AGGIORNAMENTO PROTOCOLLI FIL

LINFOMI FOLLICOLARI

Federica Cavallo

Università degli Studi di Torino

Divisione di Ematologia

A.O. Città della Salute e della Scienza di Torino

DIAGNOSI

MIRO'

Studio multicentrico di fase II per il trattamento su base molecolare dei Linfomi Follicolari stadio I/II con radioterapia locale con/senza Ofatumumab

EUDRACT NUMBER 2012-001676-11

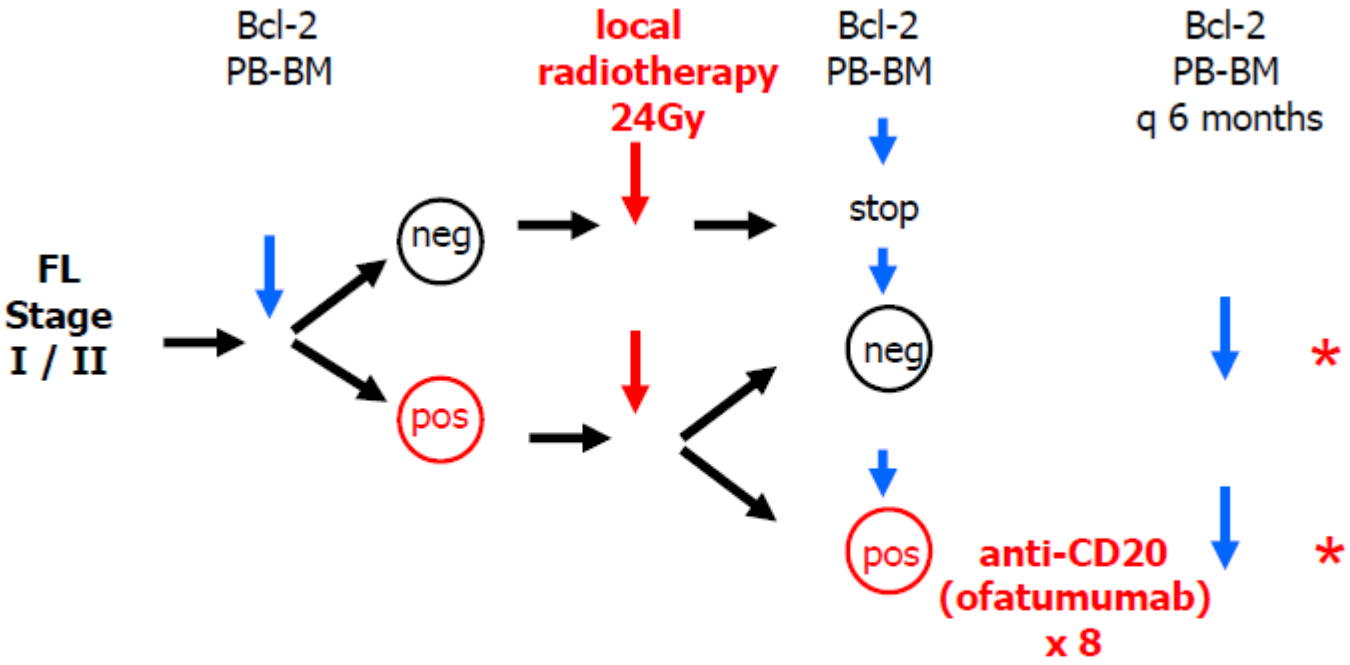
STUDY COORDINATOR Alessandro Pulsoni

PRIMARY OBJECTIVE

Evaluate

the proportion of patients obtaining **disappearance of Bcl-2-IgH rearranged cells** in peripheral blood and/or bone marrow by PCR, **after treatment with Ofatumumab**

MIRO': STUDY DESIGN



* In case of conversion from (neg) to (pos) → **anti-CD20 (ofatumumab) x 8**

MIRO': MAIN INCLUSION/ESCLUSION CRITERIA

1. Age ≥ 18 years
2. Histological diagnosis of B-Cell CD20+ Follicular Lymphoma (FL), **grade I, II, IIIa** according to the WHO 2008 classification
3. **Ann Arbor stage IA or IIA** (no more than 2 contiguous nodal regions) non bulky (< 7 cm)
4. **FLIPI ≤2; FLIPI2 ≤2**
5. **Collection BM and PB for MRD analysis**
6. No previous treatment for the lymphoma
7. Staging with PET-CT, bone marrow biopsy
8. Not pregnant or breast-feeding
9. Not current active hepatic or biliary disease
10. Negative HIV test, HBsAg, HCV
11. No other prior malignancies
12. Signed informed written consent

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

EUDRACT NUMBER 2012-003170-60

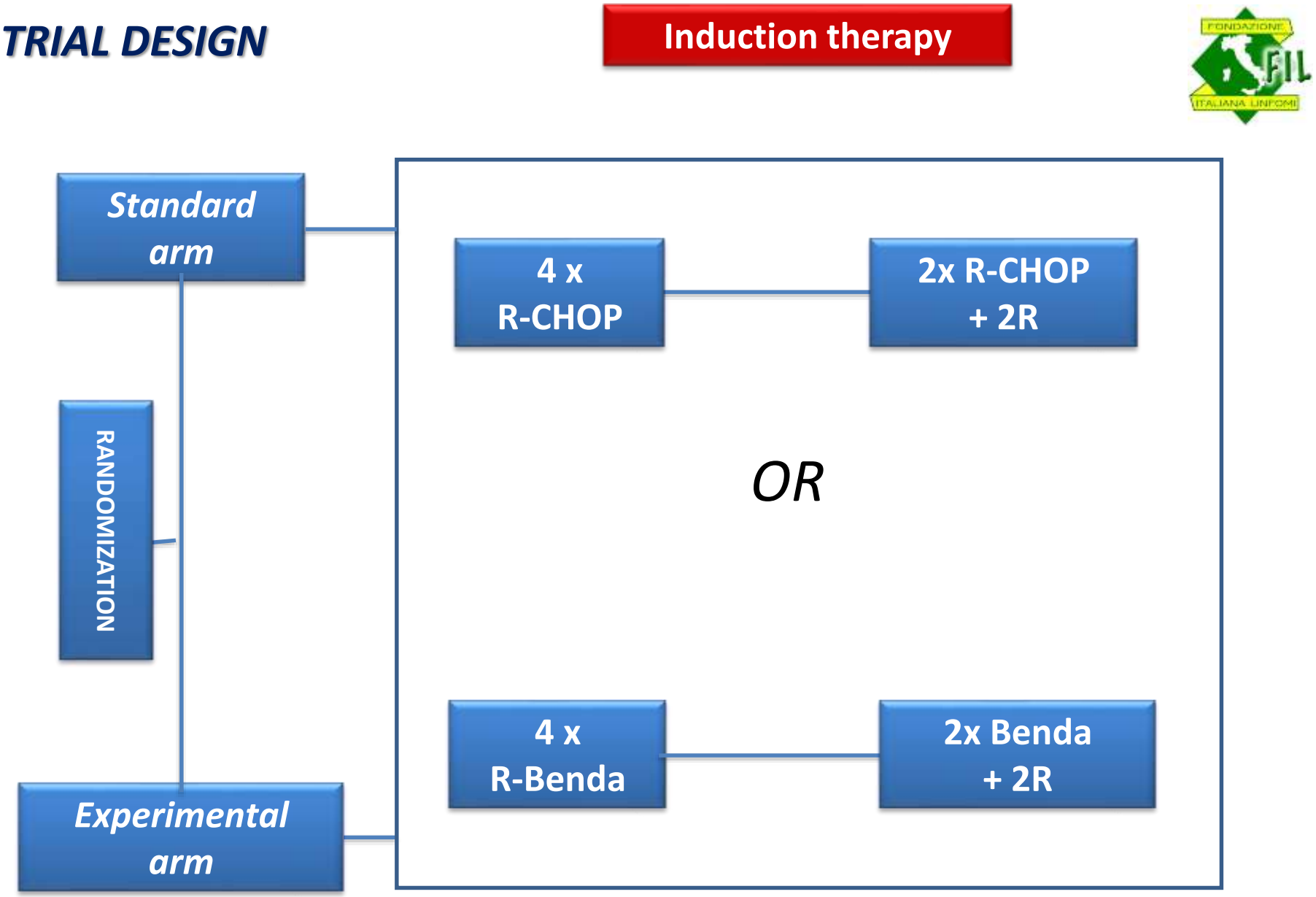
STUDY COORDINATORS Massimo Federico
Donato Mannina

PRIMARY OBJECTIVE

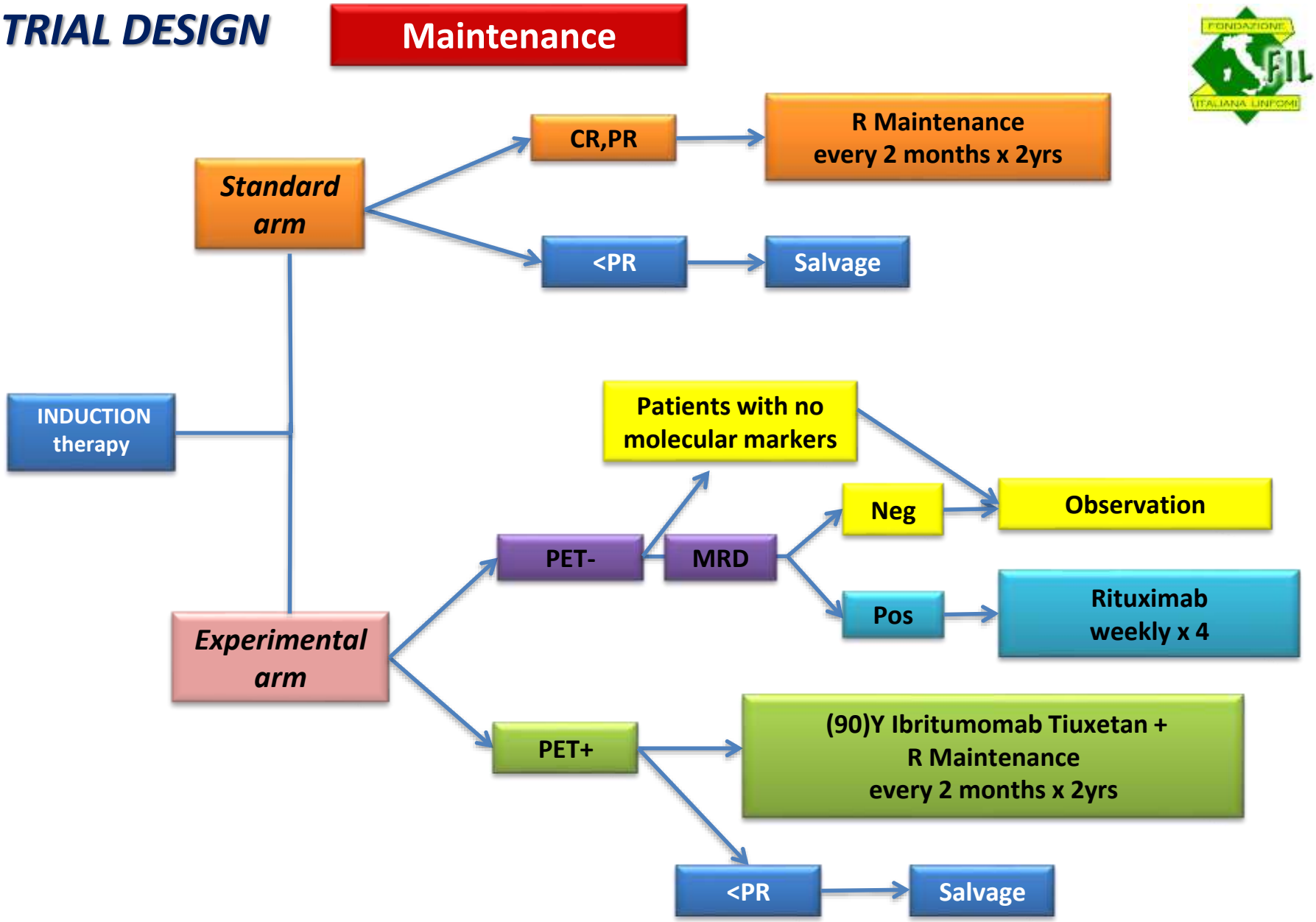
Evaluate whether

a **PET** and **MRD response-based maintenance** therapy is **not less effective** in terms of PFS than a standard maintenance therapy with R in patients with untreated, advanced FL

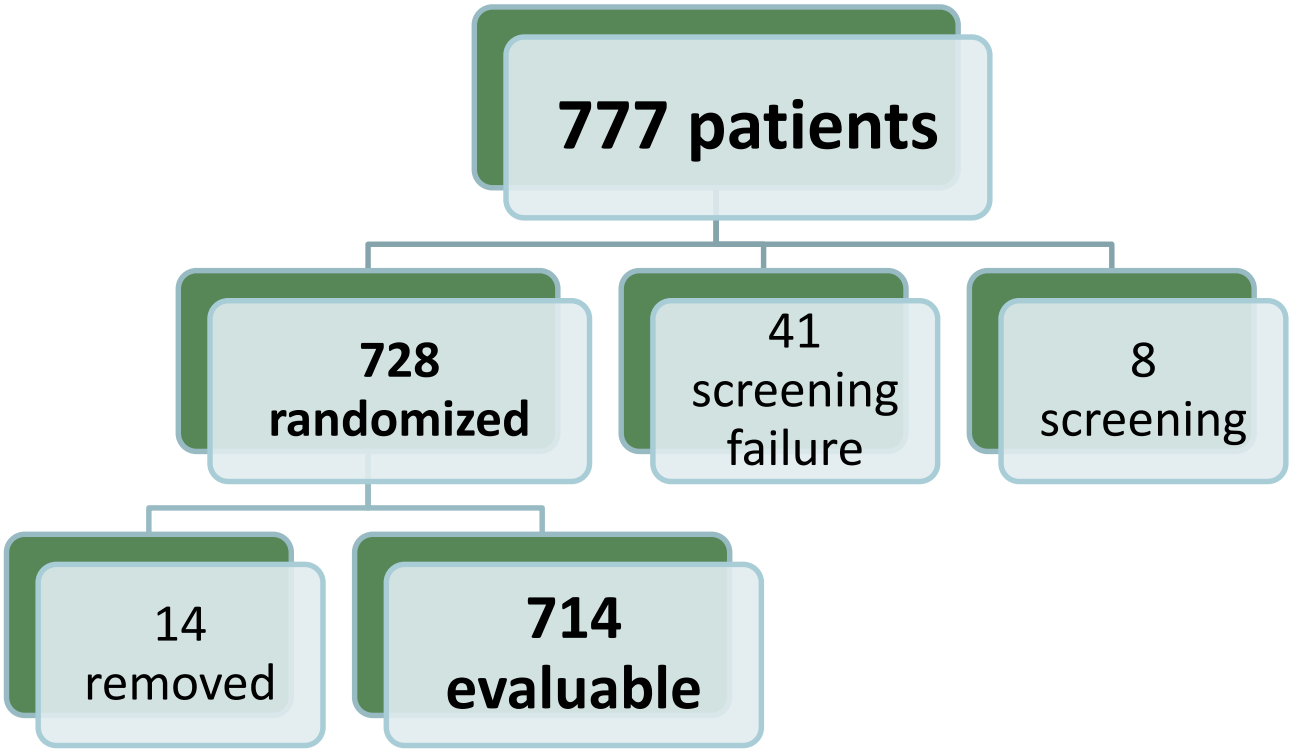
TRIAL DESIGN



TRIAL DESIGN



FIL_FOLL12 ACCRUAL 02/10/17



Sample Size **770**+ 5% dropout* **= 810 (405 by arm)**

FOLL-12: MAIN INCLUSION/ESCLUSION CRITERIA

1. Age > 18 years
2. Histological diagnosis of B-Cell CD20+ Follicular Lymphoma (FL), **grade I, II, IIIa** according to the WHO 2008 classification
3. ECOG performance status 0-2 (unless disease –related)
4. Ann Arbor stage II-IV
5. **FLIPI2>0**
6. **Collection BM and PB for MRD analysis**
7. **Clinical indication for treatment** (according to SIE and GELF criteria)
8. No previous treatment for the lymphoma with the exception of locoregional radiotherapy (IF-RT)
7. Adequate cardiac function : LVEF > 50% by echocardiography or MUGA scan
8. Not pregnant or breast-feeding
9. Willingness to use effective contraception
10. Negative HIV test, HBsAg, HCV (except for those patients without signs of active viral replication assessed by HCV-RNA copies)
11. No other prior malignancies
12. Signed informed written consent

RB OR RCHOP

424 patients treated with RCHOP (58%)
304 patients treated with RB (42%)

From amendment 1

162 patients treated with RCHOP (40%)
240 patients treated with RB (60%)

Last two months : 15 patients (8 RB, 7 RCHOP)

PET REVIEW

554 end treatment PET

479 PET- (86%)

75 PET+ (14%)

DS 4-5

RECIDIVA

FLAZ12

A phase III multicenter, randomized study comparing consolidation with 90 Yttrium-labeled Ibritumomab Tiuxetan (ZEVALIN®), radioimmunotherapy vs autologous stem cell transplantation (ASCT) in patients with relapsed follicular lymphoma (FL), aged 18-65 years

EUDRACT NUMBER 2012-000251-14

STUDY COORDINATORS ***Umberto Vitolo***
Marco Ladetto

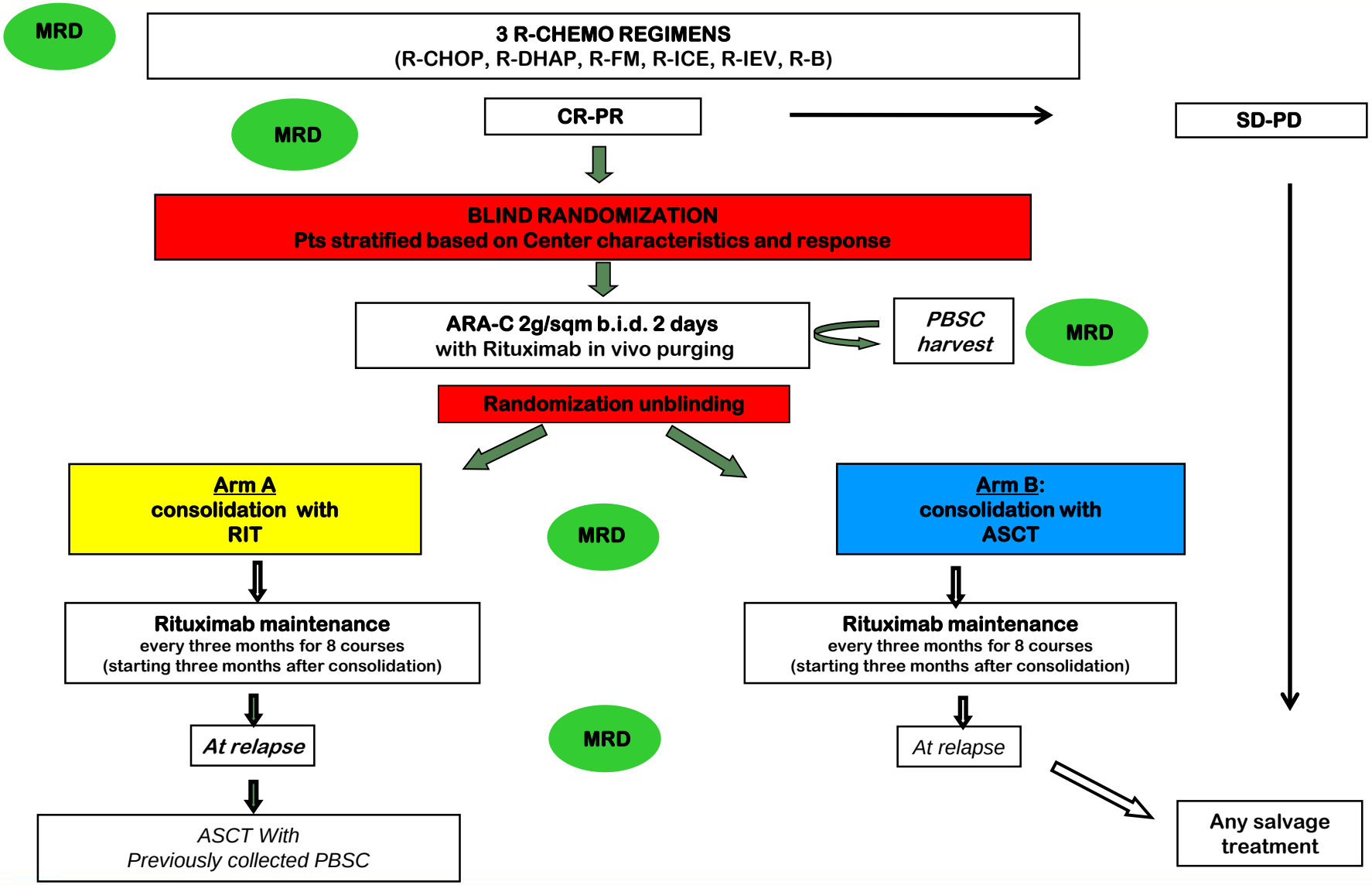
PRIMARY OBJECTIVE

To compare

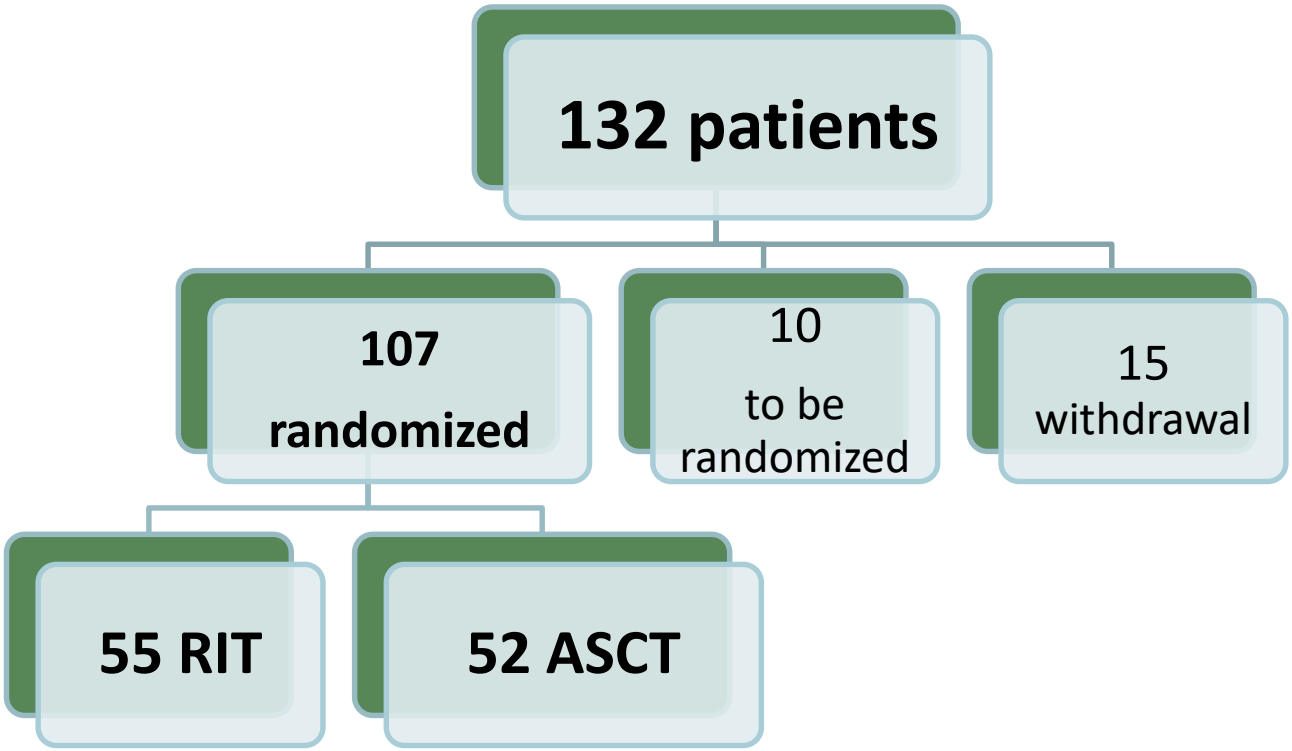
Two different consolidation regimes:

RIT (Zevalin) vs. ASCT in terms of **progression free survival (PFS)** in ***relapsed/refractory FL patients***

FLAZ-12: STUDY DESIGN



FIL_FLAZ12 ACCRUAL



Sample Size **210**

FLAZ-12: MAIN INCLUSION/ESCLUSION CRITERIA

1. Age 18-65 years
2. **Histologically documented diagnosis of grade I-IIIa** ***(no longer required biopsy if transformation is not suspected)***
3. ECOG performance status 0-2 (unless disease –related)
4. **Collection BM and PB for MRD analysis**
5. Relapsed or refractory disease after ≤ 2 chemotherapy lines
6. Clinical indication for treatment (according to SIE and GELF criteria)
7. Adequate cardiac function : LVEF > 50% by echocardiography or MUGA scan
8. Not pregnant or breast-feeding
9. Willingness to use effective contraception
10. Negative HIV test
11. No other prior malignancies
12. Signed informed written consent

FLAZ-12: CURRENT SITUATION

ADMINISTRATION OF ZEVALIN REGULAR

ENROLLMENT REMAINS LOW ALTHOUGH SLIGHTLY IMPROVING

STOP AIFA support

CRF monitoring → ongoing

Interim analysis → planned

ADVERSE EVENTS

ACTUALLY NO MAJOR PROBLEMS HAVE BEEN OBSERVED FOR ENROLLED PATIENTS

SAE	SUSAR
22	1

RENOIR

A randomized phase III multicenter trial assessing efficacy and toxicity of a combination of Rituximab and Lenalidomide (R2) vs Rituximab alone as maintenance after chemoimmunotherapy with Rituximab-Bendamustine for relapsed/refractory FL patients not eligible for autologous transplantation (ASCT)

EUDRACT NUMBER 2012-003392-18

STUDY COORDINATORS ***Umberto Vitolo***
Stefano Sacchi

PRIMARY OBJECTIVE

To evaluate

in patients responsive to induction whether the R2-MANT program may improve progression-free survival (PFS) compared to patients treated with R-MANT

RENOIR12: TREATMENT DESIGN
EMENDAMENTO

PCR analysis for Bcl-2 rearrangement on PB/BM

REALPSED/REFRACTORY FOLLICULAR LYMPHOMA NEED TO THERAPY

R-Bendamustine
R-CHOP
R-CVP
R-Fludarabine

4 cycles

Optional
2 additional courses

SD/PR

NR → **OFF**

CR/PR

Random

Restaging and PCR analysis for Bcl-2 rearrangement on PB/BM

R2

Rituximab 375 mg/m2 day 1 q 90 days (8 cycles)
Lenalidomide (10 mg dd 1-21 q 28) (24 cycles)

R alone

Rituximab 375 mg/m2 day 1 q 90 days (8 cycles)

Clinical and molecular follow-up

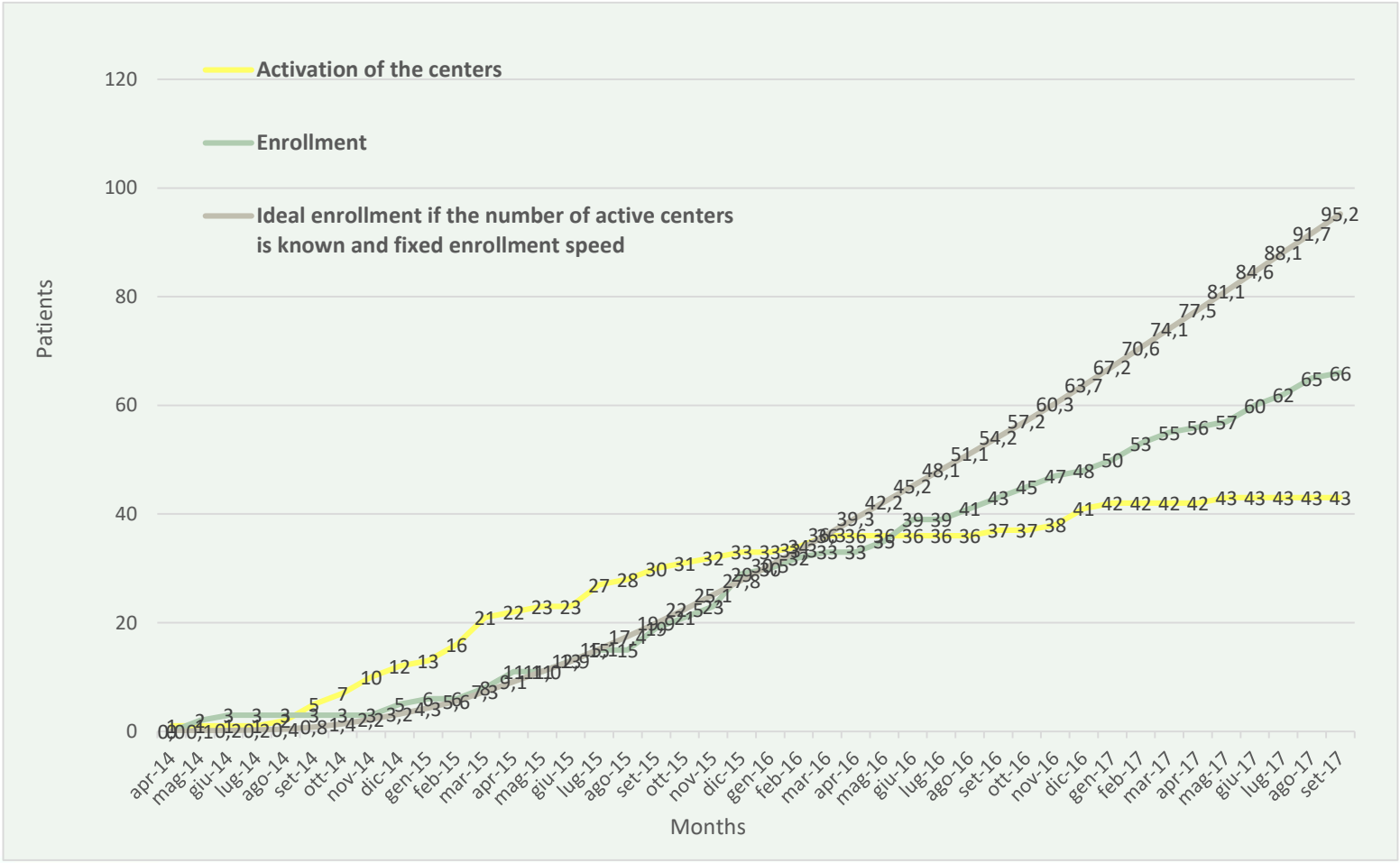
RENOIR: MAIN INCLUSION/ESCLUSION CRITERIA

1. Age >18 years
2. Histologically documented diagnosis of grade I-IIIa ***(re-biopsy if transformation is suspected)***
3. ECOG performance status 0-2 (unless disease –related)
4. Ann Arbor stage II-IV
5. **Collection BM and PB for MRD analysis**
6. **Relapsed or refractory disease after ≤ 2 R-chemotherapy lines**
7. Not eligible for ASCT
8. Clinical indication for treatment (according to SIE and GELF criteria)
9. Calculated **creatinine-clearances ≥ 40 ml/min**
10. Absolute neutrophil count (ANC) ≥ 1.5 x 10 9/L and platelets count ≥ 75 x 109/L unless due to marrow involvement by lymphoma
11. Willingness to use effective contraception
12. Negative HIV test
13. No other prior malignancies
14. Signed informed written consent

RENOIR12 STATUS

Accrual: 160 subjects

PAZIENTI ARRUOLATI	66 (41% TOTALE)



EVENTI AVVERSI

SEGNALAZIONI TOTALI: 10 SAE + 2 SUSAR

SAE

- 2 FUO
- SEPSIS
- INTESTINAL OCCLUSION BY HERNIA
- 3 PNEUMONIA
- FEBRILE NEUTROPENIA G3 - COUGH GR2 - DIARRHEA GR2
- BOWEN'S DISEASE
- GENERAL CONDITION WORSENING AND DEATH

SUSAR

- FEVER AND SHIVER - MYOCARDIAL INFARCTION - PERICARDITIS
- HEART FAILURE

GRAZIE PER L'ATTENZIONE