Simpósio Satélite

NUEVOS ENFOQUES EN MOVILIZACIÓN DE
PROGENITORES HEMATOPOYÉTICOS Y TRATAMIENTO DE PTTA

How can we ensure apheresis in one day? Looking for efficiency

Paola Charry España
Hospital Clínic de Barcelona

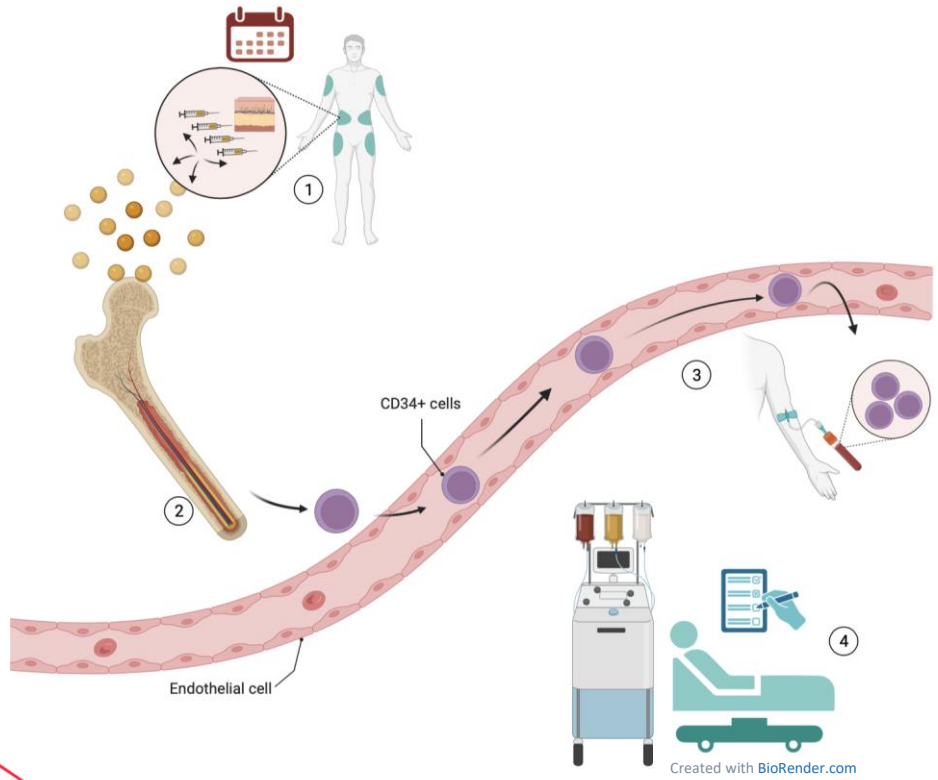
33 CONGRESO SOCIEDAD ESPAÑOLA DE TRANSFUSIÓN SANGUÍNEA Y TERAPIA CELULAR

SETS

sanofi

MAT-ES-2301508 V1 – Mayo 2023

Hematopoietic progenitor cell mobilization



- Hematopoietic cell transplantation (HCT) is a key treatment strategy in different hematologic malignancies
- Bone marrow harvesting has been replaced by collecting hematopoietic progenitor cells (HPCs) from peripheral blood (PB) after mobilization
- Two ways of mobilizing HPCs:
  - Steady-state (G-CSF)
  - Chemotherapy-based
- Risk of mobilization failure as high as 38%

Giralt S, *et al.* Biol Blood Marrow Transplant 2014;20:295-308

sanofi

Hematopoietic progenitor cell mobilization

- Plerixafor added to G-CSF has been increasingly used as a procedure to overcome mobilization failure

- Mobilization strategies:[1]
  - Delayed re-mobilization
  - Pre-emptive use or rescue or just in time
  - Up-front

- Efficacy demonstrated in two RCTs[2,3]

[1]Sancho JM, *et al*. Med Clin (Barc) 2016;147:223.e1-223.e7
[2]DiPersio JF, *et al*. Blood 2009;113:5720-6
[3]DiPersio JF, *et al*. J Clin Oncol 2009;27:4767-73

Plerixafor and apheresis on the same day

- Current recommendations:[1]
  - Plerixafor dose 0.24 mg/Kg
  - After 4-5 days receiving G-CSF (5-10 µg/Kg/day) and <20 CD34+ cells/µL
  - Start leukocytapheresis 10-12 hours after plerixafor administration

- Shorter[2,3] or longer[4,5] time schedules have been previously reported with encouraging positive results

[1]Sancho JM, *et al.* Med Clin (Barc) 2016;147:223.e1-223.e7
[2]Lefrère F, *et al.* Transfusion 2013;53:564-9
[3]Jantunen E, *et al.* J Clin Apher 2017;32:594-6
[4]Cooper DL, *et al.* Clin Lymphoma Myeloma Leuk 2011;11;267-72
[5]Harvey RD, *et al.* Biol Blood Marrow Transplant 2013;19:1393-5

Plerixafor and apheresis on the same day: Patients and methods

Clínic Barcelona | Universitat de Barcelona

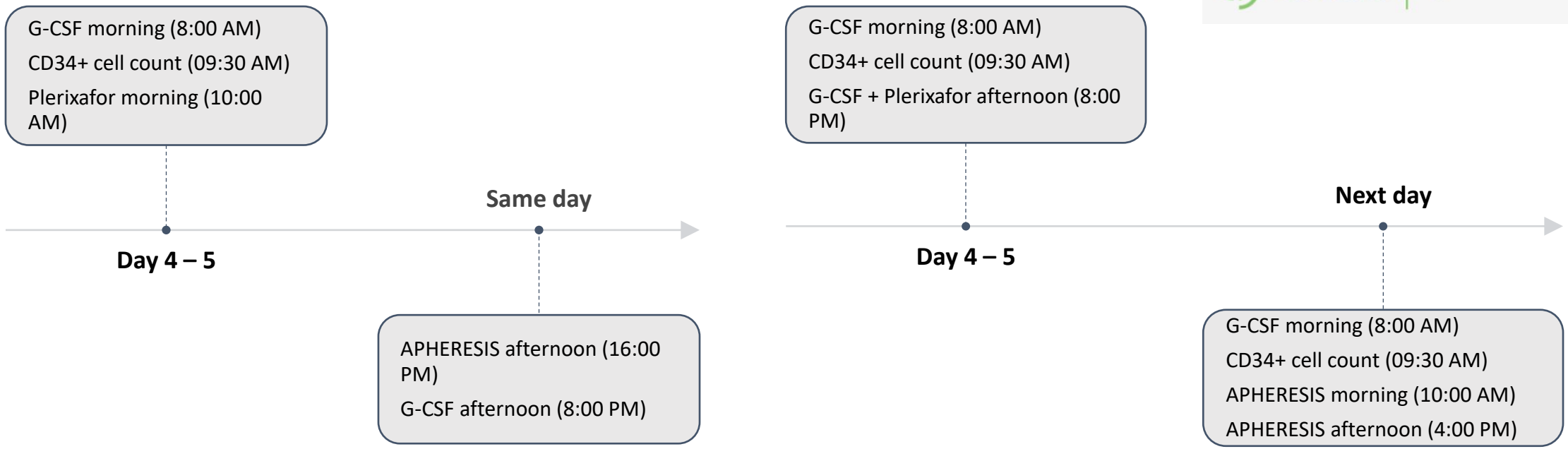
- Retrospective review of adult (≥18 years) patients
  - Received pre-emptive plerixafor
  - After mobilization with G-CSF ± chemotherapy

- Laboratory testing and statistical analyses
  - CD34+ cells quantified using single-platform analysis (ISHAGE protocol)
    - Peripheral blood
      - After G-CSF
      - After plerixafor & just before starting leukocytapheresis
      - Just after finishing leukocytapheresis
    - Collected product

Cid, *et al.* Transfusion 2020;60:779-785

Plerixafor and apheresis on the same day

Clínic Barcelona | Universitat de Barcelona



From plerixafor administration to apheresis start: 6 hours versus 14-20 hours

Cid, *et al.* Transfusion 2020;60:779-785

sanofi

Plerixafor and apheresis on the same day: CD34+ cell calculations

$$Yield = Cells\ in\ the\ product\ \left(\frac{cells}{mL}\right) * Product\ volume\ (mL)$$

$$Yield\ per\ liter = \frac{Yield}{Processed\ blood\ volume(L)}$$

$$Cell\ loss(\%) = \left(1 - \left(\frac{Postdonation\ cell\ count}{Predonation\ cell\ count}\right)\right) * (-100)$$

$$Recruitment\ factor = \frac{Postdonation\ cell\ count + Cell\ Yield}{Predonation\ cell\ count}$$

$$CE1(\%) = \left(\frac{Cells\ in\ the\ product\ \left(\frac{cells}{mL}\right) * Product\ volume\ (mL)}{\left(\frac{Predonation\ cell\ count + Postdonation\ cell\ count}{2}\right) * Processed\ blood\ volume\ (mL)}\right) * 100$$

Cid, *et al.* Transfusion 2020;60:779-785

sanofi

Plerixafor and apheresis on the same day: Results

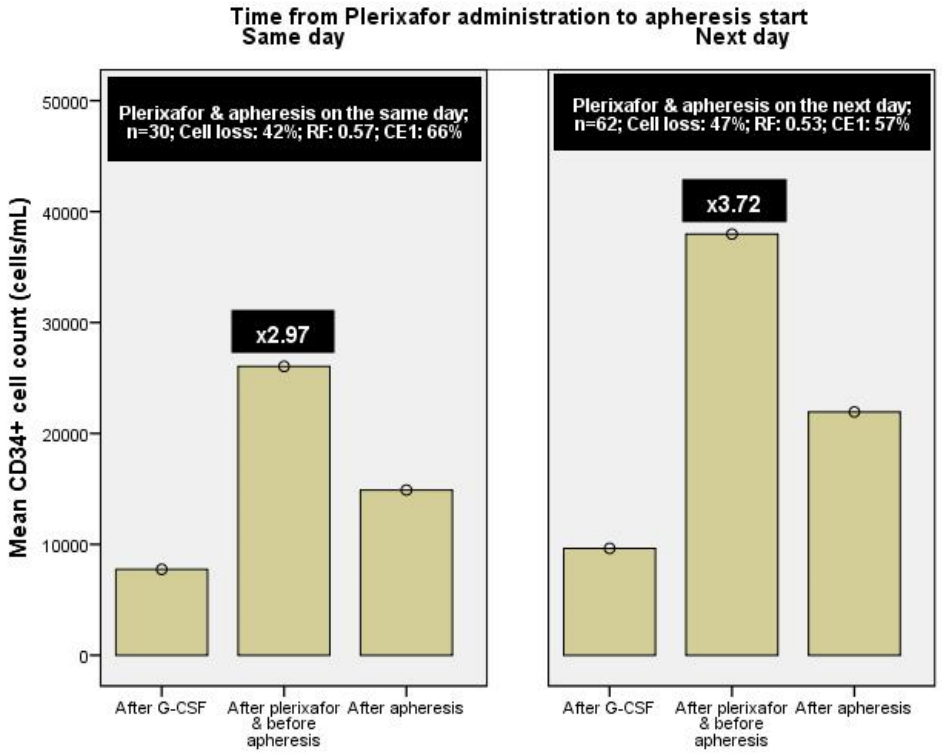
Characteristic*	Same day n=30	Next day n=62	p value
Gender Male Female	 19 (63%) 11 (37%)	 34 (55%) 28 (45%)	0.6
Age (years)	53 (45-59)	57 (46-63)	0.6
Diagnosis Lymphoma Myeloma	 17 (57%) 13 (43%)	 29 (47%) 33 (53%)	0.5
Weight (Kg)	71 (63-78)	69 (60-84.5)	1.0
Height (cm)	173 (165-179)	168 (160-175)	0.1
Blood volume (L)	4.90 (3.95-5.32)	4.47 (3.74-5.20)	0.5
Previous mobilization failure No Yes	 24 (80%) 6 (20%)	 47 (76%) 15 (24%)	0.8
Mobilization strategy G-CSF alone G-CSF+chemotherapy	 23 (77%) 7 (23%)	 51 (82%) 11 (18%)	0.7
G-CSF dose (µg/Kg/day)	20.3 (10-21.8)	18.5 (10-21.3)	0.7
Plerixafor dose (mg/Kg)	0.31 (0.26-0.35)	0.24 (0.24-0.25)	<0.01

Characteristic*	Same day n=30	Next day n=62	p value
Device Optia Spectra	 26 (87%) 4 (13%)	 35 (56%) 27 (44%)	<0.01
Venous access Peripheral veins Central line	 19 (63%) 11 (37%)	 39 (63%) 23 (37%)	1.0
Whole blood processed (L)	22.29 (18.72-25.56)	18.63 (14.91-22.70)	0.07
Whole blood processed (xTBV)	4.76 (4.14-5.25)	4.17 (3.28-5.25)	0.1
Time from plerixafor to start Minutes Hours	 375 (358-386) 6.2 (6.0-6.4)	 858 (825-885) 14.3 (13.8-14.8)	<0.01
Duration of CD34+ cell collection (min)	270 (230-297)	240 (200-286)	0.2

*Values are expressed as number of cases (%) or median (interquartile range – IQR-)

Cid, *et al.* Transfusion 2020;60:779-785

Plerixafor and apheresis on the same day: Results

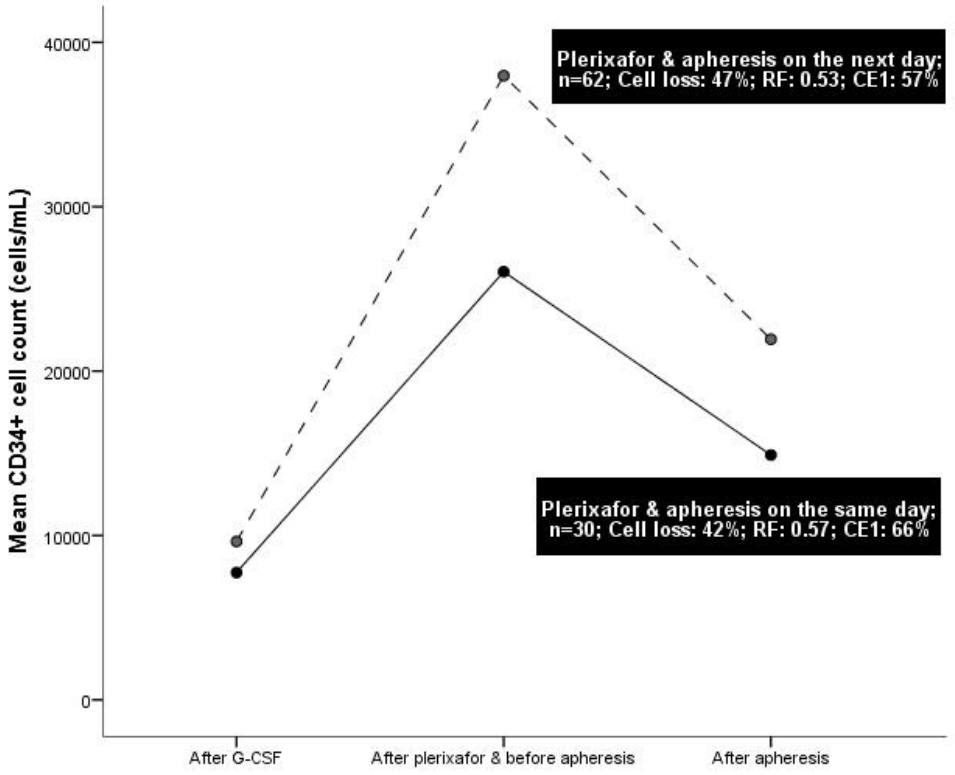


Peripheral blood cell count*	Same day n=30	Next day n=62	p value
CD34+ after G-CSF (cells/mL)	6,507 (2,120-13,370)	8,593 (4,405-13,333)	0.2
CD34+ after plerixafor & before apheresis (cells/mL)	14,868 (7,644-41,439)	27,844 (17,203-53,031)	0.06
CD34+ cell fold increase (plerixafor:G-CSF)	2.97 (2.45-4.06)	3.72 (2.88-4.85)	0.2
CD34+ after apheresis (cells/mL)	11,914 (5,007-22,445)	12,714 (7,018-30,912)	0.05

*Values are expressed as median (interquartile range – IQR-)

Cid, *et al.* Transfusion 2020;60:779-785

Plerixafor and apheresis on the same day: Results



CD34+ cell calculation*	Same day n=30	Next day n=62	p value
Yield (cellsx10^6)	223 (88-415)	226 (115-360)	0.6
Yield/L (cellsx10^6/L)	9.9 (4.9-18.1)	13.0 (5.9-21.4)	0.4
Cell loss (%)	-42.6 (-56 to -28.5)	-47.3 (-63.9 to -31.1)	0.05
Recruitment factor (RF)	0.57 (0.44-0.72)	0.53 (0.36-0.69)	0.05
Cells collected (x10^6/Kg)	2.90 (1.38-5.05)	3.09 (2.00-5.03)	0.6
Collection efficiency (CE1;%)	65.8 (55.8-78.5)	56.7 (42.8-65.4)	<0.01

*Values are expressed as median (interquartile range – IQR-)

Cid, *et al.* Transfusion 2020;60:779-785

Plerixafor and apheresis on the same day: Results

Clínic Barcelona | Universitat de Barcelona

Longitudinal linear regression analysis

Variable	CE1 of CD34+ cell change	p value
Plerixafor dose	8.6 (-63.7 to 80.9)	0.8
Apheresis device	2.5 (-5.8 to 10.8)	0.5
Time from plerixafor to apheresis start*	-0.034 (-0.047 to -0.021)	<0.01

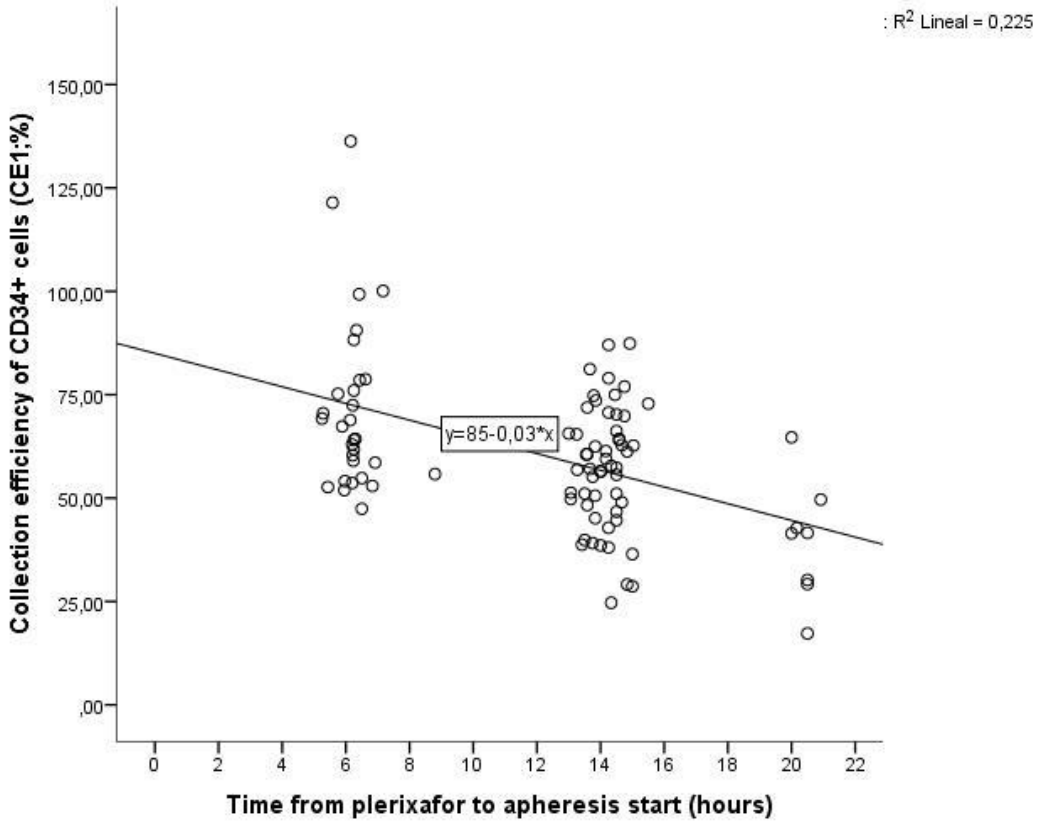
*Values are expressed as median (interquartile range – IQR-)

Cid, *et al.* Transfusion 2020;60:779-785

Plerixafor and apheresis on the same day: Results

Clínic Barcelona | Universitat de Barcelona

CD34+ cell CE1 according to plerixafor timing



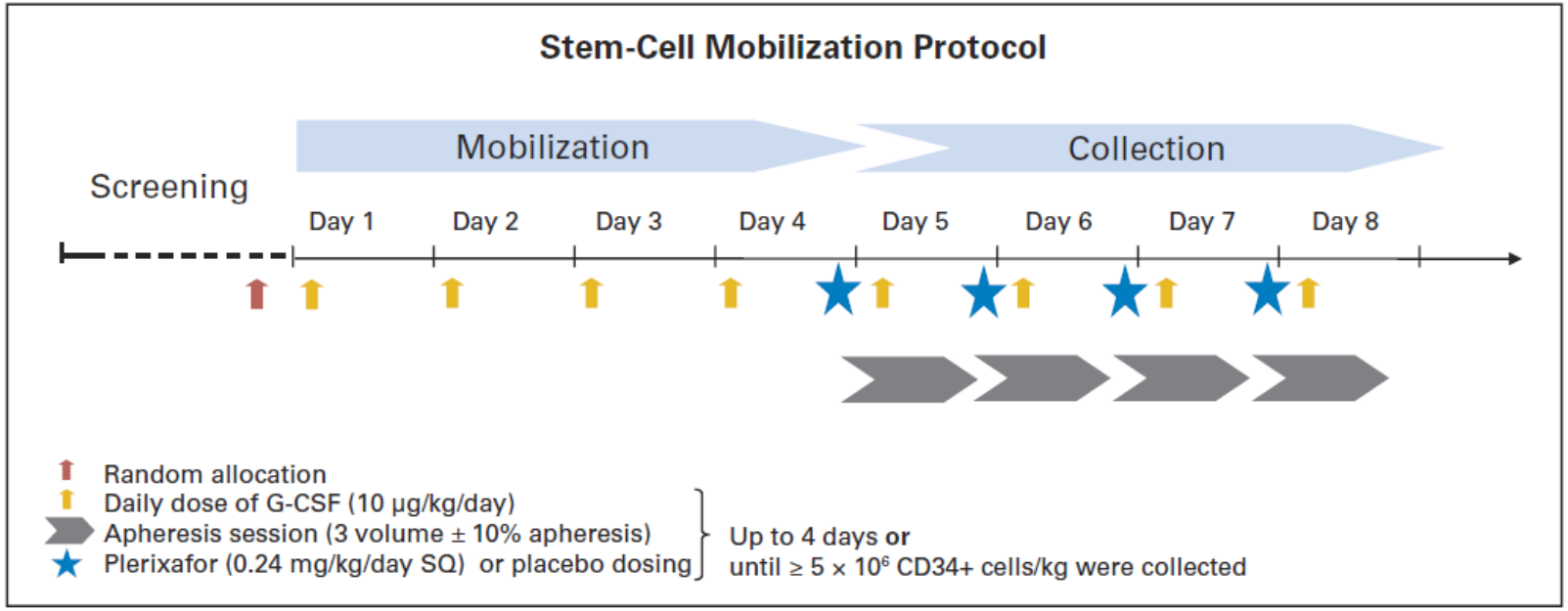
- When the time increased 1 minute, the CD34+ CE1 decreased by 0.034%
- When the time increased 8 hours, the CD34+ CE1 decreased by 16.32%
- When the time increased 14 hours, the CD34+ CE1 decreased by 28.56%

Cid, *et al.* Transfusion 2020;60:779-785

sanofi

Plerixafor and apheresis on the same day: Discussion

Plerixafor in patients



DiPersio JF, *et al.* J Clin Oncol 2009;28:4767-73
DiPersio JF, *et al.* Blood 2009;113:5720-6

Plerixafor and apheresis on the same day: Discussion

Plerixafor in patients

First author[ref]	Plerixafor administration	Apheresis start	Delay
Cooper[1]	5:00 PM	8:00 AM	15 hours
Harvey[2]	3:00 PM	8:00 AM	17 hours
Shi[3]	5:00 PM	10:00-11:00 AM	17-18 hours
Lefrère[4]	5:00-6:00 AM	9:00-11:00 AM	4-6 hours
Jantunen[5]	Morning	N.R.	3-6 hours
Cid[6]	8:00 PM 8:00 PM 10:00 AM	10:00 AM 4:00 PM 4:00 PM	14 hours 20 hours 6 hours

[1]Cooper DL, *et al.* Clin Lymphoma Myeloma Leuk 2011;11:267-72
[2]Harvey RD, *et al.* Biol Blood Marrow Transplant 2013;19:1393-5
[3]Shi PA, *et al.* Transfusion 2014;54:1263-8
[4]Lefrère F, *et al.* Transfusion 2013;53:564-9
[5]Jantunen E, *et al.* J Clin Apher 2017;32:594-6
[6]Cid, *et al.* Transfusion 2020;60:779-785

Plerixafor and apheresis on the same day: Discussion

Plerixafor in patients

TABLE 2. Results of stem cell mobilization and collection after plerixafor and G-CSF administration

Patient	Time interval between plerixafor administration and the first PB CD34+ >10 × 10⁶/L (hr)	Time interval from plerixafor administration to the beginning of apheresis (hr)	Time interval from plerixafor administration to the PB CD34+ ×10⁶/L peak (hr)	PB CD34+ peak (×10⁶/L)	Time interval between plerixafor administration and first decrease in PB CD34+ ×10⁶/L (hr)	CD34+/kg collected	Number of apheresis procedures performed after plerixafor administration
1	H+3	H+4	H+8	23	H+11	2.5	2
2	H+3	H+4	H+6	21	H+9	3.5	2
3	H+3	H+4	H+8	41	H+9	4.5	1
4	Not reached	H+7	H+6	9	H+9	1.4	2
5	H+3	H+4	H+6	17	H+9	2.75	1
6	H+3	H+4	H+8	12	H+10	2.85	2
7	H+3	H+4	H+9	55	H+11	3.6	2
8	Not reached	Not performed	H+9	4	H+12	-	Not collected
9	H+3	H+4	H+6	56	H+9	8.2	1
10	H+5	H+6	H+5	10	H+7	1.5	2
11	H+3	H+4	H+6	25	H+8	2.95	1
12	H+3	H+4	H+9	50	H+12	5.18	2
13	H+3	H+4	H+8	13	H+11	1.5	1

Lefrère F, *et al.* Transfusion 2013;53:564-9

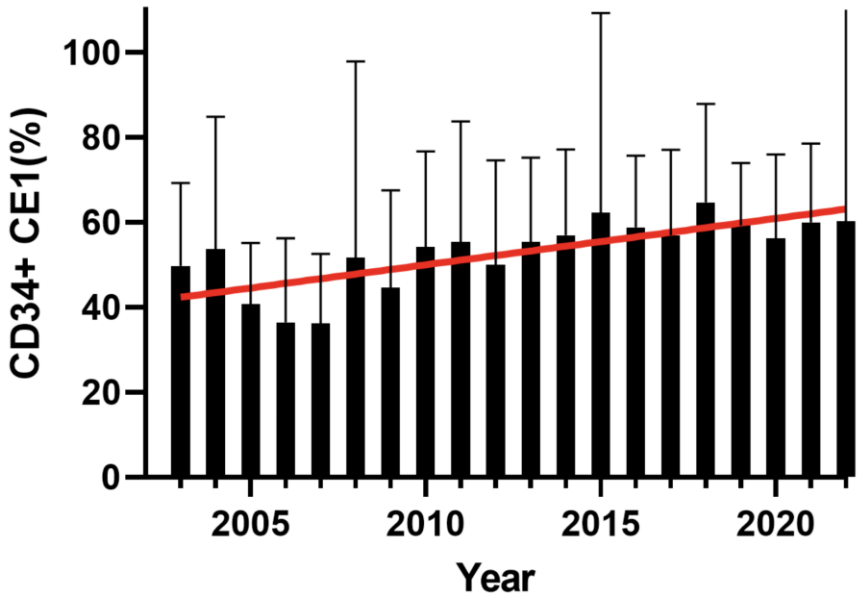
sanofi

Looking for efficiency

	Sin uso de plerixafor		
	2000-2011	2012-2022	Valor p
Donante Sano	n=229	n=251	
	38,64 (28,21-46,17)	57,73 (45,16-68,82)	<0,05
Paciente no hematológico	n=77	n=70	
	50,01 (28,73-67,96)	62,84 (44,49-70,68)	<0,05
Leucemia Aguda	n=177	n=9	
	47,68 (34,27-57,81)	53,51 (48,49-62,08)	N/A
Linfoma	n=372	n=224	
	50,3 (35,16-60,21)	64,03 (43,61-67,23)	<0,05
Gammapatía monoclonal	n=214	n=225	
	44,54 (38,61-55,33)	56,66 (46,80-65,66)	<0,05

	Con uso de plerixafor		
	2000-2011	2012-2022	Valor p
Donante Sano	n=0	n=10	
	-	71,97 (66,37-79)	N/A
Paciente no hematológico	n=2	n=20	
	38,03 (28,60-47,46)	83,57 (43,73-68,98)	N/A
Leucemia Aguda	n=0	n=0	
	-	-	NA
Linfoma	n=16	n=104	
	48,25 (32,39-53,17)	61,61 (50,00-69,17)	<0,05
Gammapatía monoclonal	n=12	n=111	
	40,63 (29,70-51,36)	59,13 (48,52-69,88)	<0,05

*Values are expressed as median (interquartile range – IQR-)



Póster presentado en SETS 2023. Brillembourg H, et al. Eficacia de recolección de progenitores hematopoyéticos en un único centro: análisis de 2123 aféresis en 23 años.

Image courtesy of Dr. Cid: Efficiency of the collection of hematopoietic progenitors at the Hospital Clínic

Conclusions

- Plerixafor added to G-CSF is a useful tool to overcome mobilization failure of HPCs
- Higher collection efficiency, calculated as CE1, of CD34+ cells was observed after administering plerixafor (at a dose of 0.24 mg/Kg or higher) followed by leukocytapheresis 6 hours later when compared with current recommendations
- Further studies are necessary to confirm this results and to explore the clinical impact of this mobilization strategy for patients undergoing auto-HCT

Simpósio Satélite

NUEVOS ENFOQUES EN MOVILIZACIÓN DE
PROGENITORES HEMATOPOYÉTICOS Y TRATAMIENTO DE PTTA

MUCHAS GRACIAS

33 CONGRESO
SOCIEDAD ESPAÑOLA DE TRANSFUSIÓN SANGUÍNEA Y TERAPIA CELULAR

SETS

sanofi