of Public Health and Primary Care, ACCENT VV, University Hospitals Leuven, KU Leuven - University of Leuven, Leuven, Belgium
[25] Department of Hematology, Oncology, and Cancer Immunology, Charité Universitätsmedizin Berlin, Campus Virchow Klinik, Berlin, Germany
[26] Department of Hematology, Hemostasis, Oncology, and Stem Cell Transplantation, Hannover Medical School, Hannover, Germany
[27] Department of Hematology, University Hospital Centre Zagreb, Zagreb, Croatia

**Introduction:** Obesity is a major health care burden and has been linked to numerous adverse outcomes including alterations of antitumor immunologic responses. Patients with high body mass index (BMI) undergoing autologous or allogeneic hematopoietic stem cell transplantation (HSCT) for hematological malignancies were repeatedly shown to have higher rates of non-relapse mortality (NRM) and relapse, translating into a reduced overall survival (OS). However, the impact of obesity on outcomes after CAR T-cell therapy has not been studied at large scale. The present study aims to investigate whether high BMI is associated with outcomes in patients receiving anti-CD19 CAR T-cell therapy.

**Methods:** This is a retrospective analysis using EBMT registry data of adult patients after first therapy with commercial CD19 CAR T-cell products for relapsed/refractory B-Non-Hodgkin lymphoma (B-NHL) between 1/1/2016 and 30/6/2022. Only patients with available information on height and weight at CAR T-cell therapy were included. Patients with a history of allogeneic stem cell transplantation were excluded. As we exclusively focused on the impact of increased BMI we excluded all patients with a BMI below 18.5 from the analysis. The primary outcome was the impact of BMI on OS. Multivariate analyses were performed with cause-specific Cox models, employing as risk factors patient age, sex, ECOG status and year of CAR T-cell therapy besides BMI categories (18.5-25, 25-30, >30).

**Results:** A total of 4576 CAR T-cell therapy patients were registered during the study period, with 3125 patients meeting inclusion criteria. Selection of patients with available height and weight including BMI of 18.5 and above resulted in a final study cohort of 1653 patients. Median follow-up was 21.2 months [95% CI: 19.6-22.6]. Patients' characteristics are summarized in Table 1. Half of the cohort had a normal range BMI, while one third was overweight (BMI 25-30) and about 18% met criteria for obesity. A significant interaction was found between age and BMI. Therefore, we divided the cohort in two groups by the median age of 62.5 years. OS was significantly reduced in younger patients with normal range BMI compared to higher BMI patients. However, this effect was not significant in the older patients (Figure 1). Upon multivariate analysis, younger patients with BMI 25-30 had a survival advantage with a hazard ratio (HR) of 0.74 (0.57-0.95, P=0.02) and patients with BMI >30 a HR of 0.68 (0.51-0.91, P=0.01) compared to normal range BMI. Progression free survival was significantly improved for younger BMI 25-30 (HR 0.79, 0.64-0.99, P=0.04) but not BMI >30 (HR 0.82, 0.64-1.05, P=0.11), and NRM was reduced only in the younger BMI 25-30 subgroup (HR 0.52, 0.31-0.9, P=0.02) but not in the obese patients (HR 0.7, 0.42-1.18, P=0.19). Multivariate analysis of BMI subgroups in patients above the age of 62.5 years did not show significant differences with regard to OS (BMI 25-30 HR 0.94, 0.74-1.18; BMI >30 HR 1.04, 0.77-1.41), PFS (BMI 25-30 HR 1.06, 0.86-1.31; BMI >30 HR 1.1, 0.83-1.47), or NRM (BMI 25-30 HR 1.35, 0.89-2.06; BMI >30 HR 1.11, 0.6-2.06).

**Conclusion:** Our European real world data on the impact of increased BMI on anti-CD19 CAR T-cell therapy for relapsed/refractory B-NHL shows that half of these patients are overweight or obese and that this seems to confer a survival benefit to younger (<62.5 years) patients. As this finding is rather surprising, future studies are required to fine tune the risk analysis, including in-depth analysis of patients' characteristics to identify protective factors linked to an elevated BMI as well as a possible selection bias. Our findings could in part be explained by the body weight-dependent dose of infused CAR T-cells for B-cell lymphoma. Therefore, for the same tumor burden, obese patients might receive more CAR T-cells than normal weight ones. A future study should test this hypothesis also in B-ALL or multiple myeloma patients, as they typically receive a fixed dose of CAR T-cells regardless of their body weight. Ultimately, our study might contribute to identify underlying mechanisms for improved outcome of CAR T-cell patients.

**Disclosures Schultze-Florey:** *Neovii:* Other: Travel support. **Yakoub-Agha:** *Novartis:* Consultancy, Honoraria; *Kite, a Gilead Company:* Consultancy, Honoraria, Other: Travel Support; *Janssen:* Honoraria; *Bristol-Myers Squibb:* Honoraria. **Scheid:** *Janssen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *BMS:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Amgen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Abbvie:* Honoraria; *Takeda:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Roche:* Consultancy; *Novartis:* Honoraria, Membership on an entity's Board of Directors or advisory committees. **Huynh:** *Jazz:* Other: travel fees, advisory board; *Novartis:* Other: travel fees, advisory board; *Pfizer:* Other: advisory board; *Servier:* Other: Advisory board; *Astellas:* Other: Advisory board; *Medac:* Other: Advisory board; *Neovii:* Other: Advisory board. **Blaise:** *Jazz Pharmaceuticals:* Honoraria. **Wulf:** *Gilead:* Honoraria, Speakers Bureau; *Novartis:* Honoraria, Speakers Bureau. **Besley:** *Kite, Novartis, Janssen and Takeda:* Honoraria. **Lopez Corral:** *Novartis:* Honoraria, Other: Travel support; *Kite/Gilead:* Honoraria, Other: Travel support; *Janssen:* Honoraria, Other: Travel support. **Vandenberghe:** *Kite, a Gilead Company:* Consultancy, Other: Travel support; *Gilead Sciences:* Consultancy, Other: Travel Support; *Miltenyi Biotec:* Consultancy; *Janssen Biotech:* Consultancy, Research Funding; *Celgene/BMS:* Consultancy; *Novartis:* Consultancy; *Pfizer:* Research Funding. **Stölzel:** *medac:* Speakers Bureau. **Glass:** *Roche:* Consultancy, Honoraria, Research Funding; *Gilead/Kite:* Consultancy, Honoraria; *Bristol Myers Squibb:* Consultancy, Honoraria; *Novartis:* Consultancy, Honoraria; *Abbvie:* Consultancy, Honoraria; *Miltenyi:* Consultancy, Honoraria; *Lonca:* Consultancy; *Jazz:* Consultancy. **Schoemans:** *Janssen:* Honoraria; *Novartis:* Honoraria, Research Funding; *Gilead:* Other: Travel Support; *Sanofi:* Consultancy; *Pfizer:* Other: Travel Support. **Penack:** *Gilead, Jazz, MSD, Novartis, Pfizer and Therakos:* Honoraria, Other: Travel support; *Incyte and Priothera:* Research Funding; *Equillium Bio, Jazz, Gilead, Novartis, MSD, Omeros, Priothera, Sanofi, Shionogi and SOBI:* Membership on an entity's Board of Directors or advisory committees. **Koenecke:** *BMS:* Consultancy; *Janssen:* Consultancy, Speakers Bureau; *Medigene:* Consultancy; *Miltenyi Biotec:* Consultancy; *Novartis:* Consultancy, Speakers Bureau; *Pierre Fabre:* Consultancy; *Roche:* Consultancy, Speakers Bureau; *Sanofi-Aventis:* Consultancy, Speakers Bureau; *Kite/Gilead:* Consultancy; *Glaxo Smith Kline:* Consultancy; *Amgen:* Consultancy; *Pfizer:* Consultancy.

**Table 1.**

| | Overall (n=1653) | <62.5 y/o (n=830) | >62.5y/o (n=823) |
|---|---|---|---|
| Age (median, range) | 62.5 (18.4-89.2) | 53.0 (18.4-62.5) | 69.7 (62.5-89.2) |
| Sex (male) | 1062 (64.2%) | 530 (63.9%) | 532 (64.6%) |
| ECOG 2-3 | 168 (10.3%) | 70 (8.4%) | 98 (11.9%) |
| BMI | | | |
| 18.5-25 | 817 (49.4%) | 394 (47.5%) | 423 (51.4%) |
| 25-30 | 547 (33.1%) | 261 (31.4%) | 286 (34.8%) |
| >30 | 289 (17.5%) | 175 (21.1%) | 114 (13.9%) |
| Disease | | | |
| LBCL | 1401 (84.8%) | 686 (82.7%) | 715 (86.9%) |
| PMBCL | 64 (3.9%) | 62 (7.5%) | 2 (0.2%) |
| MCL | 92 (5.6%) | 25 (3.0%) | 67 (8.1%) |
| FL | 44 (2.7%) | 24 (2.9%) | 20 (2.4%) |
| PCNSL | 13 (0.8%) | 7 (0.8%) | 6 (0.7%) |
| Status at CART | | | |
| PD/RD | 1111 (67.2%) | 578 (70.0%) | 533 (65.3%) |
| SD | 125 (7.6%) | 59 (7.2%) | 66 (8.1%) |
| PR | 285 (17.4%) | 131 (15.9%) | 154 (18.9%) |
| CR | 120 (7.3%) | 57 (6.9%) | 63 (7.7%) |
| CART product | | | |
| Tisa-cel | 681 (41.2%) | 313 (37.7%) | 368 (44.7%) |
| Axi-cel | 880 (53.2%) | 492 (59.3%) | 388 (47.1%) |
| Brexu-cel | 92 (5.6%) | 25 (3.0%) | 67 (8.1%) |
| Median follow-up, months [95% CI] | 21.2 [19.6-22.6] | 22.58 [20.4-23.8] | 20.05 [18.3-22.1] |
| Cause of death | 703 (42.5%) | 338 (40.7%) | 365 (44.4%) |
| Relapse | 590 (83.9%) | 301 (85.6%) | 289 (79.2%) |
| Infection related | 33 (4.7%) | 9 (2.6%) | 24 (6.6%) |
| Cell therapy related | 53 (7.5%) | 14 (4.1%) | 39 (10.7%) |
| Other | 27 (3.8%) | 14 (4.1%) | 13 (3.6%) |

**Figure 1.**

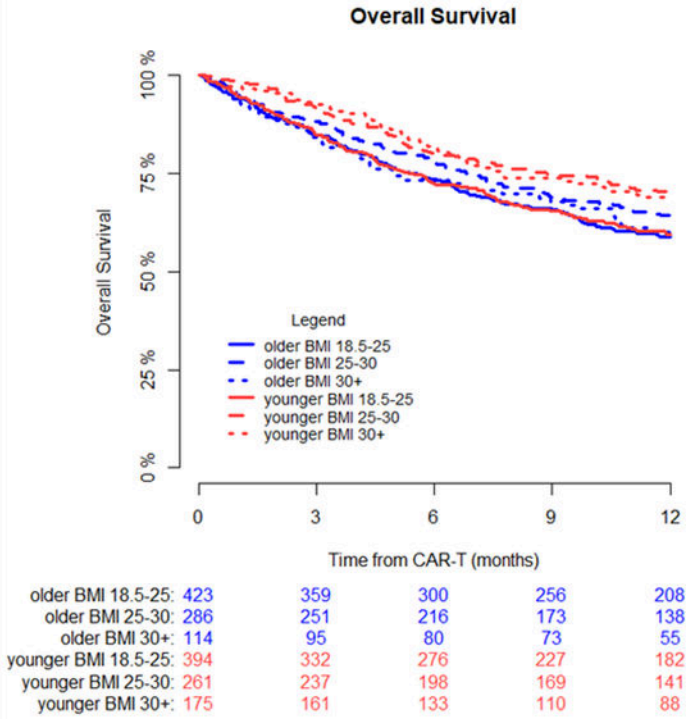


**Figure 1**

https://doi.org/10.1182/blood-2023-187393