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POSTER ABSTRACTS

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

Real-World Data Suggest Effectiveness of Allogeneic Mesenchymal Stromal (MSC-FFM) Cells in Ruxolitinib-Refractory Acute Graft-Versus-Host Disease

Peter Bader, MD PhD[1], Mareike Verbeek, MD[2], Peter Herhaus, MD[3], Lavinia Pachzelt, MD[4], Gernot Beutel[5], Christoph Schmid, MD[6], Nadine Müller, MD[7], Gesine Bug, MD[8], Arend von Stackelberg, MD[9], Johanna Tischer, MD[10], Francis A. Ayuk, MD[11], Gerald G. Wulf, MD[12], Lisa-Marie Pfeffermann, PhD[13], Bernd Jahrsdörfer, MD[14], Hubert Schrezenmeier, MD[15], Selim Kuci, MD PhD[16], Zyrafete Kuci, MD PhD[17], Anke Zens, PhD[18], Michael Tribanek, PhD[18], Robert Zeiser, MD[19], Sabine Huenecke, PhD[20], Halvard Bonig[21]

[1] Division for Stem Cell Transplantation and Immunology, University Children's Hospital Frankfurt, Frankfurt, Germany
[2] Department of Hematology and Oncology, Technical University of Munich, Munich, Germany
[3] Clinic and Policlinic for Internal Medicine III, Technical University of Munich, School of Medicine, Klinikum rechts der Isar, Munich, Germany
[4] Klinikum rechts der Isar der Technischen Hochschule München, Germany, Munich, Germany
[5] Hannover Medical School, Hannover, DEU
[6] Klinikum Augsburg, Augsburg, DEU
[7] Hematology Oncology, University Hospital Mannheim, Mannheim, Germany
[8] Klinik fuer Innere Medzin III, Ulm, Germany
[9] Charité, Med. Univ., Berlin, Berlin, DEU
[10] Dept. of Medicine 3, Klinikum Grosshadern, Munich, Germany
[11] University Hospital Hamburg, Hamburg, Germany
[12] Universitaetsklinikum Goettingen, Goettingen, Germany
[13] Goehte University, Faculty of Medicine, Institute for Transfusion Medicine and Immunhematology, Frankfurt, Germany
[14] German Red Cross Blood Service Baden-Württemberg-Hessen, University of Ulm, Institue for Transfusion Medicine and Institute for Clkinical Transfusion Medicine and Immunogenetics, Ulm, Germany
[15] University of Ulm, Ulm, Germany
[16] Department of Pediatrics, Division for Stem Cell Transplantation and Immunology, Goehte University, University Hospital, Frankfurt am Main, Germany
[17] Department of Pediatrics, Division for Stem Cell Transplantation and Immunology, Goethe University, University Hospital, Frankfurt am Main, Germany
[18] medac, Gesellschaft für medizinische Spezialpräparate mbH, Wedel, Germany
[19] Department of Medicine I, Medical Center University of Freiburg, Freiburg, Germany
[20] Department of Pediatrics, Division for Stem Cell Transplantation and Immunology, Goehte University, University Hospital, Frankfurt, Germany
[21] Faculty of Medicine, Institute for Transfusion Medicine and Immunohematology, Goethe University, Frankfurt, Germany

Introduction:
Acute graft-versus-host disease (aGvHD) remains the leading cause of treatment-related morbidity and mortality after allogeneic hematopoietic stem cell transplantation. Current first-line treatment of aGvHD is with high-dose corticosteroids, the standard for steroid-refractory aGvHD (SR-aGvHD) is the Janus kinase (JAK) inhibitor ruxolitinib.
Outcomes for patients with ruxolitinib-refractory or -intolerant aGvHD (RR-aGvHD) are poor. Thus in a recent real-world study of adult patients with RR-aGvHD (Abedin BJH 2021) median survival was 28 days (21 days for ruxolitinib refractoriness, 50 days for ruxolitinib intolerance), the probability of overall survival (OS) at 6, 12, and 24 months were about 20%, 16%, and 10%, respectively.
We assessed real-world outcomes of patients with RR-aGvHD treated with the random-donor allogeneic MSC preparation "MSC-FFM," available via Hospital Exemption in Germany.
Patients:

Between December 2017 and February 2023, 156 patients, including 33 children and adolescents (<18 years of age), received MSC-FFM for RR-aGvHD. Thirty-two German sites contributed 139 patients, while the remaining 17 patients came from seven transplant centers in France, Hungary, Norway, Sweden, and Switzerland. The adult cohort (n=123) consisted of 41% females, with an age range of 19 to 79 years (median 55 years). Except for one patient, all had been diagnosed with malignant diseases (missing information, n=3). Among the adult patients with malignant diseases, 88% (n=105) received HSCT for acute myeloid leukemia (AML), advanced myelodysplastic syndrome, myeloproliferative neoplasm or lymphoma, and 12% (n=15) for acute lymphoblastic leukemia (ALL). In the pediatric cohort (n=33), 48% of patients were females, with an age range of 0 to 17 years (median 9 years). Overall, 58% of pediatric patients (n=19) had malignant diseases as the indication for allogeneic HSCT, 42% (n=8) having ALL and 32% (n=6) with AML. The remaining 42% of pediatric patients (n=14) had non-malignant diseases as the indication for HSCT. Of the adult patients, 6 (4.9%) had grade II, 52 (42.3%) had grade III, and 63 (51.2%) had grade IV aGvHD, with no specification reported for 2 patients (1.6%). In children, 2 (6.1%) had grade II, 10 (30.3%) had grade III, and 21 (63.6%) had grade IV

Treatment:

MSC-FFM is manufactured from pooled bone marrow mononuclear cells from eight HLA-disparate healthy donors. MSCs are selected by plastic adherence, expanded until the end of passage 3, then frozen in saline-albumin with DMSO. The recommended dosing for MSC-FFM is 1-2 million cells/kg body weight (BW), for four weekly doses. The median dose administered was 1.18 million cells/kg BW, with a median number of four doses and a median inter-dose interval of 7 days.

Results:

Safety: Tolerability of MSC-FFM was good, with only five adverse drug reactions reported in three adult patients (chills, BK virus cystitis, increase in C-reactive protein [reported twice in one patient], nausea) and did not result in cessation of MSC treatment or dose reductions.

Response: The overall response rate at day +28 was 49% (95%-CI: 41-58%), with 45% (36-55%) in adults and 64% (45-80%) in children. Most responses were durable, resulting in an overall response rate of 49% (41-57%) for both adults and children at 2 months, and 40% (31-48%) at 6 months.

Survival: Overall survival at 6, 12, and 24 months was 47% (38-56%), 35% (27-44%), and 29% (21-38%) for adults, and 59% (40-74%), 42% (24-58%), and 37% (19-54%) for children, respectively (Table 1). Median overall survival was 5.8 months. These outcomes compare favourably to published overall survival estimates for adult RR-aGvHD patients not treated with MSC-FFM (Abedin BJH, see above).

Summary:

The unique MSC-preparation MSC-FFM appears to be effective against RR-aGvHD.

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