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ORAL ABSTRACTS

723.ALLOGENEIC TRANSPLANTATION: LONG-TERM FOLLOW-UP AND DISEASE RECURRENCE

Relapse Incidence Post Unrelated Allogeneic Stem Cell Transplantation with Post-Transplant Cyclophosphamide (PTCy) Versus Conventional Anti-Graft Versus Host Disease Prophylaxis in Patients with Acute Myeloid Leukemia: A Study on Behalf of the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation

Arnon Nagler, MD[1], Maud Ngoya[2], Jacques-Emmanuel Galimard[3], Myriam Labopin[4], Igor Wolfgang Blau, MD PhD[5], Nicolaus Kröger, MD[6], Tobias Gedde-Dahl, MD[7], Thomas Schroeder[8], David Burns, MD PhD[9], Urpu Salmenniemi, MD PhD[10], Alessandro Rambaldi, MD[11], Goda Choi[12], Regis Peffault De Latour[13], Jan Vydra, MD[14], Henrik Sengeloev[15], Matthias Eder[16], Stephan Mielke, MD[17], Edouard Forcade, MD PhD[18], Sergey Bondarenko, PhDMD[19], Fabio Ciceri, MD[20], Mohamad Mohty, MDPhD[21,22]

[1] Division of Hematology and Bone Marrow Transplantation, Chaim Sheba Medical Center, Tel Hashomer, Israel
[2] European Society for Blood and Marrow Transplantation, Paris, France
[3] Statistic and Statistic and Epidemiologic Research Center Sorbonne Paris Cit, Paris, FRA
[4] EBMT Statistical Unit, Sorbonne University, Saint-Antoine Hospital, AP-HP, INSERM UMRs 938, Paris, France
[5] Medizinische Klinik m. S. Hämatologie, Onkologie und Tumorimmunologie, Berlin, Germany
[6] University Hospital Eppendorf, Bone Marrow Transplantation Centre, Hamburg, Germany
[7] Oslo University Hospital, Oslo, NOR
[8] Department of Hematology and Stem Cell Transplantation, University Hospital Essen, Essen, Germany
[9] University Hospital Birmingham NHSTrust, Birmingham, United Kingdom
[10] HUCH Comprehensive Cancer Center, Stem Cell Transplantation Unit, Helsinki, Finland
[11] Department of Hematology, ASST Papa Giovanni XXIII, Bergamo, ITA
[12] University Medical Center Groningen (UMCG), Groningen, Netherlands
[13] Hôpital Saint-Louis, Paris, France
[14] Institute of Hematology and Blood Transfusion, Prague 10, CZE
[15] Rigshospitalet, Copenhagen, Denmark
[16] Department of Hematology, Hemostasis, Oncology and Stem Cell Transplantation, Hannover Medical School, Hannover, Germany
[17] Department of Cellular Therapy and Allogeneic Stem Cell Transplantation, Karolinska Institute & University Hospital, Stockholm, Sweden
[18] Service d'Hématologie Clinique et Thérapie Cellulaire, CHU Bordeaux, F-33000, Bordeaux, France
[19] RM Gorbacheva Research Institute, Pavlov University, Saint-Petersburg, RUS
[20] IRCCS Ospedale San Raffaele, Vita-Salute San Raffaele University, Milan, Italy
[21] Saint-Antoine Hospital, Sorbonne University, Paris, France
[22] Hôpital Saint Antoine, Paris, FRA

Background:
Recently, the BMT CTN 1703 phase III study compared post-transplant cyclophosphamide with tacrolimus with *mycophenolate mofetil* (PTCy/TAC/MMF) to TAC /methotrexate (MTX) as graft- *versus*-host disease (GVHD) prophylaxis post allogeneic transplantation (HSCT), demonstrating a lower incidence of severe acute (a) GVHD and chronic (c) GVHD and better GVHD-free, relapse-free survival (GRFS). The control arm did not include anti-thymocyte globulin (ATG), used in many centers for GVHD prophylaxis.
Methods: The study aim was to compare PTCy with TAC or cyclosporine A (CSA) and MMF (PTCy/TAC or CSA & MMF) to ATG combined with TAC and MTX (ATG/TAC/MTX) in acute myeloid leukemia (AML) patients (pts) undergoing HSCT from matched siblings (MSD) or 9-10/10 unrelated donor (UD) in first complete remission (CR1). Statistical tests included a multivariate analysis (MVA) adjusting for potential confounding factors using a Cox proportional-hazards regression model for main outcomes.

Results: 6050 pts met the inclusion criteria, 402 received PTCy/TAC or CSA & MMF and 5648 received ATG/TAC/MTX as GVHD prophylaxis. Median follow-up was 23.4 (IQR, 20.3-24.9) and 41.8 (IQR, 39.6-43.3) months (p<0.0001). The median year of the transplant was 2018 (2010-2020) and 2016 (2007-2020) (p<0.0001). Pts in the PTCy/TAC or CSA & MMF group were younger, with a median age of 48.7 (range 18-5.6) *versus* 51.5 (8-77.8) years (p=0.024). The diagnosis was *de novo* AML in 84.1% *vs* 85.3% and secondary (s) AML in 15.9% *vs.* 14.7% (p=0.49). The cytogenetic risk was categorized as intermediate (70.9% *vs.* 67.1%), adverse (22.2% *vs.* 25.7 %), and favorable (6.9% *vs.* 7.2%) for pts in the PTCy/TAC or CSA & MMF and ATG/TAC/MTX groups, respectively (p=0.35) (data missing for 2214 pts). Karnofsky performance status (KPS) did not differ between the groups. There was a higher frequency of pt cytomegalovirus (CMV) seropositivity and female (F) donor to male (M) pt combination in the PTCy/TAC or CSA & MMF versus the ATG/TAC/MTX groups, 77.8% vs. 71.8% (p=0.009) and 18.4% vs. 14.4% (p=0.029), respectively. More pts in the PTCy/TAC or CSA & MMF group received reduced intensity conditioning (RIC) 51.5% *versus* 41.1% in the ATG/TAC/MMT group, respectively (p<0001). Day 60 neutrophil engraftment (ANC >0.5 x 10^{9}/L) was 98.7% *vs.* 98.6% (p=0.84). Day 180 incidence of a GVHD grade II-IV and III-IV was 21.2% *vs.* 20.4% (p=0.92) and 8.1% *vs.* 6% (p=0.1), in pts receiving PTCy/TAC or CSA & MMF *versus* the ATG/Tac/MTX GVHD prophylaxis, respectively. The 2-year (y) total and extensive chronic (c) GVHD were 33.7% *vs.* 30% (p=0.09) and 10.7 % *vs.* 11.2% (p=0.81), respectively. GVHD was the cause of death in 11.6% *vs.* 13.9% of pts who died. In the MVA, both aGVHD (grade II-IV or III-IV) and cGVHD (total or extensive) did not differ between the groups with hazard ratios (HRs) =1.15 (95% CI 0.86-1.53, p=0.35), HR=0.87 (95% CI 0.56-1.34, p=0.52), HR=0.91 (95% CI 0.7-1.18, p=0. 47 and HR=1.51 (95% CI 0.96-2.36, p=0.074). Two-y NRM was significantly lower in pts that received PTCy/TAC or CSA & MMF *versus* ATG/TAC/MTX for GVHD prophylaxis, HR=1.57 (95% CI 1.07-2.3, p=0.022). Other HSCT outcome parameters did not differ between the groups. The HR for 2-y RI was 0.99 (95% CI 0.77-127, p=0. 93). The HRs for 2-y leukemia-free survival (LFS), overall survival (OS), and GRFS were HR=1.15 (95% CI 0.94-1.42, p<0.18), HR=1.18 (95% CI 0.94-1.49, p=0.16) and HR=1.12 (95% CI 0.93-1.36, p=0.22), respectively. Donor type and conditioning regimen were poor prognostic factors for grade II-IV, III-IV aGVHD, and total and extensive cGVHD. For cGVHD, additional poor prognostic factors were F donor to M pt combination and pt CMV seropositivity. Poor prognostic factors for LFS, OS, and GRFS were 9/10 UD, age (by 10 y), sAML, adverse-risk cytogenetics, lower KPS, and pt CMV seropositivity. For NRM, factors were the same apart from cytogenetics risk which was not a prognostic factor. In addition, time from diagnosis to HSCT was a prognostic factor for NRM and RI. Other poor prognostic factors for RI were lower KPS and pt CMV seropositivity. **Conclusions**: In this registry-based retrospective analysis, comparing PTCy in combination with TAC or CSA and MMF to ATG in combination with TAC and MTX as GVHD prophylaxis, we observed a similar incidence and severity of both aGVHD and cGVHD. NRM was significantly lower with the PTCy-based GVHD prophylaxis, while all other transplant outcome parameters were similar.

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Figure: Transplantation outcome – Relapse incidence (RI), non-relapse mortality (NRM), leukemia-free survival (LFS), overall survival (OS), and graft-versus-host disease (GVHD)-free, relapse-free survival (GRFS) in acute leukemia patients undergoing unrelated allogeneic stem cell transplantation with post-transplant cyclophosphamide (PTCy) compared to no PTCy (*in vivo* T-cell depletion or calcineurin inhibitor-based GVHD prophylaxis)

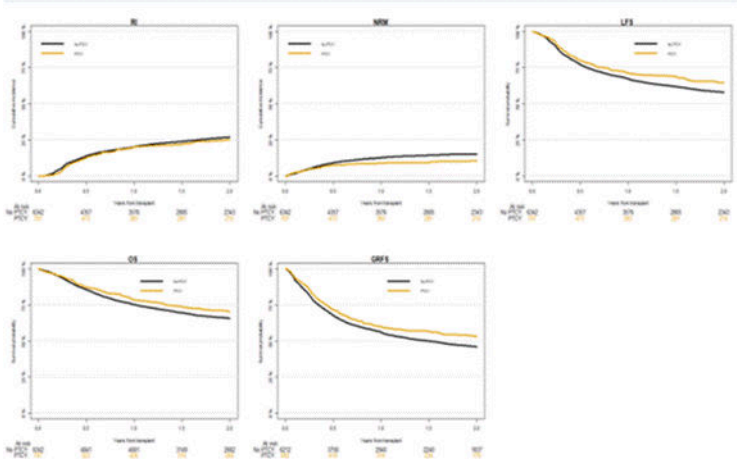

Figure 1

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