

Lymphomes

Y a t 'il une place pour
l 'allogreffe ?

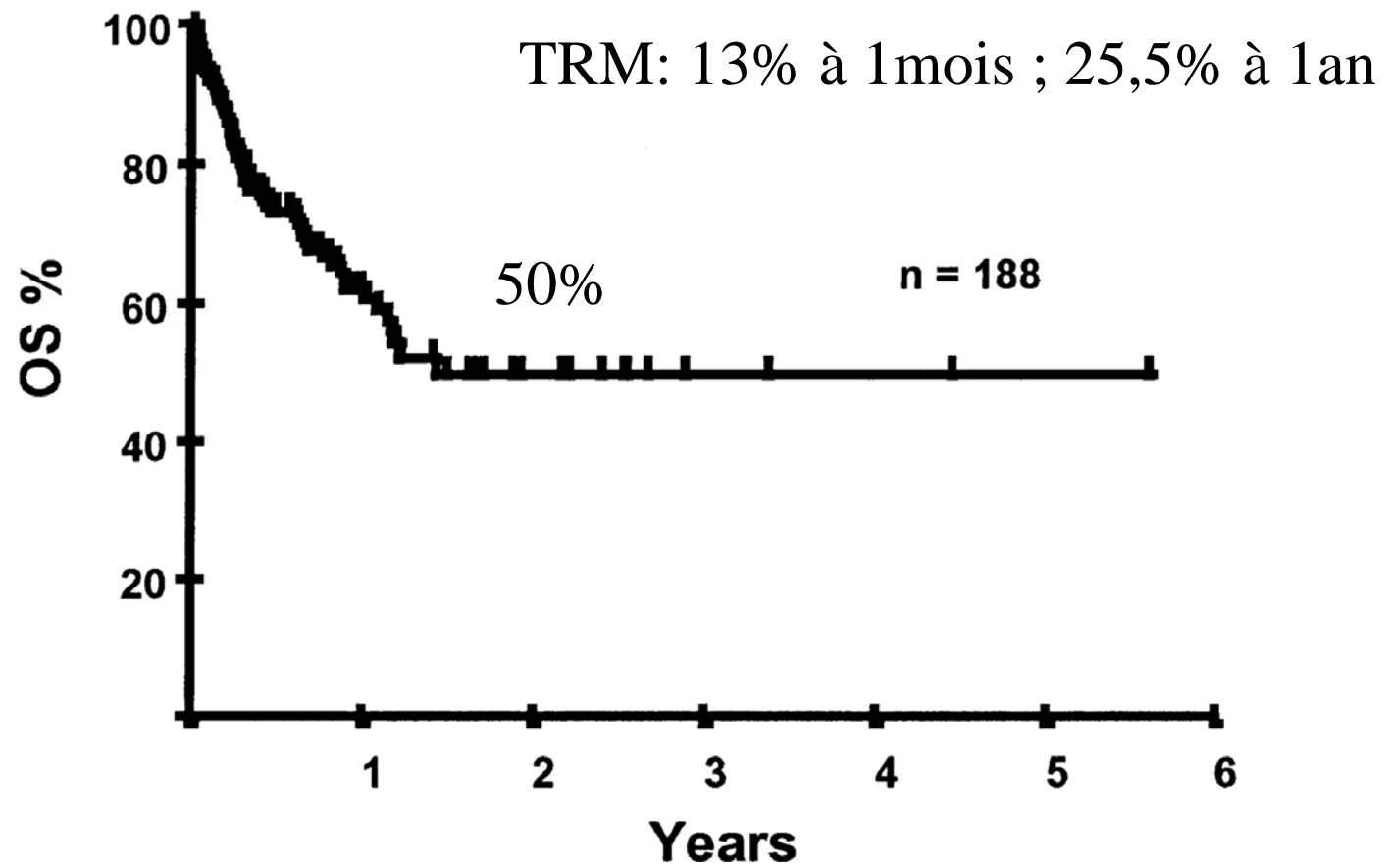
Mini allo: retrospective EBMT

**188 pts. Age médian: 40. Auto avant: 48%.
N° median ligne de chimio: 3**

84% fluda

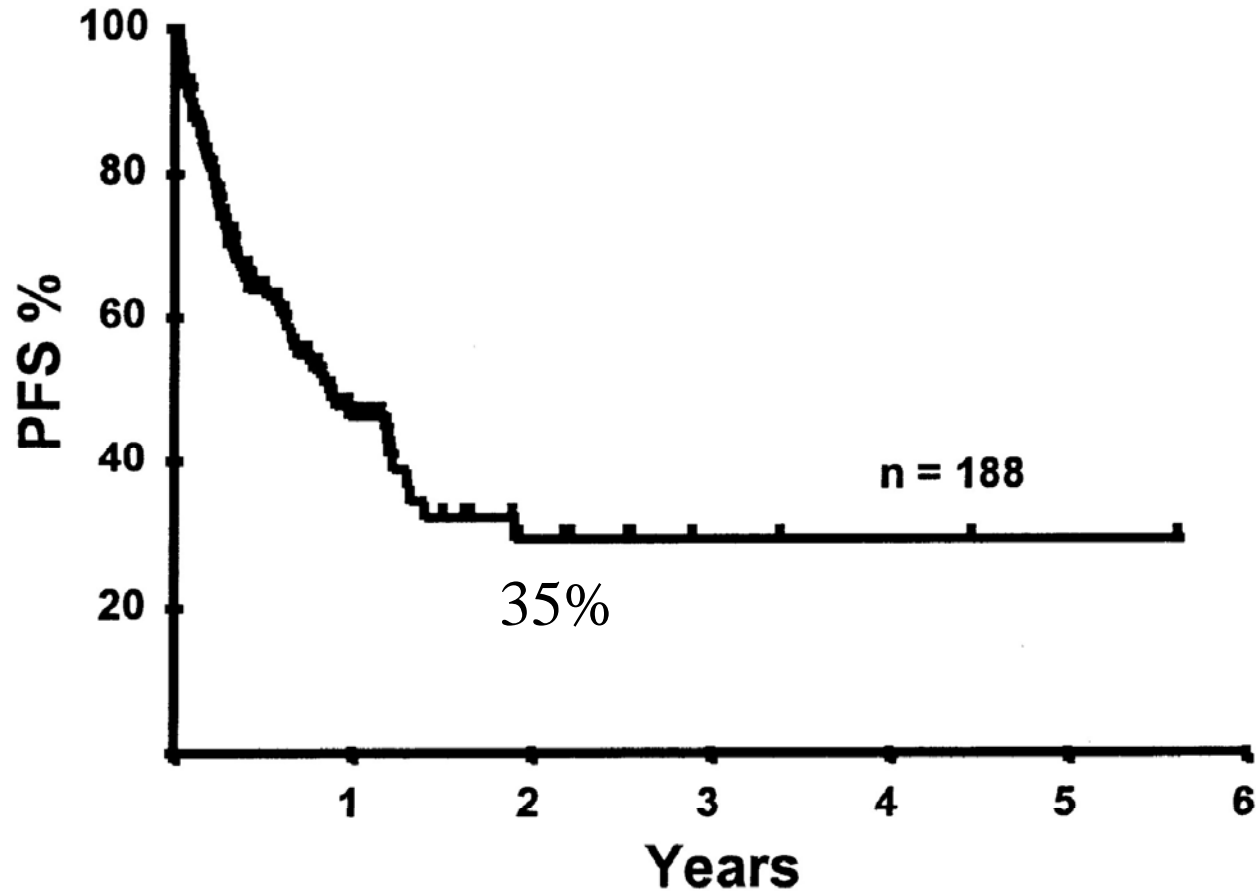
10% BEAM

Robinson SP et al Blood 2002;100: 4310



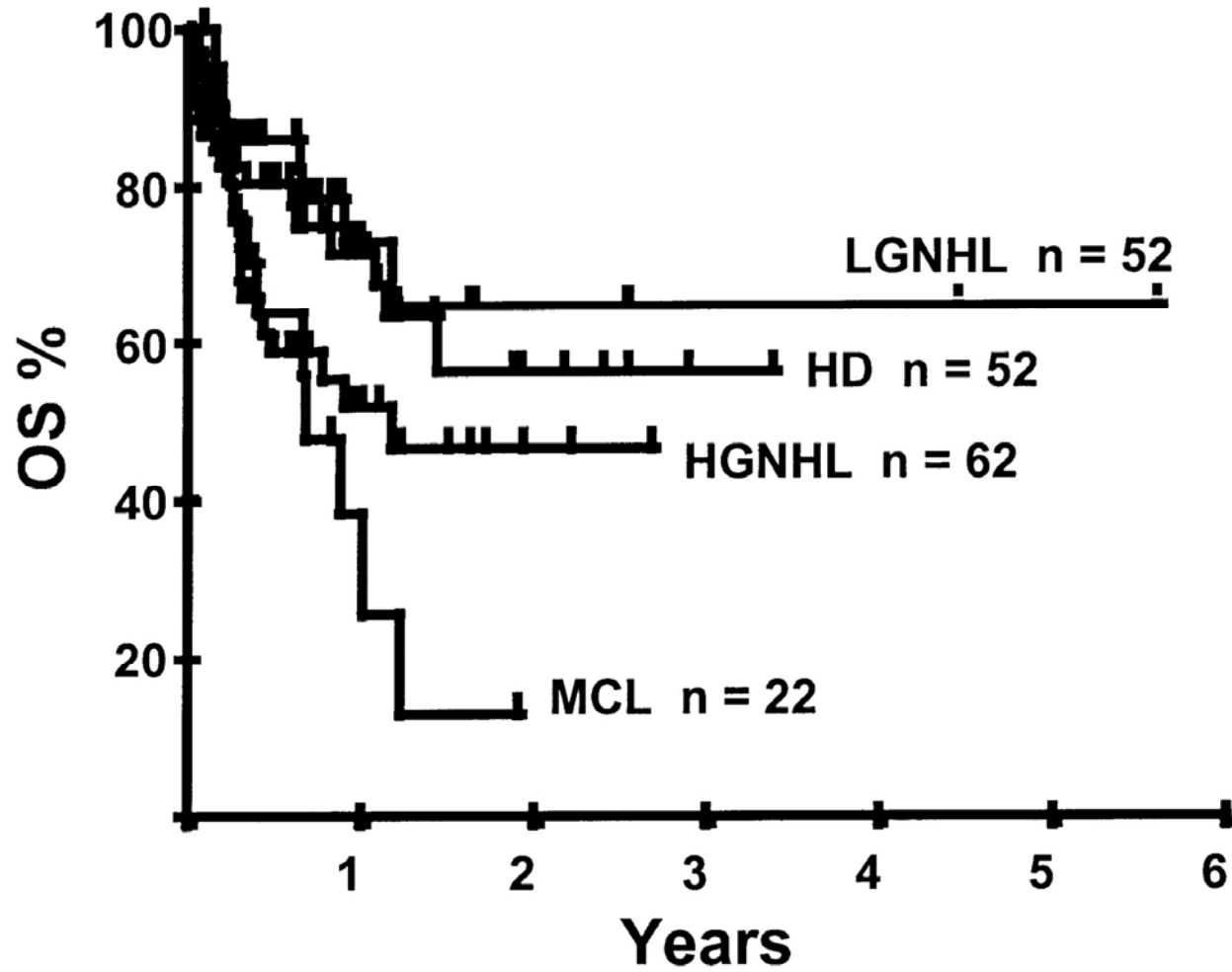
Robinson, S. P. et al. Blood 2002;100:4310-4316

Figure 7.



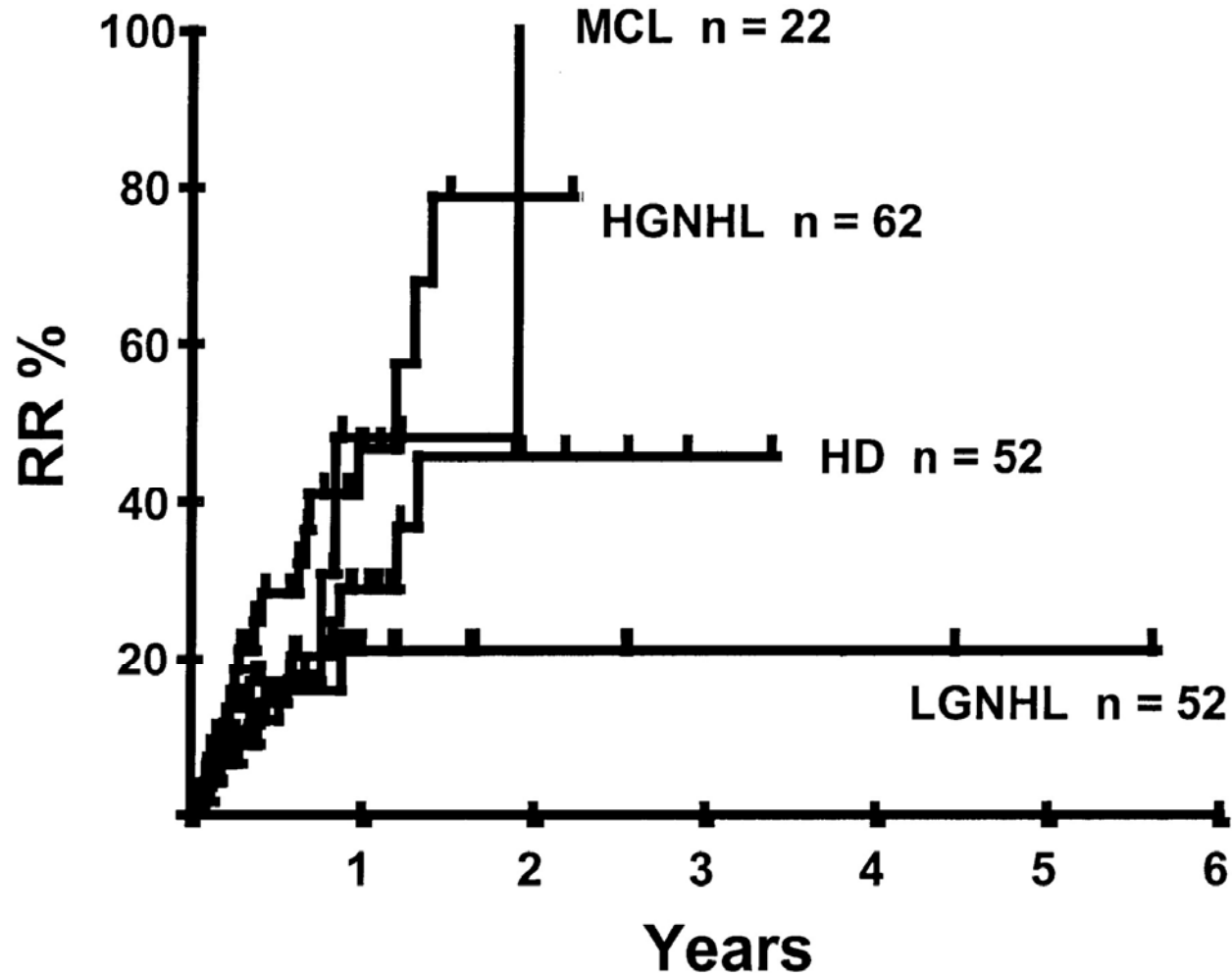
Robinson, S. P. et al. Blood 2002;100:4310-4316

Figure 3.

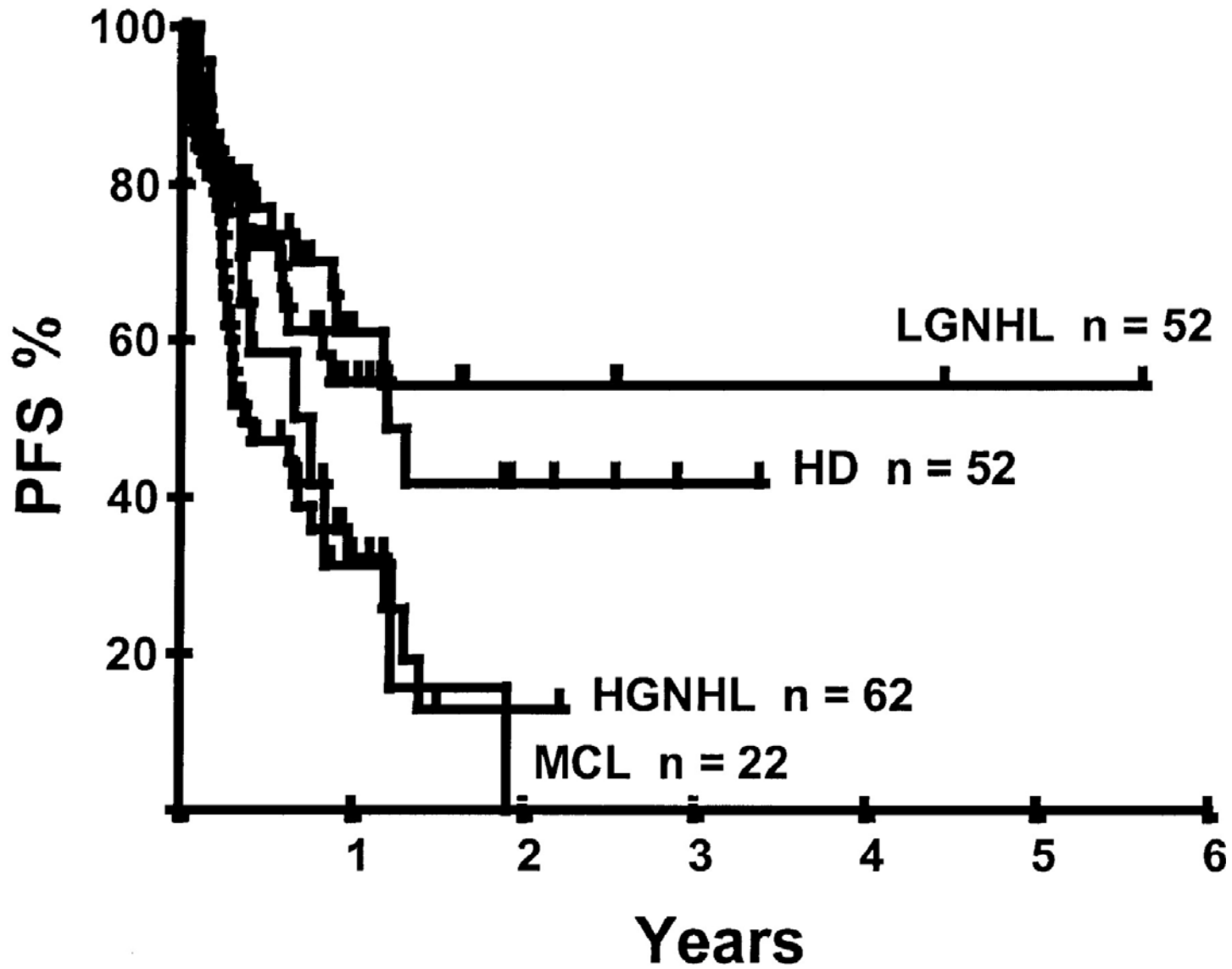


Robinson, S. P. et al. Blood 2002;100:4310-4316

Figure 6.

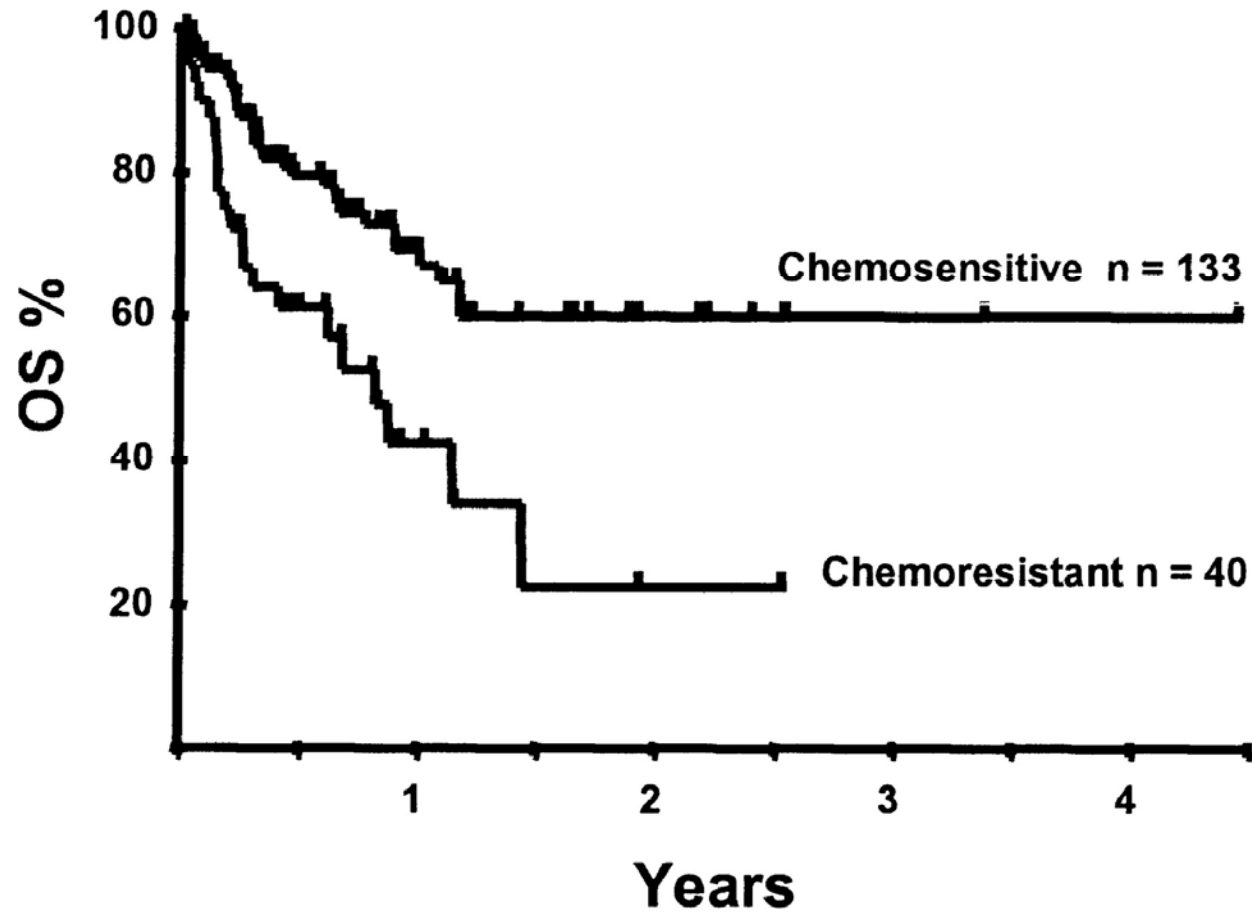


Robinson, S. P. et al. Blood 2002;100:4310-4316



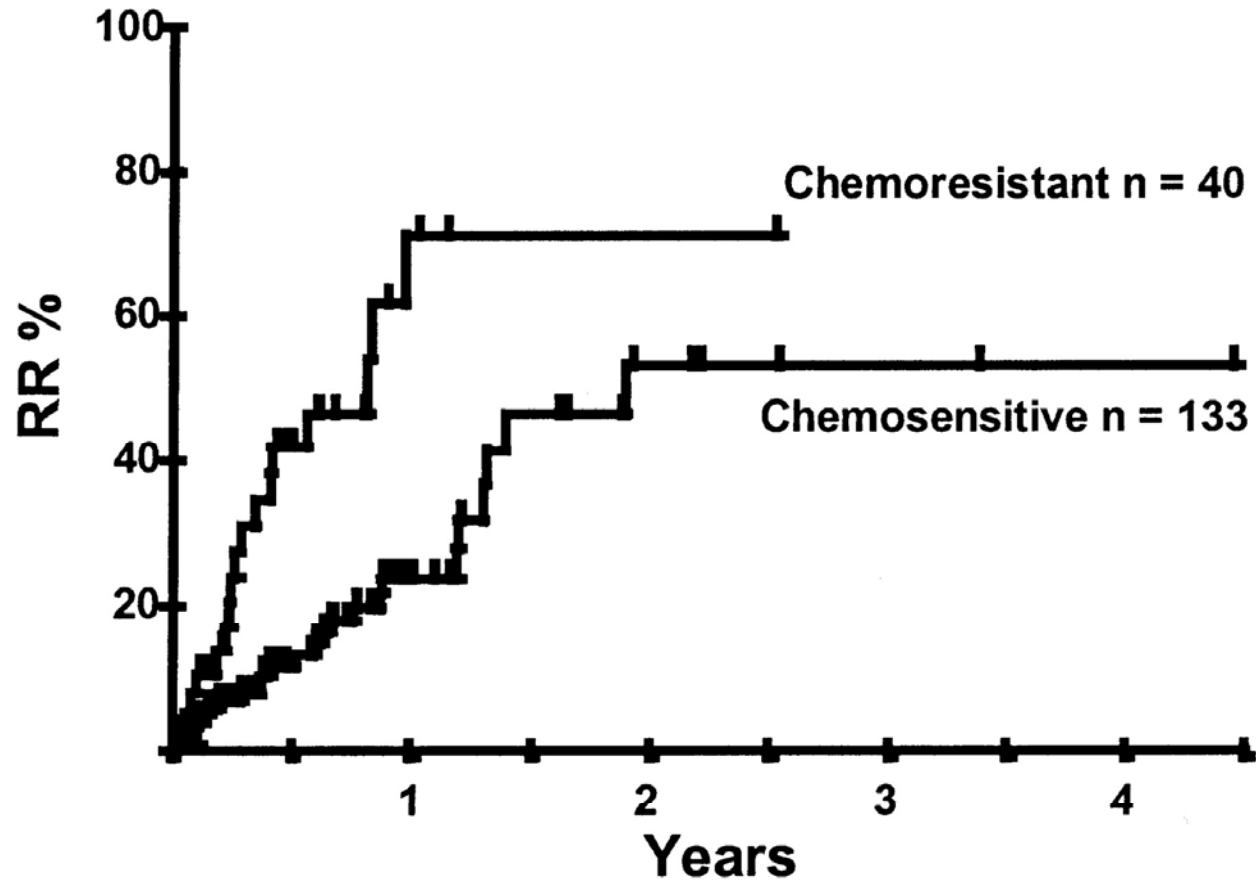
Robinson, S. P. et al. Blood 2002;100:4310-4316

Figure 2.



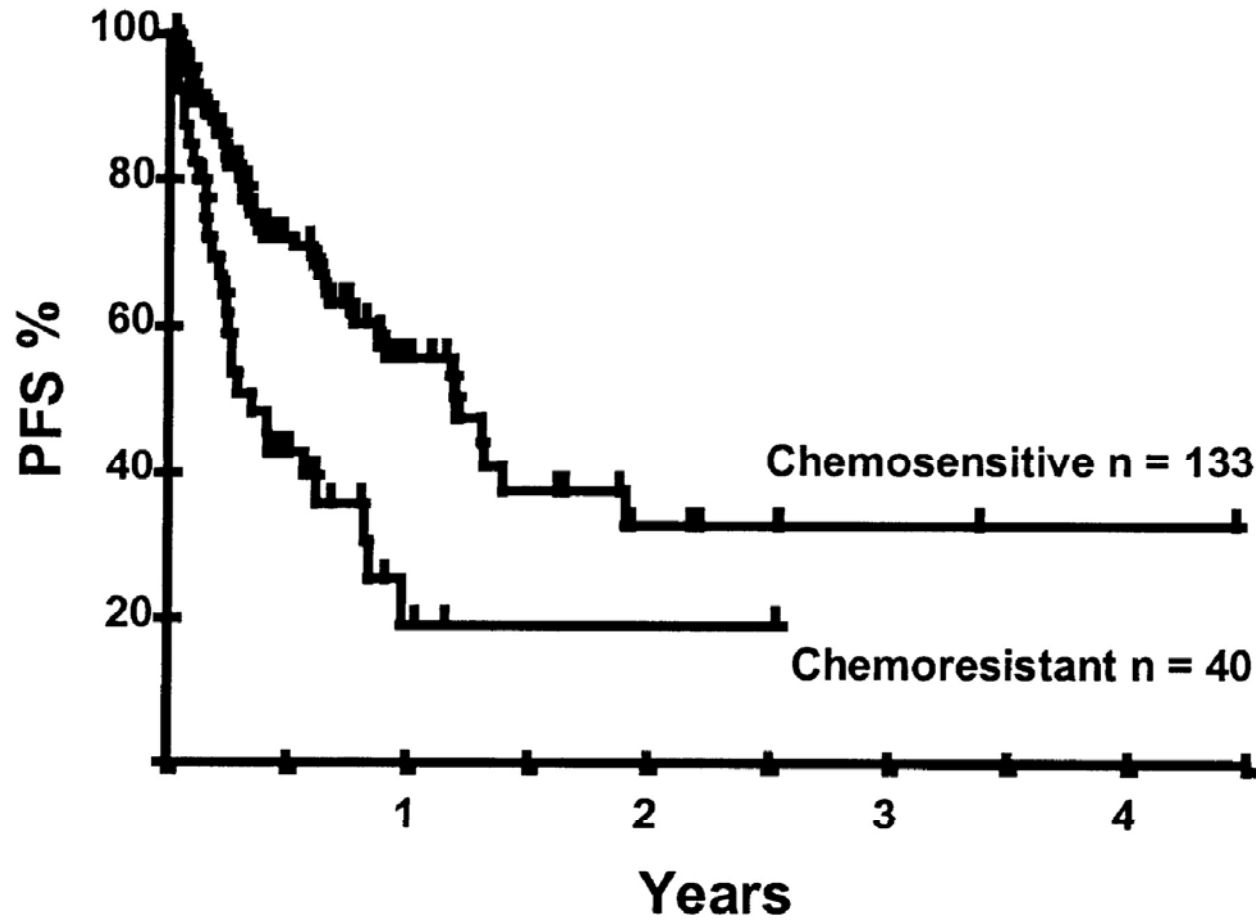
Robinson, S. P. et al. Blood 2002;100:4310-4316

Figure 5.



Robinson, S. P. et al. Blood 2002;100:4310-4316

Figure 8.



Robinson, S. P. et al. Blood 2002;100:4310-4316

Analyse multivariée

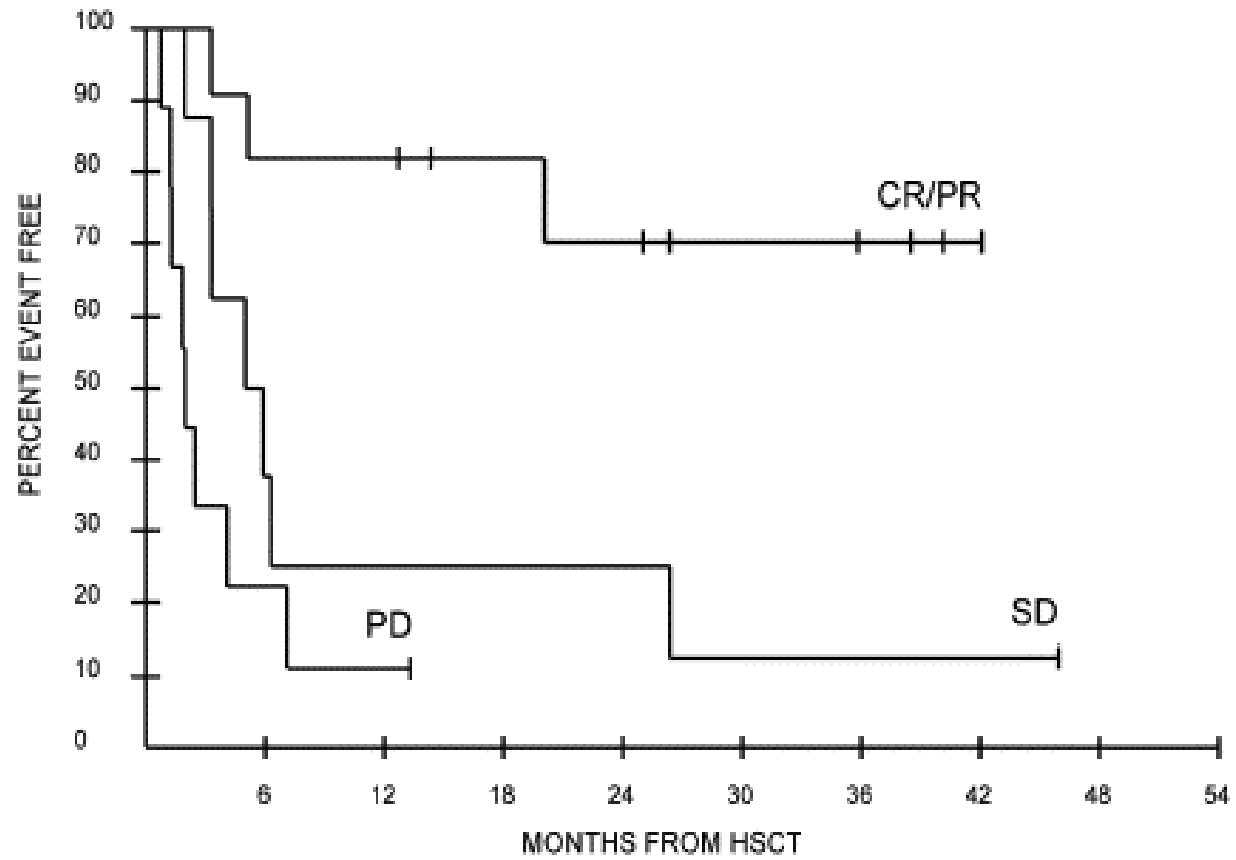
| | Variable | RR | P |
|------|------------|------|-------|
| OS | Chimiosens | 2,4 | .002 |
| PFS | Chimiosens | 2,3 | .007 |
| TRM | Age>50 | 2,02 | .041 |
| Prog | ChimioR | 3,3 | .0004 |
| GVH | Pheno | 3,7 | .0098 |
| GVH | TCD | 0.4 | .0071 |

Conclusion enseignements

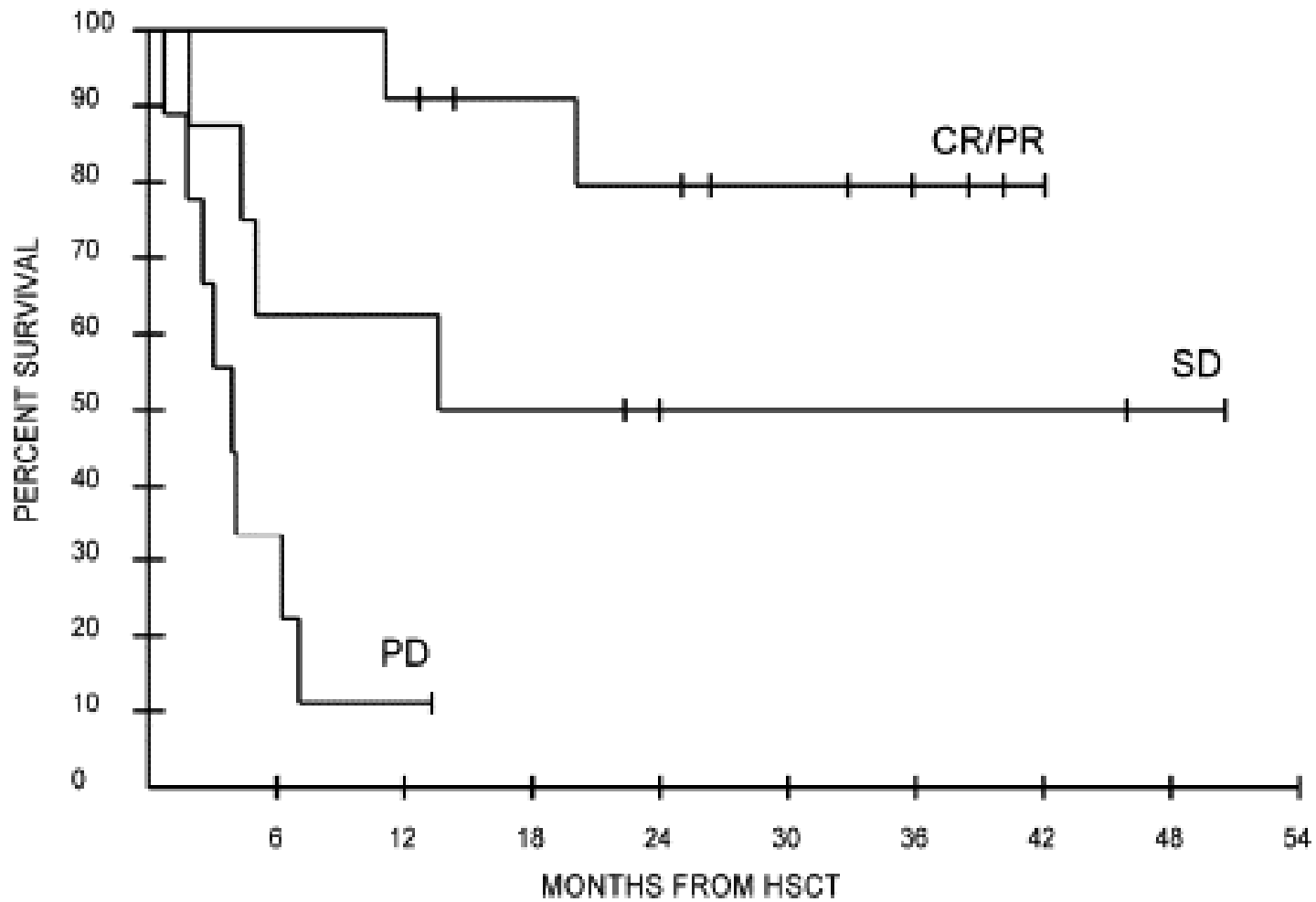
- Retrospectif,
- FU court: 283j en mediane
- Multiples situations et conditionnement.
- Meilleurs résultats si maladie chimiosensible, et si Hodgkin ou LNH de bas grade.
- Résultats plus mauvais dans Manteau et haut grade et maladie résistante

*Dean RM et al Biol Blood
Marrow transplant 2005;11:593*

- 29 pts
- NHL tous types Ref 1 ou \geq 2ème rech
- HLA geno id
- Chimio: EPOCH-F
- Conditionnement: Fluda (30/m²/j) EDX
(1200/m²/j) x 4j
- Prophylaxie GVH: Cyclo seule



Dean RM et al Biol Blood Marrow transplant 2005;11:593

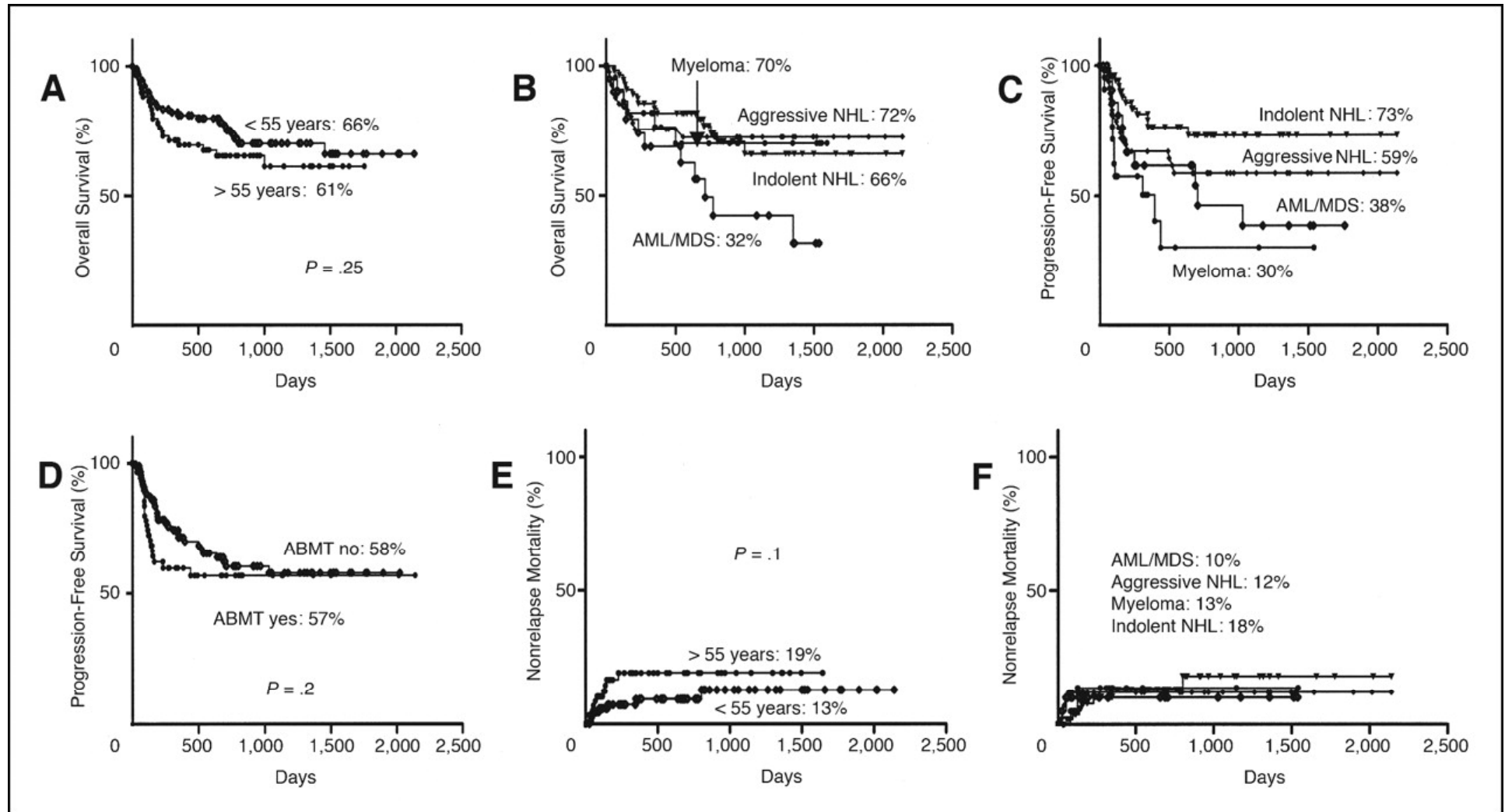


Dean RM et al Biol Blood Marrow transplant 2005;11:593

**Corradini, P. et al. J Clin Oncol; 23:6690-6698
2005**

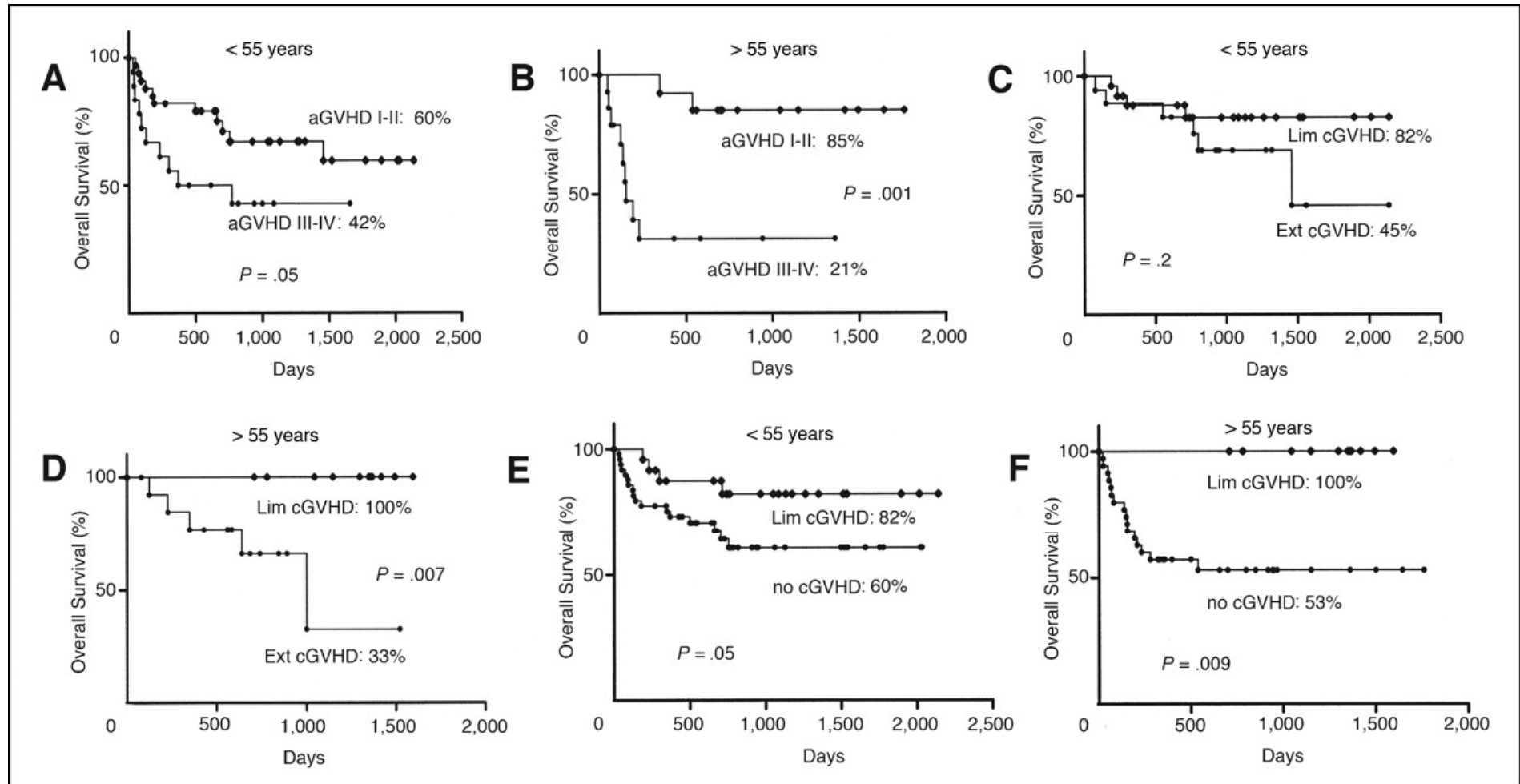
- 150 pts avec « advanced hematologic malignancies »
- Conditionnement: Thiotepa Fluda Endoxan.
- Donneur HLA id Genotypique
- Suivi médian: 927j (172-2141)

Fig 1. Survival and nonrelapse mortality (NRM) curves



Corradini, P. et al. J Clin Oncol; 23:6690-6698 2005

Fig 3. Graft-versus-host disease (GVHD) effect on survival



Corradini, P. et al. J Clin Oncol; 23:6690-6698 2005

Conclusion et enseignement

- Encore une fois retrospectif et « melting pot »
- Mais plus long suivi.
- Impact élevé de la GVH grave sur la TRM
- TRM influencée par un echec préalable de l'autogreffe.
- Resultats comparables pour LNH de haut et de bas grade? Sélection différente des hauts grades?
- Encourageant pour haut grade?

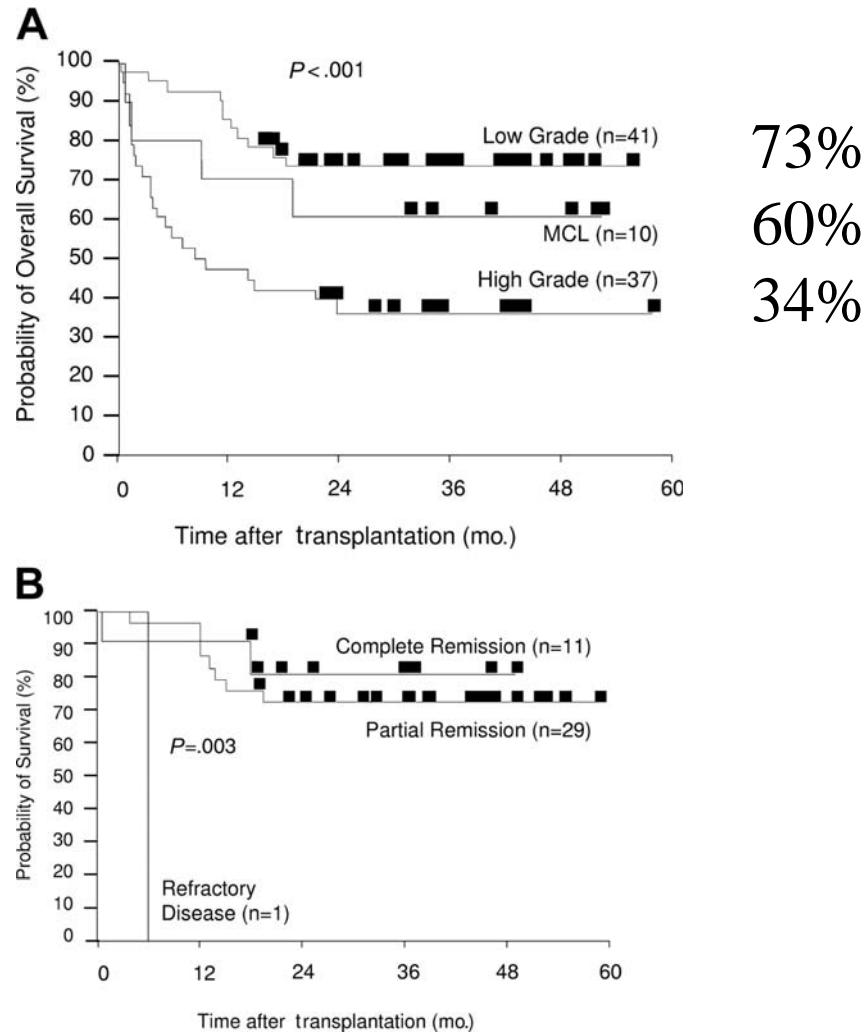
CAMPATH et RIC allo greffe pour
LNH en rechute ou refractaire

Morris, E. et al. Blood 2004;104:3865-3871

Patients

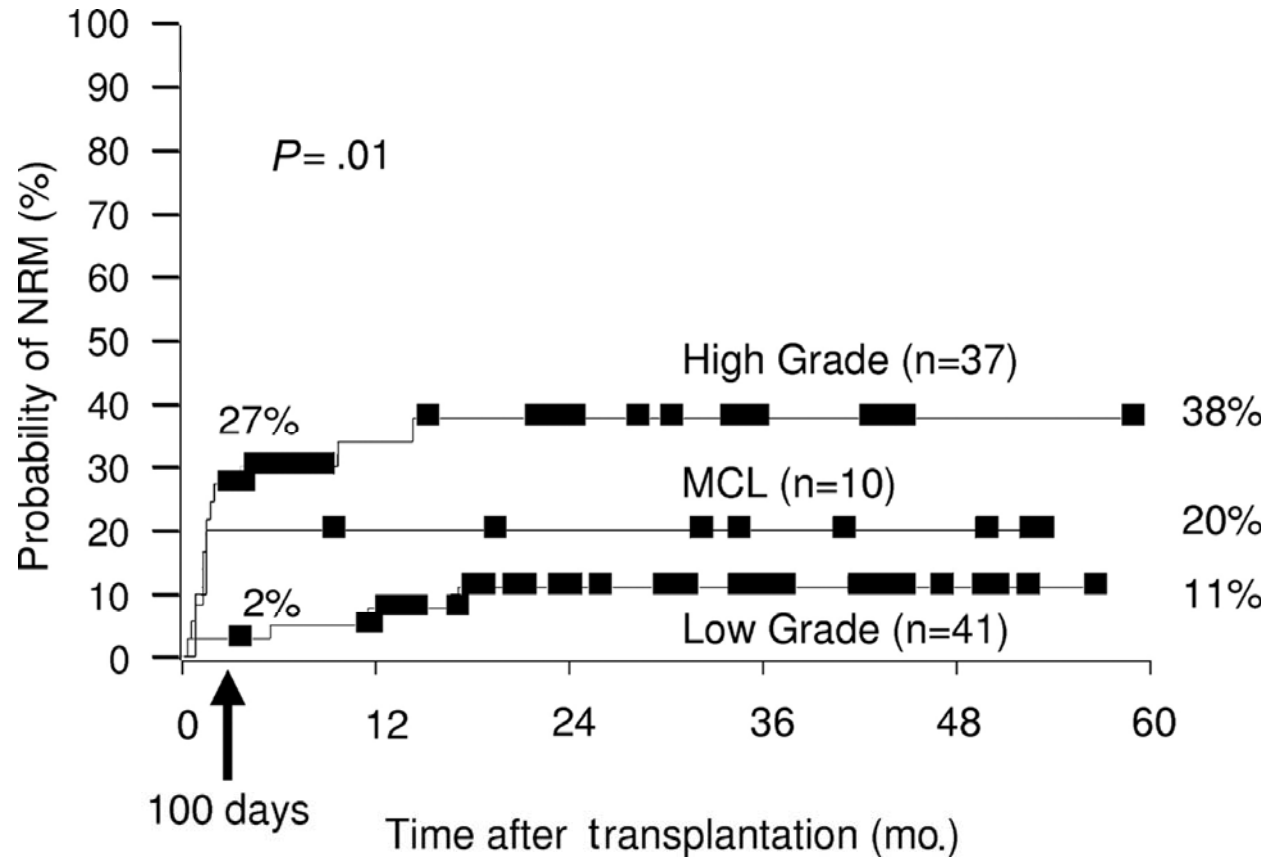
- N: 88
- LNH bas grade: 41(RC:11)
- LNH haut grade: 37 (RC:10)
- N° de chimio antérieures: 3 (1-6)
- Autogreffe antérieure: 37
- Donneurs fam(65) non fam(23)
- Conditionnement: Campath, Fluda, Melphalan

Figure 3. Kaplan-Meier plots of estimated OS



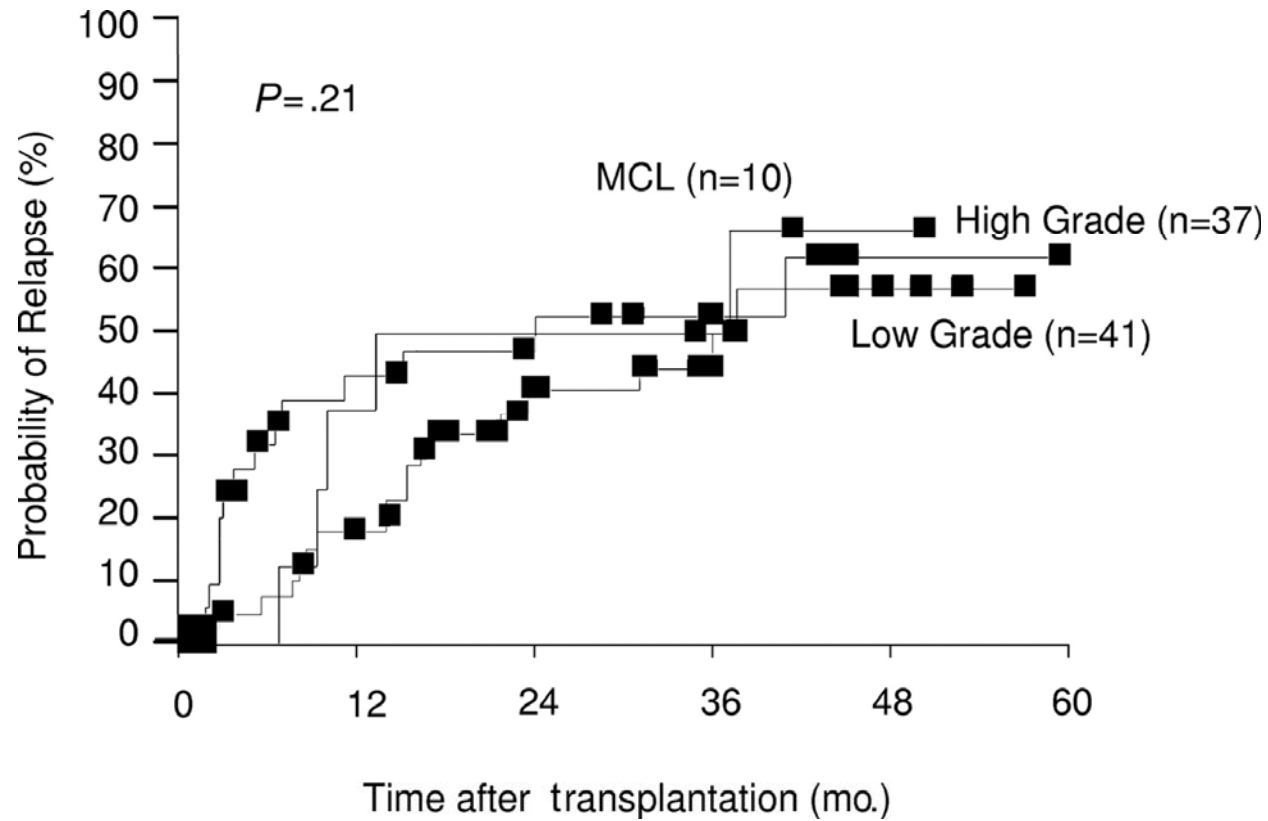
Morris, E. et al. Blood 2004;104:3865-3871

Figure 1. Kaplan-Meier plot of estimated nonrelapse mortality



Morris, E. et al. Blood 2004;104:3865-3871

Figure 2. Estimated probability of relapse by disease grade



Morris, E. et al. Blood 2004;104:3865-3871

Figure 4. Kaplan-Meier plots of estimated current PFS



Morris, E. et al. Blood 2004;104:3865-3871

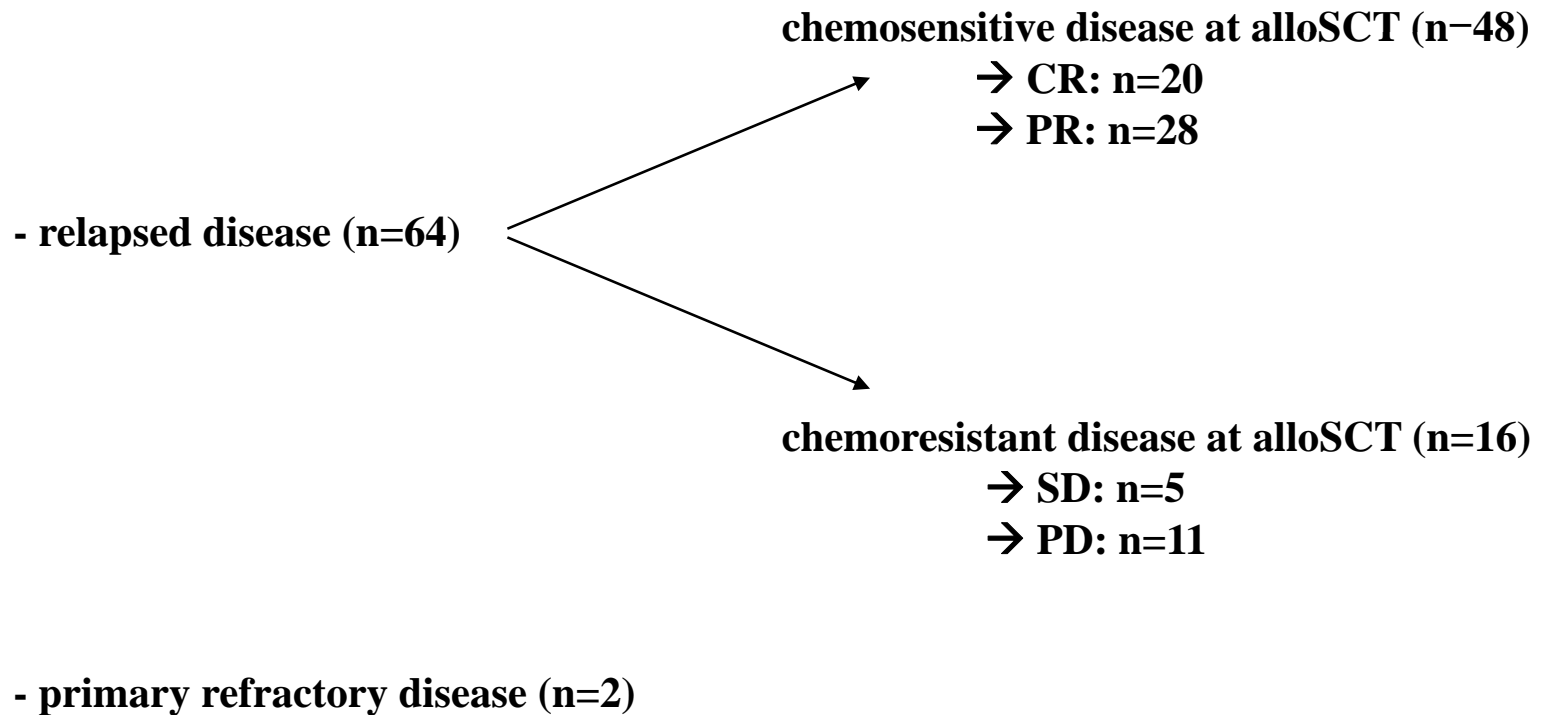
Conclusion et enseignements

- Excellent résultats dans les LNH de bas grade et ici aussi dans les LNH du manteau.
- Moins bons résultats pour les LNH de haut grade pour une raison de TRM plus élevée: Intensité des traitements préalables?
- Rôle de la chimiosensibilité préalable.
- Impact de CAMPATH vs autres immunosuppresseurs: ?

Allogeneic stem cell transplantation with reduced-intensity conditioning regimen for patients with relapsed or refractory low-grade lymphomas: a report of the French Society of Bone Marrow Graft Transplantation and Cellular Therapy (SFGM-TC)

Stéphane Vigouroux, Mauricette Michallet, Raphaël Porcher, Michel Attal, Gérard Socié, Marc Bernard, Didier Blaise, Reza Tabrizi, Frédéric Garban, Jill-Patrice Cassuto, Patrice Chevalier, Thierry Facon, Norbert Ifrah, Marc Renaud, Hervé Tilly, Jean Paul Vernant, Mathieu Kuentz, Jean-Henri Bourhis, Pierre Bordigoni, Eric Deconinck, Bruno Lioure and Noël Milpied

Figure 1. Characteristics of patients' disease at the time of allogeneic stem cell transplantation (alloSCT).



CR: complete response; PR: partial response; SD; stable disease; PD: progressive disease

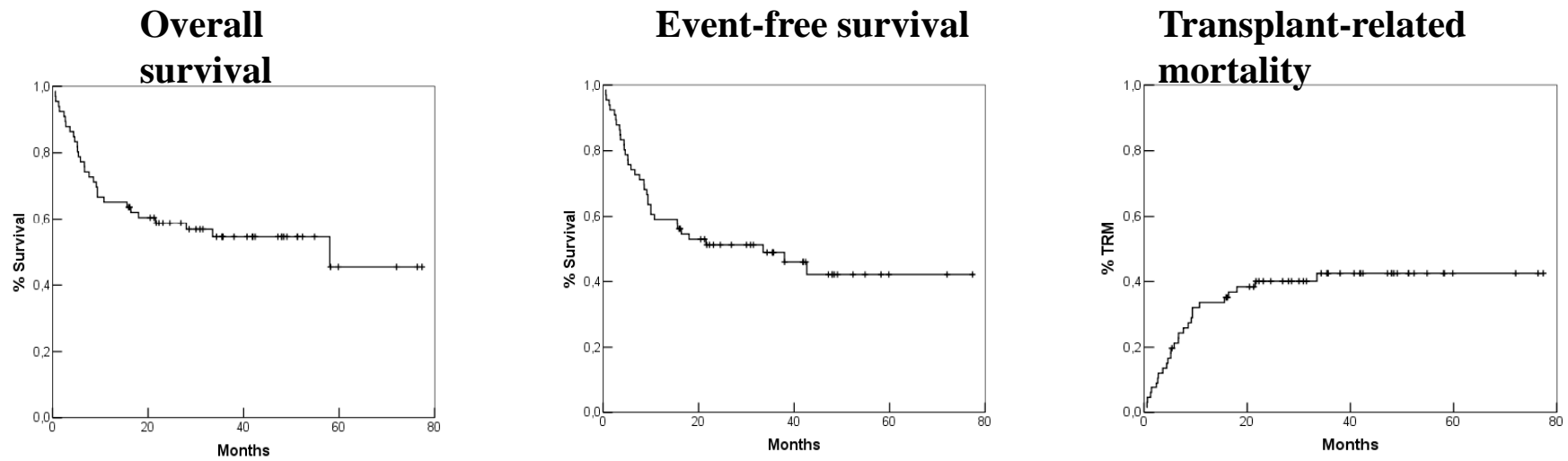


Figure 2. Survivals and transplant-related mortality of the study population (n=66).

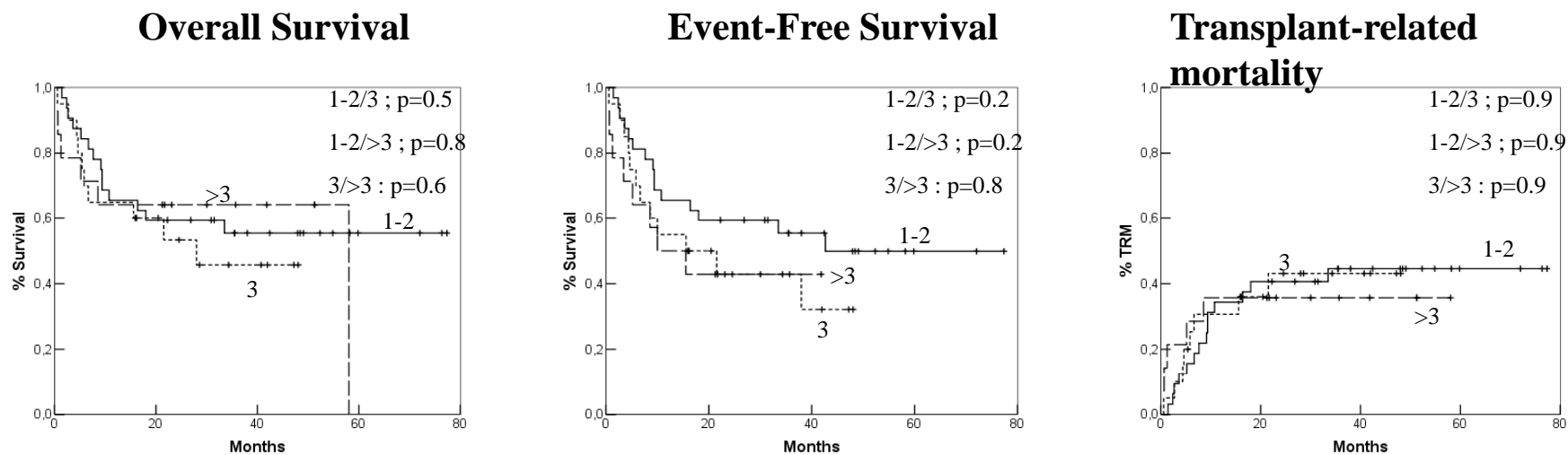
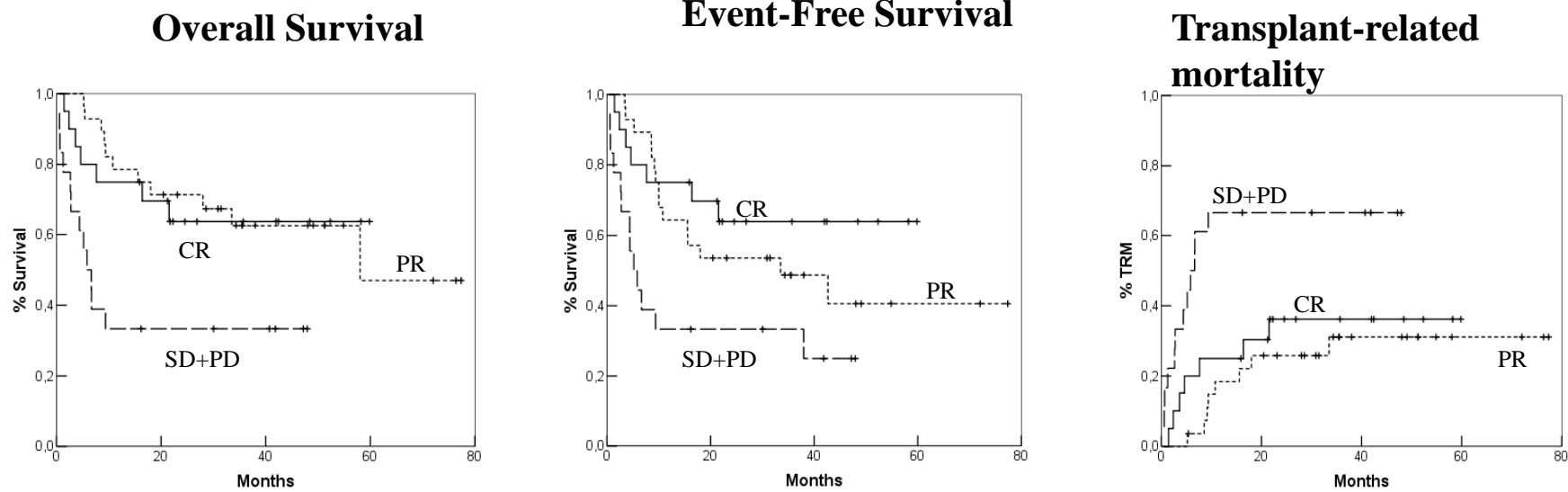


Figure 3. Survivals and transplant-related mortality according to the number of lines of therapy prior to alloSCT. 1-2 = 1 or 2 lines (n=32); 3 = 3 lines (n=20); >3 = more than 3 lines (n=14).

. Survival and transplant-related mortality according to the status of disease at alloSCT.



| | 3-year | | |
|------------------------|-----------|------------|------------|
| | OS | EFS | TRM |
| CR group(20) | 64% | 64% | 36% |
| PR group(28) | 63% | 49% | 31% |
| SD+PD group(18) | 33% | 33% | 67% |

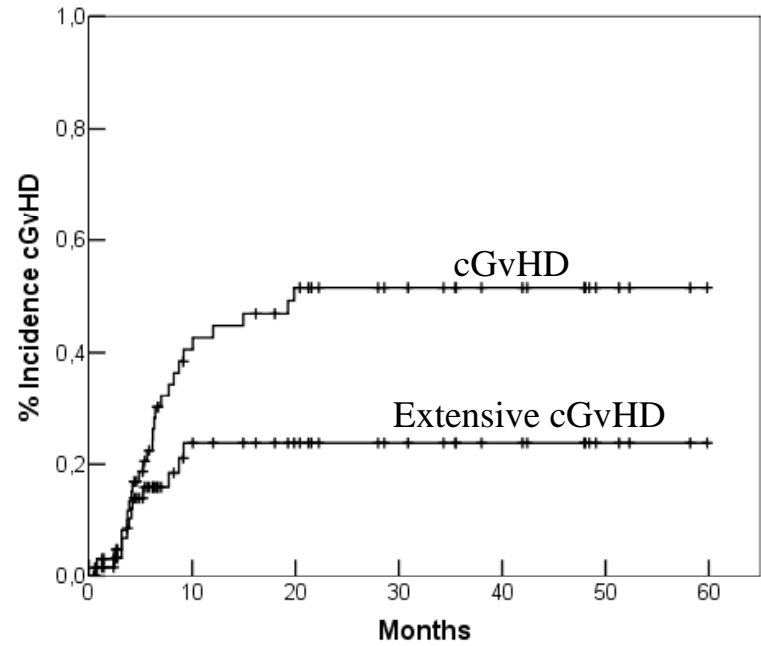


Figure 5. Cumulative incidences of chronic graft versus host disease (cGvHD) and extensive cGvHD of the study population (n=66).

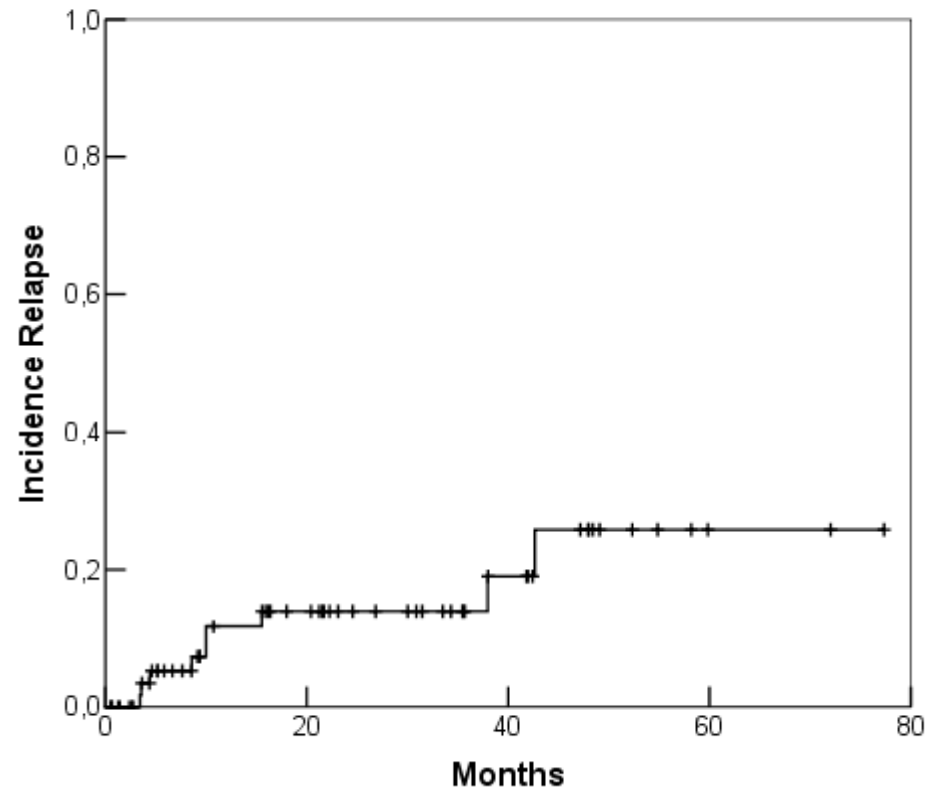
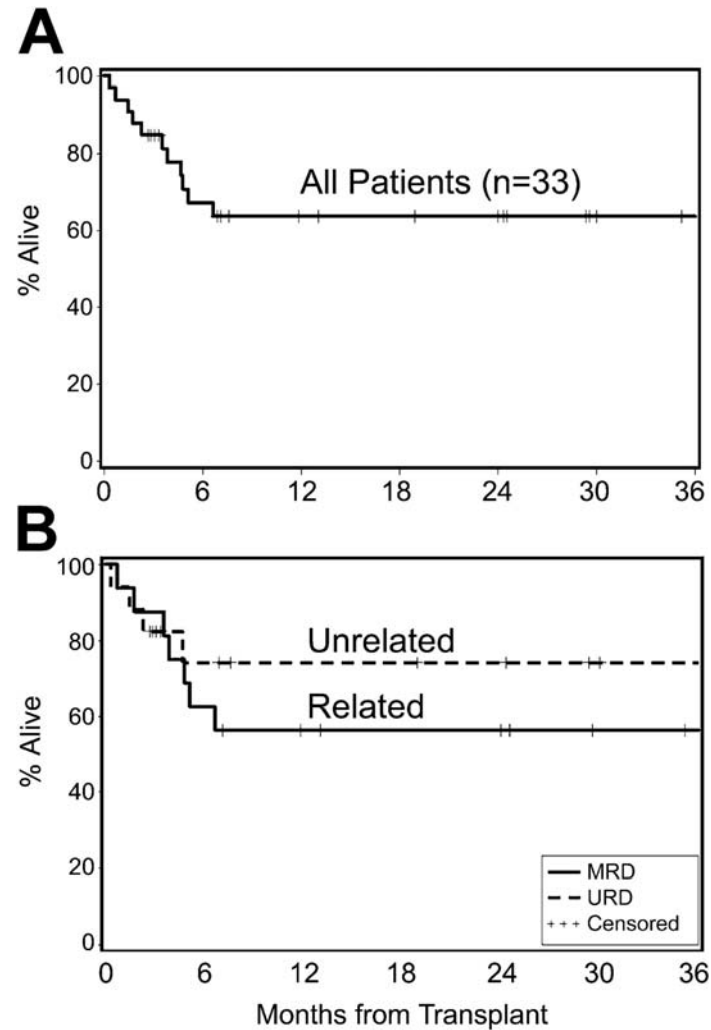


Figure 6. Cumulative incidence of relapse of the study population (n=66).

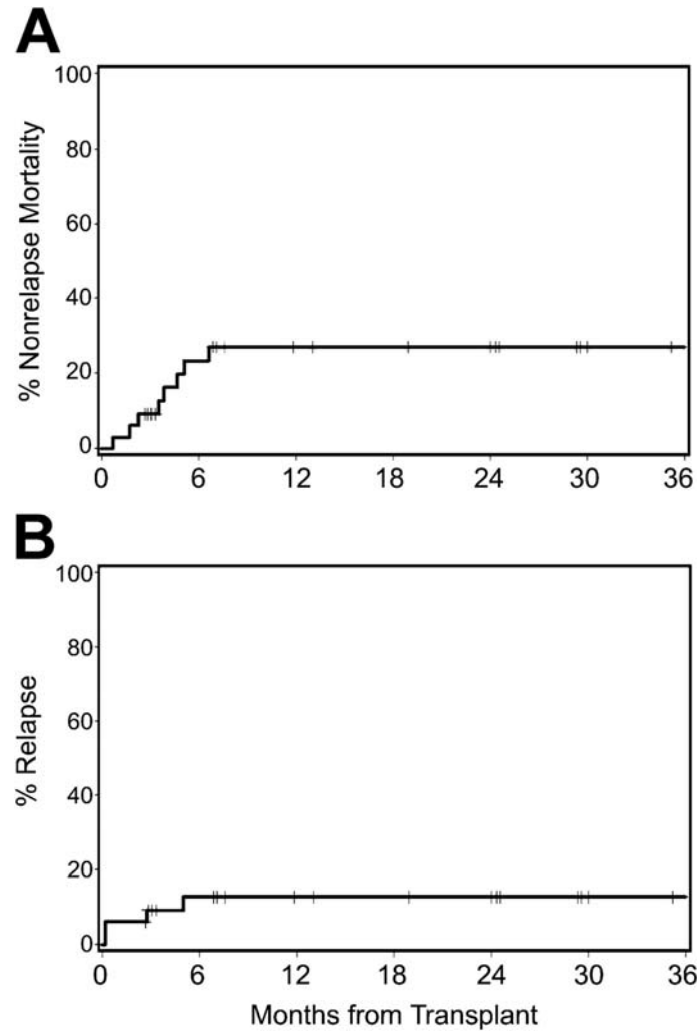
Lymphome du manteau

Figure 5. Kaplan-Meier estimates of overall survival



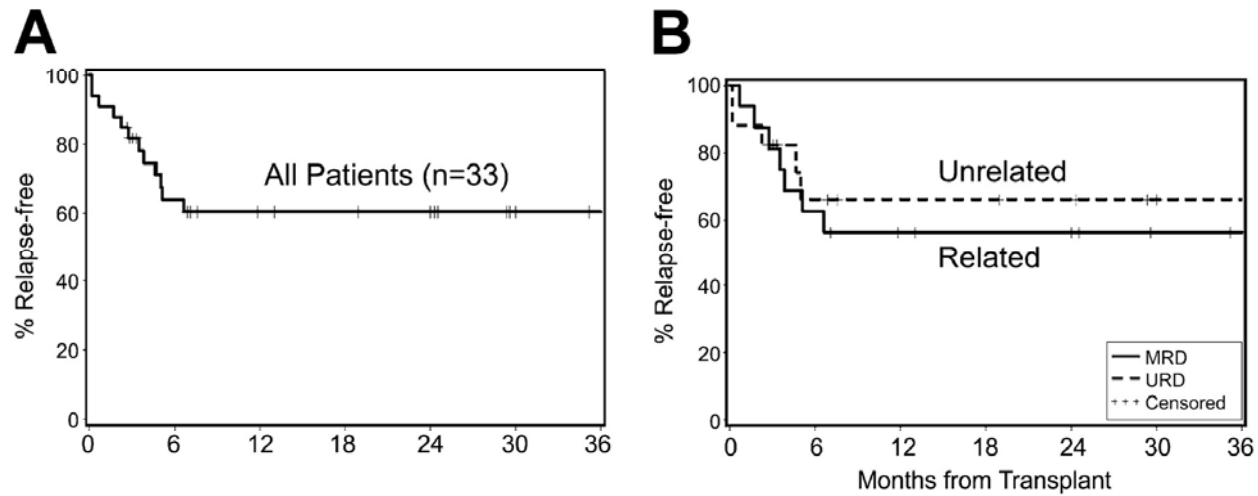
Maris, M. B. et al. *Blood* 2004;104:3535-3542

Figure 4. Nonrelapse and relapse mortality



Maris, M. B. et al. Blood 2004;104:3535-3542

Figure 3. Kaplan-Meier estimates of progression-free survival



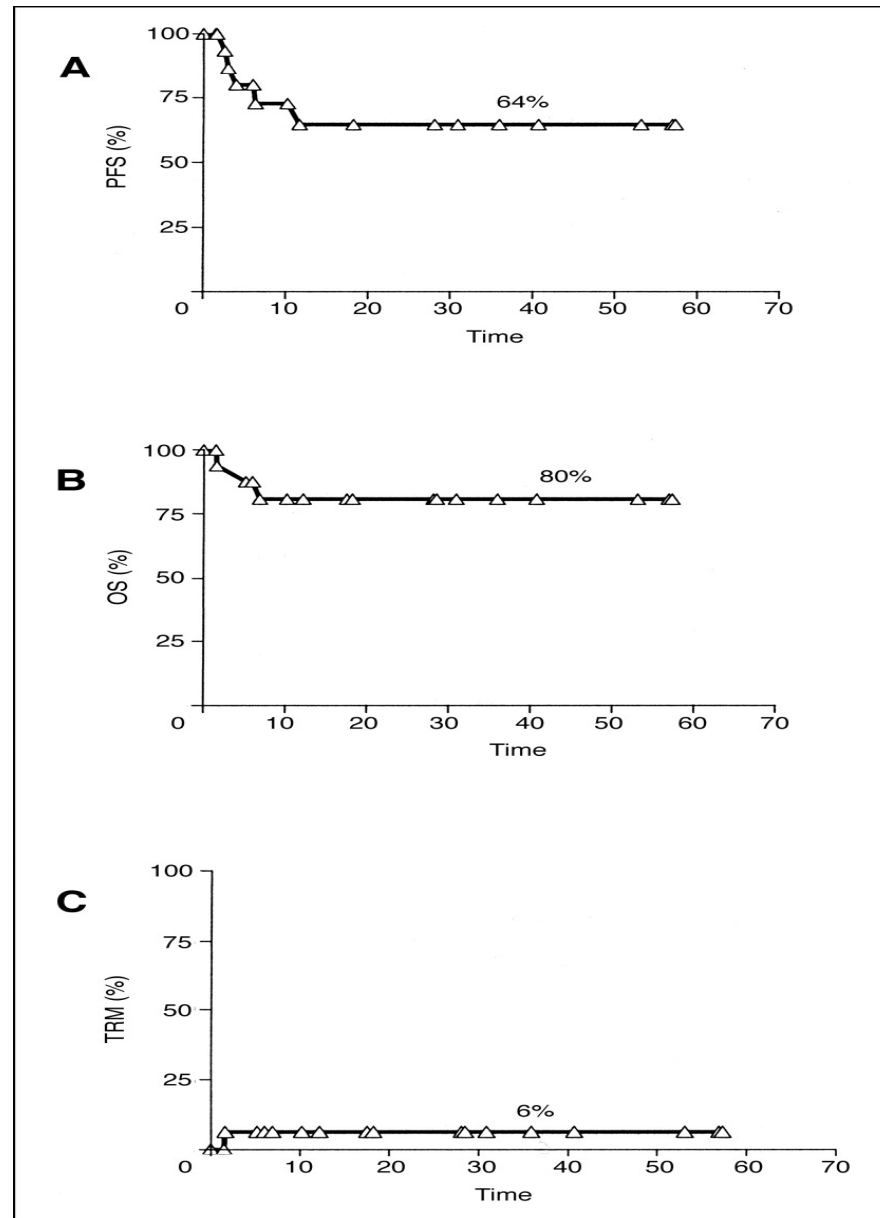
Maris, M. B. et al. Blood 2004;104:3535-3542

Allogreffe RIC pour LNH T Périphérique en rechute

Corradini, P. et al. J Clin Oncol; 22:2172-2176 2004

Fig 1. Survival and transplant-related mortality (TRM) curves

17 pts
RIC allo post salvage chimio
Condt: Thiotepa, Fluda,Cy
8 auto antérieures



Population de 22 patients

Age médian: 36 ans (16-54 ans)

Diagnostic:

Lymphome anaplasique T: 10

T périph NOS: 5

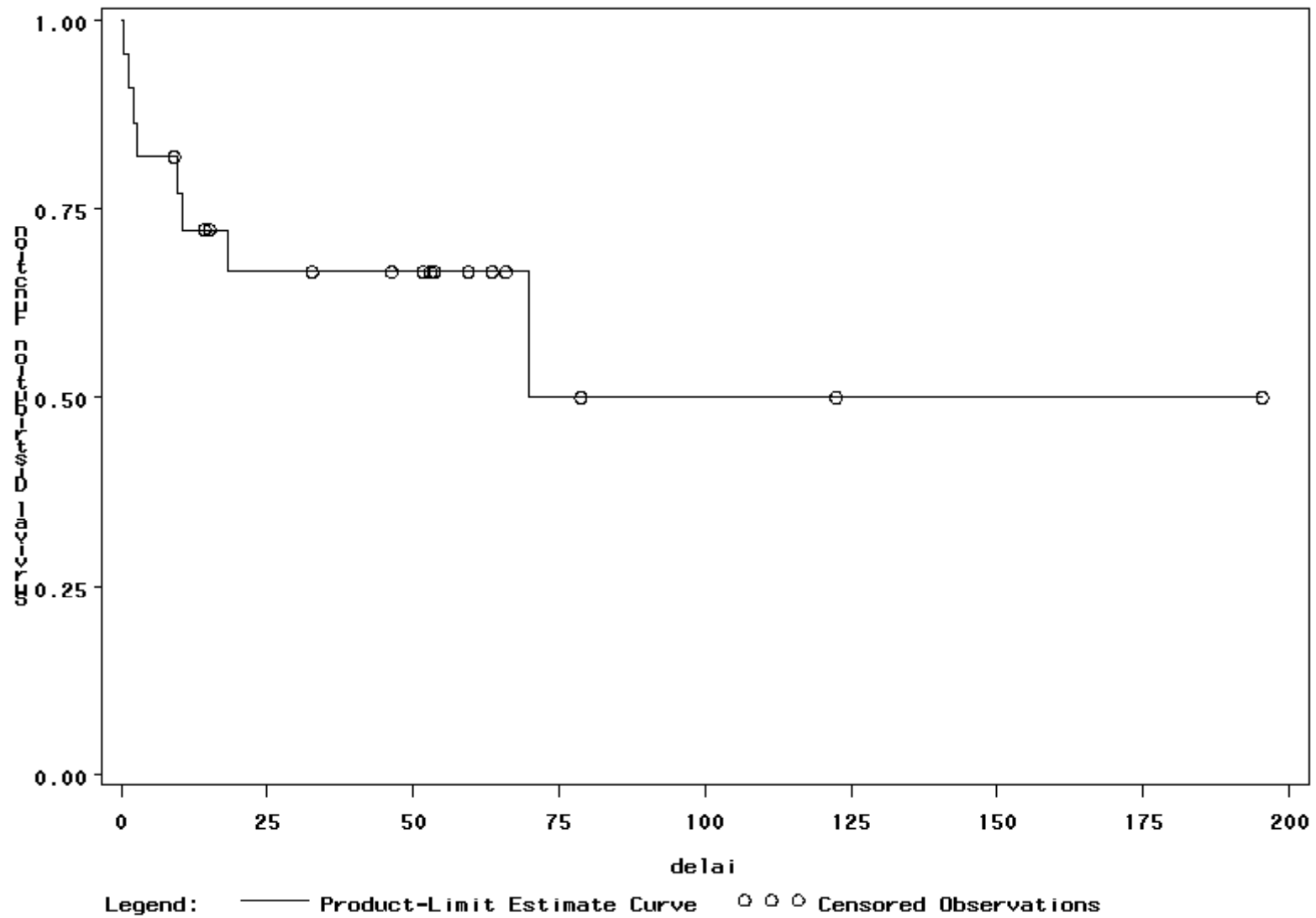
LAI: 3

Lymphome T gamma delta: 2

Leucémie LGL: 1

L nasal NK/T: 1

Ensemble de la population n=22



Le Gouill et al. Soumis pour ASH 2006

Conclusion

- Allogreffe à conditionnement atténué dans les LNH:
- Oui, pour qui?
- Chimiosensibles
- T en première ligne!
- Haut grades IPI élevés non répondeurs à la 1ère ligne (Pet scan)
- Faibles grades en transformation en 1ère ligne
- Manteau en 2ème ligne
- Hodgkin réfractaire à 2 lignes? En > 2ème réponse?

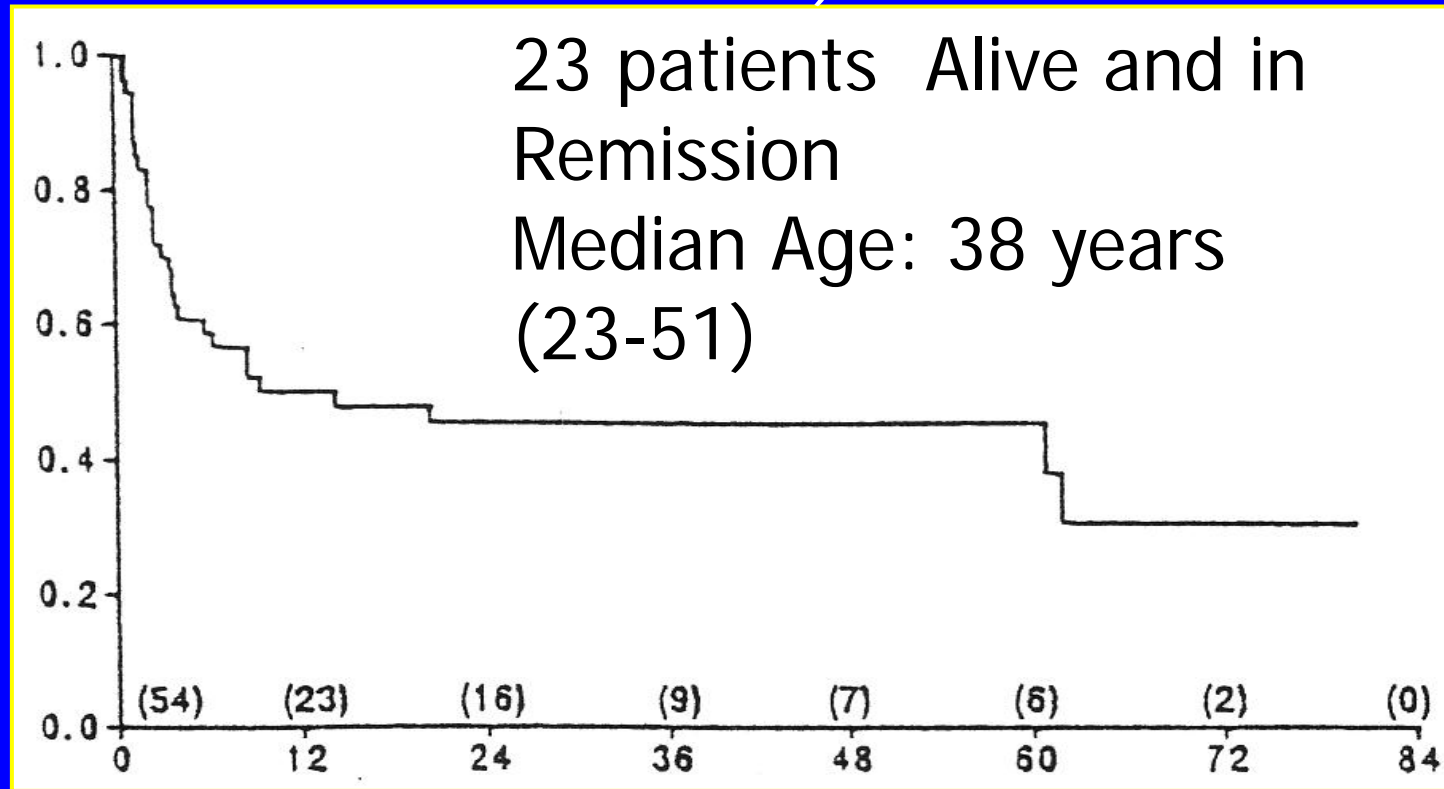
**ALLOGENEIC
HEMATOPOIETIC
STEM CELL
TRANSPLANTATION
FOR CLL**

Past and Future

M.Michallet

ALLOGENEIC TRANSPLANTATIONS FOR CLL

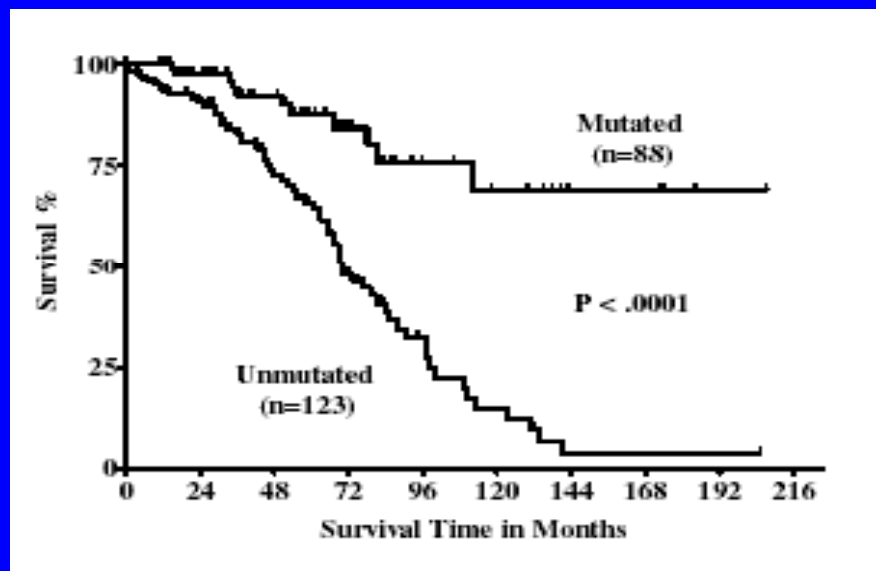
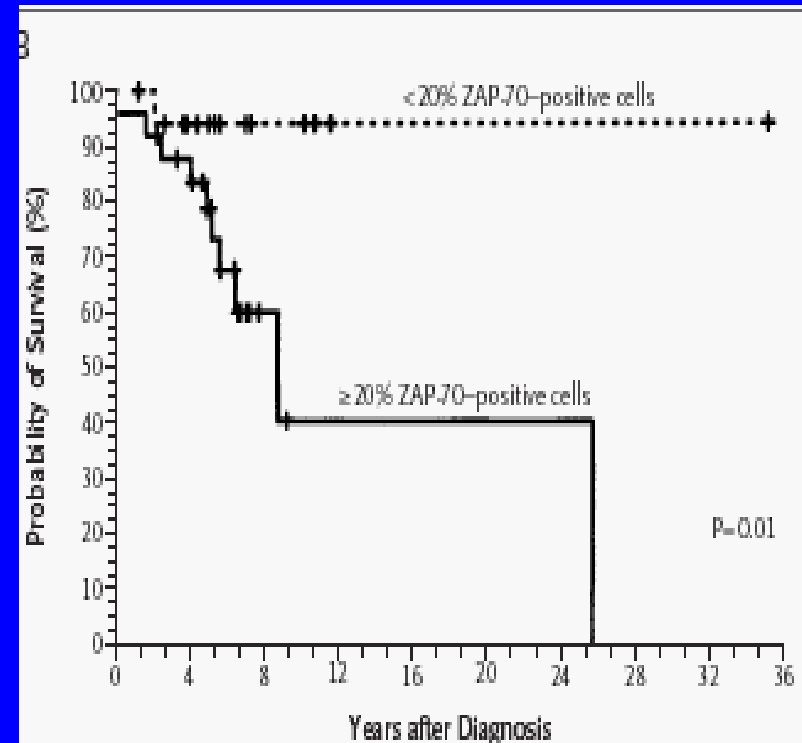
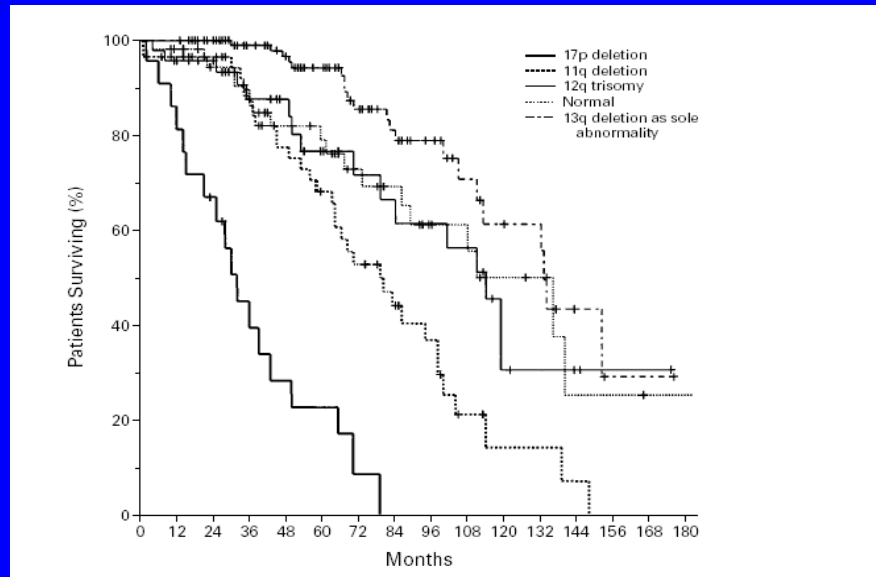
STUDY OF EBMT/IBMTR (M. Michallet *et al*/Ann Intern Med 1996)



The 3 year probability of survival was 46% (95%CI [32-60])

Median Follow-up of 27 m / Maximal Follow-up of 80 m

CLL : Biological Risk Factors



- 1.-17p-,11q-:Dohner NEJM 2000
- 2.-Unmutated VDJ:krober 2000 Blood
- 3.-Expression of ZAP 70 NEJM 2003



Survival - CLL Transplantations

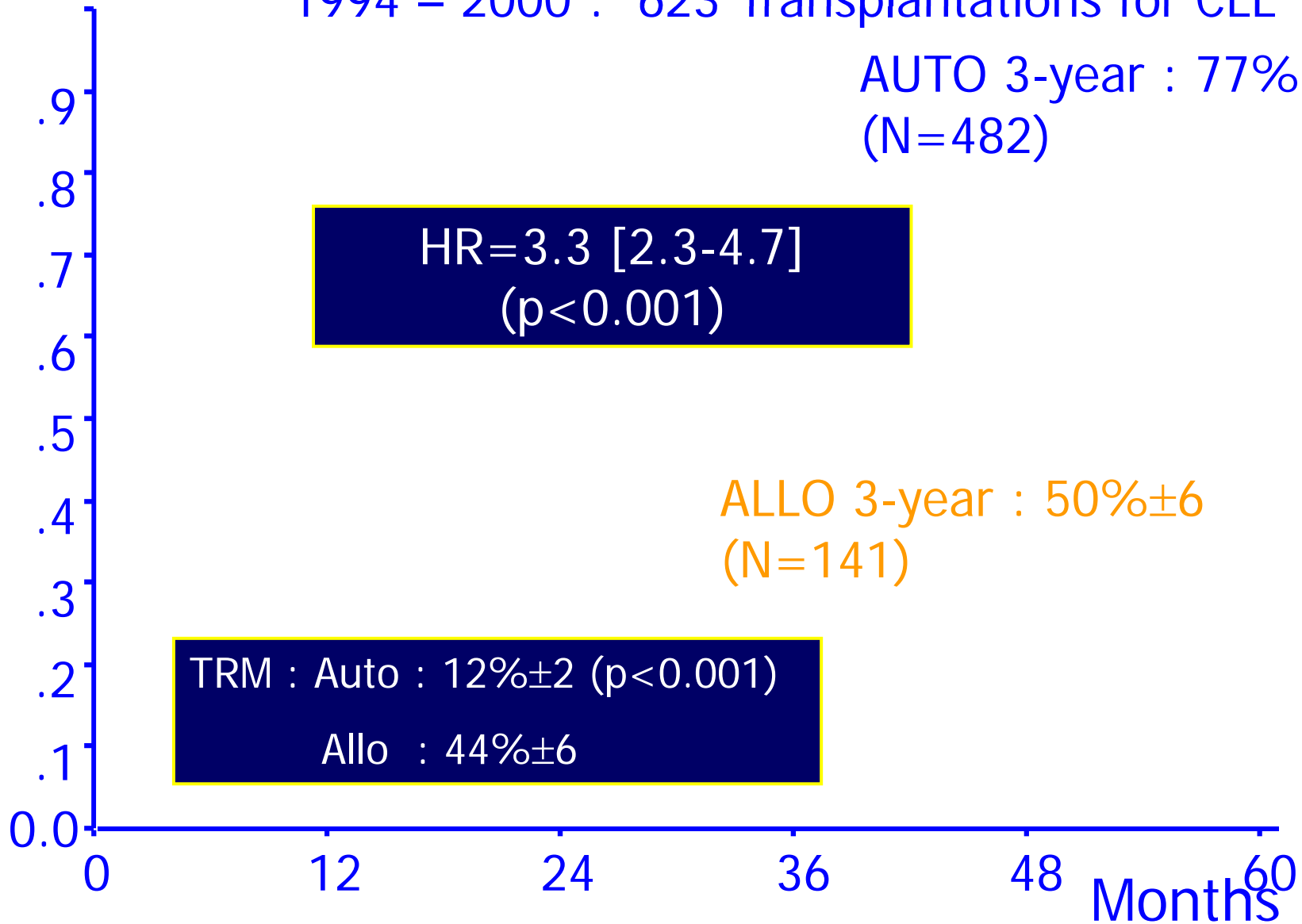
1994 – 2000 : 623 Transplantations for CLL

AUTO 3-year : 77% ±3
(N=482)

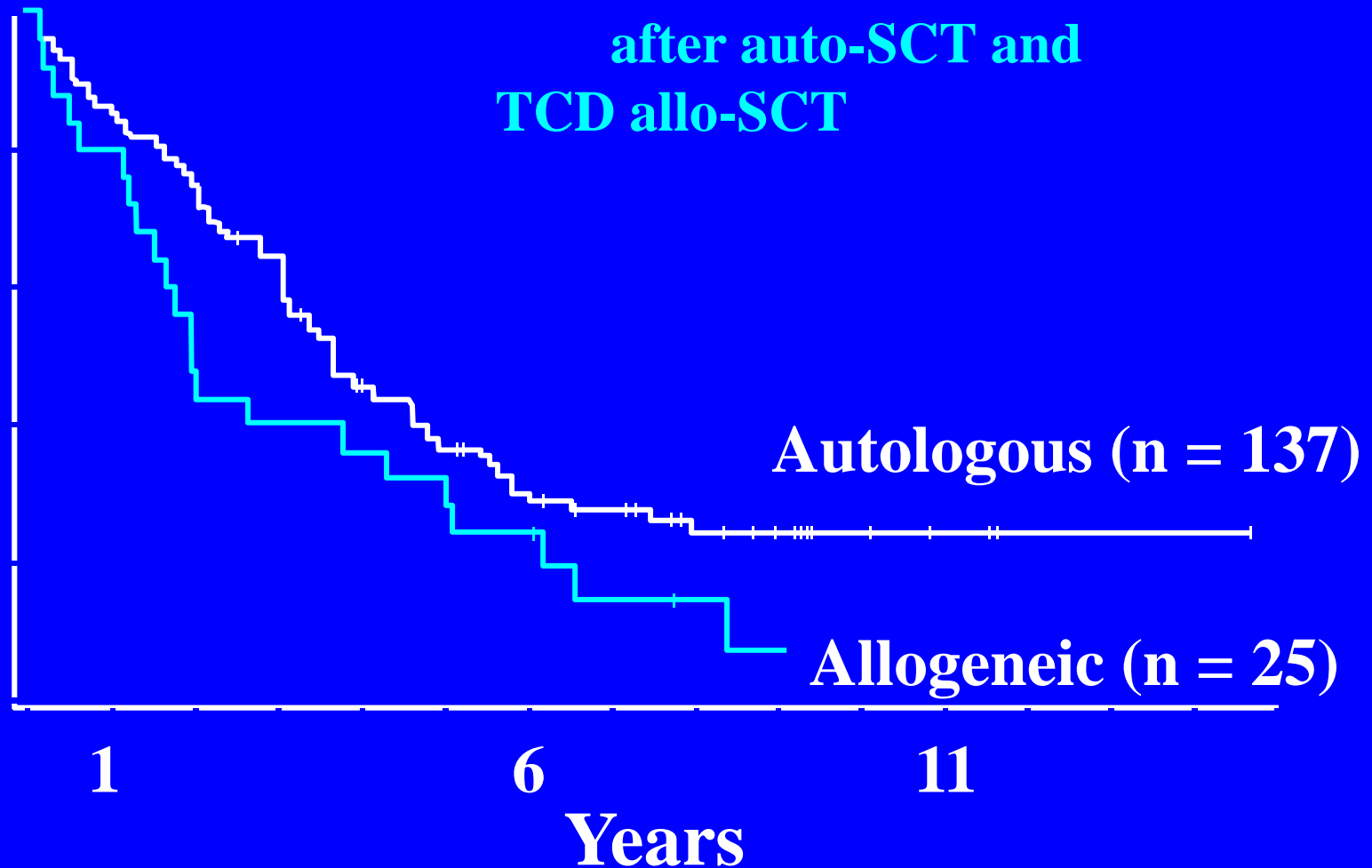
HR=3.3 [2.3-4.7]
(p<0.001)

ALLO 3-year : 50%±6
(N=141)

TRM : Auto : 12%±2 (p<0.001)
Allo : 44%±6



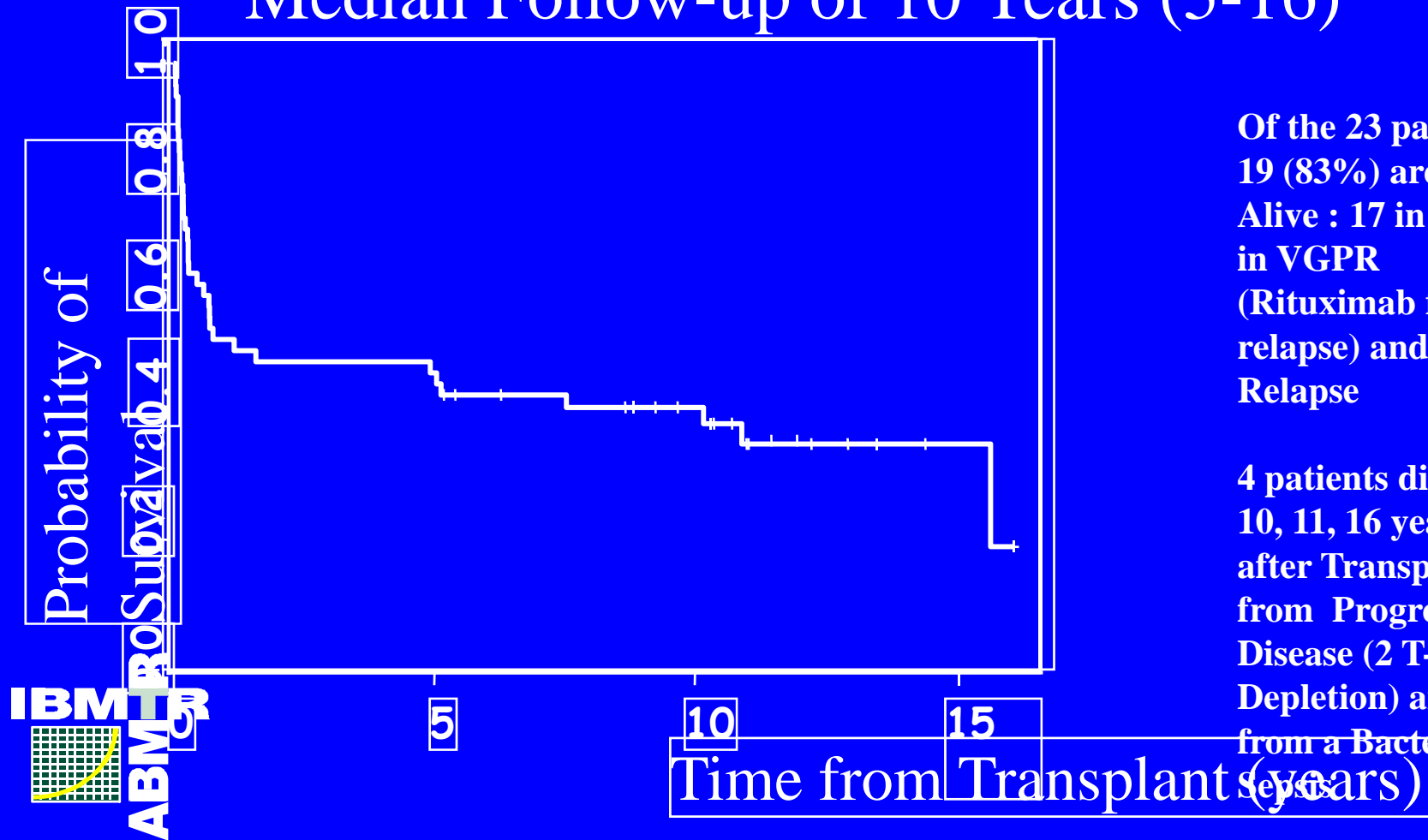
Event-free survival after HSCT for CLL



Gribben JG, *et al. Blood* 2005

STUDY OF EBMT/IBMTR UPDATE

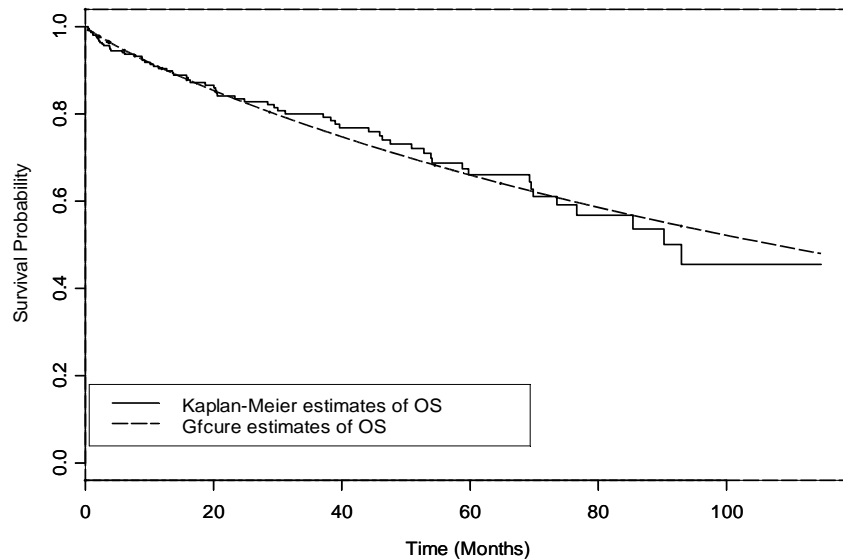
Median Follow-up of 10 Years (5-16)



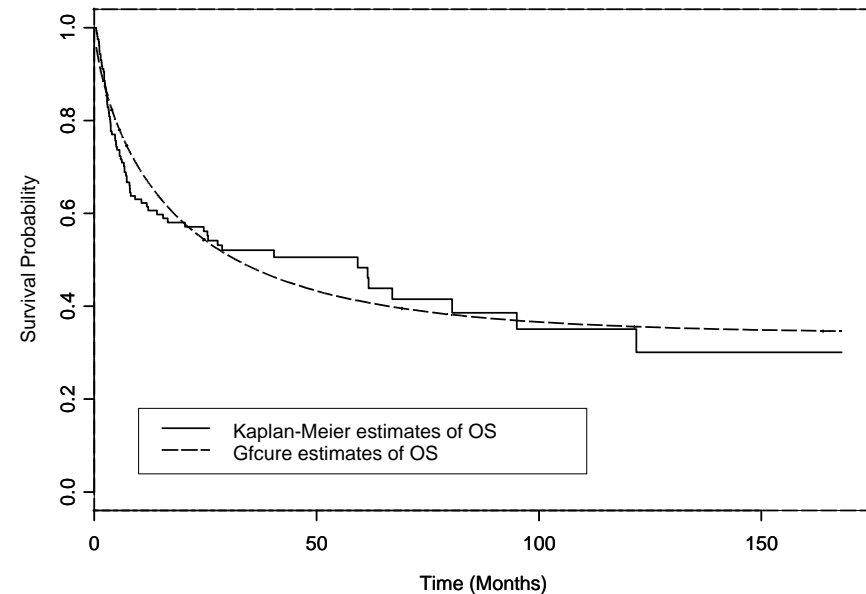
Of the 23 patients :
19 (83%) are still
Alive : 17 in CHR, 1
in VGPR
(Rituximab for
relapse) and 1 in
Relapse

4 patients died 7,
10, 11, 16 years
after Transplant : 3
from Progressive
Disease (2 T-
Depletion) and 1
from a Bacterial
sepsis

Analysis of Long Survivors



**After Autologous
Transplantation**



**After Allogeneic
Transplantation**

| Trial | IBMTR | Int. Project | Omaha | NMDP | Barcelona |
|---|---------------------|---------------------|-------------------|--------------------|------------------|
| Design | Registry | Registry | Single | Registry | Single |
| n | 54 | 46 | 23 | 38 | 23 |
| Altern Donors* | 0% | 0% | 13% | 100% | 0% |
| TRM | 44% (10y) | 31% (3m) | 30% (5y) | 38%(5y) | 17% |
| Survival | 41% (10y) | 56% (5y) | 62% (5y) | 33%(5y) | 71% |
| Relapse rate | 15% (10y) | 23% (5y) | 5% (5y) | 32%(5y) | 12% |
| Late relapses | 3 | 2 | 0 | 1 | 3 |
| Follow-up (m) | 120 (60-192) | 35 (11-176) | 26 (9-115) | 72 (36-108) | 62 |
| * matched unrelated donors or mismatched family donors | | | | | |

Allogeneic SCT with myeloablative conditioning in CLL

| Study | Salamanca | EBMT | Seattle | GCTSG | GCLLSG |
|-------------------|------------------|----------------|--------------------|----------------|----------------|
| n | 30 | 77 | 20/44 | 30 | 44 |
| % MUD | 0% | 19% | 100% | 57% | 48% |
| TRM | 22% (5y) | 18%(2y) | 20%/20%(2y) | 15%(4y) | 7%(3y) |
| REL | 7%(5y) | 31%(2y) | 5%/34%(2y) | 30%(4y) | 24%(3y) |
| REL >2y | 0 | 1 | 0/0 | 4 | 2 |
| F/U (mo) | 47 | 18 | 24 | 72 | 19 |
| OS | 72% | 72%(2y) | 74%/58%(2y) | 69%(5y) | 70%(3y) |

Allogeneic SCT with nonmyeloablative conditioning in CLL



POPULATION-MATCHED ANALYSIS

- ❑ 73 RIC cases (Survey), 82 MC cases (Registry)
- ❑ Matched for age, donor, remission status, sex
by serial Cox modeling
- ❑ RIC reduces TRM (HR 0.4 - p 0.025)
- ❑ RIC increases relapse (HR 2.7 - p 0.054)
- ❑ No influence on EFS and OS

Prospective controlled studies are needed

Dreger et al



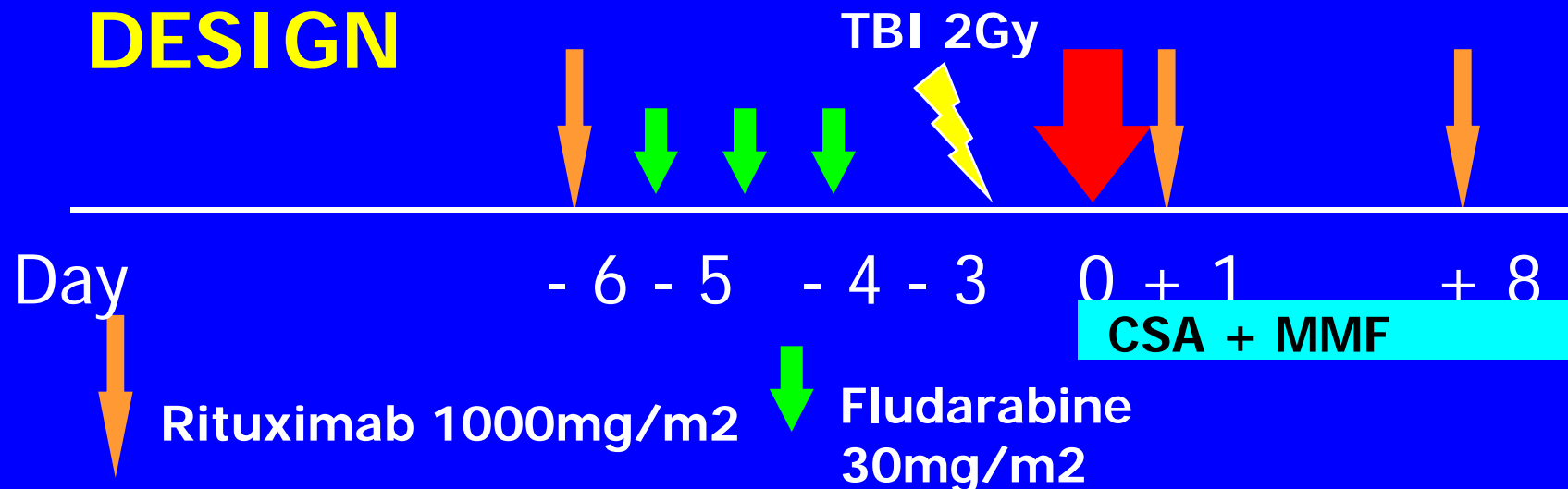
RIC for CLL

French Cooperative Group

ELIGIBILITY

B-CLL, 18-65 years, Binet B/C,
HLA-id. sibling donor available
+ failure after purine analogues (<12 mo)
or failure of auto-SCT

DESIGN



ITAC 02-02

12 PATIENTS ENROLLED

□ 7 patients Evaluated for response posttransplant : 6 CR, 1 PR

□ 7 patients Alive

- 1 month, No GVHD

- 2 mois, GVHD résolutive

- 4 months : PR

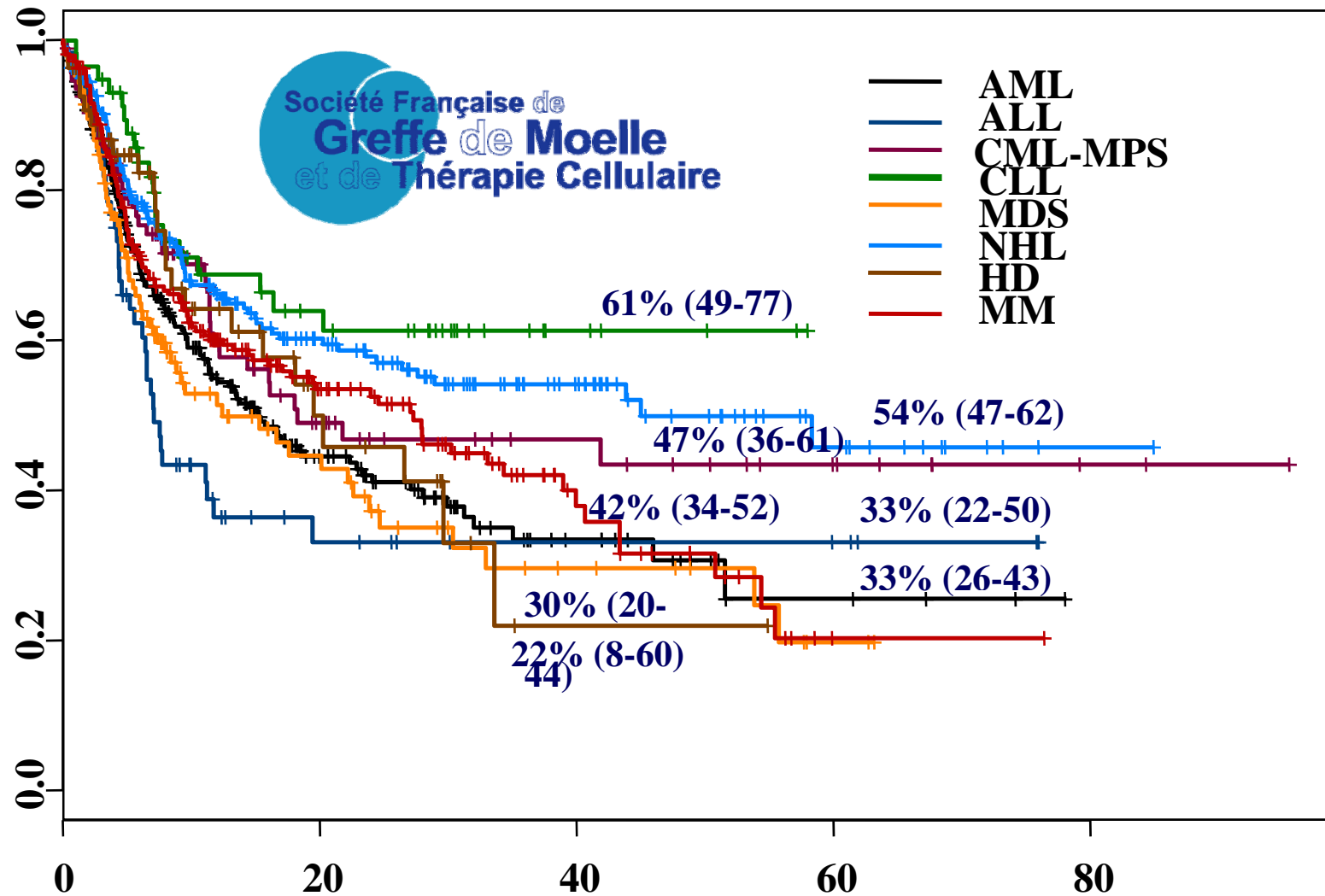
- 7 months : CR, No GVHD

- 19 months : CR, Limited cGVHD

- 29 months : CR, No GVHD

- 29 months : CR, cGVHD

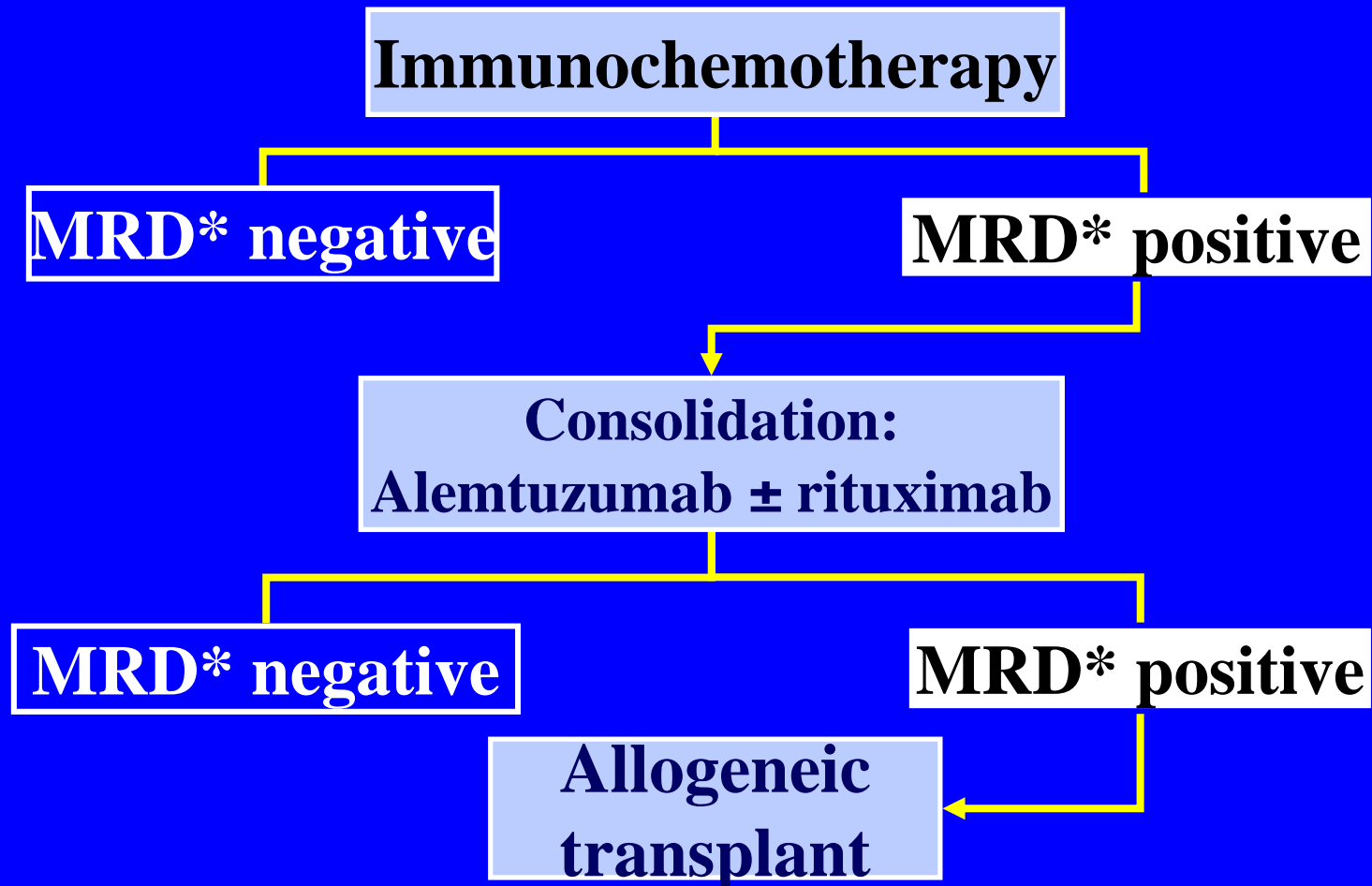
Overall Survival according to Diagnosis



Related and Unrelated Allogeneic RICT for CLL

- ❑ **Advanced CLL Patients**
- ❑ **Conditioning : 2 Gy TBI with [n = 53] or without [n = 11] Fludarabine**
- ❑ **Related (n = 44) or Unrelated (n = 20) donors**
- ❑ **Acute GVHD Grades 2, 3, and 4 : 39%, 14% and 2%**
Chronic graft-versus-host disease : 50%
- ❑ **The overall response rate : 67% (50% CR)**
- ❑ **2-year relapse/progression : 26%**
2-year relapse and nonrelapse mortalities : 18% and 22%
2-year overall and disease-free survivals : 60% and 52%
- ❑ **Unrelated HCT : higher CR + lower relapse than related**

Strategy for CLL



* MRD = minimal residual disease by PCR /flow cytometry