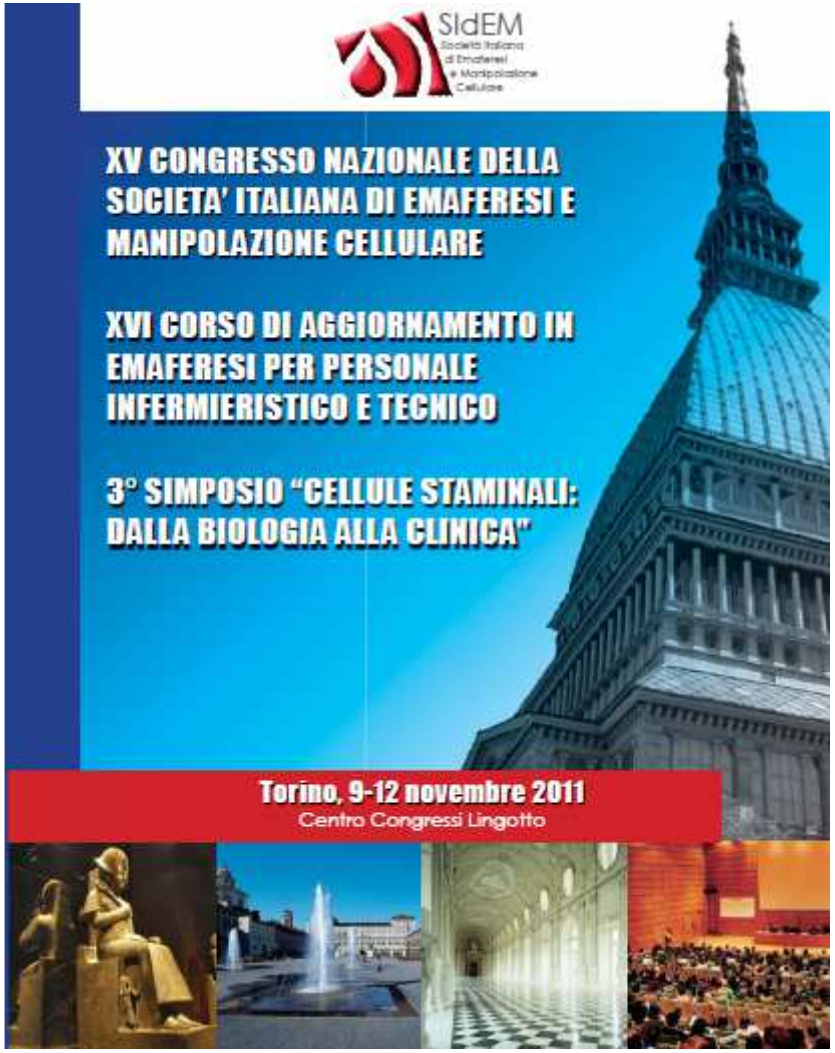

Impiego di cellule staminali autologhe da sangue periferico mobilizzate con Plerixafor nel trapianto di pazienti affetti da linfoma e mieloma multiplo.

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PLERIXAFOR

- Novel CXCR4 inhibitor
- **Effective in mobilizing PBSCs**, in combination with G-CSF
- Studies in **non Hodgkin Lymphoma** (**nHL**) and **MM** patients showed that the combination of G-CSF and Plerixafor resulted in a **significant increase in the CD34+ cell yield after aphaeresis** compared to the administration of G-CSF alone.
- Plerixafor combined with G-CSF, allowed to proceed to **ASCT** in a relevant proportion of lymphoma and MM patients and to achieve **rapid and sustained neutrophil (PMN) and platelet (PLT) engraftment** of the mobilized PBSCs .

Plerixafor Added to Chemotherapy Plus G-CSF Is Safe and Allows Adequate PBSC Collection in Predicted Poor Mobilizer Patients with Multiple Myeloma or Lymphoma

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ASBMT™ American Society for Blood and Marrow Transplantation

STUDY DESIGN

- Observational multicenter study aimed to evaluate the **feasibility of mobilization with Plerixafor after disease-oriented CHT+G-CSF** (according to the policy of each center),

  in patients with **MM** or **Lymphoma**, **at risk to mobilize poorly**, selected according to prospectively defined criteria

PREDICTED POOR MOBILIZERS: INCLUSION CRITERIA

- 1- **Mobilization failure**: at least one previously failed attempt to collect $\geq 2x10^6$ CD34+ cells/Kg after both G-CSF alone and chemotherapy followed by G-CSF
- **OR:**
- 2- Presence of **≥1 adverse factors for PBSC mobilization**

  -advanced disease,

  -prior extensive radiotherapy,

  -prolonged chemotherapy (≥2 courses),

  -past exposure to stem cell poisons (SCP)*

  -advanced age (>65 years old)

  -extensive bone marrow involvement before mobilization.

*Fluda, Lena, Mel (>4 courses)....

STUDY END POINTS

Main end point: to assess whether the use of Plerixafor after disease-specific chemotherapy followed by G-CSF would be **safe** and would allow **adequate PBSC collection for ASCT**, in **MM** and **lymphoma** patients at risk to mobilize poorly (**predicted PM**).

Secondary end points were to evaluate:

- **fold increase in CD34^{+}** cell count in PB after Plerixafor;
- **median number of aphaeresis days** needed to collect the target dose of CD34+ cells;
- percentage of **patients able to undergo ASCT**;
- **engraftment kinetics** after reinfusion of Plerixafor-mobilized PBSC;
- overall **outcome of the autografted patients**.

STUDY PATIENTS

N. Patients (April 2009 ➔May 2010)	37
MM/Lymphoma	17/20
M/F	22/15
Age median (range)	58 (20-74)
Advanced stage disease	30 pts
≥ 2 previous chemotherapy courses	28 pts
N. Chemotherapy courses median (range)	2 (1-4)
Previous Stem Cell Poisons*	17 pts
Previous mobilization failure	25 pts

***Fluda; Lena; Mel…>4 courses**

Comparison of characteristics influencing the mobilization ability in MM and Lymphoma pts

Characteristics	MM	Lymphoma	p
Age **(median)**	59	54	0.123
Standard Deviation	4.556	7.865	
Sex (M/F)	7/10	15/5	0.08
Previous chemotherapy courses **(median)**	2	2	0.637
Standard Deviation	0.899	0.745	
SCP Y/N	11/6	6/14	0.075
RX therapy Y/N	1/16	2/18	1
Previous mobilization failure Y/N	12/5	13/7	0.99
PB CD34+ cells* before Plerixafor **(median)**	6	5.5	0.718
Standard Deviation	11.425	7.048	

MOBILIZATION

- Disease-specific mobilization regimens were planned according to the local institutional guidelines.

- **G-CSF at 5-10 µg/Kg/day** was administered subcutaneously starting at 48-96 hours after the end of chemotherapy and continued until the last aphaeresis day.

- **Plerixafor (0.24 mg/Kg)** was administered subcutaneously for up to 3 days the evening before the planned leukaphaeresis (**from 9 to 11 hours before starting the procedure**). The patients received a median of 2 Plerixafor administrations (range: 1-3) after mobilization.

- TARGET: **≥ 2 x10^6 CD34+cells/Kg for a single ASCT**

  4x106 CD34+ cells/Kg for double ASCT

- ≤3 consecutive aphaeresis days

SIDE EFFECTS/ADVERSE EVENTS

- No grade 3-4 extra-hematological toxicities
- One patient developed a fever of unknown origin during the neutropenic phase.
- No significant laboratory abnormalities or worsening of liver or renal function during Plerixafor administration.

DETAILS OF MOBILIZATION

Characteristics	MM	Lymphoma
CHT mobilizing regimen	HD-CTX: 12 VP16: 3 Others: 2	DHAP: 13 HyperCVAD: 2 VP16: 2 Others: 3
Plerixafor injections median (range)	2 (1-3)	1 (1-2)
WBC before Plerixafor ($x10^3/\mu L$) median (range)	17 (2.1-68)	8.15 (1.4-61)
WBC 11 hrs after Plerixafor ($x10^3/\mu L$) median (range)	26.5 (3.5-79)	16.1 (7.2-65)
$CD34^+$ before Plerixafor ($x10^3/\mu L$) median (range)	6 (2-32)	5 (0-26)
$CD34^+$ 11 hrs after Plerixafor ($x10^3/\mu L$) median (range)	33 (6-201)	29 (0-116)
Fold-increase CD34+ count median (range)	4 (2-25)	3 (0-32)
Total number of $CD34^+$ cells collected ($x10^6/Kg$) median (range)	4.9 (0-15.2)	2.65 (0-8.2)
Total number of apheresis median (range)	2 (0-3)	1 (0-2)

Comparison of mobilization ability and harvest in the two populations

	MM	Lymphoma	p
PB CD34+ cells* after Plerixafor **(median)**	33 (SD 45.499)	31 (SD 26.946)	0.437
Fold increase **(median)**	4 (SD 5.985)	3 (SD 7.563)	0.485
CD34+ harvested (x10^6/Kg) **(mean)**	6.36 (SE 1.121)	3.8 (SE 1.063)	**0.03**
Number of leukaferesis **(median)**	2 (SD 0.845)	1 (SD 0.514)	0.059
% of pts failing to harvest$\geq$2x10^6 CD34/kg	18	35	0.24
Days for PMN>500 **(median)**	12 (SD 1.832)	14 (SD 3.795)	0.076
Days for PLT>20000 **(median)**	15 (SD 1.809)	18 (SD 22.033)	0.037
Days for PLT>50000 **(median)**	18 (SD 7.648)	30 (SD 50.904)	0.011

ASCT details and outcome

	MM	LYMPHOMA
Transplanted pts	13 (/17)	11 (3HL, 8 NHL) (/20)
Disease status before ASCT	3CR/nCR, 3 VGPR, 7 PR	5CR/nCR, 4PR, 2SD
Conditioning regimen	13 HDMel	6 FEAM, 3 BEAM, 1 TEAM, 1 Thio-Mel
ANC > 500/mcl median (range)	12 days (11-16)	14 days (10-23)
PLT>20000/mcl median (range)	15 days (11-18)	# 18 days (9-88)
PLT>50000/mcl median (range)	18 days (15-40)	# 30 days (19-180)
Response at day +90	3CR/nCR, 2VGPR, 6PR, 1 evaluable	6CR/nCR, 3 PR, 2 not evaluable
Status at day +90	12 alive, 1 dead	9 alive, 2 not evaluable

p 0.037 and 0.011

SUMMARY

- Percentage of successful collections: 73%
- 65% (13/20: 8/15 nHL and 5/5 HL) in lymphoma patients, 82% (14/17) in MM patients
- 24/37 pts (65%) with satisfactory harvests received ASCT after reinfusion of≥$2x10^6$CD34+/kg: 13MM pts and 11 Lymphoma pts (8 NHL and 3/5 HL).

CONCLUSIONS -1

- Addition of **Plerixafor** to G-CSF after chemotherapy is **safe**
  Remarkable **multiple-fold increase** (median value: 4) in the number of **circulating CD34+** cells after Plerixafor
- This strategy can effectively **rescue most PM candidates for ASCT who previously failed a mobilization attempt**, in a similar proportion to that observed in patients receiving Plerixafor+ G-CSF without chemotherapy.
- 65% of PM patients with high-risk disease, were able to be rescued with ASCT
- **Good outcome in terms of engraftment and of clinical response**.

CONCLUSIONS - 2

- **MM** patients collected significantly **higher CD34+ cell doses** than the lymphoma patients.

- The CD34+ increase rates after Plerixafor did not significantly differ (Plerixafor equally effective in the two populations).

- The higher CD34+ cell dose reinfused in the MM patients did not translate into faster PMN recovery, while a **significantly faster PLT recovery** was observed in the **MM patients**.

FUTURE PERSPECTIVES

- **Plerixafor after chemotherapy plus G-CSF allows better disease control**, especially in patients with aggressive disease. This can translate into **a higher percentage of patients eligible for ASCT** compared with G-CSF and Plerixafor alone, where the lack of disease de-bulking, could potentially lead to ASCT failures.

- The advent of **Plerixafor** will likely **change the current standards for SCT and PBSCs mobilization**: Plerixafor has broadened the therapeutic options for mobilization of PBSCs for patients in need of high-dose chemotherapy, thereby **increasing the pool of patients for whom autoSCT is an option**.

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