Second International workshop

on Interim-PET in Lymphoma

April 8th-9th Menton (France)

Current Studies with Interim-PET Non-Hodgkin Lymphoma

The Intergruppo Italiano Linfomi study

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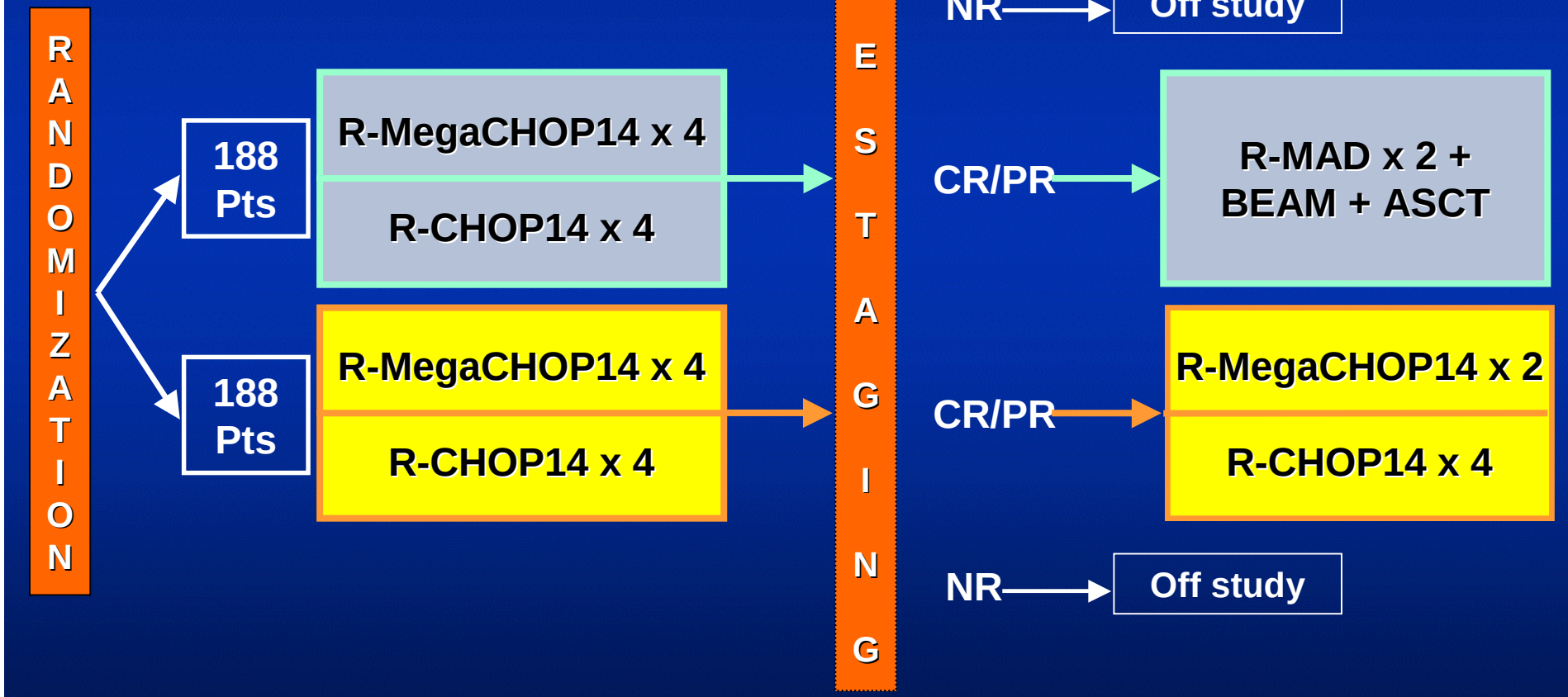
Phase III randomized, multicenter study in high-risk (IPI2-3) DLBCL young patients. Dose-dense chemotherapy + Rituximab +/- intensified and high dose chemoimmunotherapy with ASCT. Study ID: IIL-DLCL04.

INCLUSION CRITERIA

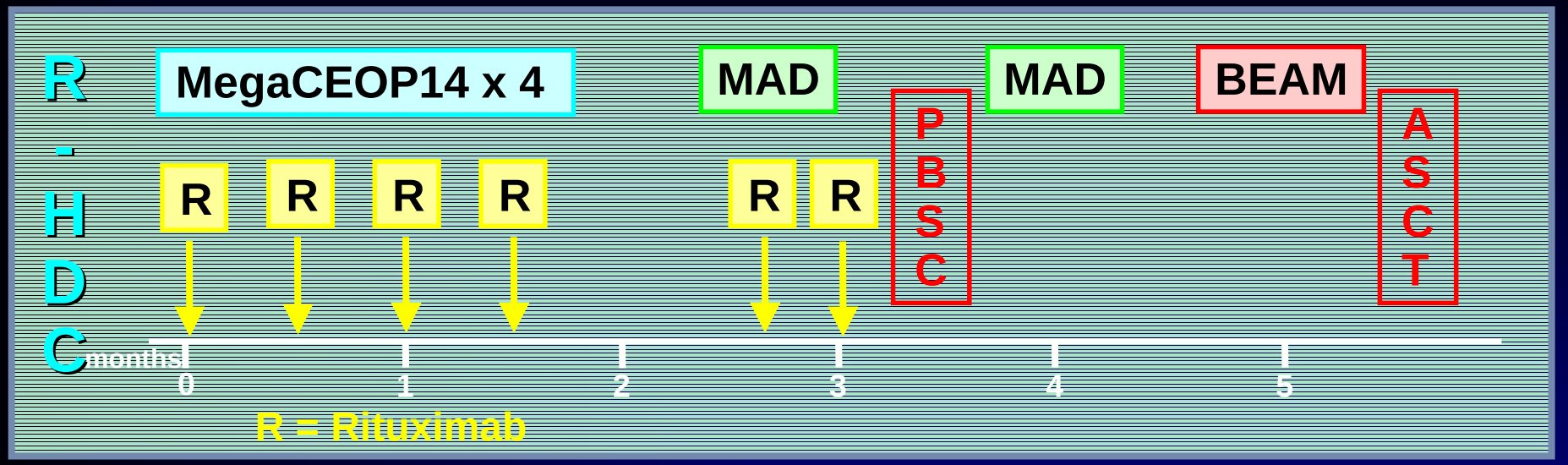
- Diffuse Large B-Cell Lymphoma CD20+ or Follicular grade IIIb
- Age 18-60
- Advanced stage II, stage III and stage IV with at least 2aa-IPI risk factors
- Age-adjusted IPI 2 or 3 Intermediate-High or High Risk
- No concomitant cardiac, liver, lung or renal disease
- HIV negativity, HCV negativity or without active replication, HBsAg –
- Centralized pathological review

Phase III randomized, multicenter study in high-risk (IPI2-3) DLBCL young patients. Dose-dense chemotherapy + Rituximab +/- intensified and high dose chemoimmunotherapy with ASCT. Study ID: IIL-DLCL04.



*Patients at risk of CNS recurrence (SIE guidelines 2006): IT Mtx 4 or 6 doses

R-Dose Dense + HDC supplemented with Rituximab + ASCT



Induction chemotherapy

Months 1 and 2

Intensified chemotherapy MAD (HD-ARAC + Mitoxantrone x 3 days)
Months 3 and 4

High dose chemotherapy BEAM + ASCT
Month 5

R-MEGACEOP14

R 375 mg/m^2 d 1
Epi 110 mg/m^2 d 3
Ctx 1200 mg/m^2 d 3
Vcr 1.4 mg/m^2 d 3
Pdn 40 mg/m^2 dd 1→ 5
G-CSF 5 mcg/kg dd 5→ 12

R-MAD

Mito 8 mg/m^2 dd 1→ 3
ARA-C 2 g/m^2/12h dd 1→ 3
Dex 4 mg/m^2/12h dd 1→ 3
R 375 mg/m^2 d 4 and d -1PBSC
G-CSF 5 µg/Kg d 4→

+/- RT-IF to bulky disease or residual mass

Vitolo U, et al. Haematologica 2009; 94: 1250-58

R-HDC: June 2002 – December 2005 94 patients

Assessed for eligibility: 97

Excluded: 3

central pathology review: 2 follicular g3a, 1 mantle cell blastoid variant

Assessed for R-HDC: 94

Received R-MegaCEOP x 4: 94

Discontinuing: 6

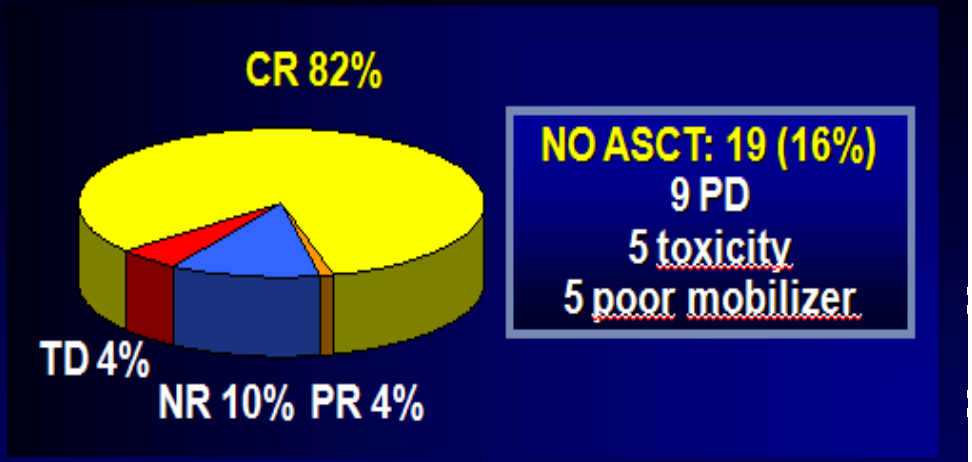
4 disease progression, 2 toxicity

Received R-MAD x 2: 88

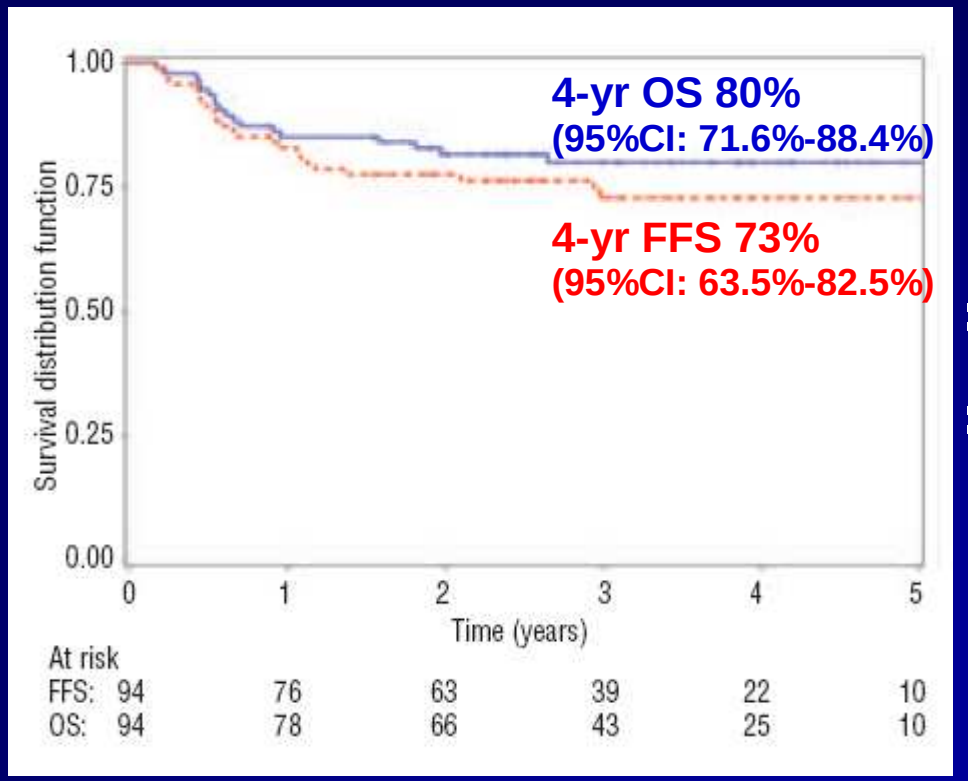
Discontinuing: 12

5 disease progression, 3 toxicity, 4 inadequate stem cell collection

Received BEAM + ASCT: 76



NO ASCT: 19 (16%)
9 PD
5 toxicity
5 poor mobilizer



4-yr OS 80%
(95%CI: 71.6%-88.4%)

4-yr FFS 73%
(95%CI: 63.5%-82.5%)

OBJECTIVE

Primary:

- To detect an increase of 15% in the probability of FFS at 2 years in favour of R-CHOP/R-MegaCHOP+ASCT arm compared with R-CHOP/R-MegaCHOP

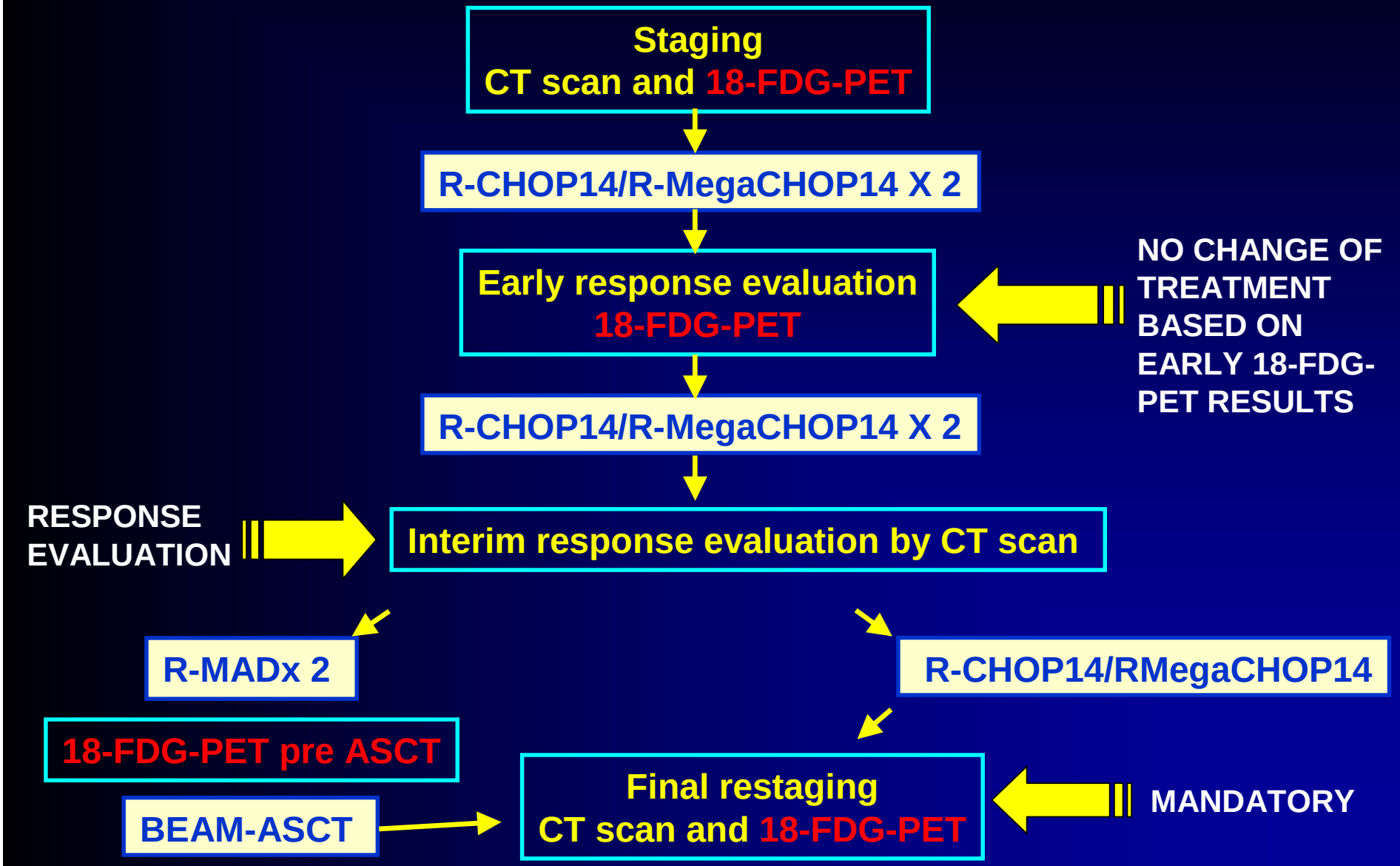
Secondary:

- To evaluate OS of R-CHOP/R-MegaCHOP + ASCT
- To evaluate 2-yr FFS of R-CHOP compared with R-MegaCHOP
- To evaluate 2-yr FFS of four randomized arms (exploratory analysis)

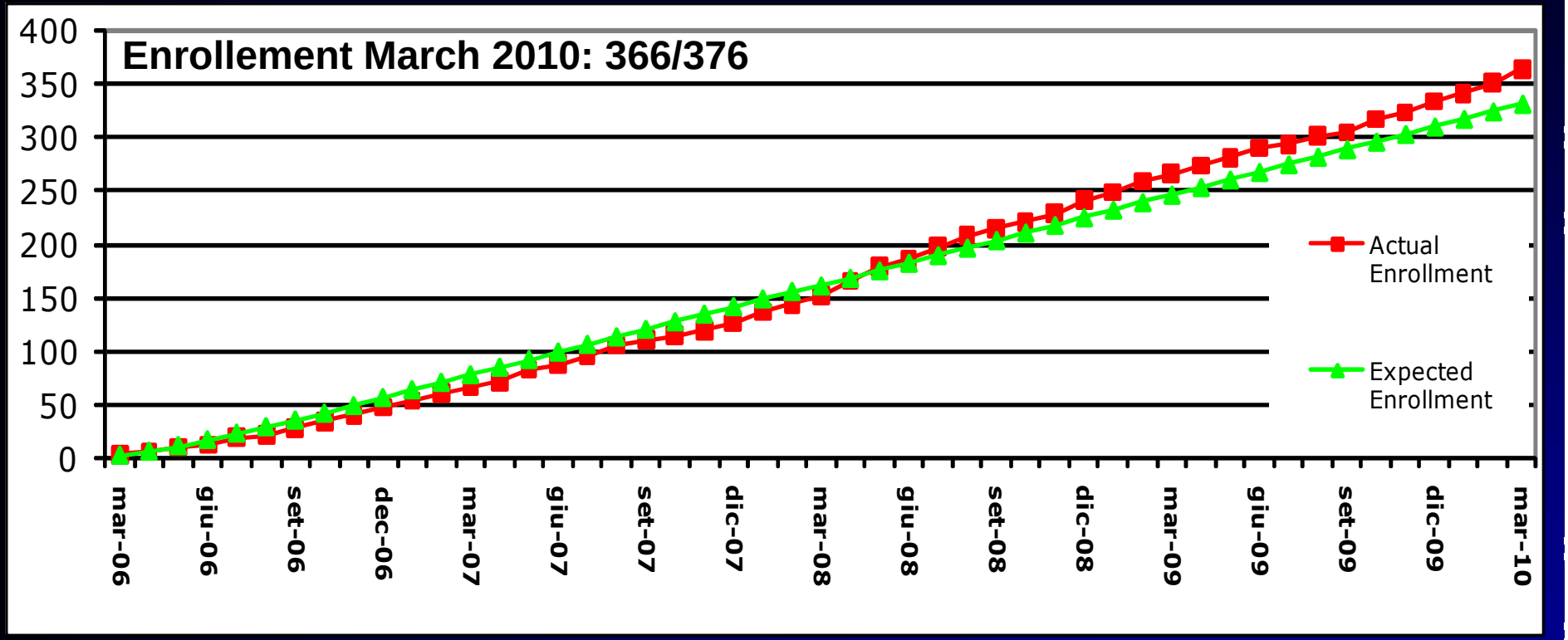
STATISTICAL METHODS

- Multifactorial 2 x 2 study, four arms randomized, open label, multicenter, phase III study
- With a two-sided α error of 0.05 and a β error of 0.20 and assuming a 50% 2-year FFS in the R-CHOP/R-MegaCHOP arm versus an expected 65% in the ASCT arm, this design required the randomization of 170 patients per arm (ASCT vs no ASCT).
- Planned sample size including drop out: 376 patients (94 in each arm)
- Time of recruitment: 4 years in 50 Italian Centres

Optional ancillary trial interim PET in IIL-DLCL04



A randomized phase III study in young patients with untreated high risk (aaIPI 2-3) Diffuse Large B-Cell Lymphoma. Study ID: IIL-DLCL04.



Enrollement in the ancillary trial interim and final PET: 142

PRELIMINARY CONCLUSION

- Dose dense chemoimmunotherapy ± HDC and ASCT is feasible and safe in a large multicenter cooperative study
- The overall results of the interim analysis show a high CR rate and a good 2-year PFS in high-risk DLBCL young patients
- The study will give new insights on the role of Rituximab-high-dose chemotherapy and ASCT compared to standard dose dense chemoimmunotherapy (R-CHOP14/R-MegaCHOP14)
- The ancillary interim-PET study is a prospective study with no change of therapy based on PET results and the results will be helpful to clarify the role of interim PET in DLBCL treated with dose-dense chemoimmunotherapy