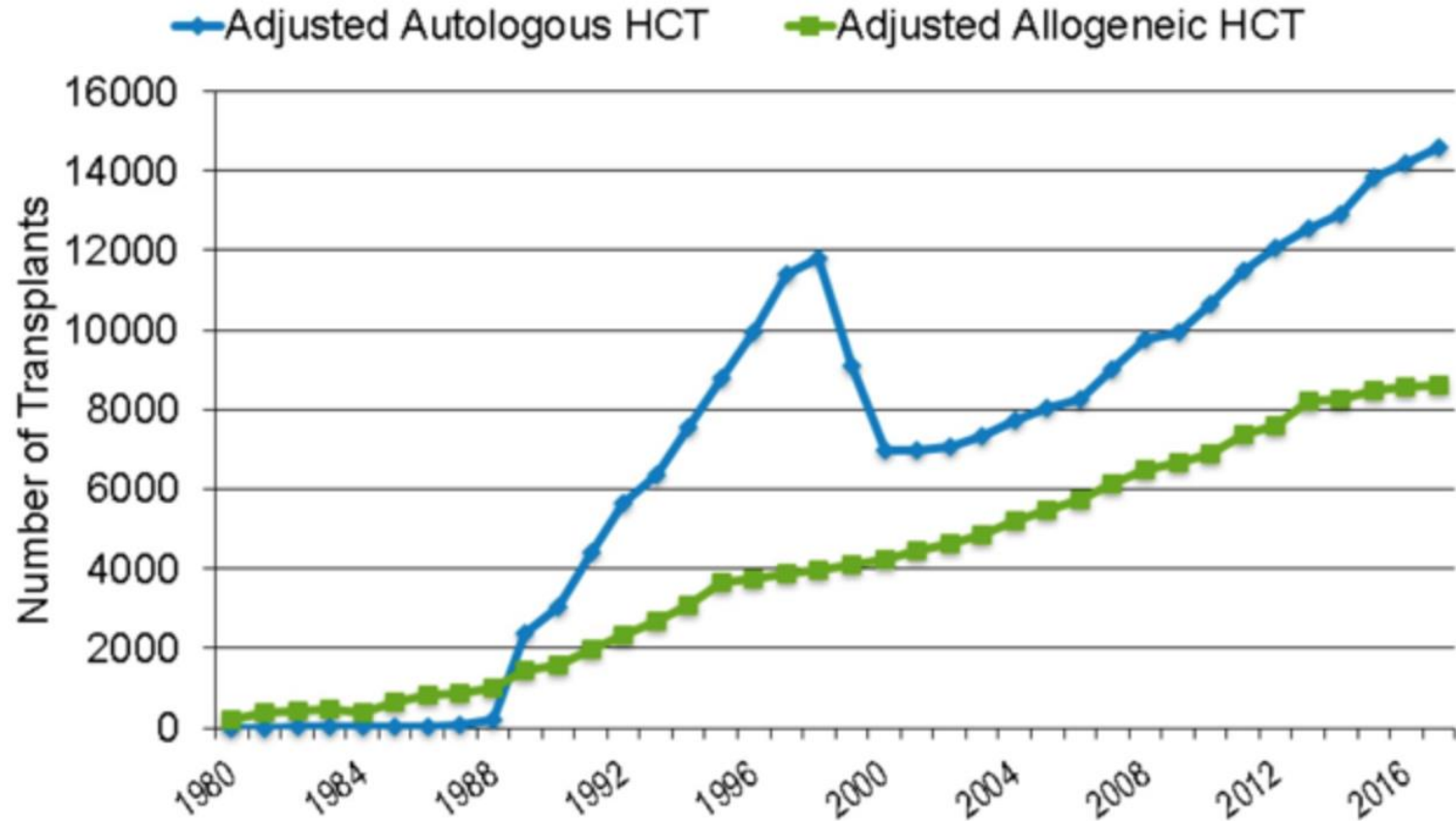


PKH Mobilizasyonunda Stratejilerin Savaşı:  
Plerixafor'un Akılcı Kullanımı  
***“Pre-emptive”***

Ozan Salim  
Akdeniz Üniversitesi, Antalya

14. Ulusal Aferez Kongresi, 23 Kasım 2019, İstanbul

# Transplant tipine göre yıllara göre veriler (CIBMTR- 2018)



## Tek OKHN için gerekli CD34<sup>+</sup> Hücre Miktarı

CD34 <sup>+</sup> Cell Dose	Possible Clinical Outcome
$> 3-5 \times 10^6/\text{kg}$	Optimal dose for a single transplant
$\geq 2 \times 10^6/\text{kg}$	Minimum dose, although a higher dose would be better for patients with lymphoma
$1.5-2 \times 10^6/\text{kg}$	Associated with delayed engraftment
$\leq 1 \times 10^6/\text{kg}$	Greater risk of erythrocyte transfusion and graft failure

# KH mobilizasyonunu etkileyen değişkenler

- Hasta popülasyonunda farklılıklar
- Farklı kemoterapi uygulamaları
- Cihaz veya teknik farklılıklar
- Farklı araştırma protokolleri
- Uygulayıcılar arası farklılıklar
- Hasta toleransı

# “Mobilizasyon başarısızlığı”nın tanımlanmasındaki farklılıklar

- “Mobilizasyon başarısızlığı” tanımında ve mobilizasyon uygulamalarında belirgin farklılıklar vardır
  - Hedef hücre sayısı farklı şekilde tanımlanabilir (optimal sayı)
    - **IMWG**: min.  $4 \times 10^6$  CD34<sup>+</sup> cells/kg, average **8-10**  $\times 10^6$  CD34<sup>+</sup> cells/kg
    - **ASBMT**: min.  $2 \times 10^6$  CD34<sup>+</sup> cells/kg (single ASCT), **> 5**  $\times 10^6$  CD34<sup>+</sup> cells/kg
  - Periferel kan CD34<sup>+</sup> miktarı 10 hücre/ $\mu$ l’nin altında olan hastalar genellikle afereze gitmediklerinden başarısızlık olarak sayılmayabilirler

# Periferik Kök Hücre mobilizasyonunda en sık kullanılan ajanlar

## -Hematopoetik büyüme faktörleri

- G-CSF + GM-CSF
- Pegfilgrastim

## -Kemoterapi+ G-CSF

- Kemo-mobilizasyon ile tek başına BF kullanımından daha fazla PKH verimi sonucu alınabilir.
- hastaların büyük yüzdesinde FEN ve yüksek oranda hastane yatışı

# Hematopoetik büyüme faktörleri ile mobilizasyonunun **avantajları**

- Mobilizasyon için tahmin edilebilir kinetikler
- Kemo-mobilizasyon ile karşılaştırıldığında düşük toksisite ve kaynak kullanımı
- Hastane yatış ve transfüzyona ihtiyaç duymama
- Uygulayıcı için kolaylık

# Kemoterapi temelli mobilizasyonun dezavantajları

- İnfeksiyon riski
- Kemomobilizasyon ve CD34+ hücre piki arasındaki geçen süre tahmin edilemez<sup>1,3</sup>
- Aferez başlatma kriteri çeşitlidir<sup>2,3,4,5,6</sup>
- Hastaneye yatış ihtiyacı
- Transfüzyon desteği ihtiyacı
- Artan maliyetler

<sup>1</sup>Hicks ML, ve ark. *Transfusion*. 2007;47(4):629-635; <sup>2</sup>Desikan KR, ve ark. *J Clin Oncol*. 1998;16(4):1547-1553; <sup>3</sup>Bargetzi MJ, ve ark. *Bone Marrow Transplant*. 2003;31(2):99-103; <sup>4</sup>Humpe A, ve ark. *Transfusion*. 2000; 40(11):1363-1370; <sup>5</sup>Venditti A, ve ark. *Bone Marrow Transplant*. 1999;24(9):1019-1027; <sup>6</sup>Arora M, ve ark. *Biol Blood Marrow Transplant*. 2004;10(6):395-404.



**Systematic Review of Randomized Controlled Trials  
of Hematopoietic Stem Cell Mobilization Strategies  
for Autologous Transplantation for  
Hematologic Malignancies**

*Dawn Sheppard, Christopher Bredeson, David Allan, Jason Tay*

- “... kemo-mobilizasyon ile görülen en yaygın advers olay febril nötropeni olup çalışmaların %43’ünde bildirilmiştir...”
- “Kemoterapinin kullanıldığı çalışmalarda, hastaların hastaneye başvurma oranı %20-48 aralığındadır”

# Periferik Kök Hücre mobilizasyonunda en sık kullanılan ajanlar

## -Hematopoetik büyüme faktörleri

- G-CSF + GM-CSF
- Pegfilgrastim

## -Kemoterapi+ G-CSF

- Kemo-mobilizasyon ile tek başına BF kullanımından daha fazla PKH verimi sonucu alınabilir.
- hastaların büyük yüzdesinde FEN ve yüksek oranda hastane yatışı

## -Plerixafor + G-CSF

- kemoterapi kadar etkili olabilir
- “just in time” “on demand” “pre emptive” olarak kullanımı etkili ve uygun maliyetli görünmekte

## Predictive factors for stem cell mobilization failure in multiple myeloma patients: A single center experience

Hakan Goker<sup>a,\*</sup>, Rafiye Ciftciler<sup>a</sup>, Haluk Demiroglu<sup>a</sup>, Mehmet Turgut<sup>b</sup>, Nilgun Sayinalp<sup>a</sup>, I.C. Haznedaroglu<sup>a</sup>, Mufide Okay<sup>a</sup>, Fatma Tekin<sup>a</sup>, Yahya Buyukasik<sup>a</sup>

<sup>a</sup> Hacettepe University, School of Medicine, Department of Hematology, Ankara, Turkey

<sup>b</sup> Ondokuz Mayıs University, Dept of Hematology, Samsun, Turkey

209/234 hastada ilk mobilizasyonda başarı oranı:  
**89.3%**

# Remobilizasyon

## Birinci Aşama Mobilizasyon

İlk Mobilizasyon  
Başarısızlığı:  
Remobilizasyona girmiş  
(n = 269)

Remobilizasyona giren her bir hasta için ilk mobilizasyonda gözlenen ortalama verim  
Ortalama aferez günü

$$0.83 \times 10^5 \text{ CD34/kg}_3$$

$$1.09 \times 10^6 \text{ CD34/kg}_4$$

$$1.03 \times 10^6 \text{ CD34/kg}_{2.5}$$

## İkinci Aşama Remobilizasyon

Kemo (n = 34)

G-CSF/GM-CSF (n = 217)

Plerixafor (n = 18)

Ortalama CD34 verimi  
Ortalama aferez günü

$$0.88 \times 10^5_2$$

$$1.22 \times 10^6$$

$$4.64 \times 10^6_{2.5}$$

**Başarısızlık Oranı**

**%73.5**

**%81.6**

**%27.8**

**Toplanmış hücreler (1. ve 2. mobilizasyon)**

Ortalama CD34 hücre/kg

$$2.11 \times 10^6$$

$$2.51 \times 10^6$$

$$5.47 \times 10^6$$

Ortalama aferez günü

Toplam başarısızlık oranı

**%47.1**

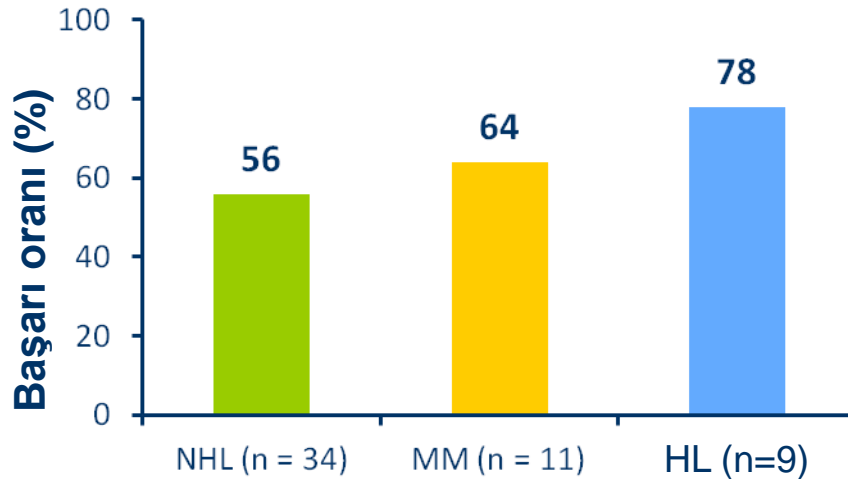
**%28.1**

**%16.7**

# İnsani amaçlı hasta erişim programı sonuçları:

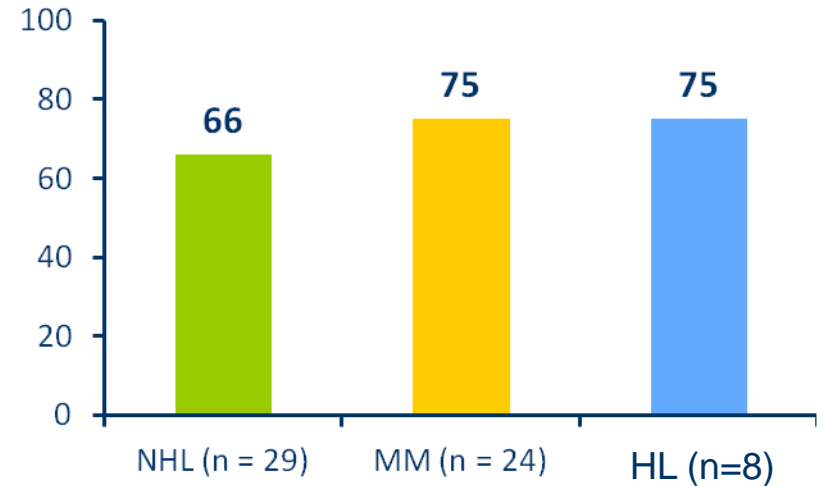
Plerixafor tedavisi sonrası  $\geq 2 \times 10^6$  CD34+ hücre/kg toplanması

Önceki sitokin tedavisinde mobilizasyonda başarısızlık grubu



Plerixafor ile remobilizasyonda tüm başarı oranı %61.0

Önceki kemo. + sitokin tedavisinde mobilizasyonda başarısızlık grubu



Plerixafor ile remobilizasyonda tüm başarı oranı %70.5

# Mobilizasyon başarısına etki eden faktörler

## Treatment related

High numbers of previous chemotherapy ( $\geq 2$  lines of chemotherapy)

Exposure to alkylating agents, purine analogs, or lenalidomide

Extended field radiotherapy to bone marrow-containing sites

## Patient related

Older age ( $>65$  y)

Female sex

Diagnosis of non-Hodgkin lymphoma

Presence of osteolytic lesion

Diabetes and smoking

## At mobilization

Low hemoglobin and low baseline platelet number ( $<1,000,000/\text{mL}$ )

Longer interval from last chemotherapy to mobilization initiation

Bone marrow infiltration by primary disease (cellularity  $< 30\%$ ) at mobilization

Preapheresis peripheral blood  $\text{CD34}^+$  cell number ( $<20 \times 10^6/\mu\text{L}$ )

Low day 1 apheresis yield

Collection procedure

Timing of apheresis,

Type of cell separator used

Rate and volume of whole blood processed

**ASCO: Oral Presentation (8003)**

**Session Name:** Hematologic Malignancies – Plasma Cell Dyscrasia

**Session Date:** 2 June 2019 | **Session Time:** 9:45 AM – 12:45 PM

**EHA: Oral Presentation: Presidential Symposium (S145)**

**Session Name:** Myeloma and Other Monoclonal Gammopathies – Clinical

**Session Date:** 14 June 2019 | **Session Time:** 15:45 – 16:00 (Hall 5)

**Phase 3 Randomized Study of Daratumumab +  
Bortezomib/Thalidomide/Dexamethasone (D-VTd) vs VTd  
in Transplant-eligible Newly Diagnosed Multiple Myeloma:  
CASSIOPEIA Part 1 Results**

P Moreau, M Attal, C Hulin, MC Béné, A Broijl, D Caillot, M Delforge, T Dejoie, T Facon, J  
Lambert, X Leleu, M Macro,  
A Perrot, S Zweegman, T Ahmadi, C Chiu, L Pei, J Vermeulen, H Avet-Loiseau, P Sonneveld  
on behalf of IFM and HOVON

**Presenter: P Moreau**

# Stem Cell Mobilization and Harvesting

	D-VTd (n = 536)	VTd (n = 538)
PBSC mobilizing agents, <sup>a</sup> n (%)		
N	506	492
Cyclophosphamide/G-CSF	506 (100)	492 (100)
<b>Plerixafor</b>	<b>110 (21.7)</b>	<b>39 (7.9)</b>
PBSC apheresis performed		
N	504	490 <sup>b</sup>
Number of days of apheresis		
Mean (SD)	1.9 (0.92)	1.4 (0.67)
Median (range)	2.0 (1-6)	1.0 (1-4)
Total number of CD34 <sup>+</sup> stem cells collected (10 <sup>6</sup> /kg) among subjects with PBSC apheresis performed		
N	504	490 <sup>b</sup>
Mean (SD)	6.7 (2.63)	10.0 (5.25)
<b>Median (range)</b>	<b>6.3 (0.5-18.7)</b>	<b>8.9 (2.2-36.9)</b>
≥2 × 10 <sup>6</sup> /kg, n (%)	501 (99.4)	490 (100)
≥5 × 10 <sup>6</sup> /kg, n (%)	380 (75.4)	434 (88.6)

Percentages were calculated with N in each group as the denominator.

Bone marrow harvest was performed for 1 patient in the D-VTd arm and no patients in the VTd arm.

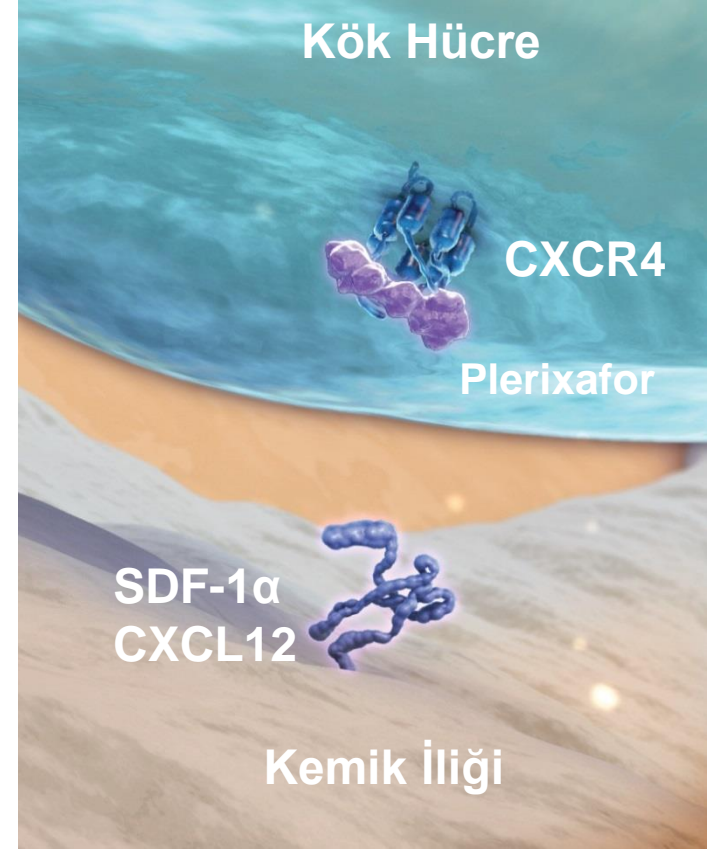
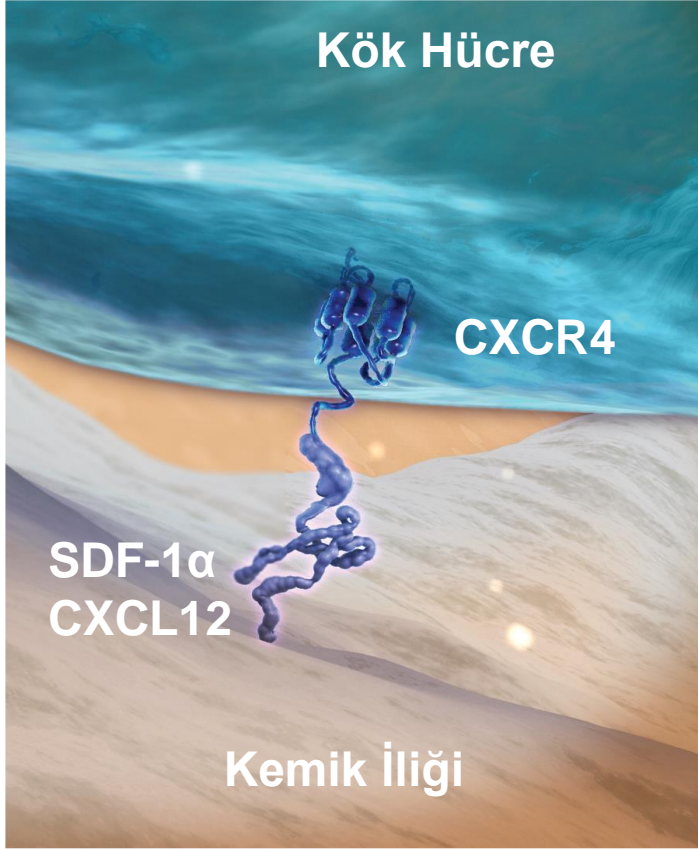
<sup>a</sup>Several PBSC mobilizing agents were possible per patient.

<sup>b</sup>Based on available information from the investigator, one patient in the VTd arm had successful CD34<sup>+</sup> stem cell collection without any prior mobilization treatment. One patient received a stem cell collection from bone marrow in addition to apheresis from peripheral blood. Here both numbers are summed up as a total of CD34<sup>+</sup> stem cells collected from this patient.

- The **median number of CD34<sup>+</sup> stem cells collected was lower** for patients receiving **D-VTd** versus VTd
  - Nevertheless, a similar percentage of patients treated with D-VTd versus VTd underwent ASCT (91.2% vs 90.0%)



# PLERIXAFOR: PKH Mobilizasyonunda kemokin reseptör inhibisyonu ile etki



CXCR4- SDF-1α/CXCL12 etkileşimini engelleyerek, kemik iliğinden dolaşıma kök hücre mobilizasyonunu sağlar

# **Efficacy and safety of plerixafor for hematopoietic stem cell mobilization for autologous transplantation in patients with non-Hodgkin lymphoma and multiple myeloma: A systematic review and meta-analysis**

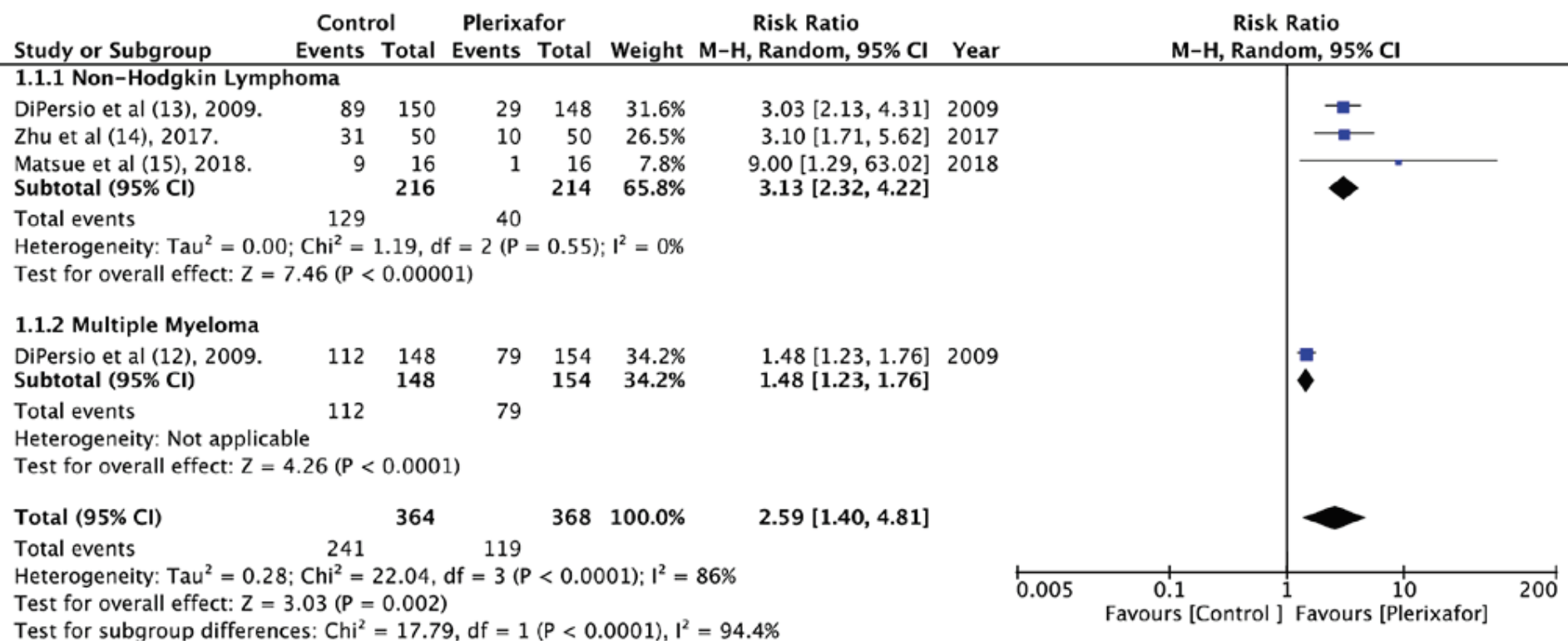
XIAOYANG YANG<sup>1</sup>, MENGJIE WAN<sup>1</sup>, FENG YU<sup>1</sup> and ZHIDONG WANG<sup>2</sup>

<sup>1</sup>Department of Hematology, Affiliated Haikou Hospital of Xiangya Medical College, Central South University and Haikou Municipal People's Hospital, Haikou, Hainan 570208;

<sup>2</sup>Department of Hematology, People's Hospital of Peking University, Beijing 100044, P.R. China

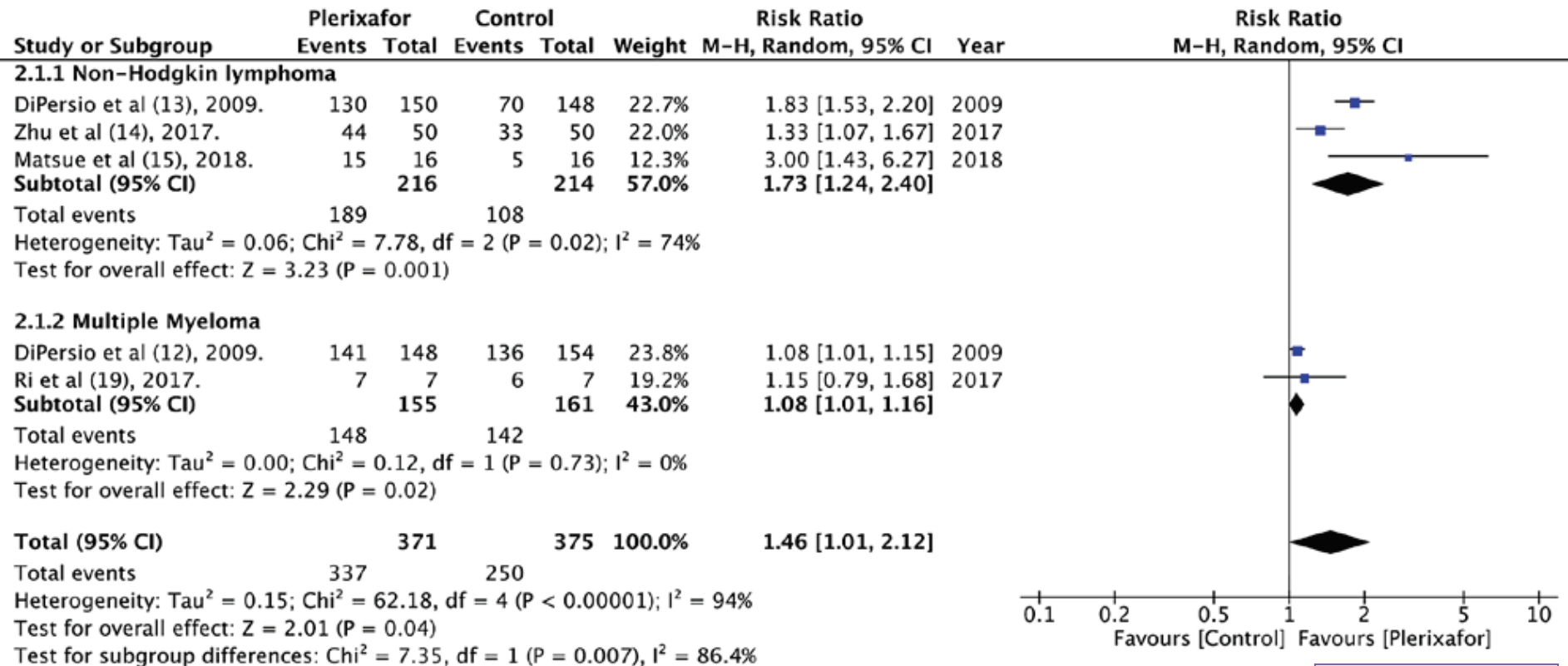
G-CSF'ye plerixafor eklenmesi, advers olaylarda bir artış olmadan daha kısa sürede yeterli HKH toplanmasını arttırır.

# Forrest plot of NHL and MM for the mobilization of optimal hematopoietic stem cells in 4 or less apheresis days



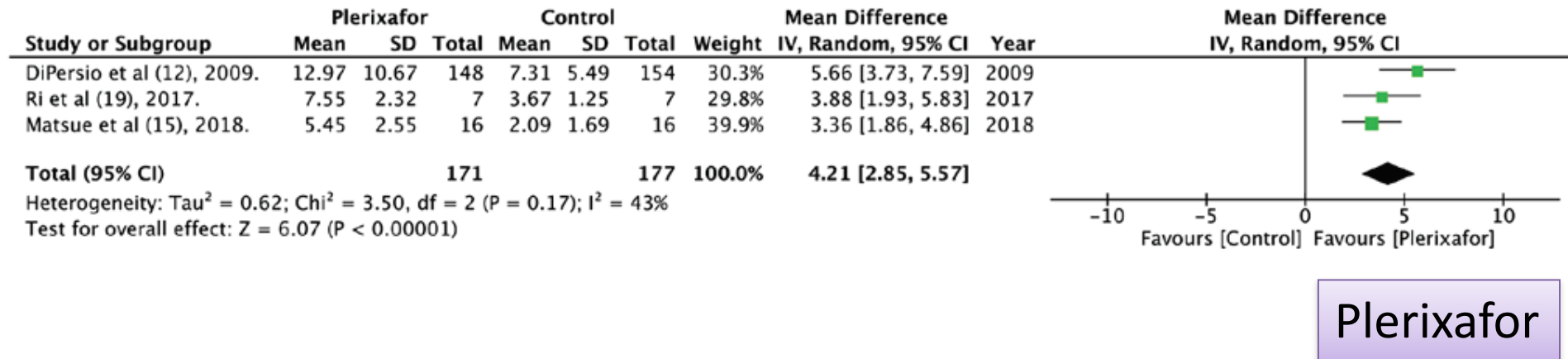
Plerixafor

# Forrest plot of NHL and MM for the mobilization of minimal hematopoietic stem cells in 4 or less apheresis days

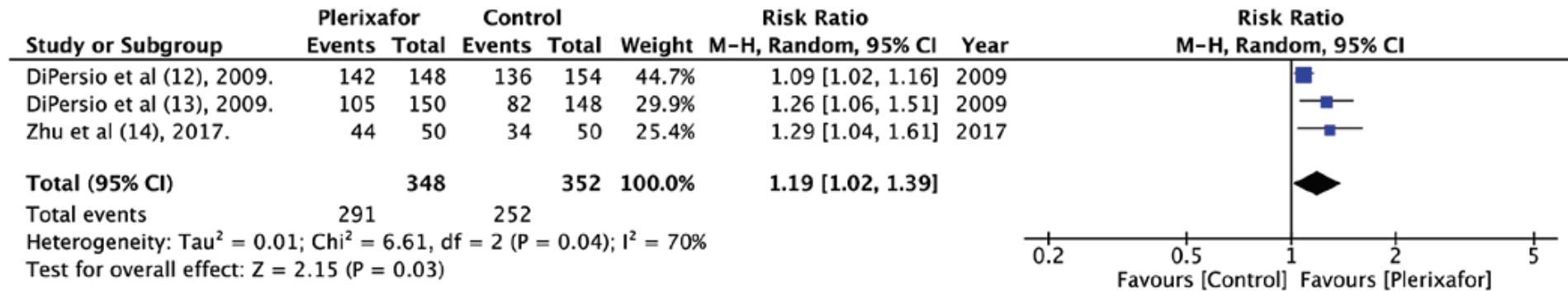


Plerixafor

## Forrest plot of mean **total** number of CD34+ cells collected in up to 4 apheresis days.

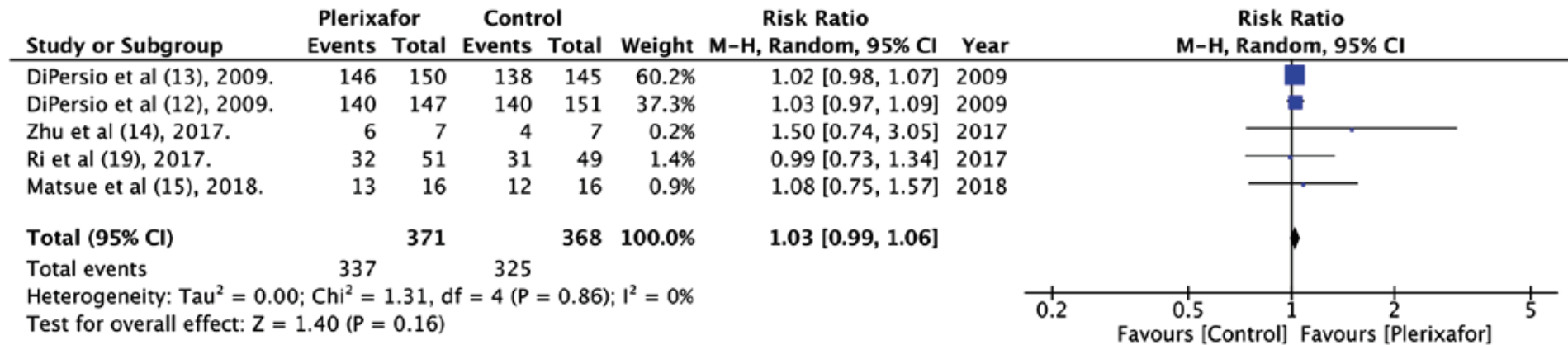


# Forrest plot of the number of patients undergoing transplantation



Plerixafor

## Forrest plot of adverse events



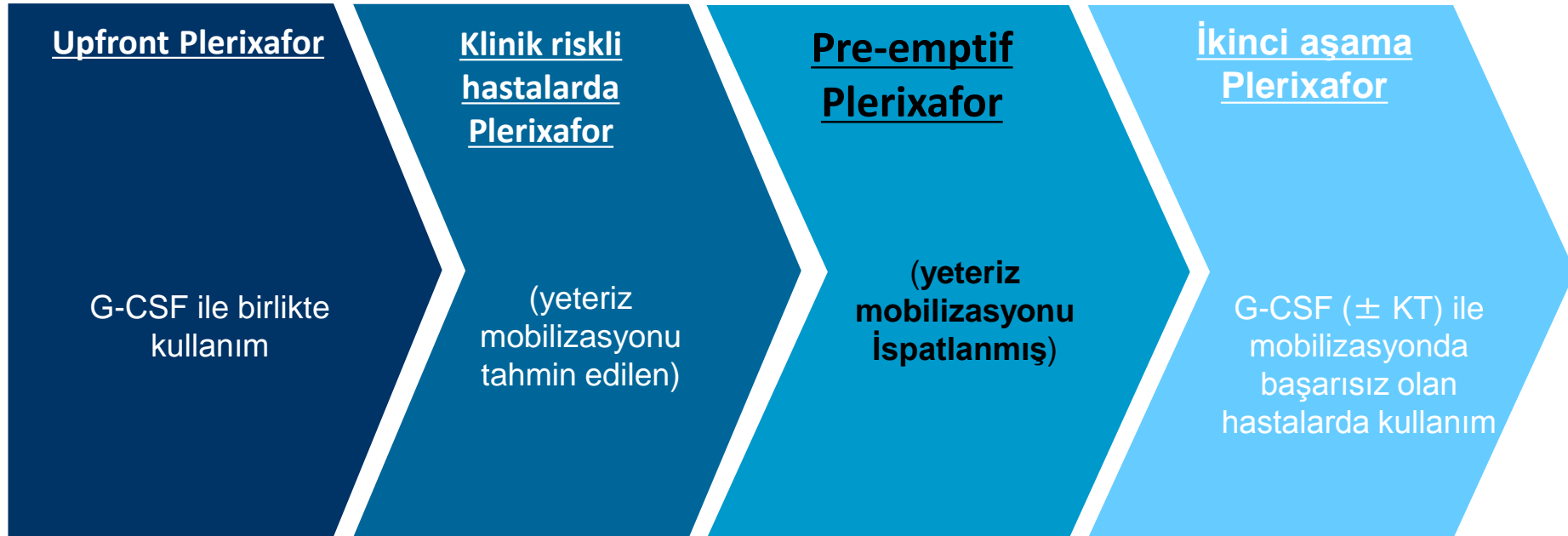


# Plerixafor genel olarak iyi tolere edilir

- yan etkiler tipik olarak;
  - hafif ya da orta şiddette
  - G-CSF'nin tek başına kullanımı ile benzer özellikte
- en sık izlenen yan etkiler;
  - GİS bozuklukları (diyare, bulantı)
  - enjeksiyon bölgesi reaksiyonları
- Plerixafor tedavisinde;
  - febril nötropeni izlenmez



# Otolog PKH mobilizasyonunda plerixafor uygulamaları



## ORIGINAL ARTICLE

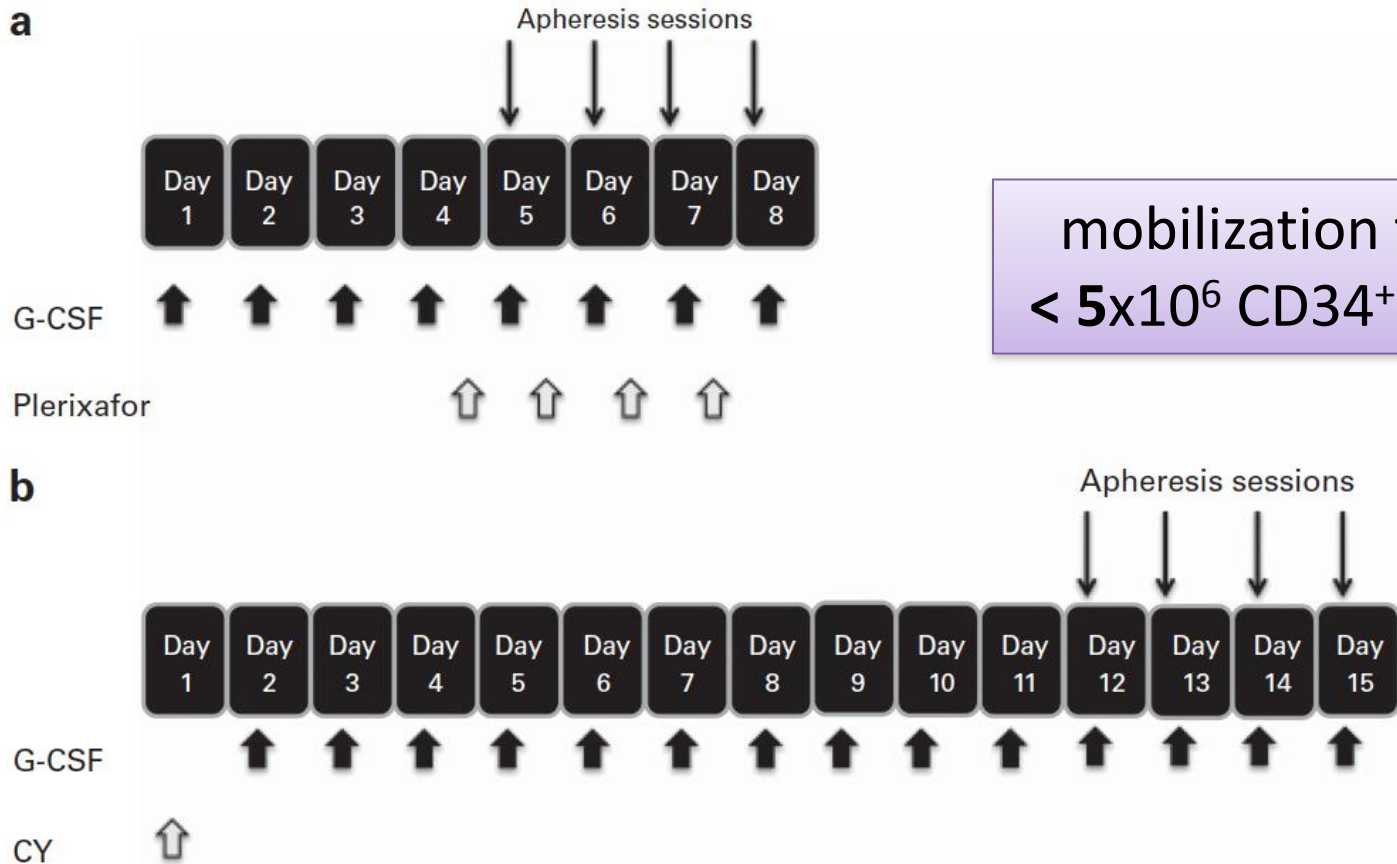
# Upfront plerixafor plus G-CSF versus cyclophosphamide plus G-CSF for stem cell mobilization in multiple myeloma: efficacy and cost analysis study

S Afifi<sup>1,2</sup>, NG Adel<sup>1,2</sup>, S Devlin<sup>2,3</sup>, E Duck<sup>2,4</sup>, J Vanak<sup>2,4</sup>, H Landau<sup>2,5,6</sup>, DJ Chung<sup>2,5,6</sup>, N Lendvai<sup>2,5,6</sup>, A Lesokhin<sup>2,5,6</sup>, N Korde<sup>2,5,6</sup>, L Reich<sup>2,5,6</sup>, O Landgren<sup>2,5,6</sup>, S Giralt<sup>2,5,6</sup> and H Hassoun<sup>2,5,6</sup>

Memorial Sloan Kettering Kanser Merkezi'nde;

- son yıllarda KH mobilizasyonu için “*upfront*” plerixafor kullanımı eğilimi  
(özellikle kemo-mobilizasyondan sonra görülen yüksek toksisite ve enfeksiyon riski)

# Stem cell mobilization schemas



**Table 2.** Patients' baseline and treatment characteristics

	<i>Plerixafor + G-CSF (n = 112)</i>	<i>Cyclophosphamide + G-CSF (n = 111)</i>	<i>P-value</i>
Median age (range)	58.5 (29–75)	60 (43–69)	0.32
Male gender (%)	62.5	65.8	0.68
Median WBC before mobilization (range)	5.65 (0.2–17.1)	4.4 (2.3–55.8)	0.003
Median platelets before mobilization (range)	214.5 (28–553)	209 (31.2–491)	0.617
Median percentage of bone marrow plasmacytosis (range)	2 (0–61)	5 (0–64)	< 0.01
B2 microglobulin (range)	3 (1.2–11)	3.2 (1–25.9)	0.39
Albumin (range)	4 (2.3–5)	4.1 (2.5–5.1)	0.194
LDH (range)	185 (93–807)	184.5 (90–511)	0.98
<i>ISS staging</i>			0.41
Stage I	57 (50%)	41 (37%)	
Stage II	29 (26%)	28 (25%)	
Stage III	19 (17%)	22 (20%)	
Unknown	7 (7%)	20 (18%)	
<i>Prognostic risk</i>			0.556
Standard risk	80 (71%)	69 (62%)	
Intermediate risk	15 (13%)	19 (17%)	
High risk	12 (11%)	13 (12%)	
Unknown	5 (5%)	10 (9%)	
Prior lenalidomide use	89 (79%)	82 (74%)	0.346
Number of cycles received before mobilization (range)	4 (1–36)	4 (1–19)	0.343
Time from induction to mobilization in months (range)	4.7 (1.5–38.3)	5.2 (2.4–34)	0.079

**Table 3.** Stem cell mobilization outcomes

	<i>Plerixafor + G-CSF (n = 112)</i>	<i>Cyclophosphamide + GSCF (n = 111)</i>	<i>P-value</i>
Mean no. of apheresis (s.d.)	2.3 (1.1)	2.6 (1.6)	0.405
Mean G-CSF doses (s.d.)	6.3 (1.1)	12.5 (2.3)	< 0.01
Median CD34+ cells/kg collected after first mobilization (range)	$11.4 \times 10^6$ (0–34.5)	$10.9 \times 10^6$ (0–45.0)	0.29
Number of patients with successful yield after first mobilization, (%) (yield $\geq 5 \times 10^6$ cells/kg)	105 (94%)	92 (83%)	0.01

**Table 4.** Mobilization charges and Medicare reimbursement

	<i>Plerixafor + G-CSF</i> (n = 112)	<i>Cyclophosphamide +</i> <i>GSCF</i> (n = 111)	<i>P-value</i>
Total charges	\$52 200	\$72 138	< 0.001
Medicare Reimbursement	\$21 143.75	\$22 958.53	0.27

**Table 6.** Engraftment outcomes

	<i>Plerixafor + G-CSF (n = 112)</i>	<i>Cyclophosphamide + G-CSF (n = 111)</i>	<i>P-value</i>
Patients transplanted, n (%)	95 (85%)	95 (86%)	0.99
Median, no. of stem cells transfused (range) <sup>a</sup>	5.2 (2–11)	4.4 (2.1–16.2)	0.03
<i>Platelet engraftment<sup>b</sup></i>			
Engrafted, n (%)	92 (100%)	94 (100%)	
Time to engraftment in days, median (range)	12 (6–47)	11 (4–36)	0.37
<i>Neutrophil engraftment</i>			
Engrafted, n (%)	95(100%)	95(100%)	
Time to engraftment in days, median (range)	10 (8–20)	11 (3–32)	0.167

## 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

*Division of Hematology/Oncology, Medical University of South Carolina, Charleston, SC, USA*

- Eşik değer  $> 14$  CD34+ hc/mm<sup>3</sup>  $\gg$  Target-CD34  $> 3 \times 10^6$  CD34+ hc/ kg;
- Eşik değer  $> 25$  CD34+ hc/mm<sup>3</sup>  $\gg$  Target-CD34  $> 5 \times 10^6$  CD34+ hc/ kg

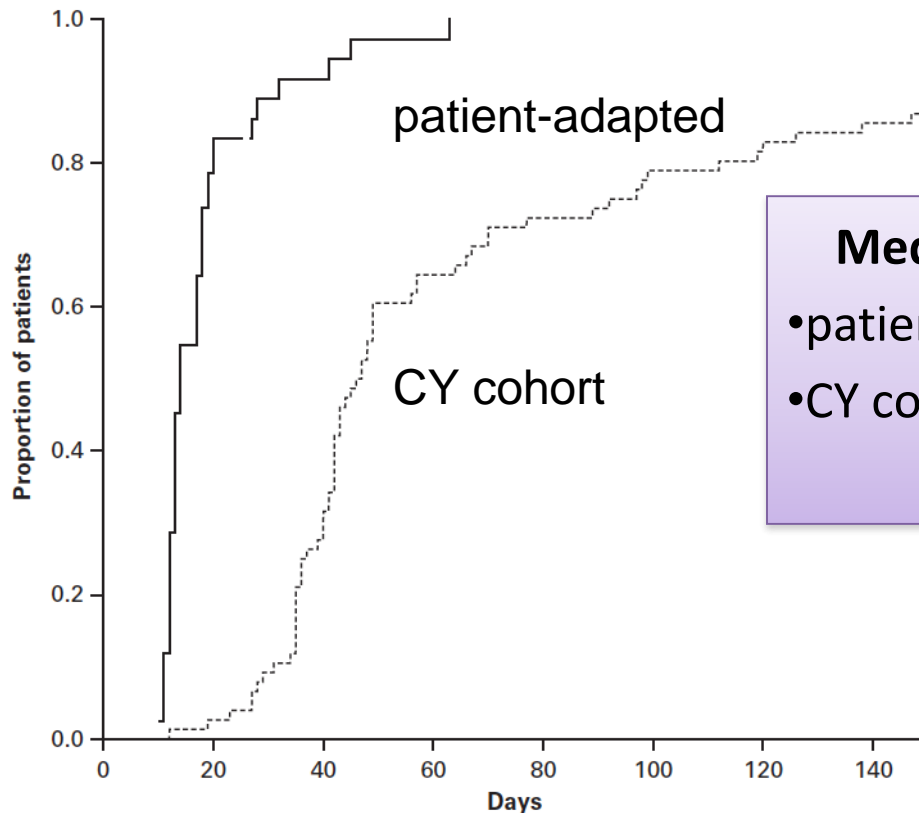
*mobilization failure rate*  
2% patient-adapted vs 22% CY cohort (P = 0.01)



G-CSF nin 4 günü akşam plerixafor (240 mg/kg/day) ve  
5. gün sabah aferez



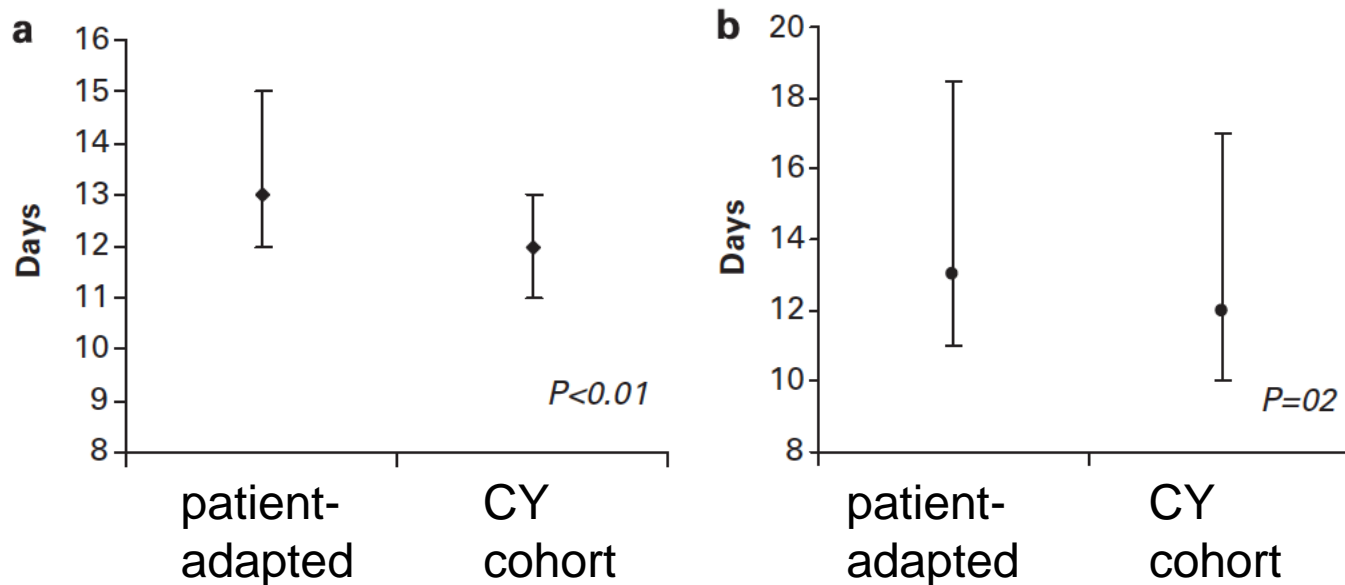
# Mobilizasyondan ilk OKHN ilerleme olasılığı



## Median zaman (Mob. >> Transplant)

- patient-adapted: 14 gün (IQR 12–18)
  - CY cohort: 43 gün (IQR 36–67)
- (P=0.01)

## Median time for neutrophil (a) and platelet engraftment (b)

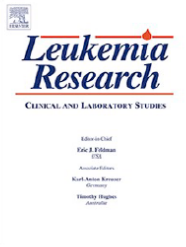




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Research paper

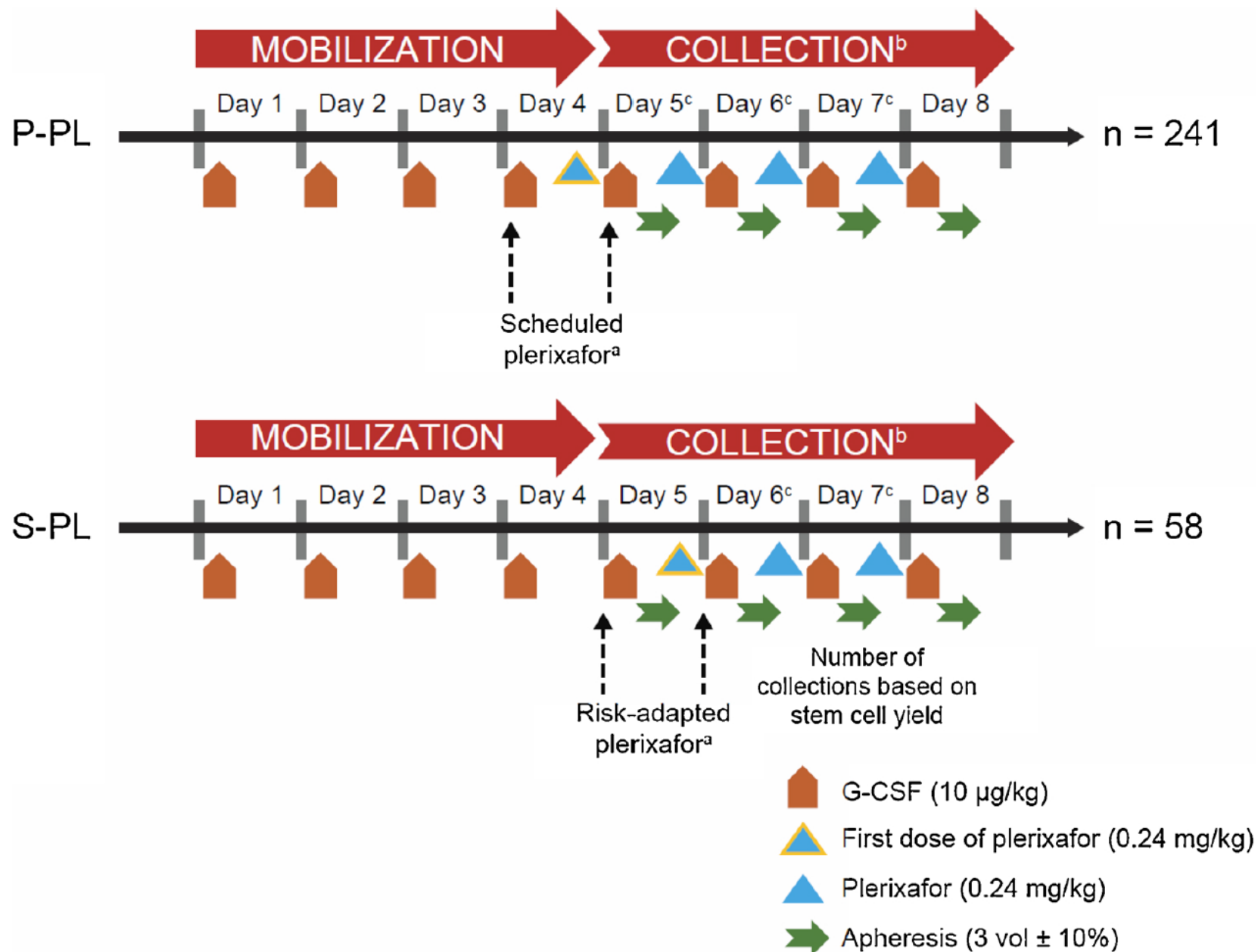
## Clinical and cost outcomes of pre-emptive plerixafor administration in patients with multiple myeloma undergoing stem cell mobilization

Leslie A. Andritsos<sup>a,\*</sup>, Ying Huang<sup>b</sup>, Ivo Abraham<sup>c,d,e,f</sup>, Keith Huff<sup>g</sup>, Scott R. Scrape<sup>h</sup>, Tao Fan<sup>i</sup>, Nimer Alkhatib<sup>c</sup>, Craig C. Hofmeister<sup>j</sup>, Edward Drea<sup>i</sup>, Ali McBride<sup>d,e,k</sup>

### Ohio State University Blood and Marrow Transplant Program

- MM hastalarına KH toplanmasının ilk gününden önceki akşam plerixafor uygulama politikası
- Başlangıçta kök hücre verimine dayanan bir tedavi algoritması kullanarak ancak yetersiz toplama parametreleri tanımlandıktan sonra plerixafor alan hastalarla etkinlik ve maliyet karşılaştırması (retrospektif)





**Fig. 1.** Dosing schedules of plerixafor: Pre-emptive (P-PL) versus standard (S-PL) administration.

# Etkinlik ve Maliyet

- median CD34+ sayısı (pre-collection):
  - (**P-PL** ; **93** (12-471) > **S-PL** ; 25 (10-218) , P = 0.01)
- median total CD34+ hücre (ilk aferez)
  - (**P-PL** ; **6.75** X 10<sup>6</sup> CD34<sup>+</sup> hc /kg > **S-PL** ; 1.96 X 10<sup>6</sup> CD34<sup>+</sup> hc/kg, P<0.01).
- Çok değişkenli analizde;
  - **P-PL** ile;
    - İlk aferezde  $\geq 2 \times 10^6$  CD34 + hc / kg toplama kabiliyeti (**OR = 4.05**,% 95 CI, 1.19–13.83, P = 0.03) ve
    - Toplamda  $\geq 5 \times 10^6$  CD34 + hc / kg (**OR = 3,09**,% 95 CI, 1,04–9,23, P = 0,04).
- **P-PL**, S-PL'ye kıyasla hasta başına 11,248 \$ (**% 46**) daha ekonomik.

## ORIGINAL ARTICLE

# Plerixafor in patients with lymphoma and multiple myeloma: effectiveness in cases with very low circulating CD34+ cell levels and preemptive intervention vs remobilization

I Sánchez-Ortega<sup>1</sup>, S Querol<sup>2</sup>, M Encuentra<sup>1</sup>, S Ortega<sup>2</sup>, A Serra<sup>2</sup>, JM Sanchez-Villegas<sup>2</sup>, JR Grifols<sup>2</sup>, MM Pujol-Balaguer<sup>2</sup>, M Pujol-Bosch<sup>2</sup>, JM Martí<sup>3</sup>, T Garcia-Cerecedo<sup>4</sup>, P Barba<sup>5</sup>, JM Sancho<sup>6</sup>, A Esquirol<sup>7</sup>, J Sierra<sup>7</sup> and RF Duarte<sup>1</sup>

PB CD34+ cell counts < 10/μL on day 4 of steady-state G-CSF mob.

**Table 2.** Results of mobilization by treatment group

	G-CSF (n = 67)	G-CSF+plerixafor (n = 38)
<i>PB CD34+ cell count on day 4 (cells per <math>\mu\text{L}</math>)</i>		
Mean (s.d.)	4.2 (2.6)	4.1 (2.4)
Median	3.7	3.5
Min-max	0.8–9.9	0.9–9.8
<i>PB CD34+ cell count on day 5 (cells per <math>\mu\text{L}</math>)</i>		
Mean (s.d.)	7.6 (6.7)	18.4 (12.5)
Median	5.25	16.1
Min-max	1.0–41.5	1.9–58
<i>Fold-expansion days 4–5</i>		
Mean (s.d.)	1.8 (1.1)	4.8 (2.9)
Median	1.6	4.04
Min-max	0.1–6.1	1.5–13.1
<i>Collection <math>\geq 2</math> CD34+ (cells <math>\times 10^6/\text{kg}</math>), n (%)</i>		
Overall	18/67 (27%)	28/38 (74%)
First apheresis only	10/67 (15%)	22/38 (58%)
<i>CD34+ yield (cell count <math>\times 10^6/\text{kg}</math>)</i>		
Overall		
Mean (s.d.)	1.02 (1.42)	2.88 (1.62)
Median	0	2.8
Min-max	0–7.38	0–7.21
First apheresis only		
Mean (s.d.)	0.6 (1.22)	2.36 (1.79)
Median	0	2.11
Min-max	0–7.38	0–7.21

**Table 3.** Mobilization with plerixafor in cases with very low PB CD34+ cell counts on day 4

	G-CSF-only cases < 3.5 CD34+ cells per $\mu\text{L}$ (n = 30)	Plerixafor cases < 3.5 CD34+ cells per $\mu\text{L}$ (n = 19)	Plerixafor cases 3.5–10 CD34+ cells per $\mu\text{L}$ (n = 19)
<i>PB CD34+ cell count on day 4 (cells per <math>\mu\text{L}</math>)</i>			
Mean (s.d.)	1.99 (0.66)	2.21 (0.69)	6.03 (1.89)
Median	1.80	2.05	6.00
Min–max	0.8–3.4	0.9–3.4	3.7–9.8
P-values	NS		< 0.001
<i>PB CD34+ cell count on day 5 (cells per <math>\mu\text{L}</math>)</i>			
Mean (s.d.)	3.42 (2.12)	12.03 (9.47)	25.09 (11.92)
Median	2.7	8.5	23.82
Min–max	1.3–9.8	1.9–39	8.8–58
P-values	< 0.001		< 0.001
<i>Fold-expansion days 4–5</i>			
Mean (s.d.)	1.69 (0.79)	5.30 (3.50)	4.21 (1.93)
Median	1.59	4.11	3.98
Min–max	0.46–3.31	1.75–13	1.47–9.97
P-values	< 0.001		0.253
<i>Collection <math>\geq 2</math> CD34+ (cells <math>\times 10^6/\text{kg}</math>), n (%)</i>			
Overall	1/30 (3%)	12/19 (63%)	16/19 (84%)
P-values	< 0.001	8/19 (42%)	0.141
First	0/30 (0%)		14/19 (74%)
apheresis only			
P-values	< 0.001		0.049
<i>CD34+ yield (cell count <math>\times 10^6/\text{kg}</math>)</i>			
Overall			
Mean (s.d.)	0.15 (0.51)	2.29 (1.64)	3.47 (1.41)
Median	0	2.47	3.48
Min–Max	0–2.19	0–6.74	1.48–7.21
P-values	< 0.001		0.015
First apheresis only			
Mean (s.d.)	0.02 (0.14)	1.59 (1.70)	3.13 (1.57)
Median	0	1.33	2.75
Min–max	0–0.78	0–6.74	1.03–7.21
P-values	< 0.001		0.002

## çok düşük (<3.5 / $\mu\text{L}$ ) periferik CD34 + hücre sayımları olanlarda;

- CD34 + hücre sayı artışı (5.3- vs 1.7 kat),
- Genel CD34 + hücre verimi
  - kg başına 2.29 vs 0.15  $\times 10^6$  CD34 + hücre
  - kg başına  $\geq 2 \times 10^6$  CD34 + hücre veren hastalar (% 63 vs% 3)



**Table 4.** Plerixafor use as a remobilization vs preemptive strategy

	Remobilization (n = 25)	Preemptive (n = 13)	P-value
<i>PB CD34+ cell count on day 4 (cells per <math>\mu\text{L}</math>)</i>			
Mean (s.d.)	3.7 (2.3)	4.9 (2.3)	0.085
Median	3.0	4.1	
Min-max	0.9-9.8	1.6-8.6	
<i>PB CD34+ cell count on day 5 (cells per <math>\mu\text{L}</math>)</i>			
Mean (s.d.)	16.2 (13.4)	22.4 (9.8)	0.058
Median	11.53	23.7	
Min-max	1.9-58	4-36.6	
<i>Fold-expansion days 4-5</i>			
Mean (s.d.)	4.7 (3.14)	4.9 (2.39)	0.888
Median	4.04	4.35	
Min-max	1.5-13	2.1-10	
<i>Collection <math>\geq 2</math> CD34+ cells <math>\times 10^6/\text{kg}</math>, n (%)</i>			
Overall	16/25 (64%)	12/13 (92%)	0.118
First apheresis only	11/25 (44%)	11/13 (85%)	0.016
<i>CD34+ yield, cell count <math>\times 10^6/\text{kg}</math></i>			
Overall			
Mean (s.d.)	2.44 (1.46)	3.73 (1.63)	0.004
Median	2.45	3.49	0.015
Min-max	0-6.74	0-7.21	
First apheresis only			
Mean (s.d.)	2.0 (1.55)	3.28 (1.79)	
Median	1.55	3.27	
Min-max	0-6.74	0-7.21	

**preemptive plerixafor vs re-mob**

- birinci aferezde CD34 + hücre verimi **(3.28 - 2.0 x 10<sup>6</sup> CD34+ hc/kg)**
- Genel toplam **(3.73 vs 2.44 x 10<sup>6</sup> CD34 + hc/kg),**
- ≥ 2 x 10<sup>6</sup> CD34 + hc/kg
  - ilk aferez (% **85** -% 44)
  - toplam (% **92** -% 64)
- daha az aferez günü
- daha az plerixafor kullanımı : (1.08 vs 1.48)

## 2136 Are We Choosing Mobilization Regimens for Autologous Stem Cell Transplantation in Multiple Myeloma Wisely?: A Single Centre Comparison of GCSF+/-Plerixafor Vs Cyclophosphamide/GCSF+/- Plerixafor

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Program: Oral and Poster Abstracts

Session: 902. Health Services Research—Malignant Conditions (Lymphoid Disease): Poster I

Hematology Disease Topics & Pathways:

apheresis, Adverse Events, Technology and Procedures, Clinically relevant

Saturday, December 7, 2019, 5:30 PM-7:30 PM

Hall B, Level 2 (Orange County Convention Center)

*Chloe Yang, MD<sup>1</sup>, Mina Dehghani, MD<sup>2</sup>, Wilma Hopman, MSc<sup>3\*</sup> and Sita D. Bhella, MD<sup>4\*</sup>*

*<sup>1</sup>Queen's University, Kingston, ON, Canada*

**GCSF +/- P ile siklofosfamid siz mobilizasyon  
inferior olmayan bir rejimdir.**

	<b>GCSF +/- plerixafor (N=47)</b>	<b>Cyclophosphamide/GCSF +/- plerixafor (N=50)</b>	<b>P Value</b>
	<b>Median (range)</b>	<b>Median (range)</b>	
<b>Age</b>	64 (38-75)	63 (44-74)	P=0.631
<b>Gender</b>	M=28 (60%) F=19 (40%)	M=26 (52%) F=24 (48%)	P=0.453
<b>Number of pts who received plerixafor</b>	15 (32%)	18 (36%)	P=0.671
<b>Number of days of plerixafor</b>	0 (0-4)	0 (0-3)	P=0.557
<b>Number of apheresis days</b>	2 (1-4)	2 (1-5)	P=0.266
<b>Total cells collected (x10<sup>6</sup>)</b>	6.06 (4.32-12.34)	10.2 (4.73-19.83)	P<0.001
<b>Pts with febrile neutropenia</b>	0	3	P=0.243
<b>Date of ASCT</b>	March 2017 to Jan 2019	Oct 2015 to March 2018	
<b>Length of stay for transplant* (in days)</b>	18 (15-52)	18 (16-49)	P=0.778
<b>Death &lt;100 days</b>	0	1	

# 4476 Incorporating Reduced-Dose Plerixafor to a Preemptive Mobilization Algorithm Increases Access to Autologous Transplantation in a Limited-Resource Setting

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Program: Oral and Poster Abstracts

Session: 711. Cell Collection and Processing: Poster III

Hematology Disease Topics & Pathways:

Biological, therapy sequence, apheresis, HSCs, Adult, Therapies, Combinations, Technology and Procedures, Cell Lineage, Study Population, Clinically relevant, Quality Improvement , transplantation, stem cells

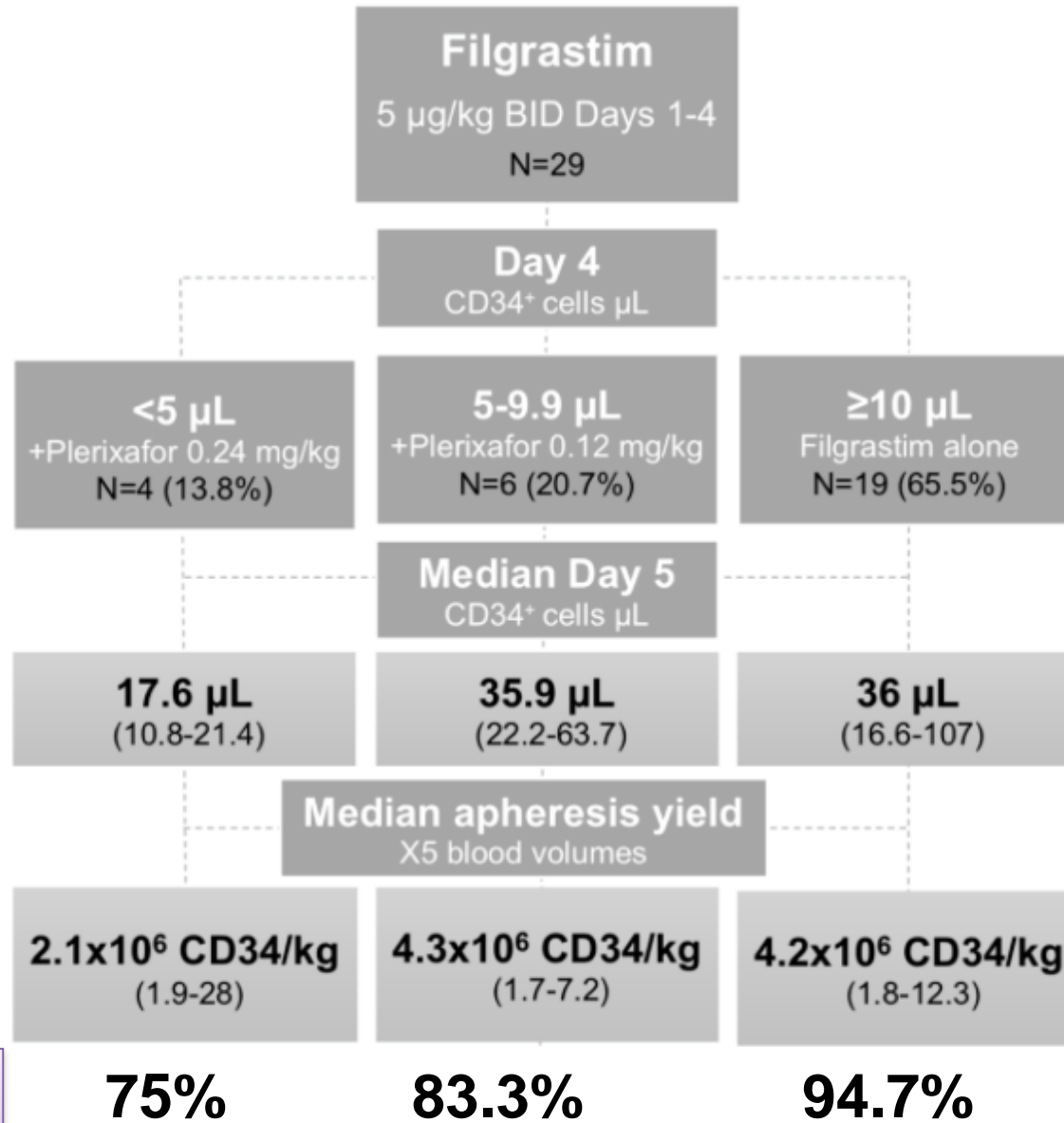
Monday, December 9, 2019, 6:00 PM-8:00 PM

Hall B, Level 2 (Orange County Convention Center)

*Andrés Gómez-De León, MD, Dalila Marisol Alvarado Navarro, MD\*, Cesar O Pezina Cantú, MD\*, Perla R. Colunga Pedraza, MD, David Gomez-Almaguer, MD, Rosario Salazar Riojas, Chem.\*, Olga Graciela Cantu Rodriguez, MD\*, Luz del Carmen Tarín Arzaga, MD\*, Jose Carlos Jaime, MD, PhD\* and Cesar Homero Gutierrez-Aguirre, PhD\**

*Universidad Autonoma de Nuevo Leon, Hospital Universitario "Dr. José Eleuterio Gonzalez", Servicio de Hematología, Monterrey, Mexico*

Maliyette \$22,000 USD azalma



Mob. başarı  
oranı:

# **Tümör hücresi mobilizasyonu?**



ELSEVIER

## Biology of Blood and Marrow Transplantation

journal homepage: [www.bbmt.org](http://www.bbmt.org)

ASBMT<sup>TM</sup>  
American Society for Blood  
and Marrow Transplantation

Autologous

# A Pilot, Exploratory, Randomized, Phase II Safety Study Evaluating Tumor Cell Mobilization and Apheresis Product Contamination in Patients Treated with Granulocyte Colony-Stimulating Factor Alone or Plus Plerixafor

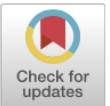
Hareth Nahi<sup>1,\*</sup>, Marina Celanovic<sup>2</sup>, Qianying Liu<sup>2</sup>, Johan Lund<sup>3</sup>, Valdas Peceliunas<sup>4</sup>

<sup>1</sup> Hematology Department, Karolinska Institute, Stockholm, Sweden

<sup>2</sup> Sanofi, Cambridge, Massachusetts

<sup>3</sup> Department of Medicine, Karolinska Institute, Stockholm, Sweden

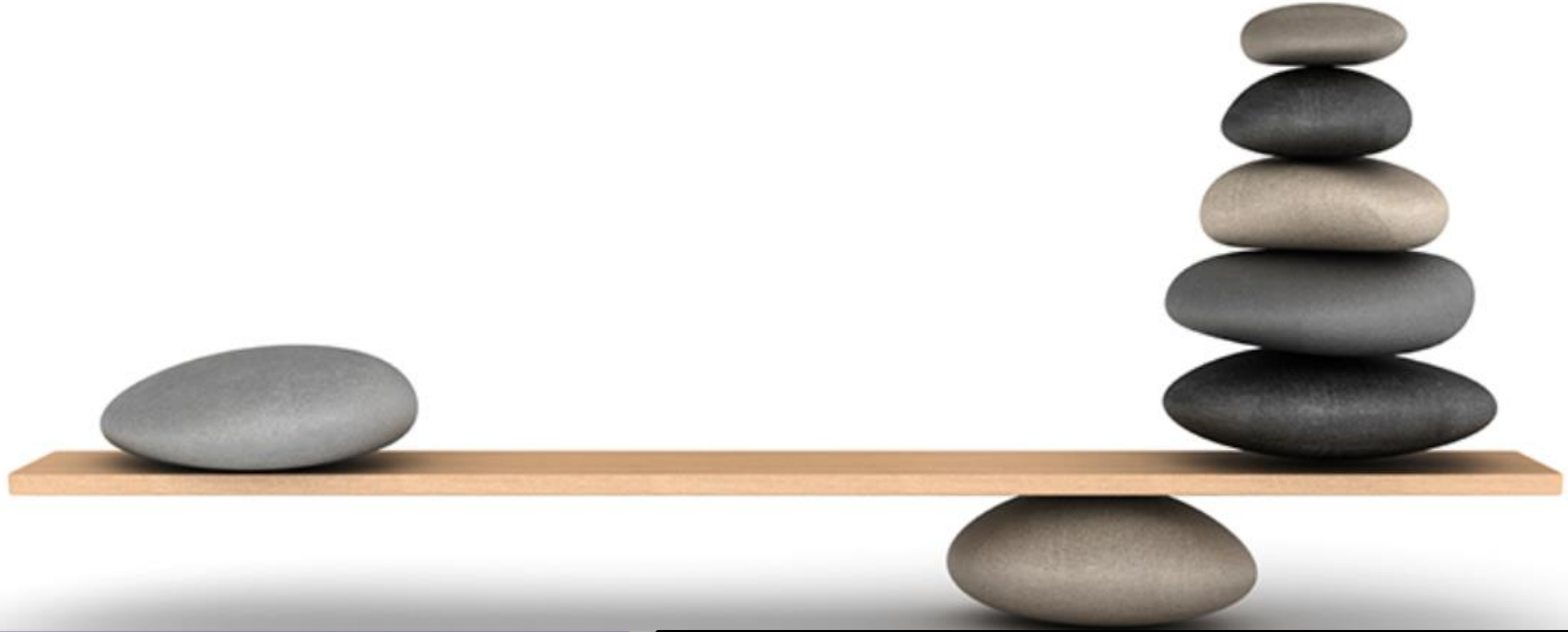
<sup>4</sup> Hematology, Oncology and Transfusion Medicine Center, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania



## 5-8. Günlerde Aferez Ürününde MM Tümör Hücreleri (10<sup>5</sup> hücre / kg)

Time Point	G-CSF Alone(n = 10)	G-CSF + Plerixafor(n =1 0)
Day 5	(n = 10)	(n = 10)
Mean ± SD	.5 ± 1.1	.5 ± 1.1
Range	.0-3.5	.0-2.8
Day 6	(n = 7)	(n = 3)
Mean ± SD	1.2 ± 2.8	.3 ± .5
Range	.0-7.4	.0-.9
Day 7	(n = 3)	(n = 1)
Mean ± SD	.0 ± .0	.0 (NC)
Range	.0-.0	.0-.0
Day 8	(n = 1)	(n = 0)
Mean ± SD	.0 (NC)	
Range	.0-.0	
Overall	(n = 10)	(n = 10)
Mean ± SD	1.3 ± 3.4	.6 ± 1.3
Range	.0-10.9	.0-3.7





### **P+G-CSF**


- Plerixaforun fiyatı yüksek


### **KT+G-CSF**

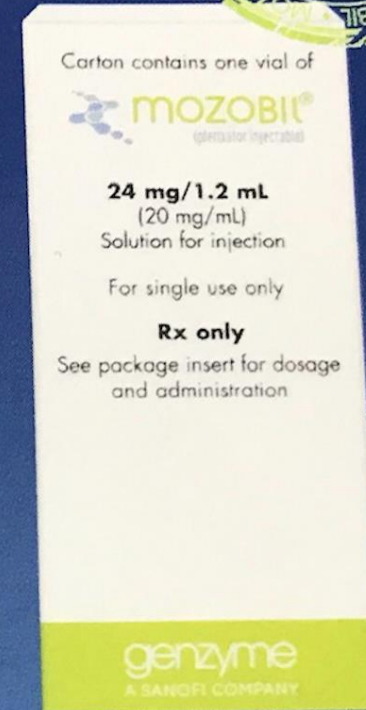
- G-CSF kullanımında artış,
- Aferez seanslarında artma,
- Kateter ve KT komplikasyonları ile ilişkili hastaneye yatış
- Kurtarma tedavisi ihtiyacına neden olan mobilizasyon başarısızlıklarının artması
- In vivo purging >> superior disease control??*

# Endikasyon

Otolog kök hücre transplantasyonu gerçekleştirmek istenen lenfoma ve multipl miyelom tanısı konmuş erişkin hastalarda,

 Sadece Granülosit Koloni Uyarıcı Faktör (G-CSF) mobilizasyonunun yeterli olacağı öngörülen hastalarda en az 1 seri 10 mikrogram/kilogram gün dozunda G-CSF uygulaması ve en az 1 seri G-CSF ve kemoterapi uygulaması ile yeterli ( $\geq 2 \times 10^6/\text{kg}$  CD34+ hücre) kök hücre mobilizasyonu sağlanamayan hastalarda,

 Sadece G-CSF ile yeterli düzeyde kök hücre mobilizasyonu sağlanamayacağı öngörülen hastalarda en az 1 seri kemoterapi ve G-CSF uygulamasına rağmen yeterli ( $\geq 2 \times 10^6/\text{kg}$  CD34+ hücre) kök hücre mobilizasyonu sağlanamayan olgularda G-CSF ile kombine olarak endikedir.



# Özet

- Plerixafor, lenfoma ve MM tanılı (*mobilizasyon başarısızlığı açısından yüksek riskli*) hastaların başarılı bir şekilde mobilize olma şanslarını önemli ölçüde arttırdı
- Plerixaforun maliyeti yüksek olduğundan ve nakile aday hastaların çoğunluğu plerixaforsuz mobilizasyon stratejileri ile yeterli PKH sayısına ulaşabildiğinden, son çabalar, plerixafordan en fazla faydalanacak hastaları belirleyen tedavi stratejilerine (“*PRE-EMPTIVE*”) odaklandı.