MaNGO

XVII ASSEMBLEA MaNGO

MILANO

16 OTTOBRE 2020

Con il Patrocinio di:

SIGO SOCIETA' ITALIANA DI GINECOLOGIA E OSTETRICIA

SIOG SOCIETÀ ITALIANA ONCOLOGIA GINECOLOGICA

ricogi Italian Group for Gynecologic Cancer Oncology Clinical Trials

ACTO

Collaborazioni ENGOT GCIG attive

Roldano Fossati **Giuseppe Funari**

Istituto di Ricerche Farmacologiche Mario Negri, Milano

MaNGO
Mario Negri Gynecologic Oncology

1. **ENGOT e GCIG sono reti intergruppo di collaborazione internazionale**
2. **GCIG si fonda formalmente nel 1997 e ENGOT (ESGO inside) nel 2007**
3. **ENGOT ha caratura Europea, GCIG coinvolge anche gruppi americani, asiatici e australiani**
4. **GCIG si finanzia con quote annuali di iscrizione e donazioni industria, ENGOT con quote per studio e donazioni industria**
5. **Entrambi prevedono incontri semestrali e propongono iniziative per la formazione dei futuri ricercatori clinici**

ENGOT e GCIG in breve

1. Gli studi vengono proposti in sede ENGOT e, solo in alcuni casi, discussi collegialmente.
2. Il gruppo leader chiede quali gruppi collaborativi siano interessati e stima quanti centri possano aggregarsi
3. Le proposte vengono discusse nel CTS di MaNGO
4. I centri afferenti al CTS spesso saturano il numero dei centri partecipanti messi a disposizione dal gruppo leader
5. Le CRO incaricate, in caso di studi ENGOT modello C si fanno carico di tutti gli aspetti operativi
6. In caso di studi ENGOT A e B, MaNGO si fa carico della gestione del trial in Italia

.

MaNGO
Mario Negri Gynecologic Oncology

Come si attuano le collaborazioni?

MaNGO
Mario Negri Gynecologic Oncology

carcinoma ovarico

Ovaio 1° linea

- ENGOT ov39 - IMaGYN
- ENGOT ov33 - TRUST
- ENGOT ov46 - DUO-O
- ENGOT ov43

MaNGO
Mario Negri Gynecologic Oncology

Ovaio recidiva platino sensibile

- ENGOT ov38 - OReO
- ENGOT ov41 - ANITA
- ENGOT ov53 - VITALIA
- ENGOT ov42 - AVATAR

Ovaio recidiva platino resistente

- ENGOT ov50
- ENGOT ov55 - MIRASOL
- ENGOT ov51 - NiTChe
- ENGOT ov34 - ovar 2.29
- EPIK-O

- ENGOT ov39 - IMaGYN
- ENGOT ov33 - TRUST
- ENGOT ov46 - DUO-O
- ENGOT ov43

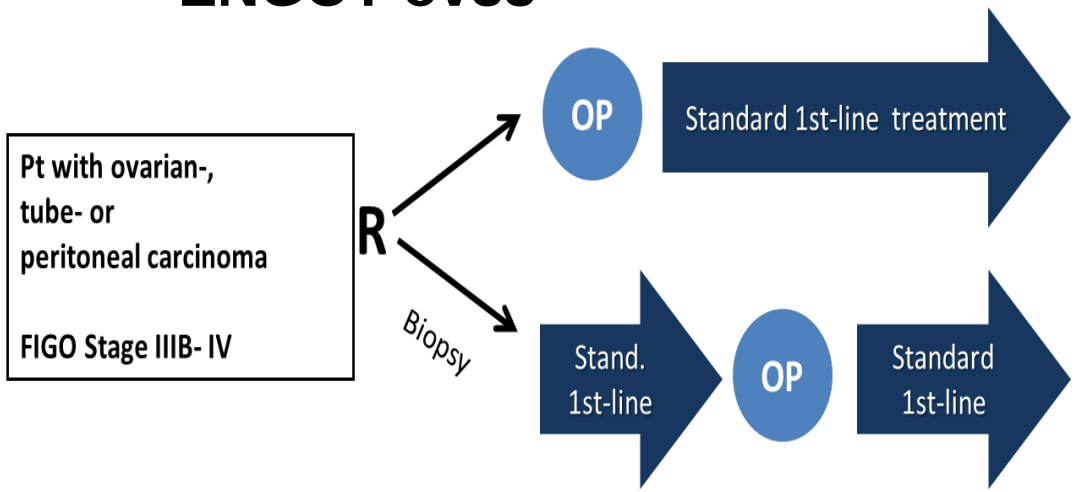
MaNGO
Mario Negri Gynecologic Oncology

- OBIETTIVI:
  - Immunoterapia (IO) in aggiunta alla chemioterapia – 1300 pazienti
  - Efficacia della strategia neoadiuvante in centri di eccellenza chirurgica - 800 pazienti
  - IO oppure IO+PARP in aggiunta alla chemioterapia+bev - 1100 pazienti wtBRCA
  - IO oppure IO+PARP in aggiunta alla chemioterapia±bev -1100 pazienti wtBRCA

TRUST – Trial on Radical Upfront Surgical Therapy

AGO-OVAR OP.7 TRUST ENGOT-ov33

ENGOT model A
Sponsor AGO Study Group



No. Pts.:	n = 726 planned / 797 randomized
First Patient In:	22-Aug-2016
Last Patient In:	07-Jun-2019
Translational Research:	Currently, collection of FFPE tumour block from either primary debulking surgery or diagnostic laparoscopy / biopsy and interval debulking surgery prioritized
Primary OS analysis:	**2024**

Country	Sites (20 SIVs / 20 active)	Group	PI	# pts screened	# pts randomized	# pts eligible*
	Berlin Charité	AGO	Sehouli, J., Muallem M., Chekerov R.	153	122	**118**
	Essen KEM	AGO	Heitz, F., Harter P., du Bois A.	358	118	**118**
	Düsseldorf, KWD	AGO	Lampe, B.	139	103	**101**
	Tübingen UFK	AGO	Krämer, B., Brucker S., Kommoss S., Taran F-A.	252	104	**97**
	München LMU	AGO	Burges, A., Trillsch F.; Mahner S.	163	53	**48**
	London, Imperial Hospital	single site / AGO	Fotopoulou, C.	92	45	**45**
	Milan, IEO	MaNGO	Aletti, G.	46ǂ	45	**45**
	Hamburg UKE	AGO	Schmalfeldt, B.	94	38	**36**
	Dresden UFK	AGO	Wimberger, P.	57	32	**30**
	München r.d.I.	AGO	Bronger, H.	36	23	**23**
	Stockholm, Karolinska	NSGO	Falconer, H.	44	18	**18**
	Paris, HEGP	GINECO	Lecuru, F.	42	18	**17**
	Milan, INT	single site / MaNGO	Raspagliesi, F.	92	15	**15**
	Copenhagen, Rigshospital	NSGO	Mosgaard, B.J.	73	15	**15**
	Naples, INT	single site / MaNGO	Greggi, S.	48	13	**12**
	Bordeaux, Institut Bergonié	GINECO	Guyon, F.	11	11	**11**
	Lund, Skane University	NSGO	Kannisto, P.	33	9	**9**
	New York, MSKCC	single site / AGO	Chi, D.	52	8	**8**
	Wien, UFK	Single site / AGO	Reinthaller, A.; Grimm, C.	5	5	**5**
	Villejuif, Inst Gustave Roussy	GINECO	Gouy, S.	2	2	**2**
			TOTAL	**1792**	**797**	**773**

* Status of December 4, 2018 (preliminary information; eligibility check via QA Board is ongoing); ǂ patient list was provided, blinded screening log needs to be provided

AGO-OVAR 23 / ENGOT-ov46
DUO-O

Olaparib and Durvalumab in addition to SoC in newly diagnosed, advanced, ovarian cancer patients

ENGOT model C; Sponsor Astra Zeneca

BRCAm cohort was closed for recruitment in Nov 2019

- Newly diagnosed advanced high grade epithelial OvC stage III-IV
- Primary surgery or interval debulking surgery (IDS)
- N~1254

Single arm

Olaparib 300mg BD (24 months)

1:1:1 n= 1104

Non-BRCAm

Arm 1 (SOC)
- CTX 6 cycles q3wk
- Bevacizumab 15mg/kg q3wk (15 months)
- Durvalumab Placebo IV q3wk (24 months)
- Olaparib placebo BD (24 months)

Arm 2
- CTX 6 cycles q3wk
- Bevacizumab 15mg/kg q3wk (15 months)
- Durvalumab IV q3wk (24 months)
- Olaparib Placebo tablets BD (24 months)

Arm 3
- CTX 6 cycles q3wk
- Bevacizumab 15mg/kg q3wk (15 months)
- Durvalumab IV q3wk (24 months)
- Olaparib 300mg BD (24 months)

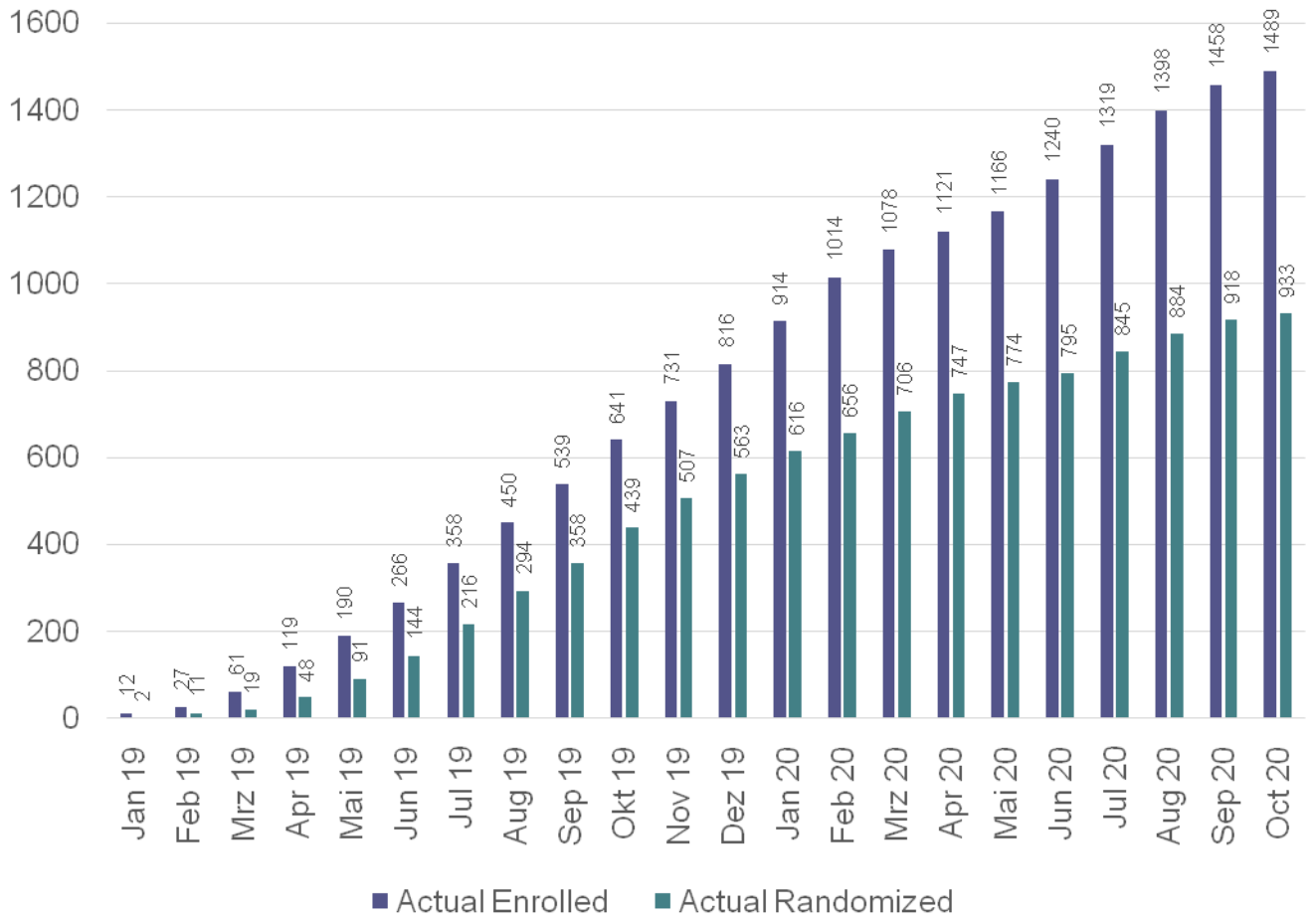
Stratification:
1) No residual macroscopic disease vs. residual or IDS
2) Region: North America; EU; RoW

★ Tumour sample from primary surgery or biopsy to be provided for central BRCA testing

DUO-O Study / AGO-OVAR 23
ENGOT-ov46

Enrolment / Randomization
(Status 7th Oct 2020)

Group	Nts enrolled	pts random.
AGO	401	231
GOG-F	188	124
JGOG	117	84
KGOG	113	84
GEICO	96	66
MITO	94	65
TRSGO	100	58
NSGO	54	35
GINECO	70	29
MaNGO	44	29
PGOG	42	27
AGO-Au	34	24
BGOG	23	15
PMHC	17	11



933 patients randomized

Completion of enrollment estimated byApril 2021

ENGOT-ov43:
Pembro and Olaparib in first-line OC

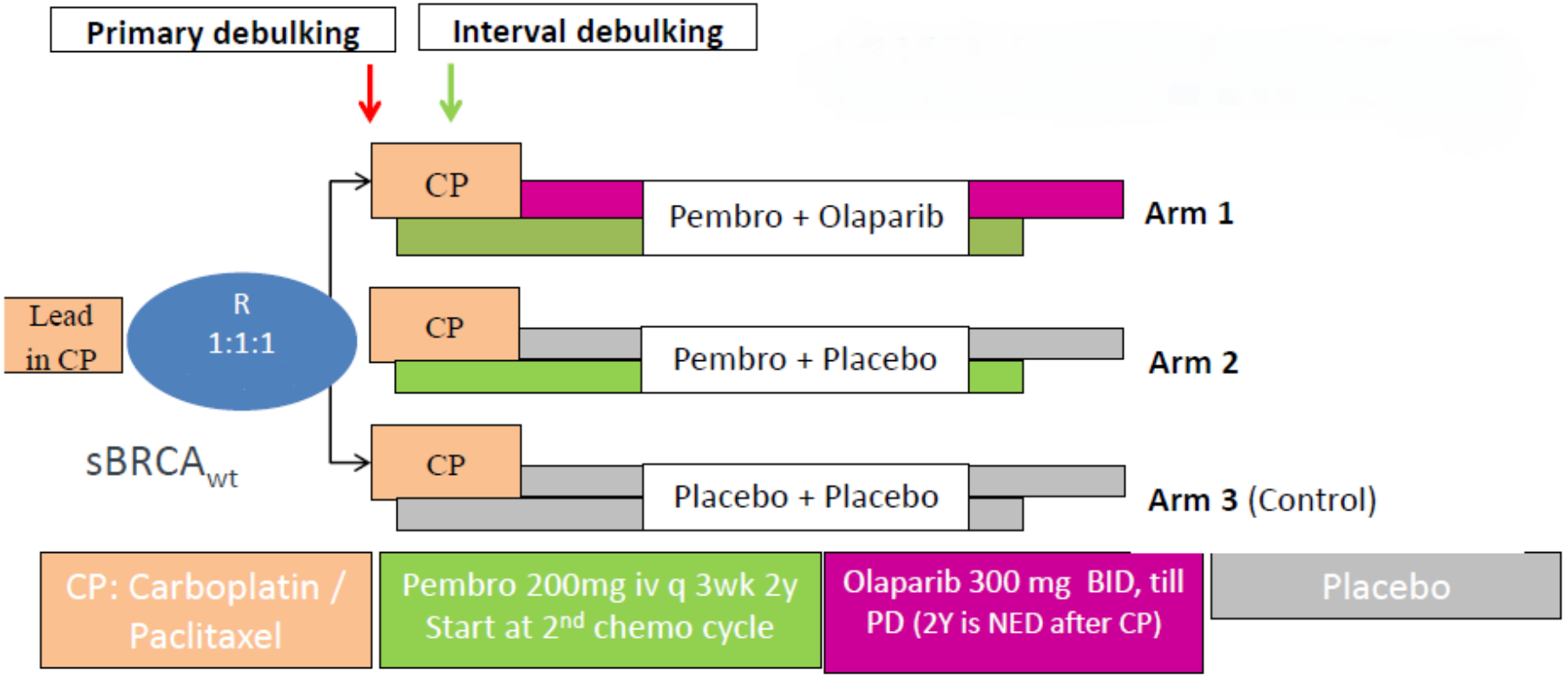
STUDY DESIGN

Trial setting: **Ovary/newly diagnosed**
Sponsor(s): **MSD**
Planned No. of patients: **1086**
FPI: **expected Q4 2018**
Co-primary Endpoints: **PFS (by PI) and OS**

First biopsy for somatic BRCA testing (taken at PDS or laparoscopy or core,…)

Randomization before 2nd chemo cycle if not somatic mutated in BRCA

Stratification: 1. Bev use 2. PDS R0; PDS R>0; NACT->IDS
3. PD-L1 status (CPS < or >= 10)



Bevacizumab allowed; to be specified in advance; randomization to be stratified by use of bev or not

ITALIAN METRICS

Commitment for Italy
78 patients

Enrollment Metrics	14OCT2020
Total Screened	158
In Screening	8
Screened Failed	70
Total Randomized	**80**
Discontinued	**19**

MaNGO sites

Investigator	Screenati	SF/lead in Failure	Randomiz.
COLOMBO	26	11	11
ARDIZZOIA	6	3	3
ZOLA	13	7	5
CONTE	15	5	10
	60	26	**29**

Current global metrics (as of Oct 20)

N = 1086
FPI = 30 Jan 2019
LPI = 30 Dec 2020

Country	Total Screened	In Screening	In Lead-in	Total Randomized	Screened Failed
BGOG	143	3	1	79	60
CEEGOG	200	3	8	99	90
GEICO	103	0	3	60	40
GINECO	31	1	0	12	18
NOGGO	12	2	3	3	4
ISGO	85	2	2	44	37
MaNGO/MITO	158	3	5	80	70
PGOG	76	4	2	36	34
TRSGOG	132	9	14	54	55
ENGOT	940	27	38	467	408
GOG-F	92	11	10	37	34
GOTIC	121	4	7	66	44
KGOG	103	1	4	55	43
PMHC	46	3	0	23	20
Taiwan	83	0	1	56	26
Australia	12	0	0	5	7
Brazil	43	6	3	12	22
Chile	72	5	5	22	40
Colombia	39	0	1	22	16
Russia	120	3	2	55	60
South Africa	38	2	1	15	20
OTHER	769	35	34	368	332
TOTAL	1709	62	72	835	740

Ovaio 1° linea

- ENGOT ov39 - IMaGYN
- ENGOT ov33 - TRUST
- ENGOT ov46 - DUO-O
- ENGOT ov43

MaNGO
Mario Negri Gynecologic Oncology

Ovaio recidiva platino sensibile

- **ENGOT ov38 - OReO**
- **ENGOT ov53 - VITALIA**
- **ENGOT ov42 - AVATAR**
- **ENGOT ov41 - ANITA**

Ovaio recidiva platino resistente

- ENGOT ov50
- ENGOT ov55 - MIRASOL
- ENGOT ov51 - NiTChe
- ENGOT ov34 - ovar 2.29
- EPIK-O

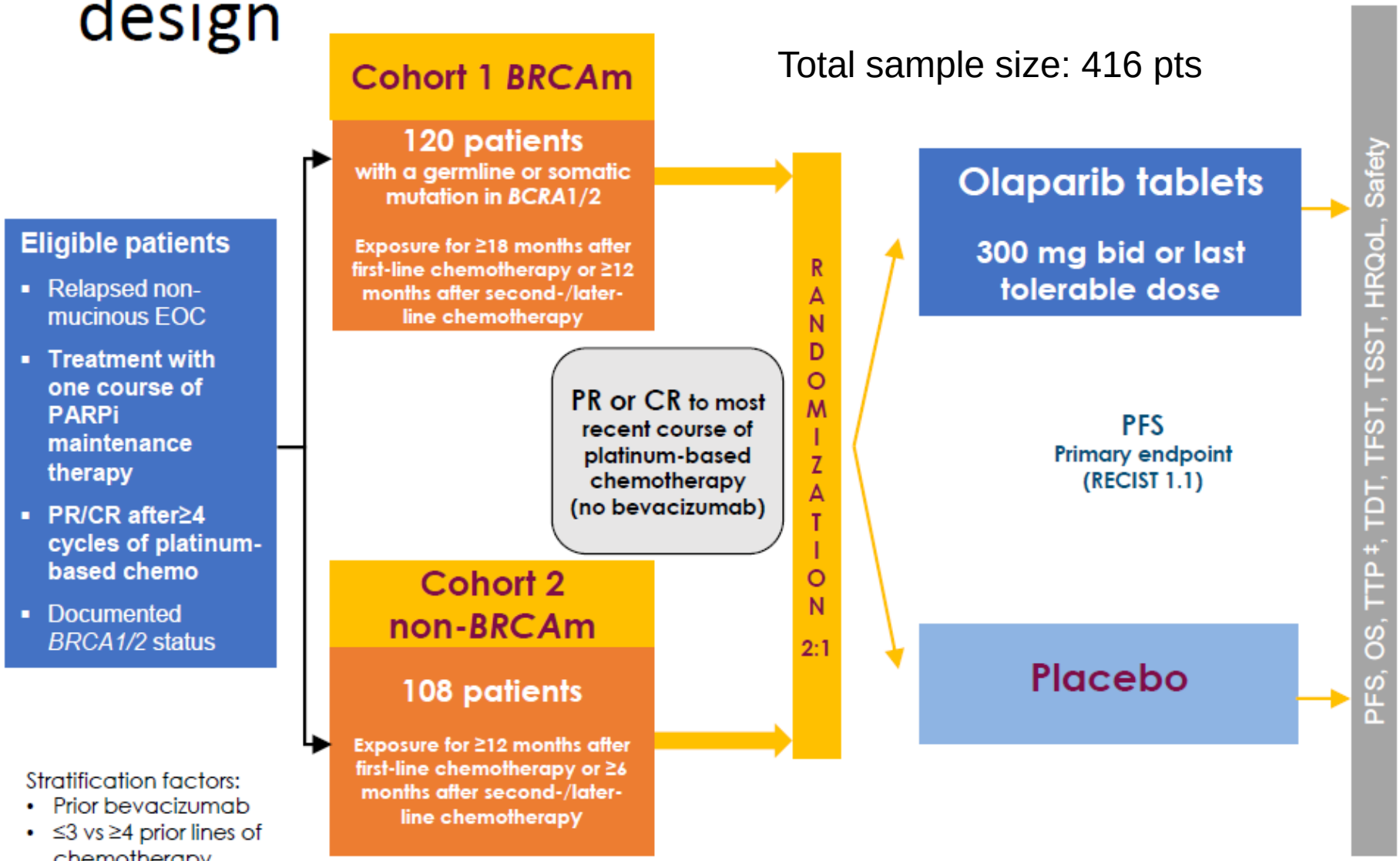
- ENGOT ov38 - OReO
- ENGOT ov53 - VITALIA
- ENGOT ov42 – AVATAR
- ENGOT ov41 - ANITA

MaNGO
Mario Negri Gynecologic Oncology

- OBIETTIVI:
  - Utilità di mantenere PARPi oltre una progressione occorsa durante PARPi – 230 pazienti
  - Efficacia di IO cellulare attiva in aggiunta a terapia standard - 800 pazienti
  - Efficacia di IO+PARPi+bev oppure PARPi+bev in confronto con chemio+bev - 423 paz
  - Efficacia di IO in aggiunta a Chemio+PARPi - 400 pazienti

ENGOT Ov38/OReO

OReO design



ENGOT Model C; Lead Group GINECO

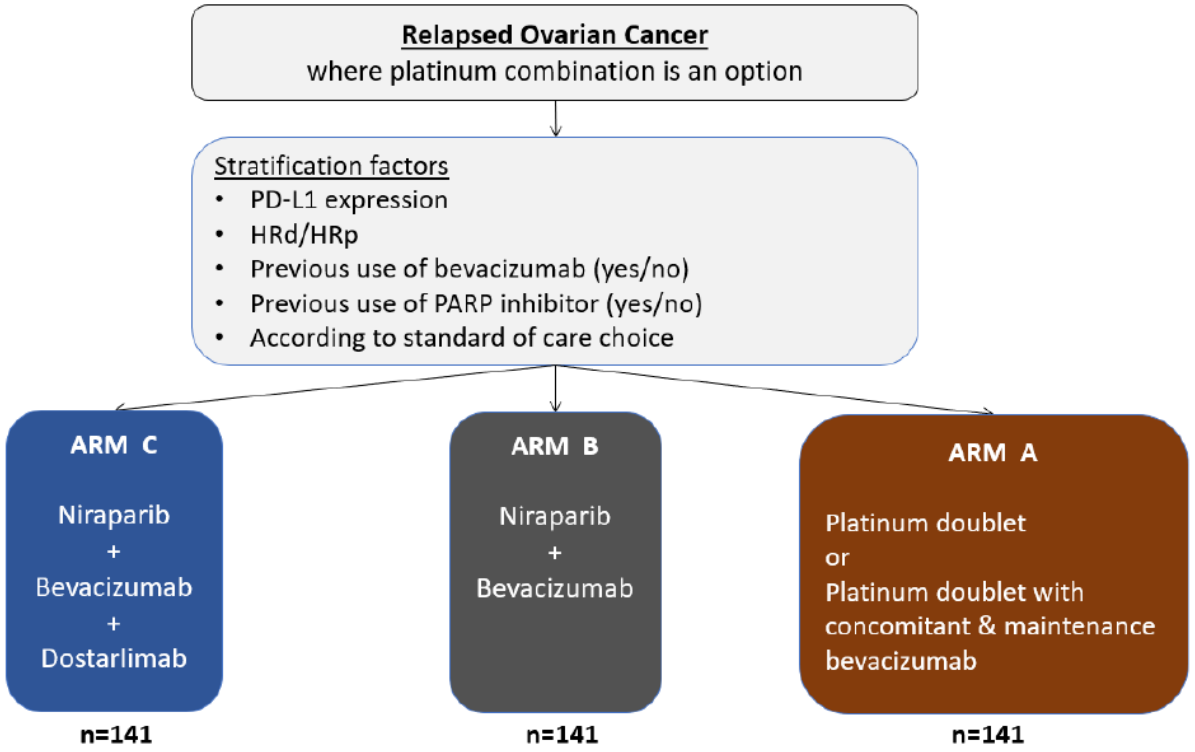
Recruitment status (28th Sep):

ENGOT/GCIG	Country	Sites Initiated	Closed Sites	Sites Active (1 patient screened at least)	Subjects Screened	Subjects in Screening	Subjects Screen Failed	Subjects Randomized	Subjects Withdrawn	# BRCA Positive Subjects Randomized	# BRCA Negative Subjects Randomized
BGOG	Belgium	3	0	2	7	0	1	6	3	3	3
PMC	Canada	3	0	2	3	0	2	1	1	0	1
NSGO	Denmark	3	0	3	5	0	0	5	5	3	2
	Norway	1	0	1	3	0	0	3	3	0	3
GINECO	France	20	1	19	66	0	12	54	44	33	21
AGO	Germany	20	7	12	43	0	19	24	19	9	15
ISGO	Israel	7	1	5	8	0	4	4	3	2	2
MANGO	Italy	7	0	4	12	0	3	9	9	8	1
MITO	Italy	11	0	8	44	2	7	35	21	21	14
PGOG	Poland	6	1	5	12	0	2	10	9	9	1
GEICO	Spain	13	0	13	59	0	15	44	32	23	21
NCRI	UK	8	0	7	12	0	5	7	5	1	6
	Totals	**102**	**10**	**81**	**274**	**2**	**70**	**202**	**154**	**112**	**90**

BRCA+	**96**	Missing BRCA-	**18**
BRCA-	**58**		

ENGOT-OV42/NSGO-AVATAR

A three-arm randomized study to evaluate the efficacy of niraparib-bevacizumab-dostarlimab triplet combination against niraparib-bevacizumab doublet combination and against standard of care therapy in Women with relapsed ovarian cancer where platinum combination therapy is an option.



ENGOT model: A
Status: Not yet recruiting
Planned number of patients: 423

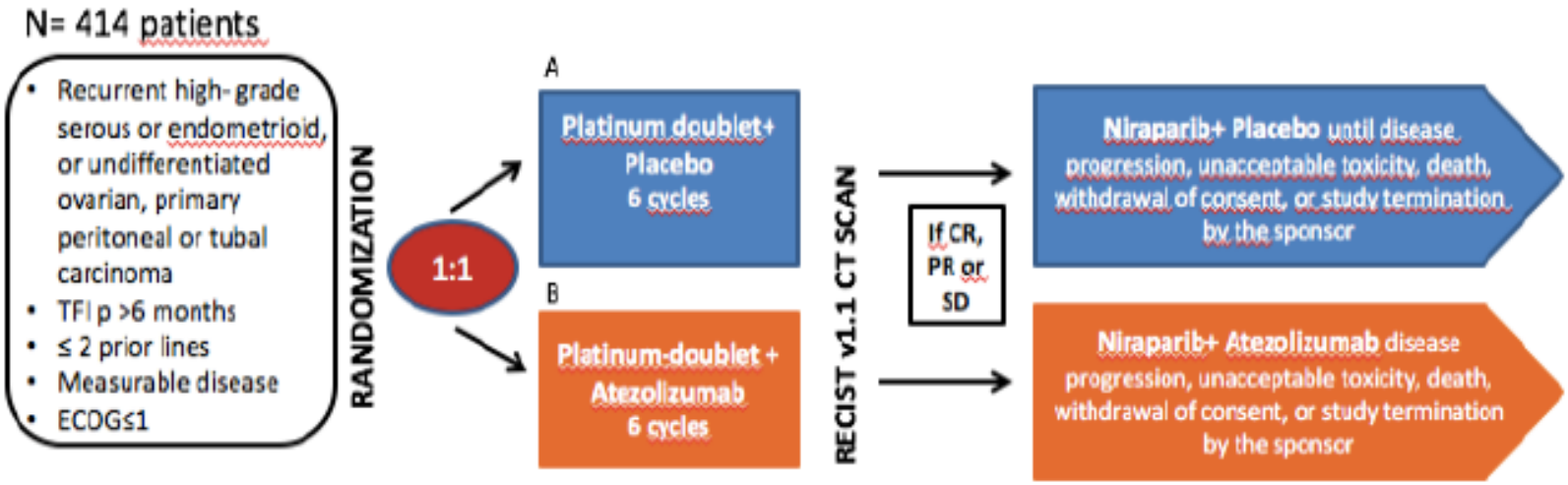
Sponsor: NSGO-CTU
NSGO-CTU Lead PI: Mansoor Mirza
NSGO-CTU PM : Nicole Buchner Vinum

Primary end-point:
Progression-free survival (PFS)

ANITA / ENGOT-ov41 / GEICO 69-O

(Atezolizumab and NIraparib Treatment Association)

ENGOT Model B; Lead Group GEICO



Stratification factors:

- Platinum based regimen selected
- PFI (6-12 months vs > 12 months)
- BRCA mutation status (mutated vs. non-mutated)
- PD-L1 expression status (positive vs negative vs non informative)

Primary Endpoint:

- PFS by RECIST v, 1.1

Secondary Endpoints

- Safety and tolerability
- TFST, TSST, PFS2, OS
- ORR, DOR
- QoL/PRO

ANITA / ENGOT-ov41 / GEICO 69-O

(Atezolizumab and NIraparib Treatment Association)

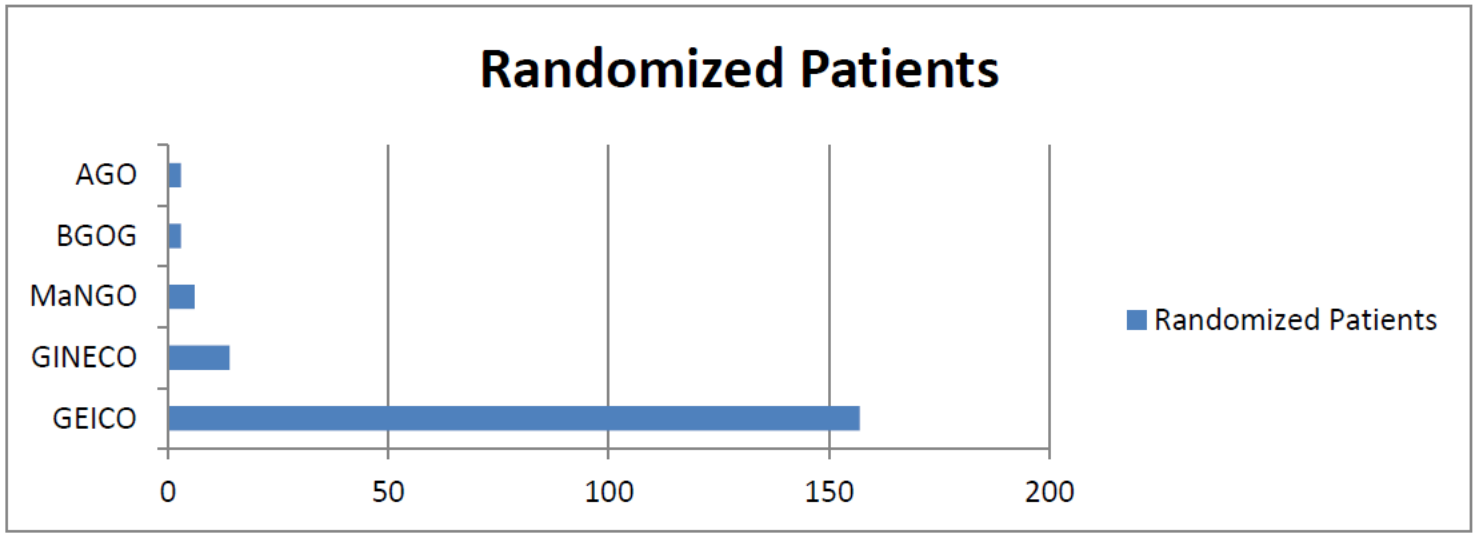
RECRUITMENT UPDATE

Total recruitment period duration: Q2 2021. Follow-up period: 24 months.

248 patients have been enrolled in the study: 183 patients have been randomized, 13 patients are currently in screening and 52 patients are screening failure.

GLOBAL Recruitment: 248 real vs 414 planned

Recruitment PER COUNTRY:



ANITA / ENGOT-ov41 / GEICO 69-O

(Atezolizumab and NIraparib Treatment Association)

MaNGO
Mario Negri Gynecologic Oncology

Site	Principal Investigator	Site Status	Screening	Screening failure	Randomized
Istituto Europeo di Oncologia IEO- Milano	Nicoletta Colombo	Active	8	0	7
Spedali Civili-Brescia	Germana Tognon	Active	1	0	1
IOV-IRCCS- Padova	Giulia Tasca	Active	1	1	0
Ospedale Mauriziano Torino	Annamaria Ferrero	Active	0	0	0
ASST- Lecco	Antonio Ardizzoia	Active	0	0	0
IRCCS Arcispedale Santa Maria Nuova Reggio Emilia	Alessandra Bologna	SIV ongoing	0	0	0
Ospedale Sant'Anna Torino	Paolo Zola	SIV not yet established	0	0	0
Total			10	1	8

Original commitment: 115 patients **Actual commitment: 93 patients**

Ovaio 1° linea

- ENGOT ov39 - IMaGYN
- ENGOT ov33 - TRUST
- ENGOT ov46 - DUO-O
- ENGOT ov43

Ovaio recidiva platino sensibile

- ENGOT ov38 - OReO
- ENGOT ov41 - ANITA
- ENGOT ov53 - VITALIA
- ENGOT ov42 - AVATAR

Ovaio recidiva platino resistente

- ENGOT ov50
- ENGOT ov55 - MIRASOL
- ENGOT ov51 - NiTChe
- ENGOT ov34 - ovar 2.29
- EPIK-O

MaNGO
Mario Negri Gynecologic Oncology

- ENGOT ov50
- ENGOT ov55 - MIRASOL
- ENGOT ov51 - NItCHE
- ENGOT ov34 - ovar 2.29
- EPIK-O

MaNGO
Mario Negri Gynecologic Oncology

OBIETTIVI:

- Efficacia di TTFields in aggiunta a wk-taxolo – 540 pazienti

- Efficacia di un citotossico veicolato da un anticorpo specifico per il recettore alfa dei folati (FRa) in pazienti con tumore che esprime FRa verso chemio - 430 pazienti

- Efficacia di IO+PARPi verso chemio - 420 pazienti

- Efficacia di IO in aggiunta a Chemio+bev - 660 pazienti

- Efficacia di inibitore della chinasi PI3K + PARPi

ENGOT-ov50
TTFields in patients with recurrent ovarian cancer not suitable for platinum (ROC-NP)

Trial setting: **Ovary/recurrent (ROC-NP)**
Sponsor(s): **NOVOCURE**
Planned No. of patients: **540**
FPI: **expected Q1 2019**

STUDY DESIGN

Primary endpoint: OS

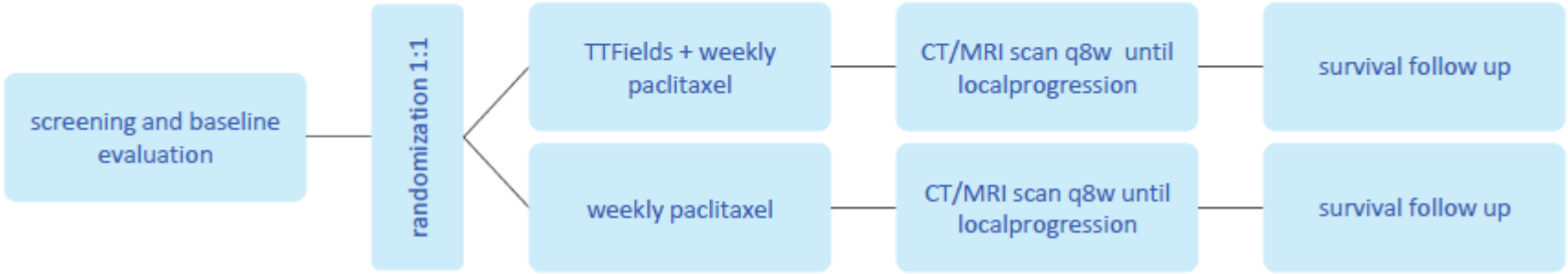
Secondary endpoints: PFS, ORR, severity and frequency of adverse events, QOL, time to undisputable deterioration in health-related QoL / death

Planned sample size: 540

Study population: Ovarian/primary peritoneal or fallopian tube carcinoma, maximum two prior lines of systemic therapy following diagnosis of platinum-resistance, ECOG 0-1

Study duration: 48 months (30 months of patient accrual)

Participant duration: expected 12 months on the trial



ENGOT-ov55/MIRASOL: Mirvetuximab-Soravtansine in FRα High Platinum Resistant Ovarian Cancer

STUDY DESIGN

MIRASOL

Enrollment and Key Eligibility

- 430 patients/330 events for PFS by INV
- Platinum resistant disease (<6 months PFI)
- Prior Bev and PARP allowed
- BRCAmut patients allowed

Statistical Assumptions

- α=0.05 (two-sided), Power = 90%, HR=0.7; control arm mPFS 3.5 mo

Mirvetuximab Soravtansine

6 mg/kg (adjusted ideal body weight) once every 3 weeks

1:1 Randomization

STRATIFICATION FACTORS
IC Chemotherapy Choice (Paclitaxel, PLD, Topotecan)
Prior therapies (1 vs 2 vs 3)

Investigator's Choice Chemotherapy
Paclitaxel, PLD†, or Topotecan

Paclitaxel: *80 mg/m² weekly*
PLD: *40 mg/m² once every 4 weeks*
Topotecan: *4 mg/m² on Days 1, 8, and 15 every 4 weeks; or 1.25 mg/m² on Days 1-5 every 3 weeks*

*BICR: Blinded Independent Central Review
†PLD: pegylated liposomal doxorubicin

Primary Endpoint

Progression-free survival by INV
BICR for sensitivity analysis*

Secondary Endpoints

Overall response rate by INV
Overall survival
Patient reported outcomes

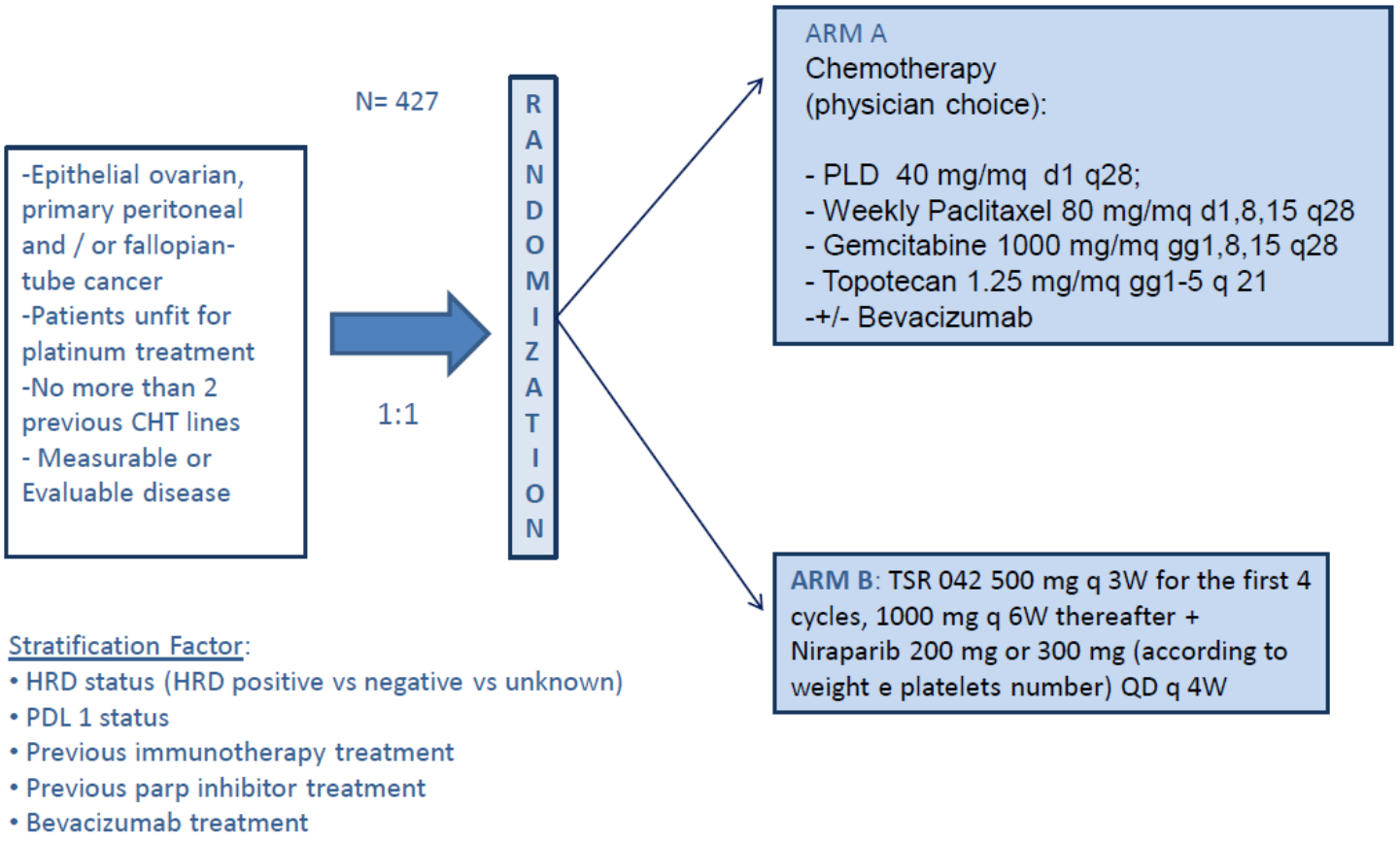
ENGOT Model: C Sponsor: Immunogen
Planned No. of patients: 430
No. of already recruited patients ENGOT: 0
Trial Status: Recruiting

ENGOT-ov55/MIRASOL: Mirvetuximab-Soravtansine in FRα High Platinum Resistant Ovarian Cancer

STUDY STATUS (1-Oct-2020)

	Site selected	SIV performed	Active sites
AGO	16		
BGOG	6	1	1
CEEGOG	10	1	1
DGOG	3		
GEICO	12	6	5
GINECO	16	1	
ISGO	6		
MANGO	7	1	
NCRI	11		
PGOG	6		

ENGOT Ov-51 Trial
MITO 33: The NItCHE trial



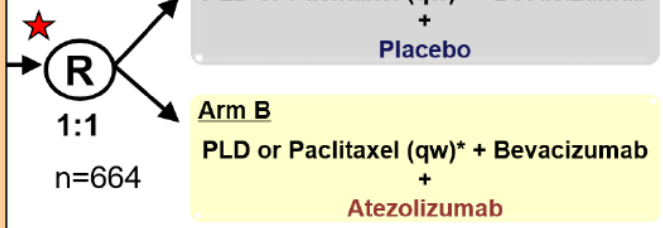
Stratification Factor:

- HRD status (HRD positive vs negative vs unknown)
- PDL 1 status
- Previous immunotherapy treatment
- Previous parp inhibitor treatment
- Bevacizumab treatment

ENGOT-ov34
AGO-OVAR 2.29

ENGOT Model A

- Epithelial ovarian, fallopian tube or primary peritoneal cancer
- **1st or 2nd relapse: TFIp < 6 months**
- **OR 3rd relapse**
- **Prior Bevacizumab allowed**
- Bev and atezolizumab specific exclusion criteria
- Archival **and** recent biopsy mandatory
- PS 0/1, life expectancy > 3 months



* In arm 1 and 2 cohorts capping: 50% PLD and 50% paclitaxel

PLD, pegylated liposomal doxorubicin; PS: performance status

★ Mandatory Biopsy

- Recruitment international: AGO Austria, BGOG, GEICO, GINECO, NSGO, SAKK
- 664 patients in about 142 sites

★ **Fresh biopsy → Central PD-L1 test prior to randomization**

Stratification factors:

- Number of prior treatment lines (1-2 vs. 3)
- Planned chemotherapy (PLD vs. paclitaxel)
- Previous administration of bevacizumab (yes vs. no)
- **Tumor PD-L1 status**

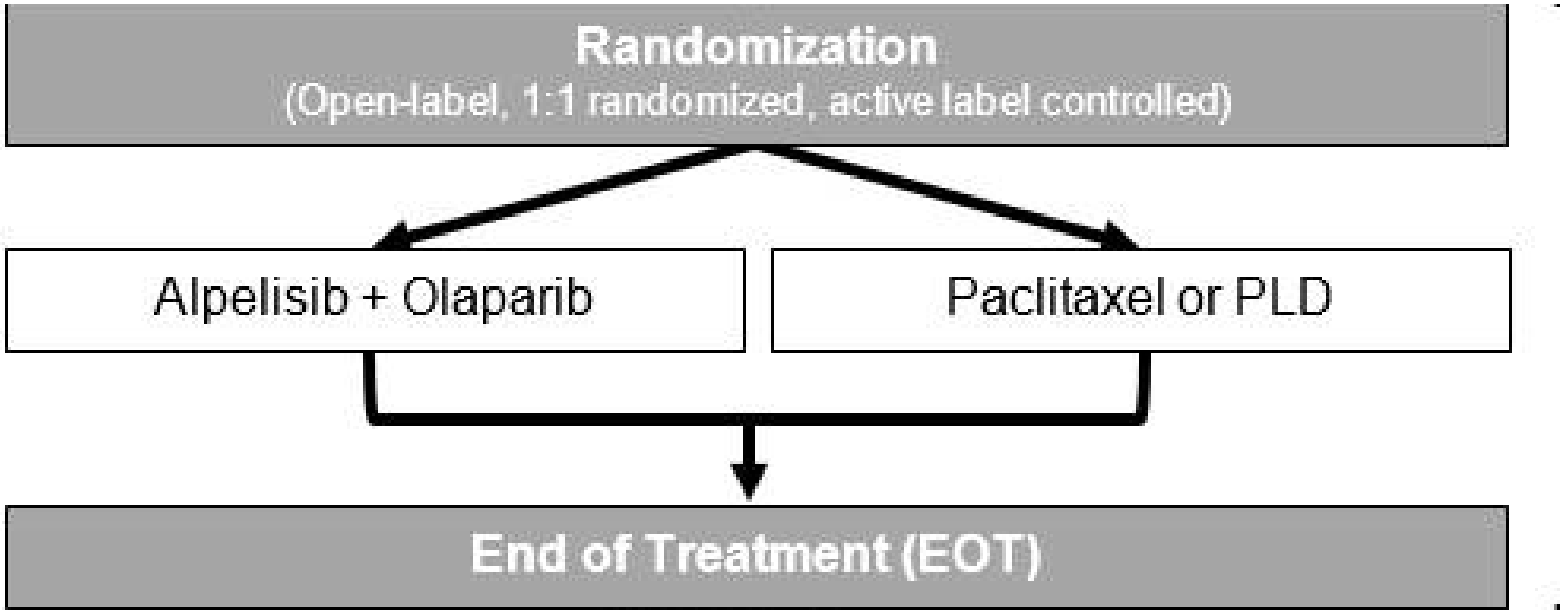
(VENTANA SP142 assay; positive IC 1/2/3 vs negative IC 0 vs non-informative).

The inclusion of patients with non-informative tissue PD-L1 status will be capped to 10% of the whole study population

Study Treatment:

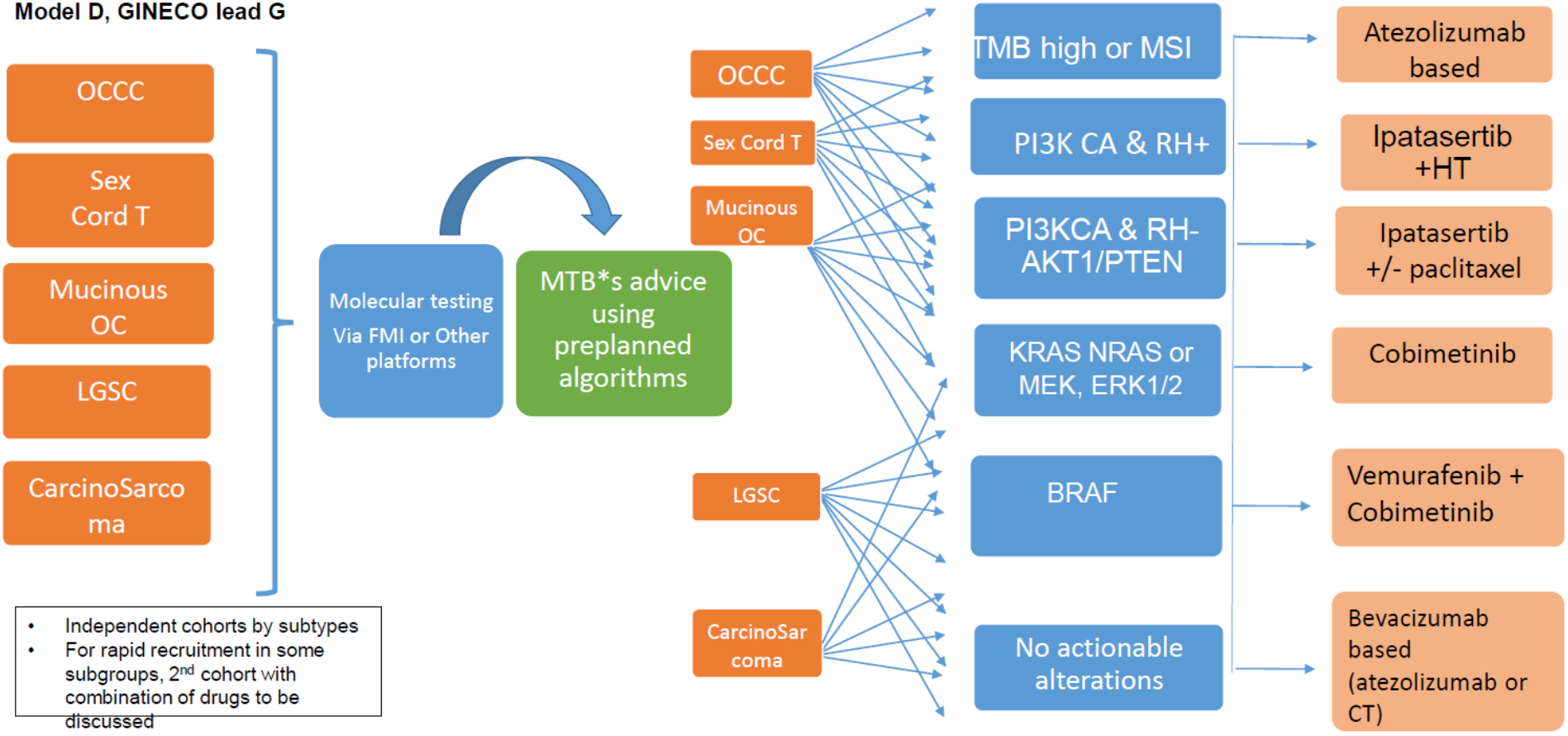
Bevacizumab: 10 mg/kg d1, q14d
Atezolizumab OR Placebo: 840 mg d1, q14d
Paclitaxel: 80 mg/m² d1, 8, 15, 22, q28d
PLD: 40 mg/m² d1, q28d

Epik-o


Randomization
(Open-label, 1:1 randomized, active label controlled)
Alpelisib + Olaparib
Paclitaxel or PLD
End of Treatment (EOT)

Petale-1-ENGOT-gyn2 trial design

Cohorts by histological subgroups
Model D, GINECO lead G



- Independent cohorts by subtypes
- For rapid recruitment in some subgroups, 2nd cohort with combination of drugs to be discussed

MaNGO
Mario Negri Gynecologic Oncology

Collaborazioni in corso

carcinoma della cervice

Cervice 1° linea

- SENTICOL III
- INTERLACE

Cervice recidiva

- ENGOT cx10 - BEAT
- ENGOT cx9- EMPOWER

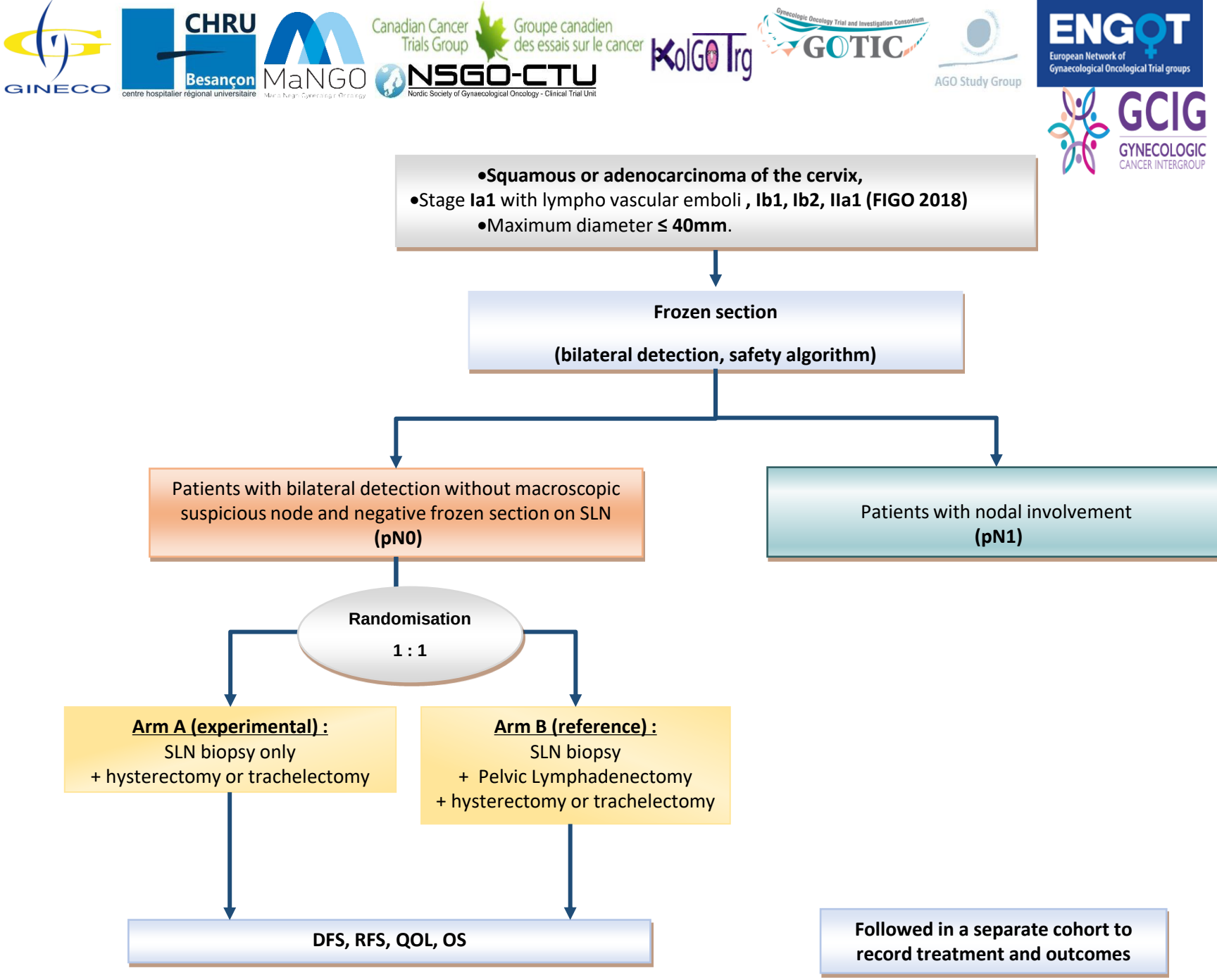
SENTICOL III : International prospective validation trial of sentinel node biopsy in cervical cancer. (GINECO-CE106 / ENGOT-Cx24)

Trial setting: tumour type/stage: cervical cancer; stage Ia1 – IIa1

Study Design: randomized, single blind phase III trial

Sponsor(s): Hospital Besançon for GINECO

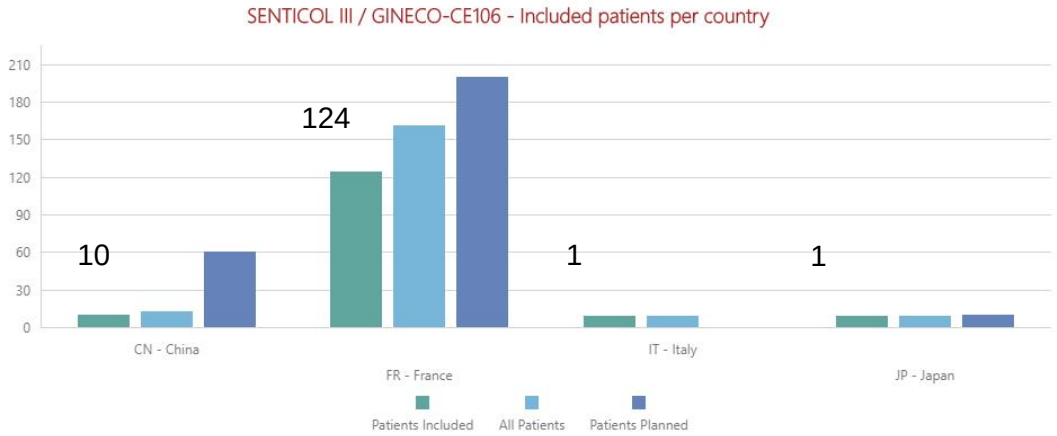
Coordinating Investigator : Pr Fabrice Lecuru


•Squamous or adenocarcinoma of the cervix,
•Stage Ia1 with lympho vascular emboli , Ib1, Ib2, IIa1 (FIGO 2018)
•Maximum diameter ≤ 40mm.
Frozen section
(bilateral detection, safety algorithm)
Patients with bilateral detection without macroscopic suspicious node and negative frozen section on SLN
(pN0)
Patients with nodal involvement
(pN1)
Randomisation
1 : 1
Arm A (experimental) :
SLN biopsy only
+ hysterectomy or trachelectomy
Arm B (reference) :
SLN biopsy
+ Pelvic Lymphadenectomy
+ hysterectomy or trachelectomy
DFS, RFS, QOL, OS
Followed in a separate cohort to record treatment and outcomes

International update

- Planned number of patients : 950
- Current accrual : 176 registered patients, 135 randomized patients and 7 patients in the pn1 cohort

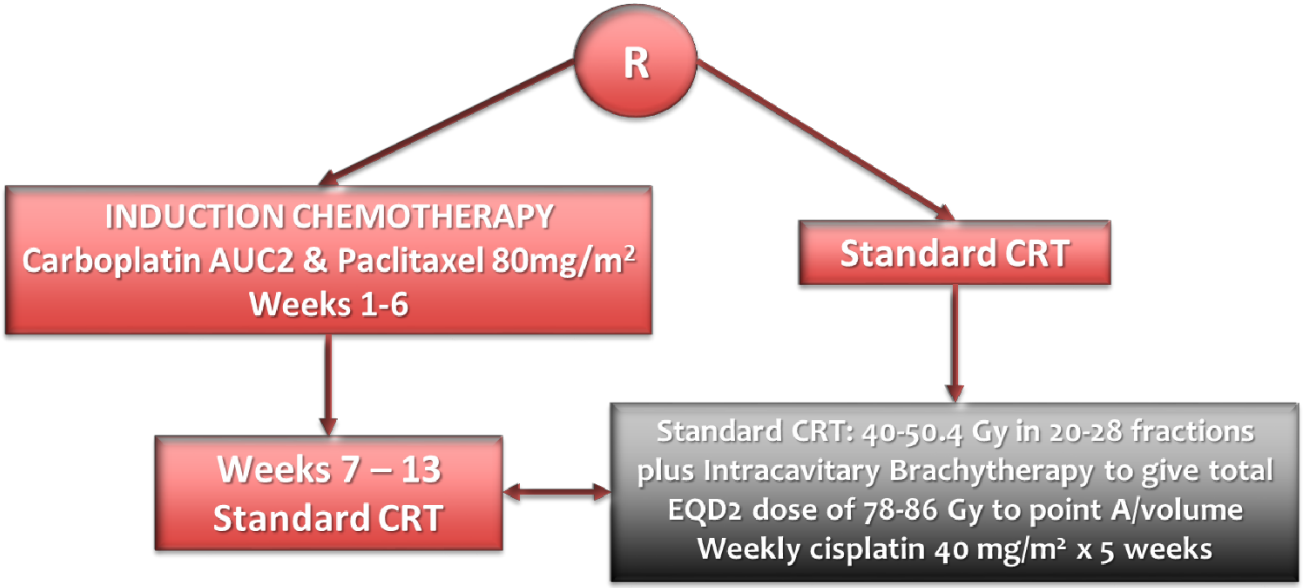
- Japan (GOTIC), China (CCRN site) and Italy (MANGO) are open (<u>10 randomized patients in China, 1 patient randomiezd in Japan, 1 patient randomized in Italy</u>)



- Pending opening : Canada (CCTG), Brazil (BrGOG and LACOG) India (KolGOTrg), Switzerland, Norway (NSGO), Germany (Ago), UK isolated sites
- May participate : Czech Republic (CEEGOG), Belgium (BGOG), Singapore (APGOT)

INTERLACE

Histologically confirmed FIGO stage Ib2-IVa squamous, adeno or adenosquamous carcinoma of cervix, fit to receive radical CRT



Follow-up
3 monthly for 2 years; 6 monthly for 3 years

INTERLACE

Recruitment Has Resumed!!

INTERLACE resumed recruitment on the 20th of May 2020. **Please notify the CTC once your Trust confirms capacity to resume recruitment into trials,** and we can work with you to get the trial reopened at your site!

We have 10 sites open to recruitment!

Current Recruitment Figures

Since resuming recruitment, **6** patients have been randomised into the trial. We are now in our final months of recruitment and we are really relying on every centre in the UK and abroad to help us complete recruitment by February 2021.

We appreciate everyone's efforts so far and we hope that you will all continue supporting the trial in its final months.

INTERLACE has recruited a total of **421** patients with **79** to Go!!

Changes to Patient FU Visits due to COVID-19

A Non-Substantial Amendment was circulated on 19Mar2020 informing all sites that telephone consolations can be carried out for FU visits. Remember to document any toxicities/adverse events, as well as any signs of recurrence. Remaining assessments performed at FU can be omitted.

ENGOT-Cx10/GEICO 68-C / JGOG1084 / GOG-3030 / BEAT cc

ENGOT Model B; Lead Group GEICO

- Primary Stage IVB, persistent or recurrent carcinoma of the cervix
- Measurable disease by RECIST v1.1
- ECOG-PS: 0-1
- No previous systemic chemotherapy for advanced or recurrent disease
- Available archival tumour for PD-L1 expression

Control Arm

Cisplatin + paclitaxel + bevacizumab **(GOG#240)** until disease progression

R: 1:1

Experimental Arm

Cisplatin + paclitaxel + bevacizumab + atezolizumab until disease progression

Safety run-in cohort: 12 pts after 2 cycles of treatment

Primary Endpoints:

- Overall survival (OS)

N=404 Pts

A tumor specimen is mandatory at study entry.

RECRUITMENT UPDATE

Total recruitment period duration: Q2 2021. Follow-up period: 24 months.

277 patients have been enrolled in the study: 227 patients have been randomized, 8 patients are currently in screening and 42 patients are screening failure.

Site	Principal Investigator	Site Status	Screening	Screening failure	Randomized
Ospedale Sant'Anna Torino	Dyonissios Katsaros	Active	4	0	4
Istituto Europeo di Oncologia IEO- Milano	Nicoletta Colombo	Active	1	1	0
IOV-IRCCS- Padova	Giulia Tasca	Active	0	0	0
Ospedale Mauriziano Torino	Annamaria Ferrero	Active	0	0	0
Ospedale San Gerardo-Monza	Andrea Lissoni	Active	0	0	0
AOU Pisana	Angiolo Gadducci	SIV ongoing	0	0	0
Total			5	1	4

Original commitment: 52 patients **Actual commitment: 43 patients**

R2810-ONC-1676 (GOG-3016/ENGOT cx-9) Newsletter

EMPOWER Cervical-1

Study Population: Patients with recurrent or metastatic cervical cancer that has progressed after platinum therapy for recurrent or metastatic cervical cancer

Screening, Randomization, and Stratification (N = 436):
Randomization – 1:1
Stratification:

- Histology– Squamous versus adenocarcinoma/ adenosquamous
- Geographic region
- Prior bevacizumab (Y/N)
- ECOG PS 0 vs 1

Experimental Therapy
REGN2810
350 mg IV Q3W

Control Therapy, Investigator's Choice
Any of the following, given IV Q3W:

- Anti-folate:
  Pemetrexed 500 mg/m^2 on Day 1(Q3W)
- Topoisomerase inhibitor
  Topotecan 1.0 mg/m^2 on Days 1-5 (Q3W)
  OR
  Irinotecan 100 mg/m^2 weekly x4 followed by 10-14 days rest (Q42D)
- Nucleoside analog:
  Gemcitabine 1000 mg/m^2 on Days 1 and 8 (Q3W)
- Vinca alkaloid:
  Vinorelbine 30 mg/m2 on days 1 and 8 (Q3W)

Duration of Treatment:
Treatment until PD, unacceptable toxicity, or until 96 weeks (16cycles, each 6 weeks)

- Option for treatment beyond progression with REGN2810
- Option for retreatment for patients who complete 16 cycles and then experience PD in post-treatment follow up

Post-Treatment Follow-up:
For safety, progression events, and OS

Study Endpoints:
Primary: OS
Key Secondary: PFS,

Study Milestones

- Current Version of Protocol: Amendment 5, dated 09Mar2019

- Study Recruitment Period: ~20 months of accrual
- First site initiated: 08Aug2017
- Actual FPFV: 13Oct2017
- **Planned LPFV: *~31May2020 Actual: 02Jun2020***
- Planned LPLV: 29Jun2023
- Planned DBL:05Sep2023
- CSR: 21Nov2023
- Enrollment Closed: 29May2020
- Randomization Completion: 07Jul2020

- **Protocol Amendment 6 released 26May2020**

Country Activity and Enrollments (as of 02 September)

Region	Country	Sites Activated	Sites Currently Active	# Patients Screened	Re-Screened Patients	# Patients SF	# Patients Randomized	# Patients Treated
NA	USA	33	11	33	1	9	24	21
NA	Canada	7	7	60	5	18	42	41
SA	Brazil	8	8	128	7	39	89	88
EU	Belgium	7	7	17	0	2	15	15
EU	Greece	4	4	11	0	2	9	9
EU	Italy	8	8	45	1	10	35	33
EU	Poland	5	5	62	2	17	45	45
EU	Russia	9	9	94	4	9	85	82
EU	Spain	10	10	73	0	7	66	63
EU	UK	6	6	3	0	1	2	2
APAC	South Korea	6	6	92	0	16	76	73
APAC	Australia	6	6	38	1	8	30	30
APAC	Taiwan	4	4	42	1	8	34	32
APAC	Japan	14	14	59	1	3	56	56
Totals		**127**	**105**	**757**	**23**	**149**	**608**	**590**

ENGOT Enrollment (as of 02 September)

Country	ENGOT Sites Selected	ENGOT Sites Initiated (Activated)	ENGOT Screened Subjects	ENGOT Total Randomized	ENGOT Total Dosed	ENGOT Total Screen Fail
GEICO	10	10	73	66	63	7
PGOG	3	3	44	35	35	9
NCRI	5	5	3	2	2	1
MITO	5	5	32	24	23	8
MaNGO	5	3	13	11	10	2
BGOG	7	7	17	15	15	2
HeCOG	6	4	11	9	9	2
ENGOT Totals	41	37	193	162	157	31

MaNGO sites Metrics (as of 28Aug2020)

PI Last Name	Institution	# Pts Screened	# Pts. Randomized	# Pts Enrolled	# Pts Screen Failed	# Pts in Screening
Ardizzoia	ASST LECCO	1	1	1	0	0
Colombo	Istituto Europeo di Oncologia	12	10	10	2	0
Bologna	AUSL, IRCCS di Reggio Emilia	0	0	0	0	0
TOTAL		13	11	11	2	0

MaNGO
Mario Negri Gynecologic Oncology

carcinoma endometrio

MaNGO
Mario Negri Gynecologic Oncology

Adiuvante

- **ENGOT-EN 11**

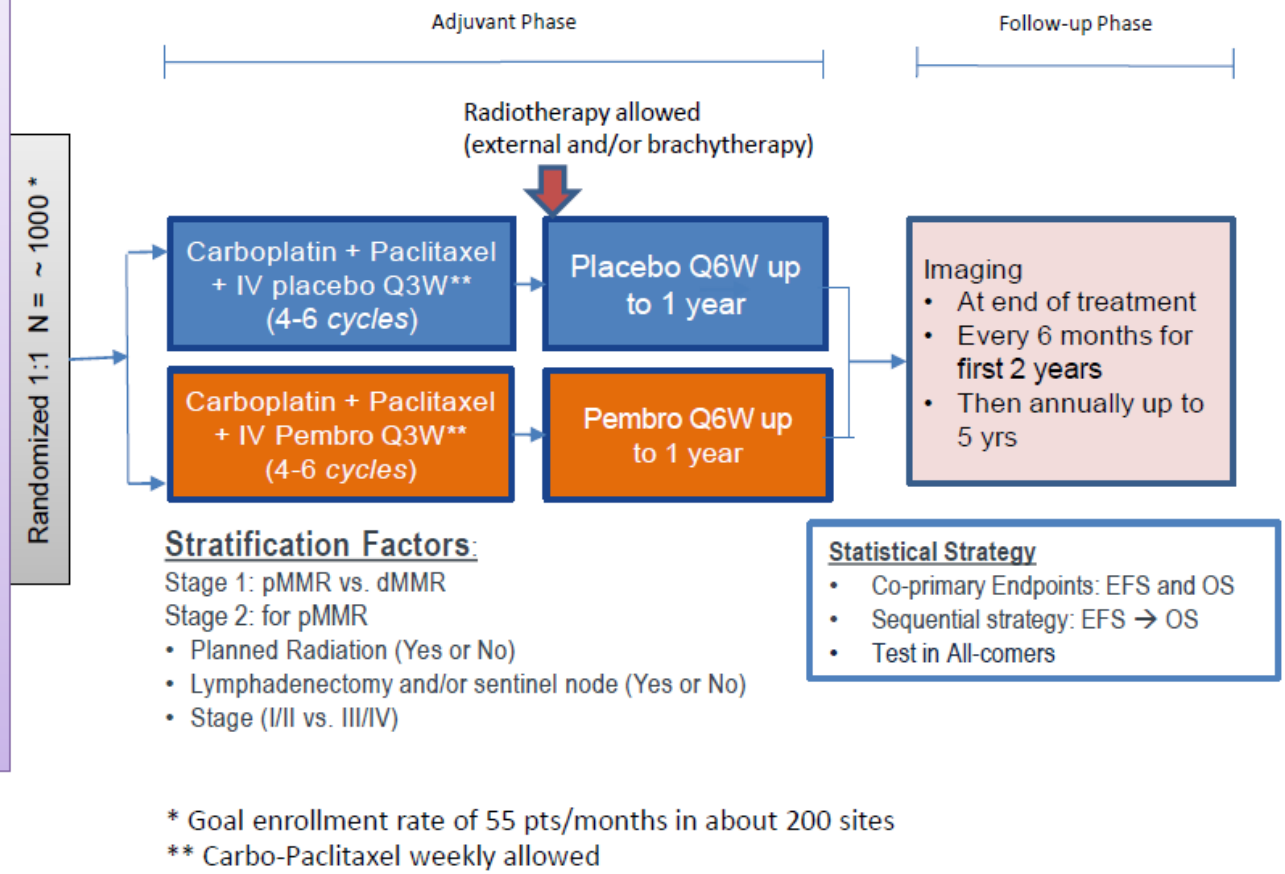
Avanzato/ricorrente

- **ENGOT-EN12 - Incyte**

Proposed Adjuvant Endometrial Cancer Study

Key Eligibility Criteria:

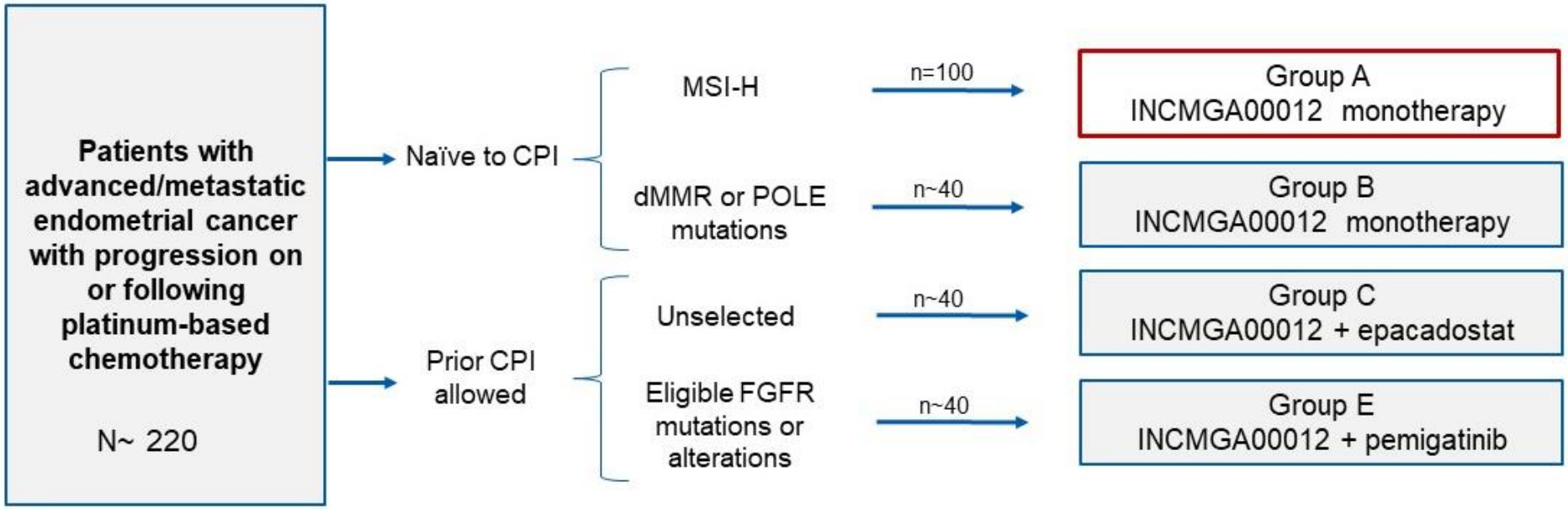
- **Newly diagnosed** Endometrial Carcinoma or Carcinosarcoma
- Undergone **curative intent surgery** with **no residual disease**
- **All-comers** with respect to PD-L1 and MMR status
- **At high risk for recurrence**:
  - FIGO Stage I/II of non-endometrioid histology
  - FIGO Stage I/II of any histology if known to be p53 mutated
  - FIGO Stage III/IVA of any histology
- **No prior radiation or systemic therapy** for EC including neoadjuvant therapy
- ECOG 0-1



* Goal enrollment rate of 55 pts/months in about 200 sites
** Carbo-Paclitaxel weekly allowed

ENGOT-EN11

ENGOT –EN12 – Incyte



CPI = Checkpoint Inhibitor Therapy

Note: Participants in Group A or Group B who experience disease progression on INCMGA00012 monotherapy may be eligible for further treatment with 1 of the combination regimens.