Impact of plerixafor plus G-CSF mobilization on CD34+ cell yield

By Edward P. Scott, MD, Principal Investigator
Key Biologics, LLC [Memphis, TN], Sponsor
October 2019

The goal of hematopoietic stem cell mobilization for transplantation is to increase the number of circulating CD34+ cells that can be collected by apheresis. As preparation for peripheral blood stem cell harvest from a normal donor, G-CSF is usually administered by daily subcutaneous injections with the leukapheresis occurring following the fifth injection, either on the same day or the following day. However, a second leukapheresis is often performed on the following day to assure an adequate cell count based on the recipient's weight to support transplantation. Shorter treatment courses, three or four days of injections with collections on the day of or the day following the last injection, have also been reported to produce adequate cell yields for transplantation.

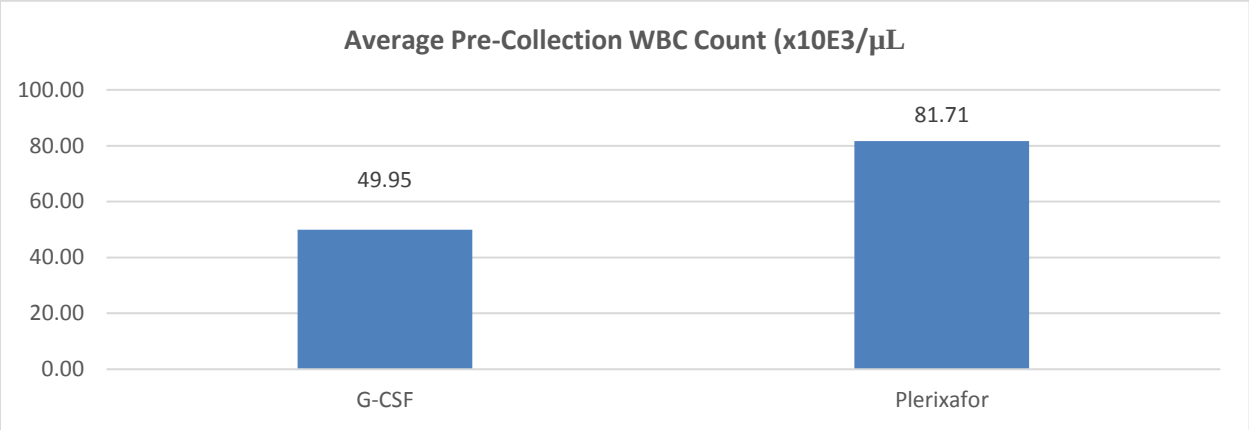
Plerixafor (Mozobil®, Genzyme, Cambridge, MA), is licensed as an adjuvant for mobilization with G-CSF for autologous transplantation for patients with non-Hodgkin lymphoma and multiple myeloma but is often used off-label to 'rescue' failed G-CSF mobilization for allogeneic transplants. It is a small bicyclam molecule originally developed as a treatment of HIV infections. HIV viral gp120 interacts with CXCR4 that is the mandatory co-receptor for the virus to enter human cells. The natural ligand of CXCR4 is stromal cell – derived factor – 1 (SDF-1). During normal subject pharmacokinetic studies of plerixafor, it was noted that the subjects' white blood cell counts rose and reached a peak roughly three times baseline levels approximately 6 hours after injection. Additionally, CD34+ cells/mL increased 10 to 20-fold after a single dose of 240µg/kg. Plerixafor's direct antagonism of SDF-1 binding to CXCRA on bone marrow stromal cells promotes release of CD34+ cells into the circulation.

A subsequent normal donor study evaluated the impact on CD34+ cell mobilization with daily injections of G-CSF at 10µg/kg for four days followed on day five by either a fifth injection of G-CSF alone (G), or injections of both G-CSF and AMD3100 (A+G). A+G increased CD34+ collection by leukapheresis to 10.0 ± 0.7 $x10^6$ cells/kg donor weight vs. 3.86 ± 0.23 $x10^6$ cells/kg donor weight for G alone.

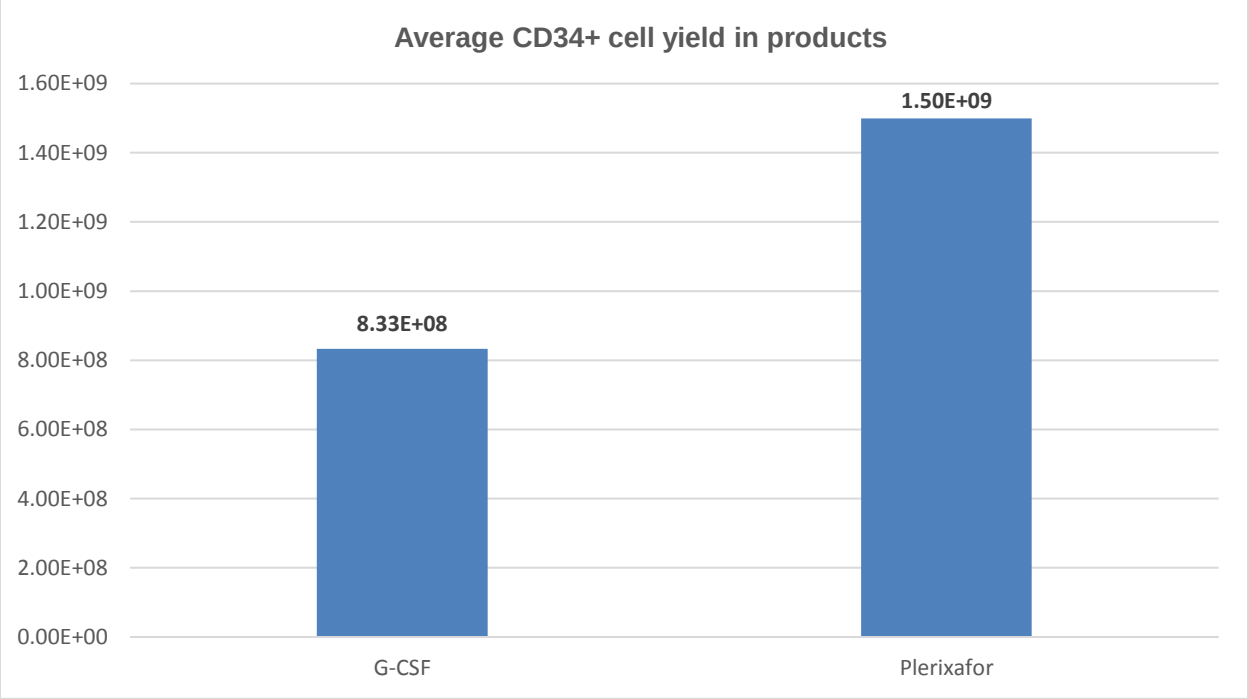
Normal donors enrolled in our research study at Key Biologics are mobilized with G-CSF plus plerixafor and undergo paired leukaphereses on day 5 and 6. Doses of G-CSF are approximately 10µg/kg BW administered on days 1-6 and plerixafor doses are approximately 0.24mg/kg BW. Plerixafor is given once in the late afternoon of day 5. Analysis of data from the paired collections allows assessment of the relative impact of the two agents on mobilization. Of note, the results following plerixafor could be enhanced by the prior injections of G-CSF.

We found that after 4 days of G-CSF injections the donors' average WBC count was 49.95x103/µL. These data were collected on the fifth day and prior to the receipt of that day's dose that was administered approximately 2 hours prior to initiation of the first leukapheresis. The plerixafor injection was administered in the late afternoon of the fifth day. On the following day and prior to the sixth dose of G-CSF, the subjects' average WBC count (in peripheral blood) was 81.7$x10^3$/µL; an increase of 64% vs. the prior day. Additionally, average WBC yields in the

post-plerixafor products were 51% higher than those in the prior, G-CSF alone, products.



The concentration CD34+ cells per microliter of product volume was 81.5% higher in the post-plerixafor (day 6) products; 7181 versus 3957 cells/µL. More importantly, the average yield of CD34+ cells increased 80%, from $8.33x10^8$ (range $3.4x10^8$ to $1.39x10^9$) in the first product to $1.5x10^9$ (range $8.79x10^8$ to $2.13x10^9$) in the second. Average product volumes and average processed blood volumes were essentially the same, within 1.5%.



If you need a source for large numbers of CD34+ cells, products collected under this protocol should give you what you need. Contact us with any questions. Product codes and prices for these collections follow below.

About the Author

Edward Scott, MD, hematologist, is the Founder of Key Biologics, LLC [Est. 2009], headquartered in Memphis, TN with sites in Lowell [Metro Boston], MA and Puyallup [Metro Tacoma], WA, whose emphasis is support of cell therapy research & development through human-derived biological products provision and associated life sciences services.

Dr. Scott, as Principal Investigator, conducts seven protocols under Key Biologics Sponsorship, working with healthy blood donors and diagnosed subjects. Key Biologics' Therapeutic Apheresis Program works with patients in national

cell therapy trials & treatment and is among the initial & ongoing apheresis providers for Dendreon's Provenge™ protocols and patients in treatment.

Formerly CEO of Key Biologics, Dr. Scott now serves as Chief Medical Officer of Key Biologics Holdings, which includes partner Astarte Biologics, Bothell [Metro Seattle], WA. Dr. Scott served as President & CEO of its antecedent company Lifeblood Biological Services from 1999-2009, and CEO & Medical Director of Mid-South Regional Blood Center / Lifeblood from 1986-2008.

Daily collections x 2 (6-day GCSF prep-10µ/kg/day + Plerixafor)	Product Codes	Price
Target blood volume processed - 10 Liters	17771 - Amicus	$55,000.00
	18771 - Optia	
Target blood volume processed - 12.5 Liters	17772 - Amicus	$60,000.00
	18772 - Optia	
Target blood volume processed - 15 Liters	17773 - Amicus	$65,000.00
	18773 - Optia	