

**Mobilizzazione CHEMIO-FREE
delle CSE
nel paziente affetto da Mieloma**

***La mobilizzazione CHEMIO-FREE,
presenta alcuni indubbi vantaggi:***

- Prodotto aferetico ricco di linfociti, adatto alla Immunoterapia Post trapianto.**
- Predicibilità del giorno di raccolta**
- Non tossicità da chemioterapia**

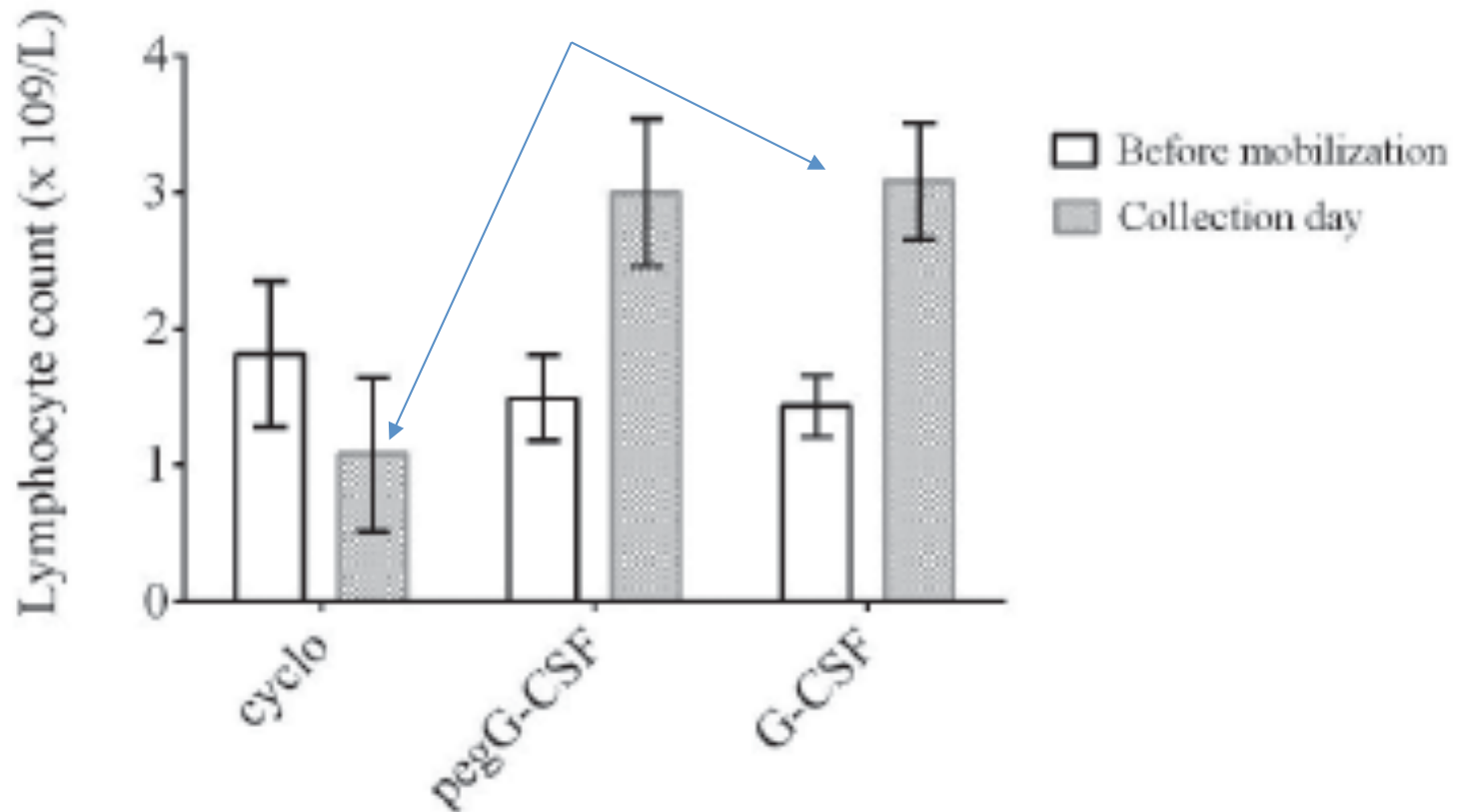
research

Mobilization with cyclophosphamide reduces the number of lymphocyte subpopulations in the leukapheresis product and delays their reconstitution after autologous hematopoietic stem cell transplantation in patients with multiple myeloma

Matevz Skerget¹, Barbara Sl¹ Department of hematology, Universit

Radiol Oncol 2016; 50(4): 402-408.

Mean lymphocyte count before mobilization and on collection day with 95% CI



Immune reconstitution

Infused peripheral blood autograft absolute lymphocyte count correlates with day 15 absolute lymphocyte count and clinical outcome after autologous peripheral hematopoietic stem cell transplantation in non-Hodgkin's lymphoma

LF Porrata¹, MR Litzow¹, DJ Inwards¹, DA Gastineau^{1,2}, SB Moore², AA Pineda², KL Bundy², DJ Padley², D Persky³, SM Ansell¹, INM Micallef¹ and SN Markovic¹

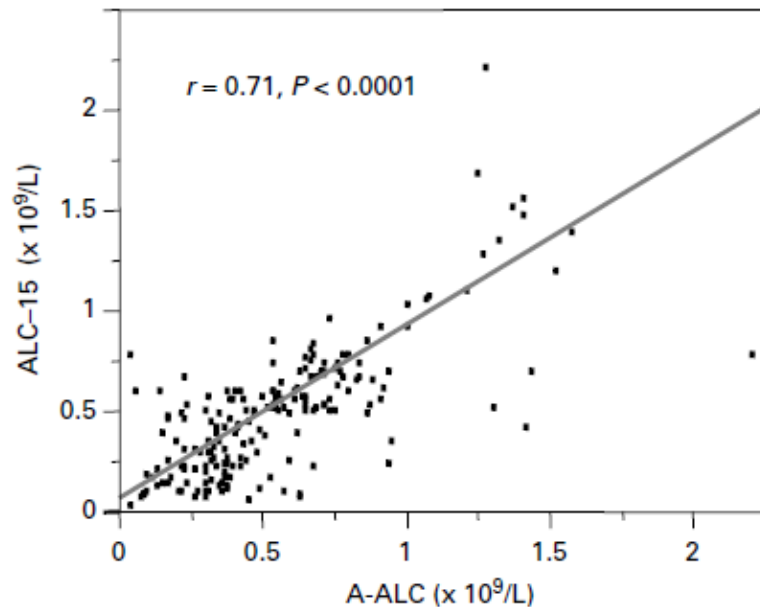
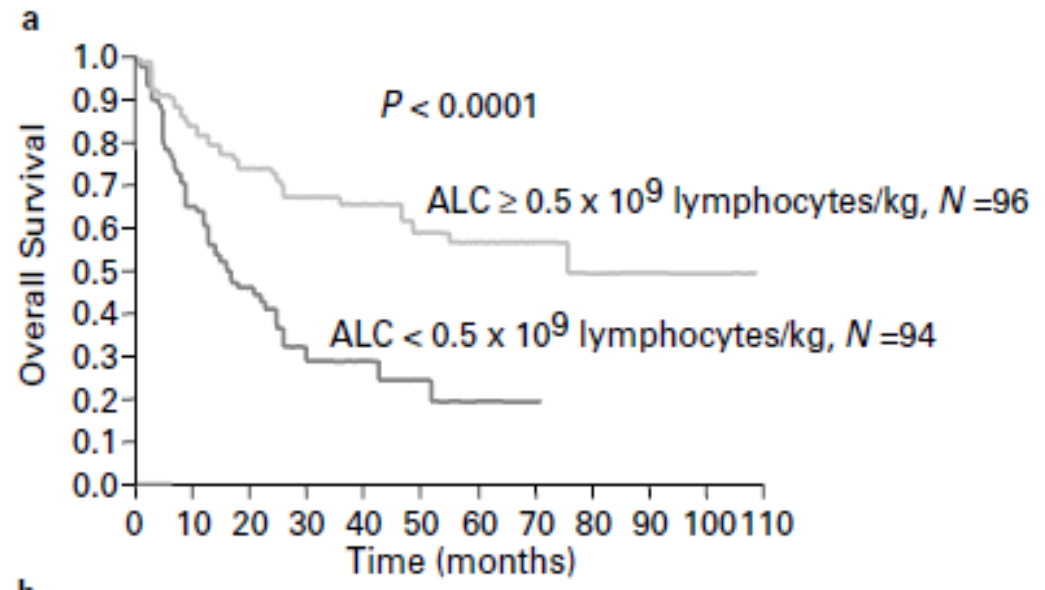


Figure 1 Scattered plot comparing the infused A-ALC and the absolute lymphocyte count (ALC) recovery at day 15 after APHSCT. Strong correlation was identified between the infused A-ALC and the ALC recovery at day 15 after APHSCT (Spearman correlation rho factor, $r = 0.71$, $P < 0.0001$).



LA NEUTROPENIA FEBBRILE DOPO G-CSF ALONE E' TIPICAMENTE ASSENTE MENTRE DOPO CTX +G-CSF LA NEUTROPENIA FEBBRILE RAPPRESENTA UN PROBLEMA NON INDIFFERENTE

AUTORE ----	DOSE CTX -----	NEUTROPENIA FEBBRILE	
Hamadani	1.5 gr	5.8%	Basse dosi CTX
Sizemore	2.0 gr	5%	
Milone	2.0 gr	5 %	
Hamadani	3 gr	16.3%	Dosi intermedie CTX
Awan	3 gr	16%	
Gertz	3 gr	10%	
Milone	4 gr	14%	
Orciuolo	3-4 gr	10%	
Fitoussi	4	70%	Alte dosi CTX
Sizemore	4	40%	
Antar	5 gr	60%	

Comparison of high-dose CY and growth factor with growth factor alone for mobilization of stem cells for transplantation in patients with multiple myeloma

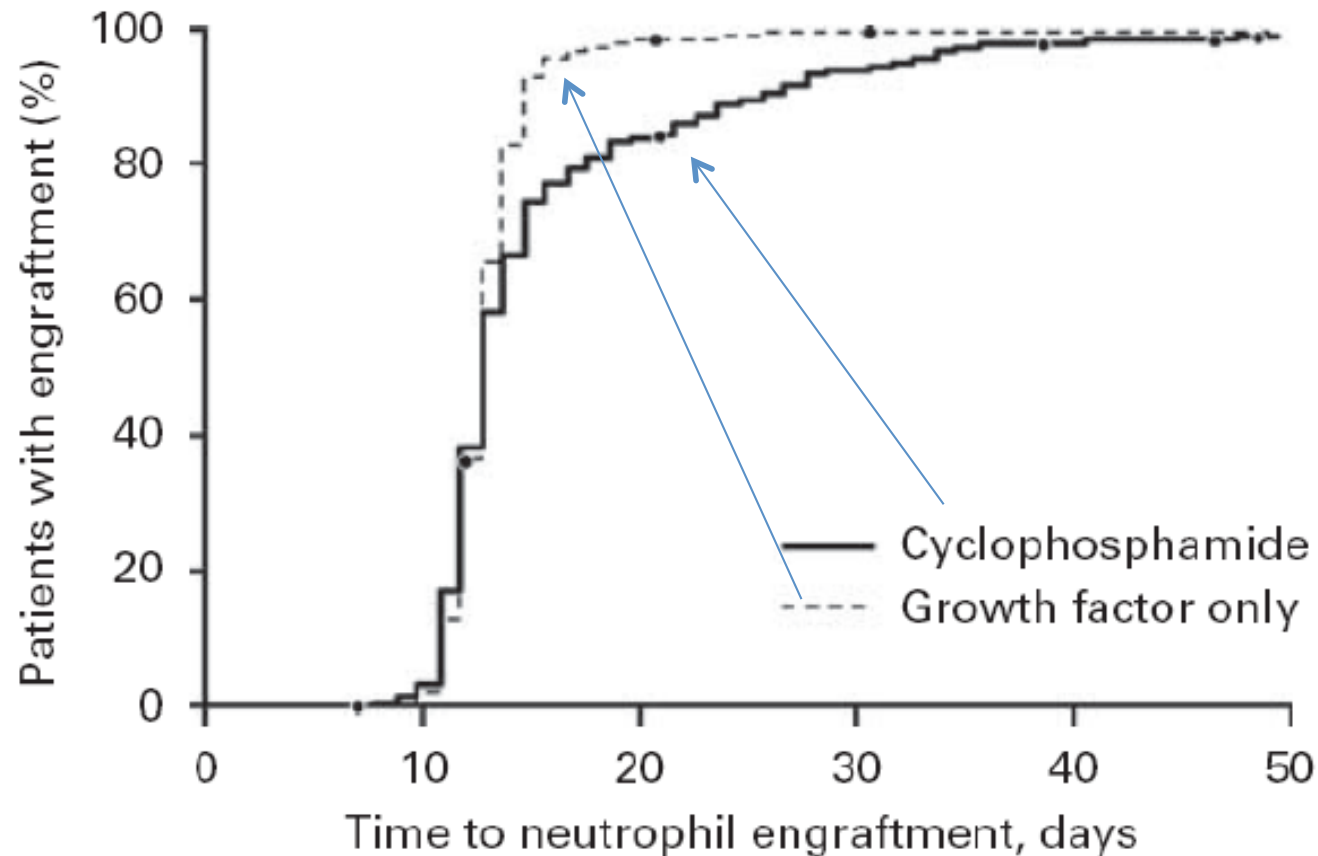
MA Gertz¹, SK Kumar¹, MQ Lacy¹, A Dispenzieri¹, SR Hayman¹, FK Buadi¹, D Dingli¹, DA Gastineau¹, JL Winters², and MR Litzow¹

¹Division of Hematology, Mayo Clinic, Rochester, MN, USA

Esisterebbe una Tossicità inaspettata da CTX, Che determinerebbe infatti un danno al Microambiente midollare con conseguente attecchimento Ritardato.

Bone Marrow Transplant. 2009 April ; 43(8): 619–625.

Gertz et al.



MOBILIZZAZIONE CHEMIO-FREE:

- **G-CSF alone**

- **PLX alone**

- **G-CSF + PLX**

- **Others agents:**

- **Balixafortide , POL-551**

- **PTH,**

- **TPO,**

- **Anti-VLA-4**

- **Meloxicam**

- **Bortezomib**

Domingues M

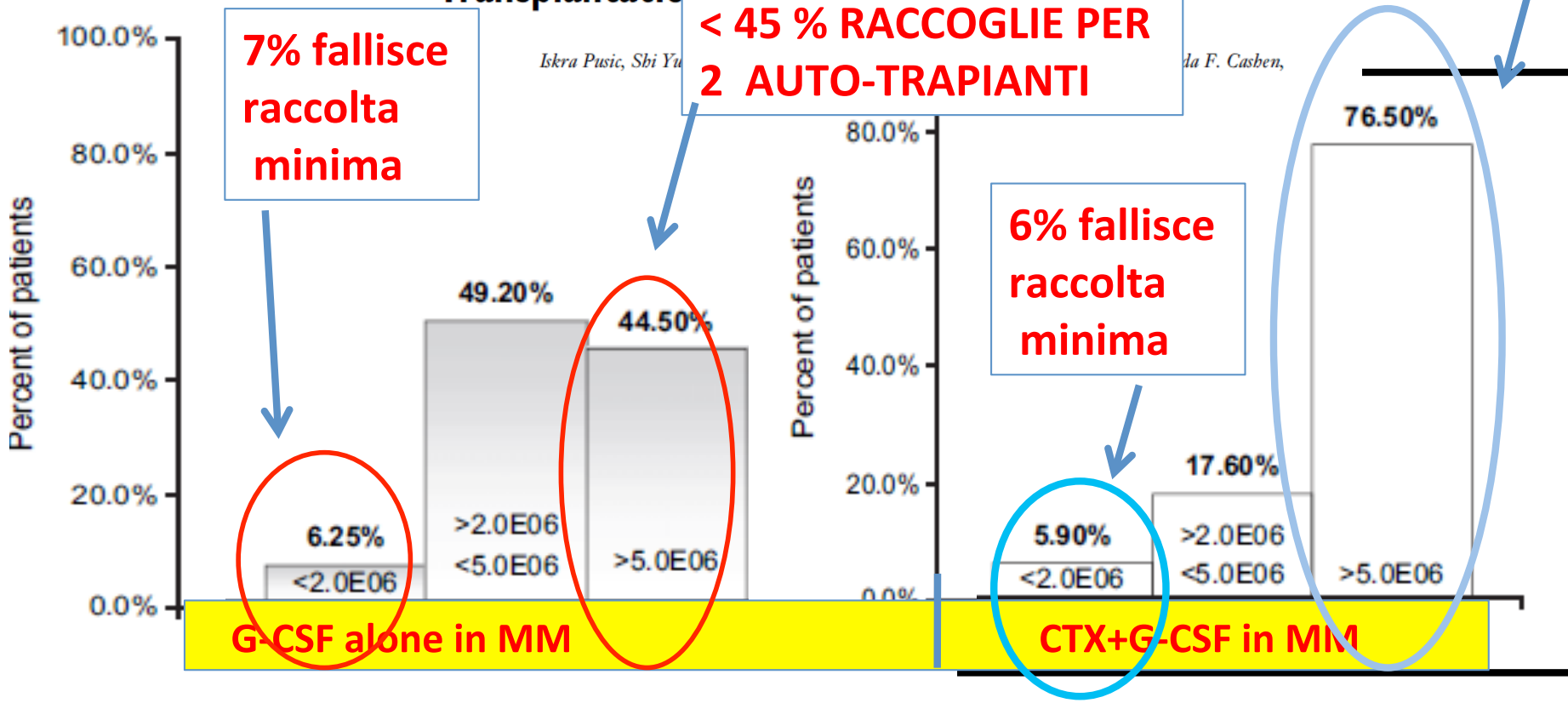
New agent in HSC mobilization

Int J Hematol 2017,105:141

LIMITI DEL “G-CSF alone” nella mobilizzazione CSE nel MM:

- **5-10 %** dei pazienti “**G-CSF alone**” fallisce la raccolta minima ($> 2 \times 10^6/\text{Kg}$).
- solo il **40-50%** dei pazienti “**G-CSF alone**” raccoglie per 2 autotrapianti ($> 6 \times 10^6/\text{Kg}$).
- Possibile inferiore risultato nei pazienti pretrattati con > 4 cicli lenalidomide.

Impact of Mobilization and Remobilization Strategies on Achieving Sufficient Stem Cell Yields for Autologous Transplantation



7% fallisce raccolta minima

< 45 % RACCOGLIE PER 2 AUTO-TRAPIANTI

75 % RACCOGLIE PER 2 AUTO-TRAPIANTI

6% fallisce raccolta minima

ANCHE CONSIDERANDO UNA QUTA MINIMA DI 5x10e6/Kg CD34+ , SOLO IL 44.5% DEI PAZIENTI RACCOGLIE PER 2 TRAPIANTI

**L'USO DI CTX+G-CSF SOLO IN PARTE OVVIA
ALLA SCARSA EFFICENZA DI MOBILIZZAZIONE DEL G-CSF ALONE**

G-CSF ALONE

CTX + G-CSF

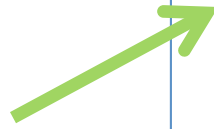
Fallimento della
Raccolta minima: 5-10%

=

Fallimento della
Raccolta minima: 5-10%

Fallimento della raccolta
ottimale: 60%

Fallimento della raccolta
ottimale: 20%

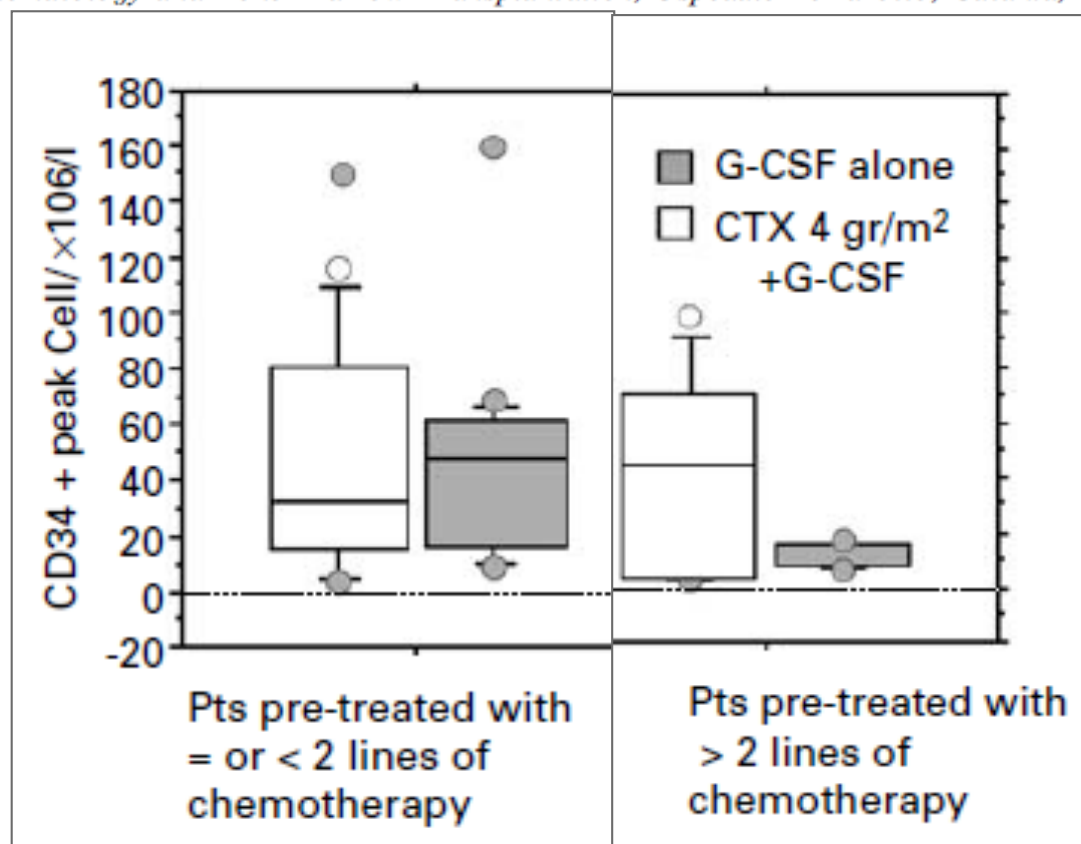


Progenitor Cell Mobilization

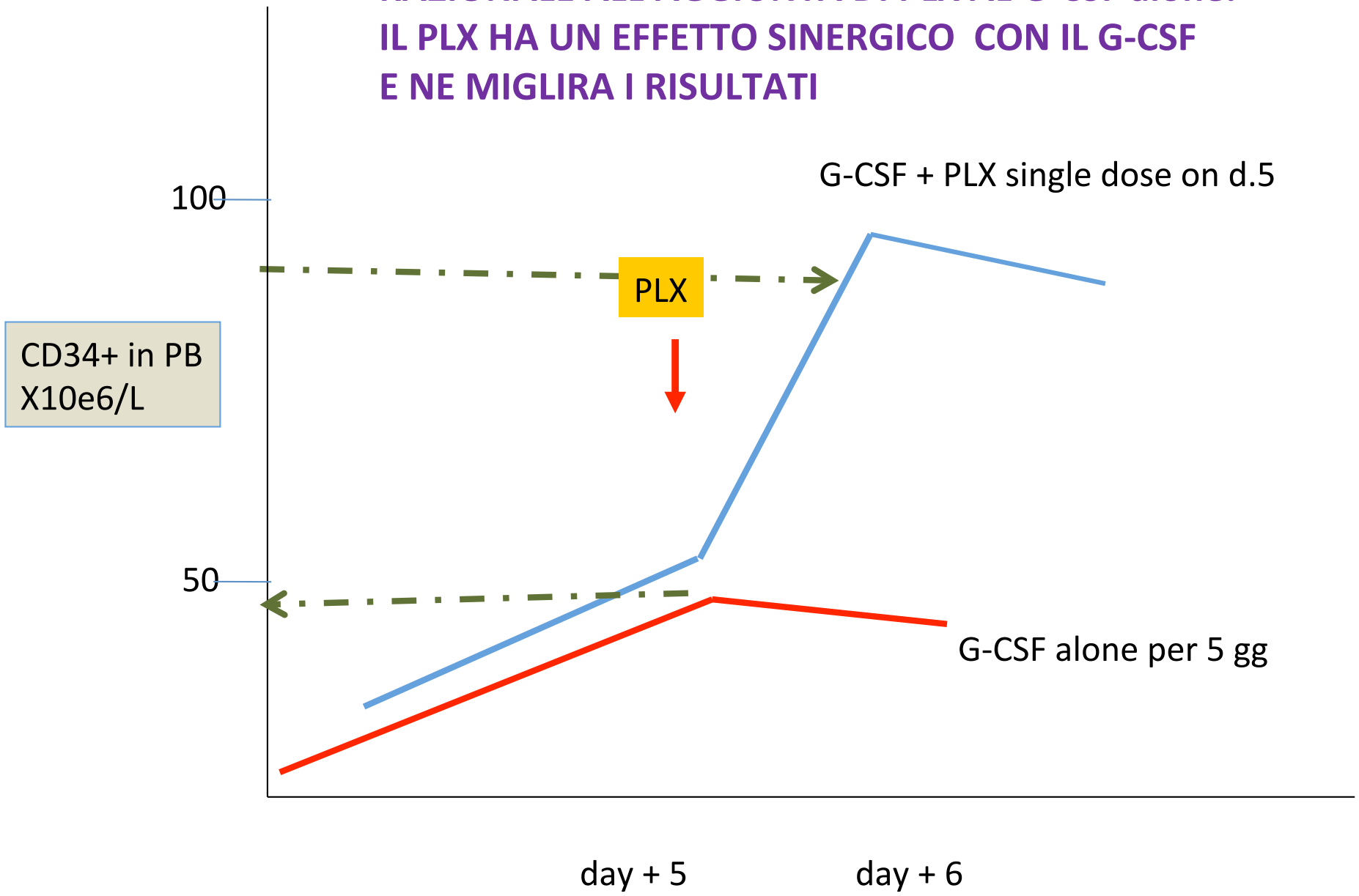
G-CSF Alone vs cyclophosphamide plus G-CSF in PBPC mobilization of patients with lymphoma: results depend on degree of previous pretreatment

G Milone, S Leotta, F Indelicato, S Mercurio, G Moschetti, F Di Raimondo, A Tornello, U Consoli, G Guido and R Giustolisi

Division of Haematology and Bone Marrow Transplantation, Ospedale Ferrarotto, Catania, Italy



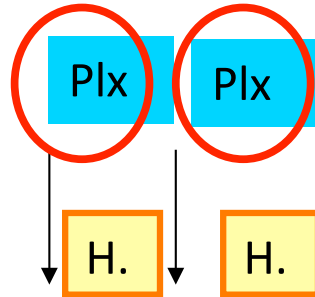
**RAZIONALE ALL'AGGIUNTA DI PLX AL G-CSF alone:
IL PLX HA UN EFFETTO SINERGICO CON IL G-CSF
E NE MIGLIRA I RISULTATI**



L'UTILIZZO DI G-CSF + PLX POTREBBE ESSERE UNA MIGLIORE MODALITA' PER OVVIARE ALLA SCARSA MOBILIZZAZIONE DI G-CSF ALONE

PLERIXAFOR
+
G-CSF

UNIVERSAL



D1 D2 D3 D4 D5 D6
↓ ↓ ↓ ↓ ↓ ↓
G-CSF 10 mcg/Kg day sc

100% dei pazienti
fa' plerixafor

**PAZIENTI che erano risultati POOR MOBILIZER CON G-CSF ALONE
SONO STATI RIMOBILIZZATI CON *G-CSF+ PLX UNIVERSAL*
CON RISULTATI MIGLIORI DI 10 VOLTE**

BLOOD, 1 SEPTEMBER 2005 • VOLUME 106, NUMBER 5

Table 4. Total CD34⁺ cells (×10⁶ cells/kg) harvested in patients who poorly mobilized with G-CSF alone

First mobilizing regimen	Collection after G-alone mobilization	Collection after A + G mobilization	Fold increase with A + G mobilization
G alone	0.08	2.8	35
G alone	0.29	2.9	10
G alone	0.73	3.7	5
G alone	1.6	8.5	6
G alone	0.55	5.2	9
A + G	0.16	5.3	33
A + G	0.36	7.6	21
A + G	0.04	4.1	102
A + G	0.63	13.6	22

Mean Increase of HARVEST X 10 fold

STUDI
PLX
UP
FRONT

CLINICAL TRIALS AND OBSERVATIONS

Plerixafor and G-CSF versus placebo and G-CSF to mobilize hematopoietic stem cells for autologous stem cell transplantation in patients with multiple myeloma

John F. DiPersio,¹ Edward A. Stadtmauer,² Ausyorn Nademanee,³ Ivana N. M. Micallot,⁴ Patrick J. Stiff,⁵ Jonathan L. Kaufman,⁶ Richard T. Maziarz,⁷ Chitra Hosang,⁸ Stefan Fröhne-Haut,⁹ Mitchell Horwitz,¹⁰ Dennis Cooper,¹¹ Gary Bridger,¹² and Gary Calandra,¹² for the 3102 Investigators

DI PERSIO 2009 MM= 148 pts

95.3% of 148 participants in the plerixafor (**HARVEST FAILURE**

4.7% more than or equal to 2×10^6 CD34+ cells/kg in two or fewer apheresis days **Versus 11.7%**.

1.6% Mobilization Failure rate:

71.6% reached CD34 cells/kg $> 6 \times 10^6$ in 2 or fewer days of apheresis (106 pts /148). Median CD34 collected: 10.96×10^6 /Kg.

IMPROVEMENT IN USING **G-CSF+PLX**
IN PBSC MOBILIZATION (MM).

75%
Raccolta sufficiente
per 2 autologhi
in max 4 aferesi.

51%
Raccolta sufficiente
per 2 autologhi
In max 4 aferesi

71.6%
Raccolta sufficiente
per 2 autologhi
in max 2 aferesi.

34%
Raccolte sufficienti
Per 2 autologhi
In max 2 aferesi

Mediana aferesi
n. 1.0

Mediana aferesi
n. 2.5



Plerixafor and granulocyte colony-stimulating factor for first-line steady-state autologous peripheral blood stem cell mobilization in lymphoma and multiple myeloma: results of the prospective PREDICT trial

Nigel Russell,¹ Kenny Douglas,² Anthony D. Ho,³ Mohamad Mohty,⁴ Kristina Carlson,⁵ G.J. Ossenkoppele,⁶ Giuseppe Milone,⁷ Macarena Ortiz Pareja,⁸ Daniel Shaheen,⁹ Arnold Willemsen,¹⁰ Nicky Whitaker,¹¹ and Christian Chabannon¹²

PREDICT (PROSPETTICO NON CONTROLLATO)

G-CSF + PLX universal

MM= n. 90 pts

98% patients within the MM group achieved minimum target cell collection ($>2 \times 10^6/\text{Kg}$)

2% Harvest Failure rate.

82% patients achieved the optimal cell collection of $\geq 5 \times 10^6$ CD34+

Median CD34 collected: $7.6 \times 10^6/\text{Kg}$.

OGUNNIYI

Leukemia and Lymphoma 2017

UPFRONT G-CSF+PLX IN MM

RETROSPECTIVE STUDY

MSKCC

**92% RACCOLGONO PER
2 TRAPIANTI**

1.4% failure rate

Retrospettivo

G-CSF+PLX

Nel MM

(138 pts mobilizzati

Upfront)

< 5.0 X10E6/Kg = 7.2%

< 4.0 X10E6/Kg = 4.3%

<2.0 X10E6/Kg= 1.4%

Multivariata per mancata risposta
(DEFINED AS A HARVEST < 5x10e6/Kg)

MULTIVARIATE IMPORTANT FOR FAILURE RATE:

- WBC <4.000**
- Razza bianca**
- Precedente prima linea con lenalidomide**

Cochrane Database Syst Rev. 2015 Oct 20;(10)

Additional plerixafor to granulocyte colony-stimulating factors for haematopoietic stem cell mobilisation for autologous transplantation in people with malignant lymphoma or multiple myeloma.

Hartmann T, Hübel K, Monsef I, Engert A, Skoetz N.

AUTHORS' CONCLUSIONS:

The results of the analysed data **suggest** that additional plerixafor leads to increased stem cell collection in a shorter time.

There was insufficient evidence to determine whether additional plerixafor affects survival or adverse events

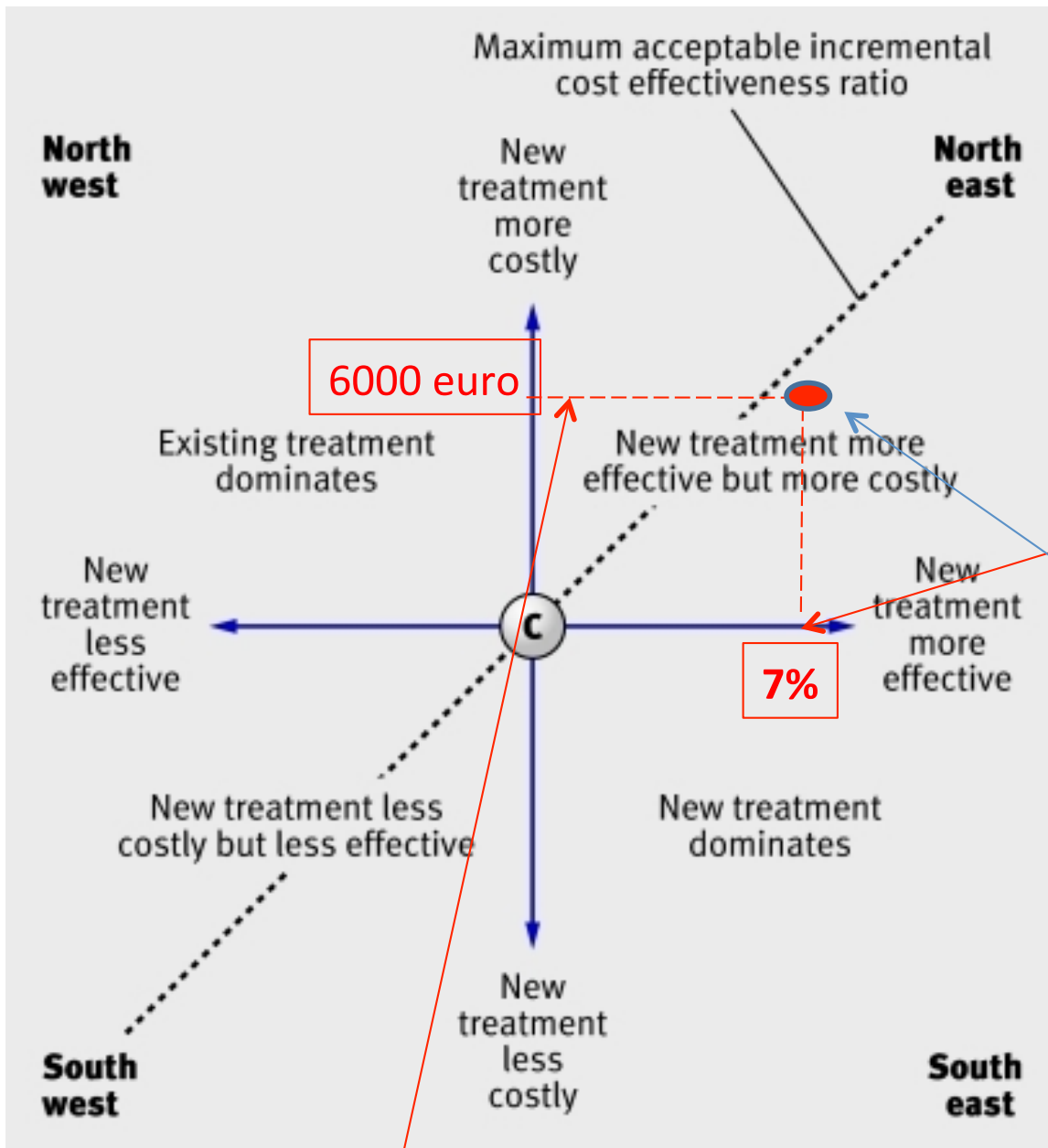
**COSTO ED EFFICACIA DI PLX + GCSF “universale”
IN CONFRONTO A G-CSF ALONE
(CONFRONTO IPOTETICO)**

	SOLO G-CSF	G-CSF + PLX		
NON MOBILIZER	11.7%	4.7%	+7%	
Aferesi	2.5	1.5	-1.0 aferesi	-1500
COSTO PLX	0	+7500		+7500
		COSTO NETTO A PAZIENTE		+ 6000

Costo PLX=

Media di 1.5 aferesi a paziente precedute da media 1.5 fiale di PLX a paziente

Per un costo di 5000 x1.5= 7500 euro.



INCREMENTAL EFFECTIVENESS OF PXL ADDED TO G-CSF=
 From 11.7% to 4.7%=
7%

Incremental Cost-Effectiveness Ratio (ICER)

Del PLX Aggiunto al G-CSF:

6000 euro / 7% =
857 EURO PER 1%
INCREASE IN success rate

Incremental Cost 6000 euro

COSTO ANNUO DI PLX PER LA MOBILIZZAZIONE CON PLX+G-CSF

In un centro medio si mobilizzano n. 30 Pazienti MM /anno
quindi

La spesa annua totale relativa al PLX per mobilizzare tutti i
paz. MM con G-CSF+PLX ammonterebbe a =

30 pazienti x 6000 euro=180.000 euro/anno

VANTAGGI=

incrementare del 7% il numero di pazienti che raccolgono e
sono provvisti di minima quota di CD34+.

Eliminare le aferesi nei week end

Consentire la previsione del giorno di raccolta

COME MIGLIORARE IL RAPPORTO COSTO EFFICACIA ?

COME OTTENERE UN MIGLIORAMENTO DEL COSTO/EFFICACIA:

- **Large Volume leuco-apheresis**
- Algoritmi **RISK ADAPTED** validati e dotati di specificita'
- Selezionare pazienti non in progressione

IMPEGNO ECONOMICO MOBILIZZAZIONE BASATA SU CTX
E' NEI PRIMI 8-9 GG

Impegno
Economico
Della degenza per
Somministrazione
CTX

1

5

7

11

13

R

R

Impegno
Economico trattamento
complicanze

IMPEGNO ECONOMICO
G-CSF+PLX NEI GIORNI DI HARVEST

Impegno
Economico
Prima sommini-
strazione PLX

Impegno
Economico
Seconda
sommini-
strazione PLX

1

2

3

4

5

6

R

R

Cost and Clinical Analysis of Autologous Hematopoietic Stem Cell Mobilization with G-CSF and Plerixafor Compared to G-CSF and Cyclophosphamide

Paul Shaughnessy,¹ Miguel Islas-Ohlmayer,¹ Julie Murphy,² Maureen Hougham,¹
 Jill MacPherson,¹ Kurt Winkler,¹ Matthew Silva,³ Michael Steinberg,³ Jeffrey Mateos,²
 Sheryl Selvey,³ Michael Maris,² Peter A. McSweeney²

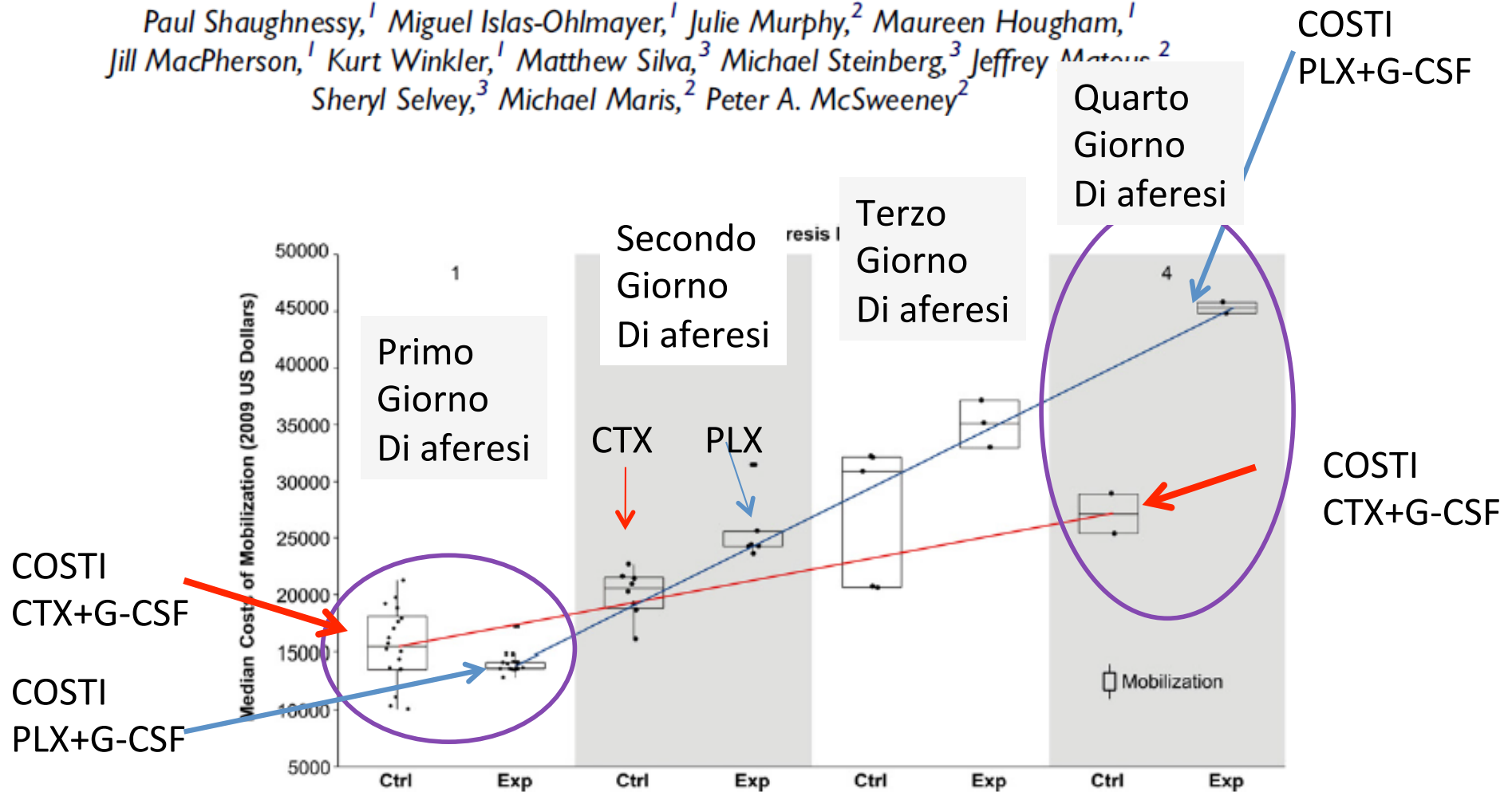


Figure 3. Total median costs associated with successive days to mobilization. The total cost of mobilization for each patient was determined through the indicated day of apheresis and medians were calculated for each group in each day of apheresis. The upper boundary of the box represents the 75th percentile and the lower boundary the 25th percentile; the line represents the median for each group.

1 Awan F ,
All collections were performed with a COBE SPECTRA apheresis system
BY PROCESSING THREE TO FOUR BLOOD VOLUMES.

2 DiPersio, for the 3102 Investigators
APHERESIS: THREE BLOOD VOLUME +/- 10%.

3 COSTA LJ .
At least THREE TOTAL BLOOD volumes were processed

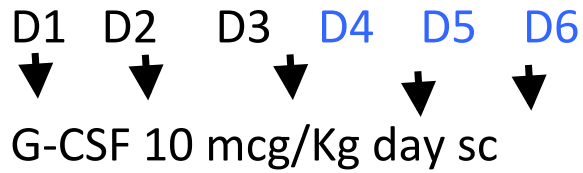
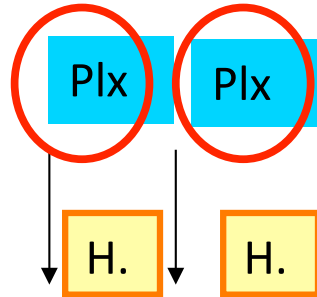
4 ABHYANKAR S BMT 2012
All patients underwent apheresis with 4–6 BLOOD VOLUMES processed.

COME OTTENERE UN MIGLIORAMENTO DEL COSTO/EFFICACIA:

- Large Volume leuco-apheresis
- **Algoritmi RISK ADAPTED** validati e dotati di specif
- Selezionare pazienti non in progressione

PLERIXAFOR
+
G-CSF

“Schema prefissato”



100% dei pazienti
fa' plerixafor

ON DEMAND
or
PRE-EMPTIVE

PLERIXAFOR
+
G-CSF

G-CSF 10 mcg/Kg day sc

D1 D2 D3 D4 D5 D6

Solo il 50%
dei pazienti
Farebbe Plx

CD34
count

>20

10-20

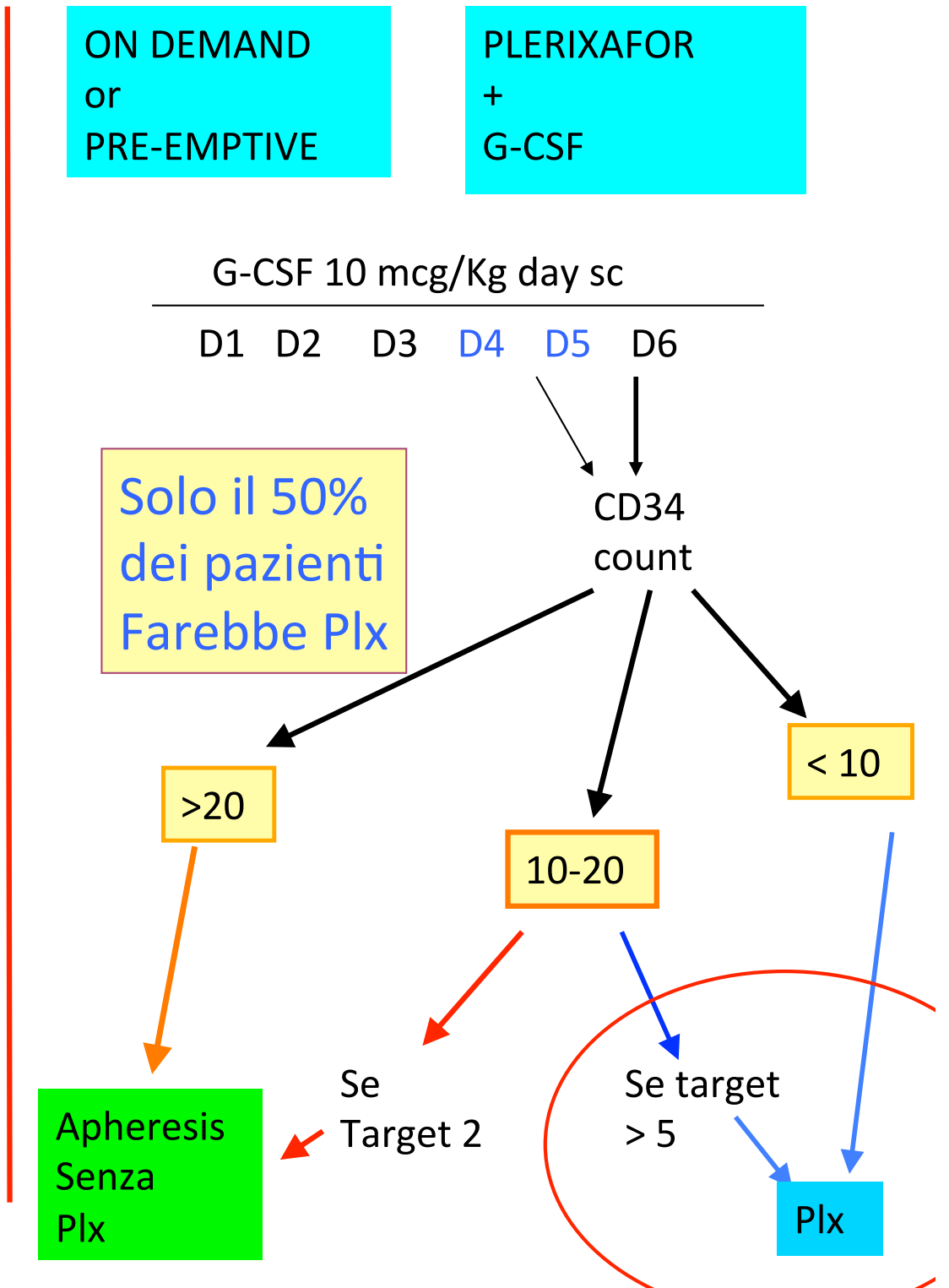
< 10

Apheresis
Senza
Plx

Se
Target 2

Se target
> 5

Plx



2 SCHEMA PLX + G-CSF Risk adapted (JUST IN TIME) or ON DEMAND sulla base di dati a +5.

HSC collection with plerixafor
S Abhyankar et al

*E' davvero indispensabile
Prefissare un
Algoritmi di mobilizzazione per gli
Studi ON DEMAND di PLX?*

Table 1 Plerixafor use algorithm

(A) Pre-collection peripheral CD34⁺ count on day 5 of G-CSF

- If CD34⁺ count is <10 cells/ μ L and patient needs a minimum CD34⁺ cell dose of 2.5×10^6 /kg
 - Administer plerixafor at 5 pm
 - Continue G-CSF (10 mcg/kg)
 - Perform collection of stem cells next morning (day 6) and assess need for more plerixafor doses based on the collection
- If CD34⁺ count is ≥ 10 and patient needs a minimum CD34⁺ cell dose of 2.5×10^6
 - No plerixafor given
 - Perform a large-volume collection (approximately 4-6 blood volume)
- If CD34⁺ is >10 but <20 cells/ μ L and patient needs a minimum CD34⁺ cell dose of 5.0×10^6 /kg
 - Perform a large-volume collection (approximately 4-6 blood volume)
 - Administer plerixafor that evening
 - Continue G-CSF
 - Continue collection the following morning and assess need for more plerixafor doses
- If CD34⁺ count is ≥ 20 cells/ μ L and patient needs a minimum CD34⁺ cell dose of 5.0×10^6 /kg
 - No plerixafor to be given
 - Perform a large-volume collection (approximately 4-6 blood volume)

(B) Day 1 collection product CD34⁺ count/kg

- If on the first day of collection the collected product contains less than one-half of the desired dose
 - Administer plerixafor that evening
 - Continue G-CSF
 - Perform collection the following morning
 - Assess need for repeating plerixafor

G-CSF+ PLERIXAFOR ON DEMAND

Abhyankar	Al Chen	Horwitz	Micallef - 1	Micallef - 2	Costa
<p>4</p> <p>d. +5 CD34+ < 10</p> <p>d.+5 CD34+ < 20 doppio tx</p>	<p>D +4° CD34+ >5 / < 15</p>	<p>d.+5 CD34 <7 /mmc</p>	<p>d.+5 CD34 <10 /mmc</p>	<p>d.+4 CD34 <10 /</p> <p>d.+4 CD34 <20 se doppio tx</p>	<p>d.+4° CD34 <14</p> <p>d. +4 CD34 < 25 Se doppio tx</p>
<p>PLX</p> <p>Necessario:</p> <p>35%</p>	<p>36-38%</p>	<p>55%</p>	<p>38% 33% MM 47% LNH</p>	<p>58% <u>53% MM</u> 69% LNH</p>	<p>68%</p>
159 paz	166 mob.	38 paz	221 mob.	100 mob.	34 paz
94.9% CD34> 2x10e6/Kg	92% CD34> 2x10e6/Kg	88% CD34> 2x10e6/Kg	95%	99%	97%
MM+LNH 5%	MM 7%	MM+LNH 11%	MM: 2% LNH: 9%	MM: 0% LNH: 3%	MM+LNH: 3%

Hematopoietic Progenitor Cell Mobilization with “Just-in-Time” Plerixafor Approach is a Cost Effective Alternative to Routine Plerixafor Use

Lauren Veltri¹, Aaron Cumpston², Alexandra Shillingburg², Sijin Wen³, Jin Luo³, Sonia

Baseline Characteristics	Routine G-CSF + Plerixafor (n=76)	Just-in-Time Plerixafor (n=60)
Disease Histology		
Myeloma	45 (59%)	30 (50%)
Lymphoma	31 (41%)	30 (50%)

Mobilization and Apheresis Results	Routine G+P (n=76)	JIT-P (n=60)
Peak peripheral blood CD34+ cell count (μ/L), mean/median (range)	77.5/61.5 (5–389)	33.1/29 (7–101)
CD34+ cells × 10 ⁶ cells/kg collected on day 1, mean/median (range)	4.3/2.9 (0.2–14.4)	2.4/2.1 (0.4–6.7)
Total CD34+ cells × 10 ⁶ /kg collected, mean/median (range)	6.7/5.8 (0.2–22.2)	4.8/4.5 (1.7–9.8)
Total number of apheresis sessions, mean/median (range)	2.2/2.0	2.4/2
Mobilization failures, N (%)	4 (5.3%)	2 (3.3%)

	Routine G+P (US Dollars, 2014)	JIT-P (US Dollars, 2014)
Average apheresis cost	9,292.01	10,336.82
Day 4 CD34+ flow cytometry, mean	Not performed	89.44
Average G-CSF costs	4,460.51	4,686.11
Average plerixafor costs	13,760.77	8,449.26
Average total mobilization costs	27,513.29	23,596.64
Average mobilization cost of patients requiring 1 session of apheresis	14,074.59	10,406.60

2 SCHEMA PLX + G-CSF

Risk adapted (JUST IN TIME) or On demand”
sulla base di dati a +5 OPPURE sui dati a +4.

PLX sera del 5° gg

se CD34 < 7 -10

< 20 (se target doppio Tx)

PLX sera del 4° gg se CD34 < 5-15

< 20-25 (se target doppio Tx)

Cost-Effectiveness Analysis of a Risk-Adapted Algorithm of Plerixafor Use for Autologous Peripheral Blood Stem Cell Mobilization

Ivana N.M. Micallef^{1,*}, Shirshendu Sinha², Dennis A. Gastineau¹, Robert Wolf³, David J. Inwards¹, Morie A. Gertz¹, Suzanne R. Hayman¹, William J. Hogan¹, Patrick B. Johnston¹, Martha Q. Lacy¹, Stephen M. Ansell¹, Francis Buadi¹, David Dingli¹, Angela Dispenzieri¹, Mark R. Litzow¹, Luis F. Porrata¹, Jeffrey L. Winters⁴, Shaji Kumar¹

**Comparazione
Algoritmi basati su
Day 5° versus Day 4°**

DAY +5

DAY +4

Table 2
Baseline Patient Characteristics

	Baseline	Plerixafor-1	Plerixafor-2
Patients (n = 592)	278	216	98
Mobilization attempts	319	221	100
Disease			
Day-1 apheresis yield	2.3 (0-26)	2.4 (0.03-28)	3.7 (0.5-29)
Mobilization failures	52 (19%)	10 (5%)	1 (1%)
Remobilizations	39 (14%)	5	1
Plerixafor use	0	82 (38%)	57 (58%)

Cost Analysis

	Baseline	Plerixafor-1	Plerixafor-2	P Value
Patients	280	219	98	
Total cost per patient*				
Median	\$12,500	\$12,500	\$20,000	
Minimum	\$3,000	\$5,000	\$5,500	
Maximum	\$146,750	\$93,500	\$89,750	.01
Mean	\$17,150	\$21,532	\$20,617	

Costo efficacia PLX + GCSF IN MODALITA' "RISK ADAPTED"

	Solo G-CSF	G-CSF + PLX		
NON MOBILIZER	11.7%	4.7%	+7%	GUADAGNO IN EFFICACIA
Aferesi	2.5	1.5	-1000	COSTO 1
COSTO PLX	0	3500	+3500	COSTO 2
			+ 2500	TOTALE COSTO

ICER $2500 / 7\% = 357$ EURO PER 1% INCREASE IN success rate

North west

Maximum acceptable incremental cost effectiveness ratio

IPOTESI DI DIFFERENTI ICER RELATIVI A:
-- G-CSF+PLX UNIVERSAL
-- G-CSF + PLX ON DEMAND

New treatment more costly

North east

G-CSF+PLX UNIVERSAL

857 E. PER 1% MIGLIORAM . IN Failure R.

6000

Existing treatment dominates

New treatment more effective but more costly

G-CSF +PLX ON DEMAND

357 E. PER 1% MIGLIORAM IN Failure R.

2500

New treatment less effective

+7%

New treatment more effective

New treatment less costly but less effective

New treatment dominates

South west

New treatment less costly

South east

COSTO ANNUO DI PLX PER LA MOBILIZZAZIONE CON PLX+G-CSF

In un centro medio si mobilizzano n. 30 Pazienti MM /anno
quindi

La spesa annua totale relativa al PLX per mobilizzare tutti i paz.
MM con **G-CSF+PLX risk adapted** ammonterebbe a =

$$\underline{30 \times 2500 = 75.000 \text{ euro/anno}}$$

VANTAGGI=

-- incrementare del 7% il numero di pazienti che raccolgono e sono provvisti di adeguata quota di CD34+.

-- Eliminare le aferesi nei week end

-- Consentire la previsione del giorno di raccolta

**E' G-CSF +PLX LA MIGLIORE DELLE
POSSIBILI STRATEGIE DI MOBILIZZAZIONE NEL MM ?**

G-CSF +/- PLX

-- G-CSF PEGHILATO

+/- PLX

-- CTX intermediate dose + G-CSF +/- PLX

-- VP16 + G-CSF

+/- PLX

	Fallimento	CD34>2x 10e6/Kg	> 5-6x10e6/Kg	COSTI		
Antar	G+P on demand	0/27	7.5	88.%	7.886	=
	CTX 5 gr + G	0/56	15.5	96%	7.536	
Awan	G+P univ.	0/33	11.6	96%	28.980	↑ +30%
	CTX 3-4 gr + G	0/55	16.6	93%	22.504	
Shanghness	G+P univ.	0/33	10.7	100%	14.224	↓ - 25%
	CTX 3-5 gr + G	0/33	11.6	90%	\$ 18.824	

NESSUNO DI QUESTI STUDI ERA RANDOMIZZATO, IL NUMERO DI PAZIENTI TRATTATO ERA ESIGUO. LA DETERMINAZIONE DEL SAMPLE SIZE NECESSARIO A RICERCARE DIFFERENZE FRA I GRUPPI ERA LONTANA DA QUELLA OTTIMALE.

VANTAGGI CLINICI

Riduzione dei fallimenti
Della mobilizzazione e
raccolta minima (dallo 11% al 2-4%)

Miglioramento della quota di pazienti
Che raccolgano per piu' trapianti (dal 30% al 80%)

No degenza per somministrazione
CTX

No episodi di neutropenia
febbrile (dopo CTX hanno incidenza 10-30%)

No degenza per complicanze

No aferesi nei week end

Ottimizzazione delle aferesi
Che diventano meglio
Programmabili, per maggiore
possibilita' di prevedere il giorno
di aferesi.

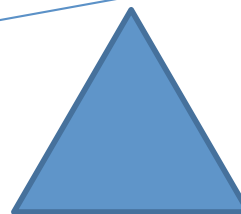
Conclusioni 1

SVANTAGGI

Costo del farmaco PLX
Da 3500 a 7500 euro a paz.
(Costi globali sono comunque
inferiori se si considera
La riduzione numero aferesi
E la riduzione delle complicanze)

Maggior numero di sacche
da criopreservare.

Per ottimizzare i costi
Consigliabile prima aferesi
Large volume (x3 VE).



Conclusioni 2

-- ESISTE LA **NECESSITA'** DI **CONFERME CON STUDI CONTROLLATI ED INDIPENDENTI SU:**

1. -- comparazione di **G-CSF + PLX versus G-CSF alone**
2. -- comparazione di **G-CSF + PLX versus CTX +G-CSF .**

però che siano:

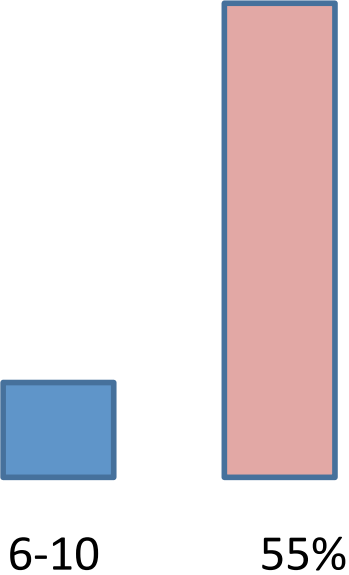
- Sufficientemente ampi e dimensionati sul fallimento di raccolta minima
- Che studino anche gli aspetti economici
- Abbiamo prefissati la modalita' di aferesi (Volume di sangue
- Abbiamo prefissati gli algoritmi decisionali per PLX.
- Abbiamo prefissato il target di raccolta.

Conclusioni 3

- **COME POSSIAMO FAR SI CHE LA MIGLIORE RIPRESA IMMUNITARIA DOPO TRAPIANTO BASATA SU CSE RACCOLTE CON PLX+G-CSF, MIGLIORI L'EFFICACIA DELLA TERAPIA ANTINEOPLASTICA ?**

GRAZIE DELLA ATTENZIONE

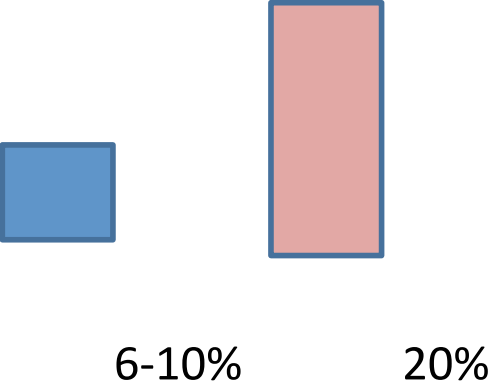
**G-CSF
alone**



G-CSF+PLX



CTX+G-CSF



Plerixafor mobilization leads to a lower ratio of CD34+ cells to total nucleated cells which results in greater storage costs

Yvette C. Tanhehco, MD PhD^{1,*}, Jill Adamski, MD PhD^{1,*}, Mary Sell, BS, MT(ASCP)¹,

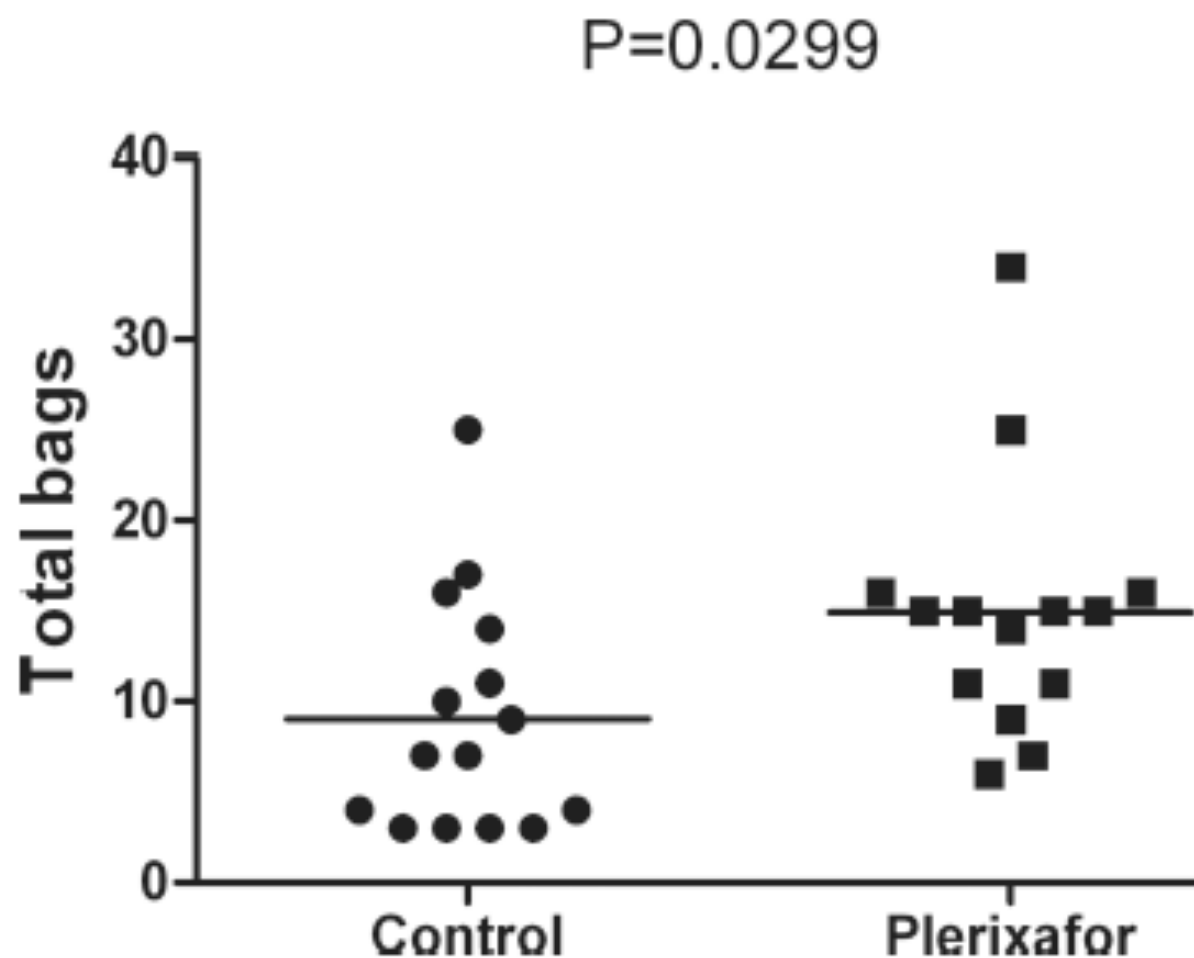
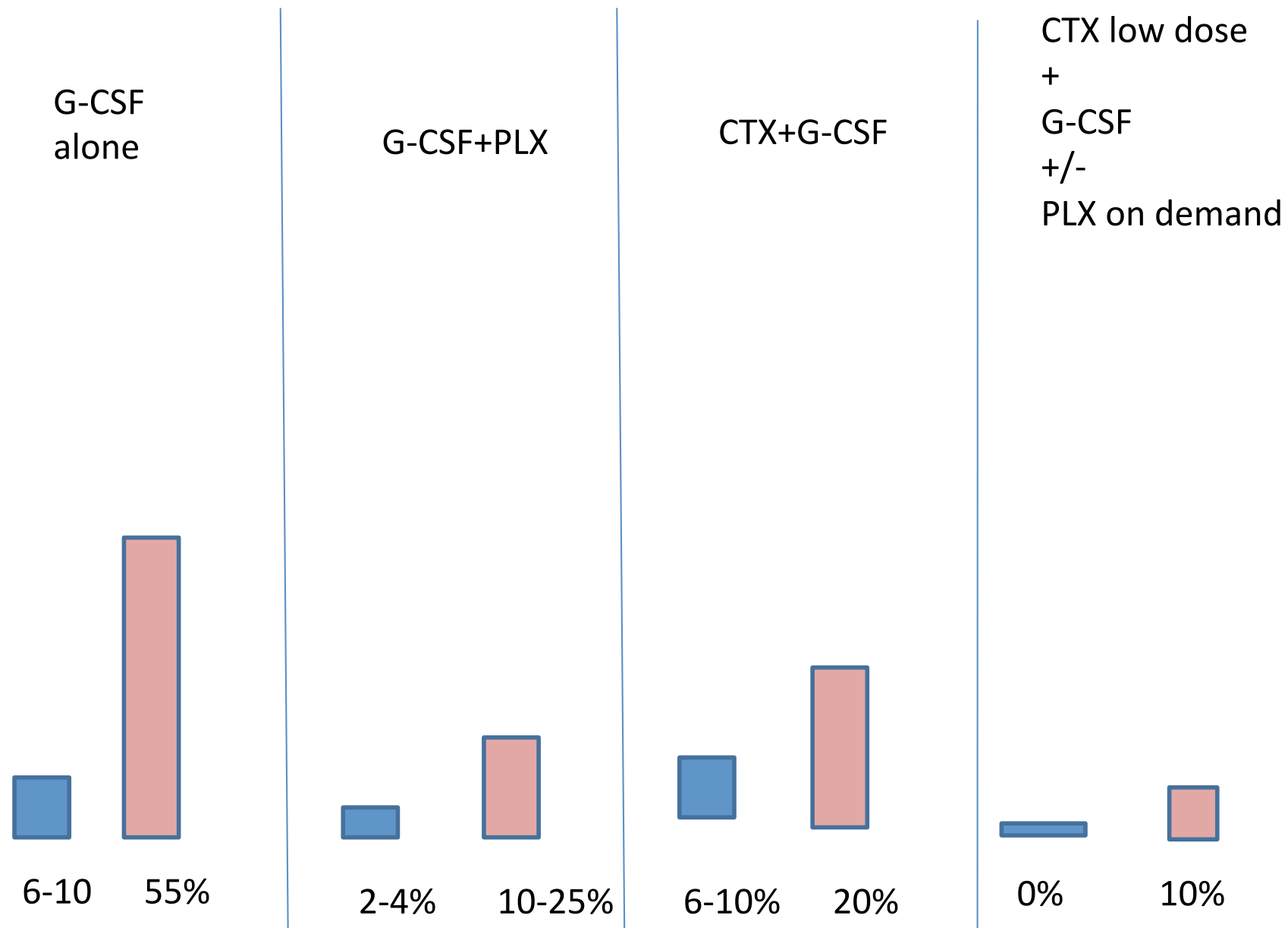


Figure 2. Plerixafor mobilization leads to increased storage bag requirements
Mean total storage bags per patient required in the control group (9 bags) was less compared to the plerixafor group (15 bags), (P=0.0299).



G-CSF
alone

G-CSF+PLX

CTX+G-CSF

CTX low dose
+
G-CSF
+/-
PLX on demand

6-10 55%

2-4% 10-25%

6-10% 20%

0% 10%

CONCLUSIONI RELATIVE AI COSTI:

- **L'aggiunta di PLX consente rispetto al G-CSF da solo di migliorare i risultati e cio' ad un costo (di farmaco) relativamente limitato (2500 euro circa a paziente quando on demand).**
- **Il G-CSF + PLX**
risulta avere dei costi economici globali che non sono dissimili rispetto a quelli della chemioterapia + G-CSF,
questo quando sono valutati non solo i costi dei farmaci ma anche i costi delle complicanze e dei giorni di degenza.
.

Conversely, CY use was associated with a high frequency of febrile neutropenia (60%), blood transfusions (27%; median number of transfusions=2), platelet transfusions (27%; median number of transfusions=1) and hospitalizations (64%; median days of hospitalization=4 days). None of the patients

ORIGINAL ARTICLE

G-CSF plus preemptive plerixafor vs hyperfractionated CY plus G-CSF for autologous stem cell mobilization in multiple myeloma: effectiveness, safety and cost analysis

A Antar¹, ZK Otrock², MA Kharfan-Dabaja³, HA Ghaddara¹, N Kreidieh⁴, R Mahfouz⁴ and A Bazarbachi¹

Table 2. Mobilization/apheresis outcomes

<i>Variables</i>	<i>CY arm (N= 56)</i>	<i>Plerixafor arm (N= 27)</i>
Peak peripheral blood CD34+ cell count, cells/ μ L; median	111.5 (21–575)	35 (5–141)
Total CD34+ cells $\times 10^6$ /kg collected, median (range)	15.5 (4.2–211)	7.5 (4–14.8)
Total number of apheresis sessions, median (range)	1 (1–2)	1 (1–2)
<i>N (%) patients collecting</i>		
$\geq 6 \times 10^6$ CD34+ cells/kg	54 (96%)	24 (88%)
$\geq 10 \times 10^6$ CD34+ cells/kg	40 (71%)	6 (22%)

on an established algorithm. Compared with plerixafor, CY use was associated with higher total CD34+ cell yield (7.5×10^6 vs 15.5×10^6 cells/kg, $P=0.005$). All patients in both groups yielded $\geq 4 \times 10^6$ CD34+ cells/kg. Conversely, CY use was associated with high frequency of febrile neutropenia, blood and platelet transfusions need and hospitalizations. The average total cost of mobilization in Lebanon was slightly higher in the plerixafor group (\$7886 vs \$7536; $P=0.16$). Our data indicate robust stem cell

Cost and Clinical Analysis of Autologous Hematopoietic Stem Cell Mobilization with G-CSF and Plerixafor Compared to G-CSF and Cyclophosphamide

Paul Shaughnessy,¹ Miguel Islas-Ohlmayer,¹ Julie Murphy,² Maureen Hougham,¹ Jill MacPherson,¹ Kurt Winkler,¹ Matthew Silva,³ Michael Steinberg,³ Jeffrey Matous,² Sheryl Selvey,³ Michael Maris,² Peter A. McSweeney²

Table 4. Mobilization and Apheresis Results

	Plerixafor/G-CSF n = 33	Chemo/G-CSF n = 33	P Value
Median total CD34 ⁺ cells × 10 ⁶ /kg, n (range)	10.7 (3.5-37.9)	11.6 (2.1-69.3)	.5
Number of patients collecting ≥2 × 10 ⁶ CD34 ⁺ cells/kg (%)	33 (100%)	33 (100%)	—
Number of patients collecting ≥5 × 10 ⁶ CD34 ⁺ cells/kg (%)	31 (94%)	25 (76%)	.04
Number of MM patients collecting ≥3 × 10 ⁶ CD 34 ⁺ cells/kg (%)	13/13 (100%)	11/13 (85%)	.14
Number of MM patients collecting ≥6 × 10 ⁶ CD 34 ⁺ cells/kg (%)	20/20 (100%)	18/20 (90%)	0.49
Median number of apheresis days (range)	1 (1-4)	1 (1-4)	.45
Number of patients initiating apheresis on scheduled day (%)	33 (100%)	29 (88%)	.04
Number of patients requiring weekend apheresis (%)	0	16 (48%)	≤.0001
Total number of weekend apheresis procedures	0	19	≤.0001

Chemo indicates chemotherapy (cyclophosphamide 3-5 g/m²); MM, multiple myeloma; NHL, non-Hodgkin lymphoma; G-CSF, granulocyte-colony stimulating factor.

ORIGINAL ARTICLE

Growth factor and patient-adapted use of plerixafor is superior to CY and growth factor for autologous hematopoietic stem cells mobilization

LJ Costa, AN Miller, ET Alexander, KR Hogan, M Shabbir, C Schaub and RK Stuart

algorithm dictates the use of plerixafor, starting on the fourth day of G-CSF mobilization, depending on PB-CD34⁺ and patient-specific T-CD34⁺. Patients

PB-CD34⁺ was checked. If PB-CD34⁺ exceeded a certain target-specific threshold (for example, threshold of 14 CD34⁺ per mm³ for T-CD34⁺ of 3×10^6 CD34⁺ per kg; threshold of 25 CD34⁺ per mm³ for T-CD34⁺ of 5×10^6 CD34⁺ per kg), apheresis was started immediately

PB-CD34⁺ equal or inferior to the target-specific threshold, daily plerixafor (at the dose of 240 µg/kg/day) was started in the evening of the fourth day of G-CSF and apheresis started in the following morning (day 5). Daily

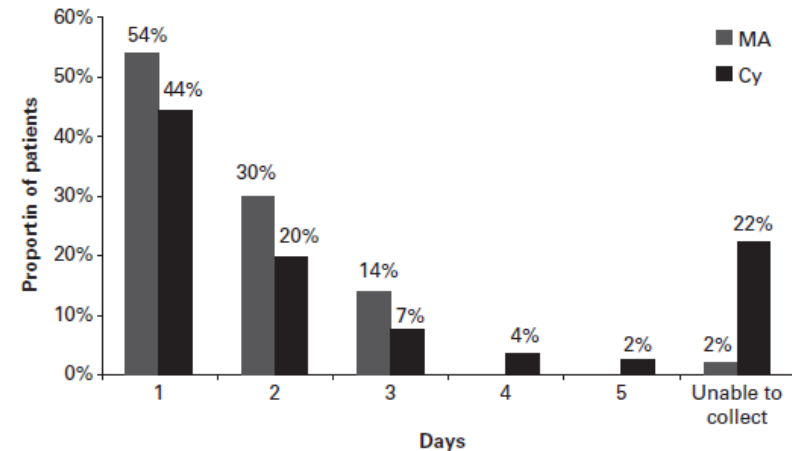


Figure 1 Distribution of number of apheresis day required to meet collection target in each cohort. Note that because there were patients in both cohorts who did not meet the collection target or did not start apheresis, the totals do not equal 100%.

cohort ($P = 0.01$). Fewer patients in the MA cohort than in the CY cohort had infectious complications during mobilization requiring hospitalization (2 vs 30%

The estimated average cost of mobilization per patient was US\$23 415.71 in the MA cohort and US\$22 884.79 in the CY cohort. However, because a higher proportion of

FAILURE RATE USING
CTX+G-CSF
IN PBSC MOBILIZATION (MM).

FAILURE RATE USING
G-CSF ALONE
IN PBSC MOBILIZATION (MM).

← **24% Di Persio 2009 (CD34 peak)**

← **19% Micallef 2012**

**Mob failure
Max 10%**

- Eta'
- Stato di malattia
- Pregresse linee trattamento
- Risorse aferetiche
- Parametro valutazione

10% Reggio Calabria

10% Monza

8.4% min harvest MUSTO

7% Pescara

5.7 % Catania: CD34 Peak

5.9 PUSIC

4% Firenze

6.7% Lee 2014

3% Moreau IFM 2005

**0
Mob failure
Min 5%**

TABLE 2. Flow cytometry analysis of the lymphocyte subsets of the cryopreserved grafts*

Blood graft content ($\times 10^6$ cells/kg)	Arm A (CY plus G-CSF), n = 17	Arm B (G-CSF), n = 19	p value†
CD3+	65.1 (28.3-283.0)	215.2 (50.4-683.6)	<0.001
CD3+CD4+	45.2 (12.6-156.4)	116.3 (29.4-502.5)	0.001
CD3+CD8+	23.1 (5.3-133.9)	90.5 (20.8-197.3)	0.001
CD19+	2.03 (0.46-11.6)	8.7 (0.3-76.7)	<0.001
NK	6.8 (0.9-36.1)	31.7 (15.5-144.7)	<0.001

* Data are reported as median (range).

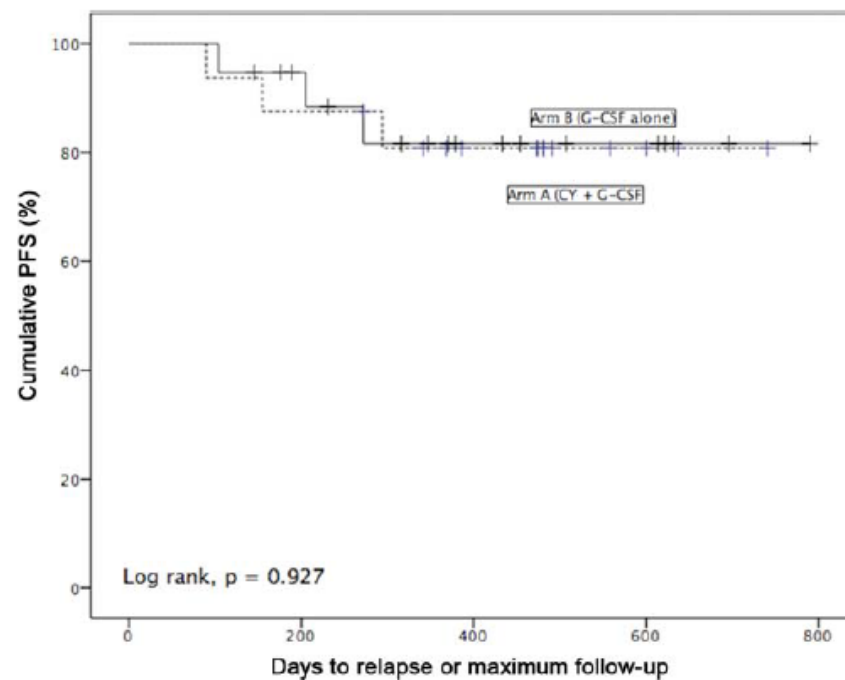
Blood flow cytometry 3 months after auto-SCT ($\times 10^9/L$)

CD3+	1.37 (0.29-2.61); 14	1.06 (0.37-2.95); 19	0.038
CD3+CD4+	0.35 (0.11-0.55); 14	0.32 (0.16-0.75); 19	0.358
CD3+CD8+	1.1 (0.17-2.1); 14	0.69 (0.22-2.42); 19	0.035
NK	0.17 (0.07-0.36); 14	0.25 (0.14-0.51); 19	0.005
CD19+	0.15 (0.0-0.38); 14	0.09 (0.05-0.29); 19	0.760

Blood graft cellular composition and posttransplant outcomes in myeloma patients mobilized with or without low-dose cyclophosphamide: a randomized comparison

Jaakko Valtola,¹ Raija Silvennoinen,² Antti Ropponen,³ Timo Siitonen,⁴ Marjaana Säily,⁴

1394 TRANSFUSION Volume 56, June 2016



A combination of granulocyte–colony-stimulating factor (G-CSF) and plerixafor mobilizes more primitive peripheral blood progenitor cells than G-CSF alone: results of a European phase II study

Stefan Fruehauf^{1,2}, Marlon Romano Veldwijk^{3,*}, Timon Seeger^{1,*}, Mario Schubert¹,

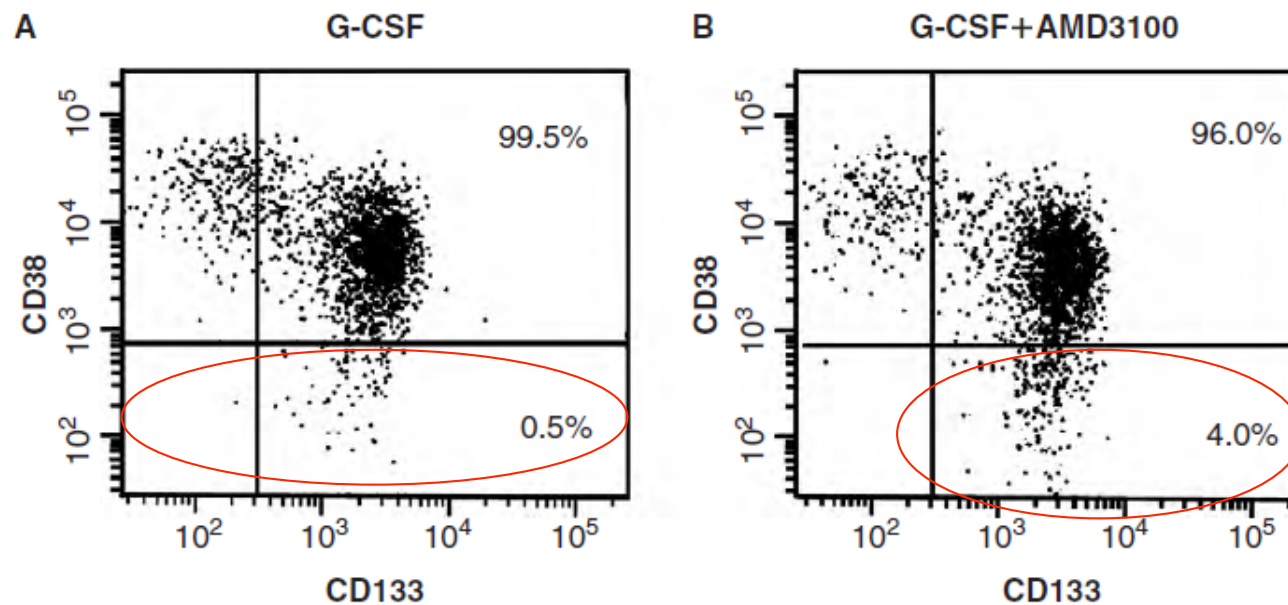


Figure 3. Differences in CD38 expression on CD34⁺ PBPC after G-CSF and G+A mobilization. Six-color FACS determination of primitive Ag expression on mobilized CD34⁺ PBPC at tp1 (A) and tp2 (B). In this representative plot, the CD34⁺ CD38⁻ subset significantly increased from 0.5% (A) to 4% following addition of AMD3100 to G-CSF mobilization (B). All cells co-expressed CD34⁺ and CD133⁺.

ORIGINAL ARTICLE

Upfront plerixafor plus G-CSF versus cyclophosphamide plus G-CSF for stem cell mobilization in multiple myeloma: efficacy and cost analysis study

S Afifi^{1,2}, NG Adel^{1,2}, S Devlin^{2,3}, E Duck^{2,4}, J Vanak^{2,4}, H Landau^{2,5,6}, DJ Chung^{2,5,6}, N Lendvai^{2,5,6}, A Lesokhin^{2,5,6}, N Korde^{2,5,6}, L Reich^{2,5,6}, O Landgren^{2,5,6}, S Giral^{2,5,6} and H Hassoun^{2,5,6}**Table 5.** Average Medicare reimbursement

	Plerixafor + G-CSF (n = 112)	Cyclophosphamide + G-CSF (n = 111)
Apheresis	4800.53	5224.47
<i>Laboratory before mobilization</i>		
INR/PT/PTT	14.06	14.06
CBC/CMP/magnesium/urine analysis/EKG	—	66.73
<i>Mobilization drug reimbursement</i>		
Plerixafor 0.24 mg/kg	11 163.18	—
Cyclophosphamide 3 g/m ²	—	1384.02
G-CSF 10 mcg/kg	4351.51	8594.84
Other drugs/IV drug administration/hydration	—	821.83
Subtotal average reimbursement for upfront mobilization	20 329.28	16 105.96
Reimbursement for hospitalization due to complications (per patient) ^a	—	1802.41 (n = 13)
Reimbursement for salvage mobilization (per patient) ^a	814.47 (n = 5)	5050.16 (n = 20)

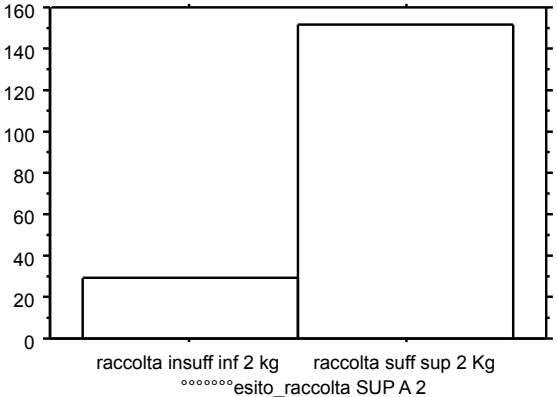
Table 3. Stem cell mobilization outcomes

	Plerixafor + G-CSF (n = 112)	Cyclophosphamide + G-CSF (n = 111)
Mean no. of apheresis (s.d.)	2.3 (1.1)	2.6 (1.6)
Mean G-CSF doses (s.d.)	6.3 (1.1)	12.5 (2.3)
Median CD34+ cells/kg collected after first mobilization (range)	11.4 × 10 ⁶ (0–34.5)	10.9 × 10 ⁶ (0–45.0)
Number of patients with successful yield after first mobilization, (%) (yield ≥ 5 × 10 ⁶ cells/kg)	105 (94%)	92 (83%)

Percents of Column Totals for ***esito_raccolta SUP A 2, GRUPPI**
Inclusion criteria: controllo+on demand 2 from OTTOBRE 2015 PLX on Demand 1+2.svd

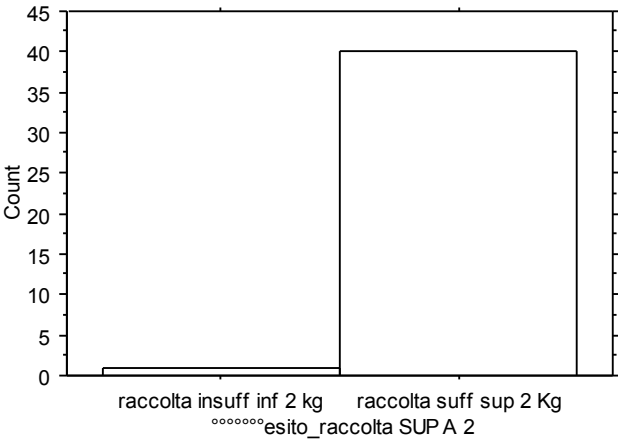
	controllo	prospettico on demand 2	Totals
raccolta insuff inf 2 kg	16.022	2.439	13.514
raccolta suff sup 2 Kg	83.978	97.561	86.486
Totals	100.000	100.000	100.000

Histogram
 Split By: GRUPPI
 Cell: controllo
 Inclusion criteria: controllo+on demand 2 from OTTOBRE 2015 PLX on Demand 1+2.svd



P=0-02

Histogram
 Split By: GRUPPI
 Cell: prospettico on demand 2
 Inclusion criteria: controllo+on demand 2 from OTTOBRE 2015 PLX on Demand 1+2.svd



Descriptive Statistics

Split By: GRUPPI

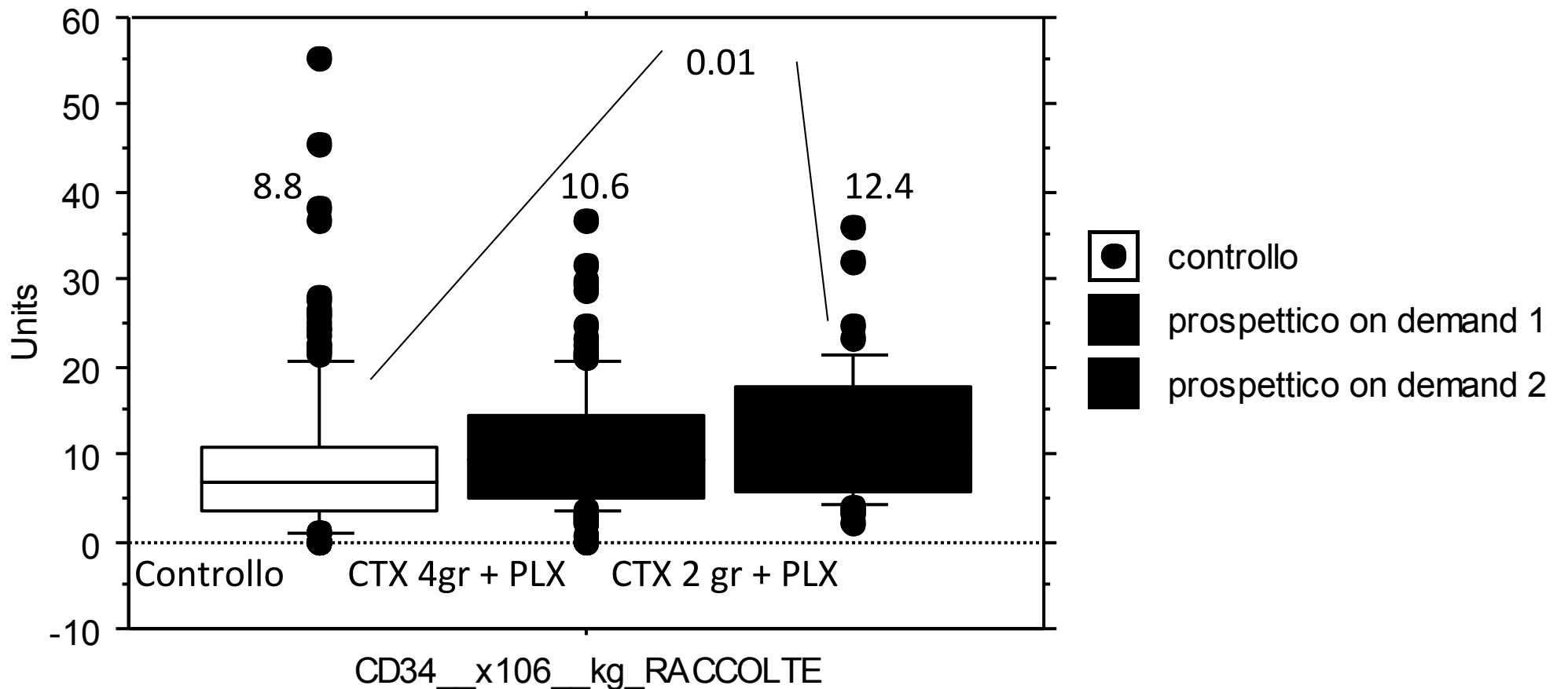
Inclusion criteria: CONTROLLO ON DEM1 ONDEM 2 from OTTOBRE 2015 PLX on Demand 1+2.svd

	CD34__x106__kg_RACCOLTE, Total	CD34__x106__kg_RACCOLTE, controllo	CD34__x106__kg_RACCOLTE, prospettico on demand 1	CD34__x106__kg_RACCOLTE, prospettico on demand 2
Mean	9.919	8.836	10.636	12.476
Std. Dev.	7.986	8.451	7.128	7.736
Std. Error	.427	.628	.632	1.208
Count	349	181	127	41
Minimum	0.000	0.000	0.000	1.850
Maximum	55.320	55.320	36.500	36.000
# Missing	0	0	0	0

Box Plot

Split By: GRUPPI

Inclusion criteria: CONTROLLO ON DEM1 ONDEM 2 from OTTOBRE 2015 PLX on Demand 1+2.svd



Percents of Column Totals for ^^^^^^^^^^^CD34 in due e 4, GRUPPI

Inclusion criteria: CONTROLLO ON DEM1 ONDEM 2 from OTTOBRE 2015 PLX on Demand 1+2.svd

	controllo	prospettico on demand 1	prospettico on demand 2	Totals
below 4×10^6 /Kg	29.834	16.535	9.756	22.636
over 4×10^6 7Kg	70.166	83.465	90.244	77.364
Totals	100.000	100.000	100.000	100.000

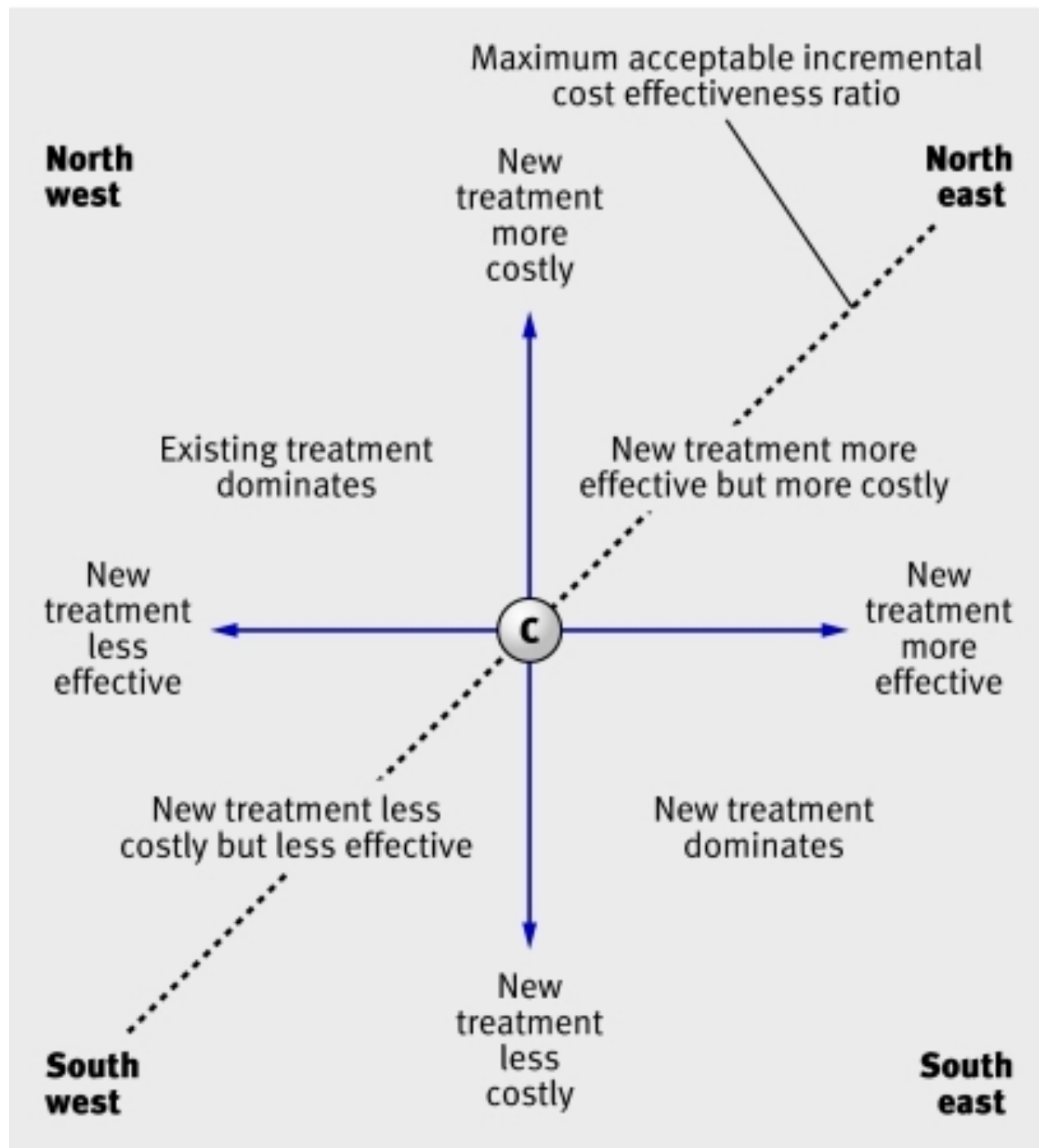
Fisher test: 0.009

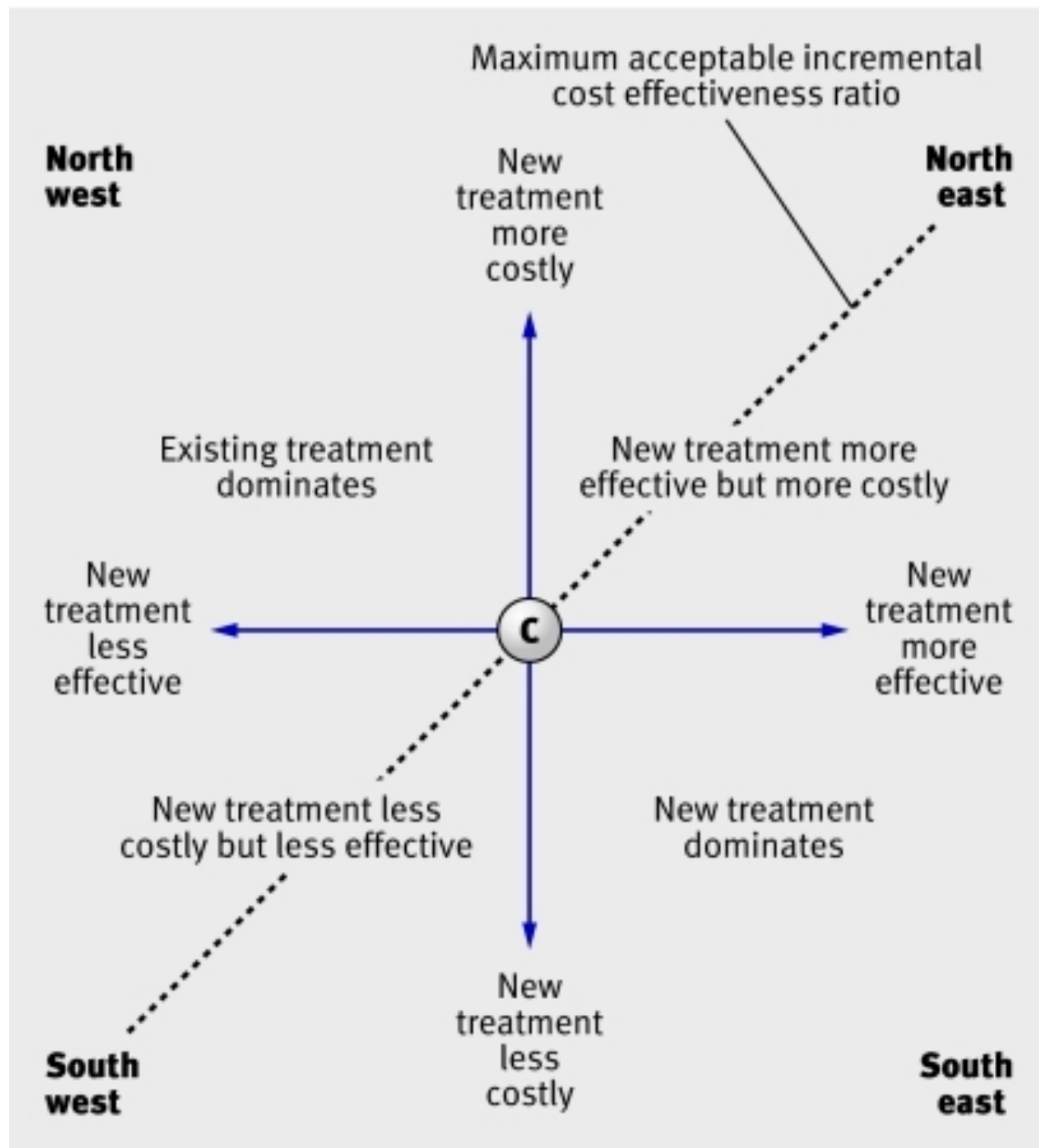
Frequency Distribution for numero_di_aferesi

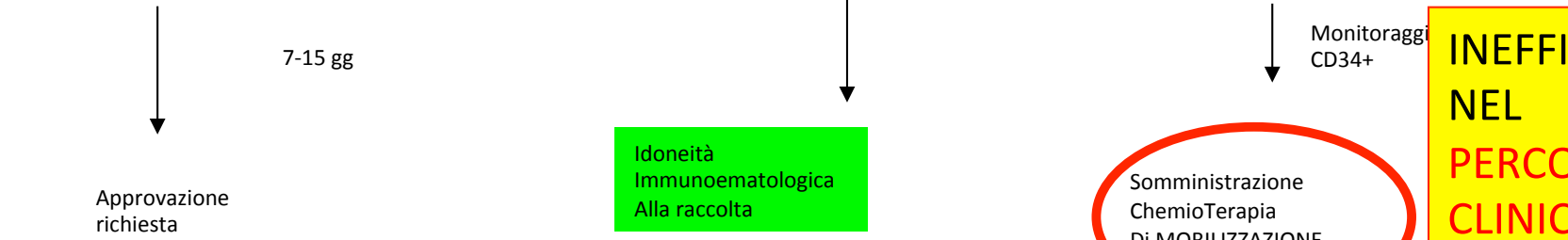
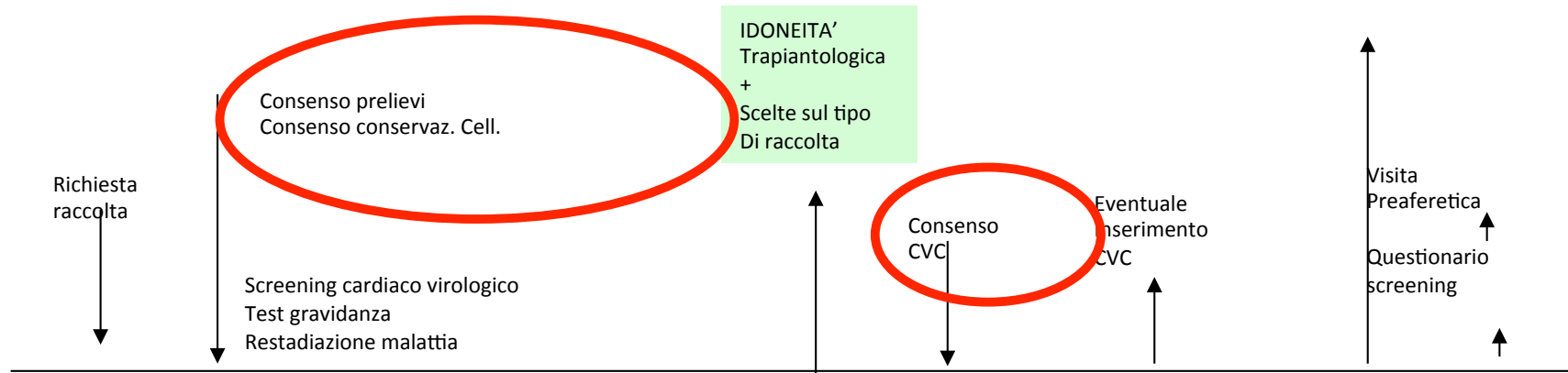
Split By: GRUPPI

Inclusion criteria: CONTROLLO ON DEM1 ONDEM 2 from OTTOBRE 2015 PLX on Demand 1+2.svd

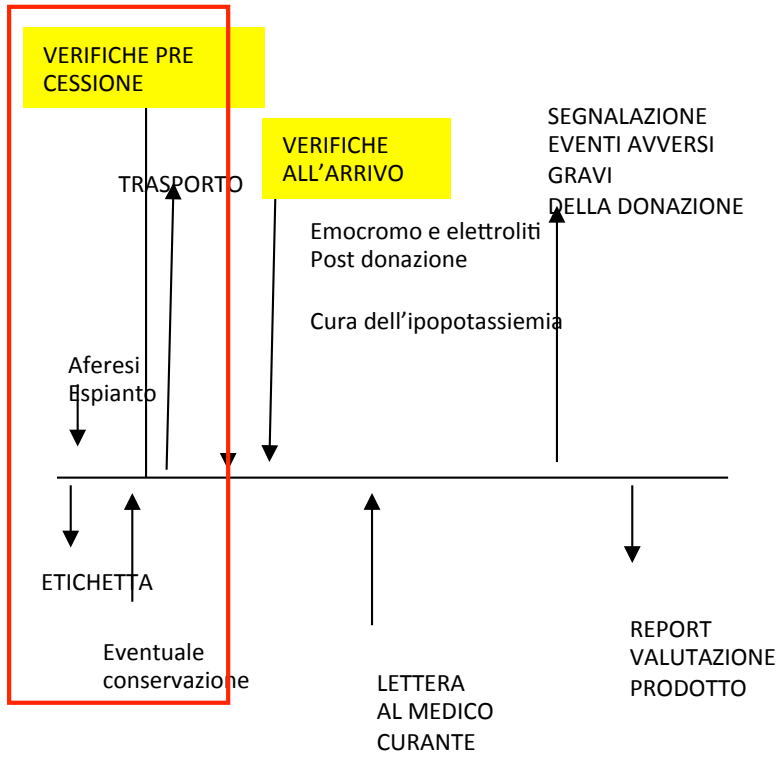
	Total Percent	controllo Percent	prospettico on demand 1 Percent	prospettico on demand 2 Percent
0	5.158	8.287	2.362	0.000
1	63.037	65.193	51.181	90.244
2	22.923	19.337	33.858	4.878
3	6.590	5.525	9.449	2.439
4	1.433	1.105	2.362	0.000
5	.860	.552	.787	2.439
Total	100.000	100.000	100.000	100.000







**INEFFICENZA
NEL
PERCORSO
CLINICO
"RACCOLTA
AFERETICA"**



NONOSTANTE IL PROCESSO MOBILIZZAZIONE E RACCOLTA AFERETICA SIA COMPLESSO RARAMENTE E' SOTTOPOSTO ALLA FORMALE IDENTIFICAZIONE DI UN "percorso diagnostico-terapeutico" e Viene lasciato alla collaborazione "spontanea" fra Ematologi e trasfusionisti.

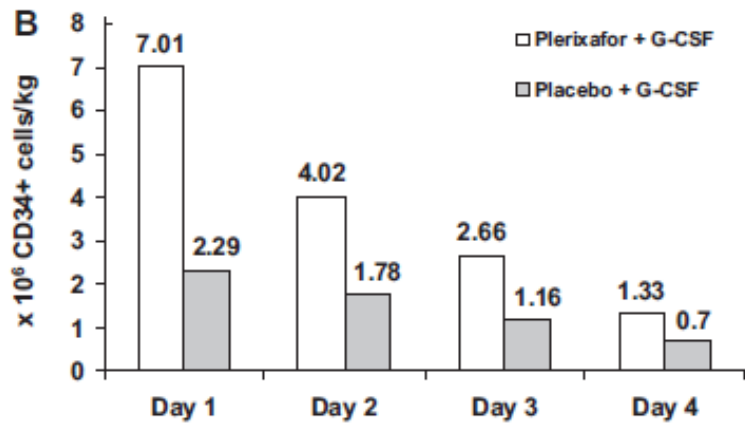
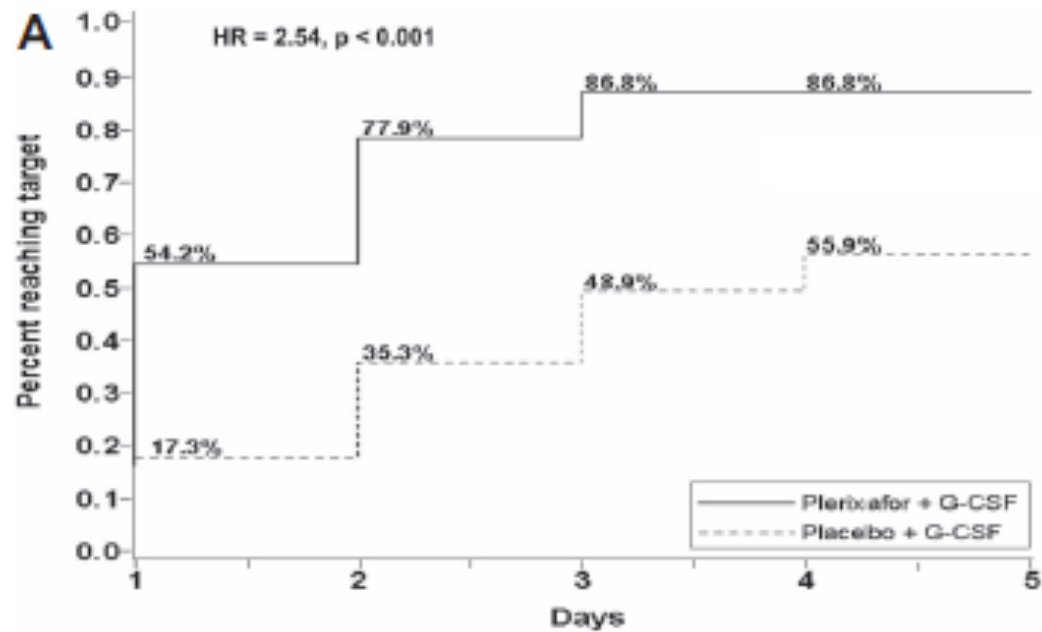


Figure 3. Kinetics of CD34/kg collection. (A) Kaplan-Meier estimate of proportion of patients reaching 6×10^6 or more CD34⁺ cells/kg. (B) Median CD34⁺ cells collected on each apheresis day.



CONCLUSIONI:

La mancanza di definizione nel processo della mobilizzazione E Raccolta delle CSE comporta inefficienze non trascurabili e sembra essere la causa dei differenti Risultati fra i vari centri.

Anche le risorse aferetiche disponibili costituiscono un fattore limitante nella Efficienza del processo.

Il Plerixafor quando impiegato on demand sulla base di algoritmi validati consente di migliorare i risultati della mobilizzazione standard del MM (CTX 4 gr) e cio' senza aggravii dei costi complessivi per paziente e con un rapporto costo/beneficio di tipo accettabile.

Ipotizziamo che l'utilizzo PLX on demand + CTX 2 gr/m² + G-CSF Possa rendere il PLX on demand ancora piu' vantaggioso nei confronti della mobilizzazione standard nel MM (CTX 4gr).

G-CSF +PLX versus G-CSF ALONE NEL MM

1) ALGORITMO SOLO SU CD34 ?

1) FALLIMENTI

MOBILIZZAZIONE (da 0 a 6,0%) (Pusic e)

1) RISORSE AFERETICHE NECESSARIE

3) COSTI E ICER

1) RICOVERI PER TERAPIA E COMPLICANZE

2) NON NEUTROPENIA FEBBRILE

	Successful mobilized / all patients	Successful harvested / all patients	Successful harvest / successful mobilized	INEFFICIENCY Number of patients “ Successfully mobilized and not successfully harvested ” / “ successful mobilized patients ”
Center 1	99/105 (94.2%)	85/105 (80.9)	84/99 (84.8%)	15/99 (15.2%)
Center 2	45/48 (93.7%)	46/48 (95.8%)	45/45 (100%)	0/45 (0%)
Center 3	25/28 (89.2%)	23/28 (82.1)	22/25 (88%)	3/25 (12%)
TOTAL	169/181 (93.3%)	154/181 (85.0)	151/169 (89.3%)	18/169 (10.7%)

USE OF PLX ON DEMAND HALVES PERCENTAGE OF POOR MOBILIZER IN MYELOMA

6-10% of patients

PUSIC	poor harvest	5.9%
PUSIC	poor harvest	6.2%
MILONE	poor mobilizers	6.7%
WUCHTER	poor mobilizer	14.0%

Management of poor peripheral blood stem cell mobilization: Incidence, predictive factors, alternative strategies and outcome. A retrospective analysis on 2177 patients from three major Italian institutions [☆]

Paolo Perseghin ^{a,*}, Elisabetta Terruzzi ^b, Maria Dassi ^a, Valentina Baldini ^a, Matteo Parma ^b,

ANCHE DOPO CTX+G-CSF NEL MM, LE FALLITE MOBILIZZAZIONI SONO IN MEDIA IL 7%

Diseases	Monza (99-07)		INT Milan (02-07)		Pescara (00-07)	
	n	<20 ^a (%)	n	<20 ^a (%)	n	<20 ^a (%)
MM	151	15 (10)	15	1 (5)	160	11 (7)

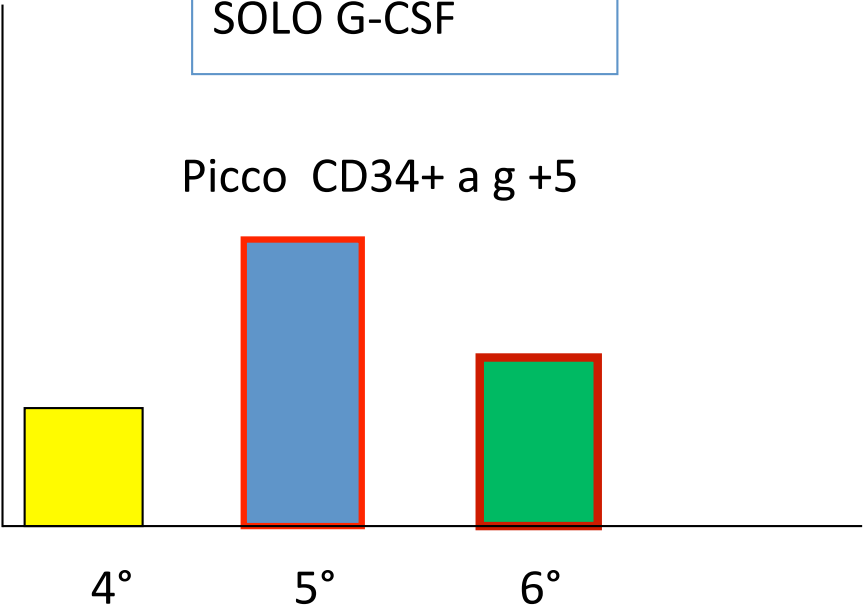
Un Gruppo Italiano (Italia Nord e Centrale) ha misurato il tasso di FALLIMENTI NELLA MOBILIZZAZIONE NEL MM (< 20 CD34+ nel SP) ottenendo un fallimento nel 5-10% dei pazienti (tot pazienti: 326)

**G-CSF + PLX gg
al 4° e 5° giorno**

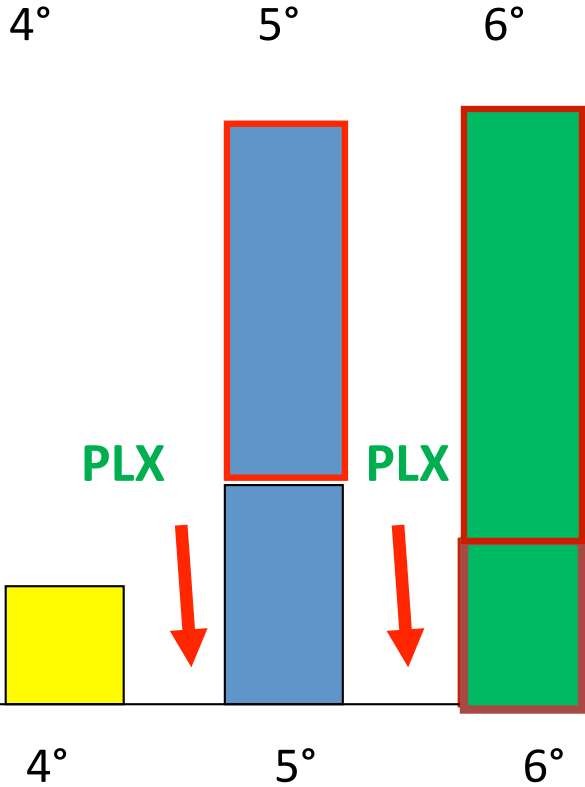
CD 34+

SOLO G-CSF

Picco CD34+ a g +5



CD 34+



SCHEMA PLX + G-CSF

Risk adapted (JUST IN TIME) or On demand”

Sulla base di dati a +4.

PLX sera del 4° gg se CD34 < 5-15

< 20-25 (se target doppio Tx)

COMPARAZIONE G-CSF ALONE versus CTX+G-CSF NEI PAZIENTI AFFETTI DA LINFOMA

Bone Marrow Transplantation (2003) 31, 747-754
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www.nature.com/bmt

Progenitor Cell Mobilization

G-CSF Alone vs cyclophosphamide plus G-CSF in PBPC mobilization of patients with lymphoma: results depend on degree of previous pretreatment

G Milone, S Leotta, F Indelicato, S Mercurio, G Moschetti, F Di Raimondo, A Tornello, U Consoli, G Guido and R Giustolisi

	<i>Pts pretreated with ≤ 2 lines of chemotherapy</i>		
	<i>G-CSF alone</i>	<i>CTX G-CSF</i>	<i>P</i>
CD34+ Peak in P.B. ($\times 10^6/l$)			
mean (range)	44.3 (8-159)	48.8 (2.0-151)	0.73
median	49	33	
Patients successfully mobilized (%)	68	64	>0.8

	CENTER 1	CENTER 2	CENTER 3	P	OVERALL	
FAILURE OF CD34+ CELL MOBILIZATION	5.7% (n.6)	6.2% (n.3)	10.7% (n.3)	<i>NS</i>	6.7%	
SUCCESSFUL CD34 + CELL MOBILIZATION	94.3% (n.99)	93.8% (n.45)	89.3 (n.25)	<i>NS</i>	93.3%	
PEAK OF CD34+ CELLS IN PB (x10⁶/L)	144.6	193.4	110.3	<i>NS</i>	150.6	
<p>MEDIA FALLIMENTI DELLA MOBILIZZAZIONE DOPO CTX 4 gr +G-CSF: 7%</p> <p>STUDIO RETROSPETTIVO CONDOTTO IN Italia Centro-Meridionale (n 181 pts).</p>						

RESULTS

Dichotomous Endpoint, Two Independent Sample Study

Sample Size	
Group 1	194
Group 2	194
Total	388

Study Parameters	
Incidence, group 1	10%
Incidence, group 2	3% 70% dec
Alpha	0.05
Beta	0.2
Power	0.8

[✎ View Power Calculations](#)



Phase I Trial of Parathyroid Hormone to Facilitate Stem Cell Mobilization

*Karen K. Ballen,¹ Elizabeth J. Sbpall,⁴ David Avigan,³ Beow Y. Yeap,¹ David C. Fisher,²
Kathleen McDermott,² Bimalangsbu R. Dey,¹ Eyal Attar,¹ Steven McAfee,¹ Marina Konopleva,⁴
Joseph H. Antin,² Thomas R. Spitzer¹*

PTH GIORNO 1-14

G-CSF GIORNI 10-14

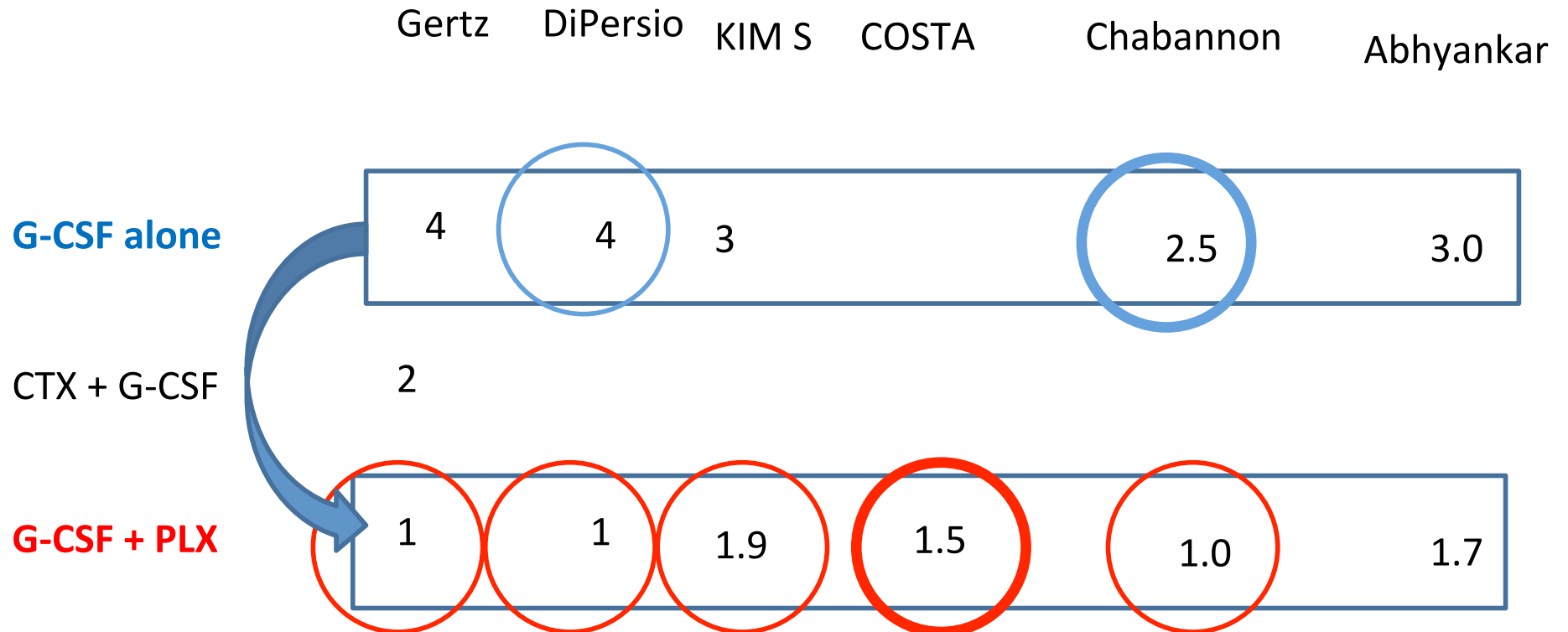
Nine of the 20 subjects previous mobilization failure
(one or two attempt) after PTH+G-CSF met
the mobilization criteria
(> 5 CD34 cells/microL) on day 14 of treatment.

40% success rate

RESOURCE UTILIZATION USING **G-CSF ALONE OR G-CSF+PLX**
IN PBSC MOBILIZATION (MM).

3

Median number of apheresis



Plerixafor and G-CSF versus placebo and G-CSF to mobilize hematopoietic stem cells for autologous stem cell transplantation in patients with multiple myeloma

John F. DiPersio,¹ Edward A. Stadtmauer,² Ausyorn Nademanee,³ Ivana N. M. Micallot,⁴ Patrick J. Stiff,⁵ Jonathan L. Kaufman,⁶ Richard T. Maziarz,⁷ Chitra Hosing,⁸ Stefan Fröhling,⁹ Mitchell Horwitz,¹⁰ Dennis Cooper,¹¹ Gary Bridger,¹² and Gary Calandra,¹² for the 3102 Investigators

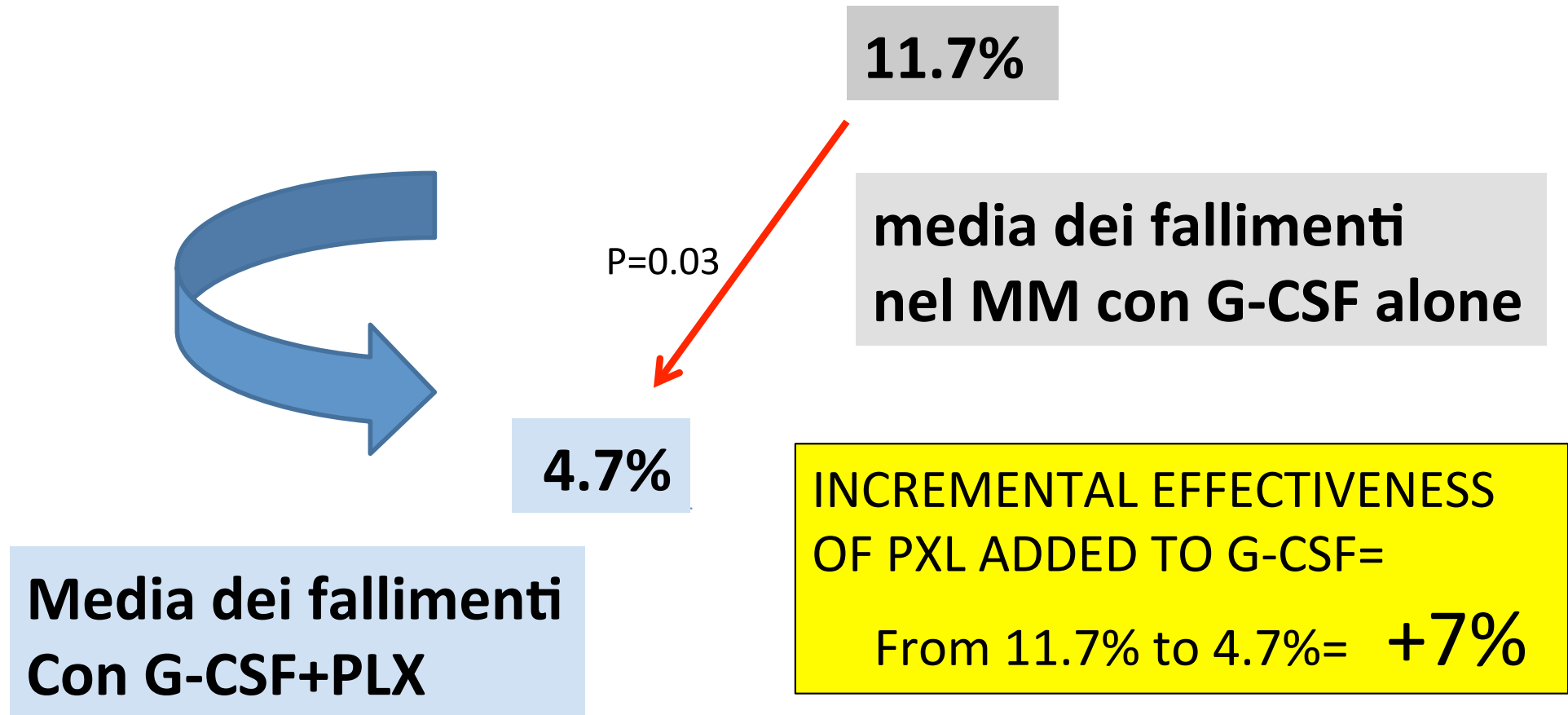
G-CSF + PLX UNIVERSAL:

DOPO G-CSF alone solo il 30% raccoglie per due trapianti in max 2 aferesi, questa quota puo essere migliorata di almeno il 20% con G-CSF+PLX ??

primary efficacy endpoint was the proportion of patients collecting more than or equal to 6×10^6 CD34 cells/kg in 2 or fewer apheresis days.

PLX UP FRONT

IMPROVEMENT IN USING **G-CSF+PLX OVER G-CSF ALONE**
IN FAILURE RATE PBSC MOBILIZATION (MM).



**Fallimento dopo CTX:
12.3%**

Predicting poor peripheral blood stem cell collection in patients with multiple myeloma

**75 % RACCOGLIE PER
2 AUTO-TRAPIANTI**

Table 2 Distribution of failure, suboptimal and optimal collections in the whole population

Parameters	Failure Number (%)	Sub-Optimal Number (%)	Optimal Number (%)
Whole population Outcome	167 (12.39)	113 (8.38)	1068 (79.23)

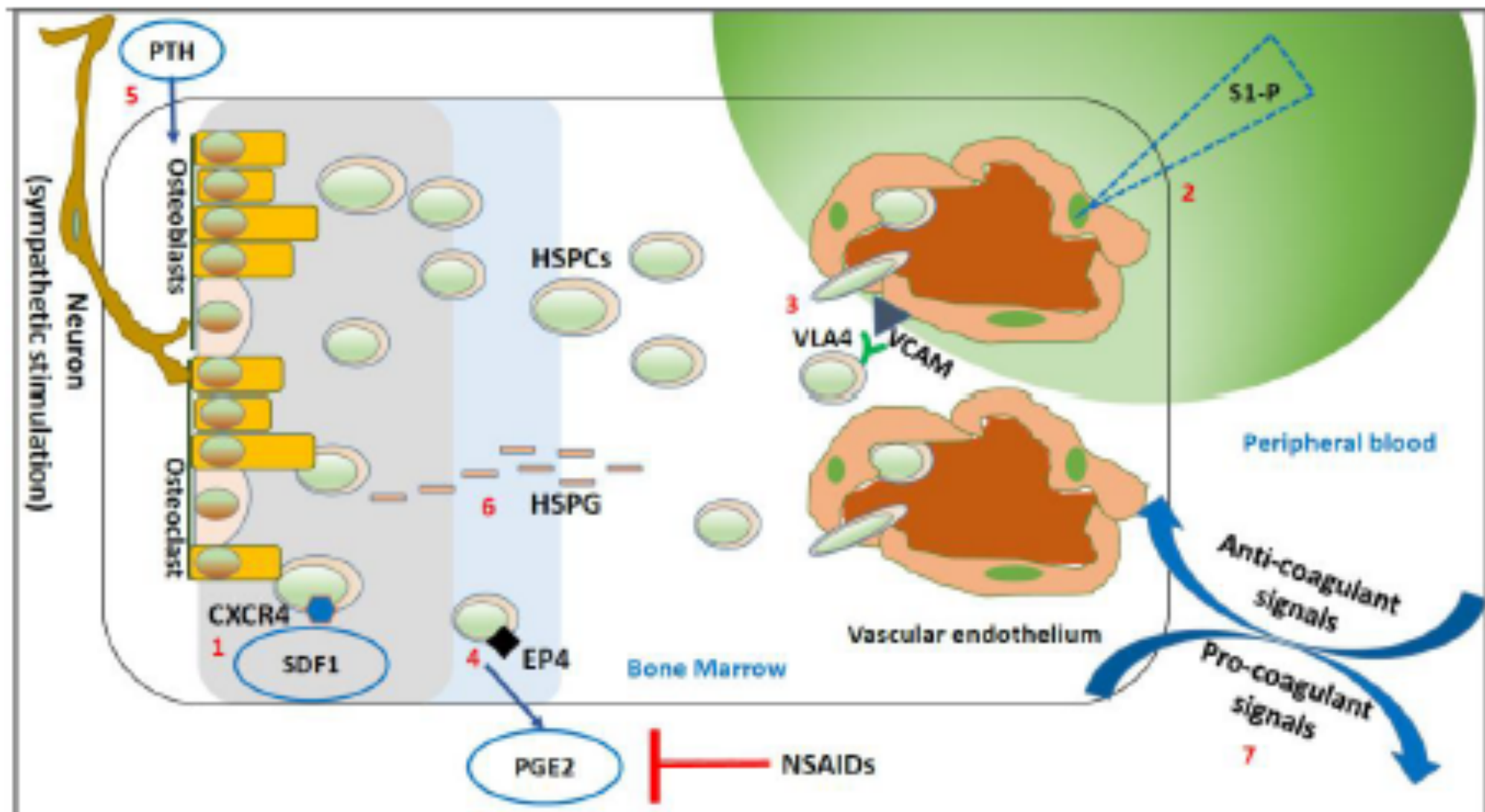


Figure 2: Novel niche pathways in HSPC mobilization. 1. CXCR4 receptors on HSCs interact with chemokine SDF-1. A disruption in this interaction causes mobilization (as modulated by G-CSF and plerixafor). Conversely, the S1P gradient draws HSCs peripherally. Hence S1P agonists are hypothesized to cause mobilization. 3. Integrin receptor, VLA4 on HSCs interacts with VCAM1 on niche vascular endothelial cells. VLA4 antagonists mediate mobilization. 4. NSAIDs block PGE2-EP4 interactions, to induce mobilization with G-CSF. PTH agonists (5), Antagonists of endogenous HSPG (6) and nitric oxide inhibitors activating niche are essential pathways (7) regulate HSC mobilization pathway.