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Peripheral Blood Stem Cell Mobilisation: Experience of Switching to Biosimilar G-CSF

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Conflicts of Interest

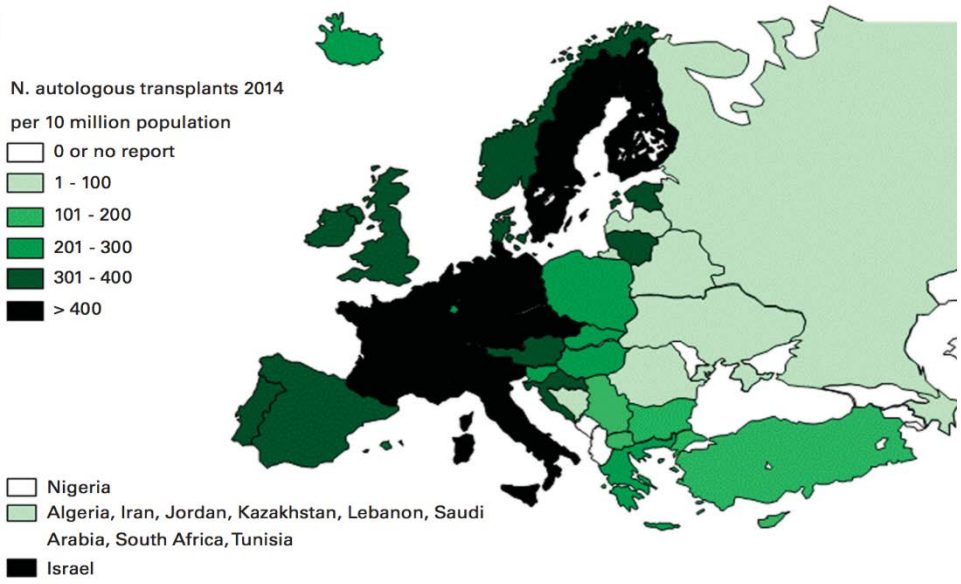
- None

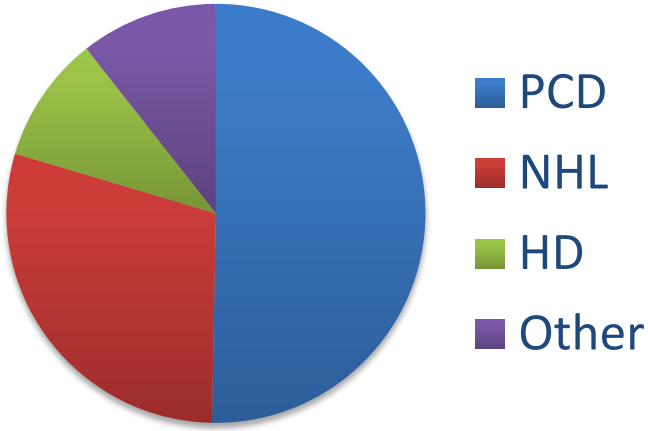
Autologous Stem cell Transplantation

- Use of high dose chemotherapy is the standard of care in “fit” patients with multiple myeloma and in certain patients with NHL and HL

- Following chemotherapy patients require an infusion of stem cells to rescue them from chemotherapy-induced aplasia

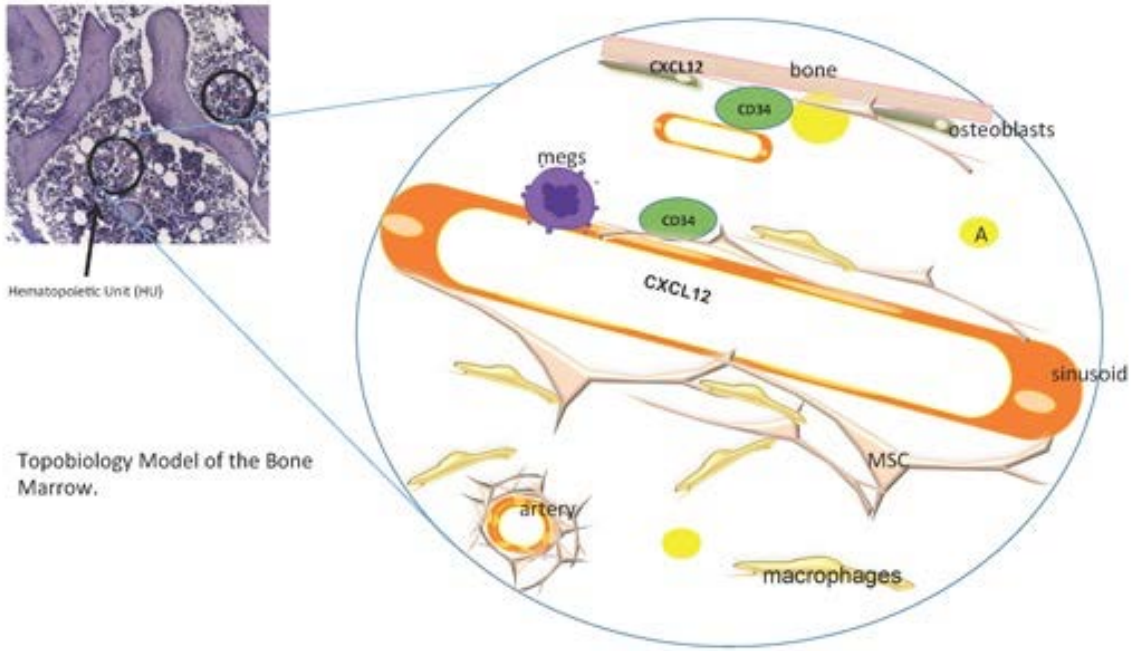
- **23,883 autografts 2014**





Mobilisation of stem cells

- Harvest BM directly
- Cause release of stem cells into blood and collect peripheral blood stem cell
  - G-CSF
  - Chemotherapy
  - CXCR4 inhibitor (Plerixafor)



Topobiology Model of the Bone Marrow.

Target Yield

- Minimum recommended dose :
  - MM 4 x 10^6 $CD34^+$ cells/kg (Target 6 x 10^6 $CD34^+$ cells/kg)
  - NHL 2 x 10^6 $CD34^+$ cells/kg (Target 3 x 10^6 $CD34^+$ cells/kg)

- Higher target doses may result in faster engraftment times, the recommended stem cell collection target is 3-5 x 10^6 $CD34^+$ cells/kg. Weigh up against number of apheresis sessions

Review

Optimizing Autologous Stem Cell Mobilization Strategies to Improve Patient Outcomes: Consensus Guidelines and Recommendations

ASBMT American Society for Blood and Marrow Transplantation

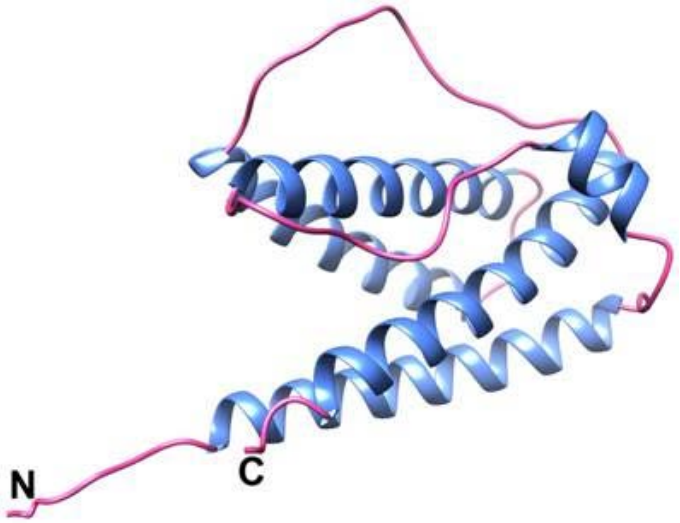
Giralt et al., Biology Blood Marrow Transplant 20 (2014) 295-308

G-CSF

- Induces the release of proteases in the marrow, which then cleave adhesion molecules such as SDF 1, releasing stem cells into PB

- <u>Biosimilar Filgrastim:</u>
  - Biologically equivalent to original product
  - Widely used in Europe since 2008
  - Cheaper than originator product

- Ongoing debate regarding efficacy and safety evidence



Schmitt, M., Publicover, A., Orchard, K.H., Görlach, M., Wang, L., Schmitt, A., Mani, J., Tsirigotis, P., Kuriakose, R. and Nagler, A., 2014. Biosimilar G-CSF based mobilization of peripheral blood hematopoietic stem cells for autologous and allogeneic stem cell transplantation. *Theranostics*, *4*(3), p.280.

Biosimilar G-CSF

- Clinically effective
  - Equivalent stem cell yields
  - Similar engraftment kinetics
- Similar side effect profile
- More affordable
- Local estimated cost saving of £500,000
  - UH Bristol switched in 2014
  - Initial concerns

Biosimilar G-CSF Based Mobilization of Peripheral Blood Hematopoietic Stem Cells for Autologous and Allogeneic Stem Cell Transplantation

Michael Schmitt[1✉], Amy Publicover[2], Kim H Orchard[2], Matthias Görlach[3], Lei Wang[1], Anita Schmitt[1], Jiju Mani[1], Panagiotis Tsirigotis[4], Reeba Kuriakose[1], Arnon Nagler[5]

Biosimilar Compared with Originator Filgrastim for Autologous Stems CELL Mobilisation: A Prospective–Historical Control Study in Multiple Myeloma REAL-Life Setting

Massimo Martino, Tiziana Moscato, Iolanda Donatella Vincelli, Francesca Ronco, Roberta Fedele, Giuseppe Irrera, Giuseppe Console, Giuseppe Messina, Eugenio Piro, Stefano Molica, and Fortunato Morabito

Blood 2014 124:5825;

Support Care Cancer (2013) 21:2925–2932
DOI 10.1007/s00520-013-1911-7

REVIEW ARTICLE

Clinical experience with Zarzio® in Europe: what have we learned?

Pere Gascón · Hans Tesch · Karl Verpoort · Maria Sofia Rosati · Nello Salesi · Samir Agrawal · Nls Wilking · Helen Barker · Michael Muenzberg · Matthew Turner

A Comparative Study of Biosimilar Filgrastim Versus Originator G-CSF for CD34+ Cells Mobilization and Autografting in Hematological Malignancies

Lucia Brunello, Luisa Giaccone, Maria Josè Fornaro, Matilde Scaldaferri, Valter Redoglia, Paola Omedè, Moreno Festuccia, Giovannino Ciccone, Massimo Massaia, Dario Ferrero, Federica Cavallo, Antonio Palumbo, Francesco Cattel, Andrea Evangelista, Mario Boccadoro, and Benedetto Bruno

Blood 2016 128:2183;

UH Bristol NHS Foundation Trust
Local Set Up

University Hospital Bristol NHS
NHS Foundation Trust

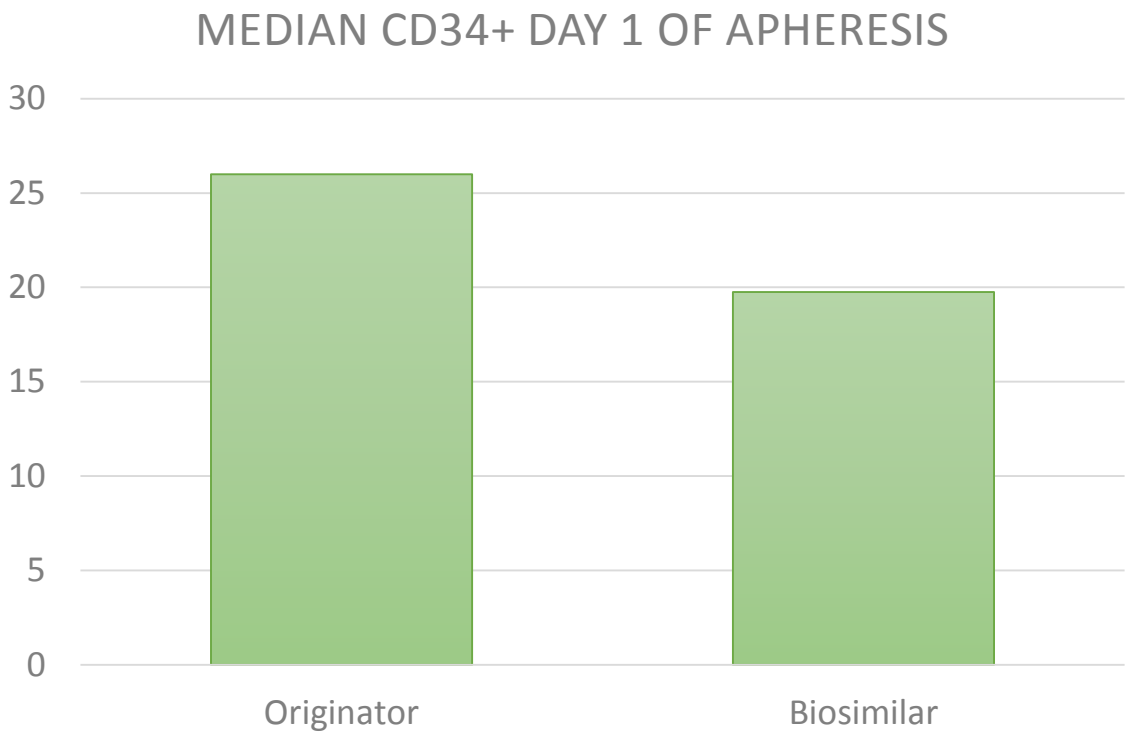
Method

- Retrospective review of UH Bristol NHS Trust Practice
- 50 patients mobilised using Originator G-CSF product (February 2012-November 2013)
- 50 consecutive patients mobilised using Biosimilar GCS-F product (Zarzio) (January 2016-January 2017)
- Study population
  - Multiple Myeloma (MM)
  - Non-Hodgkin Lymphoma (NHL)

Demographics

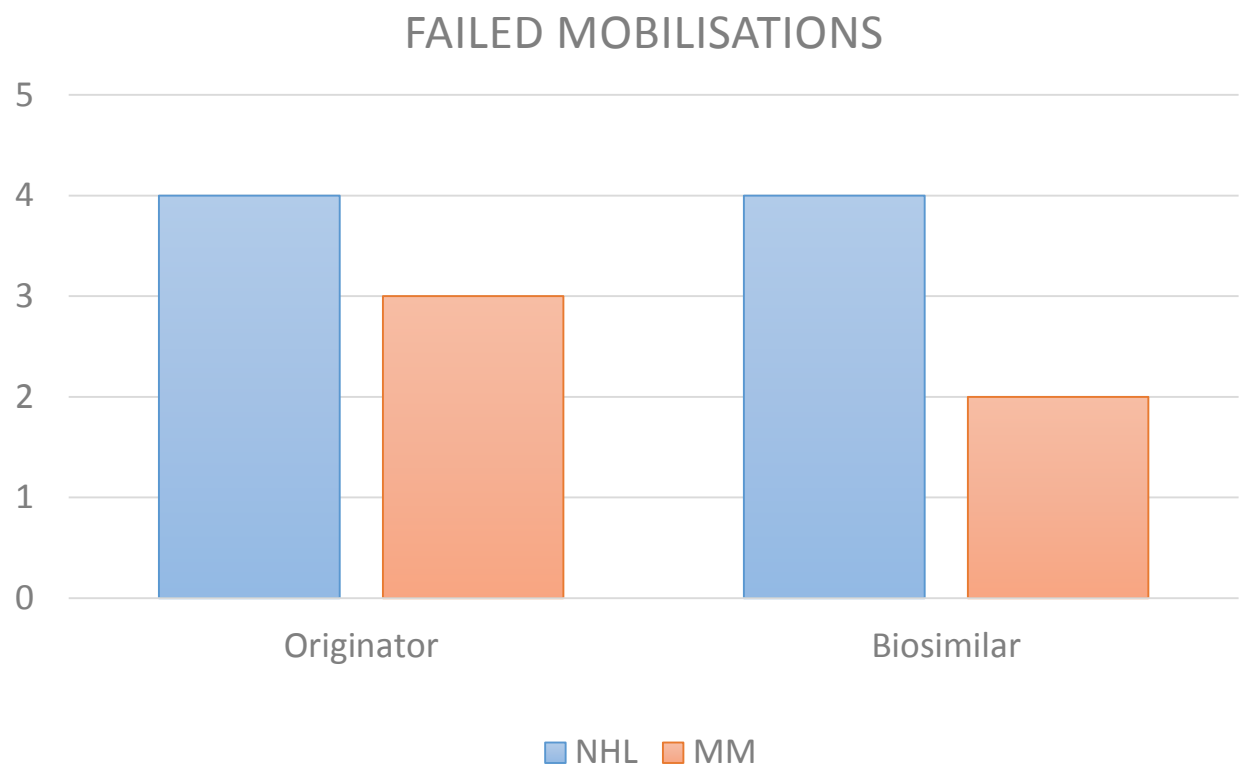
Parameter	Originator		Biosimilar	
	Multiple Myeloma	Non Hodgkin Lymphoma	Multiple Myeloma	Non Hodgkin Lymphoma
Median Age at mobilisation (range)	56.24 (48-71)	56.64 (36-73)	61.65 (48-73)	65.98 (19-70)
Sex (M/F)	21/13	15/1	18/13	4/15
Non-Chemotherapy primes	12	9	11	3
Diagnosis (%)	34 (68%)	16 (32%)	19 (38%)	31 (62%)

$CD34^+$ on Day 1



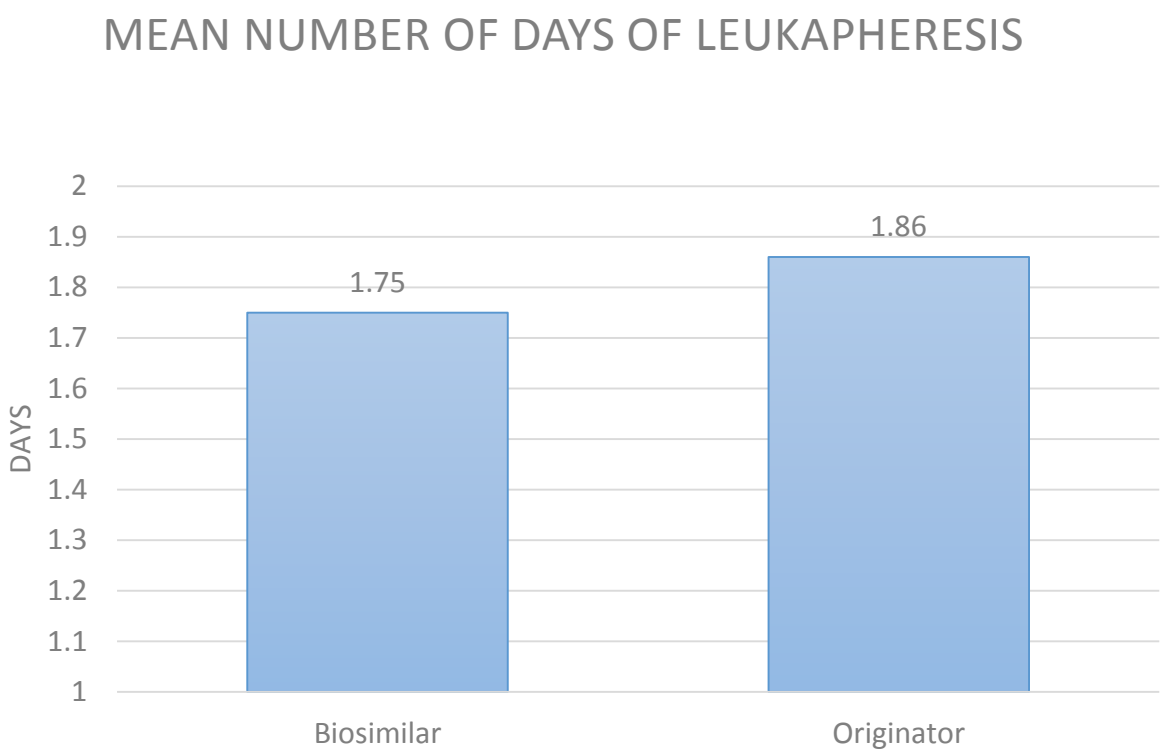
No significant difference in CD34 counts on day 1:
Originator (M= 46.09, SD= 41)
Biosimilar (M= 46, SD= 75);
t(94) = 0.52, p=0.606

Failed mobilisations



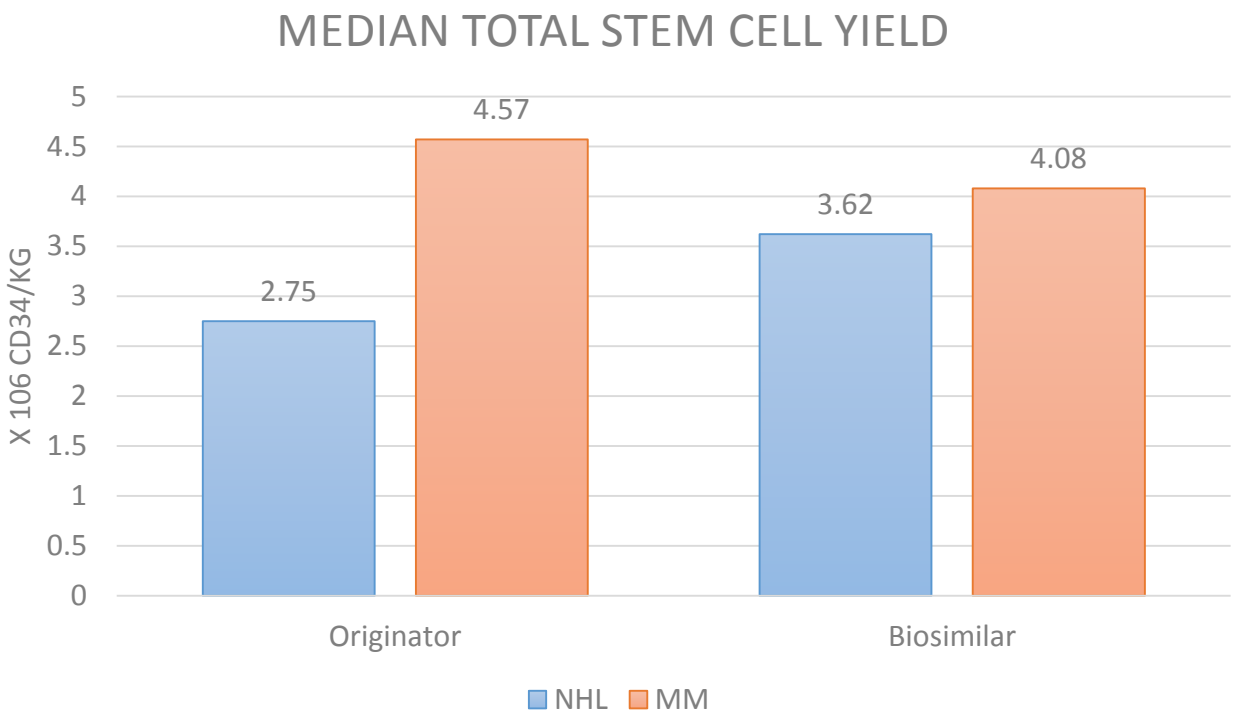
The rate of failed mobilisations was similar in both groups (Originator 7, Biosimilar 6)

Number of days of leukaphersis



The mean number of collection days was 1.86 with originator and 1.78 with biosimilar

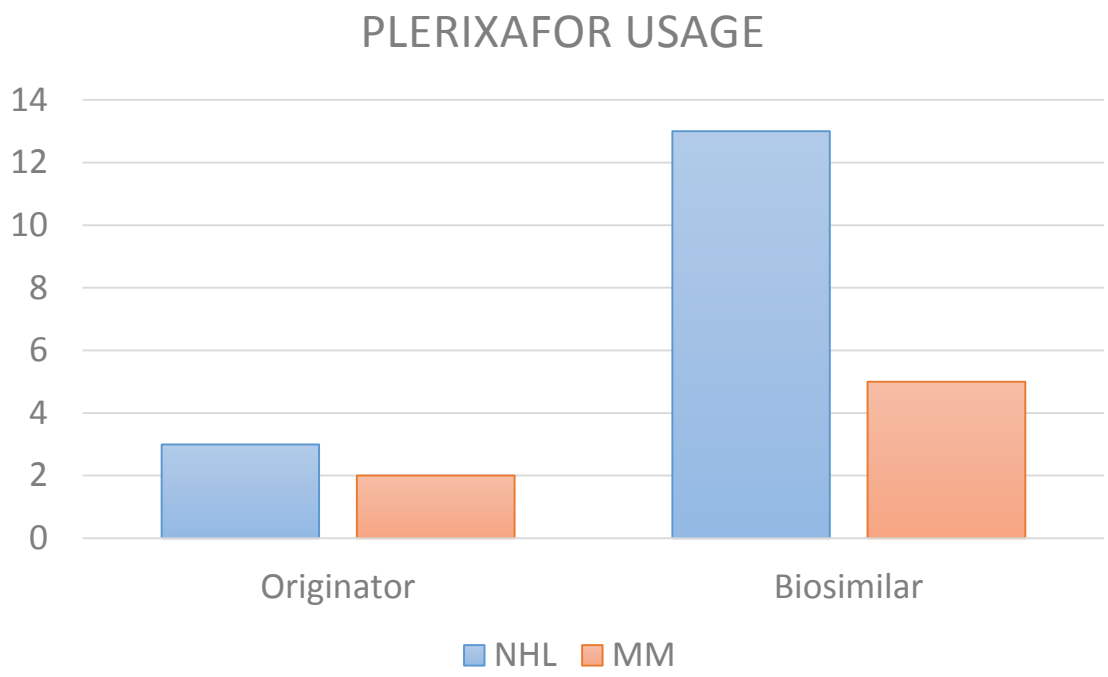
Total Yield



No significant difference in yield:

- MM p = 0.400
- NHL p = 0.056

Plerixafor usage



The use of Plerixafor was higher in the biosimilar G-CSF group compared to originator product

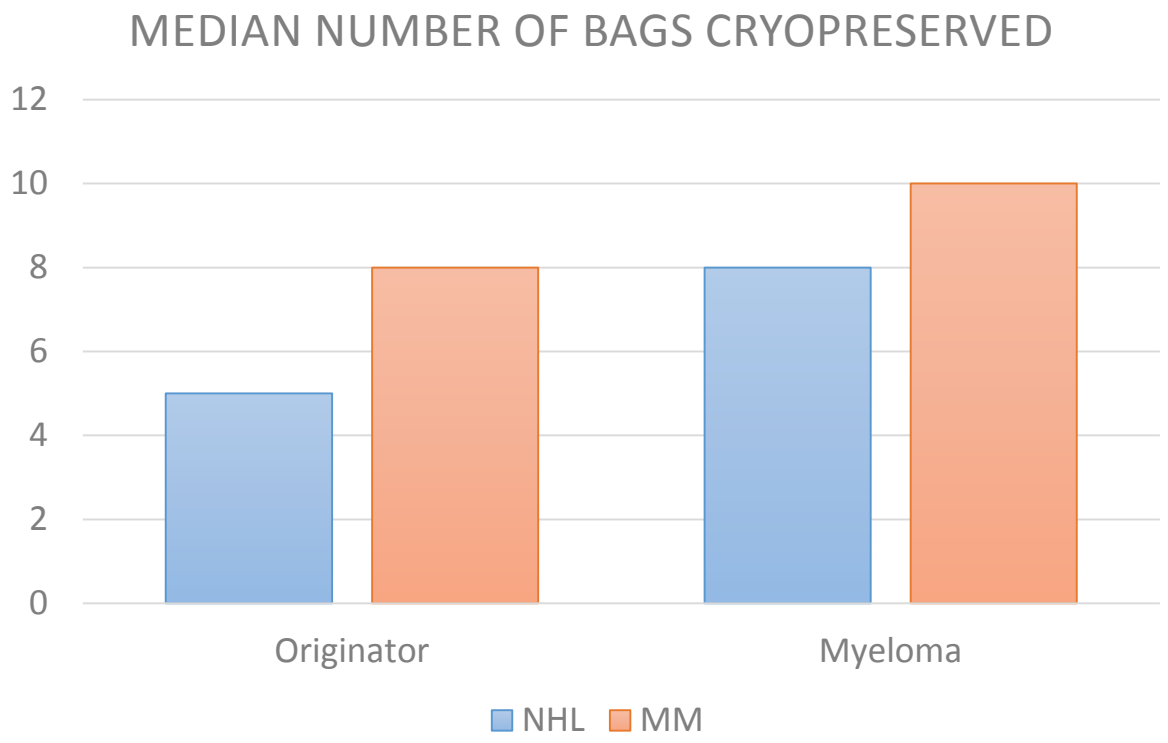
- 18 v 5 patients
- Chi squared 9.5426
- p=0.0020

Rescue for low CD34⁺ Count

<5	5-10	10-15	>15
No collection		Collection Insert Vascath if needed	
Consider plerixafor	Plerixafor		Plerixafor if previous failed collection only

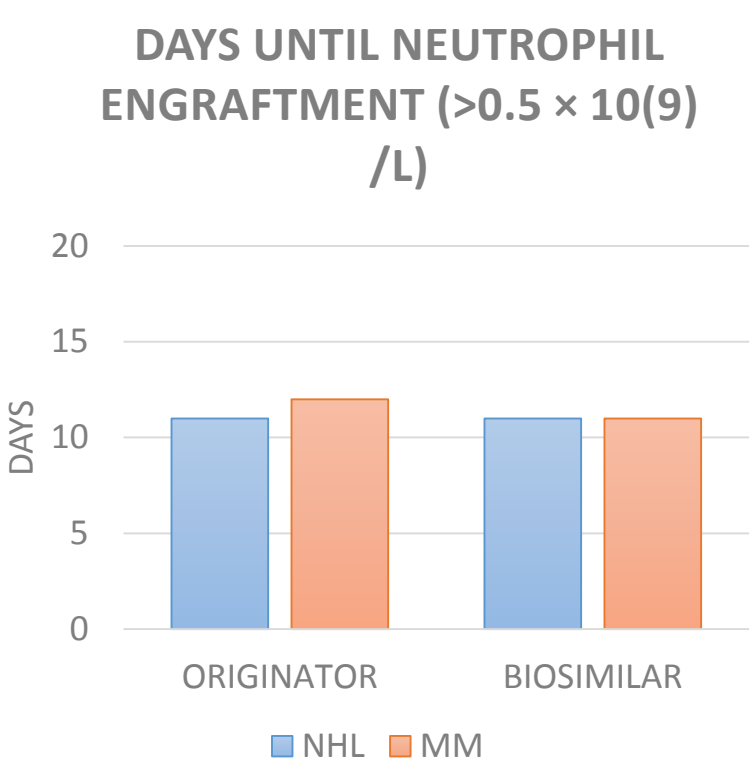
Previous Failed mobilisation

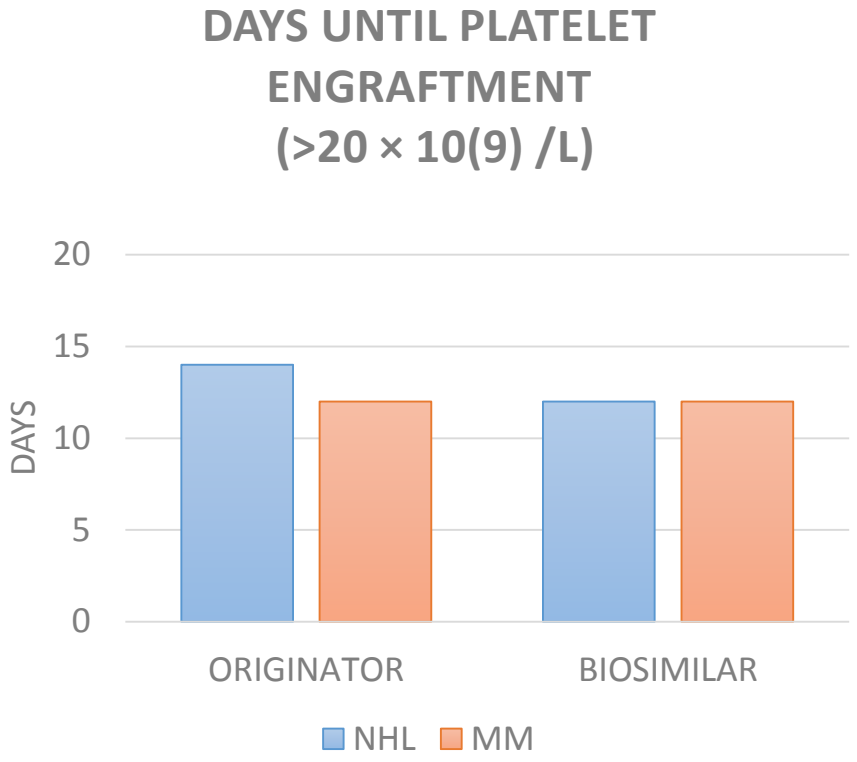
Number of bags



The number of bags stored were similar in both groups

Engraftment Data





Cost Analysis

- 71.4% mobilised ≥4 x 10^6/kg in ≤2 aphereses compared to 31.8% in the historical control.

- Patient level cost analysis
  - Mean cost with plerixafor £12679 v £11694 for historical controls.

Evaluating the Use of Plerixafor in Stem Cell Mobilisation – An Economic Analysis of the PHANTASTIC Trial

Antony P. Martin,[1]* Sarah Richards,[1] Alan Haycox,[1] Rachel Houten,[1] Claire McLeod,[1] Barbara Braithwaite,[2] Jack O. Clark,[2] Joanne Bell,[2] and Richard E. Clark[2]

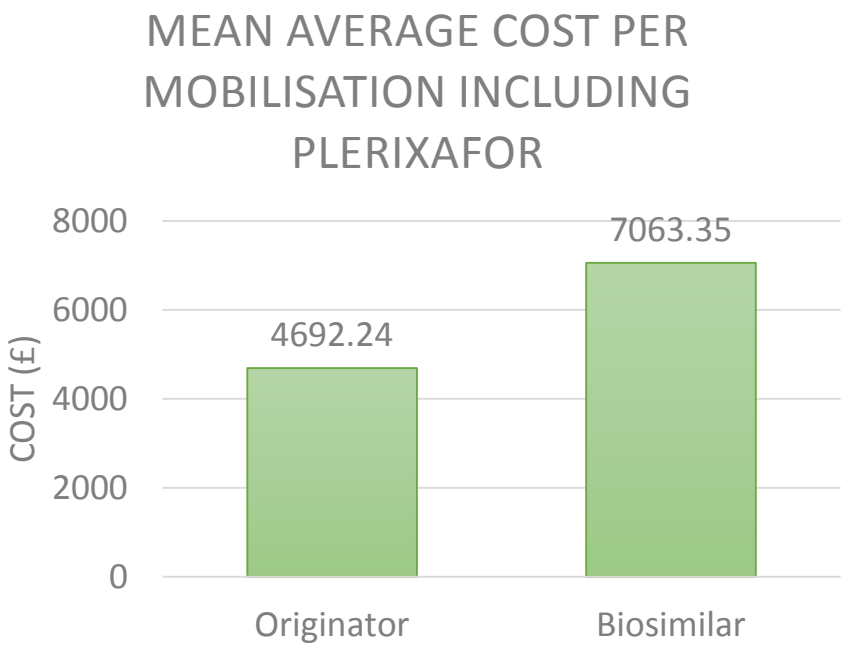
[1]Liverpool Health Economics, Department of Economics, University of Liverpool Management School, Liverpool, United Kingdom
[2]Haematology Department, Royal Liverpool University Hospital, Liverpool, United Kingdom

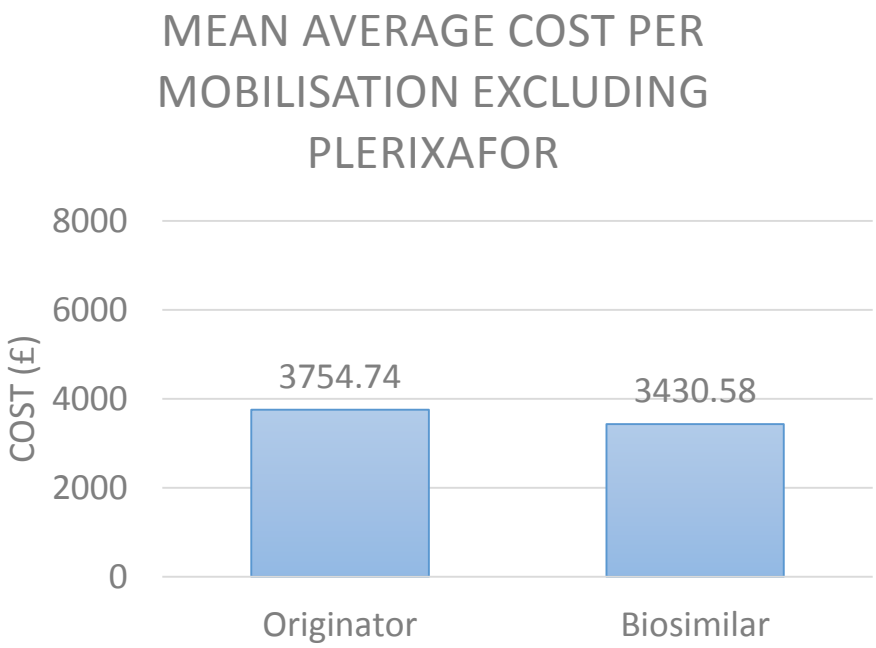
Cost Analysis

- Included:
  - Cost of GCSF
  - Cost of Plerixafor
  - Cost of Apheresis
  - Stem cell Storage

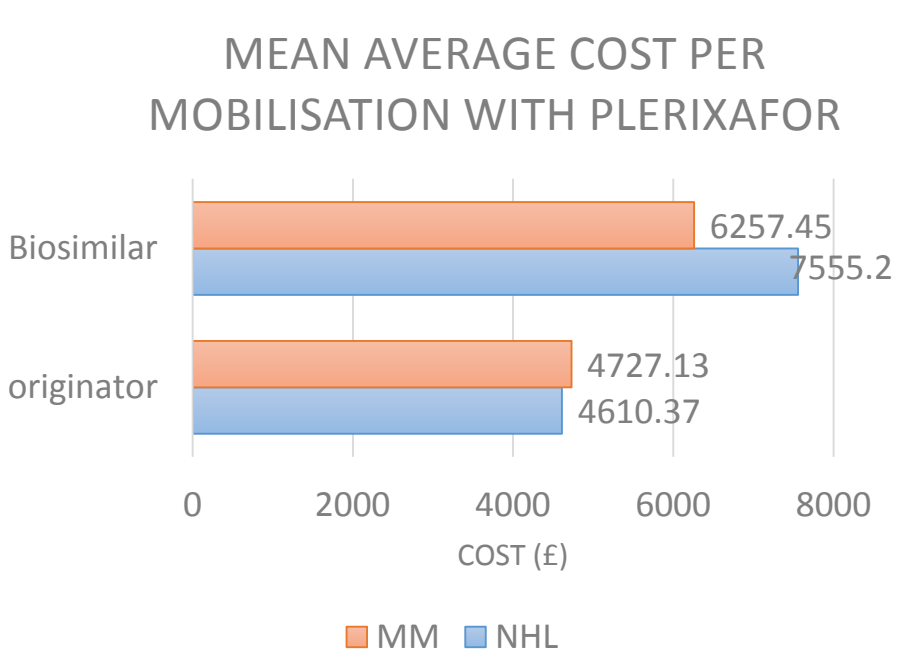
- Not Included:
  - Chemotherapy cost
  - Blood tests to assess $CD34^{+}$ numbers
  - Bed days
  - Supportive Medications

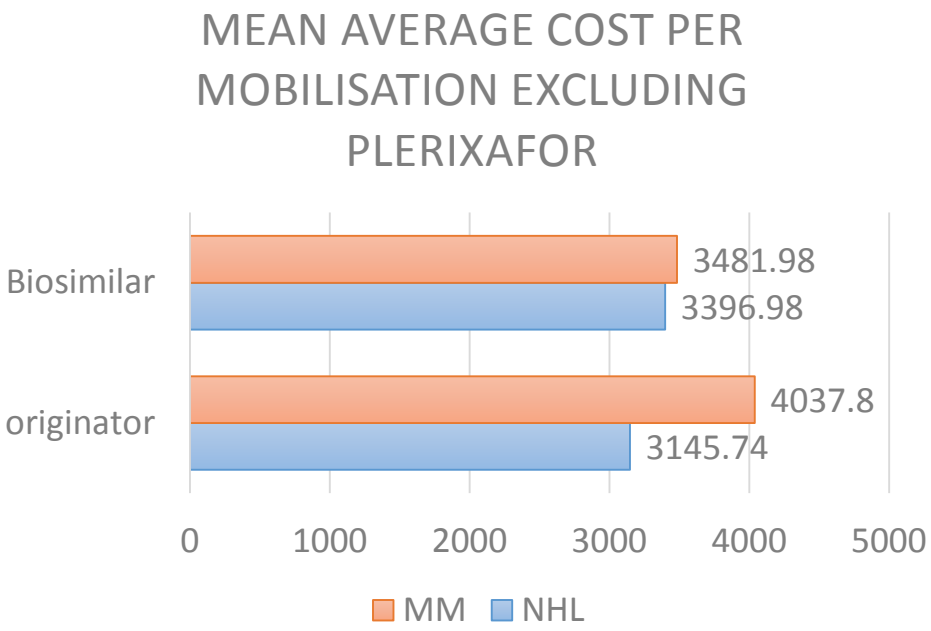
Cost Analysis





Cost Analysis





Key Conclusions

- Biosimilar G-CSF resulted in similar yields to originator product
- There was no difference in mobilisation failure rate
- Plerixafor usage went up significantly
- Overall the total NHS cost rose

What's next?

- Prospective data monitoring
- Need to continue to audit plerixafor usage
- More qualitative research into the patient experience of stem cell mobilisation

Acknowledgements

- Dr James Griffin, Haematology Consultant, NHSBT, UH Bristol NHS Foundation Trust
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- Rachel Palmer, Pharmacist, UH Bristol NHS Foundation Trust
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