6th International Workshop on PET in Lymphoma
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Ongoing PET oriented trials

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PET-based clinical trials from FIL

Disease	Stage	Patients N°	Trial	Site	Central review	PET adapted	status
HL	IIB	96/96	DDABVD	Italy	Yes	No	Closed
HL	IIB-IV	773/773	HD0607	Italy	Yes	Yes	Closed
HL	IIB-IV	512/512	HD0801/2	Italy	Yes	Yes	Closed
DLBCL	I-IV	0/90	GALILEO	Italy	Yes	No	Opening
DLBCL	II-IV	70/110	DLCL-10	Italy	Yes	Yes	Open
PMBCL	I-II	276/720	IELSG-37	World	Yes	Yes	Open
FL	II-IV	600/600	FOLL 12	Italy	Yes	Yes	Open

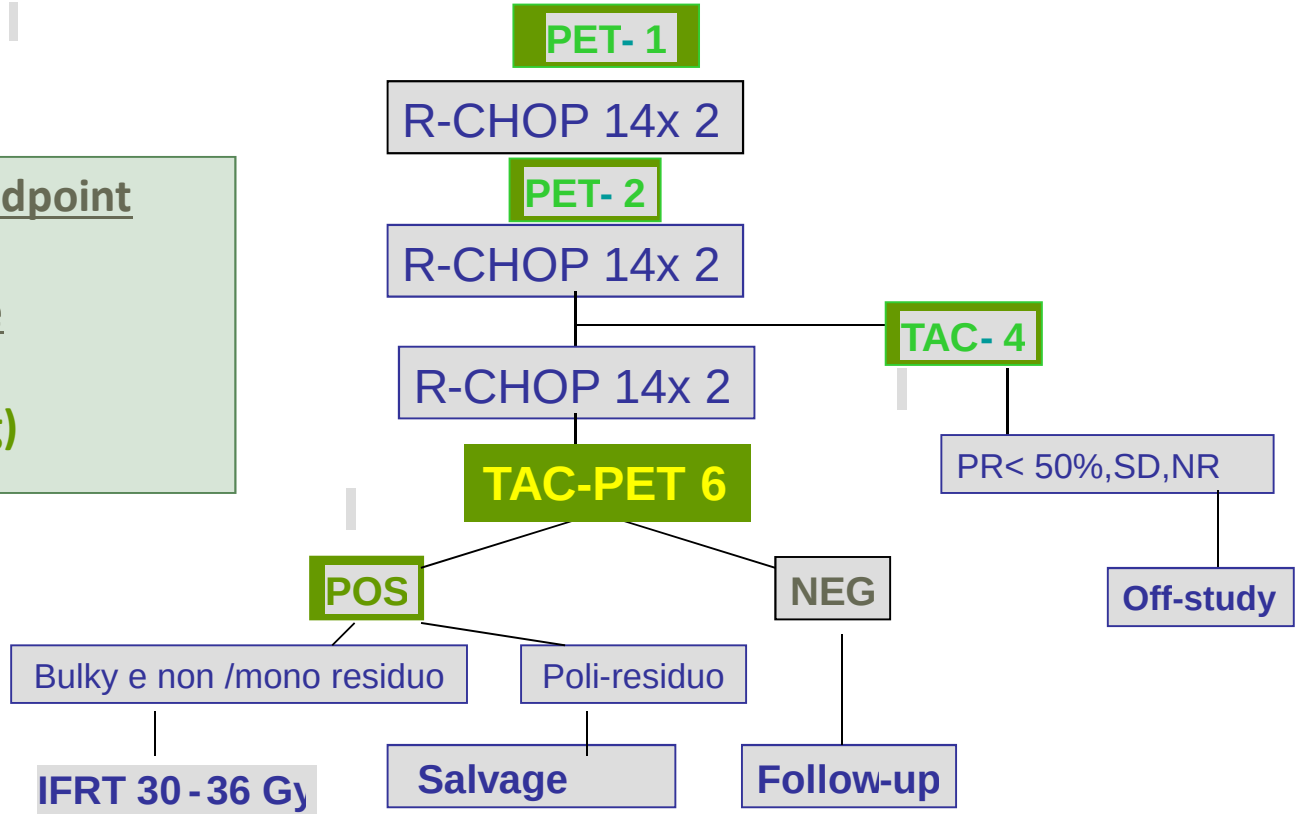
DLCL10

Prospective, multicentre phase II study with R-CHOP- 14 & consolidation PET–oriented radiotherapy in DLBCL patients with low risk profile according to age-adjusted IPI (0 with bulky or 1)

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

Primary endpoint
2-yrs PFS

Sample size
112 pts
(67 PET neg)



PI: MG Cabras , M Balzarotti - Coordinating Center : Cagliari

DLCL 10 – status on 31/08/2016

Authorized sites	40
Planned accrual	112
Current accrual	70
1° patient entered	02/01/2012

Pts registered	PET submitted for review	PET evaluated by reviewers so far	PET negative (5PS 1-2)	PET positive (5PS 3-5)
70	55	55	42	13

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 ***Maura Brugiatelli***
Massimo Federico

BACKGROUND AND RATIONALE

The standard treatment for patients with FL: initial therapy with R-CHOP combination followed by two-year maintenance with R.

Is this approach really needed for all patients with FL or some of them could benefit from a reduced intensity treatment achieving the same results in terms of outcome and survival?

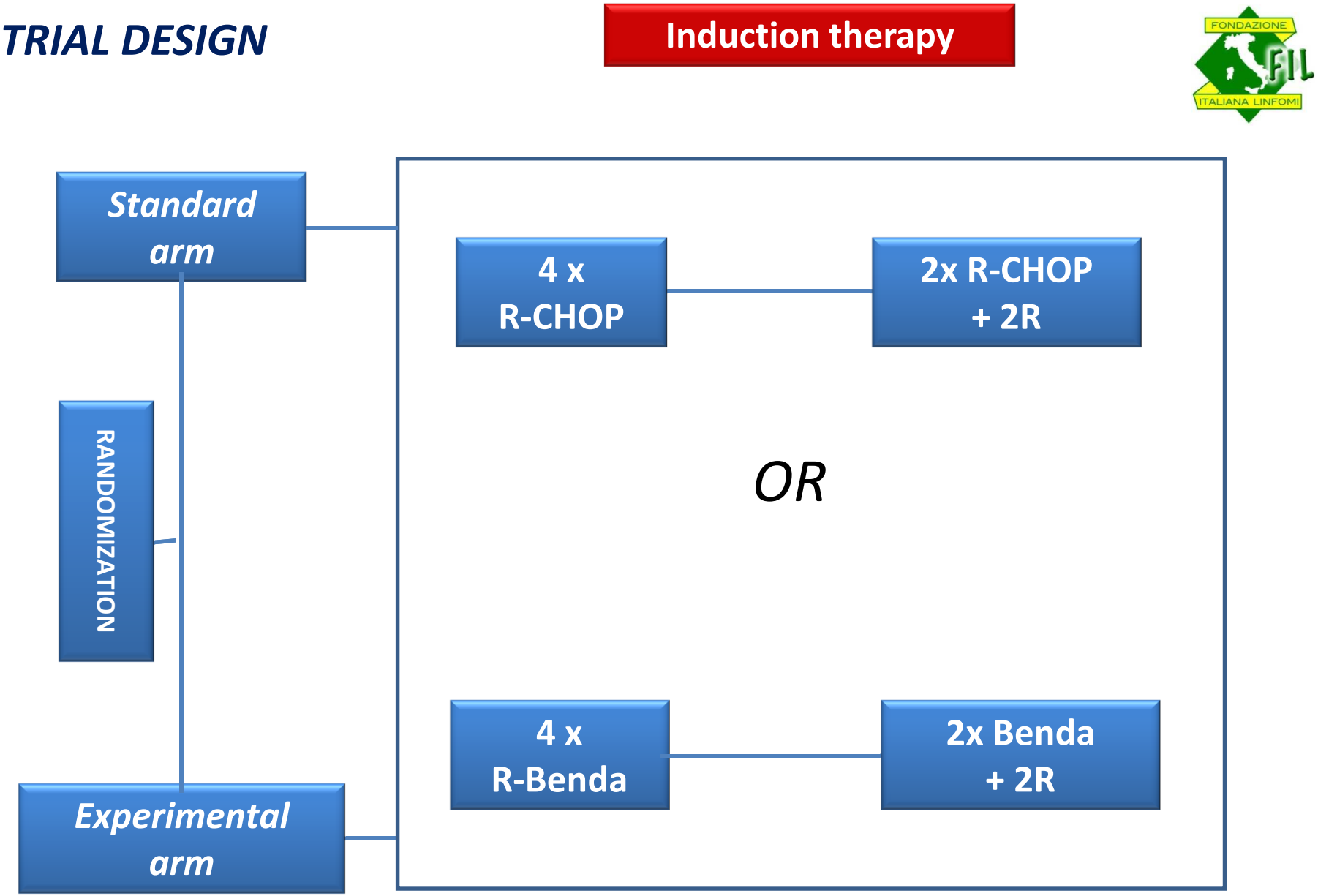
This question is of particular interest for newly diagnosed patients for whom maintenance does not affect OS.

PRIMARY OBJECTIVE

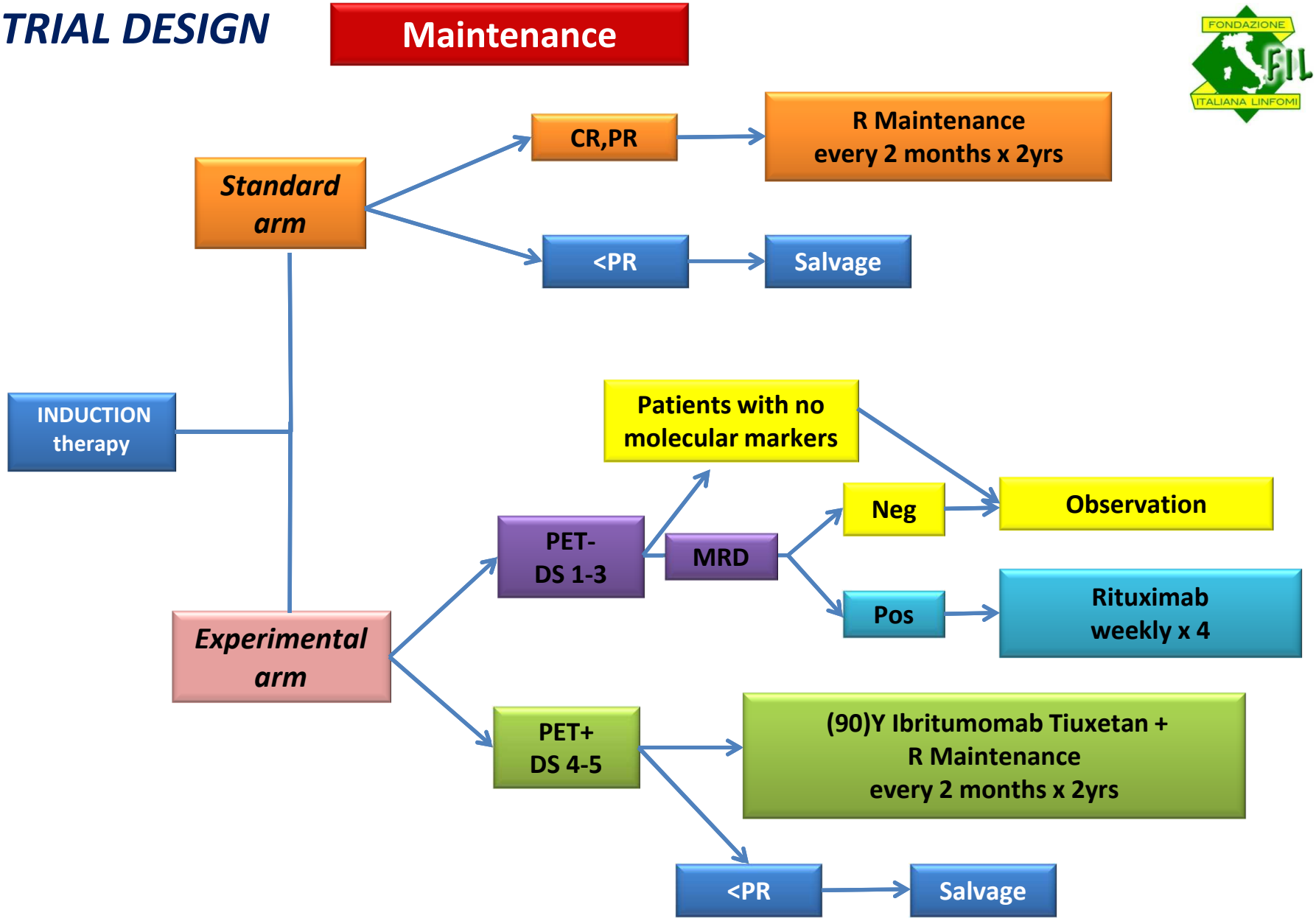
Evaluate whether

a **PET** and **MRD response-based maintenance** therapy is more effective in terms of PFS than a standard maintenance therapy with R in patients with untreated, advanced FL

TRIAL DESIGN



TRIAL DESIGN



FOLL12 STATISTICAL ASSUMPTIONS
SAMPLE SIZE

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

Expected events **210**

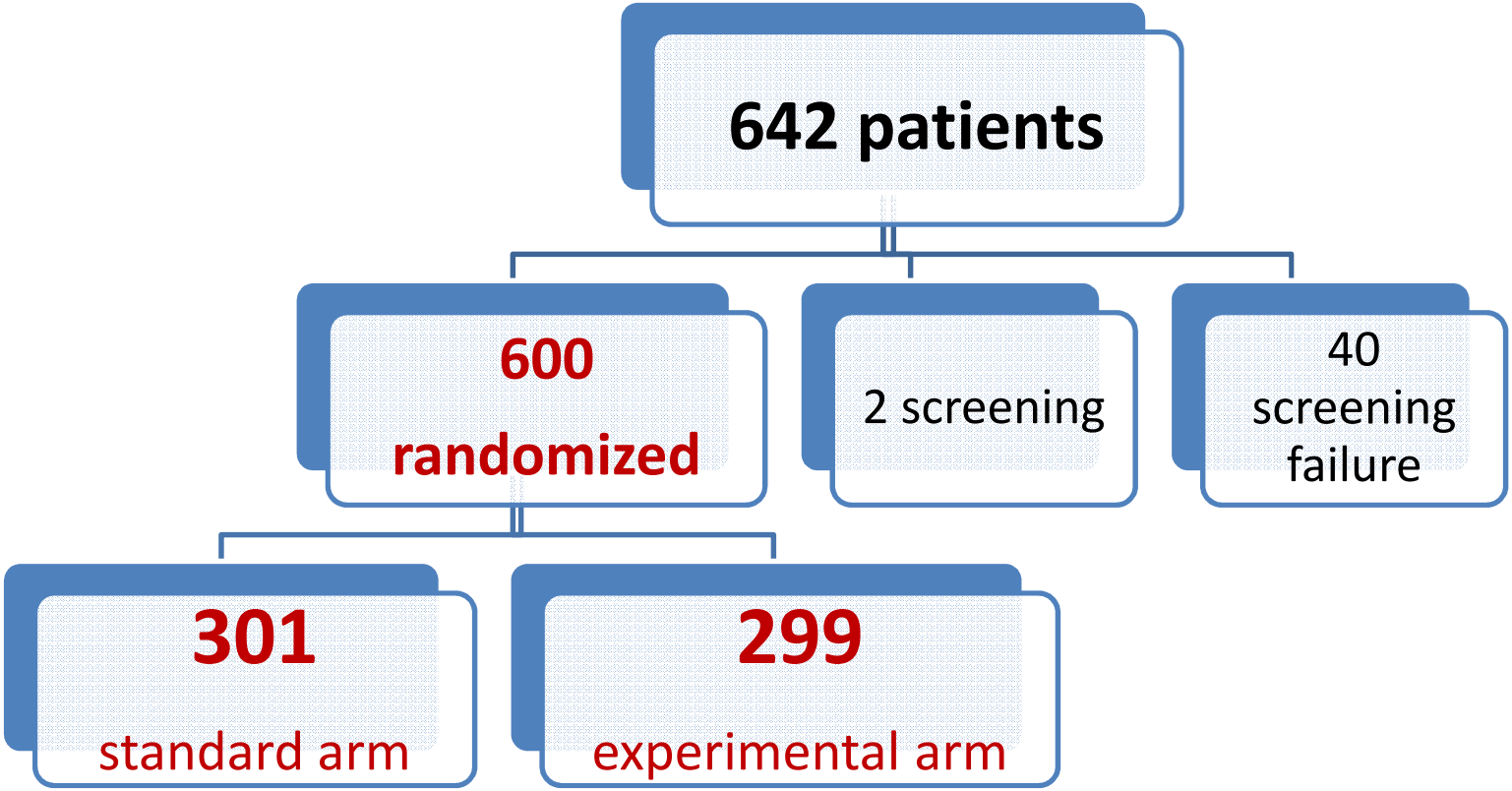
** consent retired, histological revision, concomitant neoplasia*

Two interim analysis, sequential design O'Brien-Flaming at 40% and 60% of the expected events.

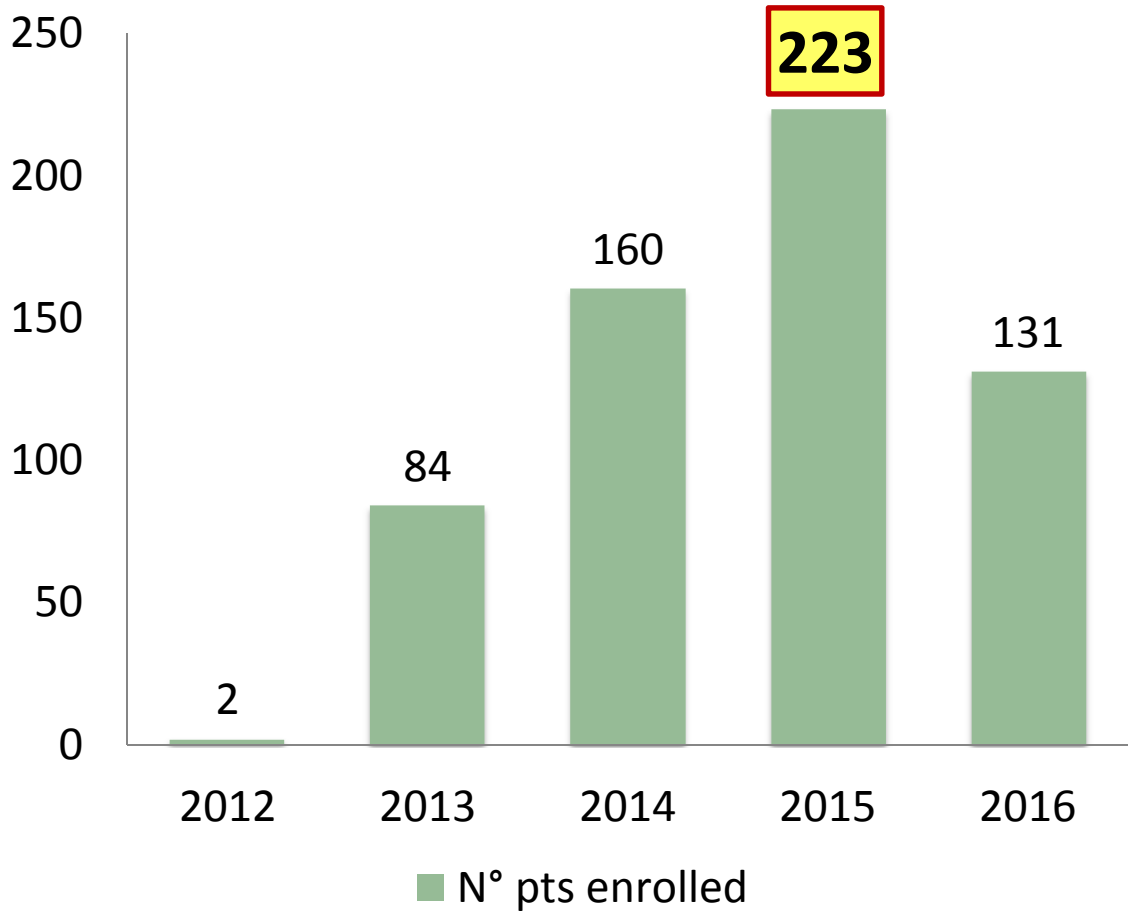
Accrual 4 years

Follow-up 3 years from the last accrued

FIL_FOLL12 ACCRUAL 15/09/16



ACCRUAL BY YEAR (UPDATED 15/09/2016)



PET REVIEW

429 end treatment PET

375 PET-

54 PET+

DS 4-5

AMENDMENT....WHY?

1. In the first 300 cases the percentage of PET + is around 13-14%, so it is reasonable to think that the PFS of the experimental arm can not be greater than that of the standard arm.

2. It is very likely, however, that the study can demonstrate unequivocally that the maintenance is not necessary in all patients, and this will determine a definite benefit in terms of reduced toxicity and of "saving" for the National Health System.

AMENDMENT….WHY?

NO MAINTENANCE for low risk

LESS TOXICITY

LESS COSTS

AMENDMENT

Phase III study, two arms randomized trial

non-inferiority design

Primary end-point: ***Progression Free Survival (PFS)***

Reference: PFS of 70% at 3 years with an inferior margin with HR = 1.31, who correspond at PFS of 63% at 3 years for the reference arm.

Than, if the PFS follow an exponential distribution, it's allowed a difference in PFS at 3 years less or equal -7% and the upper-bound of 95CI, between experimental and reference arm, will be greater of the specified margin of 1.31.

AMENDMENT

Non Inferiority trial

Error type I 5% one-sided

Power 80%

Accrual 5 years

Follow-up 3 years from the last accrued

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

A total information of 342 failures is planned under H_1, to give 80% power to demonstrate a non-inferiority between the two arms, with a an increased risk less than 1.309 in the PFS failure rate.