Transfusion and Apheresis Science xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Transfusion and Apheresis Science

journal homepage: www.elsevier.com/locate/transci

Evaluation of a new continuous mononuclear cell collection procedure in a single transplant center cohort enriched for AL amyloidosis patients

Anita Pudusseri[a,*], India Smith[a], Diane Sarnacki[a], Dina Brauneis[a], Anthony Shelton[a], Vaishali Sanchorawala[a], J. Mark Sloan[a], Shayna Sarosiek[a], Karen Quillen[a,b]

[a] Department of Medicine, Division of Hematology and Oncology, Boston University Medical Center, Boston, MA, United States
[b] Department of Pathology and Laboratory Medicine, Boston University Medical Center, Boston, MA, United States

ARTICLE INFO

Keywords:
Stem cell
Transplantation
Leukapheresis
AL amyloidosis

ABSTRACT

Background: The Spectra Optia continuous mononuclear cell (CMNC) program is newly available, and herein validated in a single-center cohort enriched with AL amyloidosis patients to collect a target CD34+ yield of 2.5×10^6 cells/kg within 2 days.

Methods: Consecutive autologous transplant patients in 2016 are included. Patients undergo leukapheresis with Optia CMNC and Spectra v4.7 over a 2-day cycle. Data collection includes collection efficiency, adverse events and engraftment kinetics.

Results: 36 leukapheresis procedures on 18 patients are included. The diagnoses are AL amyloidosis (9), myeloma (7), lymphoma (2), and scleroderma (1). Median age is 60; 12 are men. Plerixafor was employed preemptively in 6 cycles. Median blood CD34+ on Day 1 of leukapheresis was 46 cells/uL. Median number of blood volumes processed on Day 1 was 3.1. All collection cycles were completed within 2 days; only one in a heavily pretreated lymphoma patient did not reach the target requiring a second mobilization attempt. Mean collection efficiencies were comparable between the two devices. There were 2 adverse events: tubing rupture on the Optia; and one case of hypotension. All 18 patients underwent high-dose chemotherapy: median cell dose infused was 7.7×10^6 CD34+ cells/kg. Median days to neutrophil and platelet engraftment were 10 and 13 respectively.

Conclusion: The Optia CMNC collection protocol is safe and effective in a small single-center autologous stem cell transplant cohort enriched for high-risk patients with AL amyloidosis and cardiac involvement. Caution is needed for tubing setup because there is less cumulative experience with Optia.

1. Introduction

In multiple myeloma, high-dose melphalan followed by autologous stem cell transplantation (HDM/SCT) is associated with a higher response rate, improved disease-free and overall survival when compared to standard chemotherapy [1] Similarly, AL (light chain) amyloidosis is a clonal plasma cell disorder, characterized by deposition of protein derived from immunoglobulin light chain fragments. While HDM/SCT can induce complete hematologic responses and prolong survival in AL amyloidosis, the procedure is associated with significant morbidity in patients with cardiac involvement. Cardiac biomarker elevation correlates with prognosis, and has been used to develop a staging system [2,3]Selected patients with cardiac involvement who successfully undergo HDM/SCT can have durable remissions and excellent survival. In certain autoimmune diseases such as scleroderma, high dose chemotherapy and SCT have also been used to treat life- threatening complications. The rationale is that high dose chemotherapy may eradicate or modulate clones of autoreactive T-cells [4]

Peripheral blood progenitor cells have become the main source of hematopoietic stem cells for patients undergoing HDC/SCT because of the less invasive collection method (compared to bone marrow harvesting) and more rapid blood count recovery. The goal is to obtain stem cell doses between 2.5×10^6 and 10×10^6 CD34+ cells/kg, as this threshold is associated with more rapid platelet and neutrophil recovery [5]. While the most commonly used cell separator for peripheral blood stem cell (PBSC) collection of CD34+ cells from mobilized patients in the United States is the COBE Spectra Apheresis System (abbreviated as “Spectra” herein) (Terumo BCT, Lakewood, CO), many institutions are transitioning to the newer Spectra “Optia” Apheresis System (abbreviated as “Optia” herein) since the launch of the latter in

* Corresponding author at: 820 Harrison Ave FGH Building 1st Floor, Boston, MA, 02118, United States.
E-mail address: apudusseri@gmail.com (A. Pudusseri).

https://doi.org/10.1016/j.transci.2018.04.025
Received 19 December 2017; Received in revised form 17 April 2018; Accepted 24 April 2018

2010. Using a computerized automated interface system, the Optia efficiently collects mononuclear cells (MNC) via centrifugal separation while omitting erythrocytes, polymorphonuclear cells (PMNs) and platelets [6]. The MNC-rich fraction includes CD34+ hematopoietic stem cells and progenitor cells, lymphocytes and monocytes.

The aim of this study is to demonstrate that the incorporation of the continuous mononuclear cell (CMNC) program, newly introduced in 2015, on Optia into the stem cell collection process for a single center patient population enriched with fragile AL amyloidosis patients achieves a minimum target CD34+ dose of 2.5×10^6 cells/kg within 2 days of apheresis.

2. Methods

Consecutive patients who underwent stem cell mobilization followed by high dose chemotherapy and SCT in 2016 were included in this analysis. Our institutional protocol consists of 2 days of apheresis, however, the duration of apheresis on the second day may be abbreviated depending on the first day's CD34+ yield. Patients who were anticipated to require only a single day of apheresis – such as those mobilized off cyclophosphamide - were excluded. After fluoroscopic-guided placement of a tunneled apheresis catheter, patients received granulocyte- colony stimulating factor (G-CSF) dosed at 16 mcg/kg/day for 3 days, followed by leukapheresis on Day 4. Additional G-CSF is given after leukapheresis on Day 4. Patients with AL amyloidosis and cardiac involvement (modified cardiac stage II or III) received G-CSF at 10 mcg/kg/ day for 5 days, and plerixafor at 0.24 mg/kg (adjusted for creatinine clearance if necessary) in the late afternoon on Day 4, followed by apheresis on Day 5.

Patients underwent leukapheresis on Optia for one day and Spectra (Version 4.7, Terumo BCT, Lakewood, CO) for another day over a 2-day collection cycle; crossover sequence depended on device availability on any given day. Optia CMNC program was used with monitoring of the collection preference. Citrate was used exclusively as the anticoagulant without any heparin. Calcium gluconate infusion was administered through the return line, at 1 gm/h. The run target was set by time (5 h on Day 1), although initiation delay and adverse reactions could prompt shorter sessions. Serum free calcium was obtained at the end of each procedure. The leukapheresis procedures were completed as an outpatient whenever possible. Patients' weights pre- and post-procedure are recorded. The stem cell component was processed on-site with CD34+ enumeration turnaround time of 2–2.5 h. Target cell yield is 5×10^6 CD34+ cells/kg for patients receiving high-dose melphalan (200 mg/m^2); lower targets are acceptable for patients receiving modified-dose melphalan or other conditioning regimens. Collection efficiency (CE2) is calculated with the following formula:

$$\text{CE2}(\%) = \frac{(\text{CD34+ cells in product} \times \text{Product volume})}{\text{Blood volume processed} \times \text{Pre-apheresis CD34+ count in blood}}$$

Platelet loss with stem cell collection is calculated with the following formula:

$$\text{Day 1 to Day 2 Platelet decrement}(\%) = \frac{\text{Day 1 Pre-platelet count} - \text{Day 2 Pre-platelet count}}{\text{Day 1 Pre-platelet count}}$$

Patients underwent high dose chemotherapy within 6–14 days of completing leukapheresis, followed by stem cell infusion and growth factor support (G-CSF at 5 mcg/kg/day starting Day +1). Neutrophil engraftment is defined as an absolute neutrophil count (ANC) of $\geq 0.5 \times 10^9$/L (500/mm^3). Platelet engraftment is defined as platelet count $\geq 20 \times 10^9$/L at least 48 h after the last platelet transfusion.

Table 1
Patient Demographics.

Number of patients	18
Male/ female	12/6
Age (years)[a]	60 (36–70)
Weight (kg)[a]	87 (51–126)
Diagnosis	
Amyloidosis (AL) [b]	9
Multiple Myeloma (MM) [b]	7
NHL [c]	2
Scleroderma	1
Courses of mobilization	19
Courses with at least one day of Plerixafor	6

[a] median (range).
[b] One patient with dual diagnosis of Amyloidosis and MM (counted in subsequent data as AL).
[c] Non Hodgkin's Lymphoma (NHL): DLBCL, Peripheral T cell lymphoma NOS.

3. Results

Thirty-six consecutive leukapheresis procedures on 18 patients were performed between January and November of 2016. One patient with relapsed lymphoma was collected twice, one month apart. Patient diagnoses included AL amyloidosis (9), multiple myeloma (7), Non-Hodgkin's Lymphoma (2) and scleroderma (1). One patient was diagnosed with both AL amyloidosis and multiple myeloma and is included under the AL Amyloidosis cohort. Median age was 60 years (range 36–70) with 12 male patients. Patient demographics are reported in Table 1. Plerixafor was employed pre-emptively in 6 collection cycles: 4 patients with cardiac amyloidosis and the lymphoma patient who required 2 collection cycles.

3.1. Apheresis data

Apheresis parameters for each day are reported on Table 2. Two patients had only one session of leukapheresis after an unexpectedly high yield of CD34+ cells on the first day. Median total blood volume (based on actual body weight) was 6.09 liters (L) (range 3.57–7.07). Median blood volume processed on Day 1 of leukapheresis was 17.69 L (range 12.44–21.75) and 12.10 L (range 9.3–18.93) on Day 2, representing 3.1 and 2.1-fold processing of the patient's total blood volume respectively. The median WBC on Day 1 of leukapheresis was 41.4×10^9 /L (range 8.6–83.9). Median blood CD34+ cell count on Day 1 was 46.4 cells/uL (range 1.7–176). All collection series were completed within 2 days; only 1 did not reach the target harvest yield, requiring a second mobilization attempt one month later with G-CSF and plerixafor; this was a heavily pre-treated lymphoma patient for whom poor mobilization was anticipated.

Table 2
Apheresis Parameters.[a]

	Day 1	Day 2
Number of sessions	19	17
Apheresis parameters		
Total Blood Volume (L)	6.09 (3.57–7.07)	6.09 (3.57–7.07)
Blood volume processed (L)	17.69 (12.44–21.75)	12.10 (9.3–18.93)
Number of TBV processed	3.1 (2.0–3.6)	2.1 (1.6–3.3)
Pre-apheresis count		
WBC (x 10^9/L)	41.4 (8.6–83.9)	41.5 (13.1–76.4)
Platelets (x 10^9/L)	185 (54–298)	99 (24–181)
CD 34 + cells (/μL)	46.4 (1.7–176)	40.56 (2.6–94.5)

[a] Data reported as median (range).