Quantification of the Time and Effort Required For Autologous Peripheral Blood Stem Cell Collection: A European Perspective

Mohamad Mohty[1], Nabih Azar[2], John Reitan[3], Richard P. Kadota[4], Sarah Naoshy[5], Sheikh Usman Iqbal[5], Zhimin Xiao[5], Kai Hübel[6]

[1]Saint-Antoine Hospital, [2]Hematologie Clinique, Hôpital de la Pitié-Sâlpétrière, Paris, France, [3]RJM Group LLC, Crown Point, [4]Global Oncology Medical Affairs, [5]Global Evidence & Value Development, Sanofi, Cambridge, United States, [6]University Hospital of Cologne, Cologne, Germany

Abstract

Introduction: Plerixafor is approved for autologous peripheral blood stem cell mobilization in patients with Non-Hodgkin Lymphoma (NHL) or Multiple Myeloma. This agent may reduce the failure rate and/or the number of apheresis procedures required without increasing the toxicity, and this may reduce total transplant costs. With this background, the aim of this prospective noninterventional analysis is to assess resource utilization to document provider costs associated with peripheral stem cell mobilization and apheresis. Of note, the study aims to evaluate the impact on the time and effort associated and costs to the hospital when using plerixafor (P) with a primary analysis to compare measures of time/effort from patients drawn from the Pre-P versus P eras.

Materials (or patients) and methods: The study population includes NHL patients undergoing peripheral blood stem cell mobilization. Part I of the study is a retrospective medical record review study of 200 NHL patients from 7 centers in France and Germany. Selected patients will be evenly divided between two eras: 1) prior to approval of plerixafor = Pre-P era (until June 1, 2009) 2) after approval of plerixafor = P era (July 1, 2010 and onwards). Part II of the analysis is an ongoing prospective study consisting of time/motion evaluation of actual apheresis – 20 events at each center. The actual apheresis events are being measured in consecutive patients scheduled to be candidates for peripheral blood stem mobilization.

Outcome measures include number of visits for administration of mobilizing agents; duration (days) of administration of mobilizing agents; agents used as mobilizing agents; adverse events detected during mobilization; number of apheresis sessions; hours of apheresis sessions; attainment of CD34+ target (yes, no); days until CD 34+ target level was met. In addition, time-motion assessments will be obtained retrospectively (Part I) and concurrently (Part II) and included the total time to prepare the patient, perform apheresis and manage adverse events. Costs will be evaluated and quantified in terms of micro-costing group interviews with local hospital administration. The primary study end point is difference in mean time to perform apheresis (including apheresis related adverse events, if any) and costs to the hospital in terms of micro-costing per patient, between patients in the Pre-P versus P eras.

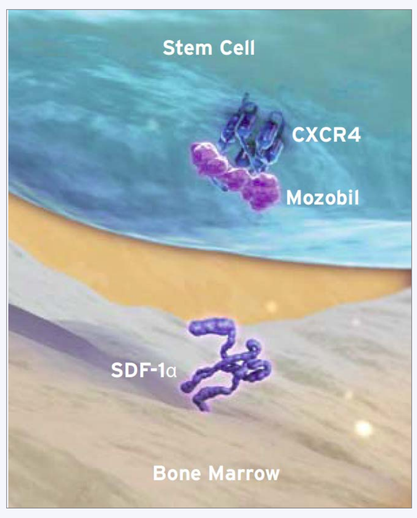
Results: At the time of abstract submission, data collection is ongoing and results will be presented during the meeting. The key findings of this study will demonstrate the favorable impact of novel interventions on the number of apheresis procedures required to reach a target peripheral blood stem cell, and failure rate of mobilization, thus translating into reduced total transplant costs without increasing the toxicity.

Discussion: The financial implications for transplant centers would be significant and would pave the way for further studies aiming to optimize staff time and resource utilization related to apheresis in real-world practice.

Background

- In Europe, plerixafor (P) is approved in combination with Granulocyte colony stimulating factor (G-CSF) to enhance mobilisation of hematopoietic stem cells to the peripheral blood (PB) for collection and subsequent autologous transplantation in patients with lymphoma and Multiple Myeloma (MM) whose cells mobilise poorly[1].
- The mechanism of action of plerixafor includes the blockage of the CXCR4-SDF-1α interaction, releasing stem cells from the bone marrow into the circulating blood[2] (**Figure 1**).
- As demonstrated by two Phase III trials for NHL (study 3101) and MM (study 3102) in patients undergoing stem cell mobilization, the addition of plerixafor to G-CSF resulted in significantly higher proportion of NHL and MM patients collecting a target number of stem cells (≥ $5x10^6$ and ≥ $6x10^6$ CD34+ cells/kg, respectively), and in fewer apheresis days, compared to G-CSF alone[3,4]. Plerixafor + G-CSF has also been shown to be effective in patients who failed prior mobilization regimens[5].
- Plerixafor may reduce the failure rate and/or the number of apheresis procedures required without increasing the toxicity, and this may reduce total transplant costs.

Figure 1
Mechanism of Action of Plerixafor[2]



Objective

Given intense competition for hospital resources and the staff required to evaluate and manage patients preparing for stem cell mobilization and transplantation, it is reasonable to assess resource utilization to document provider costs associated with peripheral stem cell mobilization and apheresis, especially when newer therapies, i.e. plerixafor is available and may be more suitable for some of these patients.

Methods

The study population includes patients aged ≥ 18 years, with a primary diagnosis of Non-Hodgkin's Lymphoma across 7 centers in France and Germany undergoing peripheral blood stem cell mobilization. The study will consist of two parts (**Figure 2**):

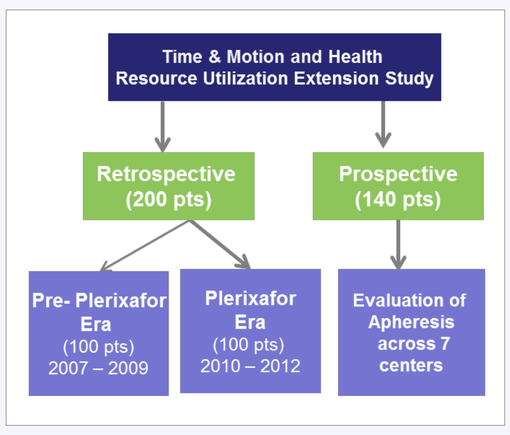
- **Part I:**
  - Ongoing retrospective medical record review study of 200 NHL patients from the sites. Selected patients will be evenly divided between two eras:
    1. **Pre-Plerixafor era (until June 1, 2009):** prior to approval of plerixafor
    2. **Plerixafor era (July 1, 2010 and onwards):** after approval of plerixafor
- **Part II:**
  - Ongoing prospective study consisting of time and motion evaluation of actual apheresis, with 20 events measured at each center

Study outcome measures include the following:

- number of visits for administration of mobilizing agents
- duration (days) of administration of mobilizing agents
- agents used as mobilizing agents
- adverse events detected during mobilization
- number of apheresis sessions
- hours of apheresis sessions
- attainment of CD34+ target (yes, no)
- days until CD 34+ target level was met

In addition, time and motion assessments will be obtained retrospectively (Part I) and concurrently (Part II) and include the total time to prepare the patient, perform apheresis and manage adverse events. Costs will be evaluated and quantified in terms of micro-costing group interviews with local hospital administration.

Figure 2
Study Schema



The primary study end points are difference in the mean time to perform apheresis (including apheresis related adverse events, if any) and costs to the hospital in terms of micro-costing per patient.

Ethics approval was obtained in France and Germany for all centers involved.

Statistical Analysis

Patient data was recorded using an electronic case report form and aggregated for clinical comparisons. An interim analysis is presented based on the retrospective patient population (Part I) collected to date. Each subject (N=54) had peripheral CD-34+count lower than 20/μL. For pre-plerixafor era patients, the peripheral CD-34+ count was that recorded immediately prior to the first apheresis, while for plerixafor era patients, it was that recorded immediately prior to plerixafor administration.

Statistical analysis was performed using SAS version 9.3 (Cary, NC). For categorical variables, comparisons between pre-plerixafor era and plerixafor era patients were made using Chi Square or Fisher's Exact, as appropriate. For linear variables, Student's t-test was used when data was normally distributed, and Wilcoxon rank sum was used when distributions were not normal. Differences between groups were considered significant when $p < 0.05$.

Results

Patient Characteristics

- At time of this interim data analysis, there are 54 total patients available with 17 in the pre-plerixafor era and 37 in the plerixafor era. The majority of patients included in the analysis are collected from the French centers.
- Baseline characteristics were similar in both treatment arms (**Table 1**).
- The majority of patients were stage IV NHL at time of first diagnosis across both groups.

Table 1
Patient Characteristics, Demographics and Relevant Cancer History at Baseline by Era

Characteristics	Pre-Plerixafor Era (*n = 17*)	Plerixafor Era (*n = 37*)	P value
Gender, *n* (%)			
Male	11 (65%)	22 (59%)	0.71
Mean age, y (SD)	51 (13)	55 (12)	0.28
Mean weight, kg (SD)	74 (17)	72 (13)	0.67
Mean Height, cm (SD)	172 (10)	171 (10)	0.86
Non-Hodgkin's Lymphoma subtype, *n* (%)			
Follicular Lymphoma	4 (24%)	6 (16%)	0.88
Diffuse Large B Cell Lymphoma	5 (29%)	13 (35%)	
Mantle Cell Lymphoma	2 (12%)	6 (16%)	
Other*	6 (35%)	12 (32%)	
Country *n* (%)			
France	14 (82%)	26 (70%)	0.51
Germany	3 (18%)	11 (30%)	
Disease stage at time of first diagnosis *n* (%)			
Stage I	1 (6%)	1 (3%)	0.57
Stage II	1 (6%)	5 (14%)	
Stage III	2 (12%)	5 (14%)	
Stage IV	10 (59%)	24 (65%)	
Missing	3 (18%)	2 (5%)	
Time since diagnosis (months)			
Mean (SD)	24 (29)	34 (56)	0.94

*"Other" Lymphoma sub-types include: Angioimmunoblastic T Cell Lymphoma, Extranodal NK TCell Lymphoma, NK Cell Leukaemia, Burkitts Lymphoma, Lymphoma Large Cell, Low Grade Lymphoma (Indolent), Lymphoma (Indolent) 2, T Cell Lymphoma 2, Anaplastic T Lymphoma, Large B Cell NHL, T Cell NHL 2, Peripheral T Cell Lymphoma, B-NHL

Efficacy

- CD34+ cell yields
  - There was approximately 75% higher yield of CD34+ cells at the first apheresis session with the use of plerixafor when compared to the pre-plerixafor patients.
  - The total aphereses yield of CD34+ cells was not significantly different between the two groups.

Aphereses sessions

- There was a statistically significant decrease in the mean number of apheresis sessions and total minutes of apheresis that is associated with the use of plerixafor. While the total blood volume also decreased between the groups, it was not statistically significant.

Table 2
CD34+ Yield and Volume of Aphereses between the Pre-Plerixafor and Plerixafor Eras

Parameter	Pre-Plerixafor Era (*n = 17*)	Plerixafor Era (*n = 37*)	P value
Peripheral CD34+ cell count ($1X10^6$ CD34+/L)			
Mean (SD)	15.3 (3.9)	8.6 (4.5)	p<0.001
Median (range)	16 (8 - 20)	8 (1 - 18)	
Number of Apheresis Sessions (n)			
Mean (SD)	2.4 (0.9)	1.6 (0.7)	0.003
Median (range)	2 (1 - 5)	2 (1 - 4)	
Total apheresis blood volume (ml)			
Mean (SD)	21.3 (9.2)	17.4 (7.5)	0.11
Median (range)	22.3 (3.4 - 36.1)	17.4 (4.1 - 39.9)	
Total minutes of apheresis			
Mean (SD)	460 (209)	345 (132)	0.04
Median (range)	410 (170 - 1,065)	335 (145 - 880)	
Total Apheresis Yield CD34+ Cells ($1x10^6$/kg)			
Mean (SD)	4.3 (1.5)	4.1 (1.5)	0.66
Median (range)	4.5 (1.7 - 6.9)	3.7 (1.4 - 9.3)	
First Apheresis Yield CD34+ Cells ($1x10^6$/kg)			
Mean (SD)	1.6 (0.8)	2.8 (1.6)	p<0.005
Median (range)	1.3 (0.7 - 3.7)	2.5 (0.3 - 5.8)	

Discussion

- This retrospective study of patients mobilized with or without plerixafor has shown that when plerixafor was added to the regimen, there was decreased number of mean apheresis sessions and minutes of apheresis. The total blood volume collected was also decreased in the plerixafor group, though not statistically significant.
- The total aphereses yield of CD34+ cells was not significantly different between the two groups even though plerixafor era patients had significantly lower levels of PB CD34+ cells prior to administration of plerixafor.
- This is an interim analysis, and data collection is still ongoing in all of the centers. As more patient data will be collected, final study results will further confirm this trend. The results of costs and health resource utilization comparison are concurrently being collected.

Conclusion

The initial trend observed from this interim analysis demonstrated the favorable impact of plerixafor on the number of apheresis procedures, total blood volume collected and total apheresis time required to reach the targeted PBSC. It is hypothesized that final study results (including the cost component) will continue to demonstrate this trend and may have significant financial implications for transplant centers.

References

1. European Medical Agency: Summary of product characteristics for plerixafor http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/001030/WC500030686.pdf
2. Genzyme: Plerixafor injection Product Monograph
3. DiPersio JF, Micallef IN et al. Phase III prospective randomized double-blind placebo-controlled trial of plerixafor plus granulocyte colony-stimulating factor compared with placebo plus granulocyte colony-stimulating factor for autologous stem-cell mobilization and transplantation for patients with non-Hodgkin's lymphoma. *J Clin Oncol*. 2009;27(28):4767-73
4. DiPersio JF, Stadtmauer EA et al. Plerixafor and G-CSF versus placebo and G-CSF to mobilize hematopoietic stem cells for autologous stem cell transplantation in patients with multiple myeloma. *Blood*. 2009; 113(23):5720-6.
5. Calandra G, McCarty J et al. AMD3100 plus G-CSF can successfully mobilize CD34+ cells from non-Hodgkin's lymphoma, Hodgkin's disease and multiple myeloma patients previously failing mobilization with chemotherapy and/or cytokine treatment: compassionate use data. *Bone Marrow Transplant*. 2008; 41(4):331-8.

40th Annual Meeting of the European Society for Blood and Marrow Transplantation; 30 March - 2 April 2014; Milan, Italy; PH-P243. Funding provided by Sanofi.