EBMT LWP

EBMT study code: 2019-R-05

Title: A Comparison between ATG and PT-CY graft-versus-host-disease prophylaxis in patients with lymphoma undergoing reduced intensity conditioning regimen HSCT from 1 antigen MMUD

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Background: Post Transplant-Cyclophosphamide (PT-CY) has been first used for prevention of acute and chronic graft-versus-host-disease (GVHD) in the setting of haploidentical transplantation (HAPLO) almost 10 years ago. Subsequently, different studies have reported promising results with respect to non-relapse mortality (NRM), GVHD and infections for HAPLO PT-CY compared to other donor sources. As a consequence, this platform has also been investigated in the setting of HLA-identical sibling and matched unrelated donor (MUD). To date, two single-center studies have compared outcomes of patients with various hematological malignancies undergoing mismatched unrelated donor (MMUD) with either PT-CY or Anti-thymocyte globulin (ATG) as GVHD prophylaxis in small cohorts. More recently, a matched pair analysis was conducted in AML patients with results indicating lower incidence of grade III-IV acute GVHD and higher LFS for the PT-Cy group. So far, no other studies have compared the use of PT-CY to ATG in the setting of MMUD 9/10 in a homogeneous cohort of lymphoproliferative disorders.

Study design: Retrospective registry analysis

Objective: to retrospectively analyze outcomes after first allogenic hematopoietic stem cell transplantation (HSCT) from MMUD 9/10 with a reduced intensity conditioning (RIC) regimen comparing outcomes of PT-CY versus ATG as GVHD prophylaxis in patients with lymphoproliferative disorders.

Primary endpoint: cumulative incidence (CI) of acute grade II-IV GVHD

Secondary endpoints: CI of neutrophil engraftment, CI of grade III-IV acute GVHD, CI of chronic GVHD, CI of extensive chronic GVHD, non-relapse mortality (NRM), relapse incidence (RI), progression free survival (PFS), overall survival (OS) and GVHD-free/relapse-free survival (GRFS)

Inclusion criteria:

-Patients who received a 9/10 HSCT

-First HSCT (previous autologous transplantation accepted)

-High-resolution HLA allele typing at loci A, B, C, DRB1 and DQ available

-Stem Cell source (bone marrow or peripheral blood stem cells)

-Year of HSCT from 2010 to 2018

-All type of B and T cell lymphomas (NHL and HL, aggressive and indolent)

-All disease status at HSCT

-RIC regimen

-In vivo T cell depletion (TCD) with ATG (other in vivo TCD excluded) or PT-CY

Exclusion criteria:

-Cord Blood as stem cell source

-Other type of unrelated HSCT (matched unrelated, more than 1 mismatch)

Variables to be analyzed:

Patient

Age (Med A)

Gender (Med A)

Karnofsky score at HSCT (Med A)

Sorror score (Med A)

Disease status at HSCT (Med A)

Diagnosis (Med A)

Previous auto (Med A)

HLA typing (Med A)

ABO group, Rhesus (Med B)

CMV status (Med A)

Donor

Age (Med A)

Gender (Med A)

HLA typing (Med A)

ABO group, Rhesus (Med B)

CMV status (Med A)

Transplant

Stem cell source (Med A)

CD 34 cell dose (Med B)

CD 3 cell dose (Med B)

Conditioning regimen RIC (Med A)

PT-Cy (yes/no) (Med A)

T-cell depletion ATG (yes/no) (Med A)

Year of HSCT (Med A)

GVHD prophylaxis (Med A)

Outcomes to be analyzed:

-Time to neutrophil recovery (Med A)

- Time to platelet recovery (Med A)

- Acute GVHD (yes/no; grade if yes) (Med A)

- Chronic GVHD (yes/no; extension if yes) (Med A)

- Date of Acute GVHD (Med A)

- Date of Chronic GVHD (Med A)

- Status at last follow-up (Med A)

- Date of last follow-up (Med A)

- Relapse (yes/no) (Med A)

- Date of relapse, if applicable (Med A)

- Cause of death, if applicable (Med A)

- Date of death, if applicable (Med A)

Strategy for data collection:

An invitation to participate will be sent to all EBMT centers who reported RIC HSCT from MMUD 9/10 for HL or NHL after January 1, 2010.

Statistical analysis: Probabilities of OS and PFS will be calculated using the Kaplan-Meier estimate; the log-rank test will be used for univariate comparisons. Cumulative incidence curves will be computed for RI and NRM, death and relapse being competing risks. Gray's test will be used for univariate comparisons. Multivariate analysis will be performed using Cox proportional hazards for OS and PFS, Fine-Gray model for RI, NRM and acute and chronic GVHD. The composite endpoint GRFS in which events include grade 3-4 acute GVHD, systemic therapy-requiring chronic GVHD, relapse or death in the first post-HCT year will also be analyzed.

Data collection: Data will be collected from Med A, Med B and Med C items to be requested from the centers

Deadline: data analysis should be completed for September 30th, 2020 for EBMT 2021 Abstract submission.

Feasibility: a preliminary analysis identified in EBMT registry 540 patients who satisfy the following criteria (age>18years, first HSCT MMUD 9/10, year of HSCT 2010-2018, RIC conditioning regimen, diagnosis: B or T cell lymphomas).
FL (n=94), MCL (n=70), DLBCL (n=95), HL (n=137), BL (n=2), other B cell (n=14), T-cell (n=93), and other (n=35).