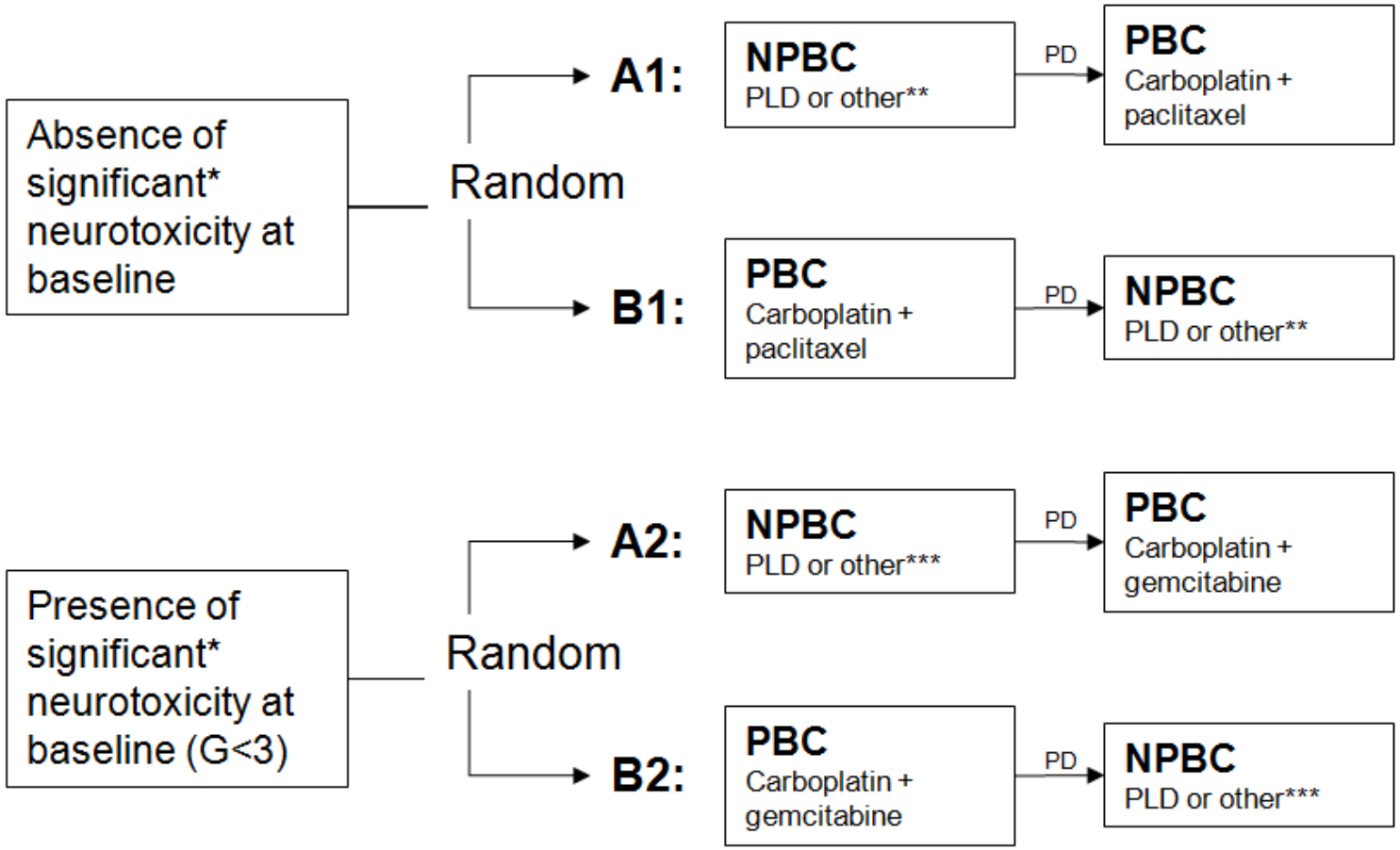
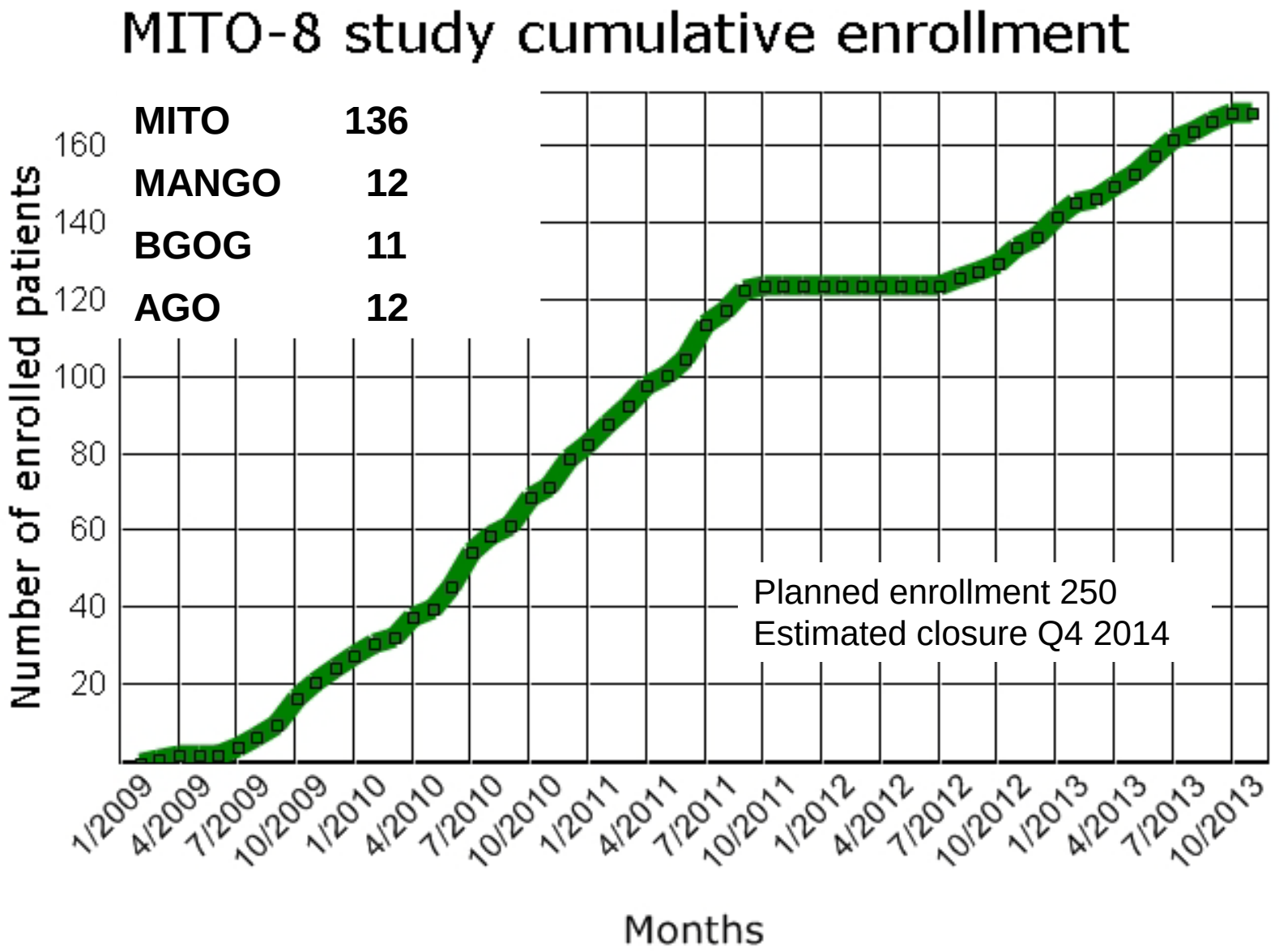
ENGOT Ov-1 Trial
MITO 8; AGO-OVAR 2.16
Study Design

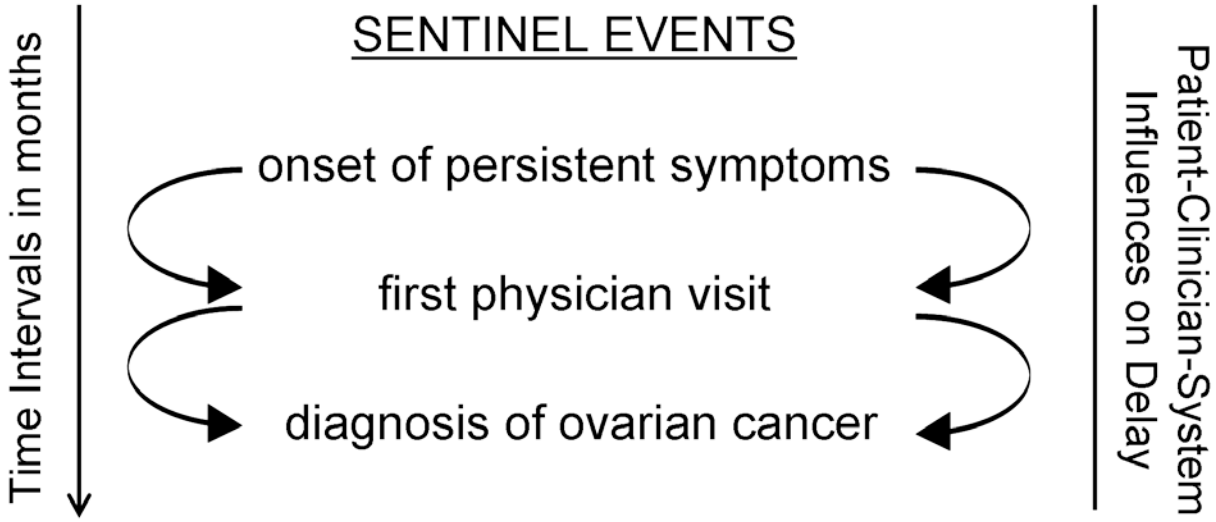


•The clinical significance of residual neurotoxicity at baseline assessment will be judged by the Investigator
** Topotecan or Gemcitabine or other drugs registered for the indication
*** Topotecan or other drugs registered for the indication

ENGOT Ov-1 Trial
MITO 8; AGO-OVAR 2.16
Recruitment 04/10/2013 n = 173



ENGOT Ov-12 Trial
MITO -12
Recruitment CLOSED 10/09/2013 n =695



Cooperative Group	Patients
MITO	**537**
MANGO (MITO 7 only)	**53**
BGOG	**33**
NOGGO	**72**

ENGOT Ov-17 Trial
MITO 16b; MANGO-OV2b
Study Design

- Ovarian Ca
- Platinum-sensitive
- Previous Bevacizumab
- ECOG 0-2
- Availability of samples for translational res.
- No Beva contraindications

R

ARM 1: 6 cycles

CBDCA AUC5 + PAC 175 mg/m2 q3w
or
CBDCA AUC4, d1 + GEM 1000mg /m2, d1&8 q3w
or
CBDCA AUC5+PLD 30mg/m2 q4w

ARM 2*: 6 cycles

CBDCA AUC5 + PAC 175 mg/m2 q3w
Plus bevacizumab** 15mg/kg q3w
or
CBDCA AUC4, d1 + GEM 1000mg /m2, d1&8 q3w
Plus bevacizumab 15mg/kg q3w
or
CBDCA AUC5+PLD 30mg/m2 q4w
Plus bevacizumab 10mg/kg q2w

*Patients without PD after 6 cycles of combined treatment will receive Bevacizumab maintenance until PD
**Bevacizumab will be provided by Roche ltd

ENGOT Ov-17 Trial
MITO 16b; MANGO-OV2b
Study Design

Statistical parameters:

- primary endpoint: PFS, defined as occurrence of progression or death, whichever comes first**. PFS is assessed by the local investigator**
- two-tailed significance level / alpha: 0.05
- power 90%
- median expected PFS in the control arm: **8 months**
- Hazard ratio to be detected: **0.67**
- median expected PFS in the experimental arm: **12 months**
- number of events required: **265**
- with **400 patients** to be recruited and an enrolment rate of 20 patients per month, the expected study duration should range from **24 to 26 months.**

MITO16b Status

Study Start Date: July 2013
Participating centers: 60
Approval from the Ethical Committee: 4
Active Centers: 2
Enrolling centers: 0
Patients enrolled: 0/400

GINECO: start December 2013
HECOG: submitted to EC
SAKK: submitted to EC

Hyperthermic intra-peritoneal chemotherapy (HIPEC) in Ovarian cancer recurrence: Randomized trial on Survival Evaluation PROTOCOL ID: HORSE – MITO 18 (NCT01539785)

EudraCT Number: *2012 -002872-15*
INSURANCE Number: *n. A.1201232799*
Power: *from h 24.00-09/09/2012 to h 24.00-09/05/2015*
Insurance Company: *Sindacato Lloyd's 1218 Newline*

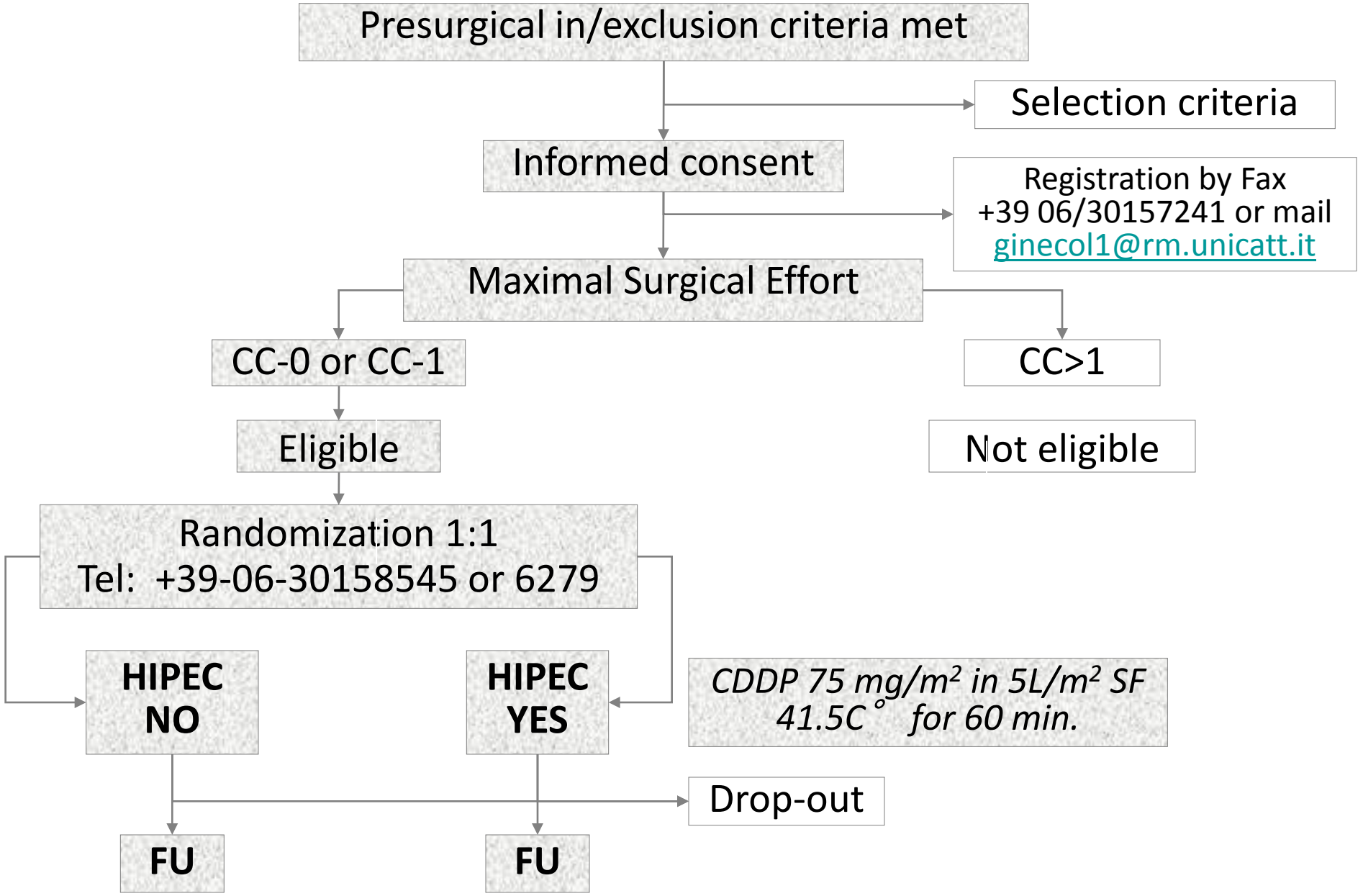
Inclusion/Exclusion Criteria

- First EOC recurrence, after ≥6 months from primary platinum based treatment, with measurable or evaluable disease (upwards of Ca125 for 2 consecutive assessments).
- Disease limited to the abdominal cavity with or without extraperitoneal spread considered resectable at i.o. evaluation

Objectives

- Primary: disease free survival
- Secondary: overall survival, morbidity and mortality
- Others: pattern of recurrence, complete cytoreduction rates, quality of life, systemic CHT within 5 weeks from HIPEC, stratifications

Study Design



Statistical Analysis

Assuming a median PFS in the control arm of 18 months (hazard ratio 0.5 on a total period of 36 months), it will be possible define a survival benefit in a period greater than or equal to 6 months (hazard ratio 0.66 on a total period of 36 months).

The sample needed to highlight this result with a power of 80% and an alpha-error of 0.05 (one-tailed) is of 144 patients (72 per arm), which becomes 158 patients (79 per arm) considering a dropout of 10%.

Status

Study Start Date: September 2012
Participating centers: 20
Approval from the Ethical Committee: 9
Active Centers: 8
Enrolling centers: 4
Patients enrolled: 25/158
Estimated Primary Completion Date: May 2015 (Final data collection date for primary outcome measure)

Interest from GEICO, KGOG

Contact: anna.fagotti@rm.unicatt.it