Allogeneic HSCT in PTCL "European perspective"

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ISTITUTO NAZIONALE
PER LO STUDIO
E LA CURA DEI TUMORI

Dislosures

- Speaker or advisory boards or research support:
- Celgene, Janssen, Takeda, Novartis, Roche Gilead, Kyowa Kirin, BMS, MSD

Rationale for allogeneic SCT in PTCL

1. Results of conventional or high-dose chemotherapy at relapse are still largely unsatisfactory even with new drugs

2. T-cells can be a good target for donor derived immune cells: the so called "Graft-Versus-Lymphoma" effect

3. Allogeneic grafts are free from tumor cell contamination.

Survival and transplant-related mortality (TRM) curves

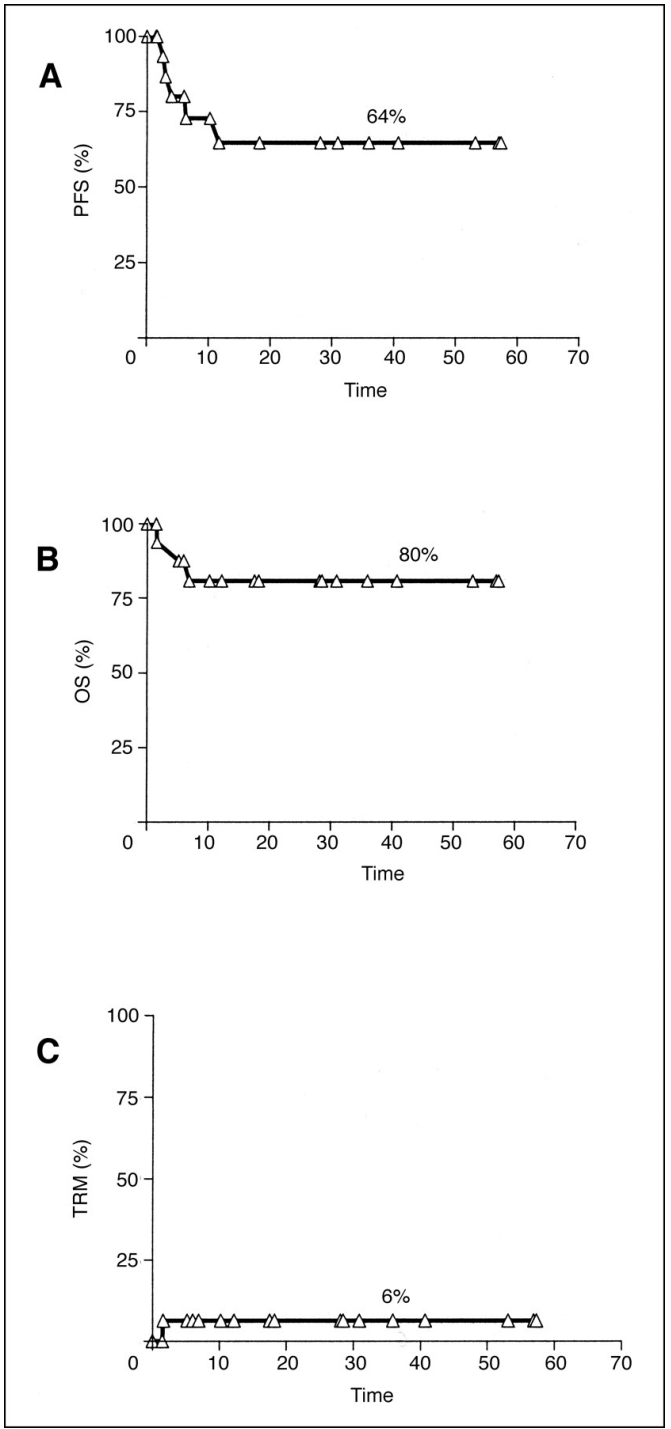
17 patients

(15 chemosensitive)

Estimated OS 80%,

PFS: 60% at 3 yrs

NRM: 6% at 2 yrs



Corradini, P. et al. J Clin Oncol 2004

Graft versus lymphoma effect for aggressive T-cell lymphomas

- French study - (Le Gouill et al. JCO 2008)

-**77** aggressive T-cell lymphoma

-57 (75%) myeloablative,

20 (25%) RIC

-Median age:36

-**Results**:

-5-year **OS** 57%

-5-year **EFS** 53%

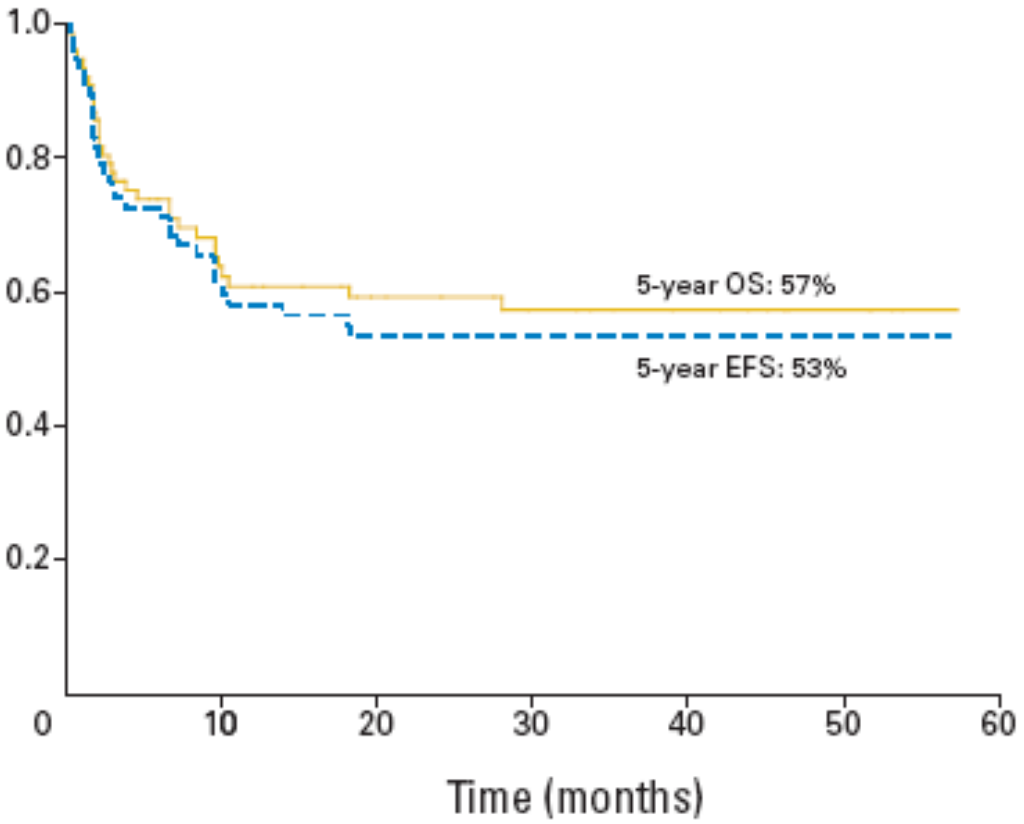
-**23** patients in PR at transplant

→ **17 CR (74%)**

-**23** patients in SD/PD/refractory

→ **13 CR (56%)**

-TRM → 34%



Disease status at transplant influence OS

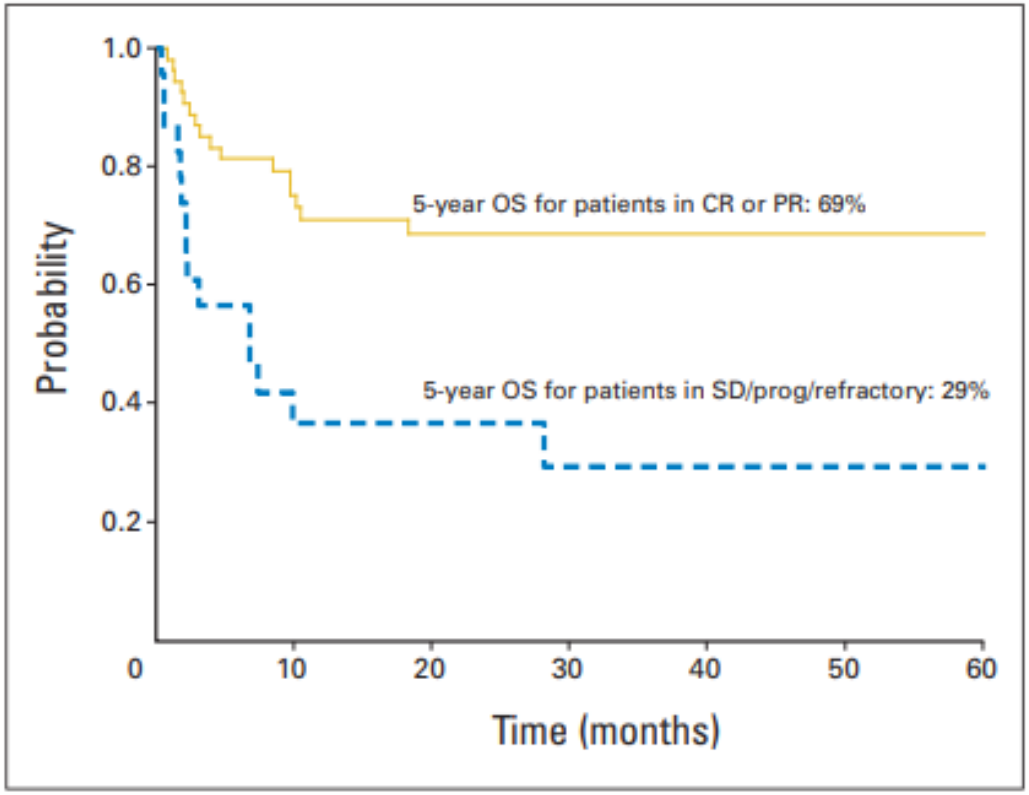


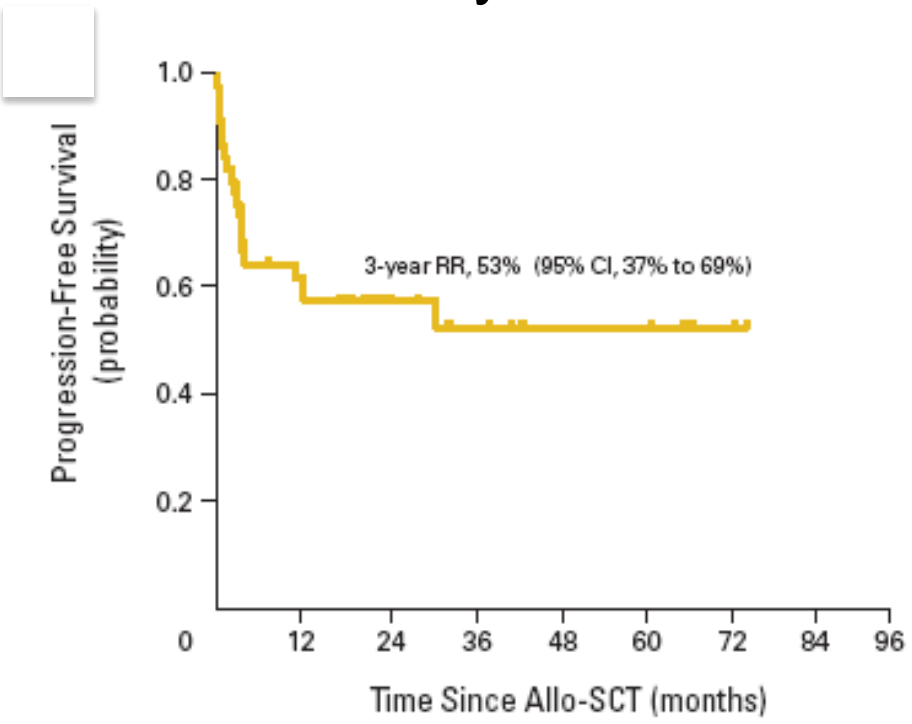
Fig 3. Five-year overall survival (OS) after allogeneic stem-cell transplantation according to disease status at transplantation. CR, complete remission; PR, partial response; SD, stable disease; prog, progression.

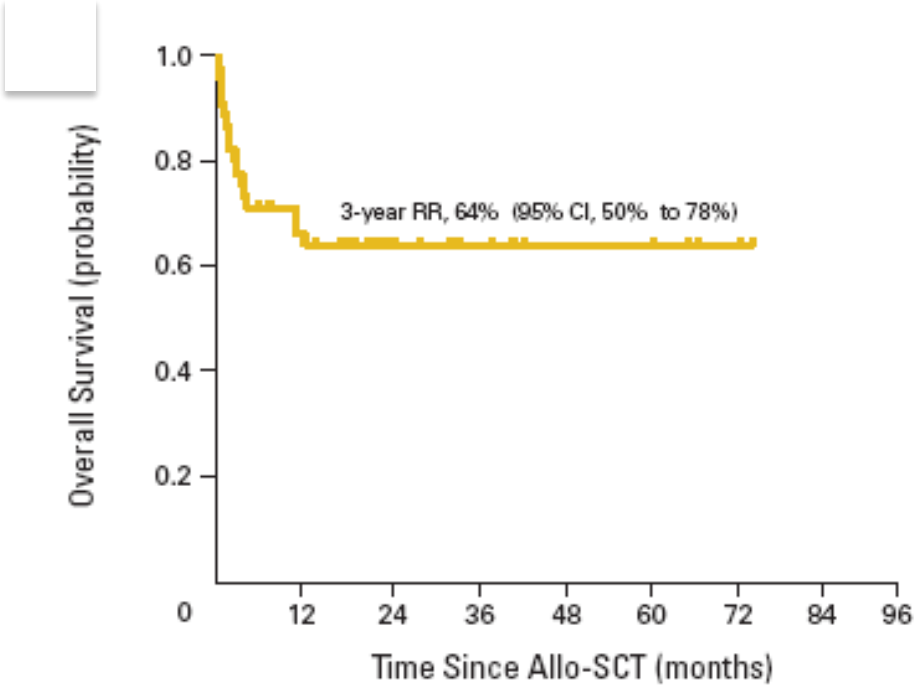
Le Gouill et al. JCO 2008

Allogeneic SCT in angioimmunoblastic

(Kyriakou C, JCO 2009)

- EBMT retrospective study; 45 pts, median, age 48 yrs
- Before allo-SCT: 60% chemosensitive disease
- 56% myeloablative, 44% RIC.
- NRM 25% 1 year





Chronic GVHD has a protective effect on disease relapse

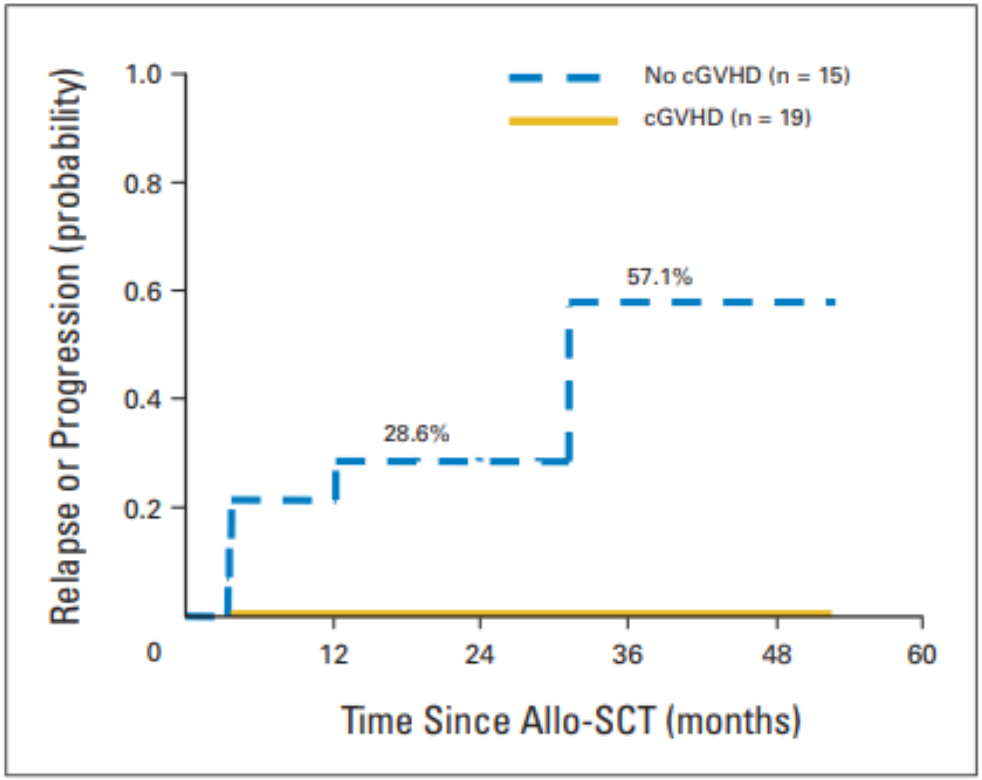


Fig 1. Impact of chronic graft-versus-host disease (cGVHD) on the relapse rate after transplantation. alloSCT, allogeneic stem-cell transplantation.

Kyriakou C, JCO 2009

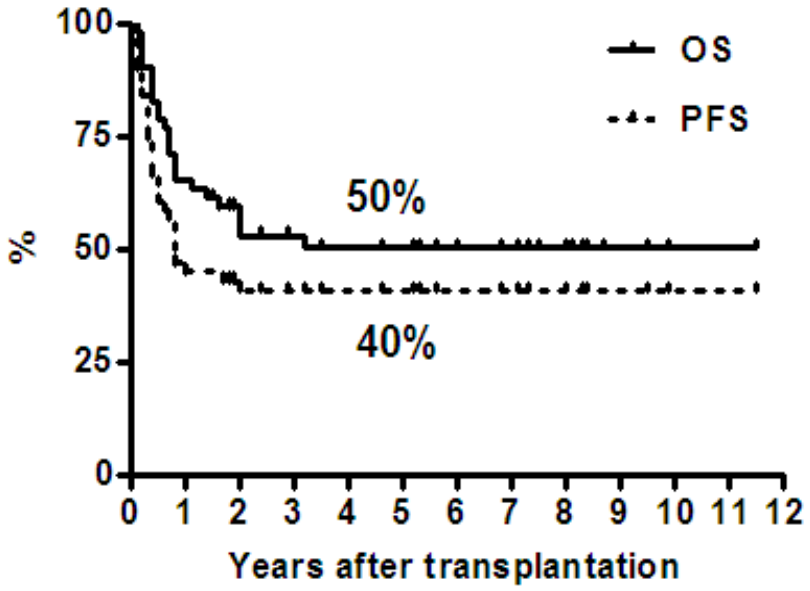
RIC alloSCT in 52 rel/ref PTCL: long-term outcome

Median Age at Diagnosis (range)	47 years (15-64)	%
Sex (Men/Female)	33 /19	64%/37%
Subtypes PTCL-NOS AITL ALCL Other	 23 9 11 9	 45% 17% 21% 17%
Median Time from Dx to AlloSCT (range)	18 (4-99 months)	-
No. Lines of Treatment ≤ 2 > 2	 34 18	 65% 34%
Previous Autograft	27	52%
Disease Status at alloSCT CR/PR Refractory	 39 13	 75% 25%
Donor Type HLA matched sibling Unrelated/Haploidentical	 33 13/6	 64% 25%/11%

Dodero A et al Leukemia 2012

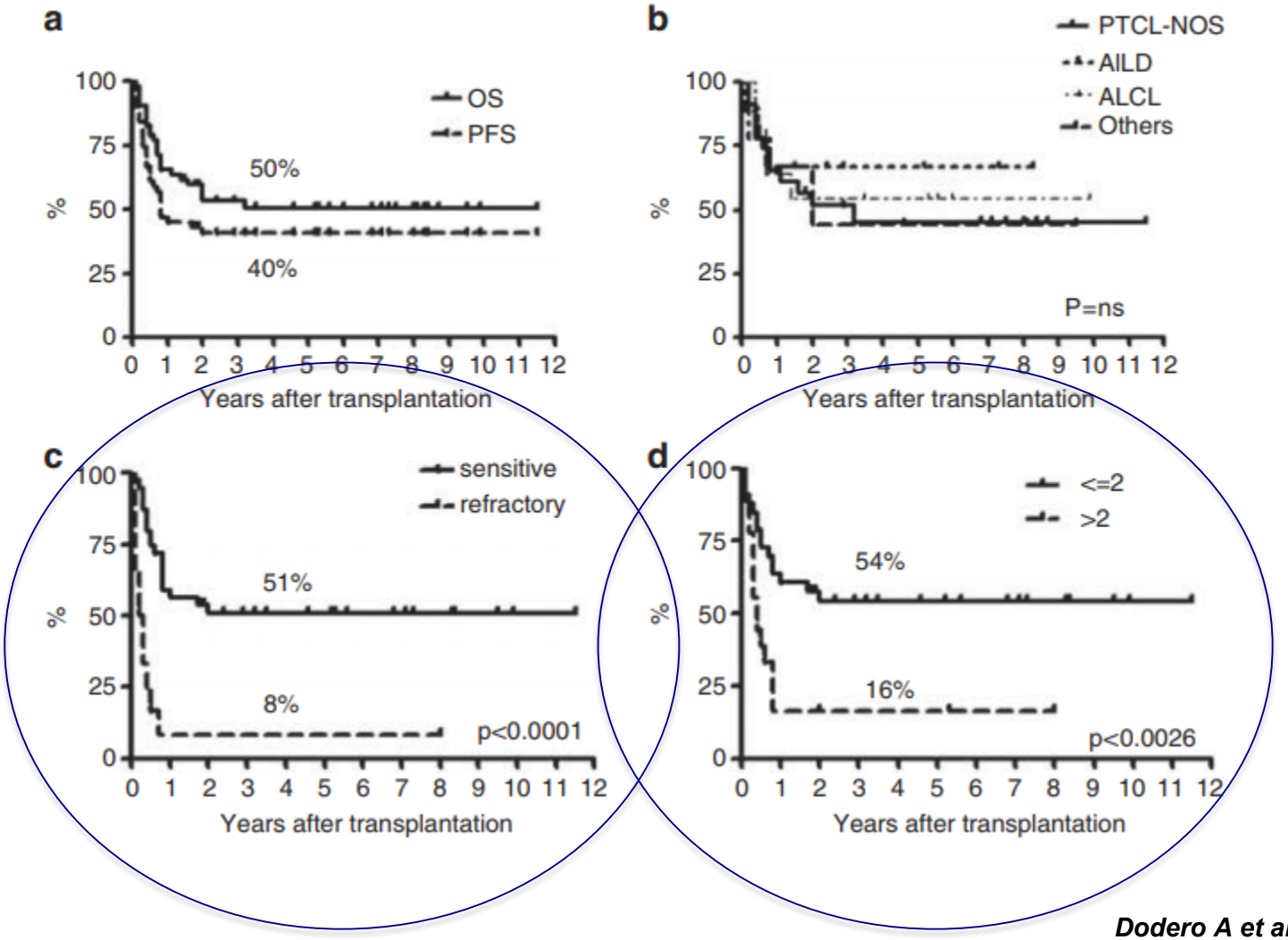
RIC alloSCT in 52 rel/ref PTCL

Survival curves: PFS and OS



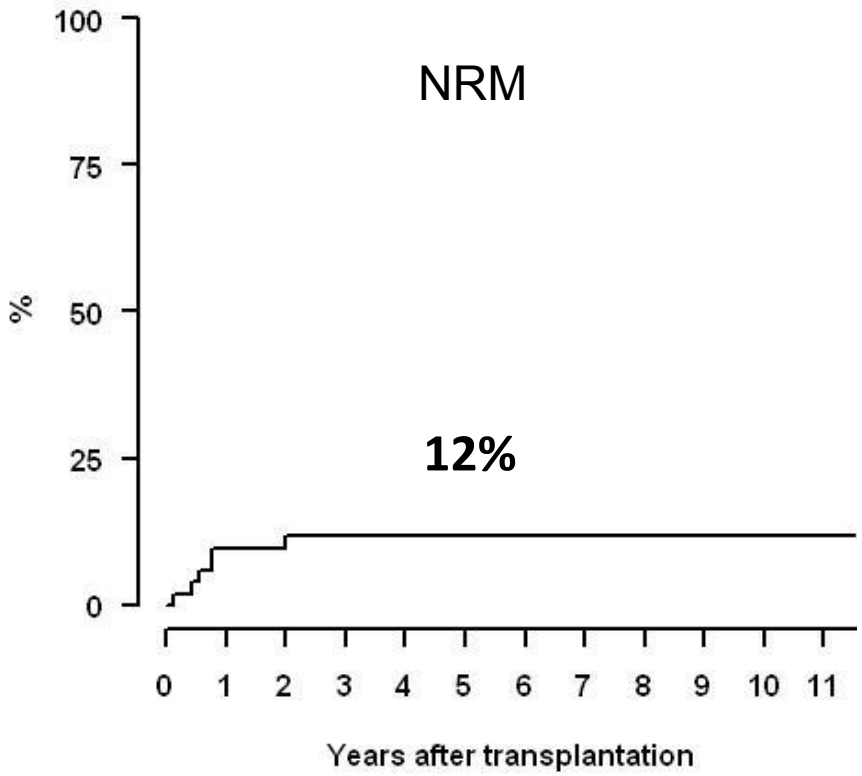
Median follow-up: 67 months (range 18-138 months)

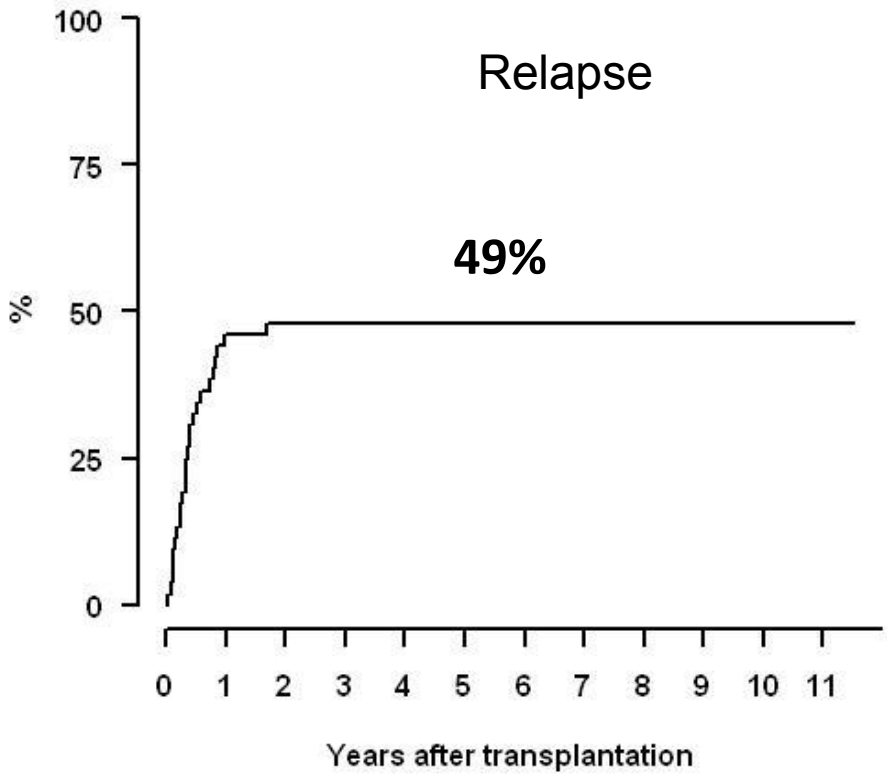
Chemorefractory disease at transplant influence survival



Dodero A et al, Leukemia, 2012

Non Relapse Mortality and Relapse incidence





Intensive Chemo-immunotherapy as First-line Treatment in Adult Patients With PTCL

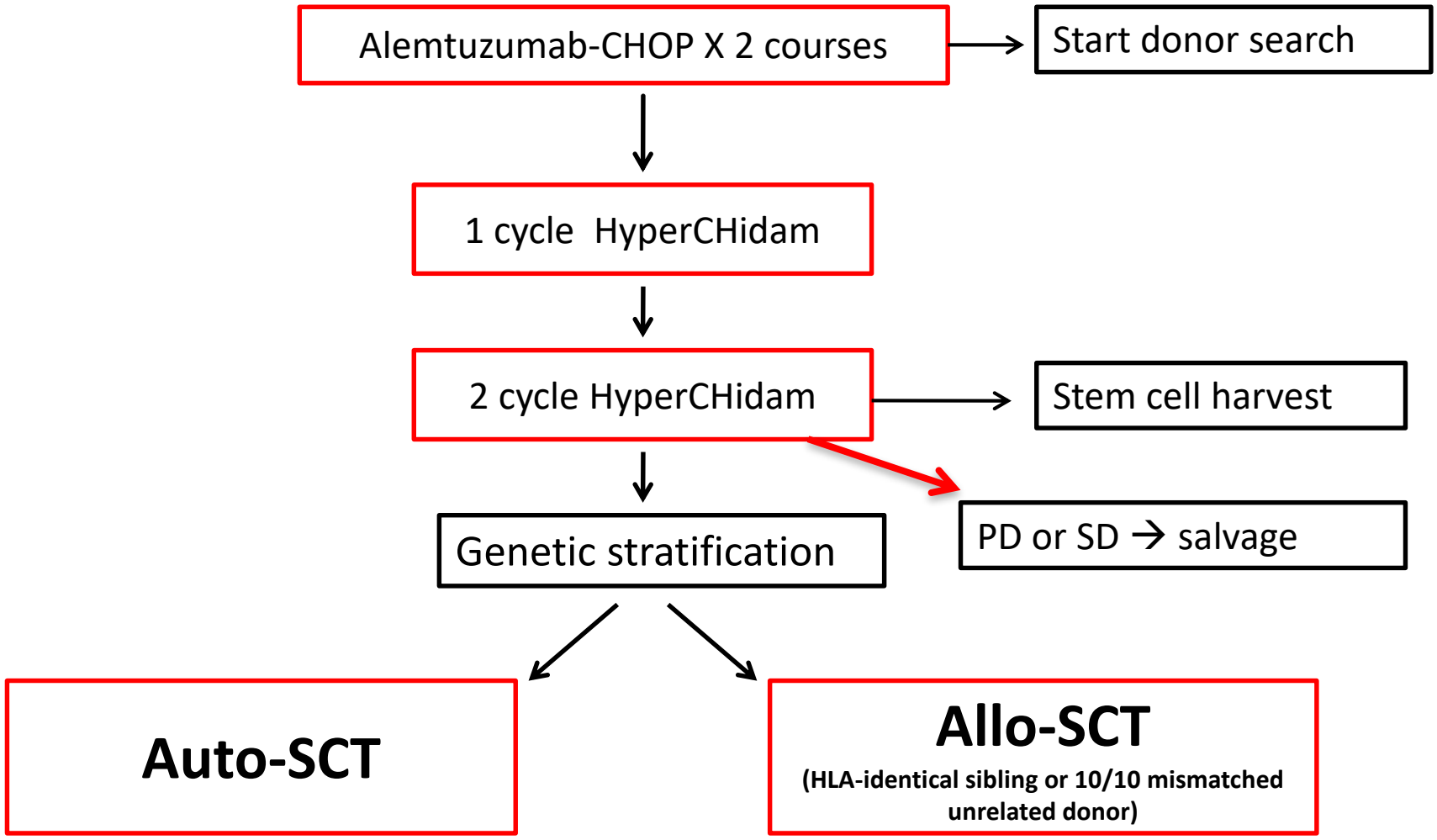
- GITIL and IIL national prospective trial (2006) -

AIM OF THE STUDY: A "global" approach to improve the outcome of PTCLs reducing the primary refractory and early PD patients

1. Inclusion of alemtuzumab at diagnosis
2. HD chemo before transplant with drug crossing the blood-brain barrier
3. First study with allogeneic SCT frontline

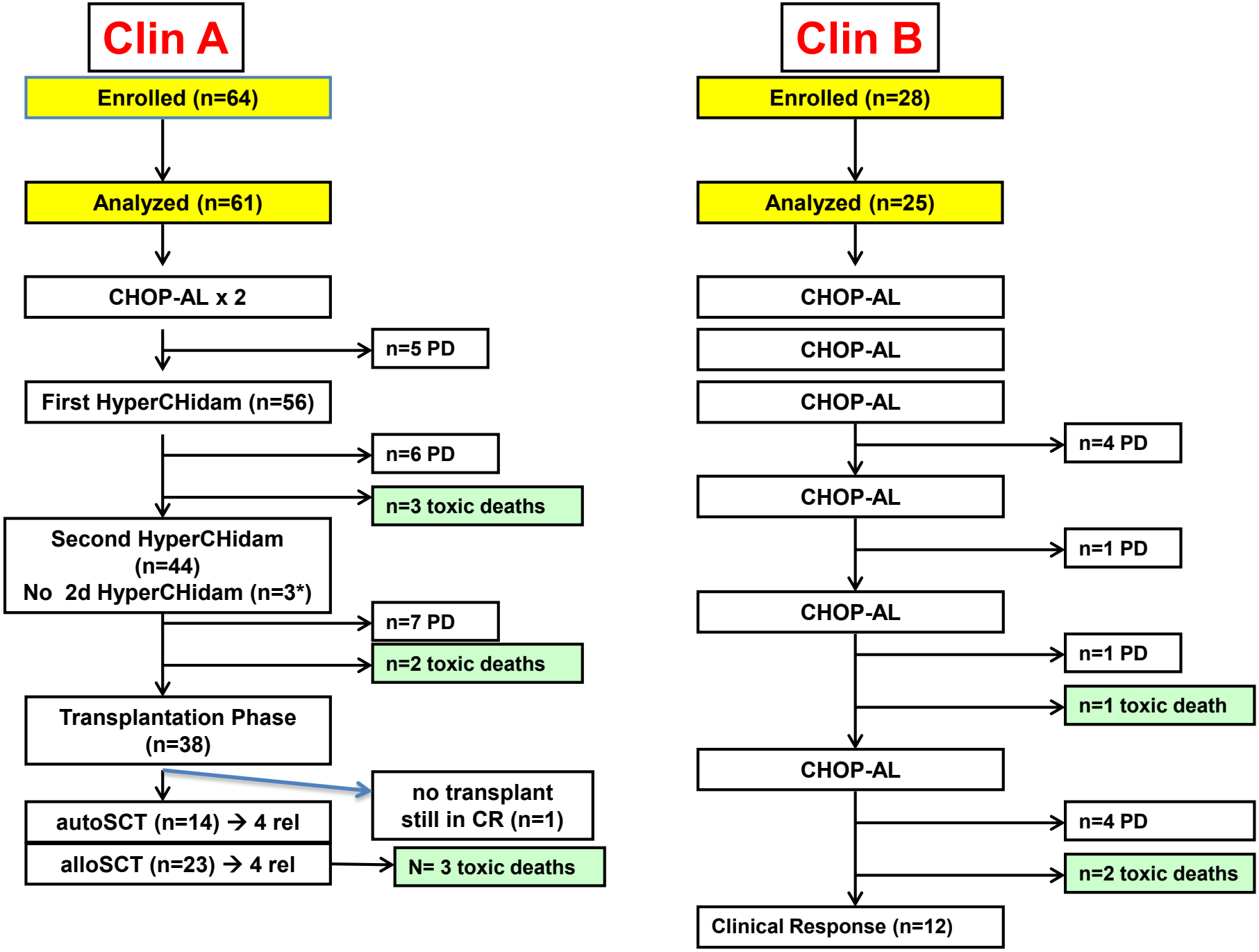
Corradini P Leukemia 2014.

Outline of Clin A Study



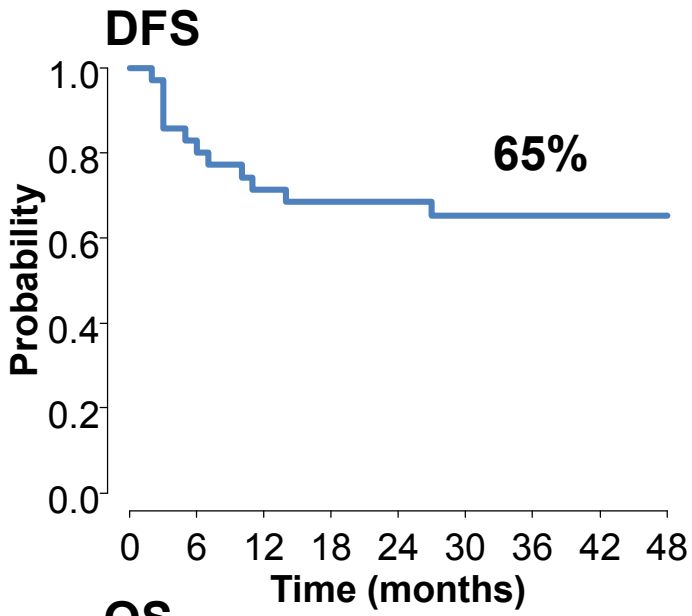
HyperCHidam, Hyperfractionated cyclophosphamide with high-doses of arabinosylcytosine and methotrexate

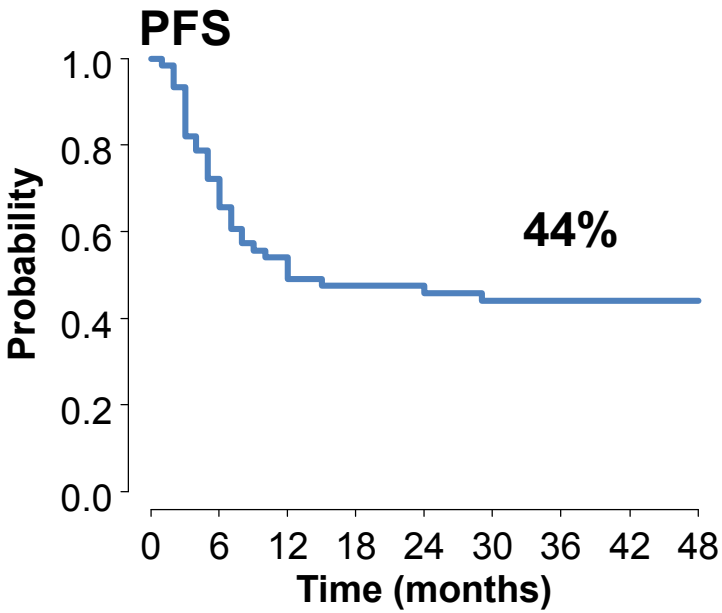
EudraCT Number 2006-004234-33

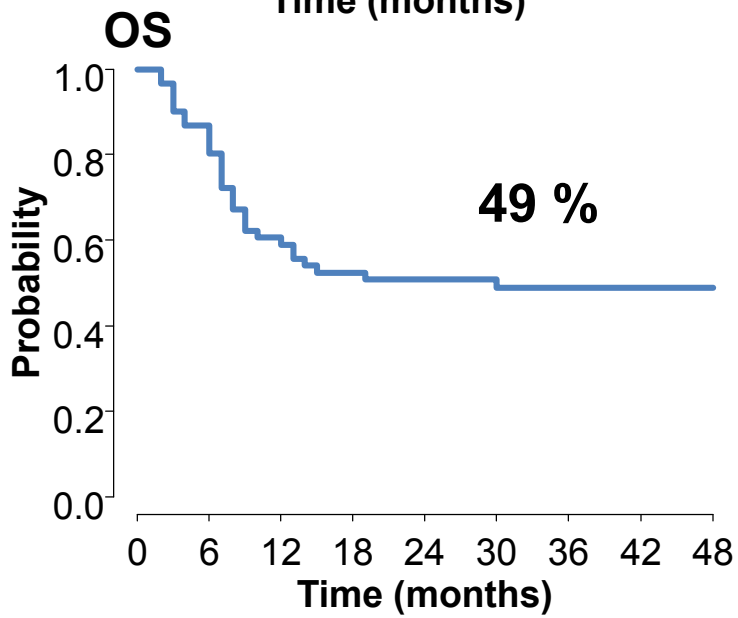


*these 3 patients received directly transplantation

Clin A – Survival Outcomes



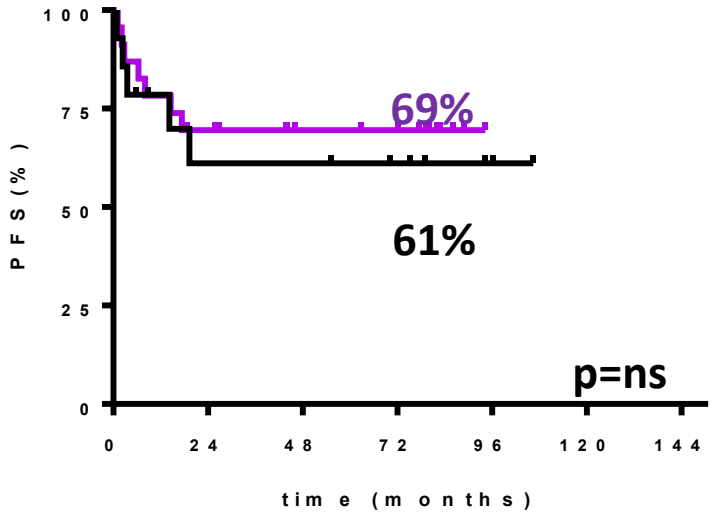


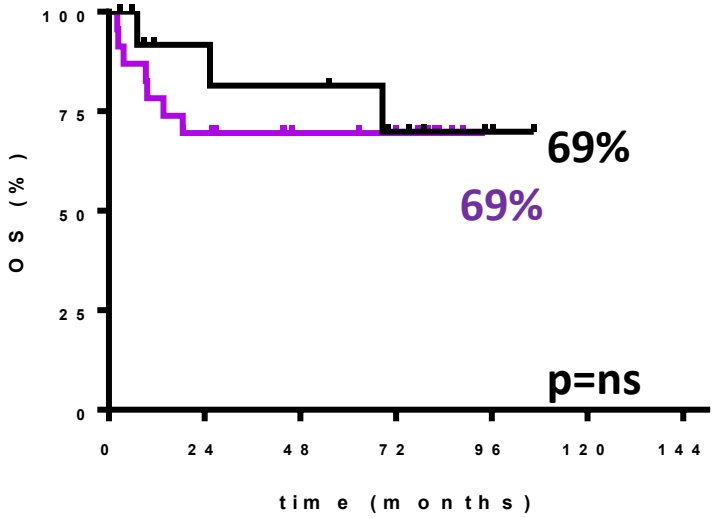


- **Median follow-up: 40 months**
- **8 of 61 patients died for treatment-related causes with a cumulative incidence of non-relapse mortality of 13%.**

Corradini P et al. Leukemia 2014

Intensified Chemo-immunotherapy with auto or allo-SCT - Only transplanted pts: up-date December 2016-



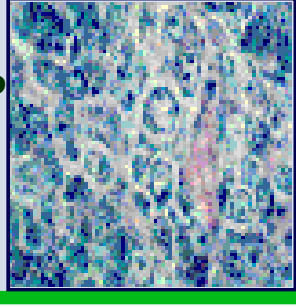


3 patients relapsed after AutoSCT were rescued by alloSCT

Median Follow-up 60 months

THE LYMPHOMA STUDY ASSOCIATION (LYSA Lymphomes T)

GERMAN HIGH-GRADE LYMPHOMA STUDY GROUP (DSHNHL)



Allogeneic or Autologous Transplantation as First-Line Therapy for Younger Patients with Peripheral T-Cell Lymphoma

Results of the Interim Analysis of the AATT Trial

Norbert Schmitz, Maike Nickelsen, Bettina Altmann, Marita Ziepert, Kamal Bouabdallah, Christian Gisselbrecht, Sébastien Maury, Guillaume Cartron, Emmanuel Gyan, Arnaud Jaccard, Laurence Sanhes, Philippe Gaulard, Andreas Rosenwald, Lorenz Truemper, Bertram Glass, Peter Reimer, Wolfgang Herr, Martin Wilhelm and Olivier Tournilhac

THE LYMPHOMA STUDY ASSOCIATION (LYSA Lymphomes T)

GERMAN HIGH-GRADE LYMPHOMA STUDY GROUP (DSHNHL)

Inclusion criteria

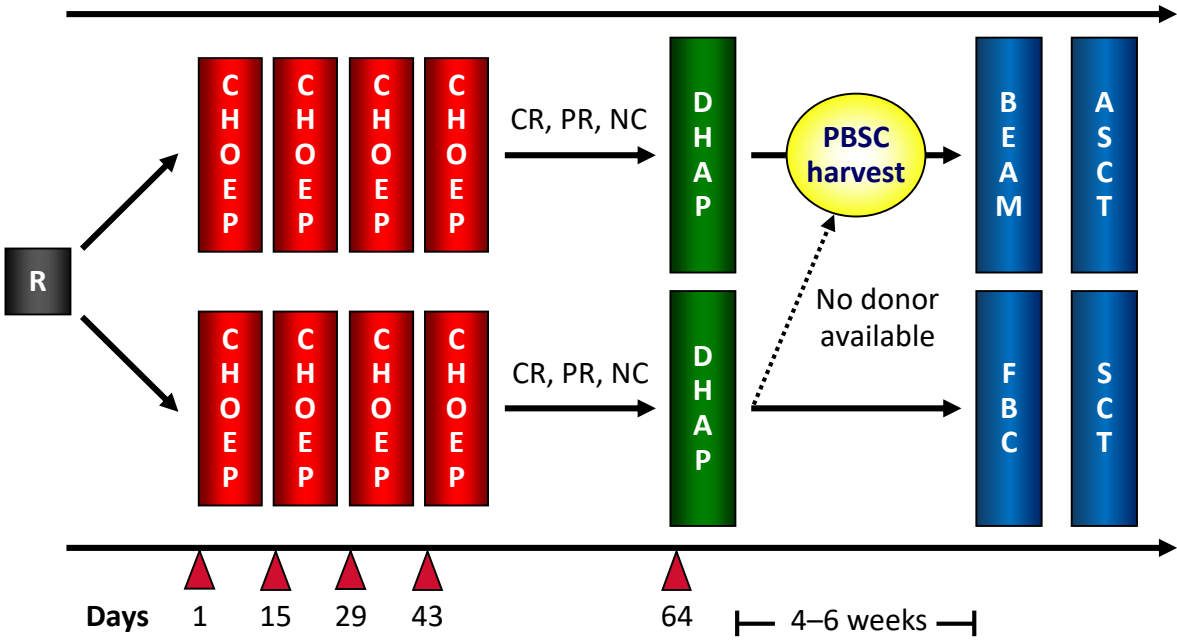
- Patients 18-60 years
- ECOG 0-3

with

- **Peripheral T-cell lymphoma, NOS**
- **Angioimmunoblastic T-cell lymphoma**
- **Anaplastic large cell lyphoma, ALK negative**
- Extranodal NK/T-cell lymphoma, nasal type
- Enteropathy type T-cell lymphoma
- Hepatosplenic T-cell lymphoma
- Subcutaneous panniculitis-type T-cell lymphoma

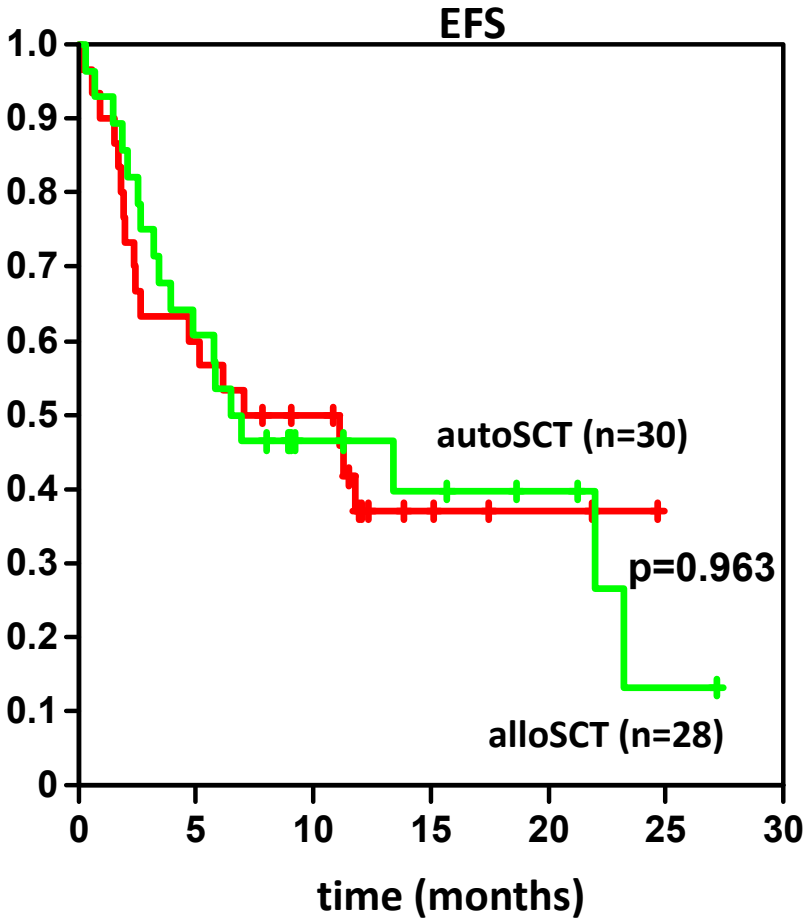
- All stages and IPI except stage I and aaIPI 0

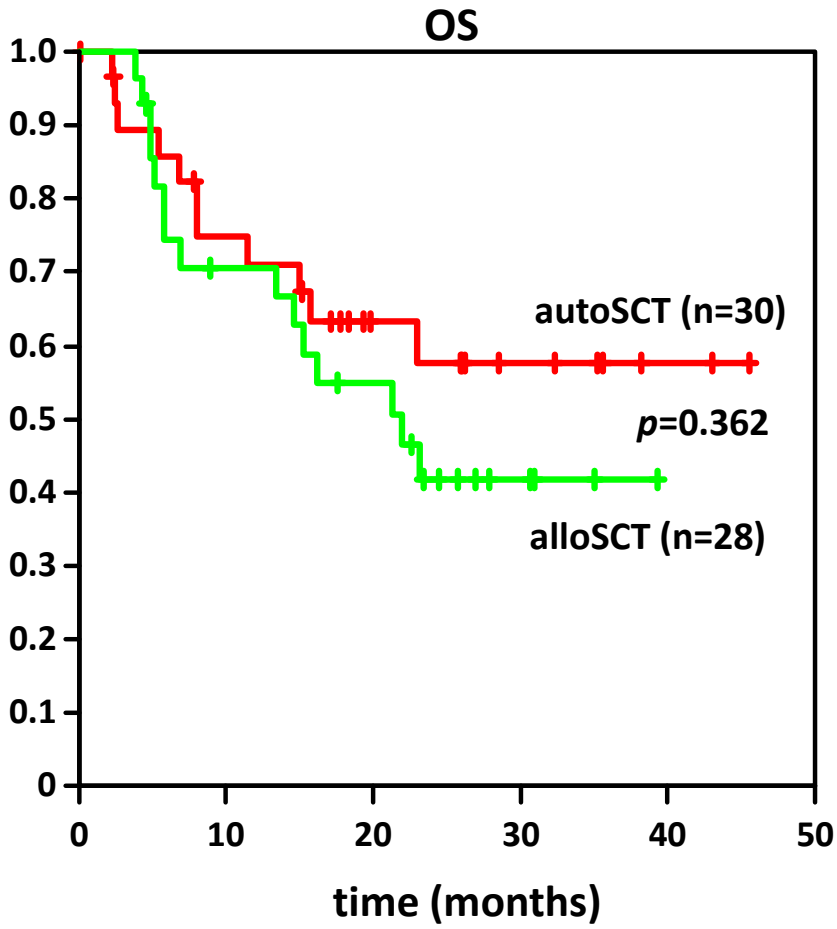
Study design



BEAM: BCNU 300 mg/m^2, Ara-C 800 mg/m^2, VP-16 800 mg/m^2, Mel 140 mg/m^2
FBC: Fludara 125 mg/m^2, Busulfan 12 mg/kg, Cyclo 120 mg/kg

AATT study:
Results of interim analysis (n=58)





median observation time: 26 months

Analysis on 104 patients is expected

Courtesy from N.Schmitz

Ann Oncol. 2015 Feb;26(2):386-92.

Upfront allogeneic stem-cell transplantation for patients with nonlocalized untreated peripheral T-cell lymphoma: an intention-to-treat analysis from a single center.

Loirat M[1], Chevallier P[1], Leux C[2], Moreau A[3], Bossard C[3], Guillaume T[1], Gastinne T[1], Delaunay J[1], Blin N[1], Mahé B[1], Dubruille V[1], Augeul-Meunier K[1], Peterlin P[1], Maisonneuve H[4], Moreau P[5], Juge-Morineau N[6], Jardel H[7], Mohty M[8], Moreau P[1], Le Gouill S[9].

All patients that presented with advanced PTCL in our institution at diagnosis were scheduled to undergo upfront allo-SCT after induction chemotherapy. From 2004 to 2012, **49 newly diagnosed PTCL** patients were scheduled to receive upfront allo-SCT. A human leukocyte antigen-matched donor was found for 42 patients: related to the patient in 15 cases, unrelated in 20 cases, and suitable cord blood units were used in 7 cases.

RESULTS: After induction chemotherapy, 17 patients reached complete remission and **29 (60%) proceeded to upfront allo-SCT**. For all patients, the 1 and 2-year overall survival (OS) rates were 59% [95% confidence interval (CI) 47-75] and 55% (95% CI 43-71), respectively. The most frequent reason we did not proceed to allo-SCT was disease progression or insufficient response after induction. **For transplanted patients, the 1- and 2-year OS were 76% (95% CI 62-93) and 72.5% (95% CI 58-91), respectively. Toxicity-related mortality (TRM) 1 year after allo-SCT was only 8.2%** (95% CI 0-18.5). The 2-year progression-free survival (PFS) rate of patients who did not proceed to allo-SCT (n = 20) was below 30%. The disease status at the time of transplantation was a strong predictive marker for both PFS and OS in transplant patients.

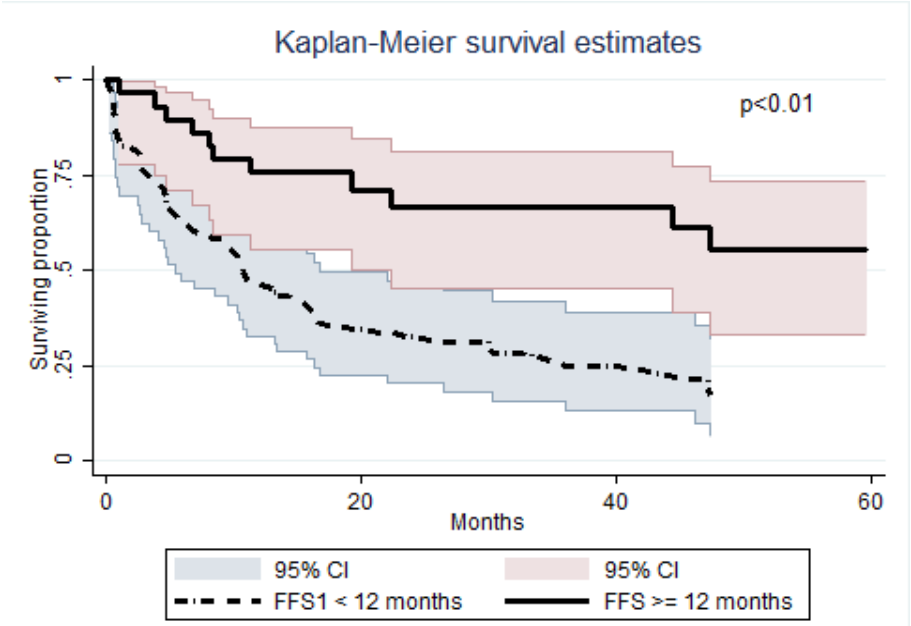
CONCLUSIONS: Upfront allo-SCT in PTCLs is feasible with low TRM, and it provides long-term disease control. However, one-third of patients remain chemo-refractory .

Retrospective study on transplant eligible patients at first relapse

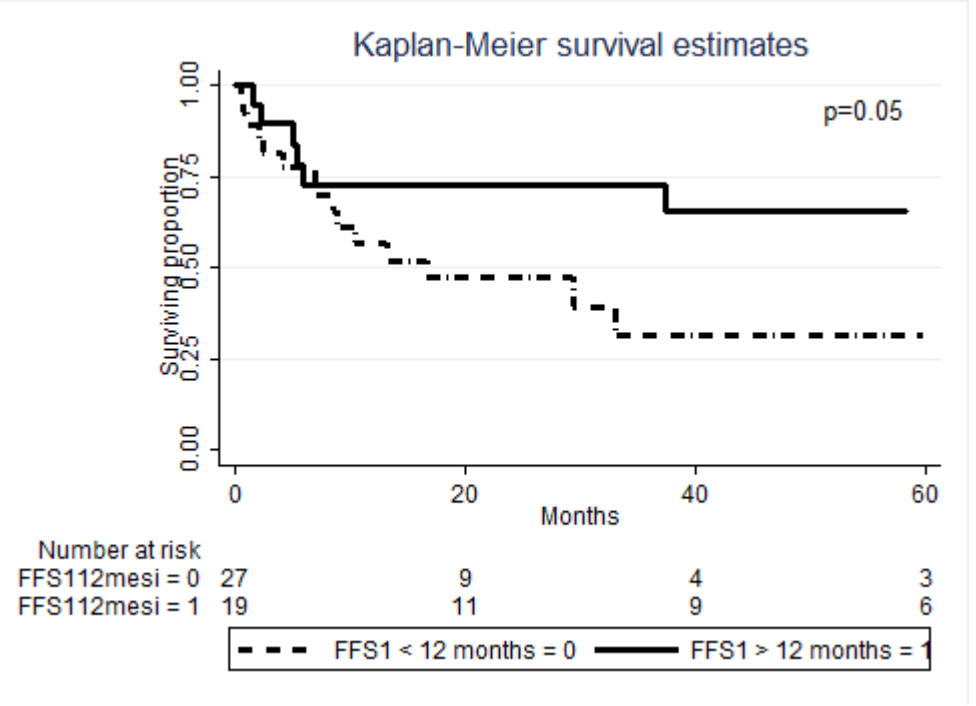
Patients (age)	Histology	AlloSCT	No alloSCT	Median Survival	Risk factors
79 (50 yrs)	31 PTCL-U 23 ALC 16 AITL 9 other	46(58%)	34(42%): -27 Progression -6 Unfit -1 No donor	4-year 31%	•Extranodal disease at Dx •FFS1<12 months

Corradini P et al manuscript in preparation

The first FFS (less than 12 mos) influence also the outcome alloSCT



Relapsed/refractory cohort (79 patients)



AlloHCT cohort (46 patients)

Conclusions

- AlloSCT is a potentially curative therapy for 40-50% of rel/ref PTCLs (possible GvL effect).
- It should be reserved after first relapse or progression in chemosensitive disease.
- Only a 50-60% of transplant-eligible patients will be able to receive allogeneic SCT. Chemorefractory disease is the main problem.

Ice Fall - Avers Monster, Suisse Alps

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