



INOVATYON



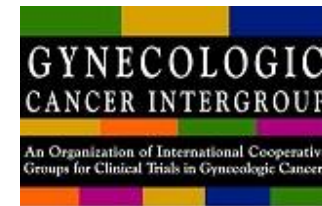
Phase III international, randomized study of **Trabectedin plus Pegylated Liposomal Doxorubicin (PLD)** versus **Carboplatin plus PLD** in patients with **relapsed ovarian cancer progressing within 6-12 months of last platinum**

- **Sponsor:** Mario Negri Institute, MaNGO group, Milan, Italy
- **PI:** Nicoletta Colombo, European Oncology Institute, Milan, Italy

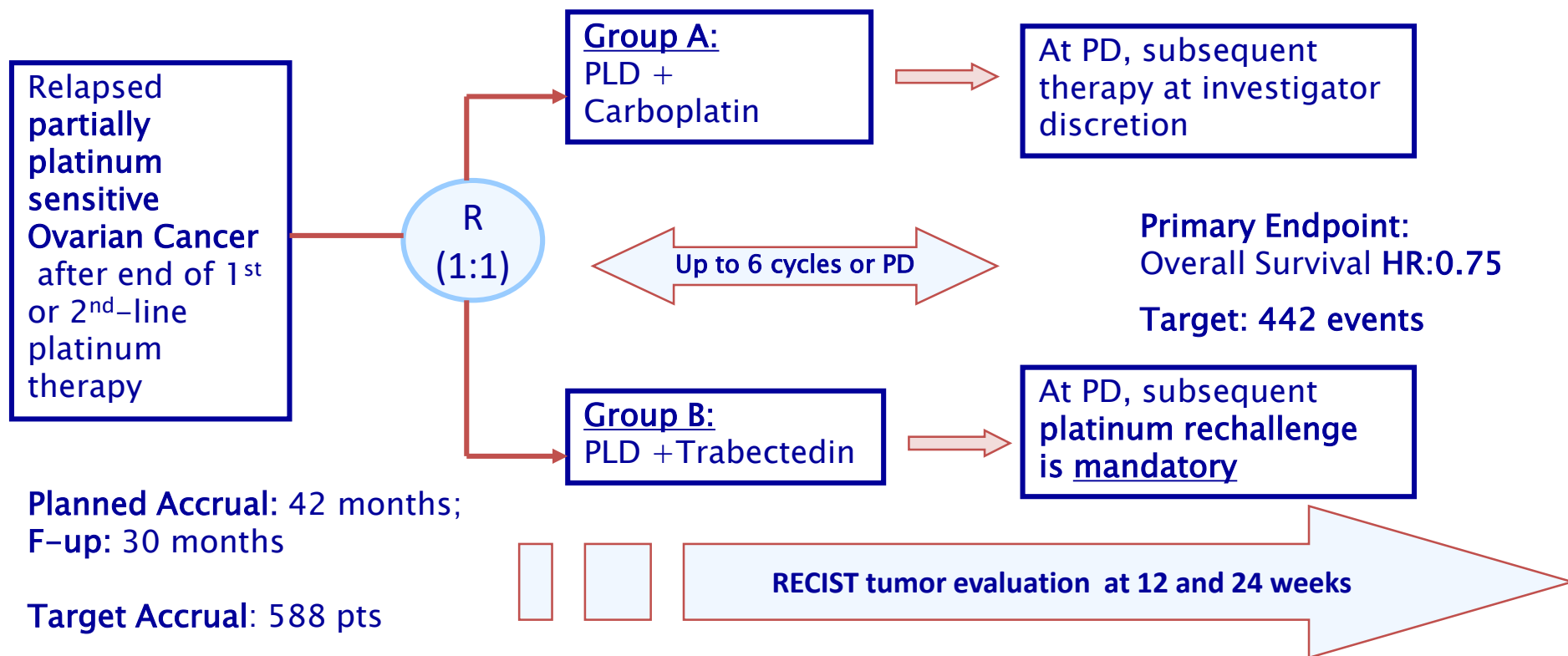
**Giuseppe Funari– XVI Assemblea MaNGO
Reggio Emilia, 22 Giugno 2019**



Grupo Español de Investigación en Cáncer de Ovario



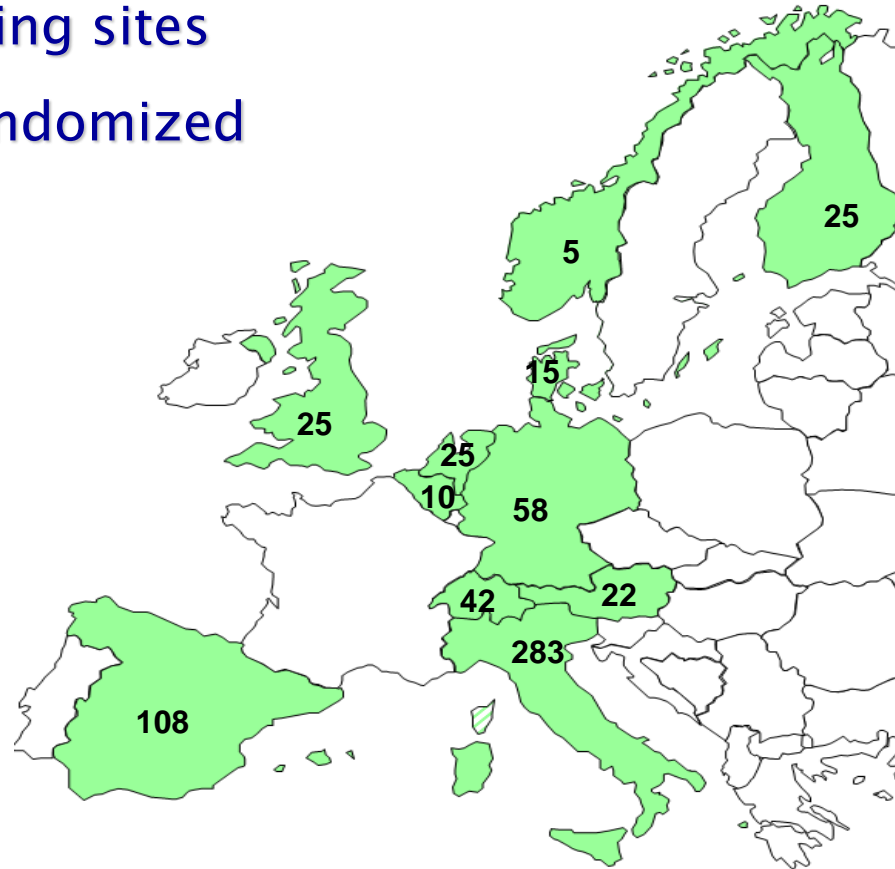
INOVATYON



Accrual

117 participating sites

618 patients randomized



Target sample size reached in September 2017

44 months of accrual

INTERIM ANALYSES & FINAL ANALYSES

Second interim analysis



- AIMS: To test superiority and to evaluate trial early closure for efficacy
- WHEN: September 2018, two thirds of the expected events (about 295 deaths)
- HOW: The trial would have been stopped in case of clear OS advantage in the experimental arm, setting the significance level at 0.014

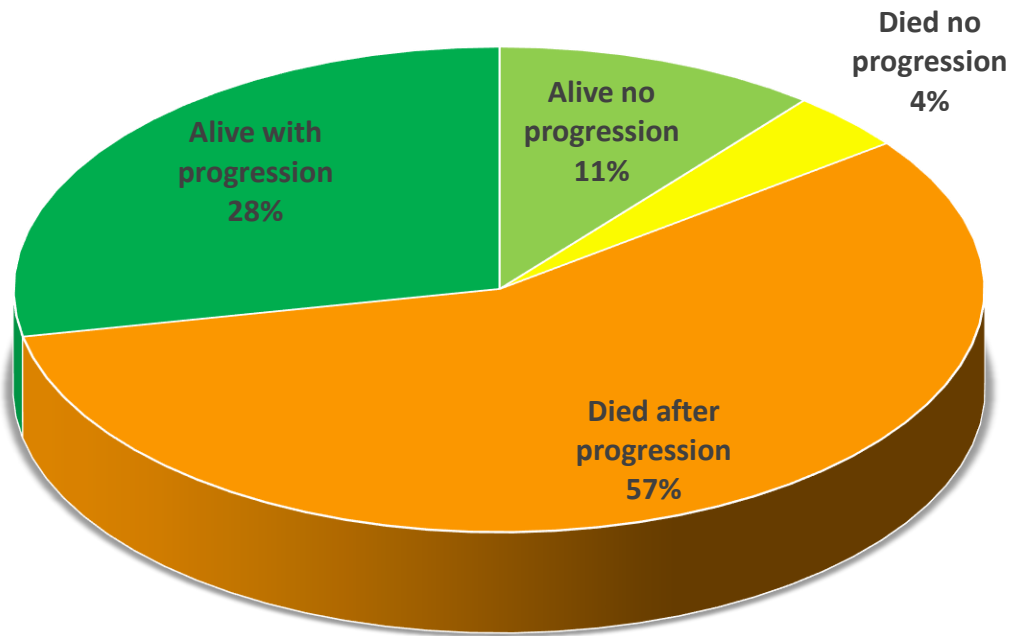
Second interim analysis

Conclusions



- Results did not meet the efficacy criteria for early closure of the trial
- The combination with trabectedin resulted in higher toxicity. However DSMC members deemed that continuing the trial would not have harmed any patient, as the safety profile of trabectedin was in line with what was expected according to Reference Safety Information

DSMC members agreed to continue the follow-up of the trial as planned in the protocol to obtain final result of efficacy



As of June 2019:

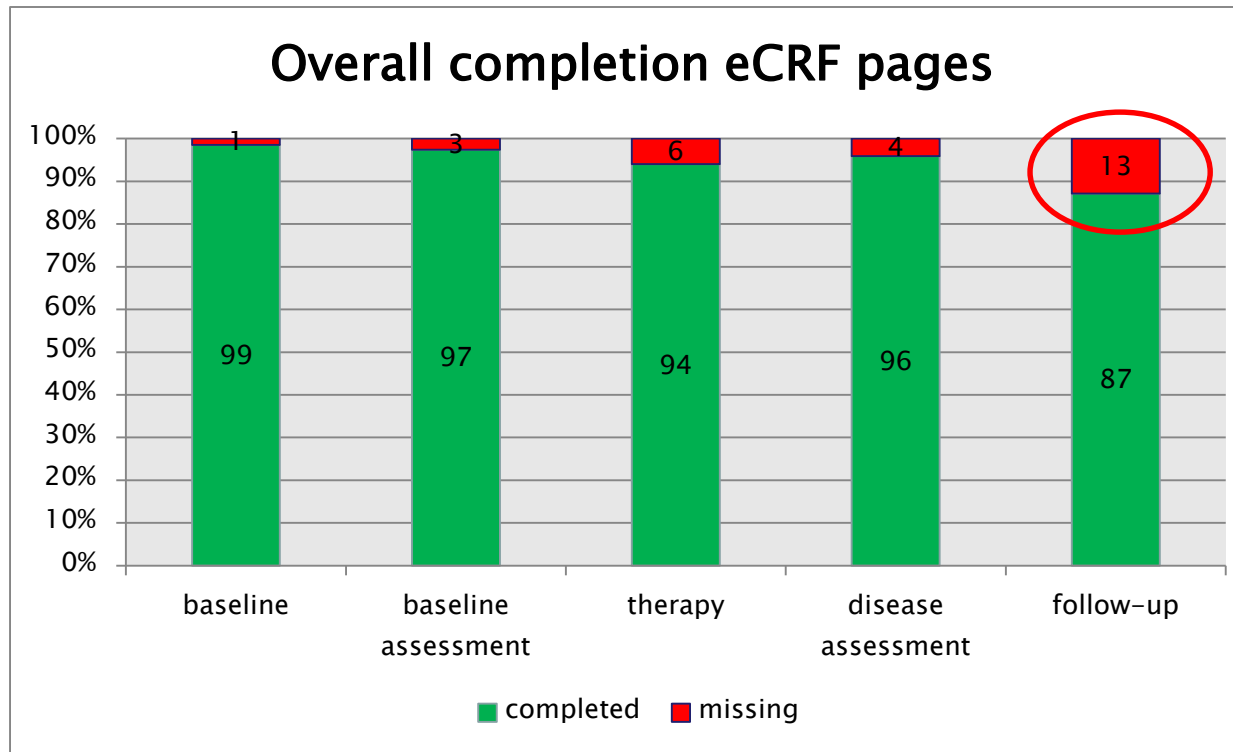
66 Alive without progression
 172 Alive with progression
 24 Died without progression
 349 Died after progression

85% of overall survival events reached

373 Died → **442 expected for Final analysis**

The final analysis is planned for June 2020

eCRF overall completion



Update of follow up forms is crucial to collect the events needed for final analysis

INOVATYON Germline BRCA status



BRCA1 and BRCA2 unknown	270 (44%)
BRCA1 and BRCA 2 missing	62 (10%)
BRCA1 and BRCA 2 known	286 (46%)

BRCA1 mutated	42/286 (15%)
BRCA2 mutated	21/286 (7%)

Pt with at least one BRCA mutation	62
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For unknown data

We are still chasing information to reduce the unknown and missing data as much as possible

TRANSLATIONAL STUDY

Only for a few italian sites

Circulating tumor DNA (ctDNA) to monitor the effects of temporal heterogeneity on prognosis of patients enrolled in the INOVATYON clinical trial: a prospective, multicentre study



To investigate the mutations of:

BRCA1 , BRCA2, TP53, ATM, ATR, EMSY, XPG, XPF, TOP2A,
MLH1

PIK3CA , EGFR, DICER1, FN1, ARID1A, TGFB3, IGF1R, VCAM1, COL3A1,
CDH1, CTNNB1, ZEB1

in liquid biopsies

Before treatment, at the end of treatment and at relapse

Traslational study Update

Centri	Pazienti traslazionale	Braccio di trattamento
Ospedale Santa Chiara Pisa - Gadducci	4	1 Trabectedina + PLD 3 Carboplatino + PLD
A.O. Spedali Civili di Brescia - Tognon	2	1 Trabectedina + PLD 1 Carboplatino + PLD
Istituto Oncologico Veneto - Padova - Nicoletto	4	1 Trabectedina + PLD 3 Carboplatino + PLD
Azienda Ospedaliera S. Croce e Carle – Cuneo - Di Costanzo	1	Carboplatino + PLD
Nuovo Ospedale di Prato S. Stefano - Prato - Zafarana	2	1 Trabectedina + PLD 1 Carboplatino + PLD
Alessandria - Fusco	1	Trabectedina + PLD
IRCCS Policlinico S. Matteo - Pavia - Babilonti	1	Trabectedina + PLD
Policlinico S.Orsola Malpighi - Bologna - Zamagni	1	Carboplatino + PLD
IRCCS - Arcispedale S. Maria Nuova Reggio Emilia - Bologna	3	3 Trabectedina + PLD
IRST Meldola e Cesena - De Giorgi	1	Carboplatino + PLD
totale pazienti	20	Tot Carbo + PLD: 11 Tot Trabe + PLD: 9

Thanks for your collaboration in **INOVATYON study!**

Mario Negri Institute study staff:

Roldano Fossati, Elena Biagioli (Responsible)

Giuseppe Funari (Study Coordinator)

Eliana Rulli (Study Statistician)

Fabio Galli (Data quality Verifier)

Clara Caudana (Software helpdesk)

Davide Poli (Responsible for the monitoring activities in Italy)

Francesca Scellato (Clinical Monitor)

Paola Tonto (Clinical Monitor)