AGGIORNAMENTI DI PROTOCOLLI FIL

Linfomi Follicolari

Dr.ssa Carola Boccomini

SC Ematologia

AO Città della Salute e della Scienza

Torino

61st Annual Meeting and Exposition (December 7-10, 2019)

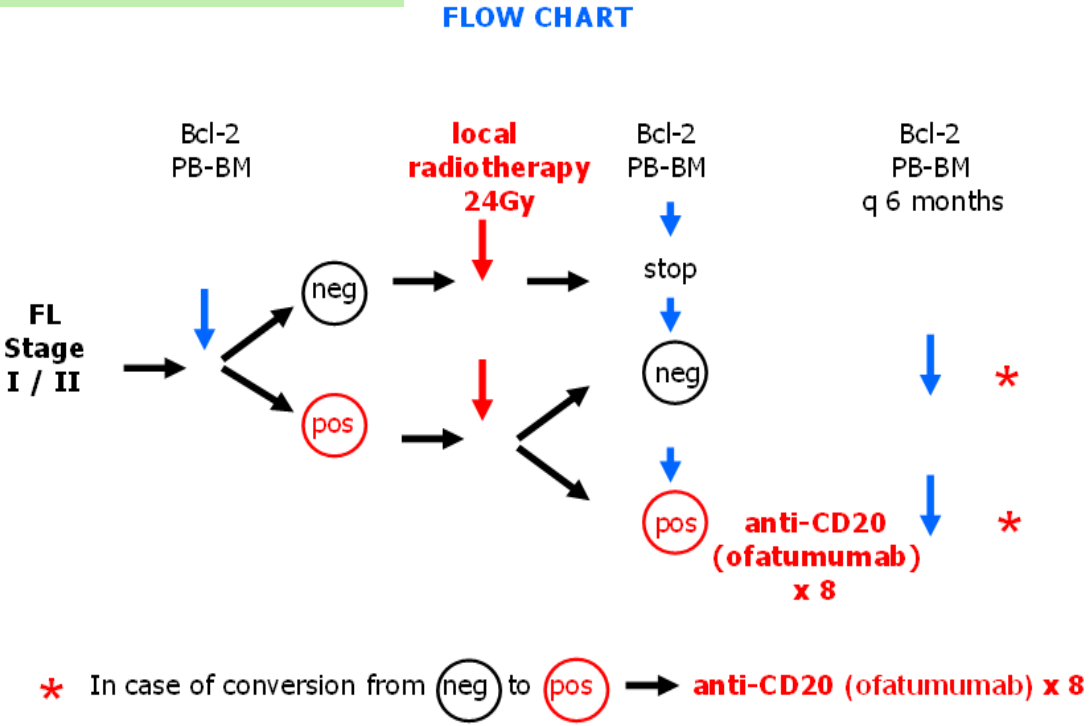
FIL_MIRO'

Studio "MIRO" (Molecularly Immuno-radio-therapy Oriented): studio multicentrico di fase II per il trattamento su base molecolare dei Linfomi Follicolari stadio I/II con radioterapia locale con/senza Ofatumumab

Coordinating Investigator:
Alessandro Pulsoni

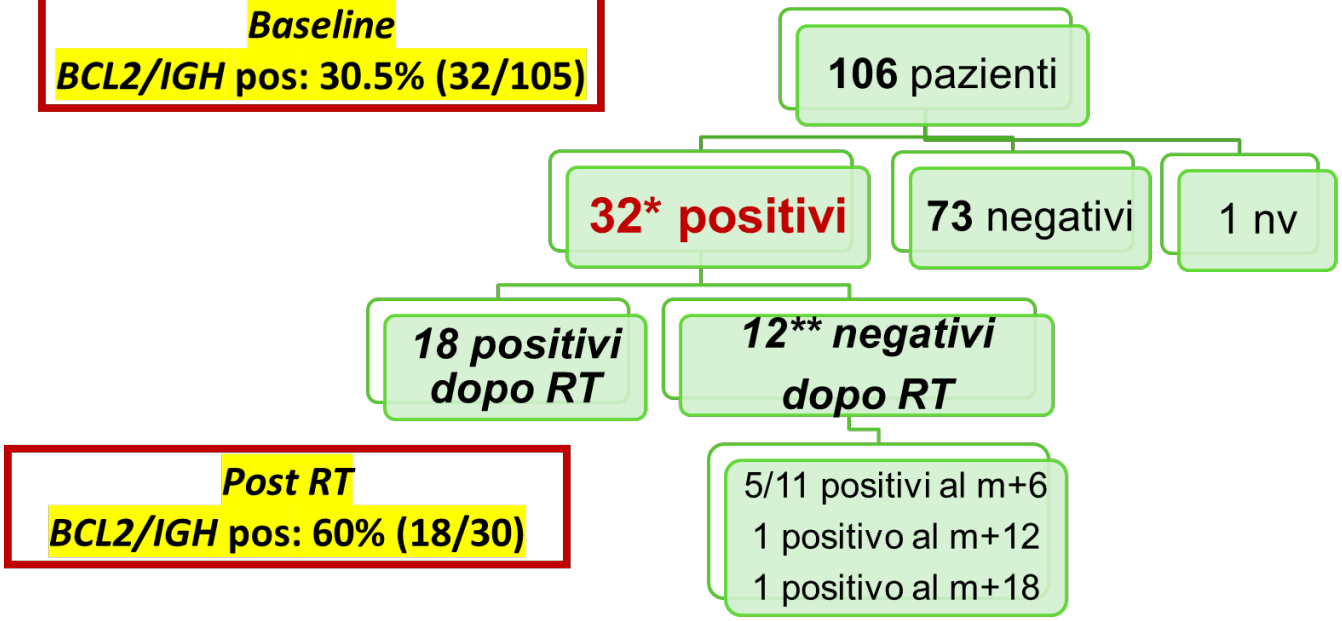
11/06/2015 – 10/05/2018: ARRUOLAMENTO COMPLETATO

FIL Mirò



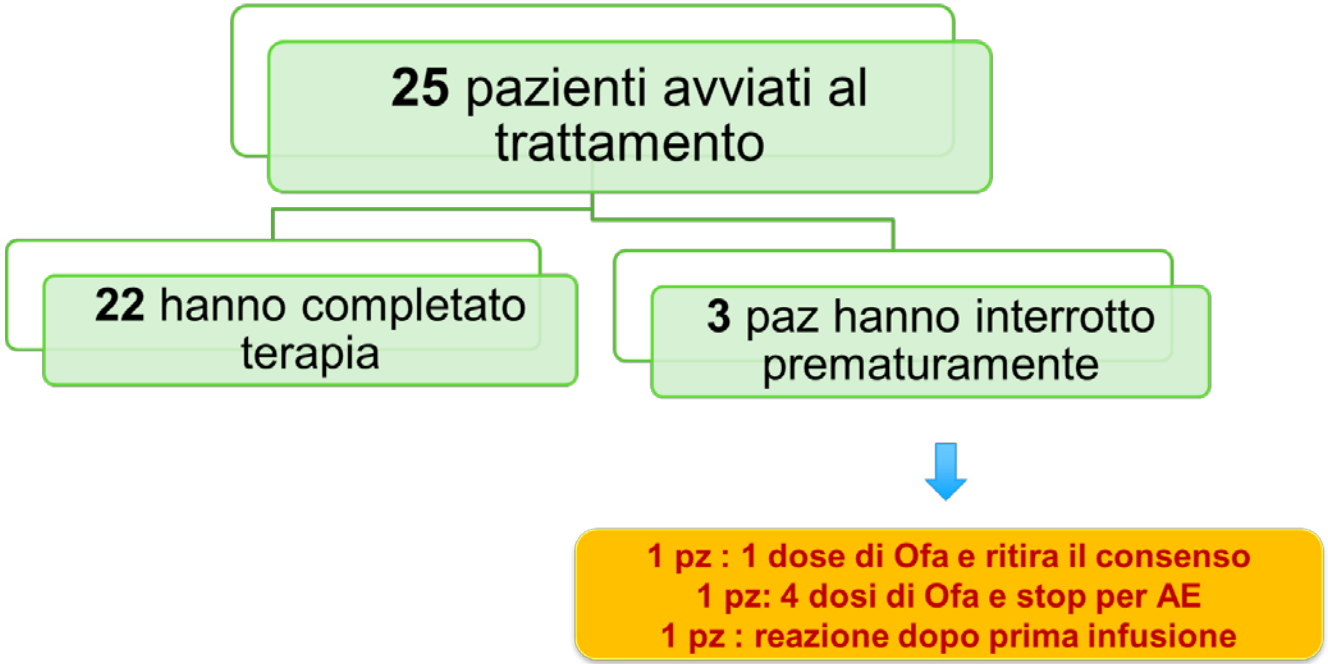
Obiettivo primario: % di pazienti che ottiene MRD neg dopo ofatumumab

Arruolamento pazienti



*pz deceduto in corso di radioterapia, 1 paziente è risultato in progressione dopo RT
** un paziente uscito per PD prima di rivalutazione mese 6

Trattamento al 04/11/2019



Risposta al trattamento

- Nessuna differenza nel tasso di recidiva tra pazienti che hanno il marcatore molecolare e quelli che non lo hanno
- MRD- post Ofatumumab: 91% (20/22), molto più elevata dell'atteso (50%)
- MRD- post Ofatumumab considerando 2 paz che hanno eseguito trattamento incompleto + 1 negativizzazione tardiva: 92% (23/25)
- La RT è in grado di indurre una risposta molecolare solo nel 37% dei pazienti con effetto duraturo soltanto nella metà dei casi.
- Il trattamento con anticorpo monoclonale è in grado di indurre una risposta molecolare nella quasi totalità dei pazienti trattati
- **La strategia di RT + immunoterapia è pertanto in grado di garantire un tasso di remissioni complete anche molecolari maggiori, il cui impatto clinico potrà essere stabilito soltanto con l'allungamento del follow-up**

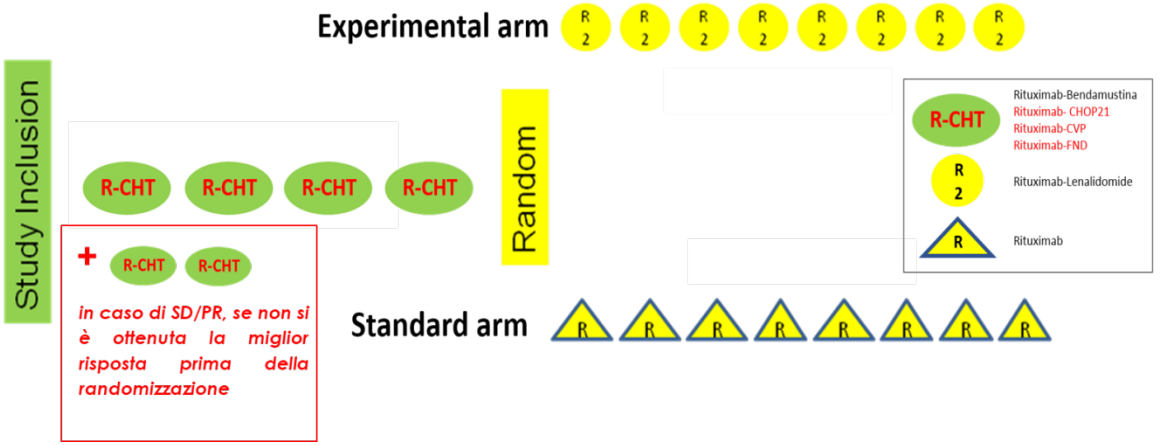
FONDAZIONE ITALIANA LINFOMI

FIL_RENOIR12

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-chemotherapy (R-CHT) for relapsed/refractory FL patients not eligible for autologous transplantation (ASCT)

Coordinating Investigators:
Umberto Vitolo, Barbara Botto

FIL_RENOIR12: study design



- Terapia di induzione: R- bendamustina, R-CHOP, R-CVP, R-FND
- Terapia di induzione: fino a 6 cicli di R-CHT in caso di SD/PR
- Autorizzato uso Rituximab sottocute e biosimilare anti-CD20

This is a multicenter phase III trial with one randomization step that will compare two maintenance regimens (in patients responsive to induction):

R2-MANT program versus standard R-MANT

- Random will be done in 1:1 ratio and stratified by clinical response (PR or CR) after induction
- Lenalidomide supplied by Celgene
- PET not mandatory but reccomended

FIL_RENOIR12: objectives

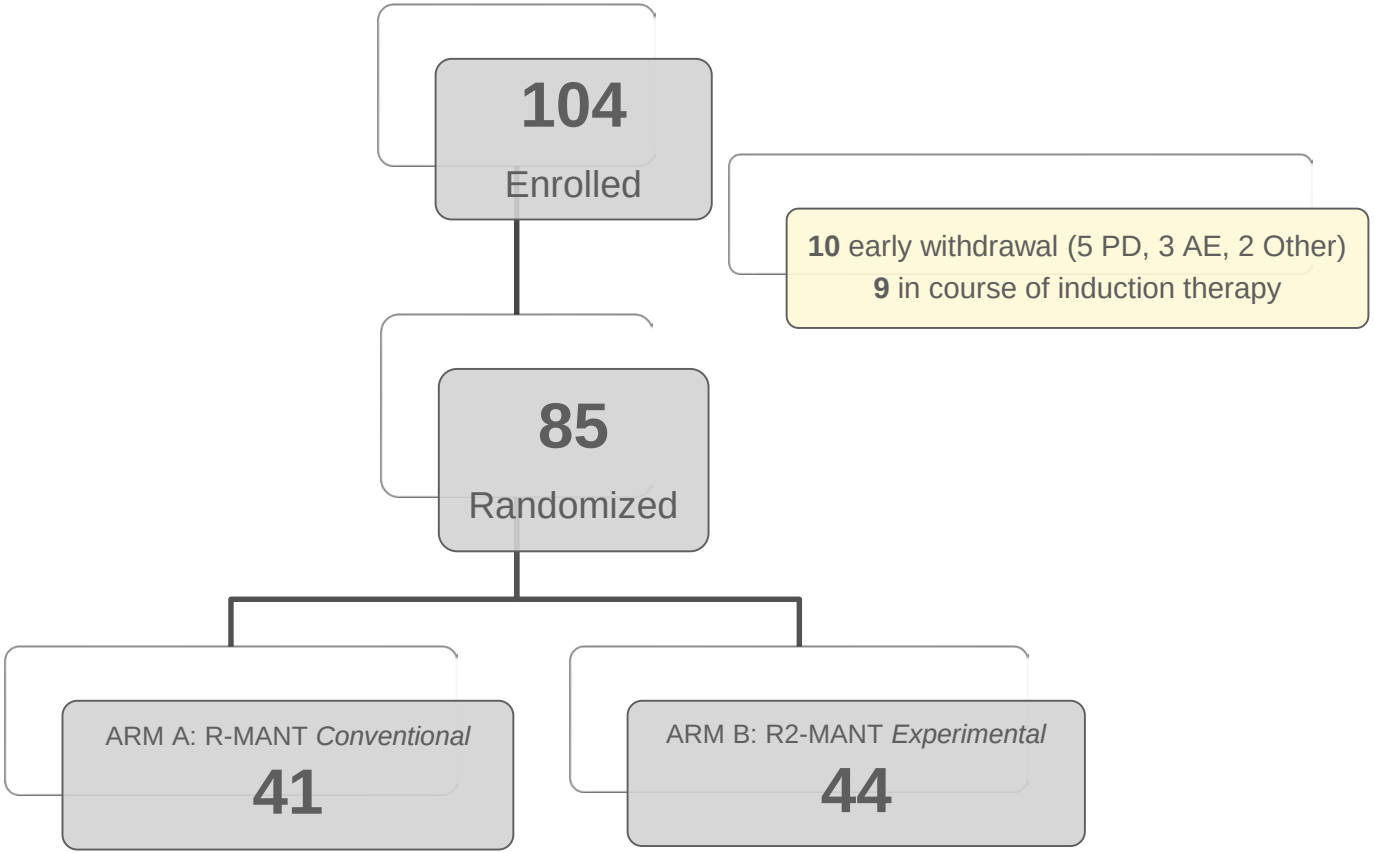
Primary

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

Secondary

- To compare the R2-MANT vs the R-MANT program for: safety (grade III-IV adverse events) and efficacy (OS)
- To evaluate the activity of maintenance program on minimal residual disease (MRD) in the bone marrow (BM) and peripheral blood (PB).
- To assess the prognostic impact of molecular persistence and molecular relapse on PFS and OS.
- To assess quality of life (QoL) during tretament and maintenance, using the EORTC QLQ-C30C questionnaire
- To compare the cost-effectiveness of treatment arms

FIL_RENOIR12: enrollment status



FIL_RENOIR12: centri partecipanti

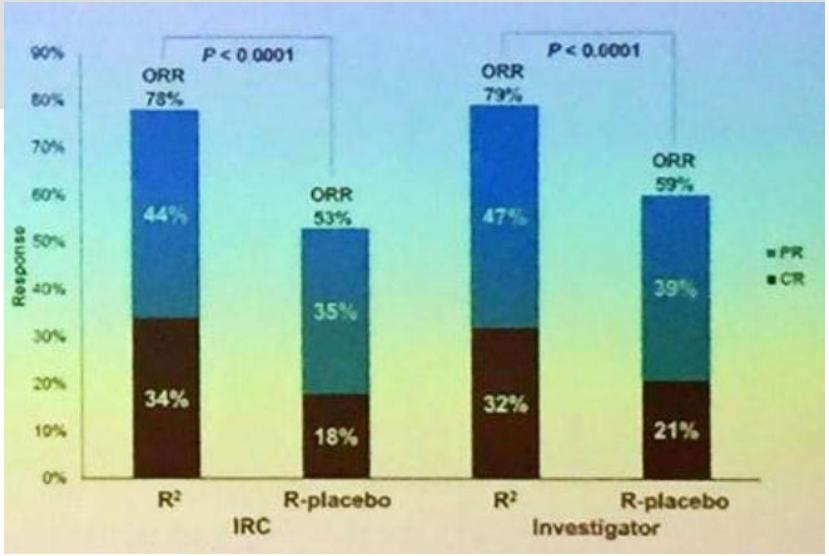
- Centro Coordinatore: SC Ematologia , AOU Città della salute e della Scienza di Torino, Presidio Molinette – Dr. Umberto Vitolo, Dr.ssa Barbara Botto
- Centri partecipanti all'avvio dello studio: **53**
- CENTRI CHIUSI PER MANCATO INTERESSE (ottobre 2018): **17** *Barletta, Catania-Consoli, Civitanova Marche, Latina, Matera, Mestre, Milano-Baldini, Milano-Ferrari, Oristano, Pagani, Parma, Perugia, Roma-Palombi, Salerno, San Giovanni Rotondo, Sassari, Treviglio*
- Centri attivi/Centri partecipanti: **36/36**
- Centri arruolanti/Centri attivi: **26/36**

! **10 centri attivi, non arruolanti**

AUGMENT PHASE III STUDY: LENALIDOMIDE/RITUXIMAB (R^2) IMPROVED EFFICACY OVER RITUXIMAB/PLACEBO IN RELAPSED/REFRACTORY FOLLICULAR PATIENTS IRRESPECTIVE OF POD24 STATUS

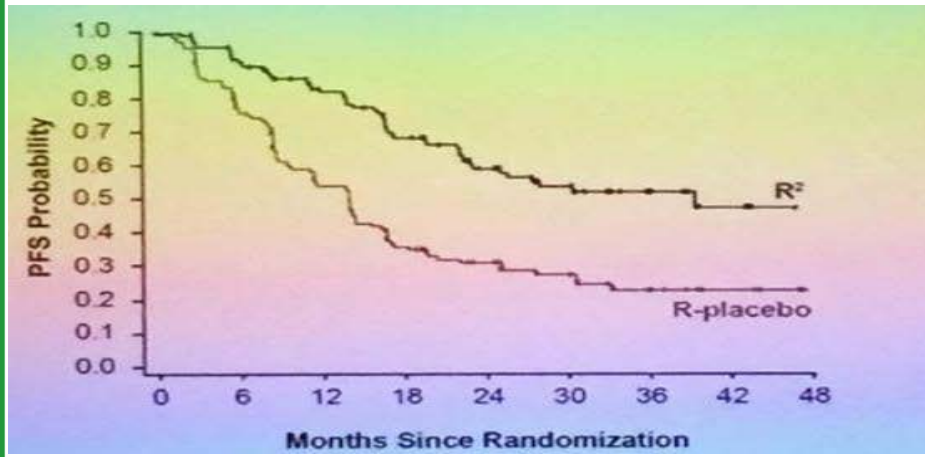
- To examine the potential impact of POD24 in relapsed/refractory FL pts receiving Lenalidomide + Rituximab (R2) vs Rituximab + placebo
- **Treatment: Rituximab standard dose cycle 1 d1-8-15-22 and d1 cycles 2-5 ± Lenalidomide 20 mg/day d1-21/28 x 12 cycles**
- 295 pts

ORR and CRR significantly improved for R2 vs R/placebo

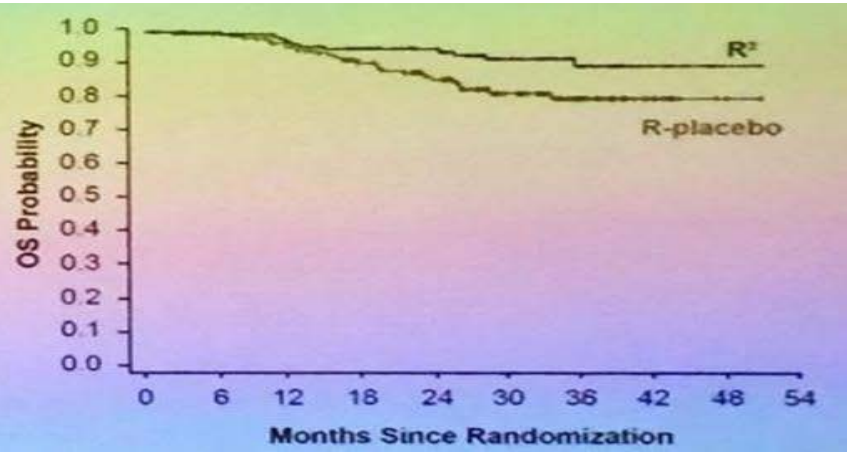


AUGMENT PHASE III STUDY: LENALIDOMIDE/RITUXIMAB (R^2) IMPROVED EFFICACY OVER RITUXIMAB/PLACEBO IN RELAPSED/REFRACTORY FOLLICULAR PATIENTS IRRESPECTIVE OF POD24 STATUS

PFS

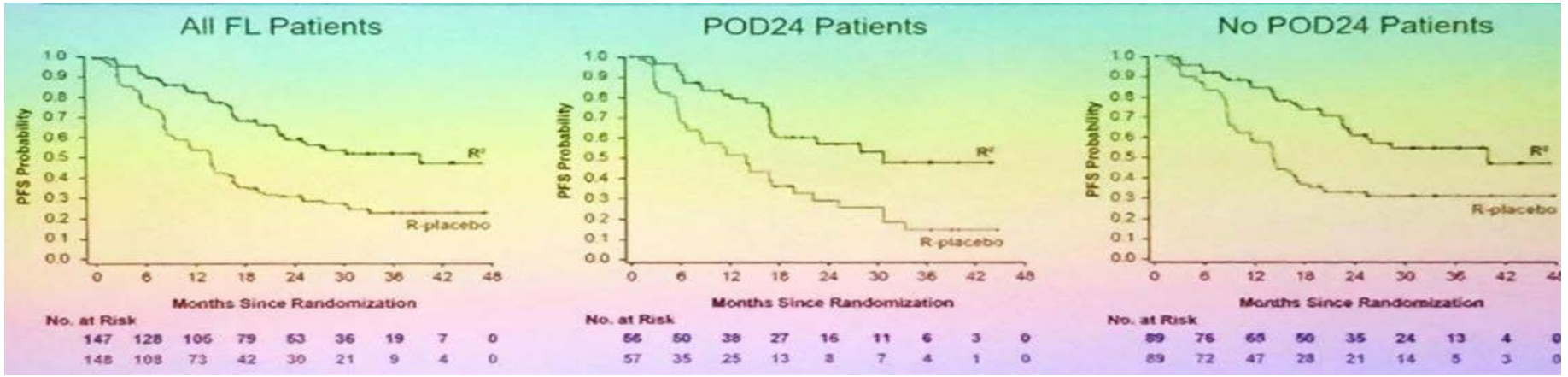


OS



AUGMENT PHASE III STUDY: LENALIDOMIDE/RITUXIMAB (R^2) IMPROVED EFFICACY OVER RITUXIMAB/PLACEBO IN RELAPSED/REFRACTORY FOLLICULAR PATIENTS IRRESPECTIVE OF POD24 STATUS

- For all pts and subgroups based on POD24 status, median PFS was improved in the R2 vs R/placebo arm
- **R2 demonstrated superior efficacy over R/placebo, including those with POD24**



FIL_RENOIR12: timeline

Aprile 2017 — *Settembre 2019* — *Dicembre 2022*

FPI 15/05/2014

Protocollo 1° versione_Aprile 2014

PLANNED SAMPLE SIZE

253 (202 randomize) in 40 Italian Centres

EXPECTED ACCRUAL TIME

36 months (aprile 2017)

52 pts

Protocollo 2° versione_Gennaio 2018

PLANNED SAMPLE SIZE

160 (128 randomize) in 60 Italian Centers

EXPECTED ACCRUAL TIME

68 months (settembre 2019)

104 pts (85 randomized)

Protocollo 3° versione_in corso

EXPECTED ACCRUAL TIME

88 months (dicembre 2022)

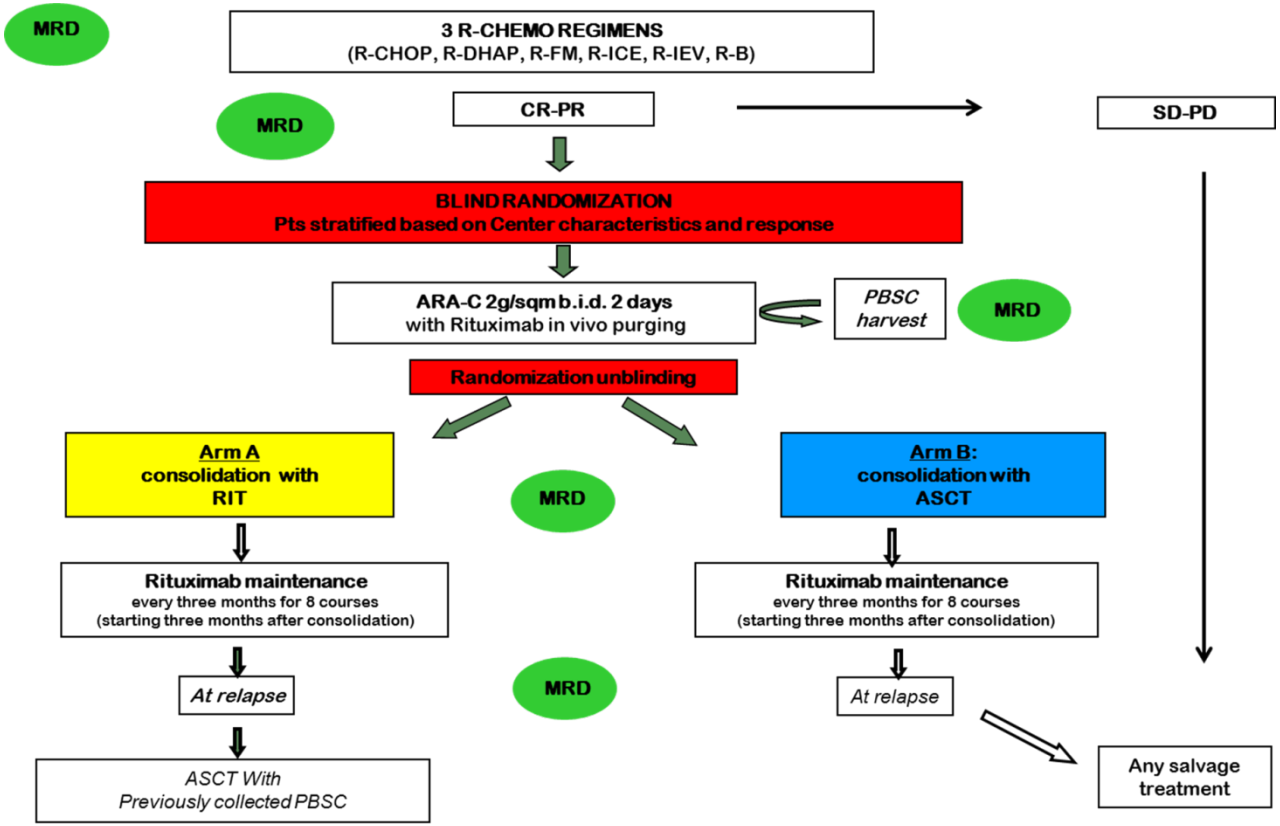
FONDAZIONE ITALIANA LINFOMI

FIL_FLAZ12

A PHASE III MULTICENTER, RANDOMIZED STUDY COMPARING CONSOLIDATION WITH 90YTTRIUM-LABELED IBRITUMOMAB TIUXETAN (ZEVALIN®) RADIOIMMUNOTHERAPY VS AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT) IN PATIENTS WITH RELAPSED/REFRACTORY FOLLICULAR LYMPHOMA (FL) AGED 18-65 YEARS

Coordinating Investigators:
Marco Ladetto, Umberto Vitolo

Study design



STUDY OBJECTIVES

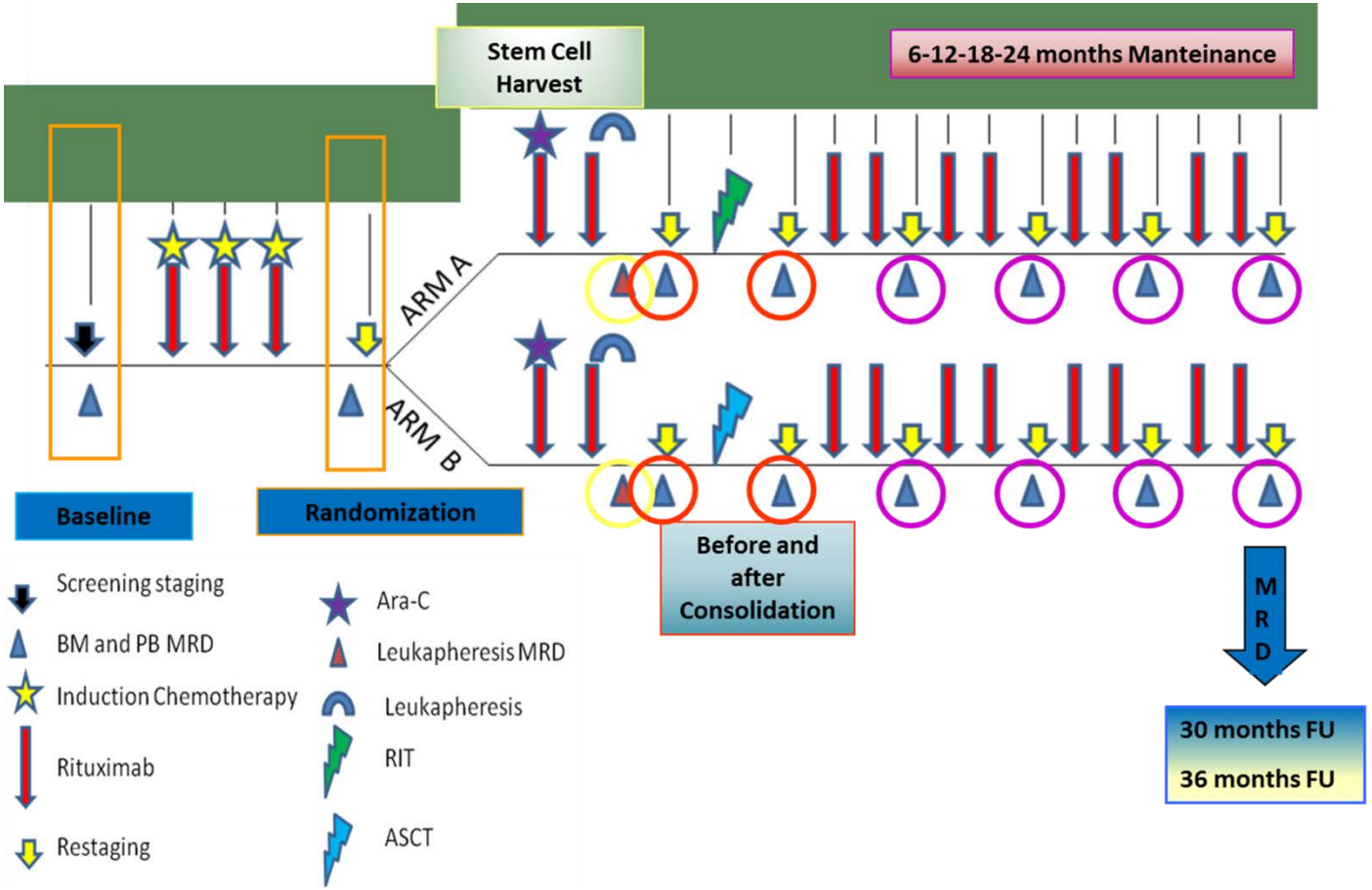
PRIMARY

- Compare 2 different consolidation regimes: ***RIT (Zevalin) vs. ASCT*** in terms of **progression free survival (PFS)** in ***relapsed/refractory FL patients aged 18-65.***

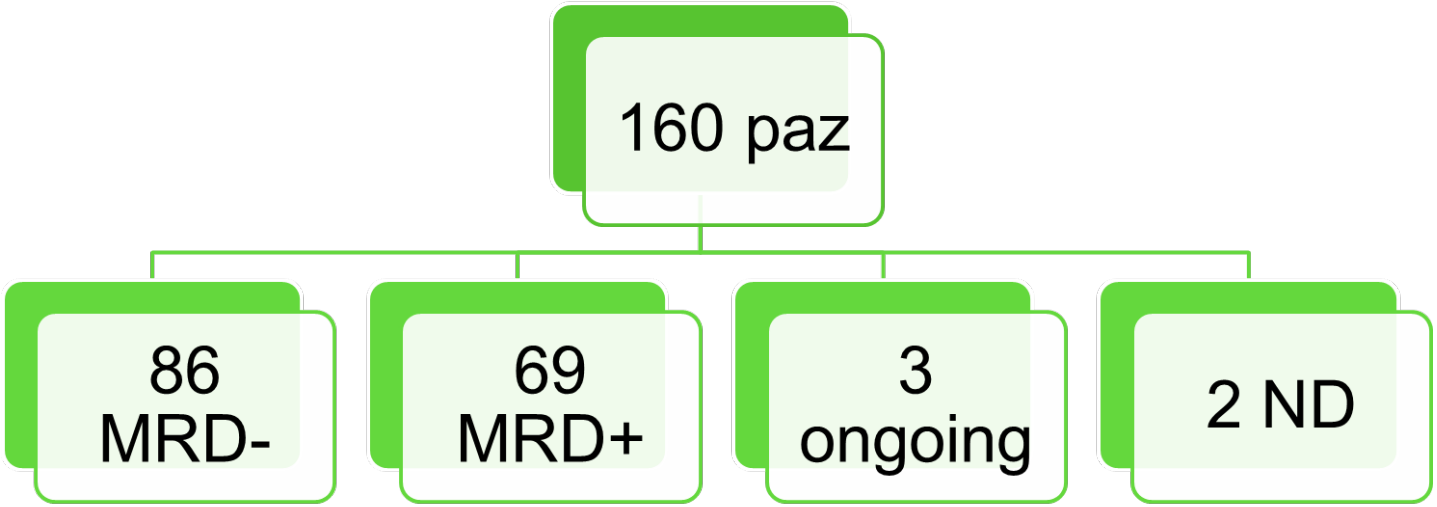
SECONDARY

- Complete Remission **(CR)** and Overall Response Rate **(ORR)**
- Events-free Survival **(EFS)**, Treatment-free survival **(TFS)** from randomization and Overall Survival **(OS)**
- Effect of ASCT vs RIT on **minimal residual disease (MRD)** in terms of: molecular response rate, molecular relapse rate, kinetics of disease assessed by real-time PCR on bone marrow and peripheral blood
- Prognostic impact of **molecular disease persistence** on PFS and OS
- Assess feasibility, toxicity and efficacy (ORR, PFS and OS) **of ASCT after RIT faillure**
- Assess **toxicity** in both arms during induction, consolidation and maintenance
- Compare **cost-effectiveness** of both treatment regimens **(eliminato nell'emendamento)**
- Check the impact of the two treatment on **quality of life** in the short and long term **(eliminato nell'emendamento)**

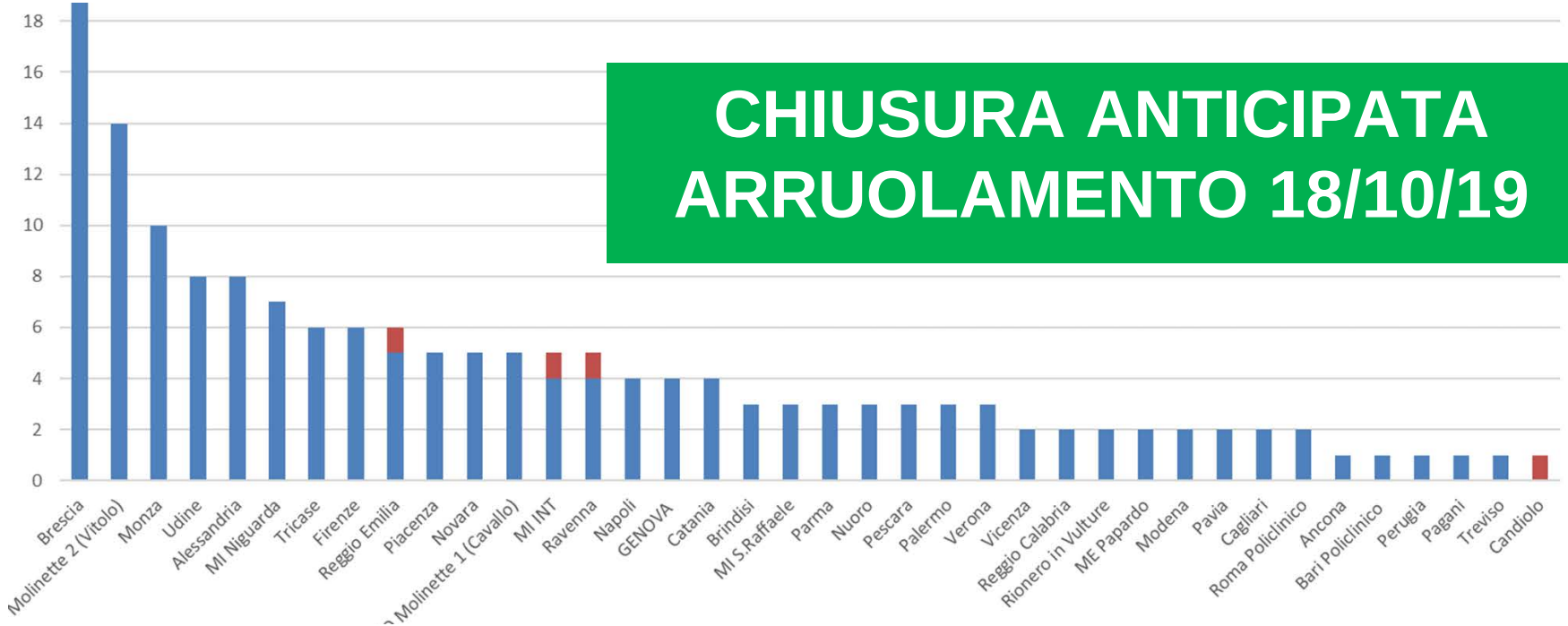
MRD planned timepoints



BCL-2 at baseline



SITE ENROLLMENT



CHIUSURA ANTICIPATA ARRUOLAMENTO 18/10/19

Il numero considerevole di pazienti arruolati ed il numero di eventi non trascurabile fornirà informazioni importanti alla comunità scientifica

FONDAZIONE ITALIANA LINFOMI

FIL_GAUDEALIS

“Idelalisib Plus Obinutuzumab In Patients With Relapsed/Refractory Follicular Lymphoma: A Phase 2, Single-Arm, Multicentric Study.”

Coordinating Investigator:
Pier Luigi Zinzani

Objectives & Endpoints

Primary Objective and Endpoint

- Evaluate the ***efficacy*** in terms of clinical response of the combination Obinutuzumab + Idelalisib
- **Overall response rate (ORR)** after the 6th cycle (end of induction phase) of the combination Obinutuzumab + Idelalisib (2014 Lugano criteria).

Secondary Objectives and Endpoints

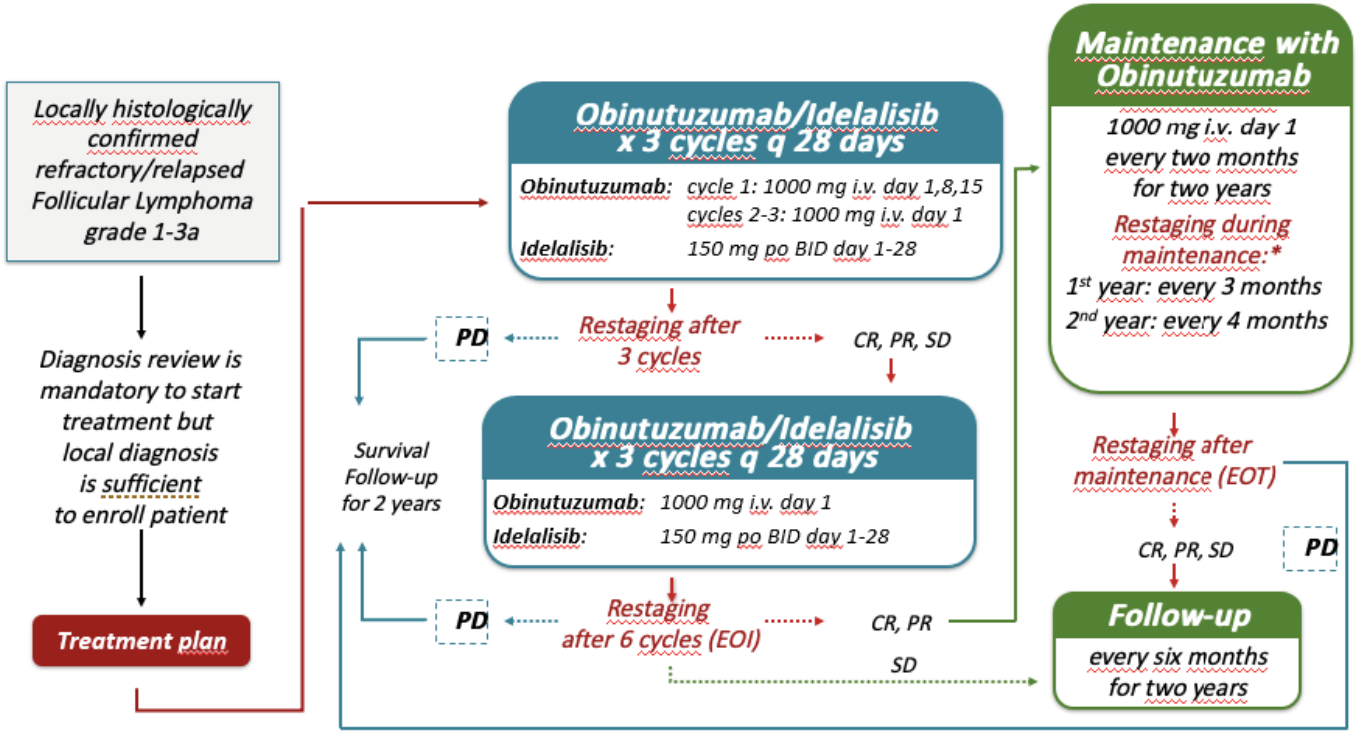
- Efficacy in terms of **PFS and OS**
- **Safety and feasibility** of the combination of Obinutuzumab + Idelalisib
- **Overall survival (OS)** rate, measured from the date of starting therapy to the date of death from any cause.
- **Progression-free survival (PFS)** rate, measured from the date of starting therapy to the date of disease progression, relapse or death from any cause.
- **Treatment safety** through the measurement of: patients' withdrawal rate, incidence, type and grade of any adverse event (AE) and serious adverse event (SAE), hospitalization rate throughout the study, and patients' compliance to oral treatment.

Study Design

- This is a prospective, multicenter, single arm, phase II study.
- A total of **43 patient** will be enrolled in the study: **15 patients at the Stage 1** of the study, **28 in the Stage II.**

- Duration of the study:
- - 2 years (including 6 months for interim analysis) for enrollment
- - 6 months of induction of LP
- - 2 years of maintenance
- - 2 years of follow up after EOT
- For a total of **6,5 years**

Flow Chart



* Patients in PD at any restaging during maintenance will be addressed to Survival follow-up

Relevant Inclusion/Exclusion Criteria

- Relapsed or refractory, histologically confirmed **CD20-positive follicular non-Hodgkin's lymphoma, grade 1, 2 or 3A** according to the WHO 2017 classification.
- **At least 2 prior systemic therapies** for follicular lymphoma including both any antibody directed against the CD20 antigen and a chemotherapy combination.
- **At least 1 of following treatment indications:** bulky disease, at least one B-symptom, symptomatic splenomegaly, compression syndrome, lymphoma-related cytopenias, pleural or peritoneal serous effusions, ECOG-PS ≤ 2.
- Patients must agree to undergo **Pneumocystis jirovecii pneumonia (PJP)** prophylaxis throughout the treatment period and 2-6 months thereafter (before consulting with Medical monitor).

- Grade 3b follicular non-Hodgkin's lymphoma or evidence of transformation to high-grade non-Hodgkin's lymphoma.
- On-going inflammatory bowel disease.
- On-going alcohol or drug addiction.

Participating Centers and Authorization Process

Participating Centers = 12
Coordinating Center = Institute of Hematology "L. and A. Seràgnoli ", AOU Policlinico S. Orsola-Malpighi, University of Bologna

AIFA Authorization = 13/06/2019
Favourable Opinion Coordinating Ethics Committee = 22/05/2019

List of centers (3/12 già attivi)

Centre	Center Type	PI
Aviano	Satellite	Spina Michele
Bari	Satellite	Guarini Attilio
Bologna	**Coordinator**	**Zinzani Pier Luigi**
Brescia	Satellite	Rossi Giuseppe
Firenze	Satellite	Bosi Alberto
Milano INT	Satellite	Corradini Paolo
Napoli Pascale	**Satellite**	**Pinto Antonio**
Novara	Satellite	Gaidano Gianluca
Roma	Satellite	Pulsoni Alessandro
Torino	Satellite	Boccomini Carola
Trieste	**Satellite**	**Zaja Francesco**
Udine	Satellite	Olivieri Jacopo

PROTOCOLLI ATTIVI PRESSO LE 2 EMATOLOGIE "CITTA' DELLA SALUTE E DELLA SCIENZA DI TORINO"

PCYC-1141-CA
Studio di Fase 3, multicentrico, randomizzato, in doppio cieco, con placebo, sull'inibitore della Tirosin Chinasi di Bruton (BTK), Ibrutinib, in combinazione con rituximab rispetto a placebo in combinazione con Rituximab in pazienti con linfoma follicolare naive al trattamento.

GS-US-313-1580
Studio di ottimizzazione della dose di Idelalisib (ZYDELIG) nel linfoma follicolare.

INCB 50465-203 – CITADEL-203
Studio di fase II, multicentrico, in aperto, di INCB050465, un inibitore PI3K, nel linfoma follicolare recidivante/refrattario.

GO29833
Studio di fase II che valuta la sicurezza e l'efficacia di Obinutuzumab in associazione con Polatuzumab Vedotin e Venetoclax in pazienti con linfoma follicolare o diffuso a grandi cellule B recidivante/refrattario.

UTX-TGR-205
UTX-TGR-205 – A Phase 2b Randomized Study to Assess the Efficacy and Safety of the Combination of Ublituximab + TGR-1202 with or without Bendamustine and TGR-1202 alone in Patients with Previously Treated Non-Hodgkin's Lymphoma

Grazie dell’attenzione!