

# Interim PET in Diffuse Large B Cell Lymphoma. The GEL/TAMO experience



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Chair of The GEL/TAMO Group*

*Menton ,9 april 2010*

# Disclosures for Dolores Caballero

|                           |                                     |
|---------------------------|-------------------------------------|
| Research Support/P.I.     | N/A                                 |
| Employee                  | N/A                                 |
| Consultant                | N/A                                 |
| Major Stockholder         | N/A                                 |
| Scientific Advisory Board | Janssen-Cilag, Mundipharma, Celgene |



# Interim PET analysis in patients with intermediate risk DLBCL treated with R-CHOP 14

# Inclusion criteria

- Patients  $\geq 65$  years with non localized disease
- Patients  $< 65$  with non localized disease ,IPI 0-2
- Diagnosed of DLBCL CD20+
- ECOG 0-2

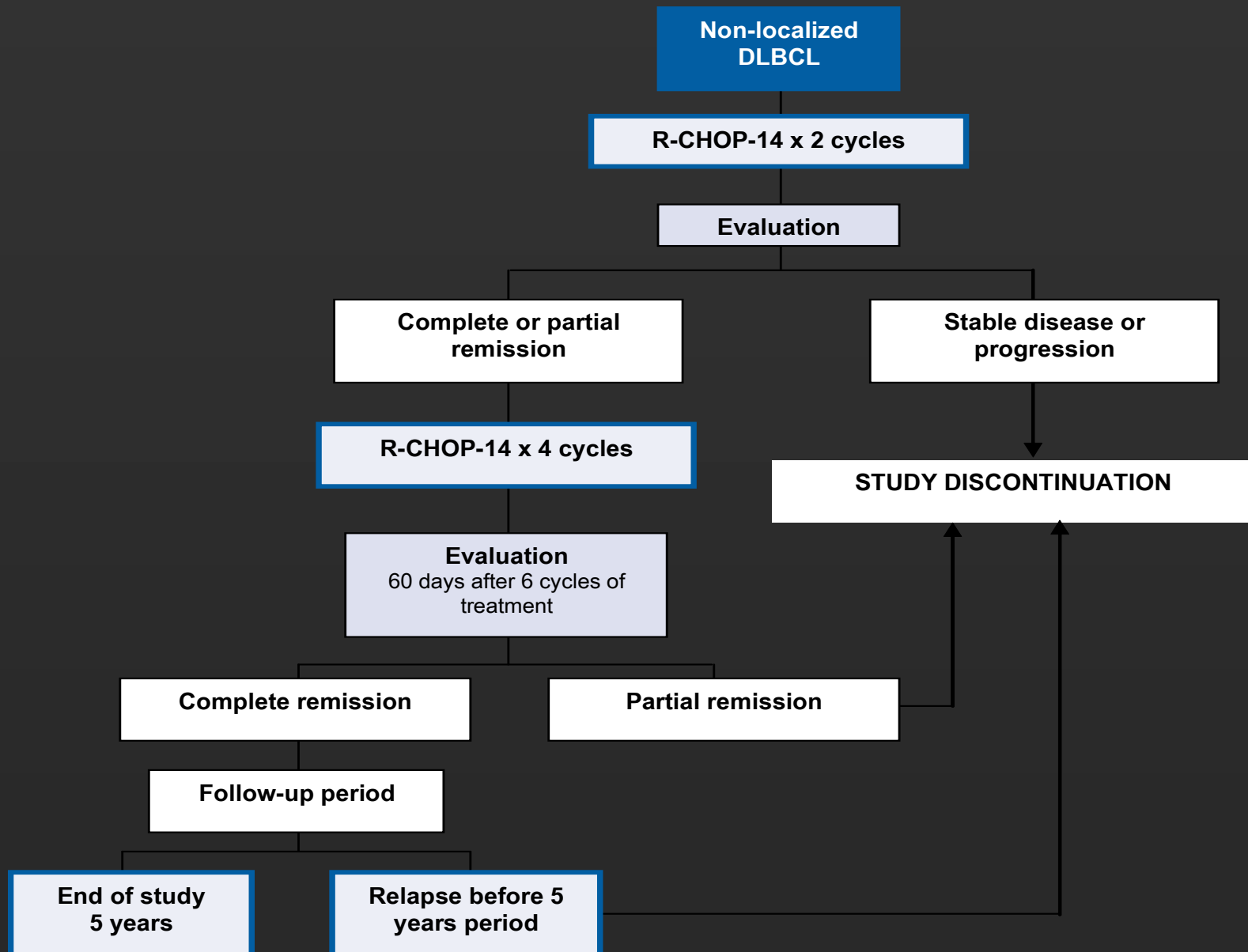
*Phase II multicenter prospective Trial*

# Objetive

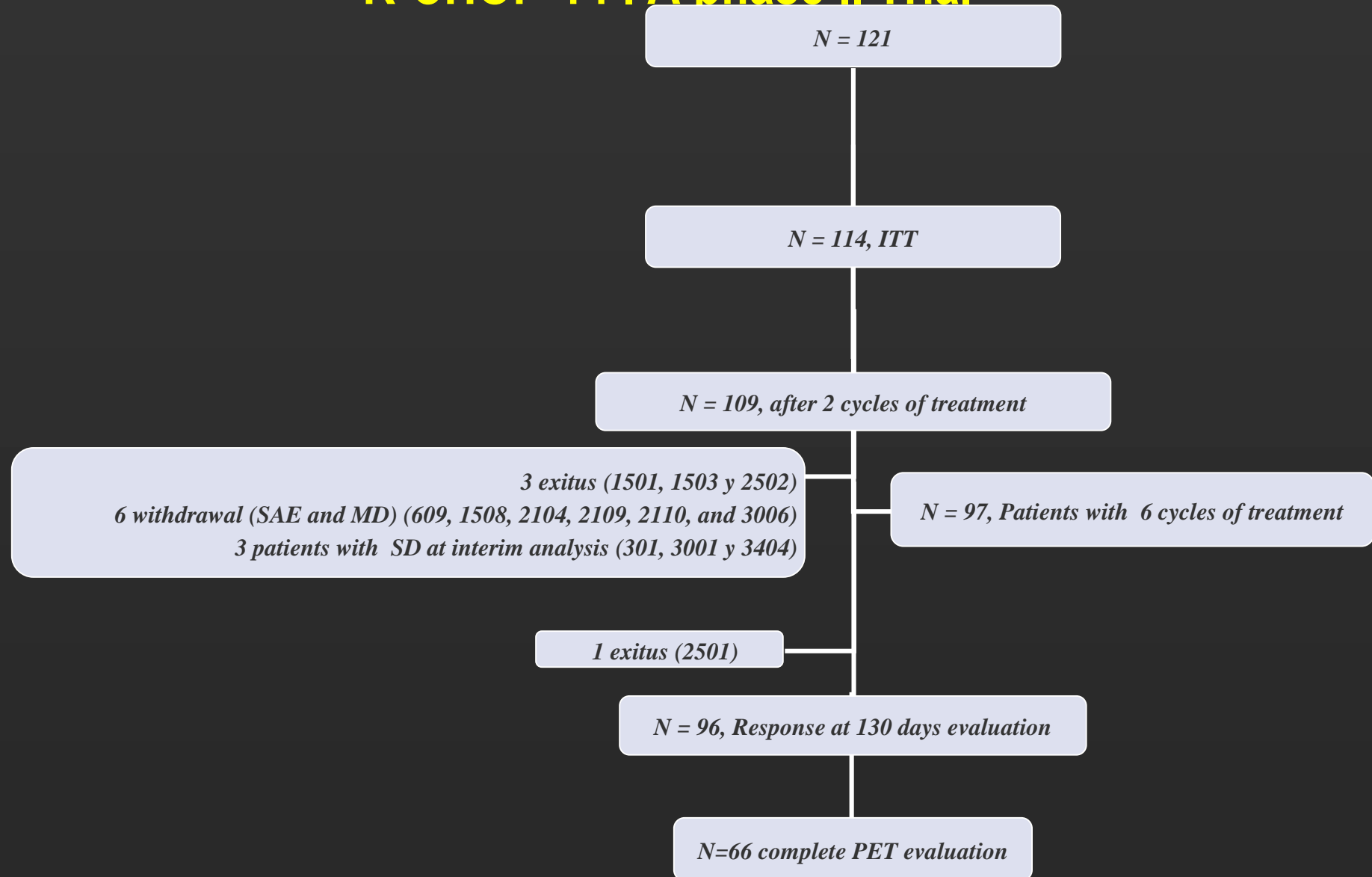
- Progression Free Survival
- Influence of an interim PET (after 2 R-CHOP 14 cycles) and PET at the end of treatment (6 R-CHOP) in Overall Survival and Progression Free Survival in patients with DLBCL.

*Phase II multicenter prospective Trial*

# Interim and End-of-Treatment 18F-FDG-PET in DLBCL after 6 R-CHOP-14 . A phase II Trial



# Interim and End-of-Treatment 18F-FDG-PET in DLBCL after 6 R-CHOP-14 . A phase II Trial





# Patients characteristics (n=66)

|                           |                   |
|---------------------------|-------------------|
| Median age                | <b>57 (18-79)</b> |
| >65 y                     | <b>47%</b>        |
| Gender M/F                | <b>53/47</b>      |
| Bulky mass (>10 cm)       | <b>23%</b>        |
| Ann Arbor Stage III,IV    | <b>64%</b>        |
| High LDH                  | <b>48%</b>        |
| High beta2 microglobuline | <b>35%</b>        |
| PS >1                     | <b>14%</b>        |
| IPI 0-2                   | <b>69%</b>        |
| IPI 3-5                   | <b>33 %</b>       |

*González-Barca E ASH 2009*



# Interim and End-of-Treatment <sup>18</sup>F-FDG-PET in DLBCL after 6 R-CHOP-14

**66 patients**

Interim PET (after 2 cycles of R-CHOP/14)

**PET+**  
**33 (50%)**

**PET-**  
**33 (50%)**

Final PET (at the end of treatment)

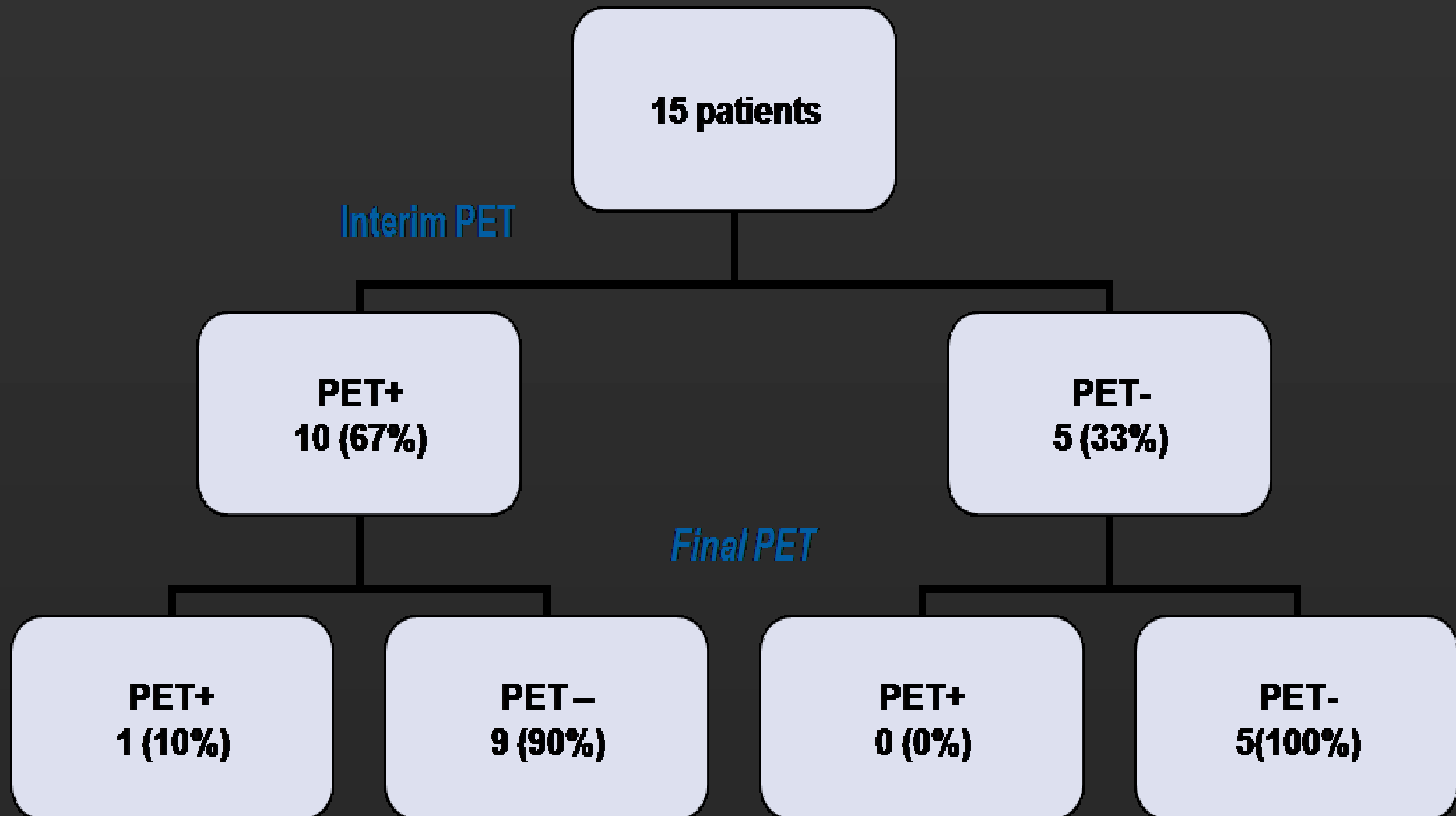
**PET+**  
**9 (27%)**

**PET-**  
**24 (73%)**

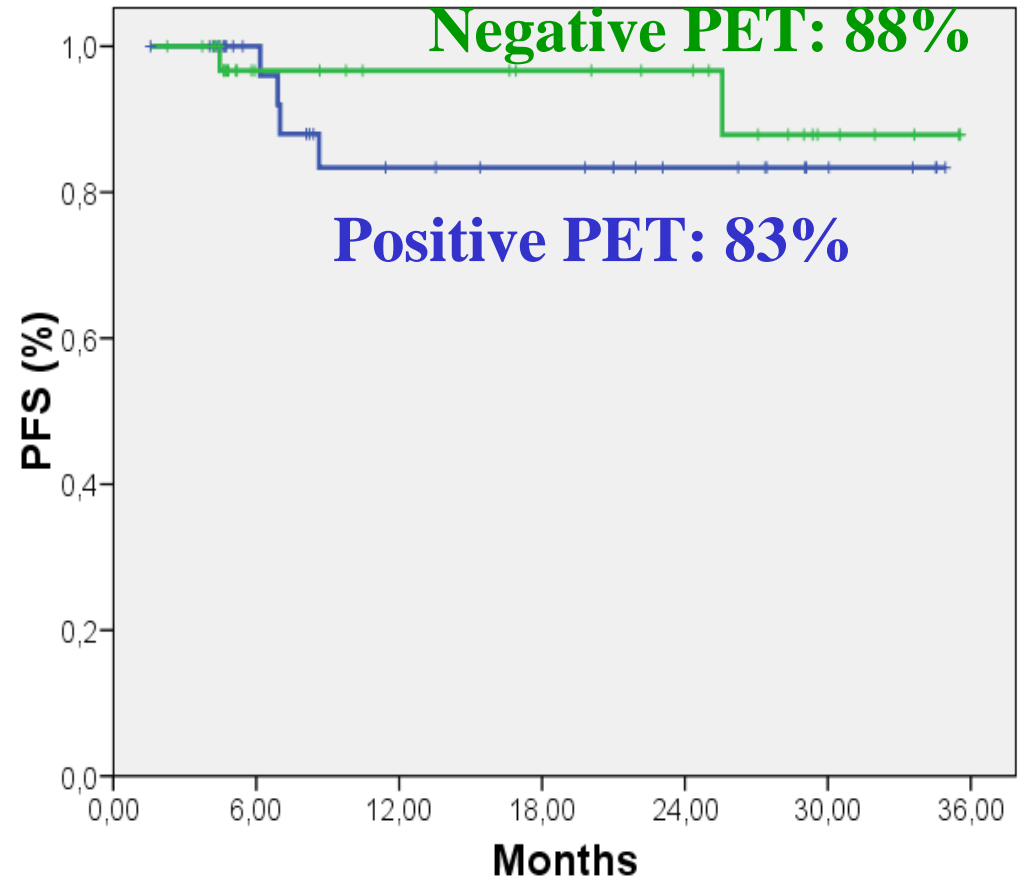
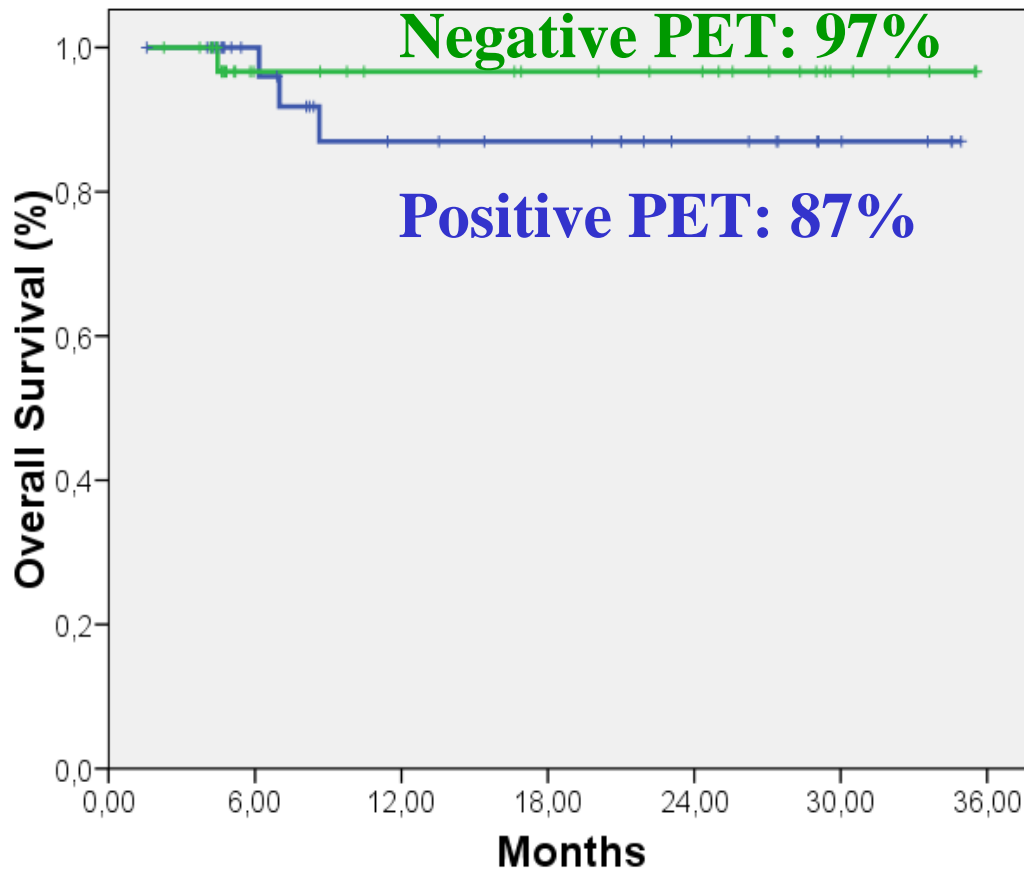
**PET+**  
**2 (6%)**

**PET-**  
**31 (94%)**

# Interim analysis with PET in patients with bulky disease



# Influence of early PET on Overall Survival and PFS



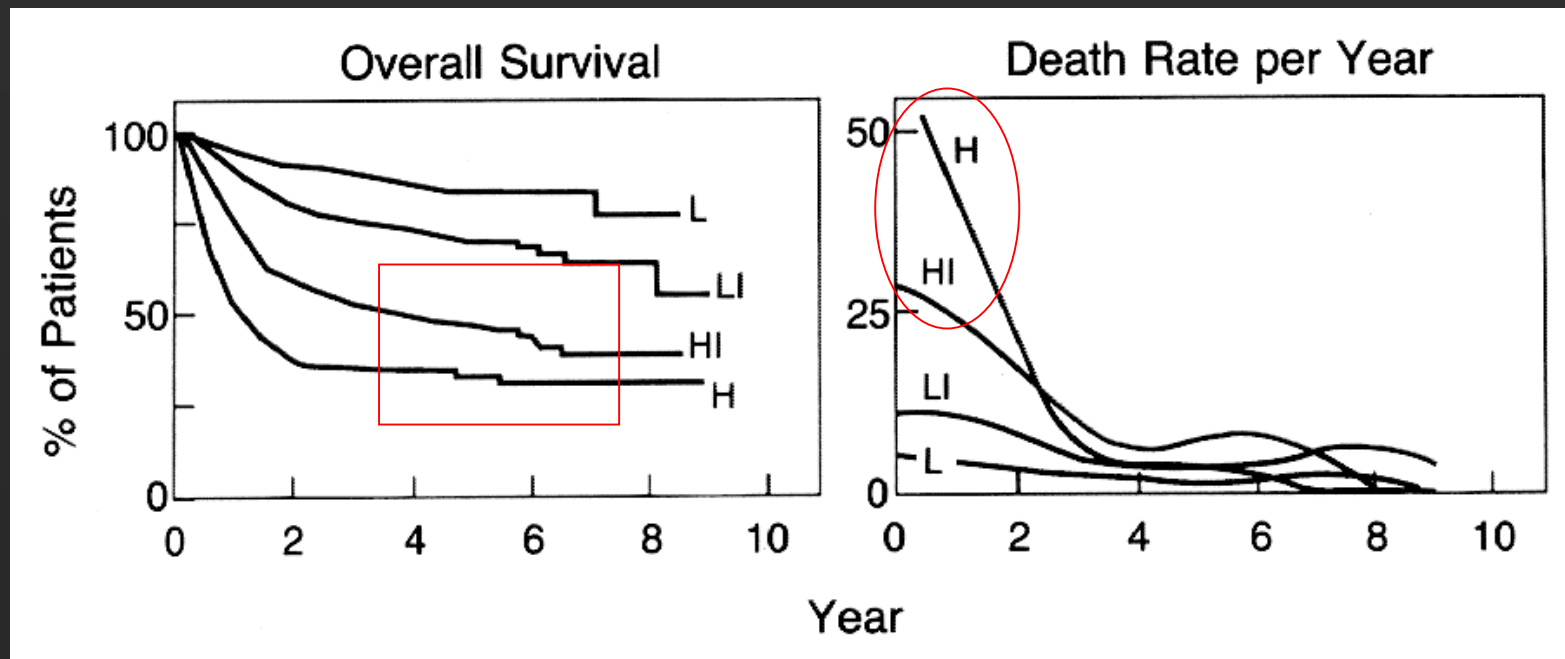
*Median follow up 10 mo (2-31)*



# Treatment stratification based on an early PET/CT evaluation in patients with high IPI DLBCL

# Complete Remission and Survival In Young Patients with IPI 2,3

| Risk     | Score | CR (%) | 5-year OS (%) |
|----------|-------|--------|---------------|
| High/Int | 2     | 57     | 46            |
| High     | 3     | 46     | 32            |





Registry at Dx

# MEGACHOP +-IFE

*DLBCL, IPI 2,3 or IPI 1 and high beta2m,*

Mega-CHOP x 3

Evaluation

CR, CRu, PR  
CT neg or pos  
*GA<sup>67</sup> Scan neg*

PR, SD, PD  
CT pos  
*GA<sup>67</sup> Scan pos*

Stem cell collection

Mega-CHOP x 1

IFE x 2 ± Rituximab

CT Evaluation

ASCT  
(BEAM regimen)

CR, Cru, PR

Less than PR

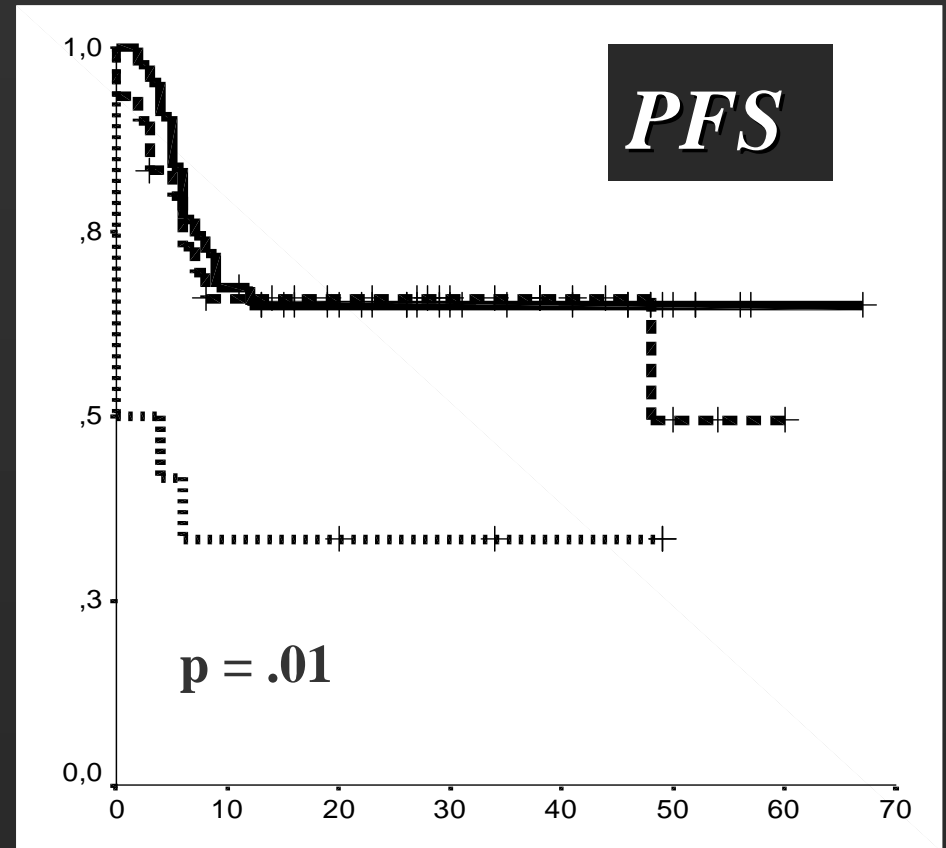
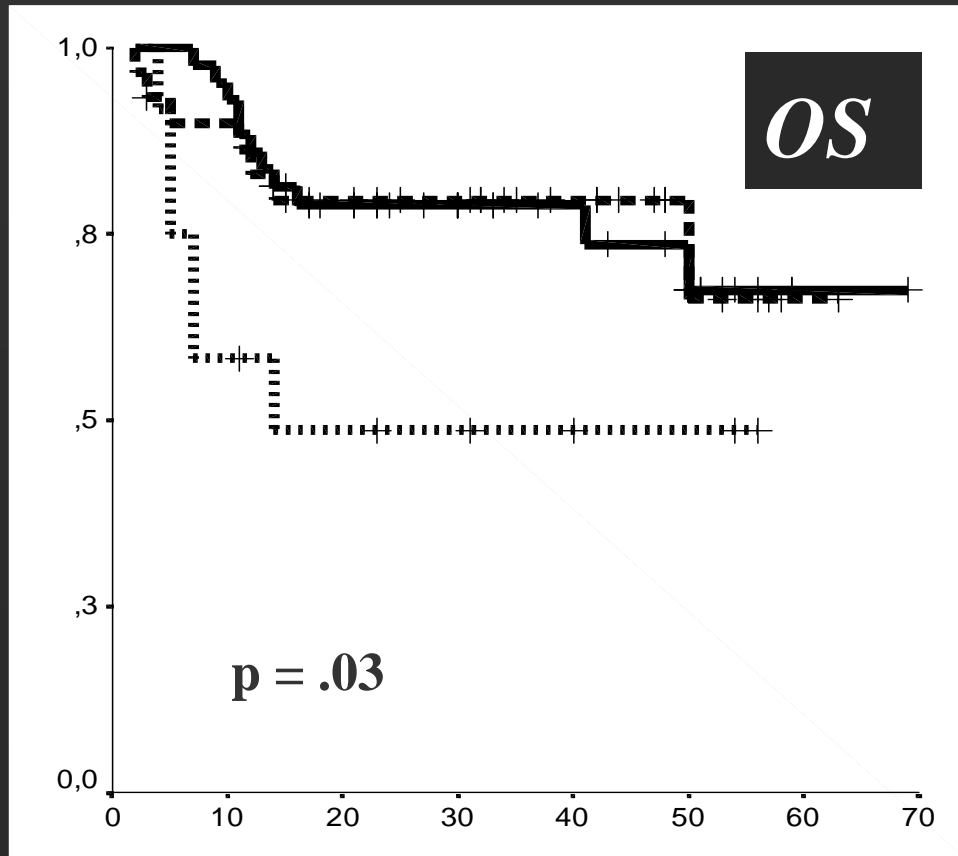
Out off



# Patients characteristics (n=86)

|                                  |                   |
|----------------------------------|-------------------|
| Median age                       | <b>53 (18-68)</b> |
| Gender M/F                       | <b>48/38</b>      |
| B Symptoms                       | <b>51 (58%)</b>   |
| Bulky mass (>10 cm)              | <b>36 (42%)</b>   |
| Ann Arbor Stage III,IV           | <b>76 (88%)</b>   |
| <b>Infiltrated bone marrow</b>   | <b>24 (29%)</b>   |
| High LDH                         | <b>70 (82%)</b>   |
| <b>High beta2 microglobuline</b> | <b>40 (51%)</b>   |
| PS >1                            | <b>40 (48%)</b>   |
| <b>aIPI 2,3</b>                  | <b>68 (79%)</b>   |

# OS and PFS according to gallium 67 scan response after 3 MEGACHOP +/- IFE salvage



Continuous line: CR/ PR with negative Ga<sup>67</sup>S treated with MegaCHOP followed by BEAM/ ASCT.  
Dashed line : PR positive Ga<sup>67</sup>S treated with MegaCHOP + IFE followed by BEAM/ ASCT.

Arranz, EHJ2008 Dotted line : TF after MegaCHOP+ IFE.



# Influence of the rituximab induction in survival according the IPI

% of patients

OS at 5 y

**IPI**

**RIPI**

|       |    |    |
|-------|----|----|
| 0,1   | 35 | 72 |
| 2     | 27 | 50 |
| 3     | 22 | 43 |
| 4,5   | 16 | 26 |
| 0     | 10 | 92 |
| 1,2   | 45 | 82 |
| 3,4,5 | 45 | 58 |



PET/CT positive

R-Mega-CHOP x 3

Evaluation (PET/CT)

**R-MEGACHOP +/- R-IFE +/-  
ASCT in patients with DLBCL IPI  
2,3 or IPI 1 and high beta2m  
Phase 2 Trial**

CR  
*PET neg*

PR, SD, PD  
*PET pos*

R-Mega-CHOP x 3

R-IFE x 2

PET Evaluation

Follow up

Less than PR

CR  
*PET neg*  
PR  
*PET pos*

Out off

Stem cell  
colection

ASCT  
(BEAM regimen)

# Objetives

□ To evaluate Event free survival in:

- Patients PET/CT positive after 3 R-MEGACHOP receiving R-IFE + ASCT and in
- Patients PET/CT negative after R-MEGACHOP receiving other 3 R-MEGACHOP courses



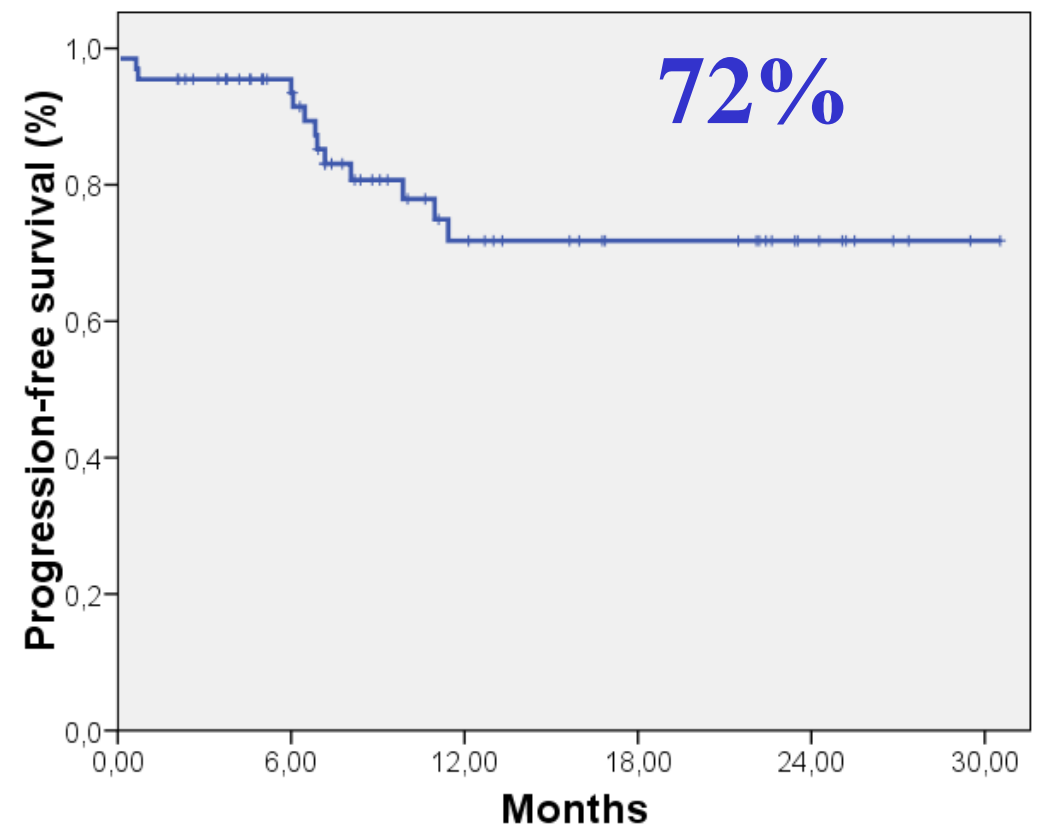
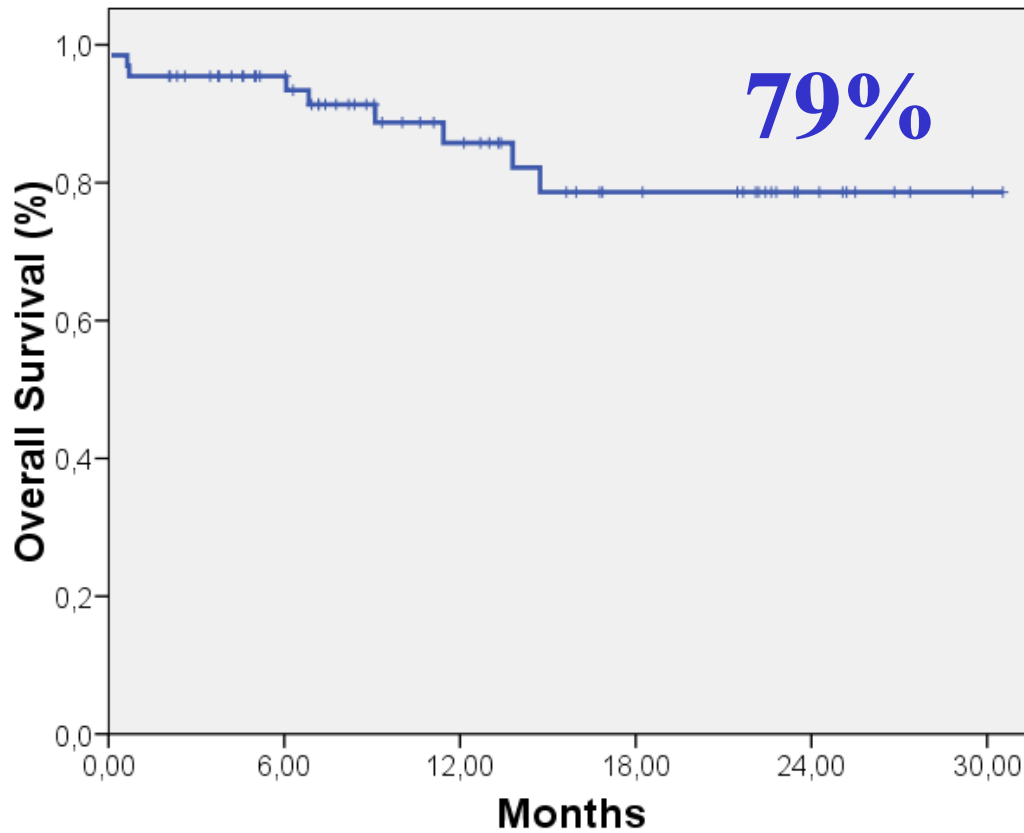
## Patient's characteristics (n=71)

|              |                   |
|--------------|-------------------|
| Median age   | <b>55 (25-69)</b> |
| Gender M/F   | <b>58/42 %</b>    |
| High LDH     | <b>70 (82%)</b>   |
| High beta2 m | <b>(51%)</b>      |
| aIPI 2,3     | <b>(83%)</b>      |

# Preliminary results

| Response                | After 3 R-<br>MEGACHOP | After 2 R –IFE+/-<br>ASCT | Last follow up |
|-------------------------|------------------------|---------------------------|----------------|
| CR<br>PET/CTneg         | 36 (51%)               | 12 (17%)                  | 44 (66 %)      |
| PR<br>PET/CTpos         | 27 (38%)               | 9 (13%)                   | 6 (8%)         |
| PGR PET<br>pos<br>or NR | 2 (3%)                 | 2 ( 3%)                   | 6 (8%)         |
| Non EV                  | 5 (8%)                 | 4 ( 6%)                   | 3 (4%)         |
| Toxic death             | 1 (1,5%)               |                           | 7 (9,9%)       |
| Total                   | 71                     | 26                        | 66             |

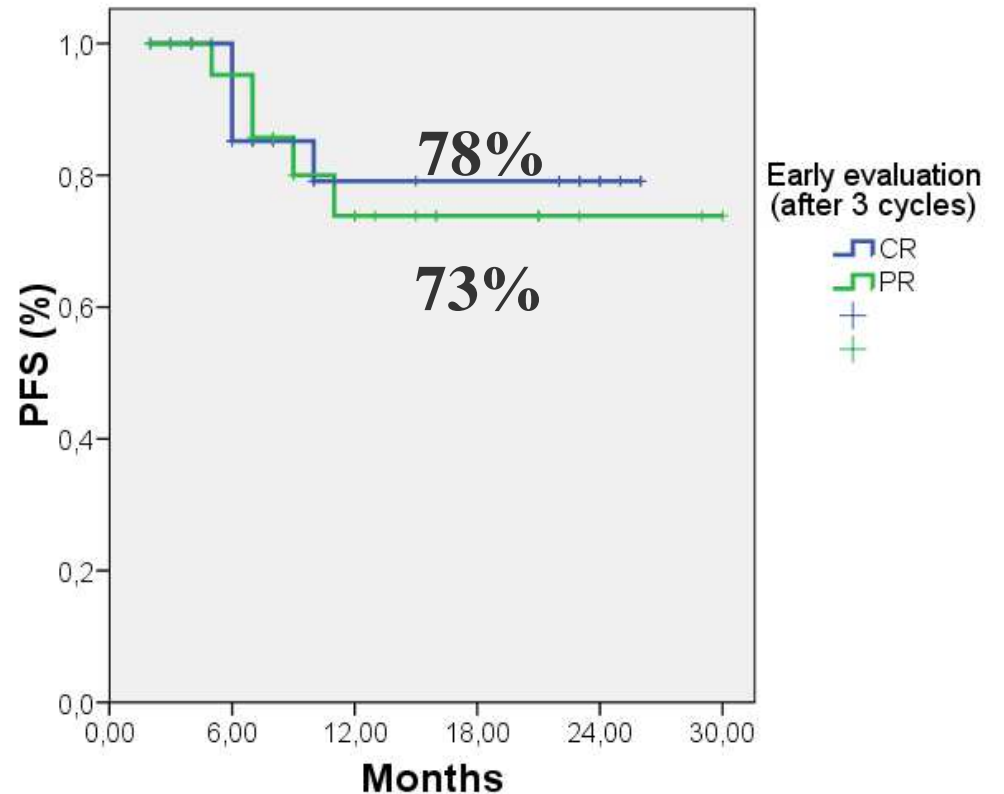
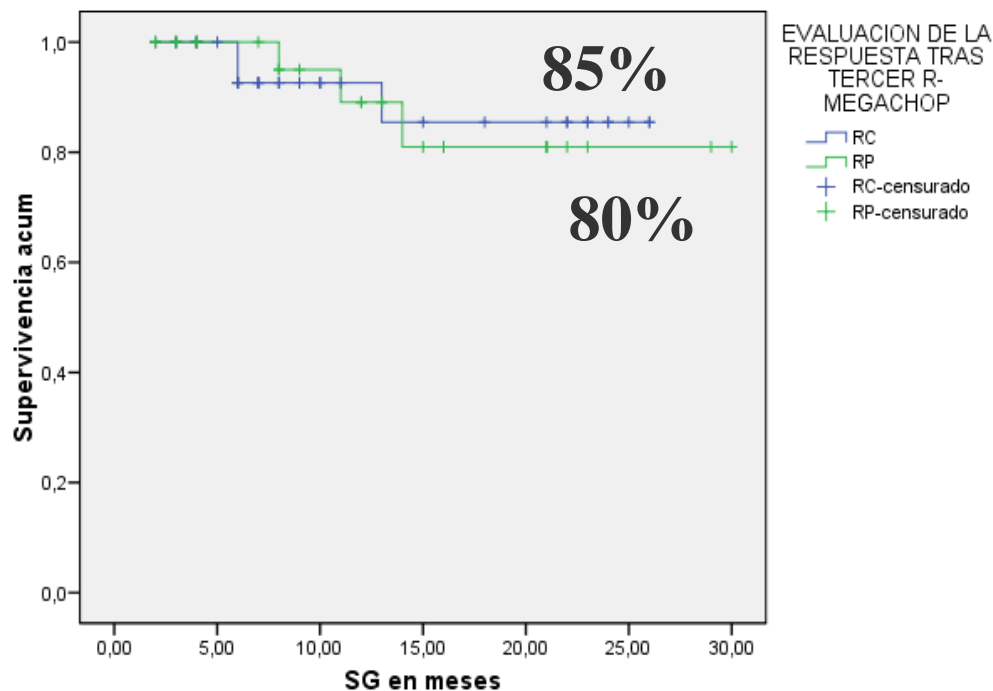
# Overall Survival and PFS



*Median follow up 10.6 mo (2-30)*

# PFS and OS according to early response to PET/CT after 3 R-MEGACHOP

Funciones de supervivencia



# Comments and future

- ◆ Centralised retrospective PET review in these two studies
- ◆ **First final analysis (may 2011)**
- ◆ The role of PET/CT in our next trials ??
- ◆ Prospective centralised review in future trials







# R-ESHAP as salvage therapy previous to ASCT. Influence of rituximab and of PET evaluation

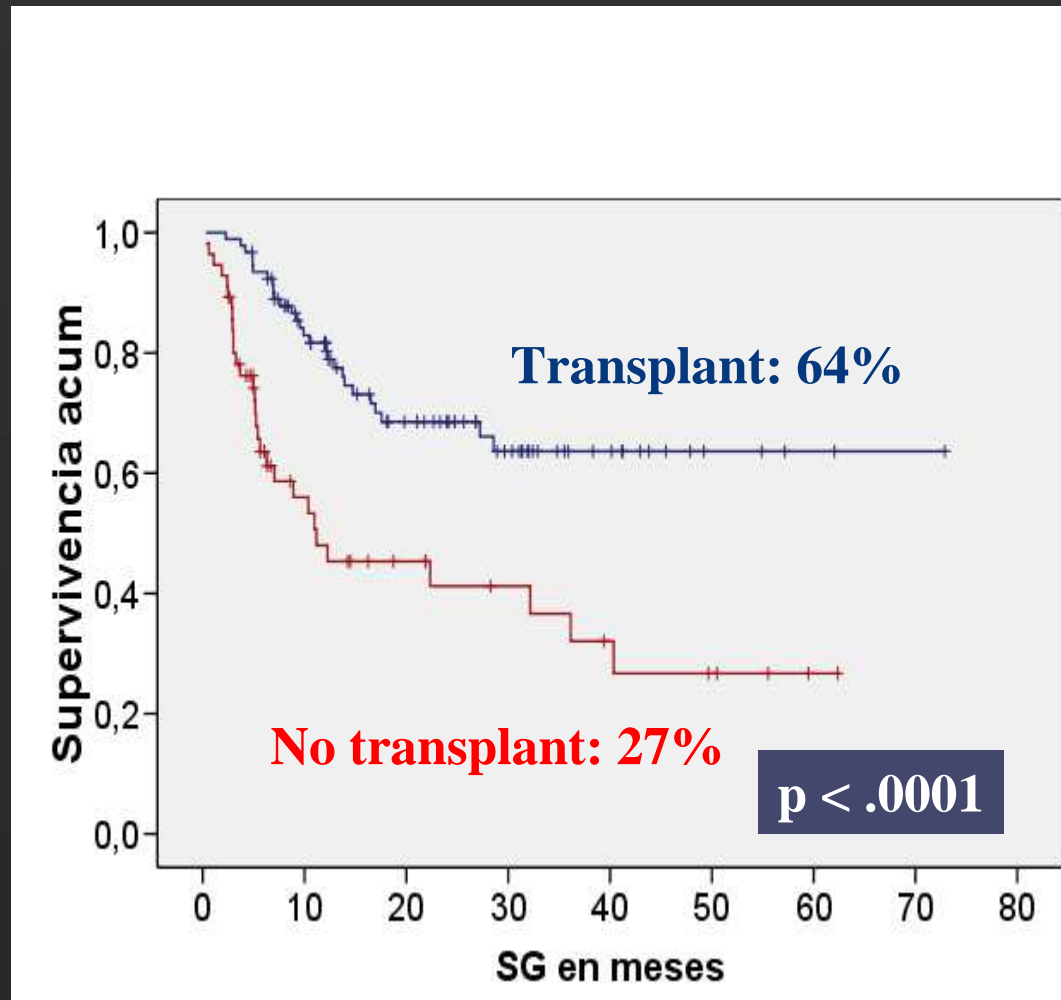
# R-ESHAP as salvage regimen in 151 patients with DLBCL



| at R-ESHAP                                                            | number (%)          |
|-----------------------------------------------------------------------|---------------------|
| age (median)                                                          | 54 (range: 19 – 70) |
| Sex: male                                                             | 86 (58)             |
| III-IV stage                                                          | 95 (63)             |
| Extranodal disease                                                    | 74 (49)             |
| bulky (>10 cm)                                                        | 41 (27)             |
| <b>IPI</b>                                                            |                     |
| 0-1 (low risk)                                                        | 66 (46)             |
| <b>2-3 (intermediate)</b>                                             | <b>67 (47)</b>      |
| <b>4-5 (high risk)</b>                                                | <b>9 (6%)</b>       |
| <b>Disease status</b>                                                 |                     |
| <b>primary refractory disease</b><br>(less than CR after 1st regimen) | <b>35 (41)</b>      |
| 1st relapse                                                           | 83 (55)             |
| >1st relapse                                                          | 2 (1)               |

*94 patients received an ASCT*

# R-ESHAP in DLBCL. Impact of ASCT in Overall survival





# Influence of Rituximab induction in the transplant outcome

## Rituximab before R-ESHAP

