# Evaluation de la maladie résiduelle dans les lymphomes non hodgkiniens

*C Tarella, Torino*

| Molecular techniques for monitoring MRD | Target | Sensitivity |
|---|---|---|
| Southern Blot | • IgH rearrangements<br>• Translocations | $10^{-2}$ |
| FISH | • Translocations<br>• deletions<br>• karyotypic alterations | $5 \times 10^{-2}$ |
| PCR | • IgH rearrangements<br>• Translocations | $10^{-4}$-$10^{-6}$ |

❖ **the Molecular Remission (*MR*) achievement is a relevant issue in the management of non-Hodgkin's lymphoma presenting with BM involvement (BM+), in particular follicular lymphoma (FCL), mantle-cell lymphoma (MCL) and in selected cases of chronic lymphocytic leukemia (CLL)**

❖ **a *MR* achievement should always be associated with a Clinical Complete Response**

❖ **the need of a *MR* achievement is strictly related to:**

- **disease prognostic presentation**
- **type of treatment employed (i.e.: intensive vs. conventional therapeutic approach)**

**you no longer need to be a transplanter to achieve molecular remission in FCL patients**

since the use of more effective schedules (i.e. CHOP, FND) as well as the introduction of RITUXIMAB, FCL patients might have some chances of achieving a Molecular Remission with no need for intensified treatments

## Clinical and molecular response assessed in PB in 194 patients with FL at different time points from the beginning of treatment*

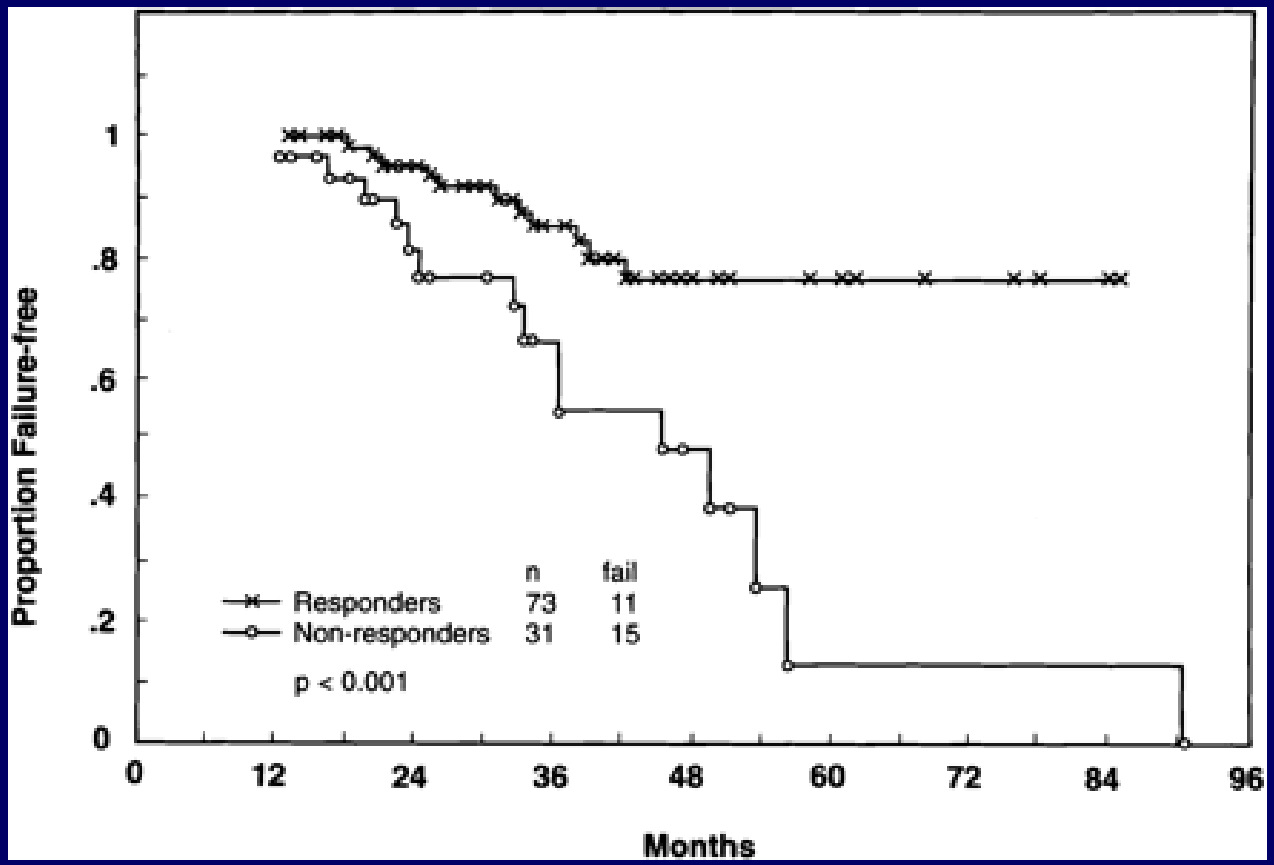
| Time point months | No of patients | Clinical CR rate (%) | Molecular (Response rate %) |
|---|---|---|---|
| 3-5 | 118 | 29 | 37 |
| 6-8 | 86 | 63 | 53 |
| 9-14 | 101 | 86 | 56 |
| 15-19 | 74 | 97 | 66 |

*** Therapy was ATT in 87 cases, FND in 24 and CHOP in 12**

**Lopez-Guillermo, Blood 91, 2955; 1998**

# The Clinical Significance of Molecular Response in Indolent Follicular Lymphomas

**By López-Guillermo et al.: Blood, Vol. 91: 2955-2960; 1998**




**FFS from 1 year after the start of treatment according to the molecular response status within the 1st year (Responders: PCR-negative; Nonresponders: PCR-positive status)**

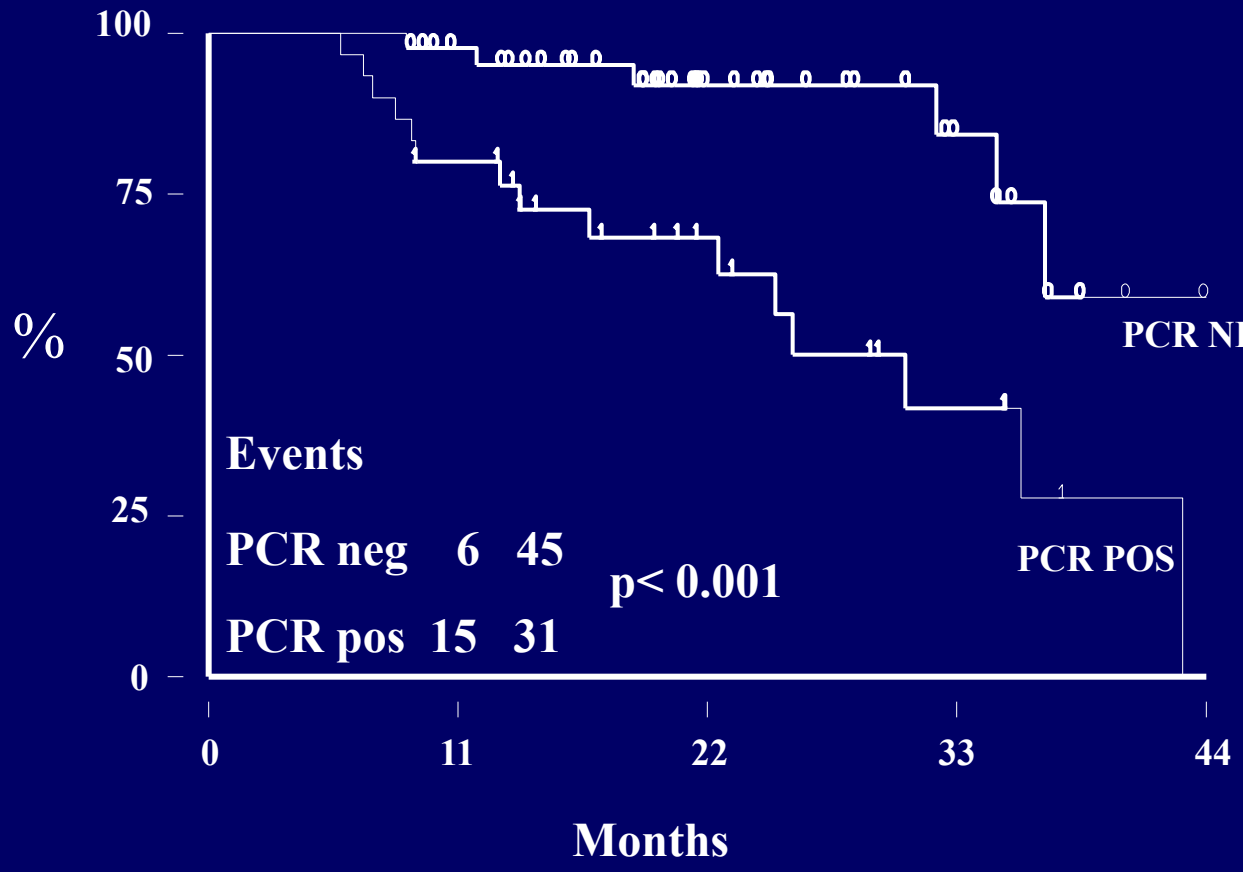
**A Rambaldi et al, Blood 2002, 99: 856-62**

**Molecular monitoring after sequential CHOP (6 cycles) and Rituximab administration as front line treatment in 128 FCL patients**

**after CHOP** → **36% BM PCR neg**

**after Rituximab** → **74% BM PCR neg**

# Freedom from recurrence after CHOP-Rituximab according to the PCR status in the BM at week +44




Rambaldi A. et al.: Blood; 99(3):856-62; 2002

❖ **several prospective studies have shown that the *MR* achievement following conventional chemo-immunotherapy (= negative PCR in at least 2 consecutive evaluations, at 6-12 mos. After treatment completion) is a favorable prognostic factor, associated with a prolonged failure-free survival (FFS)**

❖ ***however*:**

- **there is no demonstration of clear advantages in terms of overall survival**

- **quite a few patients have disease recurrence following MR achievement**

**At present, *MR* does not appear to be an essential "target" in the management of FCL patients when treated with conventional chemo-immunotherapy**

# Management of indolent non-Hodgkin's nodal lymphomas

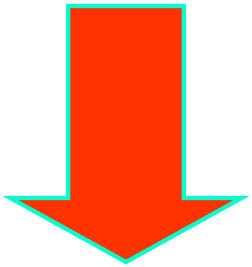
**Practice guidelines by SIE, SIES and GITMO**

***Prof. S. Tura coordinator***

❖ *“ Molecular Response should be checked at the end of first-line therapy in all the patients with an informative probe and a complete clinical remission ”*

❖ *“ Patients who have achieved a Partial Remission after first-line therapy should be considered for consolidation treatment with one of the following options: Rituximab, autologous SCT, radiotherapy, radioimmunoconjugates (either tositumomab or ibritumomab) “*

**FCL e MCL managed with an intensive approach including BM o PBPC autograft**



**Evidence that achievement of both Clinical and Molecular Remission have a relevant impact on the long-term outcome**

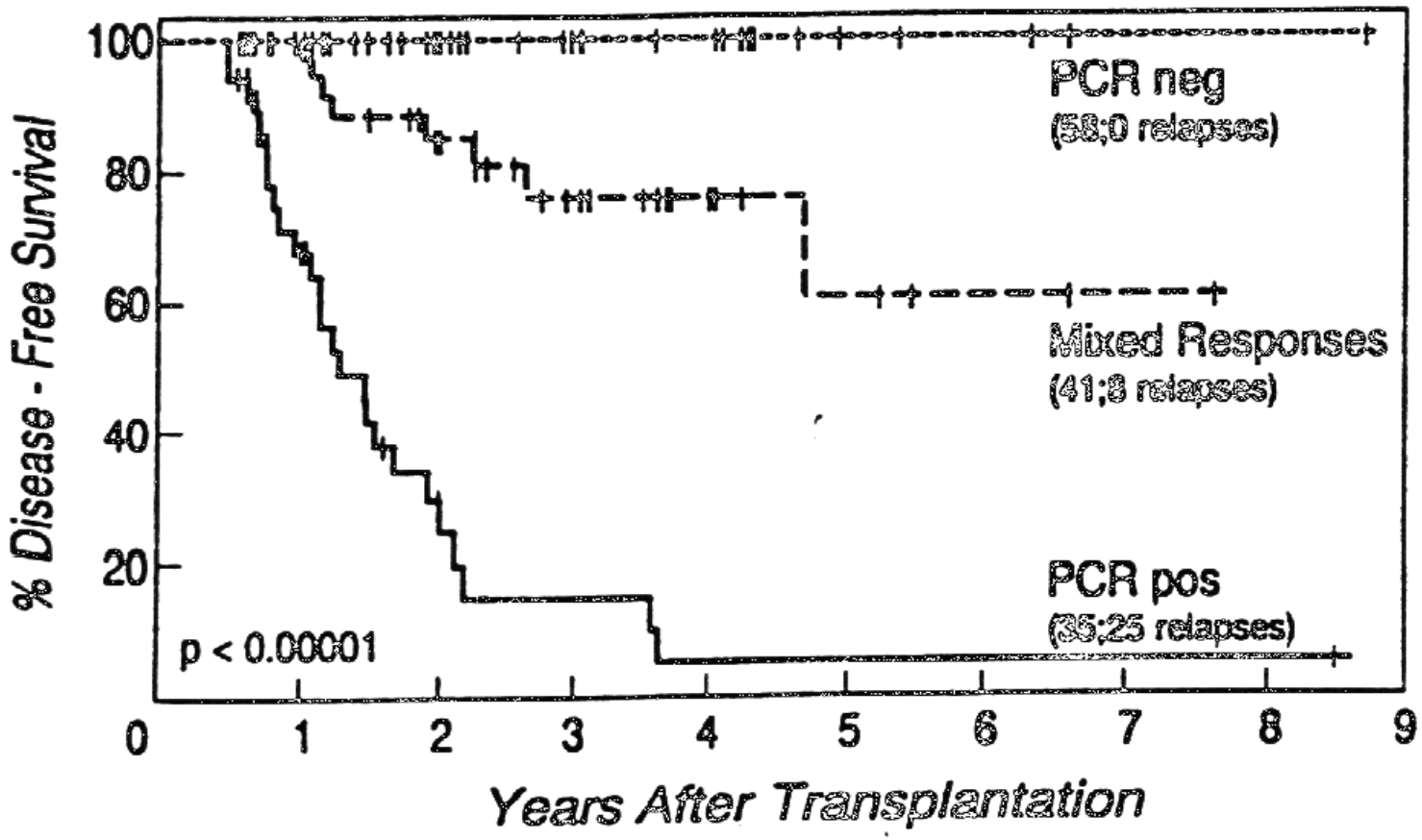
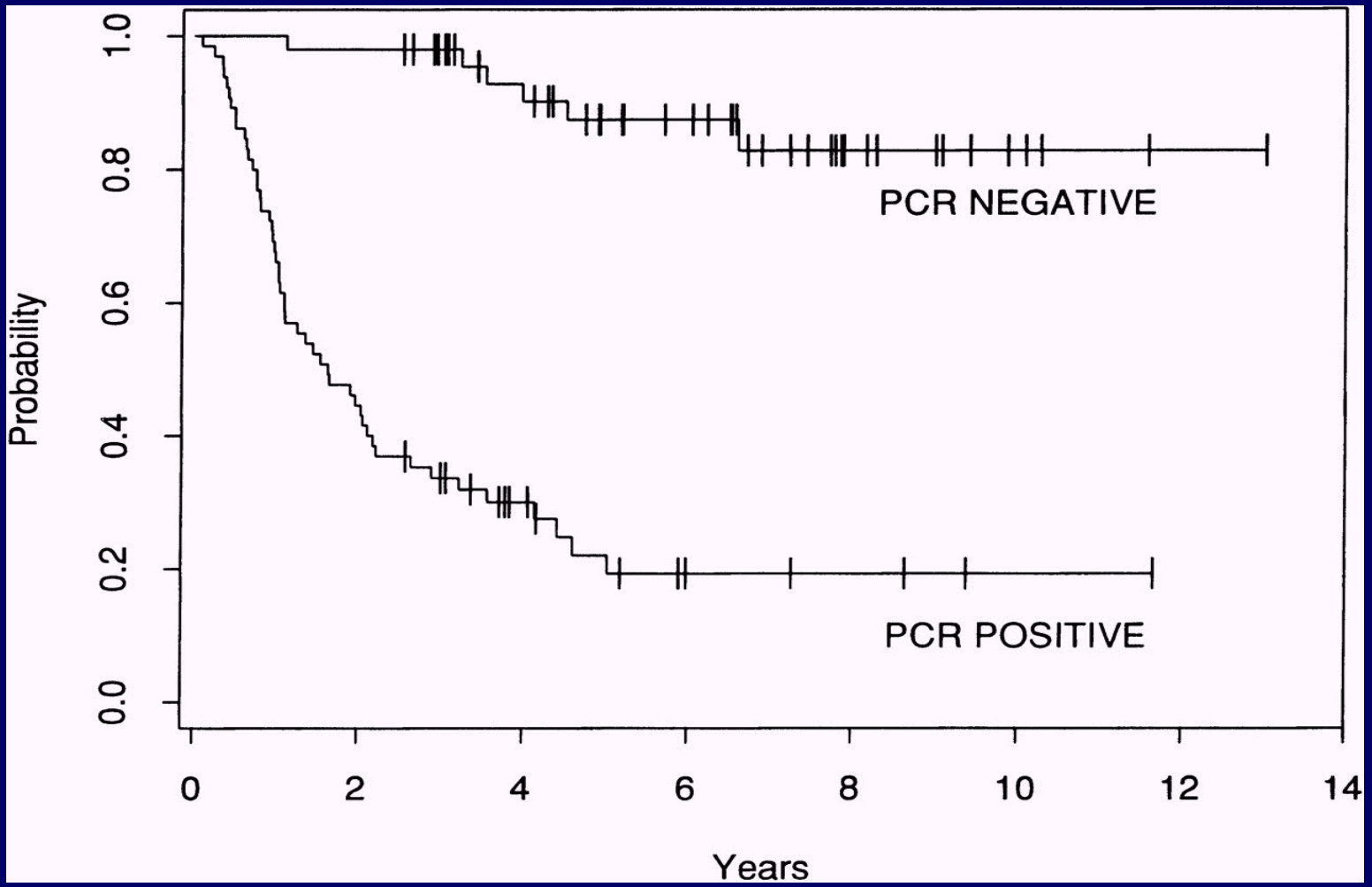



**Fig 1. Actuarial probability of disease-free survival after ABMT in 134 patients with B-cell non-Hodgkin's lymphoma.**

J.G. Gribben et al Blood 1993

# Disease-free survival according to PCR status in FCL patients




*Freedman et al, Blood 1999, 94: 3325-3333*

# Dana Farber study in MCL
# Blood 90:4212, 1997

* **complement-mediated in vitro purging of BM cells**

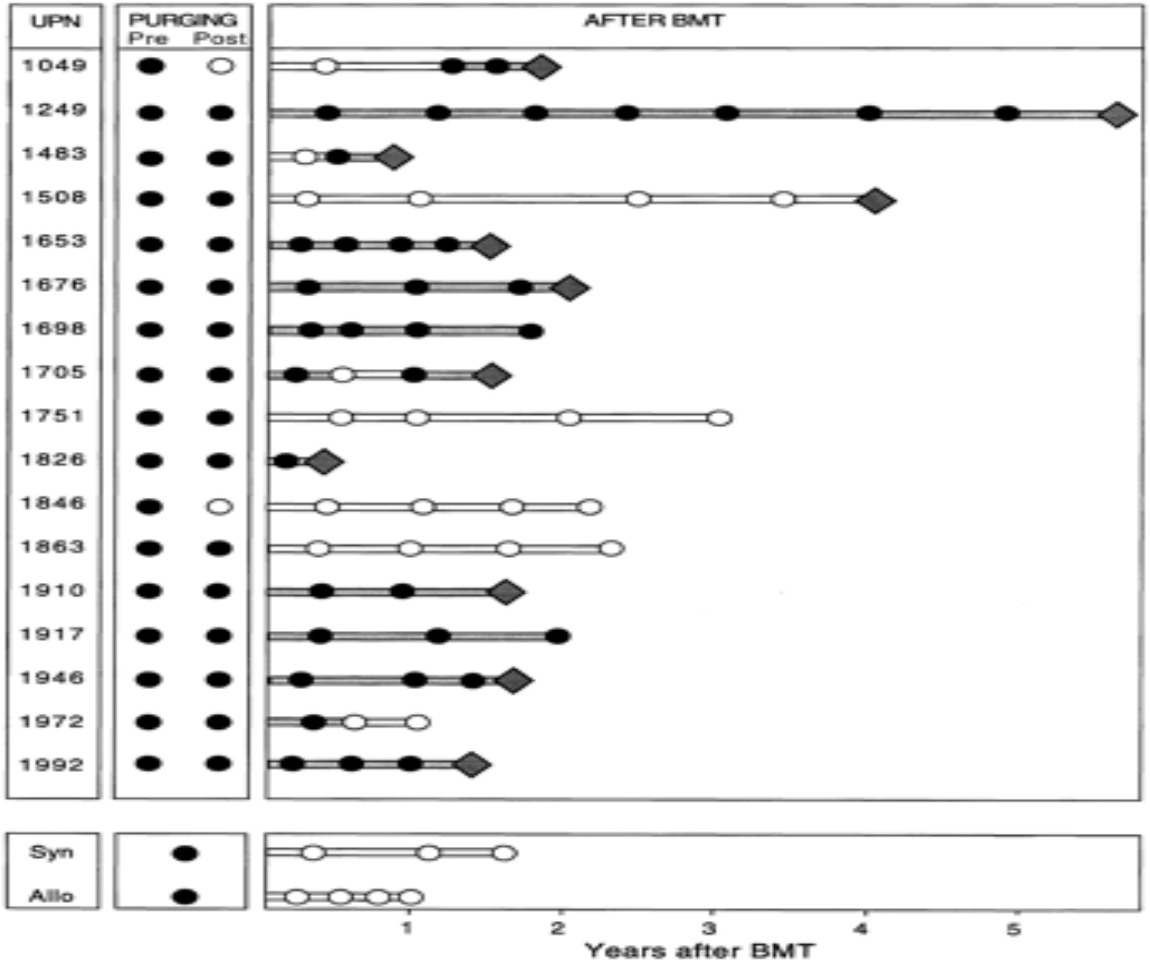
* **MRD assessed by PCR on BM harvest post-purging**

  **MRD + in 17/19 pts.**

  ***( ---> in follicular NHL, post-purging MRD negative in 50% of pts.)***

* **more than half of the mantle-cell lymphoma pts. relapsed within 2 yrs.following autograft**

# Relapse incidence and PCR status in MCL patients




***Andersen et al, Blood, 1997: 90,4212-4221***

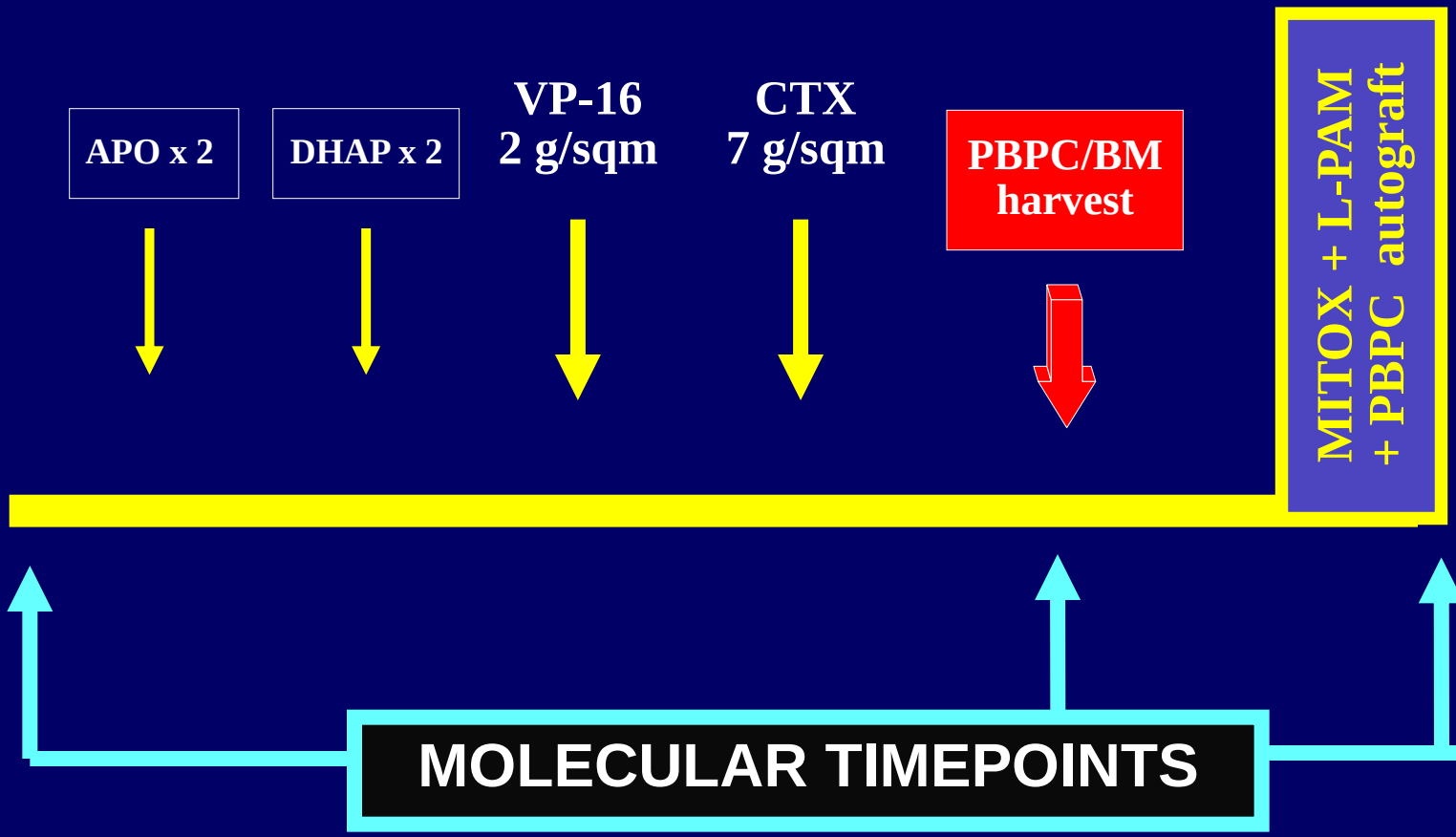
# Turin experience

- **when:** since 1990

- **treatment:** high-dose, "purging-free", chemotherapy regimen, including intensive debulking and then PBPC autografting

- **patients:** advanced-stage FCL, SLL and MCL, with adverse prognostic features

# I-HDS SCHEME FOR BM+, INDOLENT LYMPHOMAS



***Long-term clinical and molecular evaluation***

***of 70 patients with low-grade lymphoma***

***(follicular - mantle-cell - lymphocytic)***

***all treated with the same intensive approach***

***Including peripheral blood progenitor cell***

***(PBPC) autograft***

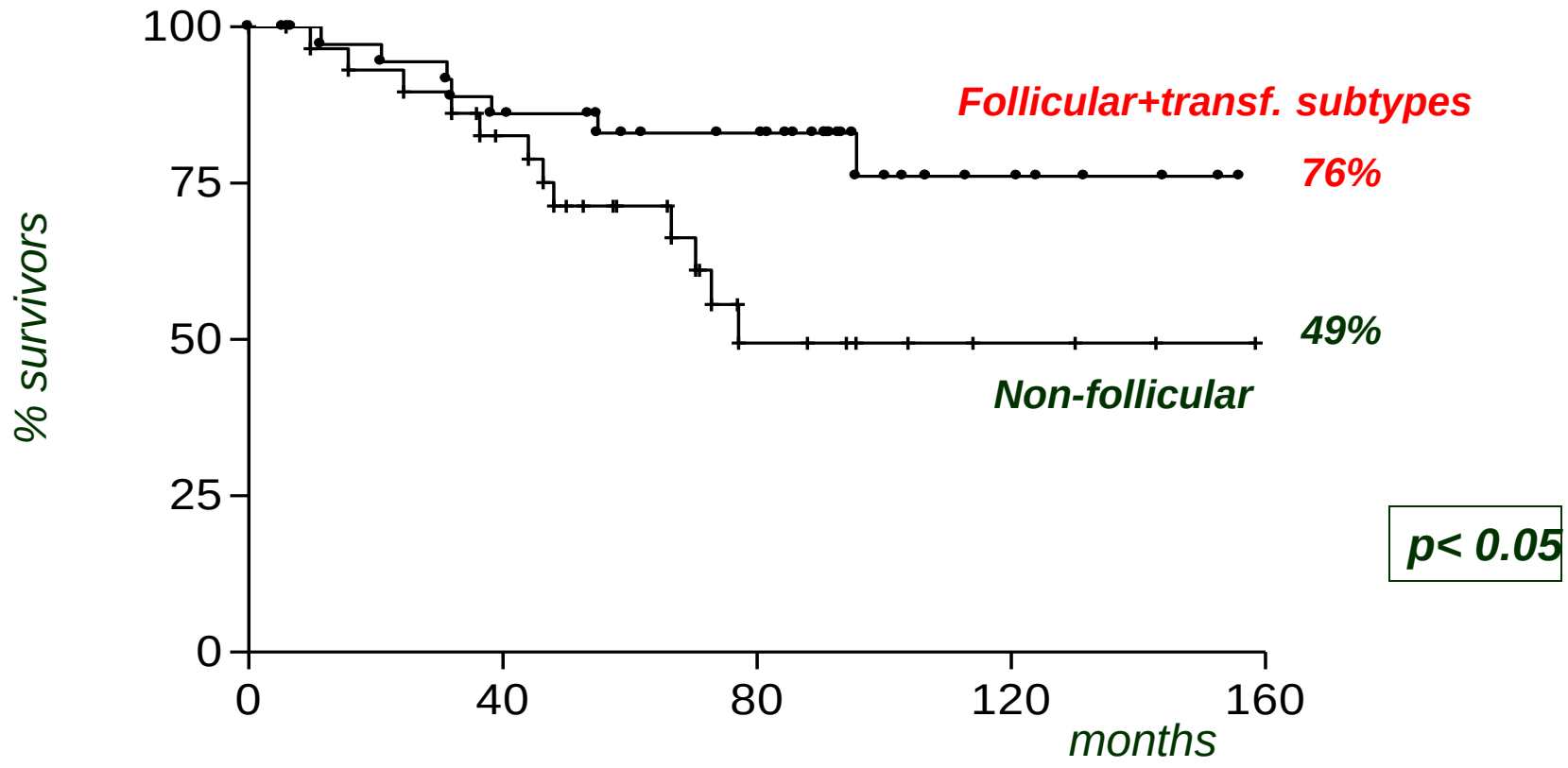
***Corradini et al. J Clin Oncol, Apr 15, 2004***

# Table 1. Main clinical features of the patients entered in the study

| *Parameter* | *n* | *(%)* |
|---|---|---|
| • Age, median (range), years | 47 | (32-61) |
| • Male/female ratio | 43/27 | |
| • Diag./rel. | 61/9 | |
| • Histology | | |
| lymphocitic | 14 | 20 |
| Follicular | 29 | 41 |
| Transformed | 11 | 16 |
| Mantle cell | 16 | 23 |
| • Stage IV | 61 | 87 |
| • Tumor-related symptoms | 45 | 65 |
| • Bone marrow involvement | 57 | 81 |
| • aaIPI score ≥ 2 | 30 | 43 |

*Figure 2 A*

# OVERALL SURVIVAL



# Long term molecular monitoring

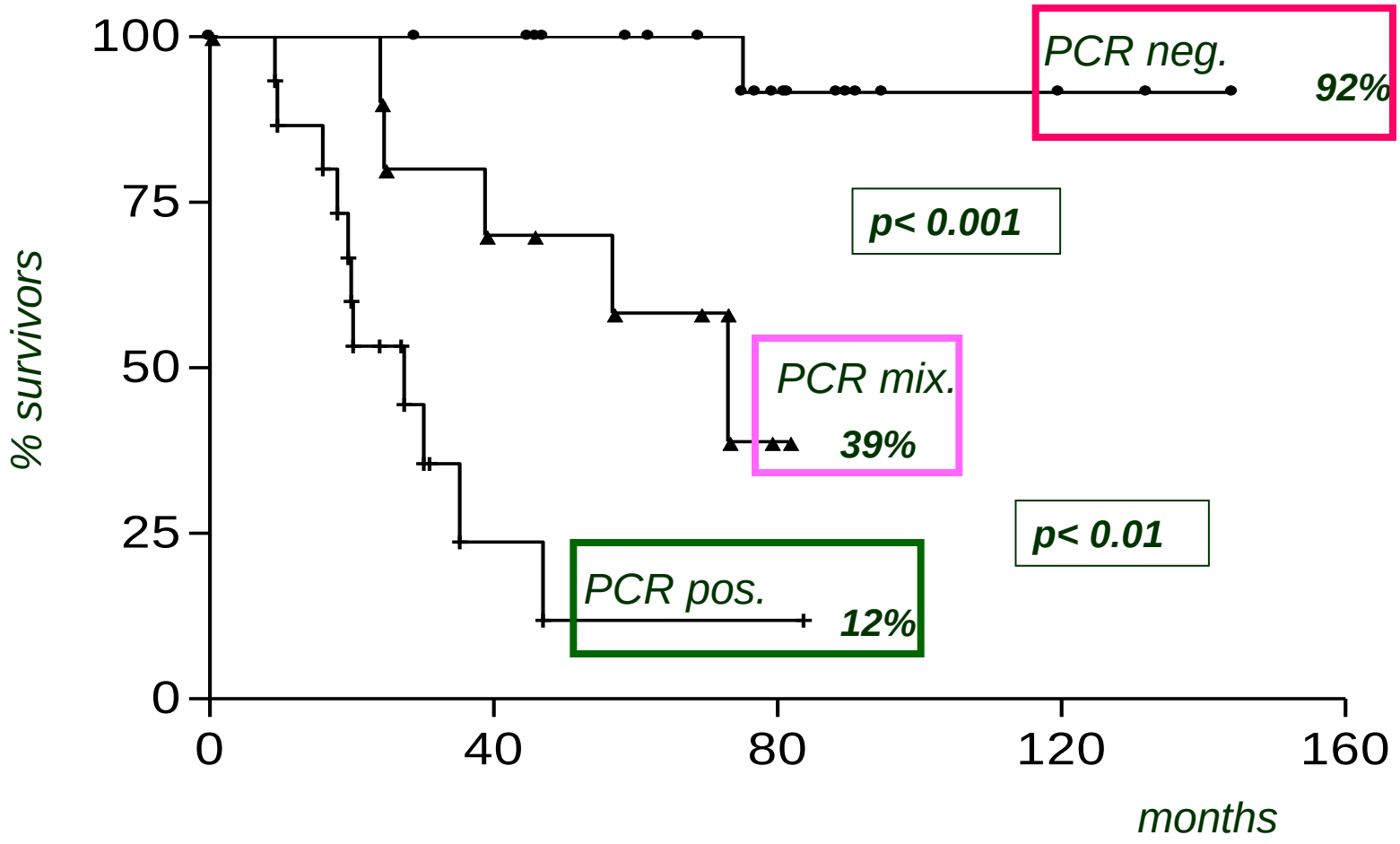
*(Median follow-up : 75 months)*

- ***Patients with a molecular marker:*** ***60 (86%)***

***PCR negativity***

| | *post-harvest* | | *post-ABMT* | | *last follow-up* | |
|---|---|---|---|---|---|---|
| | ***n=*** | ***(%)*** | ***n=*** | ***(%)*** | ***n=*** | ***(%)*** |
| ***Follicular*** | **19/35** | **(54)** | **21/30** | **(70)** | **18/22** | **(82)** |
| ***Non follicular*** | **3/25** | **(12)** | **5/20** | **(25)** | **1/20** | **(5)** |

# Disease free survival according to PCR status during molecular follow-up



# Multivariate analysis

| | *Overall survival as end point* | | | *Event-free survival as end point* | | |
|---|---|---|---|---|---|---|
| ***Characteristics*** | Risk ratio | 95% CI | p value | Risk ratio | 95% CI | p value |
| **CR achievement:** | | | | | | |
| ***-NO*** | **6.29** | **1.9-21.2** | **0.003** | **9.8** | **3.7–25.6** | **<0.0001** |
| **MR achievement:** | | | | | | |
| **-NO** | **46.9** | **5–465** | **0.001** | **24.4** | **3.1 – 191** | **0.0023** |

# CONCLUSIONS - 1

- **FCL e non-FCL patients display a significantly different outcome in terms of:**
  - **PCR-negative harvests**
  - **Achievement of post-autograft Molecular Remission**
- **Post autograft *MR* persistence is highly predictive of prolonged overall and disease-free survival**

**Thus, *MR* achievement seems an essential "target" in the autograft setting**

are high-dose therapies with autograft reproducible at a multicenter setting ?

***1997: GITMO study to evaluate reproducibility in a multicenter setting of i-HDS as front-line therapy for advanced-stage FCL < 60 y.o.***

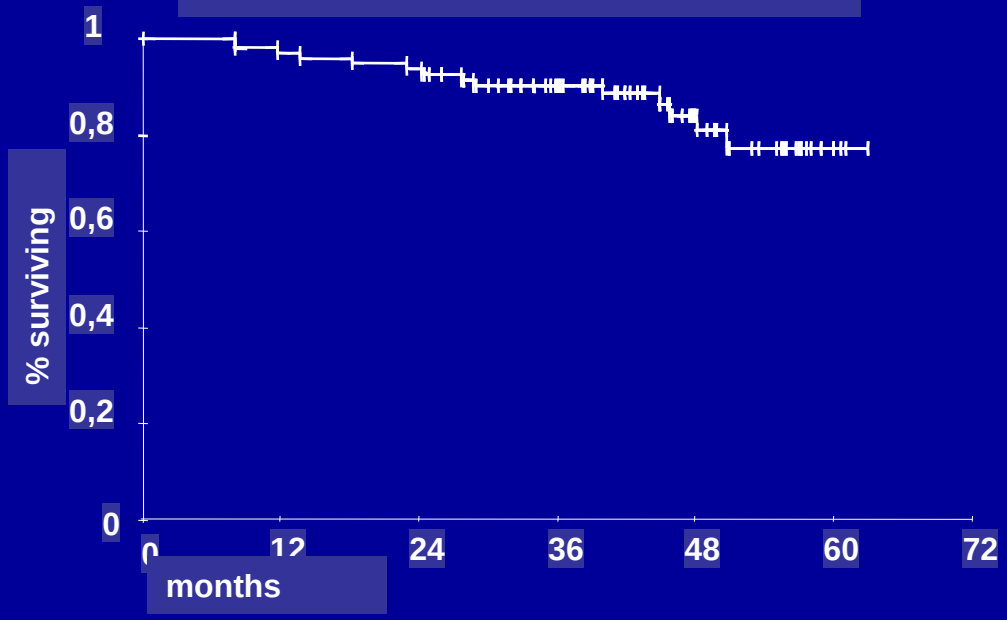
**THE MULTICENTER GITMO TRIAL HAS BEEN LAUNCHED IN DECEMBER 1996**

**20 ITALIAN CENTERS HAVE BEEN INVOLVED IN THIS STUDY**

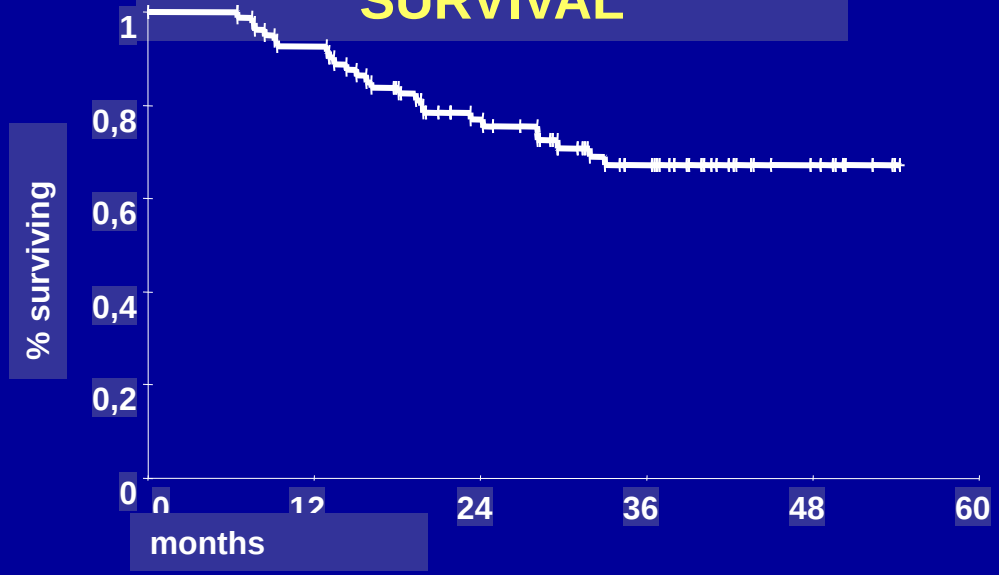
**92 PATIENTS WERE CONSIDERED EVALUABLE ON AN INTENTION TO TREAT BASIS**

***three patients were excluded due to inappropriate inclusion (1MCL, 1CLL, 1CNS involvement)***

## OVERALL SURVIVAL



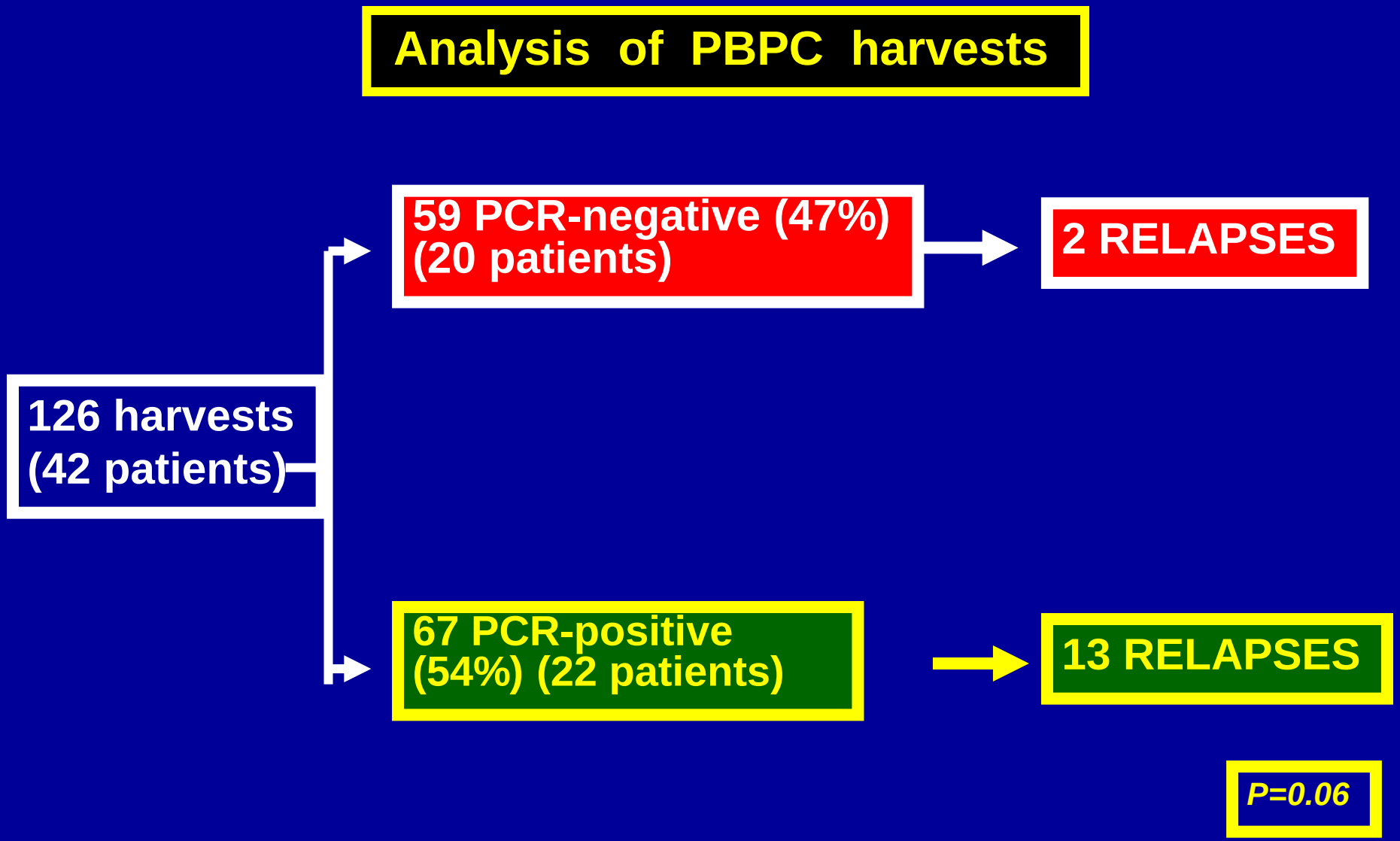

## DISEASE-FREE SURVIVAL



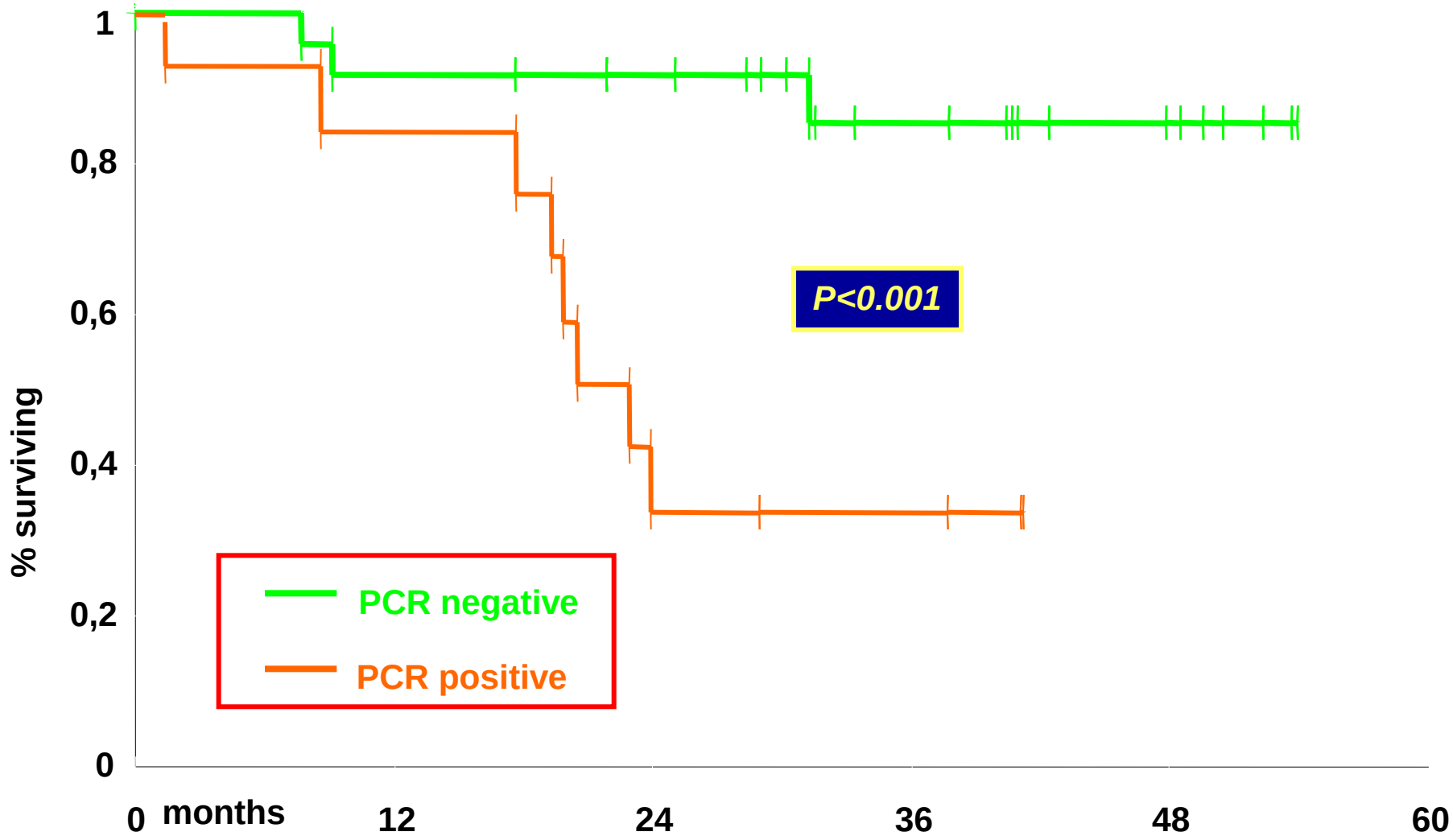

**High rate of clinical and molecular remissions in follicular lymphoma patients receiving high-dose sequentila chemotherapy and autograft at diagnosis: a multicenter prospective study by the Gruppo Italiano**

***LADETTO et al, Blood 2002, 100: 1559-65***

# *GITMO multicenter study*
# MOLECULAR RESPONSE assessed by PCR



# *GITMO multicenter study*
# DISEASE FREE SURVIVAL according to post-transplant PCR status



# CONCLUSION - 2

**Both single-center and multicenter studies have demonstrated that *MR* achievement is an essential "target" in indolent lymphoma patients undergiong an intensified program with autograft**

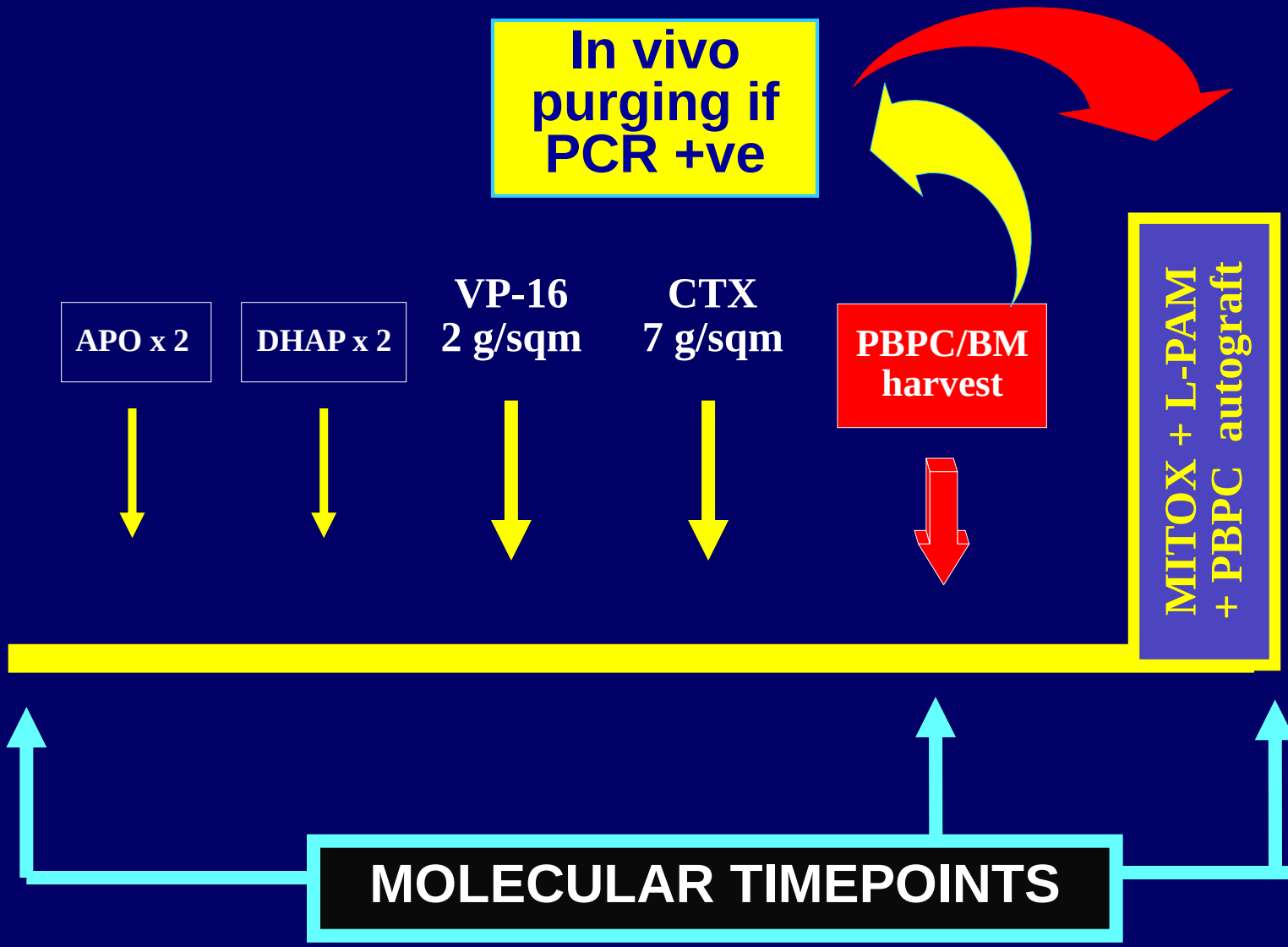
**May we increase the number of patients achieving MR**

# IN VITRO MANIPULATION ("ex-vivo purging ") OF CIRCULATING HEMOPOIETIC PROGENITORS

*in follicular and mantle-cell lymphoma patients treated with i-HDS, and displaying molecularly detectable minimal residual disease in the harvests*

**Tarella C. et al., Leukemia 1999, 13: 1456**

# I-HDS SCHEME FOR BM+, INDOLENT LYMPHOMAS



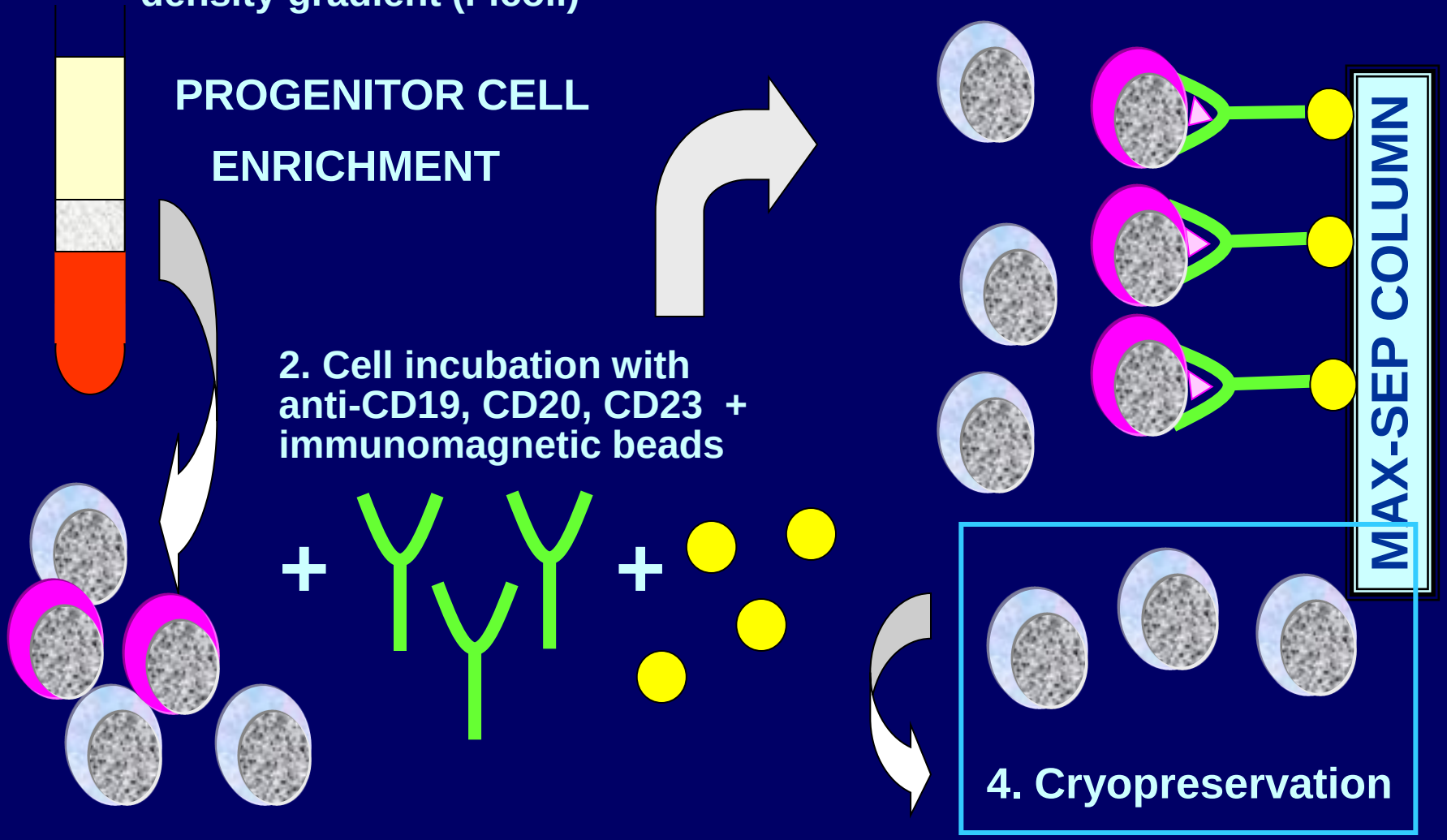
# immunomagnetic negative ex-vivo purging procedure

1. Cell separation on density gradient (Ficoll)

PROGENITOR CELL ENRICHMENT

2. Cell incubation with anti-CD19, CD20, CD23 + immunomagnetic beads

3. Lymphoma Cell separation through a passage on a Max-Sep column



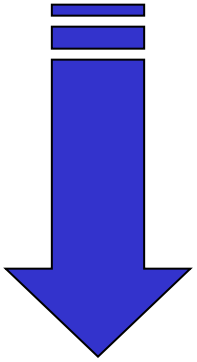
# PCR assessmemnt of the “ex-vivo purging” efficiency

| | Evaluable pts. |
|---|---|
| Follicular Lymphoma | 8 |
| • post-purging PCR neg | 3 |
| • post-autograft PCR neg | 3 |
| • *total achieving PCR neg* | *6* |
| Mantle Cell Lymphoma | 3 |
| • *post-purging PCR Neg* | *none* |
| • *post-autograft PCR Neg* | *none* |

***Andersen NS, et al. (Dana Farber group, Boston)***
***Blood 90: 4212-4221, 1997:***

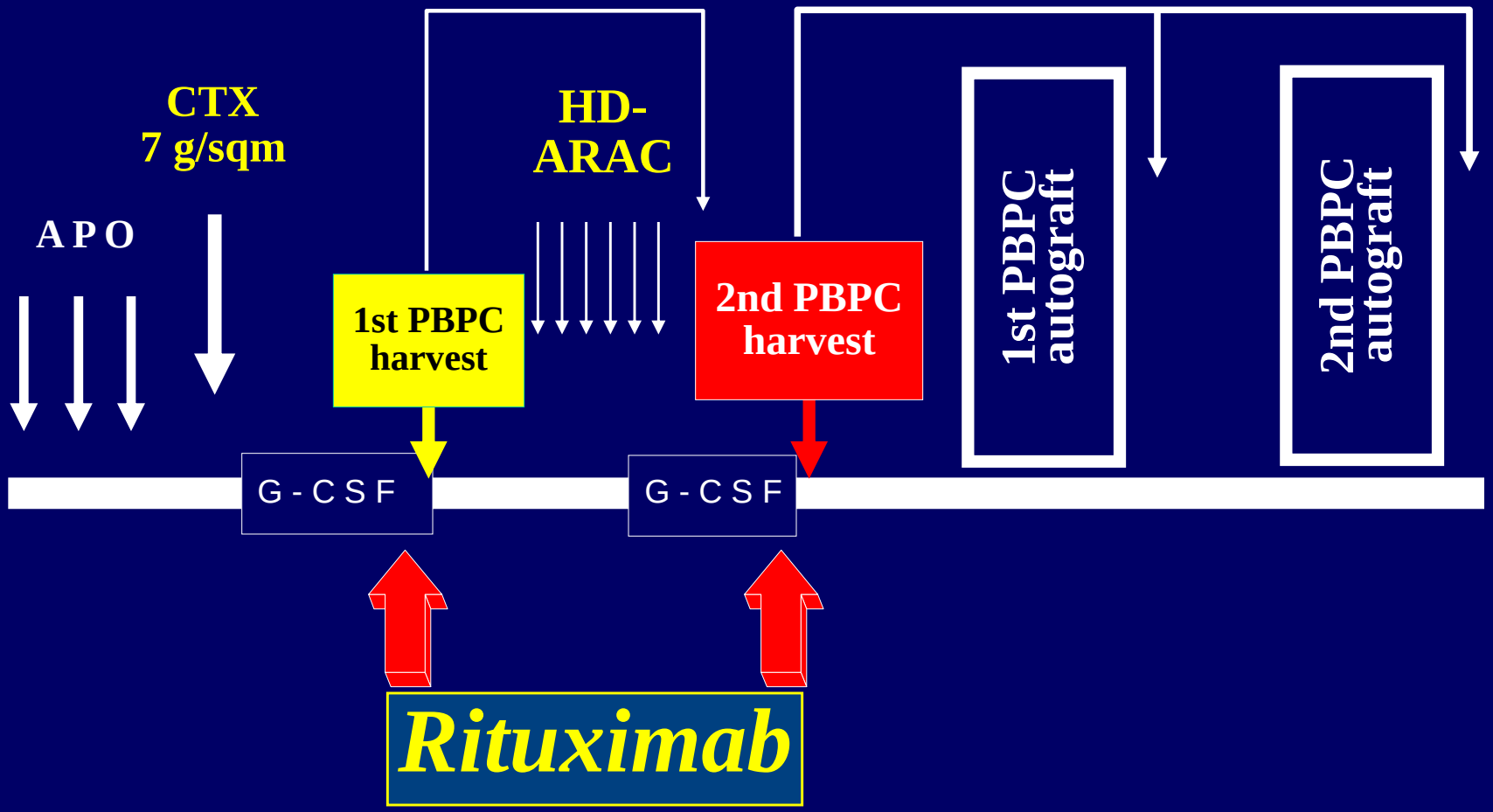
**Failure of immunologic purging in Mantle-cell lymphoma assessed by polymerase chain reaction detection of minimal residual disease**

# Searching for new approaches able to icrease the chances of harvesting PCR- PBPC

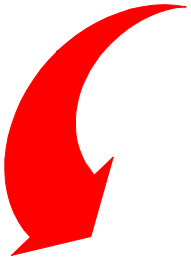


***the potential use of Rituximab in combination with autograft with the aim of exploiting an in vivo purging effect prior to PBPC harvesting***

# MODIFIED HDS WITH RITUXIMAB (R-HDS) GIVEN PRIOR TO PBPC COLLECTIONS



***A RITUXIMAB-SUPPLEMENTED HDS REGIMEN HAS BEEN PROVED TO BE FEASIBLE AND EFFECTIVE IN MCL AND IN RELAPSED FCL***



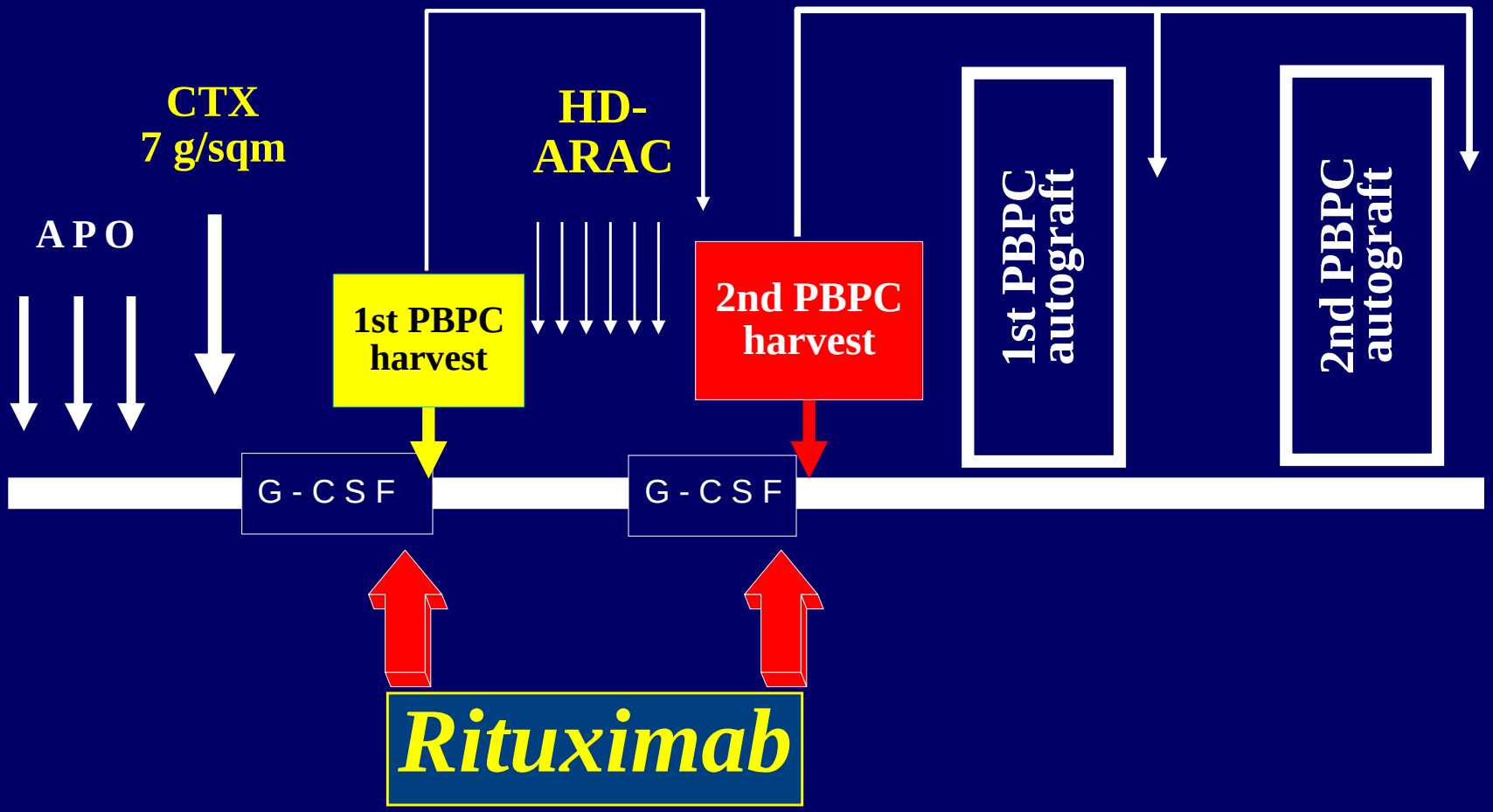
**SUCCESSFUL IN VIVO PURGING OF CD34-CONTAINING PERIPHERAL BLOOD HARVESTS IN MANTLE CELL AND INDOLENT LYMPHOMA: EVIDENCE FOR A ROLE OF BOTH CHEMOTHERAPY AND RITUXIMAB INFUSION**

*Magni M, Di Nicola M, Devizzi L, Matteucci P, Lombardi F, Gandola L, Ravagnani F, Giardini R, Dastoli G, Tarella C, Pileri A, Bonadonna G, Gianni.* ***Blood 2000, 96:864***

# R-HDS vs. HDS pilot study
# Main Patient Characteristics

| | R-HDS *n=15* | HDS *n=10* |
|---|---|---|
| Age, median (range) | 43 (34-58) | 46 (36-53) |
| Female/Male (No.) | 4/11 | 5/5 |
| Histology (No.) | | |
| *- follicular* | 7 | 7 |
| *- mantle* | 7 | 3 |
| - marginal | 1 | - |
| BM involvement | 11 | 7 |
| PCR+ only | 4 | 3 |
| PB lymphoma cells | 6 | 3 |

# MODIFIED HDS WITH RITUXIMAB (R-HDS) GIVEN PRIOR TO PBPC COLLECTIONS



# Quantity and quality of harvested PBPC in R-HDS treated and group patients

| | *R-HDS (n=15)* | *Controls (n=10)* |
|---|---|---|
| **CD34+x10$^6$ /kg p-CY** | **10,5** | **14,5** |
| **PCR neg p-CY** | **57%** | **20%** |
| **CD34+x10$^6$ /kg p-AraC** | **23** | **22,5** |
| **PCR neg p-AraC** | **93%** | **44%** |

## *Preliminary experience at the Turin Center With the Rituximab-HDS approach As 1st line therapy for MCL (april 1999 – november 2003)*

- *11 patients have been treated, all of them achieved CR, with MR achievement in 6/6*
- *at a median follow-up of 36 mos., 11/11 patients are alive*
- *so far, 1 single recurrence has been recorded: this patients is now in his 2nd remission after allogeneic transplant)*

# *efficacy of the Rituximab-supplemented approach in high-risk FCL and in relapsed/progressing B-DLCL*

**CONCURRENT ADMINISTRATION OF HIGH-DOSE CHEMOTHERAPY AND RITUXIMAB IS A FEASIBLE AND EFFECTIVE CHEMO/IMMUNOTHERAPY FOR PATIENTS WITH HIGH-RISK NON-HODGKIN'S LYMPHOMA.**

*Marco Ladetto, Francesco Zallio, Sonia Vallet, Irene Ricca, Alessandra Cuttica, Daniele Caracciolo, Paolo Corradini, Monica Astolfi, Selina Sametti, Federica Volpato, Paola Bondesan, Umberto Vitolo, Mario Boccadoro, Alessandro Pileri, Alessandro M. Gianni, Corrado Tarella.*

**LEUKEMIA, 2001, 15: 1941**

# R-HDS in high-risk FCL results

| | refr./rel n= | at diag. n= |
|---|---|---|
| Clinical CR | 5/7 | 10/11 |
| Molecular CR | 5/6 | 10/10 |
| T R M | 1 | 0 |
| C C R | 5/7 | 10/11 |

4-yr. Overall Survival: 84% (median follow-up: 2 yrs.)

# CURRENTLY ONGOING RANDOMIZED GITMO TRIAL

## *IN POOR-RISK FCL AT DISEASE ONSET*

***RITUXIMAB*-supplemented HDS (R-HDS)**

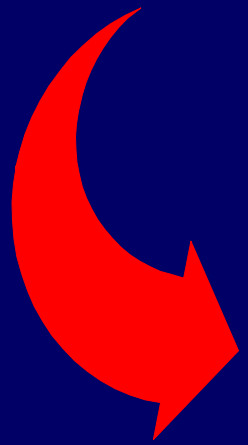
**versus**

***RITUXIMAB*-supplemented CHOP (CHOP then R)**

**involving 50 Centers associated to GITMO**

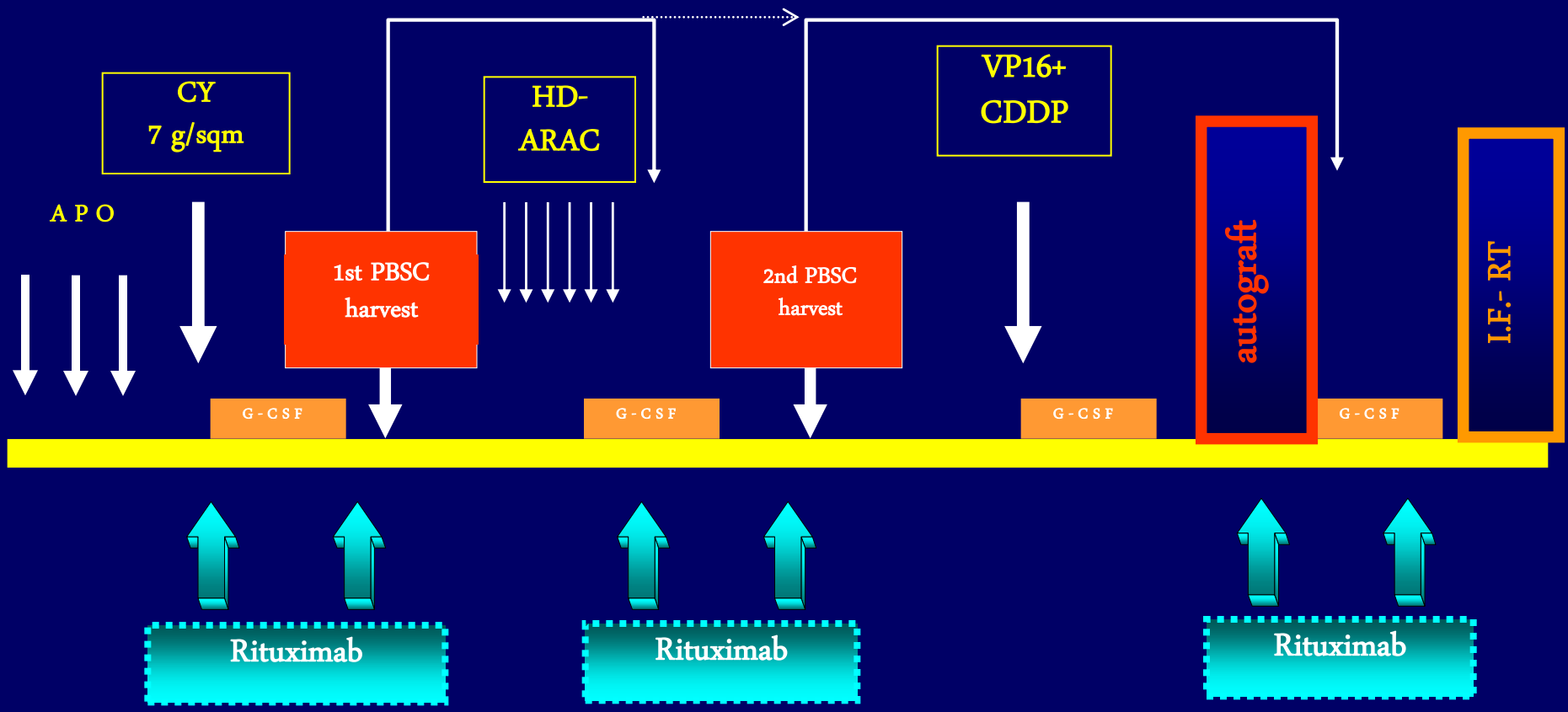
# R – HDS in aaIPI 2-3 DLCL

## *a multicenter experience of the GRUPPO ITALIANO TERAPIE INNOVATIVE NEI LINFOMI (GITIL)*



***Preliminary results***

# RITUXIMAB-SUPPLEMENTED HDS SCHEME FOR HIGH-RISK B-CELL DLCL

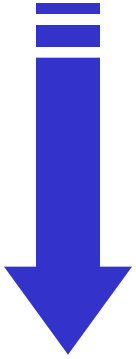


# R-HDS multicenter study protocol
## *Main Patient characteristics*

| *Parameter* | *patients (n =95)* |
|---|---|
| • Age, median (range), yrs. | 48 (18-66) |
| • aaIPI 2 vs 3 | 58 vs 33 |
| • Extranodal sites | 57 |
| - BM invasion | 29 |
| • Histological transformation | 7 |

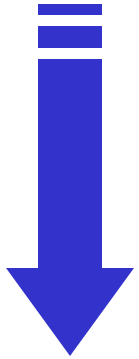
**18 out of 29 (62 %) B-DLCL patients with 2-3 aaIPI score and *BM involvement* are presently alive in CCR following R-HDS, at + 10 up to + 35 mos. since treatment conclusion**

**Several recent studies have confirmed the efficacy of Rituximab for "in vivo purging" purposes, allowing the collection of PCR – in most patients**



**The use of Rituximab is advisable whenever patients with B-cell lymphoma, with BM involvement, are enrolled in intensive programs with PBPC autograft**

# Is there any indication for the early treatment of “molecular recurrence” ?



**Again, at present the treatment of molecular recurrence should be considered only for high-risk patients, if managed with programs aimed to disease eradication or at least maximal tumor cytoreduction**

# Molecular Recurrence of the Bcl-2/IgH Rearrangement in FL Following ABMT

- IS AN UNCOMMON BUT WELL DEFINED EVENT
- IS ASSOCIATED WITH A HIGH RISK OF RELAPSE

**EARLY TREATMENT OF MOLECULAR RELAPSE?**

# THE HIGH INCIDENCE OF NNBR IN THE PB OF HEALTHY SUBJECTS

?

## MAJOR CONFOUNDING FACTOR IN THE SETTING OF PCR-ANALYSIS

...the current PCR protocols seem to be inappropriate as the sole technique for monitoring MRD in FL. (Summers et al JCO, 2001 15: 420-424)

CAN AT LEAST A PROPORTION OF THE SO-CALLED MOLECULAR RELAPSES BE ASSOCIATED TO NLABR AND NOT TO THE REAPPARENCE OF THE ORIGINAL TUMOR CLONE ?

**Recent study to verify the nature of molecular relapses occurring in our patient population**

*Ladetto M et al, Exp Hematol 2003, 31(9):784-8*

# PATIENT SAMPLE

119 FCL patients enrolled in prospective clinical trials including high-dose sequential chemotherapy + autologous transplantation with or without Rituximab supplementation (16 vs 103)

# DEFINITIONS

**MOLECULAR REMISSION (MR)**: any CR patient achieving PCR-negativity on two separate BM samples obtained after an interval of at least three months

**MOLECULAR RELAPSE**: any MR patient reverting to PCR positivity on two separate BM samples taken after an interval of one month.

# 119 patients with Bcl-2/IgH+ FL

## 8 MOLECULAR RECURRENCES

6 PATIENTS HAD THE SAME REARRANGEMENT DETECTED AT DIAGNOSIS

2 PATIENTS HAD A NOVEL UNRELATED REARRANGEMENT (different VH usage and/or N-insertions)

# Summary of the Results

- MOLECULAR RECURRENCE DUE TO UNRELATED REARRANGEMENTS OCCURRED ALWAYS AFTER THREE OR MORE YEARS FROM TRANSPLANT

- THESE NOVEL UNRELATED REARRANGEMENTS PERSISTED FOR SEVERAL MONTHS (20 in one subject)

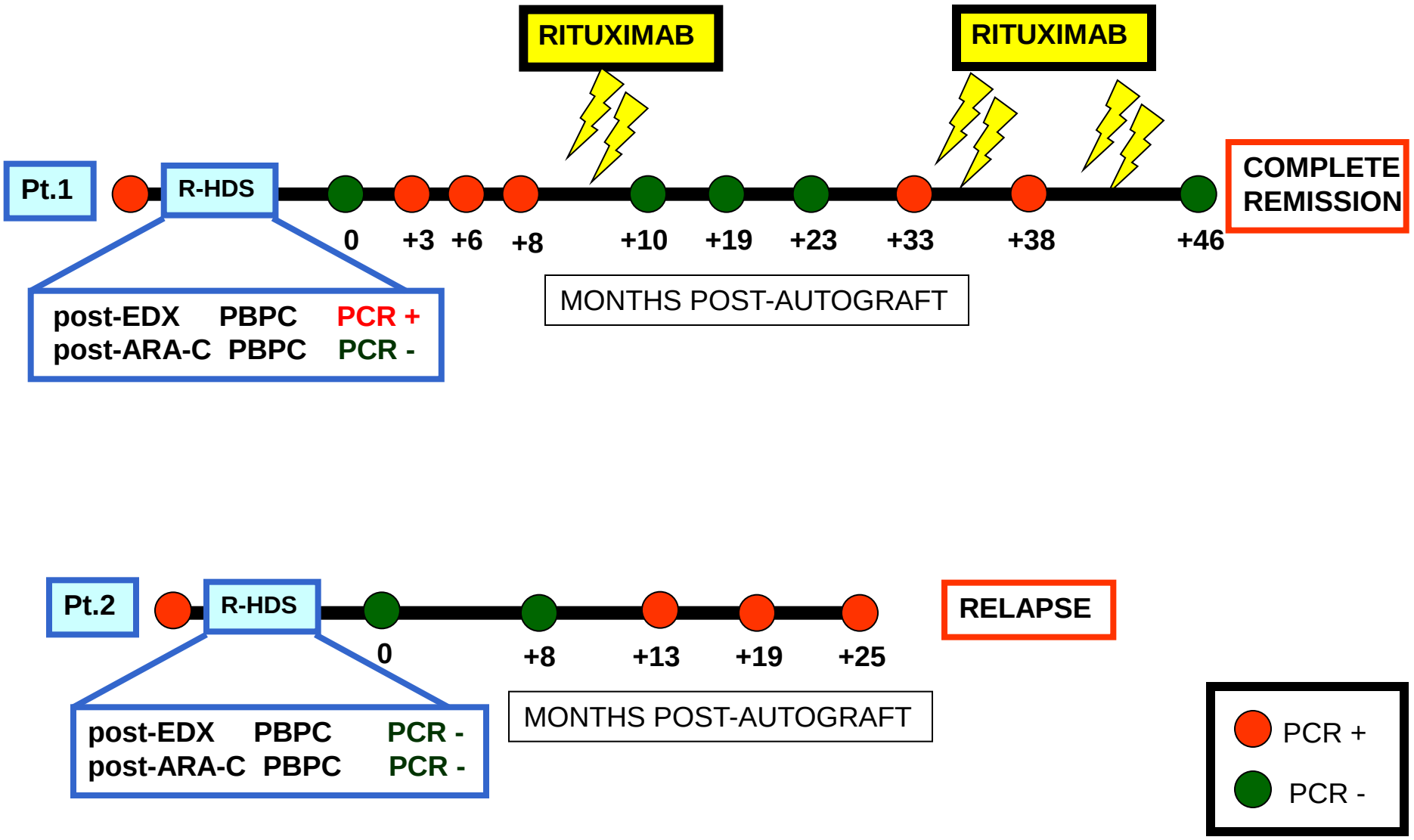
- NONE OF THE SUBJECTS WITH UNRELATED REARRANGEMENTS SHOWED EVIDENCE OF ACTIVE LYMPHOPROLIFERATIVE DISEASE

# R-HDS protocol for *Mantle Cell Lymphoma (MCL)*

***the risk of a "misdiagnosed" molecular relapse due to a non-neoplastic bcl-2 rearrangement does not apply to mantle-cell lymphoma***

# Relationship between post-graft PCR status and clinical outcome

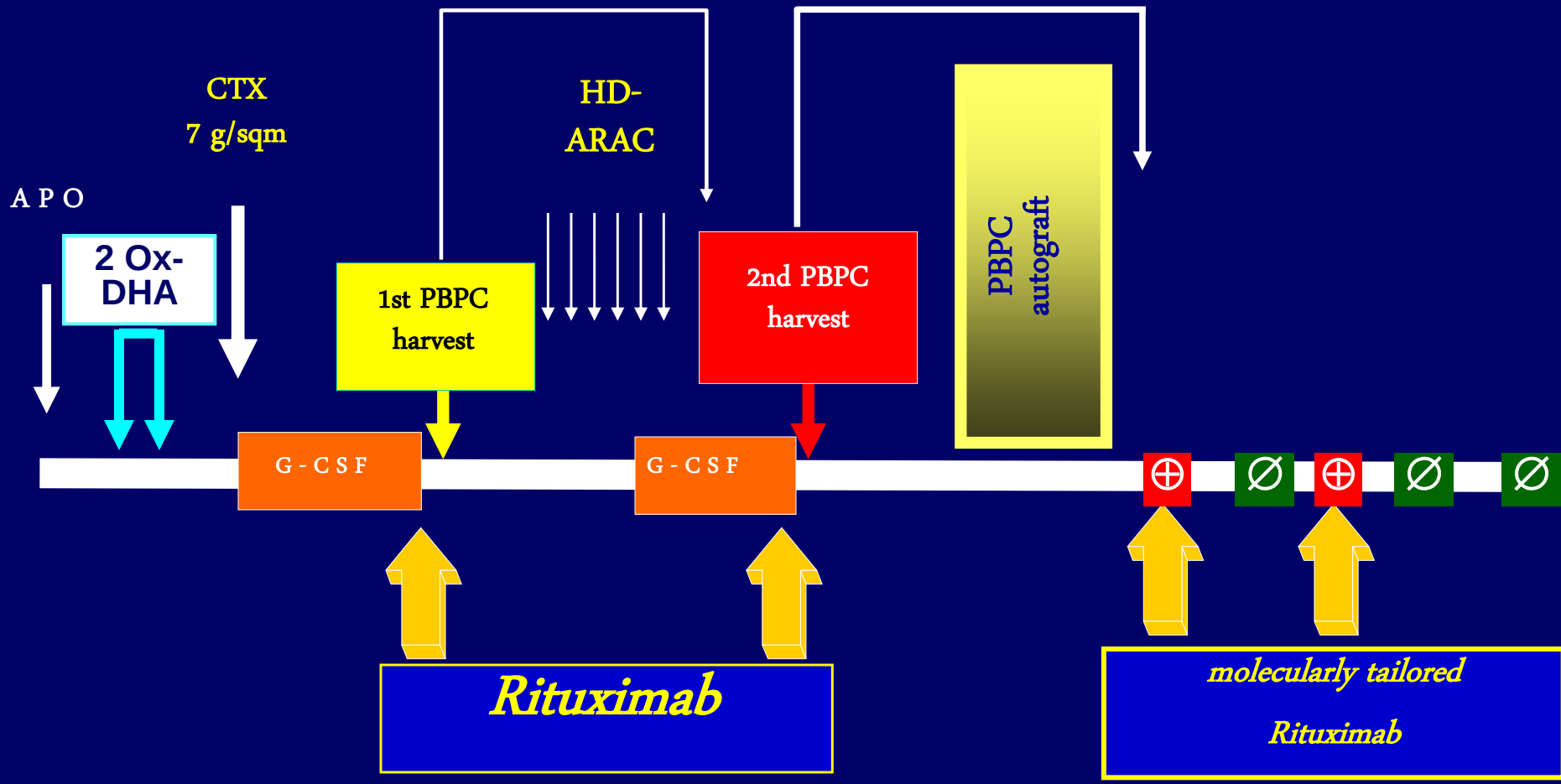
## *the lesson learned from two cases treated at diagnosis with R-HDS*



# R-HDS protocol for *Mantle Cell Lymphoma (MCL)*

***the possible post-autograft Rituximab administration "tailored" on the molecular monitoring of the minimal residual disease***

# NOVEL MULTICENTER STUDY PROGRAM FOR *LMANTLE-CELL LYMPHOMA*



# MR as an essential "target" in the management of non-Hodgkin's Lymphoma *conclusions*

- although MR achievement seems associated with a better outcome, at present there are no sufficient data to support the need of MR achievement in indolent lymphoma patients treated with conventional chemo-immunotherapy
- On the other hand, MR achievement seems an essential goal for patients enrolled in intensive programs with autograft
- In B-cell lymphoma, MR of PBPC harvests can be easily achieved by adding Rituximab as an "in vivo purging" agent
- Treatment of "molecular relapse" is not a minor issue in patients potentially curable with intensive treatments

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**ALL CENTERS PARTICIPATING TO HDS-BASED STUDY PROTOCOLS FOR HIGH-RISK NHL**

# Clinical significance of MRD in MM

**Molecular monitoring of MRD has been used for the following purposes:**

- **to evaluate the effectiveness of purging procedures**
- **to evaluate whether PCR negativity predicted a reduced risk of relapse**

# Clinical significance of molecular analysis in MM

- **Molecular disease in MM is currently assessed by PCR-based methods**
- **In nearly 70% of MM patients it is possible to identify a molecular marker (IgH specific rearrangement)**
- **Molecular disease significance has been explored in different settings**

# Prognostic significance of MRD

**Auto-SCT can induce in a small proportion of patients a long term survival (>5 yrs)**

**It has been hypothesized that molecular status can predict long term survival after auto-SCT**

# MRD after auto-SCT

**Corradini et al.**

- **12/12 patients** were PCR positive after auto-SCT. (Blood 1995)
- **14/15 patients** were PCR positive after auto-SCT. (JCO 1999)

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**Martinelli et al.**

- **25/30 patients** were PCR positive after auto-SCT and PCR negativity was not predictive of prolonged survival . (JCO 2000)

# Prognostic significance after autologous stem cell transplantation (auto-SCT)

- **Early studies demonstrated that molecular remission after auto-SCT is uncommon.** (Corradini Blood 1995, Martinelli JCO 2000)
- **Molecular follow up after auto-SCT is not ususally performed since the rare molecular remissions are not predictive of long term disease free survival.** (Corradini JCO 1999, Martinelli JCO 2000)

# In vitro purging procedures

**Autologous stem cell transplantation (auto-SCT) has been identified as the gold standard therapy for patients aged less than 65 years.**

**However, virtually all patients relapse after auto-SCT.**

# PCR analysis of purified stem cells (2)

**Stewart et al.**

**(JCO 2001)**

- **190 patients were randomized to receive an autograft of CD34-selected or unselected PBSC**
- **a median 3 log depletion (limiting dilution assay) of plasma cells was achieved**
- **50% were PCR-negative**
- **selected and unselected patients had similar outcomes.**

# PCR analysis of purified stem cells (3)

**Voena et al.**

**(BJH 2002)**

- **6/12 patients of CD34 selected PBSC were PCR positive in small scale selection**
- **Taqman analysis of large scale CD34 selected PBSC showed a 2 log reduction of tumor cell contamination.**

# Evaluation of purging procedures

- Purging manipulations of PBSC (CD34 positive selection +/- negative selection) have been shown to be ineffective, since residual tumor cells persist after purging. (Lemoli BJH 1999, Lemoli Blood 2000)
- Despite a 3 log reduction of tumor contamination, patients transplanted with purged PBSC have similar outcome respect to non-purged patients. (Stewart, JCO 2001)

# Conclusions

- **Molecular monitoring of MRD by means of PCR-based methods is feasible in 70-80% of cases**
- **PCR analysis of purged stem cells is, at present, poorly useful**
- **PCR follow up of auto-transplanted patients seems unnecessary**

**Allo-SCT can induce long term survival. Identification of patients at impending risk of relapse can facilitate early immune-therapeutical interventions (↓toxicity, ↑efficacy)**

**It has been hypothesized that molecular status can precede disease changes after allo-SCT**

# Prognostic significance after allogeneic stem cell transplantation (allo-SCT)

- Early studies have shown that molecular negativity after allo-SCT is achieved in 50% of patients in clinical remission. (Corradini Blood 1995, Martinelli JCO 2000)
- A recent analysis of 48 patients in clinical remission has shown that <u>molecular negativity correlates with a low risk of relapse</u> (Corradini Blood, in press)

# MOLECULAR REMISSION AFTER MYELOABLATIVE ALLOGENEIC STEM CELL TRANSPLANTATION PREDICTS A BETTER RELAPSE-FREE SURVIVAL IN MULTIPLE MYELOMA: an EBMT study

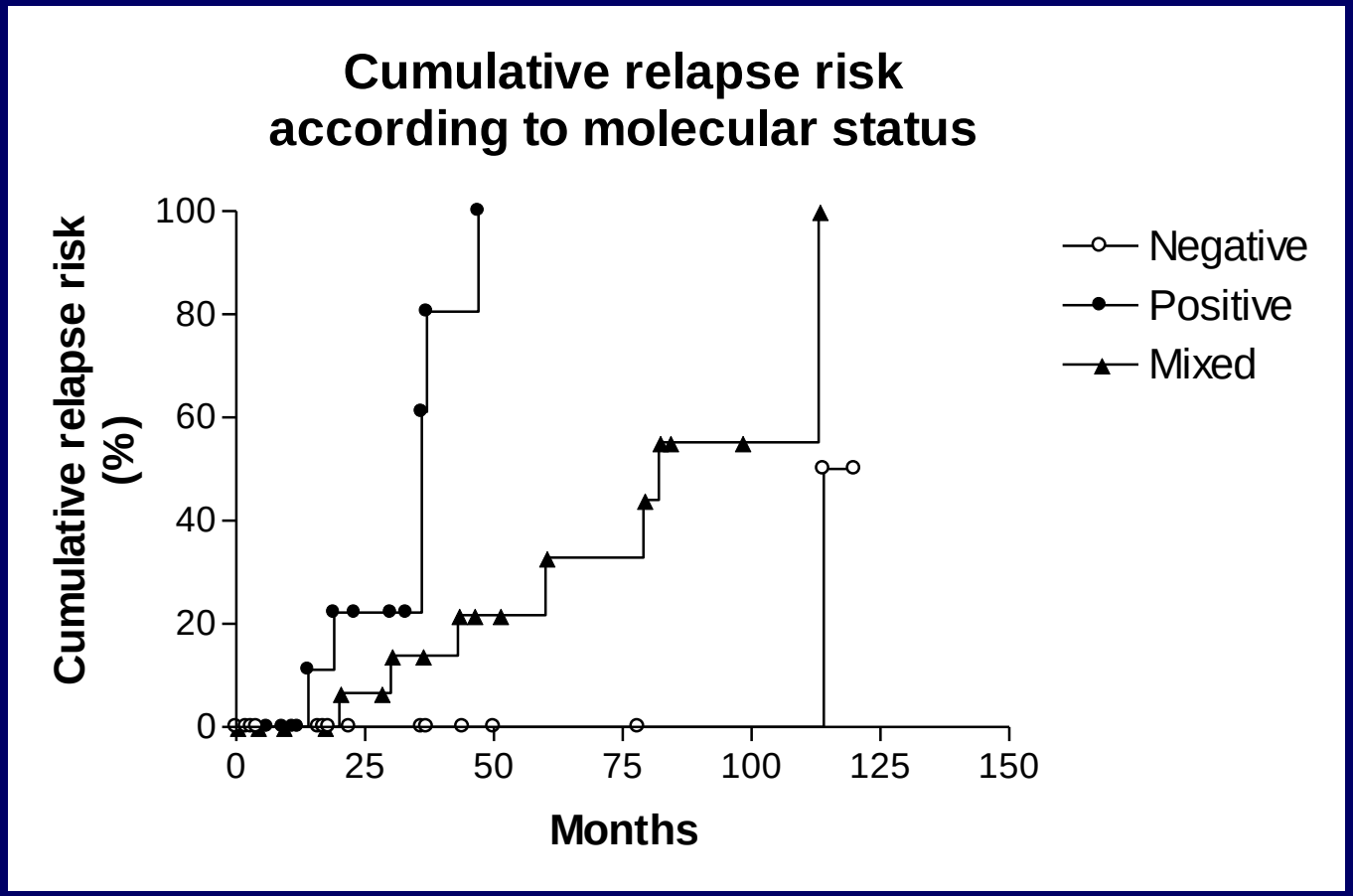
**70 patients in CR after allo-SCT:**

**48/70 (68%) had a molecular marker**

- **16 pts (33%) were persistently PCR-negative**
- **13 pts (27%) were persistently PCR-positive**
- **19 pts (40%) had a mixed pattern**

***Corradini P et al, Blood 2003***

# Molecular remission after myeloablative alloHSCT predicts a better relapse-free survival in MM




**The cumulative risk of relapse at 5 years for NEG, MIX and POS patients was 0%, 33% and 100%, respectively**

Corradini et al. Blood, 2003

**Continuous PCR negativity is predictive of a reduced risk of relapse respect to continuous PCR positivity (P=0.0001) and mixed pattern (P=0.001).**

- **PCR analysis of allo-transplanted patients has a prognostic significance and could have clinical implications**
- **Quantitative molecular monitoring of MRD after allo-SCT seems promising**
- **New drugs can be highly effective against MM and molecular monitoring can play a role in assessing the disease response.**

# Autograft and Molecular Monitoring in FCL

## *Conclusions*

- the autograft experience has shown that disease eradication may be pursued in indolent lymphoma, specifically in FCL

- the notion of disease eradication is mainly supported by molecular monitoring results

- due to its high predictive value, a post-transplant PCR positive status needs careful clinical evaluation and possibly an early treatment

- however, for FL patients reverting to PCR-positivity following a prolonged period of molecular remission confirmatory direct-sequencing analysis is recommended

*Figure 2 B*

# DISEASE FREE SURVIVAL

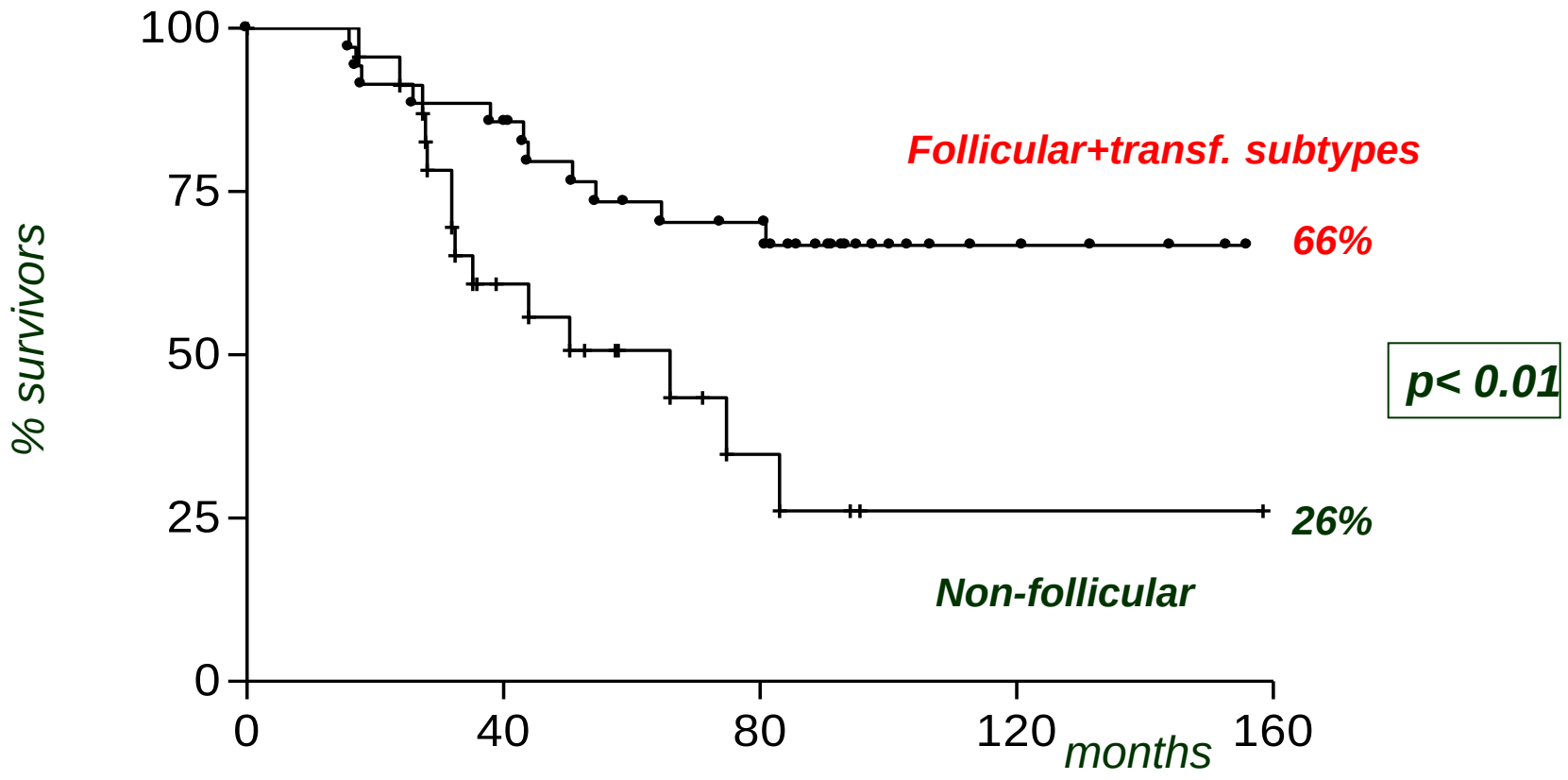
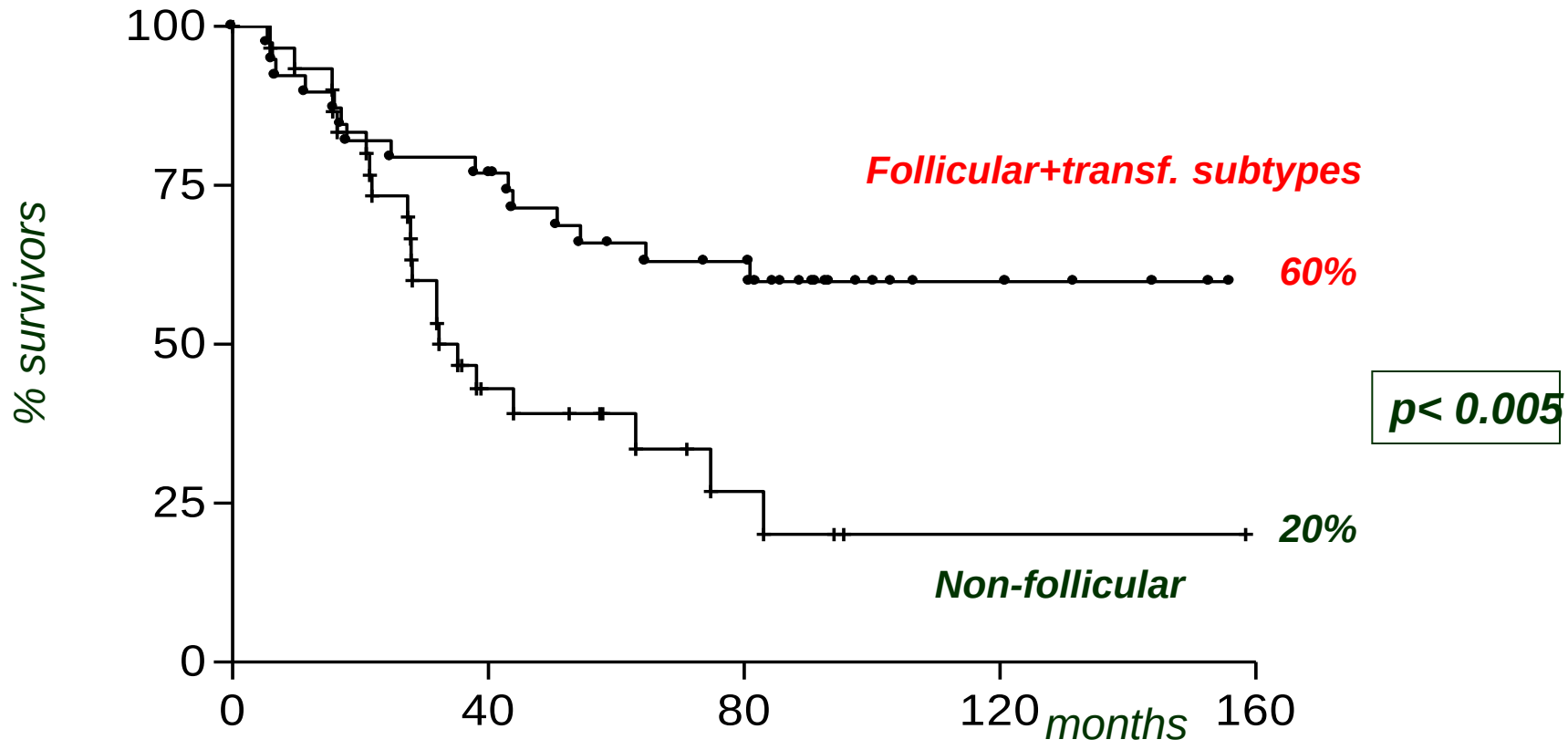
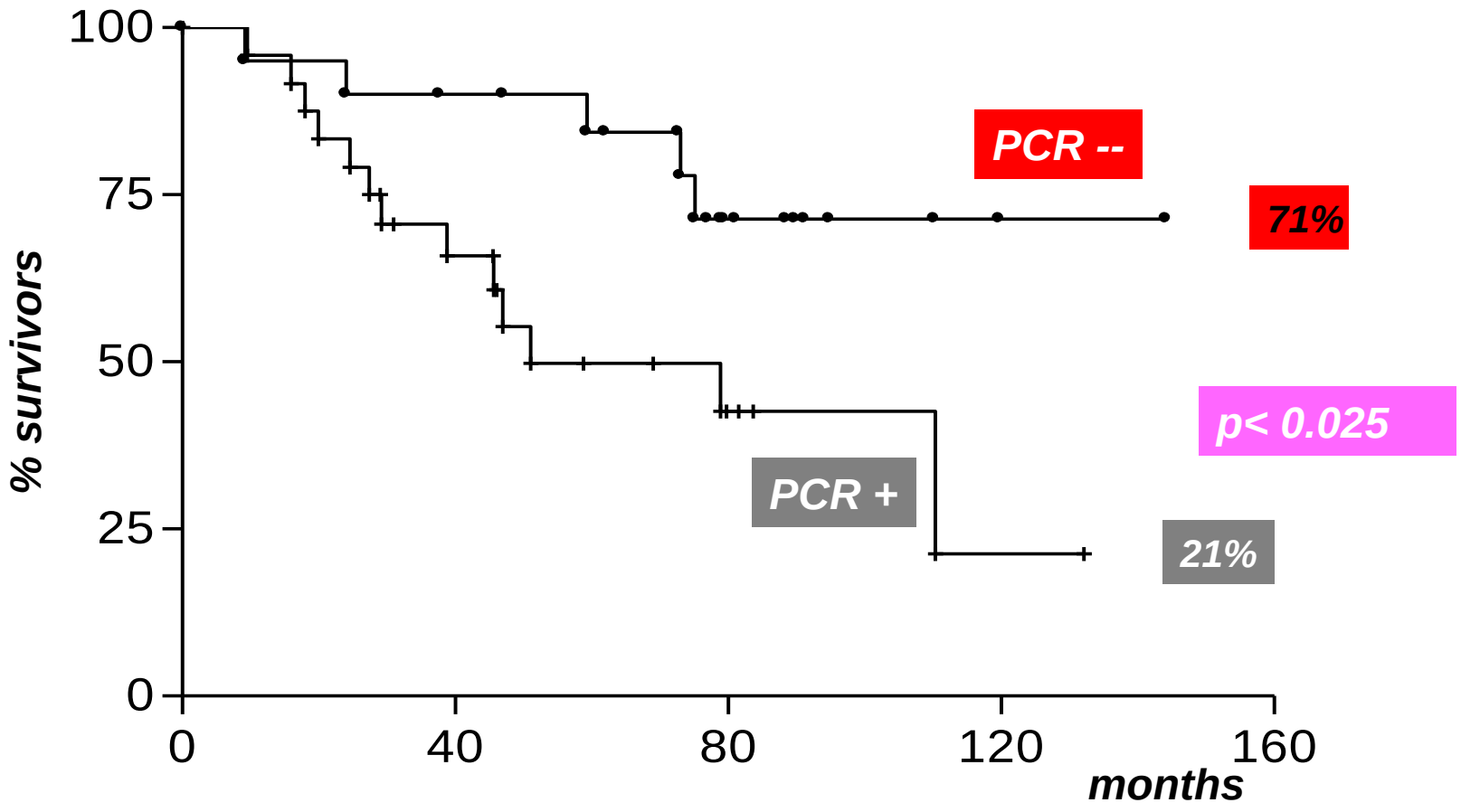


*Figure 2 C*

# PROGRESSION FREE SURVIVAL



# Disease free survival according to collection of one or more PCR-negative harvests



# Long-Term Follow-Up of Autologous Bone Marrow Transplantation in Patients With Relapsed Follicular Lymphoma

**By Freedman A et al.: Blood, 94: 3325-3333, 1999**


no more an exclusive job of the transplanter

**FFR after ABMT for 113 informative patients who were either PCR- or PCR+ after ex vivo purging**