



MGTA-145 in Combination with Plerixafor Rapidly Mobilizes High Numbers of Hematopoietic Stem Cells and Graft-Versus-Host Disease Inhibiting Myeloid Derived Suppressor Cells in Nonhuman Primates

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Magenta Therapeutics

Cambridge, MA

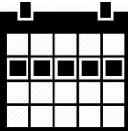


MGTA-145 + Plerixafor Enables Rapid and Robust Mobilization of HSCs

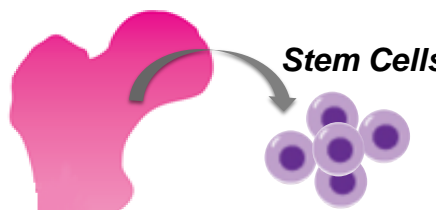
G-CSF Induced Mobilization

Time to Mobilization

Days



Stem Cells



**65,000 transplants annually
70% use mobilized peripheral blood**

Limitations to current Standard of Care

- Requires 4-6 days
- Unpredictable yields
- Associated adverse events
- Contraindicated for certain diseases


Benefits of novel mobilization regimen

- Mobilize more HSCs
- Shorten time required for mobilization
- Fewer adverse events

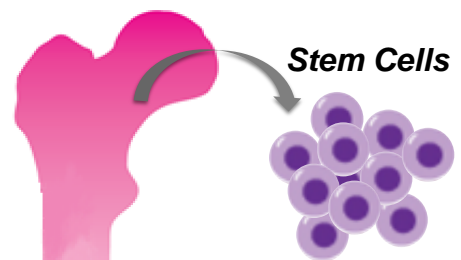
Magenta Mobilization

Time to Mobilization

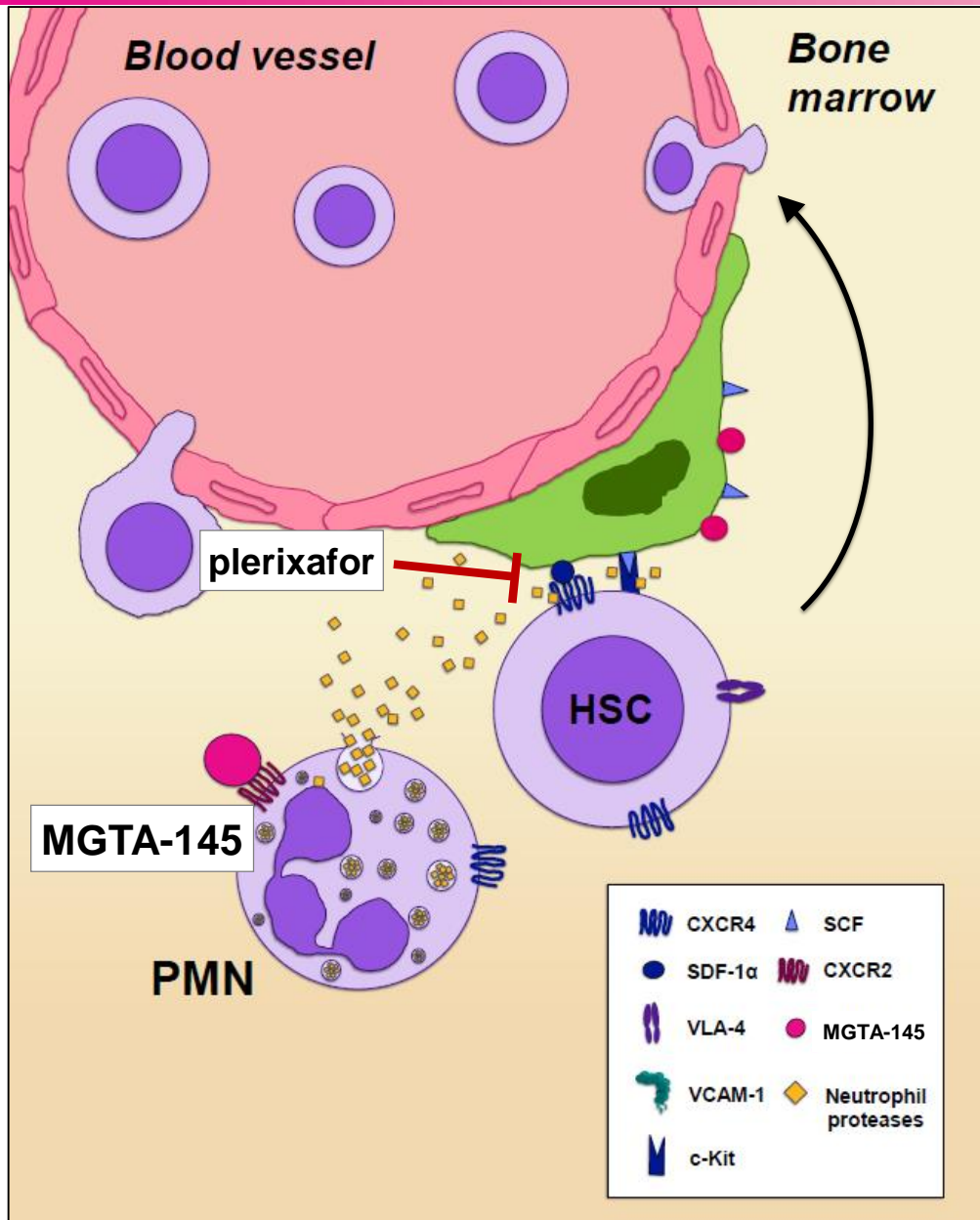
Minutes



Stem Cells



MGTA-145 and Plerixafor Work Synergistically to Rapidly Mobilize HSCs



Novel mobilization agent:

MGTA-145 (GroβT) + **plerixafor** (AMD3100)
CXCR2 agonist *CXCR4 antagonist*

Key features:

- Rapid & robust mobilization of HSCs in mice
- Well-tolerated
- Mimics physiological response

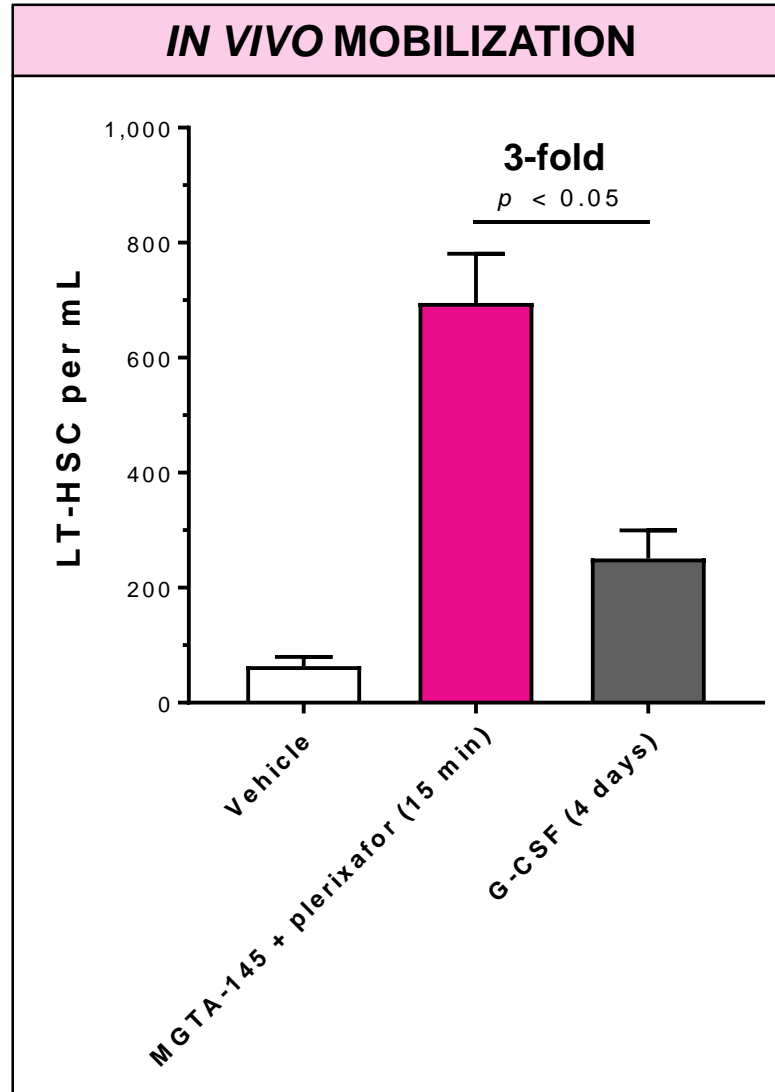
Cell

Article

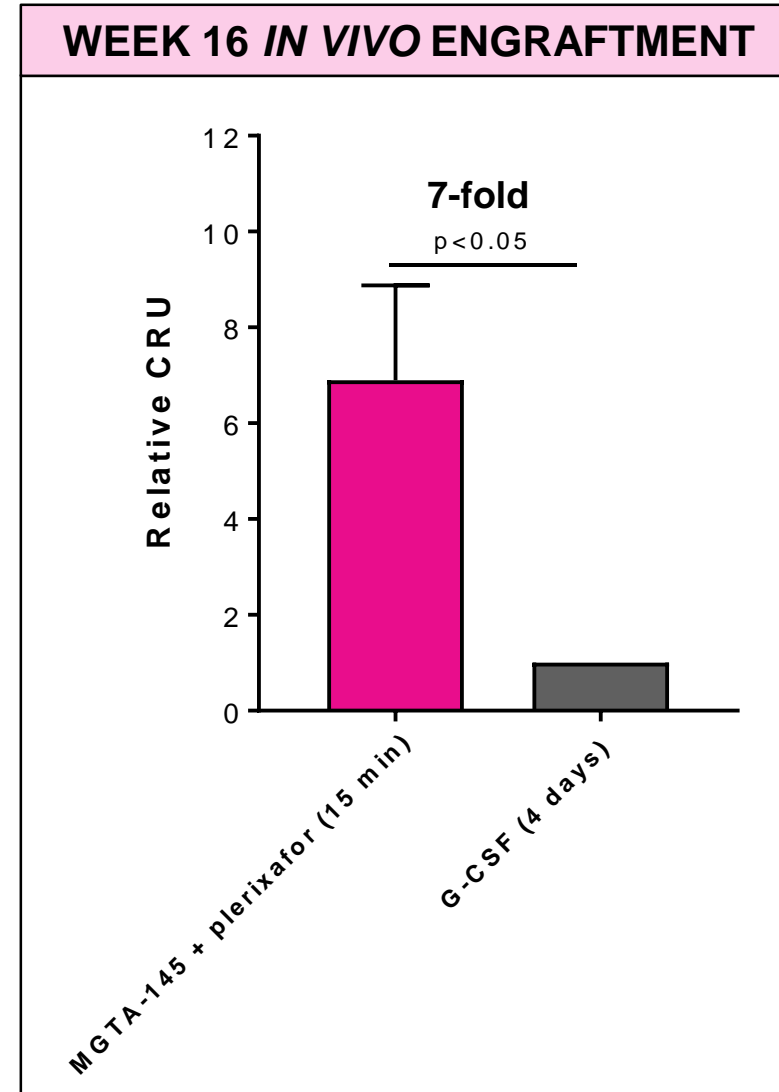
Rapid Mobilization Reveals a Highly Engraftable Hematopoietic Stem Cell

Authors
 Jonathan Hoggatt, Pratibha Singh,
 Tiffany A. Tate, ..., Dwight M. Morrow,
 David T. Scadden, Louis M. Pelus

MGTA-145 + Plerixafor Mobilizes Large Numbers of Long-Term HSCs in Mice



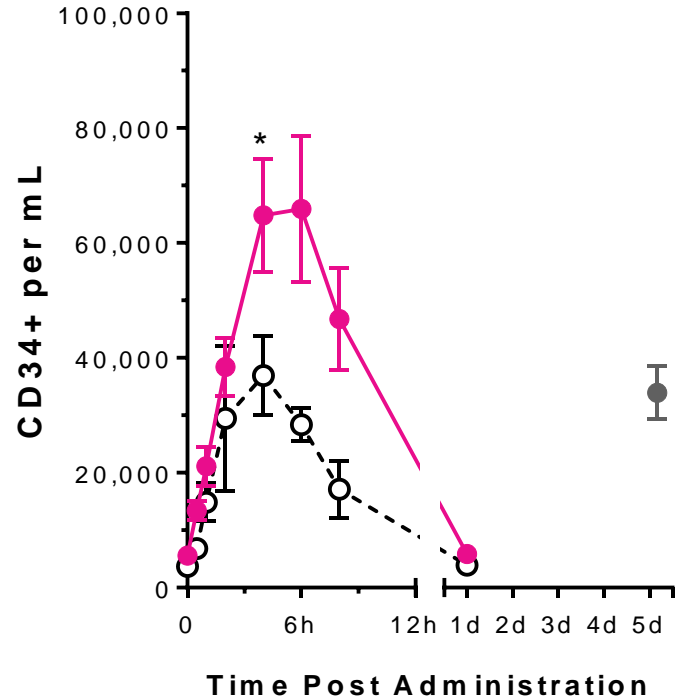
LT-HSC = Lin⁻ c-kit⁺ Sca-1⁺ CD150⁺ CD48⁻



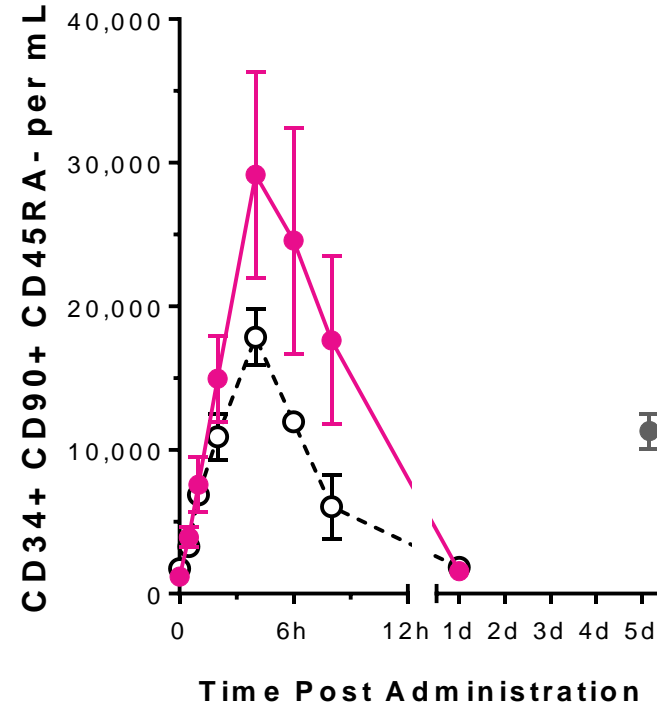
CRU = Competitive Repopulating Unit

A Single Injection of MGTA-145 + Plerixafor Rapidly Mobilizes Large Numbers of HSCs into Peripheral Blood in Nonhuman Primates

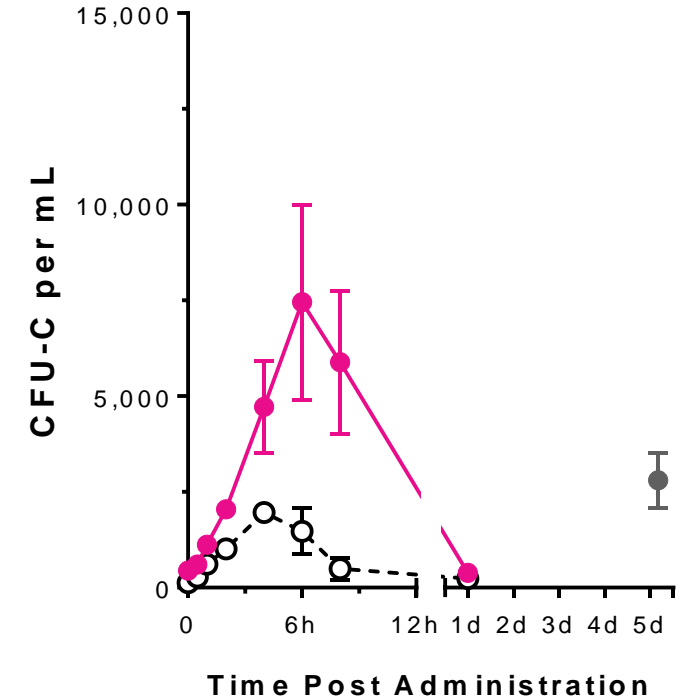
CD34+ CELLS



CD34+CD90+CD45RA- CELLS



COLONY FORMING UNITS

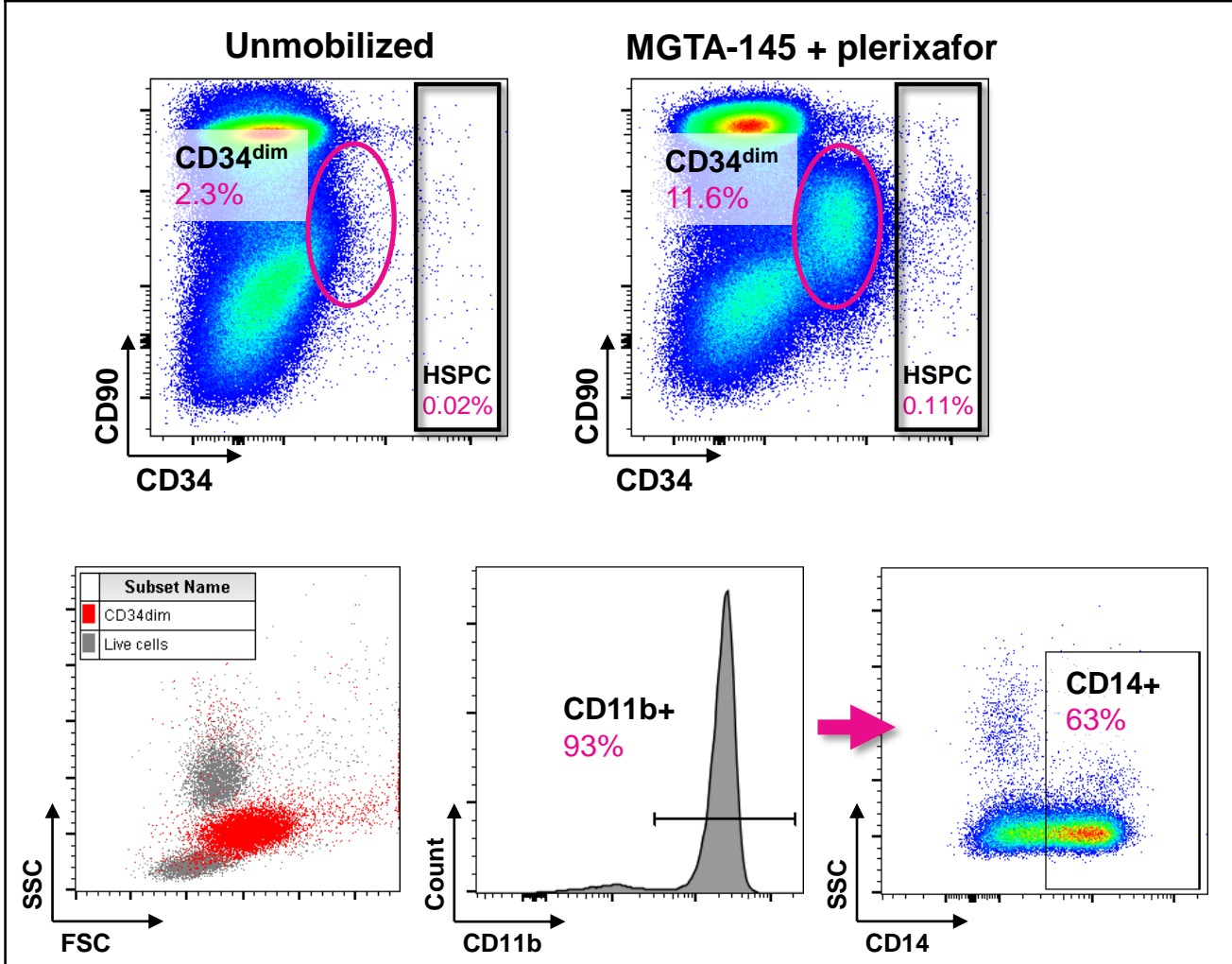


- MGTA-145 + plerixafor
- plerixafor
- G-CSF (5 Days)

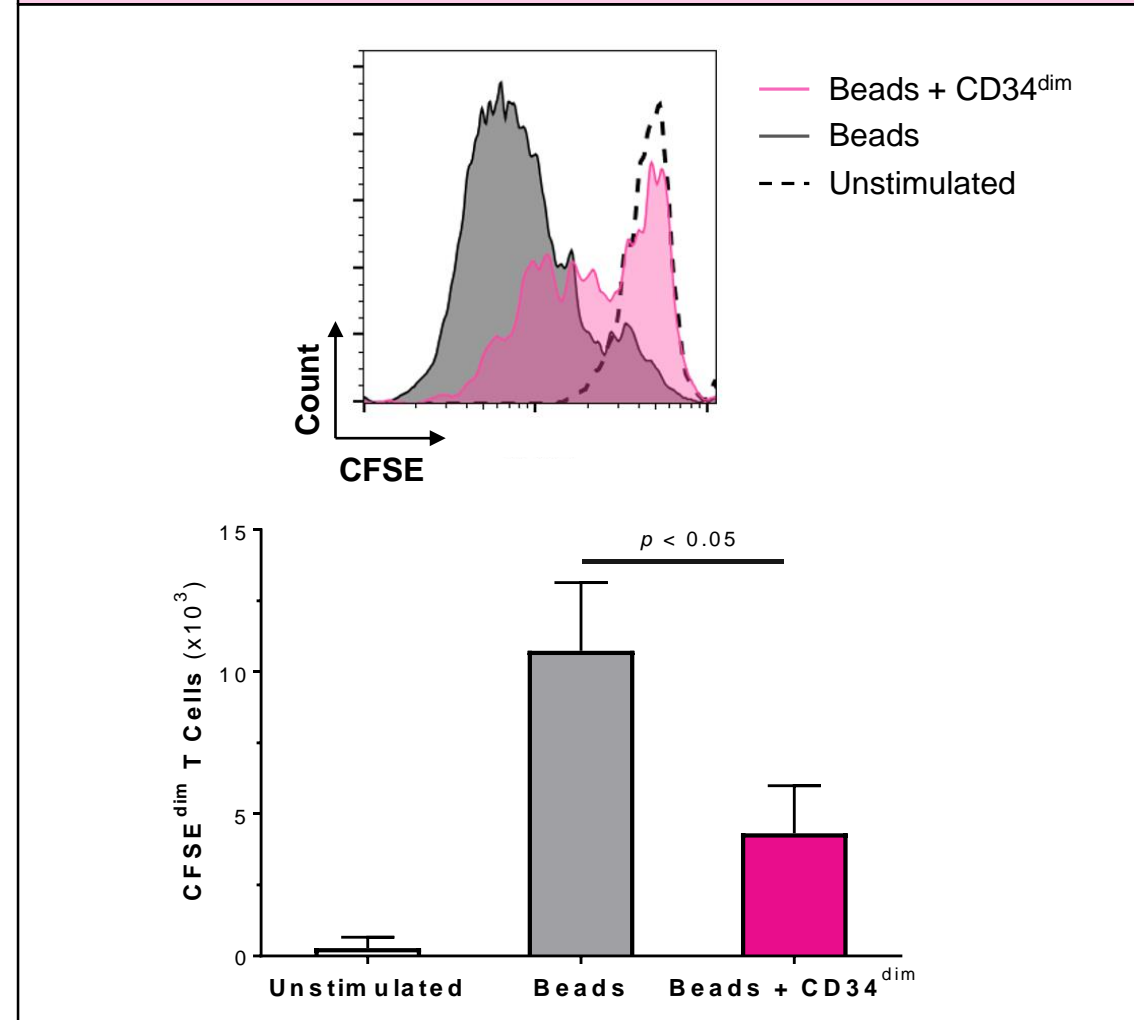
n=3-13 NHP per treatment

MGTA-145 + Plerixafor Leads to a Significant Increase in CD34^{dim} Cells in Peripheral Blood of Nonhuman Primates

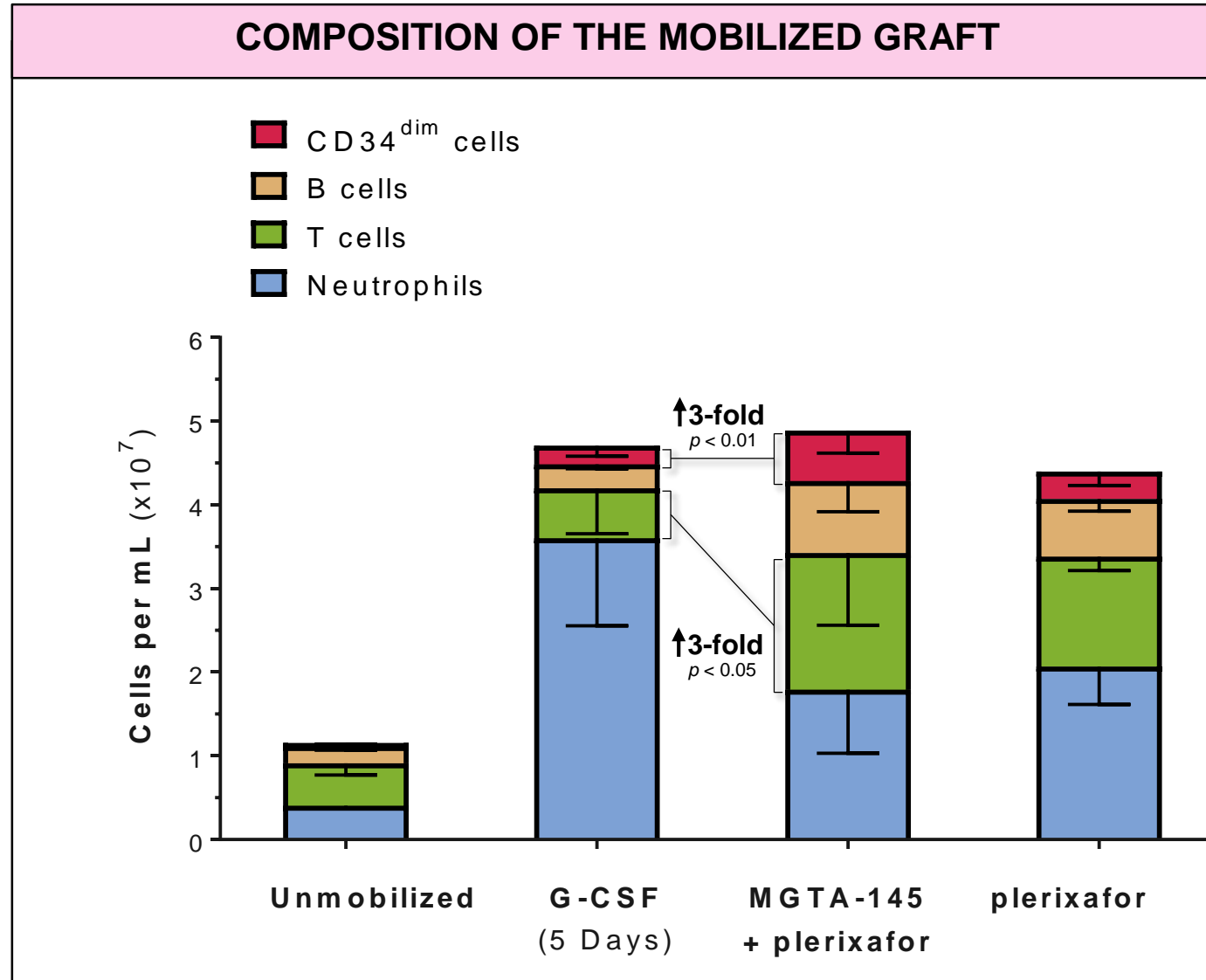
REPRESENTATIVE MOBILIZATION OF CD34^{dim} CELLS



CD34^{dim} CELLS SUPPRESS T CELL ACTIVATION *IN VITRO*



MGTA-145 + Plerixafor Mobilized Graft is Distinct from G-CSF in Nonhuman Primates



How would this graft perform following allogeneic transplantation?

MGTA-145 + Plerixafor Mobilizes an Immunosuppressive Graft

EXPERIMENTAL DESIGN

MOBILIZATION



Unmobilized
MGTA-145 + plerixafor
plerixafor
G-CSF (5 Days)

n=3-5 per regimen

ISOLATE PBMCs

XENO TRANSPLANTATION IN NSG MICE

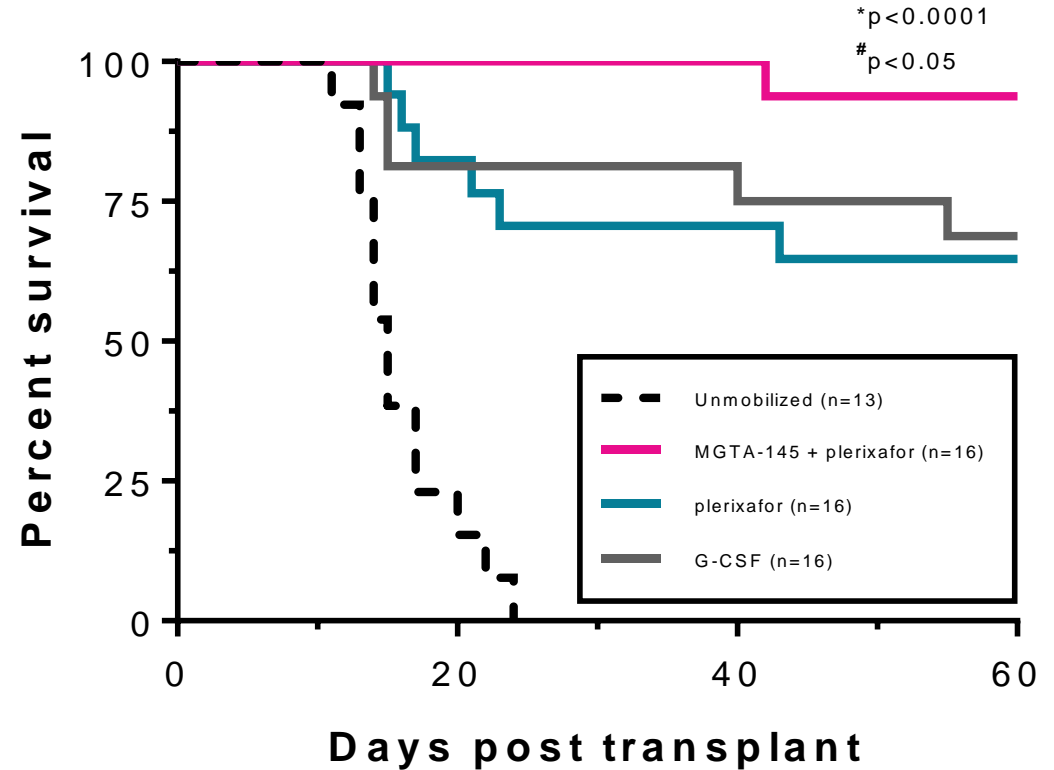


NSG mice
200 cGy

6×10^6 PBMCs
per mouse

n = 13-16 per regimen

XENO TRANSPLANTATION



* Compared to Unmobilized
Compared to plerixafor

A Single Injection of MGTA-145 + Plerixafor Rapidly Mobilizes Sufficient CD34+ Cells for Transplant in Four Hours

EXPERIMENTAL DESIGN

In collaboration with Dr. Hans-Peter Kiem

MOBILIZATION & LEUKAPHERESIS

MGTA-145
+ plerixafor



CD34+ SELECTION

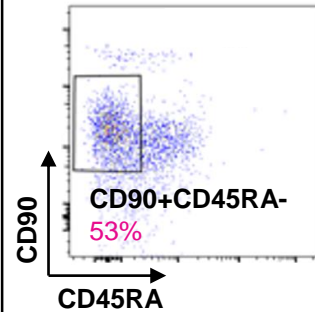
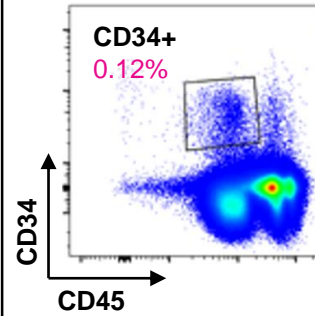
AUTOLOGOUS TRANSPLANTATION



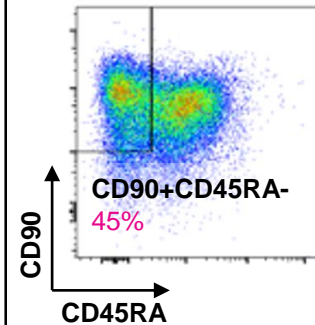
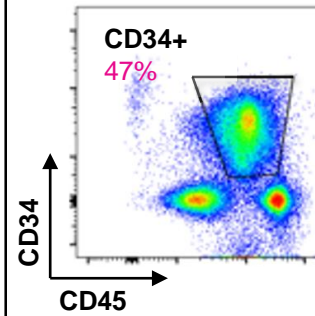
1080 cGy

MOBILIZATION & COLLECTION

APHERESIS PRODUCT



POST ENRICHMENT



4 Hour Collection

Cells Harvested

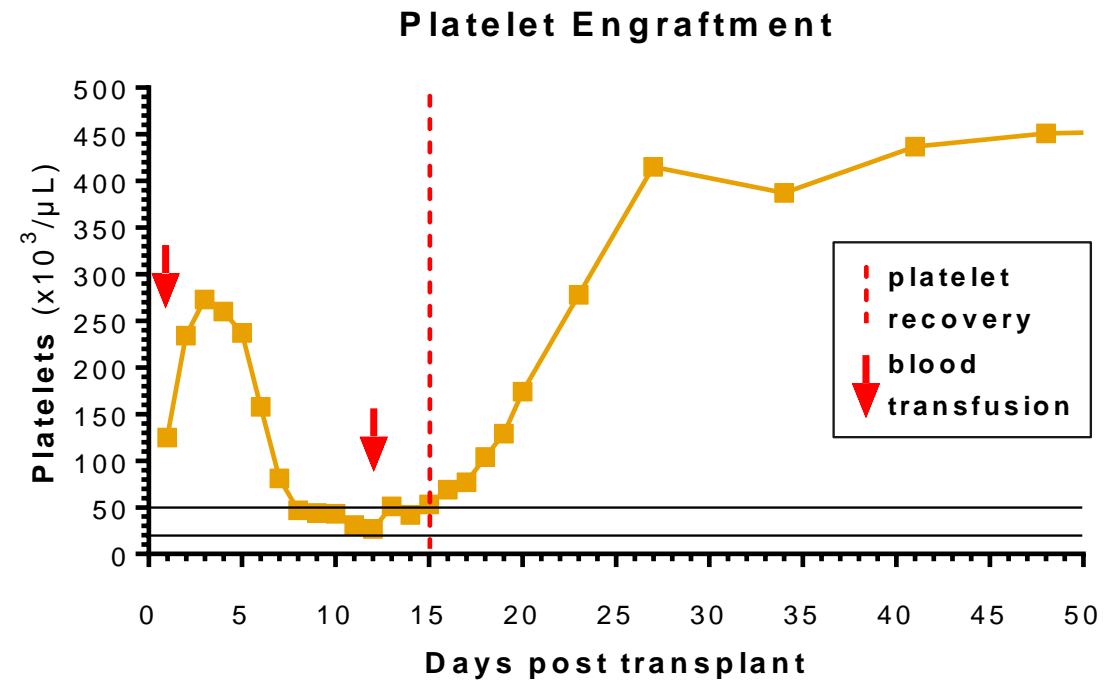
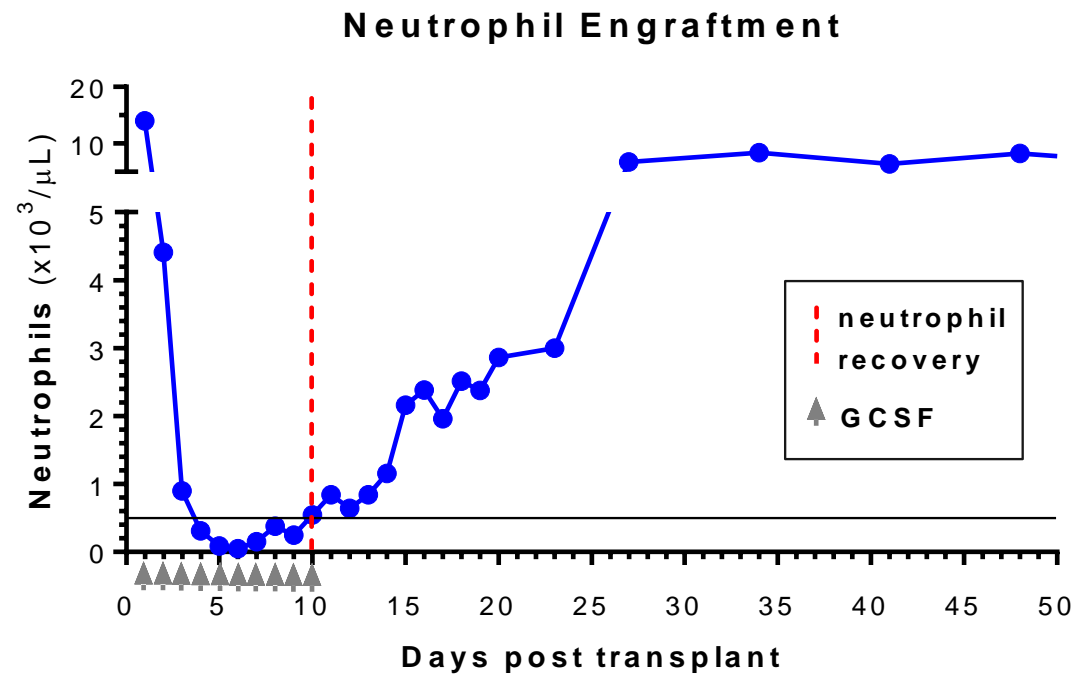
Cell Type	Dose
CD34+	$2.3 \times 10^6 / \text{kg}$
CD34+CD90+CD45RA-	$0.9 \times 10^6 / \text{kg}$

Cells Infused

Cell Type	Dose
CD34+	$1.8 \times 10^6 / \text{kg}$
CD34+CD90+CD45RA-	$0.8 \times 10^6 / \text{kg}$

MGTA-145 + Plerixafor Mobilized CD34+ Cells Rapidly Engraft Following Autologous Transplantation in Nonhuman Primate

AUTOLOGOUS TRANSPLANT

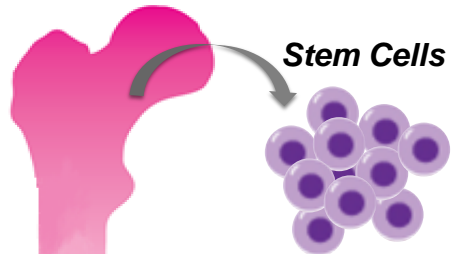


A Single Injection of MGTA-145 + Plerixafor Mobilizes Large Numbers of Engraftable HSCs and Immunosuppressive Monocytes

Magenta Mobilization



Minutes



MGTA-145
+ plerixafor

BENEFITS OF MGTA-145 + PLERIXAFOR

Single injection of
MGTA-145 + plerixafor



Rapid and robust
mobilization of HSCs

Mobilization of CD34^{dim} monocytes
capable of suppressing GvHD

Rapid engraftment in large
animal transplant model

**MGTA-145 + plerixafor is moving into the clinic
in the first half of 2019**

Acknowledgments



MAGENTA RESEARCH TEAM

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Stefan Radtke
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BACK UP
