FIL ongoing programs with decisional PET

Massimo Federico

Decisional PET in which Pts?

Hodgkin Lymphoma	Non-Hodgkin Lymphoma, Aggressive	Non-Hodgkin Lymphoma, Indolent, Follicular	Non-Hodgkin Lymphoma, Indolent, non Follicular
HD0801 *(interim PET)*	DLCL10 *(after CHT)*	FOLL12 *(after CHT)*	**none**
HD0802 *(after salvage CHT)*	IELSG37 *(after CHT)*		

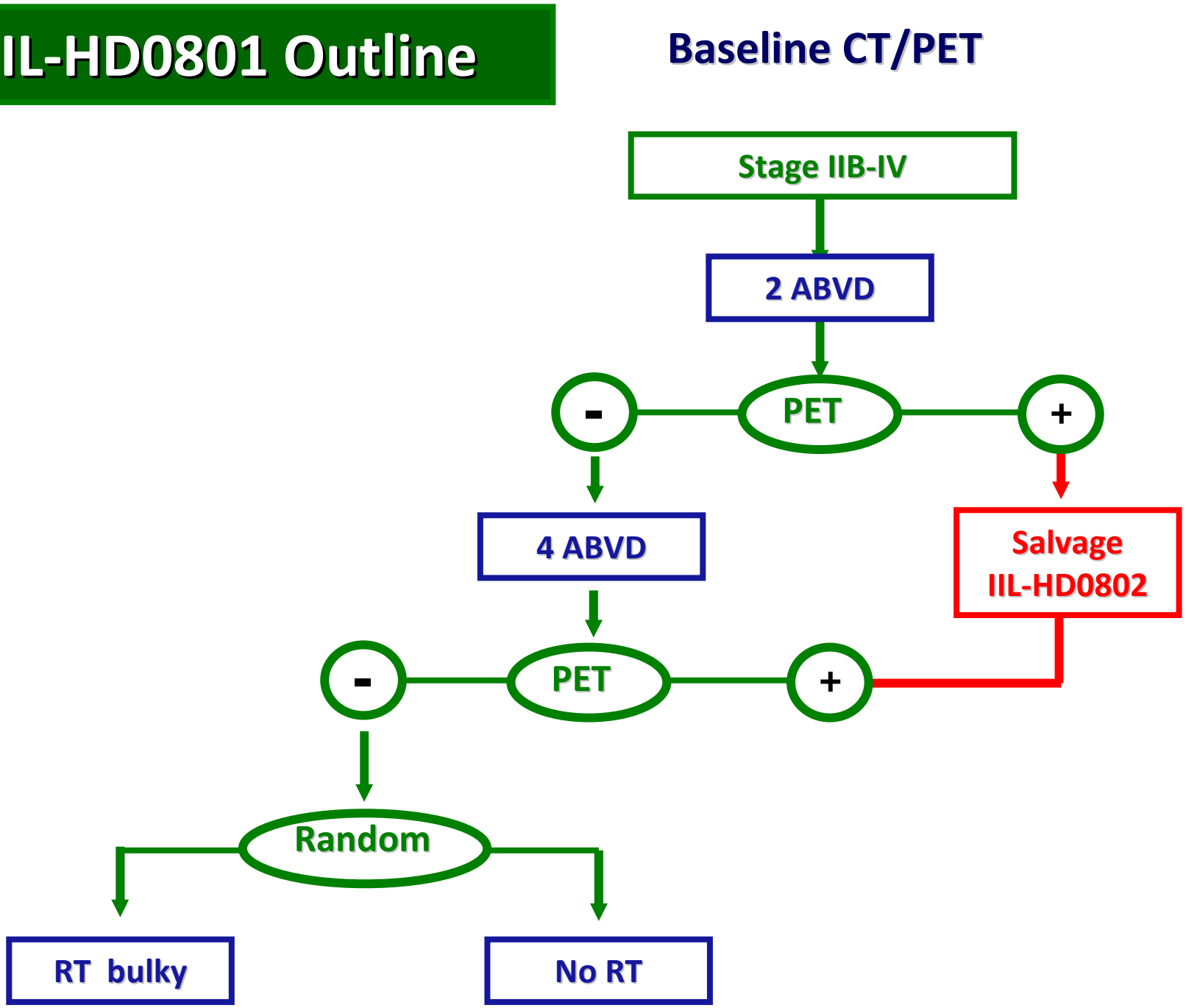
HD0801

Early salvage with high dose chemotherapy and stem cell transplantation in advanced stage Hodgkin's lymphoma patients with positive positron emission tomography after two courses of ABVD (PET-2 positive) and comparison of radiotherapy versus no radiotherapy in PET-2 negative patients

OBJECTIVES

- To evaluate if patients with PET-positivity after the first two courses of ABVD (PET-2 positive), can be salvaged by early shift to high-dose chemotherapy supported by stem cell rescue.
- To assess if patients achieving early complete response (PET-2 negative), can be spared radiotherapy on areas of initial bulky disease, at the end of the planned six courses of ABVD.

IIL-HD0801 Outline



Inclusion criteria

- Histologically confirmed Hodgkin's lymphoma of the classical type (nodular lymphocyte predominance excluded)
- Stage IIB-IV.
- Age 18-70.
- No prior therapy for Hodgkin's lymphoma
- Written informed consent.
- ECOG performance status grades 0-3
- Baseline FDG-PET scan.

HD0801 sample size and activation status

Accrual 4 years

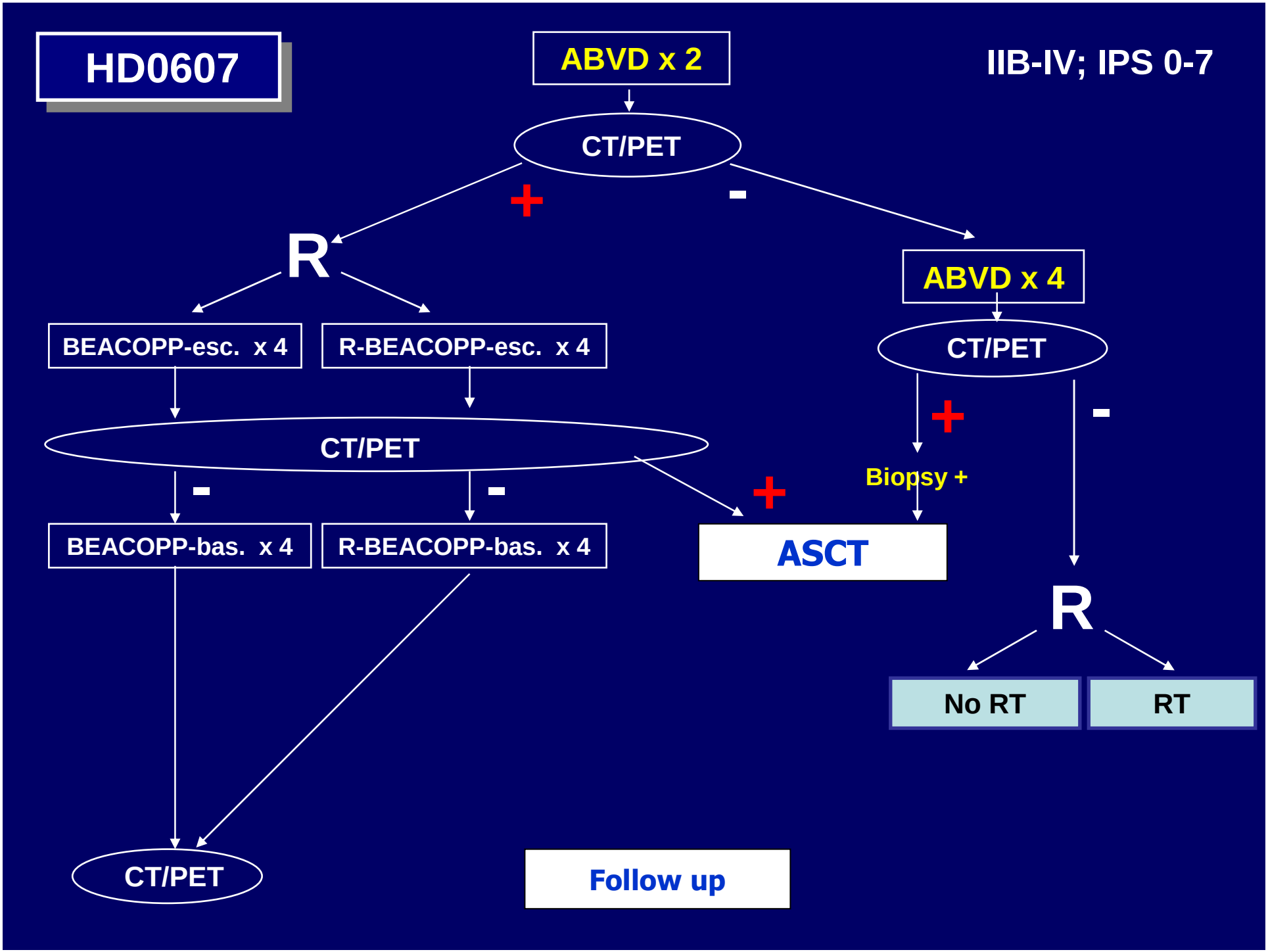
Follow-up 1-2 years from the last accrued

Sample Size **300**

31 participating sites

27 active sites

Actual Accrual 400 patients at the end of June of 2012


HD0607
ABVD x 2
IIB-IV; IPS 0-7
CT/PET
+
-
R
ABVD x 4
BEACOPP-esc. x 4
R-BEACOPP-esc. x 4
CT/PET
CT/PET
+
-
Biopsy +
-
-
+
BEACOPP-bas. x 4
R-BEACOPP-bas. x 4
ASCT
R
No RT
RT
CT/PET
Follow up

HD0607

End Points

Start date: **Mar'08**
Accrual: **372 pts**
on 25/09/2011

Primary end-point:
- **3-yr FFS**

- ***Secondary end-points:***
- **Program feasibility**
- **Early and late toxicity**
- **Superiority of R-BEACOPP vs. BEACOPP in PET2 + pts (3-y PFS)**

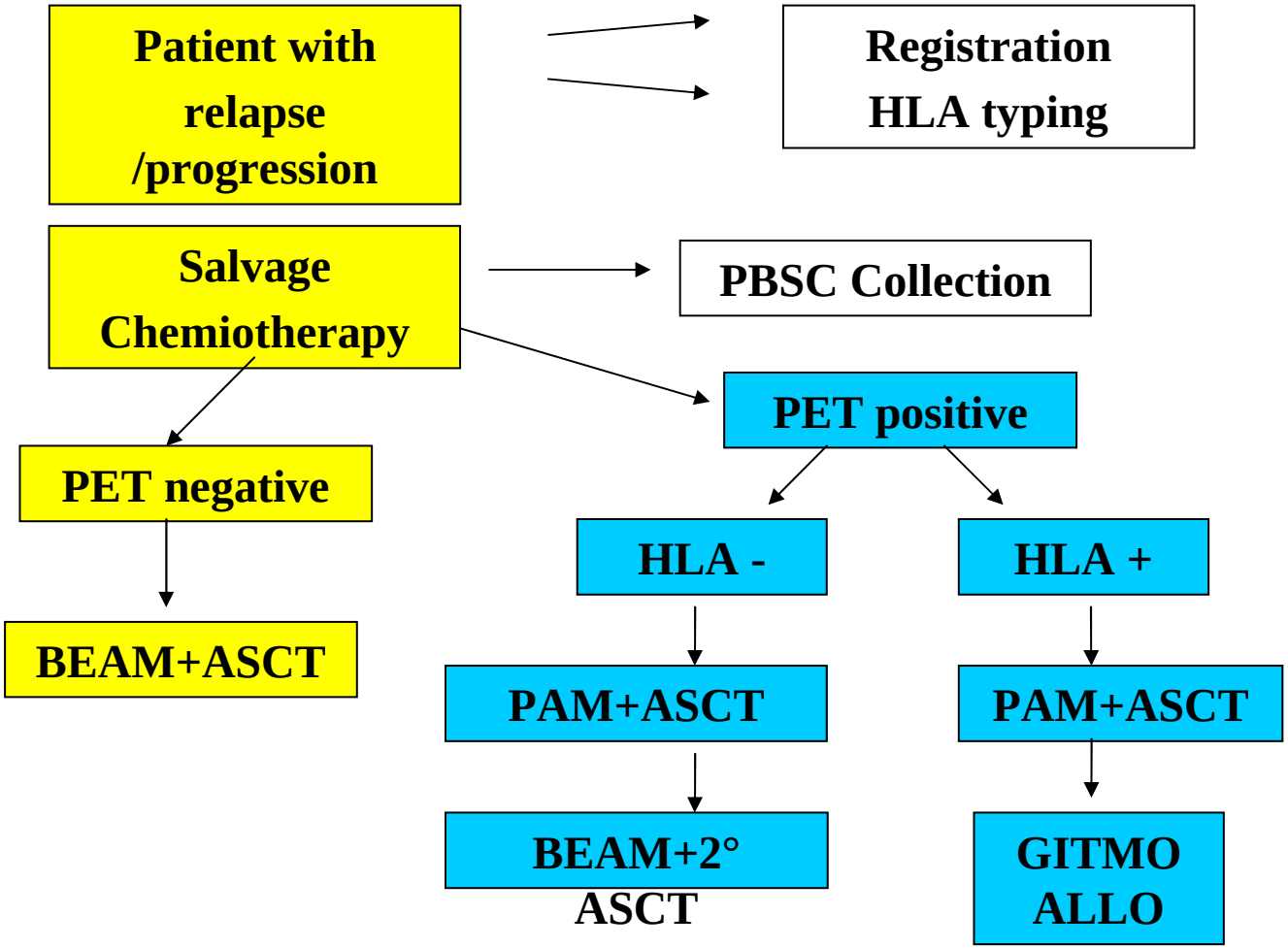
HD0802

Salvage Therapy in patients with Relapsed or Refractory Hodgkin's Lymphoma.

Inclusion criteria

- Patients not responding to first-line therapy, or with early or late relapse
- Age ≥ 18 years
- Life expectancy > 3 mesi
- Normal Cardiac, Pulmonary, Renal and Hepatic functions
- Written informed consent.

HD0802 study design



OBJECTIVES

PET -negative patients after salvage therapy

Primary objectives

- overall survival and progression free survival

OBJECTIVES

PET -positive patients after salvage therapy

Primary objectives

- To evaluate the role of allogeneic transplantation in this setting of patients after salvage chemotherapy and to compare the results with those obtained after 2 cycles of high-dose chemotherapy with stem cell reinfusion

Secondary objectives

- To evaluate complete remission rate
- To evaluate haematological and extra-haematological toxicity (including acute and chronic GvHD, infections)
- To evaluate chimerism

HD0802 sample size and activation status

Accrual 3 years

Follow-up 2 years from the last accrued

Sample Size **at least 40 Pts PET pos after induction CHT**

350 Pts PET neg after induction CHT

33 participating sites

22 active sites

Actual Accrual 142 patients (63 patients are from HD801 study)

DLCL10

Prospective multicentre Phase II study with R-CHOP-14 and consolidation radiotherapy PET-oriented for the treatment of patients with diffuse large B-cell lymphoma (DLBCL) with IPI = 0-1 and unfavorable clinical profile

OBJECTIVES

Primary objective

- To evaluate if a dose-dense chemotherapy + Rituximab (RCHOP-14) + / - consolidation radiotherapy for residual masses PET-TC positive improves the prognosis (in terms of PFS at 2 years) compared to an historical series of patients treated with R-CHOP-21 and radiotherapy administered on bulky masses irrespective of the PET-TC result

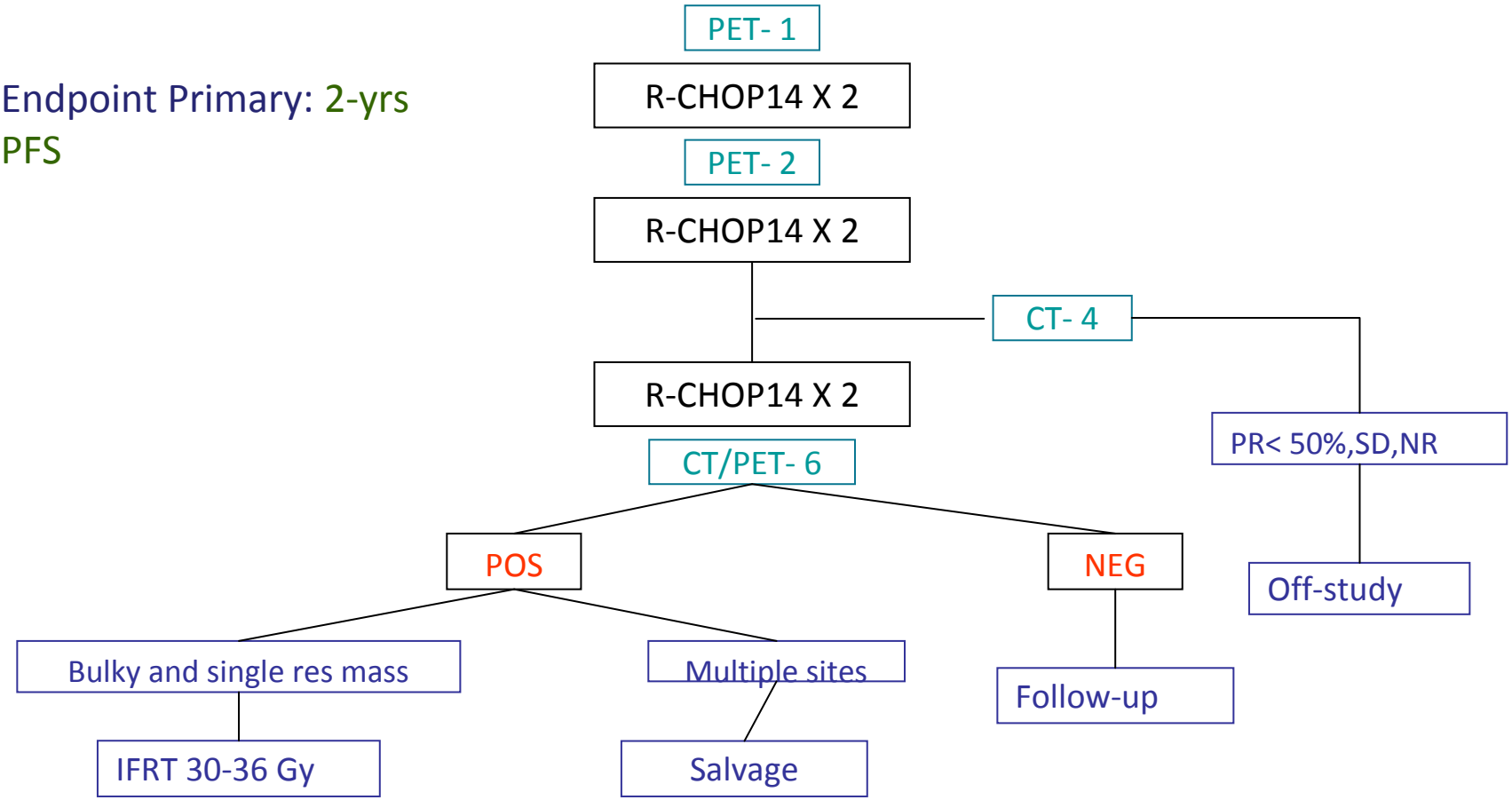
Secondary objectives

- To evaluate the efficacy of IF radiotherapy on residual PET-positive sites of disease in terms of improved clinical response measured as ORR (CR+PR) and CRR
- To evaluate ORR and CRR after the first 4 cycles and at the end of the planned 6 cycles of R-CHOP-14
- To evaluate the predictive role of early PET after 2 cycles (PET-2) in terms of FFS at 2 years.

DLCL10

- ✓DLBCL, FL grade IIIB, DLBCL T-cell rich
- ✓18-70 years
- ✓aaIPI=1 +/- bulky
- ✓aaIPI=0 + bulky (> 7,5 cm)

Endpoint Primary: 2-yrs
PFS



Inclusion criteria

- Diagnosis of diffuse large B-cell (CD20 +) lymphoma, follicular lymphoma grade IIIB grade, T-cell rich large B-cell lymphoma
- Age 18-70 years
- aaIPI=1 +/- bulky and aaIPI=0 with bulky (>7.5 cm)
- ECOG-perfomance status < 3 if not due to lymphoma
- Cardiac ejection fraction> 50%
- Normal hepatic, renal, pulmonary functions
- Negative markers for HIV and HBV
- Written informed consent

DLCL10 sample size and activation status

Accrual 2 years
Follow-up 2 years from the last accrued
Sample Size **112 Patients**

40 participating sites

Actual Accrual 10 patients

IELSG37

A randomized, open-label, multicentre, two-arm phase III comparative study assessing the role of involved mediastinal radiotherapy in Primary Mediastinal Large B-Cell Lymphoma (PMLBCL).

OBJECTIVES

Aim of the study

- To evaluate the possibility to spare radiotherapy in PMBCL patients who have become “PET-negative” after a combined R-chemotherapy.

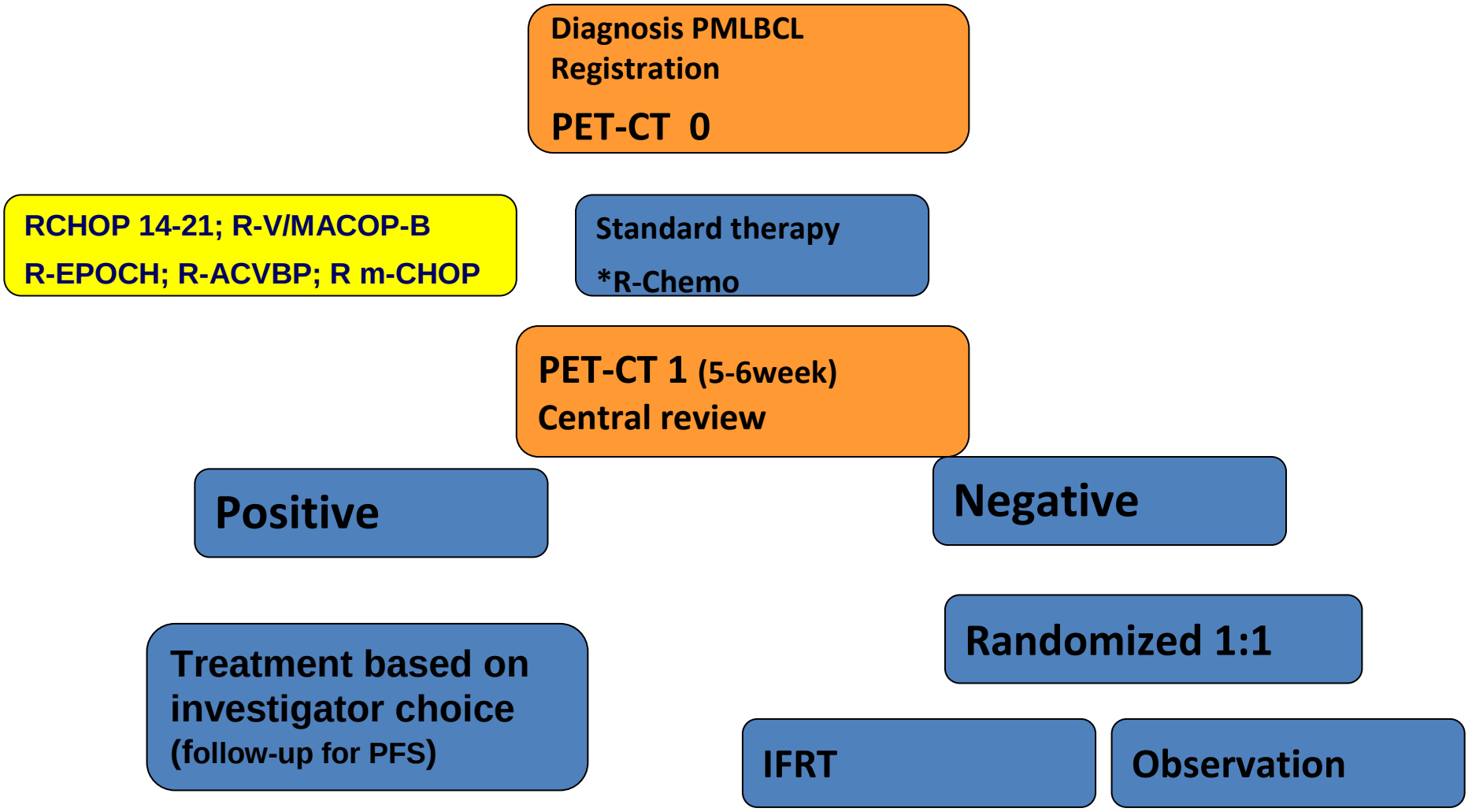
Primary objectives

- Progression free survival (PFS) at 2 years from the randomization
- The trial is planned according to a non-inferiority design aimed at demonstrating that PFS after the experimental treatment (observation) is not worse than after the standard comparator (mediastinal irradiation).

Secondary objective

- Overall survival (OS) at 5 years from registration

Study design



Inclusion criteria

- Previously untreated PMLBCL, CD20 positive. Patients must have histological confirmation of the diagnosis.
- Must have *a dominant mass* within the anterior mediastinum without evidence of extranodal disease outside the chest including spleen and bone marrow.
- Age ≥18 years.
- Fit to receive chemotherapy and radiotherapy with curative intent.
- Treatment phase consisting in a Rituximab combined with any *anthracycline-containing chemotherapy regimen without consolidation with ASCT* (e.g. CHOP14-21, DA-EPOCH, Mega-CHOP, V/ MACOP-B, or ACVBP).
- At least 6 courses of Rituximab should be administered
- Able and willing to give informed consent, and to undergo staging including PET scanning
- Histological diagnostic material available for review.

IELSG37 sample size and activation status

Accrual	3 years
Follow-up	2 years from the last accrued
Sample Size	**752 to be registered to have at least 376 PET neg Pts at the end of CHT**

.... participating sites

FOLL12

A multicenter, phase III, randomized study to evaluate the efficacy of a response-adapted strategy to define maintenance after standard chemoimmunotherapy in patients with advanced-stage Follicular Lymphoma

OBJECTIVES

Primary objective

To evaluate whether a PET and MRD response-based maintenance therapy is more effective in terms of Progression-Free Survival (PFS) than a standard maintenance therapy with Rituximab in patients with untreated, advanced, follicular lymphoma.

Secondary objectives

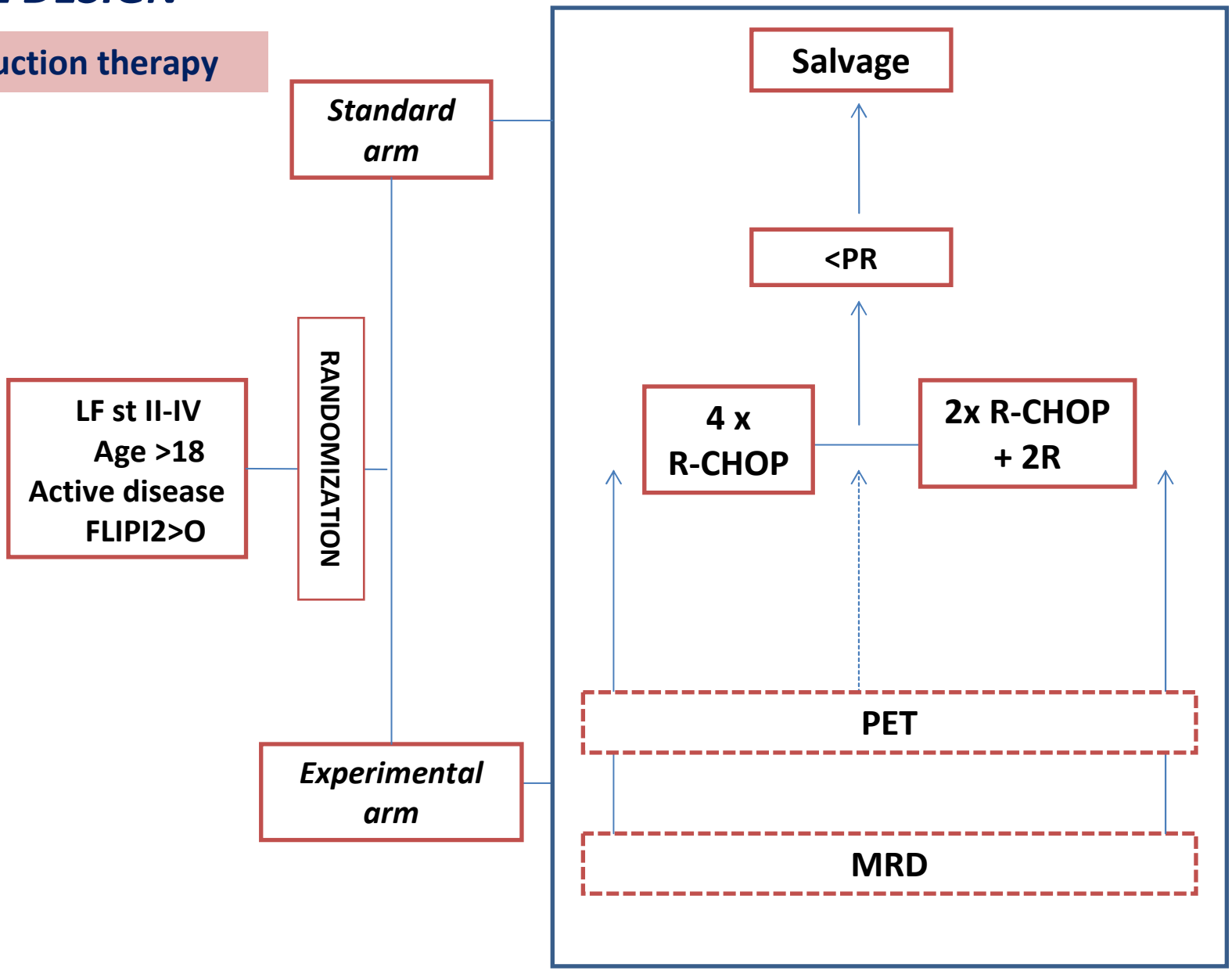
- To evaluate the efficacy of maintenance with observation or pre-emptive Rituximab therapy administered on the basis of MRD status in patients at low risk of progression after induction chemoimmunotherapy.

- To evaluate the efficacy of intensified maintenance with (90)Y Ibritumomab Tiuxetan followed by Rituximab maintenance therapy in patients at high risk of progression after induction chemoimmunotherapy.

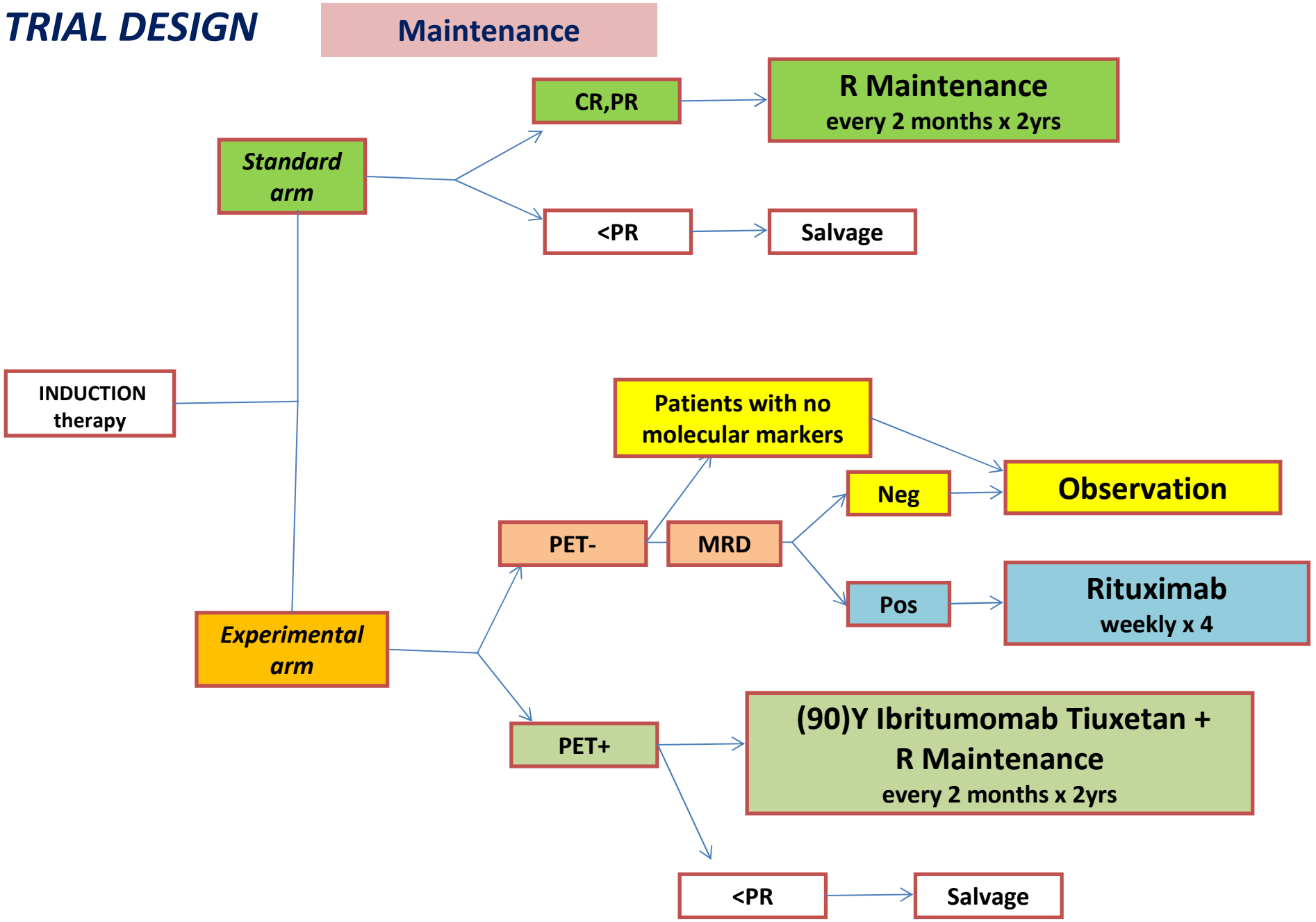
- To compare a response-based maintenance therapy with a standard maintenance therapy in terms of toxicity.

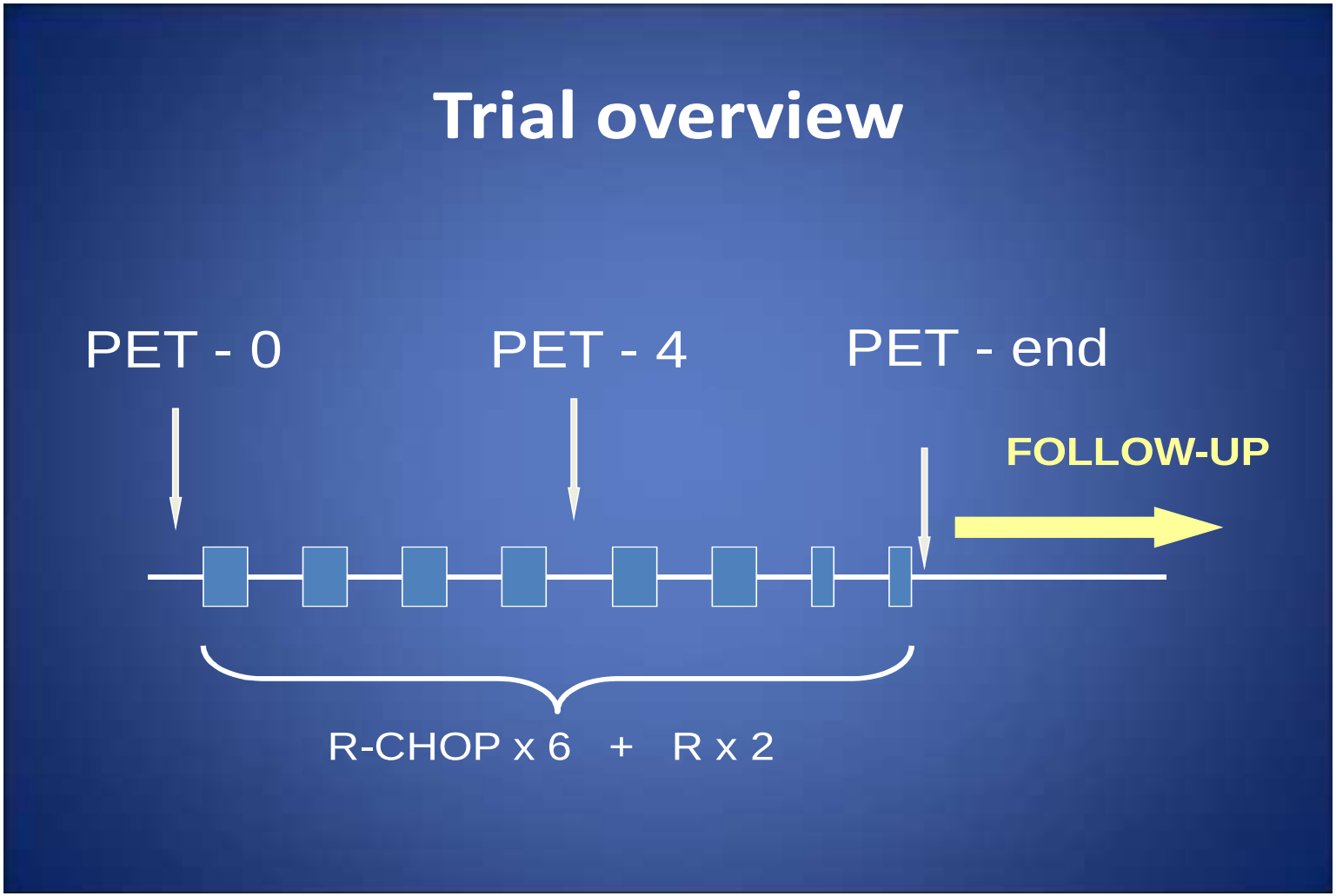
TRIAL DESIGN

Induction therapy



TRIAL DESIGN





Central review:

Five expert nuclear medicine reviewers will score the scans according to the Deauville score.

Inclusion criteria(1)

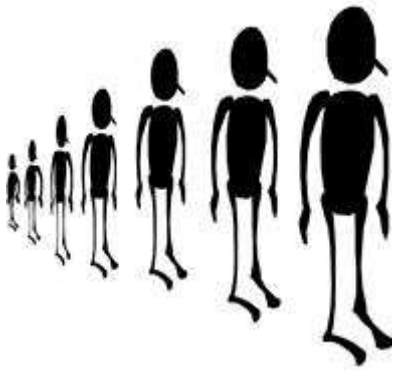
- Histological diagnosis of B-Cell Follicular Lymphoma (FL), grade I, II, IIIa according to WHO classification
- ECOG performance status 0-2
- Age ≥18 years
- Ann Arbor stage II-IV
- FLIPI2 score > 0
- Presence of evaluable/measurable disease after diagnostic biopsy

Inclusion criteria(2)

- At least one of the following criteria for defining **active disease**:

  - systemic symptoms
  - cytopenia due to bone marrow involvement
  - LDH> upper normal value
  - any nodal or extranodal tumor mass with a diameter >7cm
  - involvement of >= 3 nodal sites, each with a diameter of >= 3cm
  - extranodal disease
  - rapidly progressive disease

FOLL12 sample size and activation status



Accrual 4 years

Follow-up 3 years from the last accrued

Sample Size **546** + 10% dropout* = **602 (301 by arm)**

70-75 participating sites

First active site : **Messina Papardo**

(EC approval 25/07/2012)