Abstract: PB3190

Title: IMPACT OF PREVIOUS ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION ON CHIMERIC ANTIGEN RECEPTOR (CAR) T CELL TREATMENT WITH IDECABTAGENE-AUTOLEUCEL FOR RELAPSED/REFRACTORY MULTIPLE MYELOMA I

Abstract Type: Publication Only

Topic: Gene therapy, cellular immunotherapy and vaccination - Clinical

Background:

Anti-BCMA-directed chimeric antigen receptor (CAR) T cells are effective treatment for patients with refractory/relapsed multiple myeloma (RRMM). However, little is known about the impact of previous allogeneic hematopoietic stem cell transplantation (allo-HSCT) on lymphocyte collection for production of CAR T cells and subsequent treatment with CAR T cells.

Aims:

We performed a retrospective analysis of cellular composition of lymphocyte collections, CAR T cell expansion and treatment outcomes of RRMM patients undergoing therapy with idecabtagene vicleucel (ide-cel) with and without history of allo-HSCT.

Methods:

Between June 2022 and February 2023, 27 patients of which five with prior history of allo-HSCT, were treated with ide-cel in our institution. Median age of the whole cohort was 63 (range 39-75) years and 16 (59%) were male. The patients had median 8 (range 4-13) prior treatment lines. Most of the patients (63%) were suffering from IgG Kappa RRMM, and 56% had adverse genetics, inclusive 4/5 patients with history of prior allo-HSCT. The vein-to-vein time was median 58 (range 49-165) days. Allo-HSCT was performed in median 5.5 (range 1.9-6.7) years prior to the reinfusion of ide-cel.

All collections were performed with Spectra Optia device (Terumo BCT) using continuous MNC program, version 11. The apheresis volume was set at three-times of the estimated blood volume and collection time was limited to maximum five hours according to the national standards.

CAR T cells were determined from peripheral blood of the patients 7, 14, 30 and 100 days after the reinfusion of ide-cel. Quantification of CAR T cell specific DNA was performed by semiquantitative real-time polymerase chain reaction (PCR).

Results:

Prior to apheresis, the white blood cell, absolute lymphocyte counts, CD3+ cells and monocytes did not differ in patients with and without prior allo-HSCT.

All patients underwent a single apheresis with median of 31.5 (range 4.9-171.6) x108 CD3+ cells collected. The CD3+ yields in patients with and without prior allo-HSCT did not differ (p=0.45) and were 37.9 (13.6-171.6)x108 and 28.0 (range 4.9-155.0)x108 respectively. We also noticed no differences regarding CD3+CD4+ (p=0.42) or CD3+CD8+ yields (p=0.35), Figure 1A.

The patients were infused with median 431.2 (range 25.7-489.1) CAR T cells without difference regarding prior allo-HSCT status (p=0.35). One patient without history of prior allo-HSCT was infused with out-of-specification product with only 25.7x106 CAR T cells and is in complete remission 191 days thereafter.

The highest expansion of CAR T cells was detected between day 7 after infusion with median 563 (range 66-4423)/103 cells and showed no difference in patients with and without previous allo-HSCT with 410 (74-

3149)/103 and 837 (range 66-4423)/103 respectively (p=0.71). Low-grade cytokine release syndrome occurred in 22 patients and 10 required tocilizumab. Neurotoxicity was not detected.

One year after ide-cel infusion, the progression-free survival and overall survival of patients with and without previous allo-HSCT did not differ with 60% and 45% respectively (p=0.58) and 66.7% and 74% respectively (p=0.84), Figure 1B.

No graft-versus-host disease during the follow-up was detected.

Summary/Conclusion: Our data confirm that the treatment with ide-cel is feasible for patients with prior allo-HSCT. Furthermore, allo-HSCT did not influence cellular composition of lymphocyte collections, clinical outcome or in vivo expansion of ide-cel.

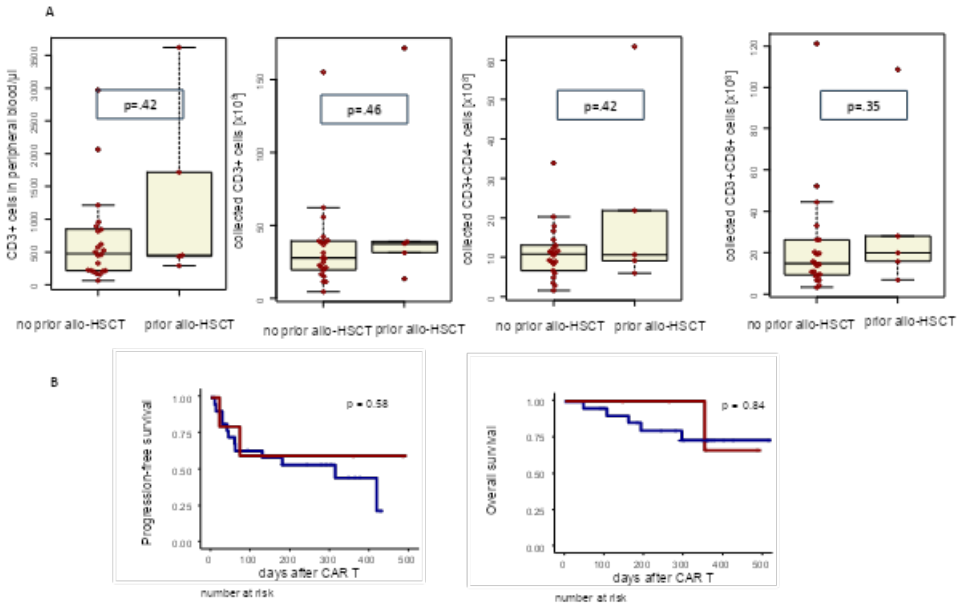

Figure 1: A. CD3+ cells in peripheral blood prior to apheresis and collected yields for CD3+, CD4+ and CD8+ cells. B. Progression-free survival and overall-survival of patients with and without prior allo-HSCT

Keywords: Multiple myeloma, CAR-T, Hematopoietic cell transplantation, Allogeneic hematopoietic stem cell transplant