MaNGO
Mario Negri Gynecologic Oncology

XVIII ASSEMBLEA MANGO

Ricerca Clinica e Traslazionale in Ginecologia Oncologica

MILANO, 2-3 LUGLIO 2021

Con il Patrocinio di:

AIOM Associazione Italiana di Oncologia Medica

FICOG | Federation of Italian Cooperative Oncology Groups

SOCIETA' ITALIANA DI CANCEROLOGIA

SIGO SOCIETA' ITALIANA DI GINECOLOGIA E OSTETRICIA

ACTO ALLEANZA CONTRO IL TUMORE OVARICO

Studi sul carcinoma ovarico

Collaborazioni

ENGOT e GCIG

Giuseppe Funari
Roldano Fossati
Istituto di Ricerche Farmacologiche Mario Negri, Milano

ENGOT e GCIG in breve

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

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 tramite il Mario Negri si fa carico della gestione del trial in Italia

Ovaio 1° linea

- ENGOT ov33 - TRUST
- ENGOT ov46 - DUO-O
- ENGOT ov43
- ENGOT ov63 NIRVANA (new)
- ENGOT ov57 AGO-OVAR 28 (new)

Ovaio recidiva platino sensibile

- ENGOT ov38 - OReO
- ENGOT ov41 - ANITA

Ovaio recidiva platino resistente

- ENGOT ov51 - NiTChe
- ENGOT ov50
- ENGOT ov55 - MIRASOL
- EPIK-O
- ENGOT-ov66 (ARAVIVE)

Carcinoma ovarico di basso grado

- ENGOT-ov60

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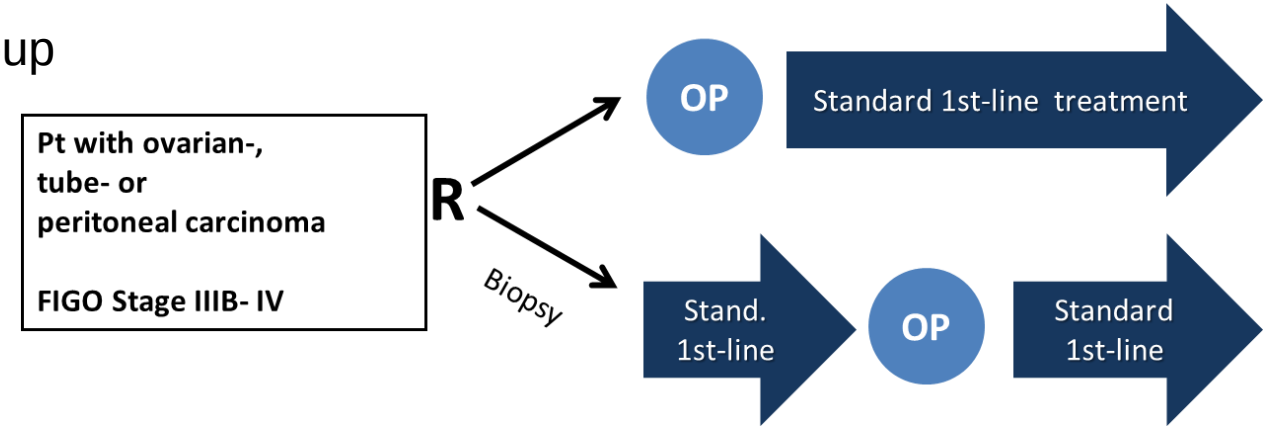
- OBIETTIVI:
  - Efficacia della strategia neoadiuvante in centri di eccellenza chirurgica > 800 pazienti
  - IO+PARP oppure solo IO in aggiunta alla chemioterapia+bev > 1100 +1100=2200 pazienti wtBRCA
  - PARP + bev oppure solo PARP > 390 + 970=1360 pazienti

TRUST – Trial on Radical Upfront Surgical Therapy

ENGOT-ov33 – TRUST

ENGOT model A
Sponsor AGO Study Group



Final No. of Patients.: n = 726 planned / 797 randomized
(FPI: 22-Aug-2016; LPI 07-Jun-2019)

Translational Research:
→ **FFPE tumour block from either primary debulking surgery or diagnostic laparoscopy / biopsy and interval debulking surgery (sample collection ongoing)**
→ optional blood plasma samples for ctDNA analysis (sample collection completed)

Primary OS analysis: **after 380 events have been observed in eligible patients (modified ITT analysis ~ 2024)**

T*R*U*S*T

Recruitment status 07.06.2019

797/772 patients randomized (= 103.2 %)

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**
			TOTAL	**1792**	**797**	**773**

ENGOT-ov46 - DUO-O

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

ENGOT model C

Sponsor AstraZeneca

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

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

1:1:1 n= 1104

n ~150

Single arm

CTX 6 cycles q3wk

Olaparib 300mg BD (24 months)

BRCAm cohort was closed for recruitment in Nov 2019

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

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)

Screening for non-BRCAm cohort was closed on 9-Apr-2021, last patient was randomized in Jun 2021

ENGOT-ov46 - DUO-O

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

- Primary Objective: To determine the efficacy of durvalumab and olaparib assessed by PFS in the first line treatment of non-tBRCAm patients with newly diagnosed advanced ovarian cancer
- Final No. of recruited patients: **1284 patients (planned: 1259)**
- Status: Last Patient randomized on 17-Jun-2021, Treatment & Follow Up ongoing
- Participating groups: AGO-Au, BGOG, GEICO, GINECO, GOG-F, JGOG, KGOG, MaNGO, MITO, NSGO, PGOG, TRSGO
- Other important information: New protocol version 5.0 released (Switch to Bevacizumab biosimilars allowed; Inclusion of a China cohort to allow inclusion of 120 non-tBRCA patients into the China cohort after global recruitment is closed, addition of exploratory analysis comparing Arm 2 and 3 to address regulatory requirements)

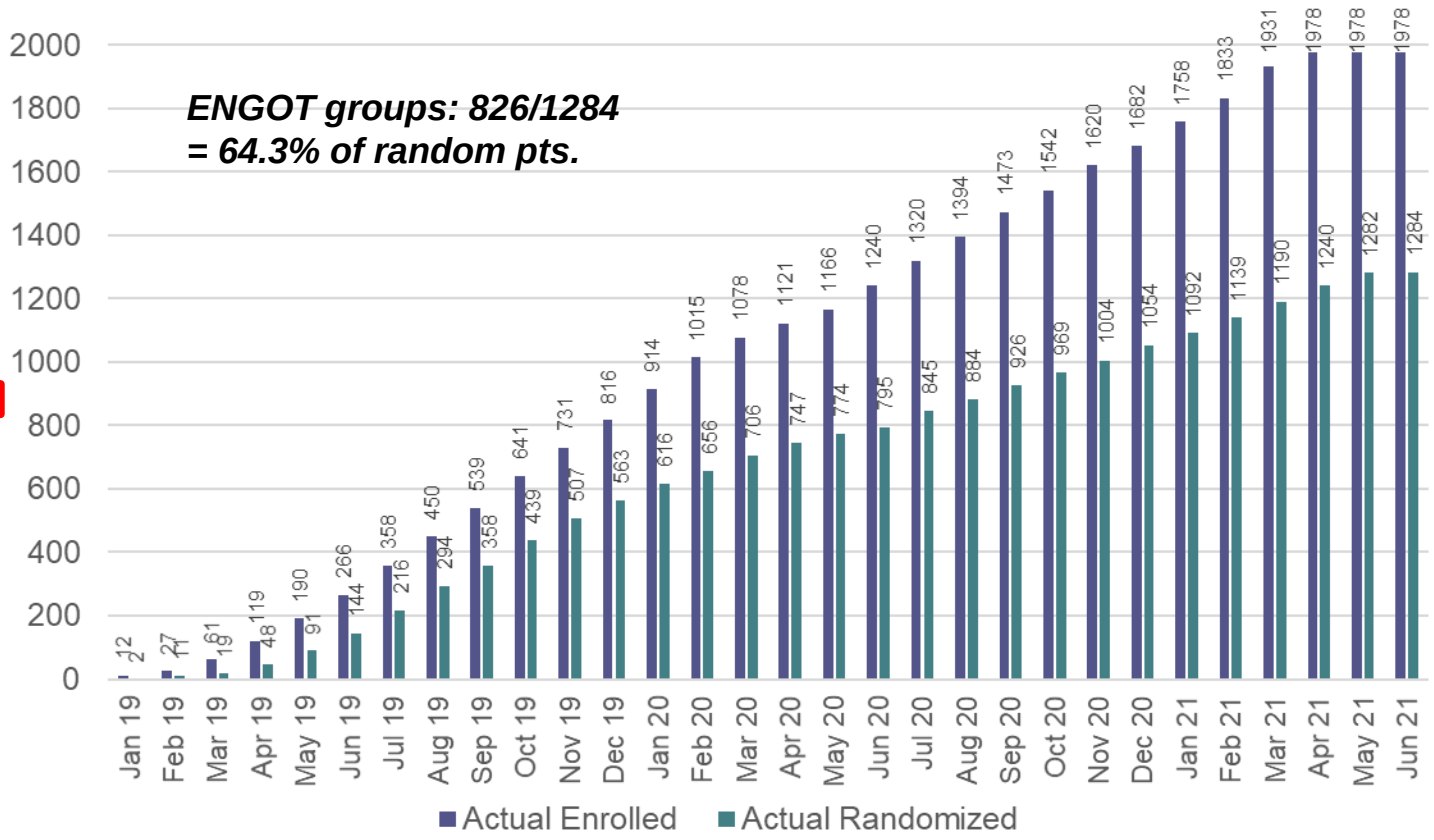
Primary PFS analysis of DUO-O is anticipated in Q2/2023

ENGOT-ov46 - DUO-O

Final Enrolment / Randomization

Group	Nts enrolled	pts random.
AGO	521	**321**
GOG-F	188	**124**
JGOG	136	**101**
KGOG	125	**93**
GEICO	124	**83**
TRSGO	130	**80**
MITO	107	**73**
GINECO	124	**72**
NSGO	87	**58**
MaNGO	58	**42**
PGOG	60	**40**
AGO-Au	46	**33**
PMHC	43	**27**
BGOG	32	**24**
Hungary via AZ	72	47
Bulgaria via AZ	50	28
Brazil via AZ	33	17
Peru via AZ	32	15
Romania via AZ	8	5
China via AZ	2	1

ENGOT groups: 826/1284
= 64.3% of random pts.



Status MaNGO sites as of 28-June-2021

- Participation with 6 sites planned, 4 of them have enrolled / randomized patients

PI Name	Centre Number	Centre Status	Centre Activation Date	Subjects Enrolled	Subjects Screen Failed	Subjects Randomised
Colombo,Nicoletta	4101	Active	2019-Jul-11	31	7	24
Tognon,Germana	4105	Active	2019-Aug-27	12	4	8
Ardizzoia,Antonio	4106	Active	2020-Feb-27	10	3	7
Ferrero,Annamaria	4104	Active	2020-Sep-17	5	2	3
Katsaros,Dionyssios	4103	Not Activated	-	0	0	0
Bologna,Alessandra	4102	Not Activated	-	0	0	0
TOTAL				**58**	**16**	**42**

durvalumab plus olaparib DUO ovarian cancer

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

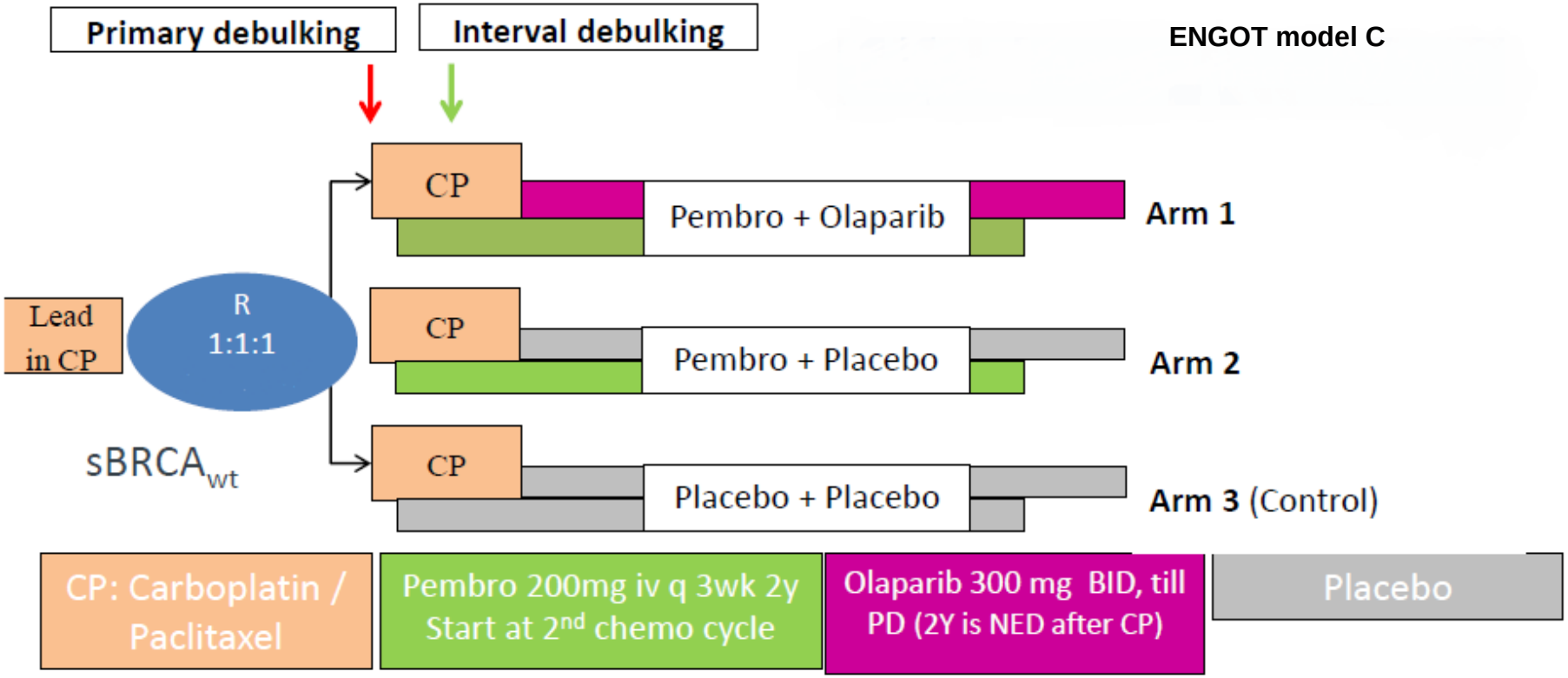
STUDY DESIGN

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

ENGOT OV43 : Enrollment Closed, GLOBAL

Country	Total Screened	In Screening/ In Lead-in	Screen Fail/ Lead-in Fail	Total Randomized	Discontinued
Australia	24	2	12	10	2
Belgium	189	5	75	109	49
Brazil	74	0	49	25	4
Canada	79	3	36	40	17
Chile	113	1	65	47	14
Colombia	61	0	28	33	8
Czech Republic	110	2	59	49	18
France	74	4	35	35	9
Germany	67	7	20	40	4
Hungary	57	0	29	28	9
Israel	116	3	55	58	35
Italy	218	8	96	114	37
Japan	145	4	55	86	42
Korea, Republic of	123	0	54	69	24
Poland	115	5	51	59	21
Russia	150	2	73	75	28
South Africa	60	2	32	26	4
Spain	148	9	62	77	32
Taiwan	90	2	29	59	22
Turkey	183	5	90	88	26
Ukraine	107	5	39	63	27
United States	243	22	97	124	17
Total	**2,546**	**91**	**1,141**	**1,314**	**449**

ENGOT OV43 : Enrollment Closed, LOCAL

Enrollment Metrics		
Total Screened	218	
In Screening	1	
Screened Failed, %	18	14%
Rescreened	0	
Lead In	199	
Lead In Failed, %	78	39%
Randomized	114	
Randomized and Active	82	
End of Treatment, %	39	34%
Discontinued, %	39	34%
Completed	0	
Unblinded By Site	11	

Country	Site #	Active	Total Screened	In Screening	Total Lead In	Screened Failed	Total Lead in Fail	Total Randomized
Italy	1100	Colombo	46	1	42	3	18	22
Italy	1101	Ardizzoia	8	0	6	2	1	4
Italy	1104	Zola	21	0	20	1	10	10
Italy	1105	Scambia	67	0	62	5	27	35
Italy	1107	De Placido	15	0	14	1	8	6
Italy	1108	Naglieri	4	0	3	1	1	2
Italy	1109	Caldara (Trento)	3	0	3	0	0	3
Italy	1110	Scollo	14	0	13	1	4	9
Italy	1111	Palaia	5	0	5	0	2	3
Italy	1112	Febbraro	1	0	0	1	0	0
Italy	1113	Conte	15	0	14	1	4	10
Italy	1114	Andreetta	8	0	6	2	3	3
Italy	1115	Raspagliesi	11	0	11	0	0	7
								114

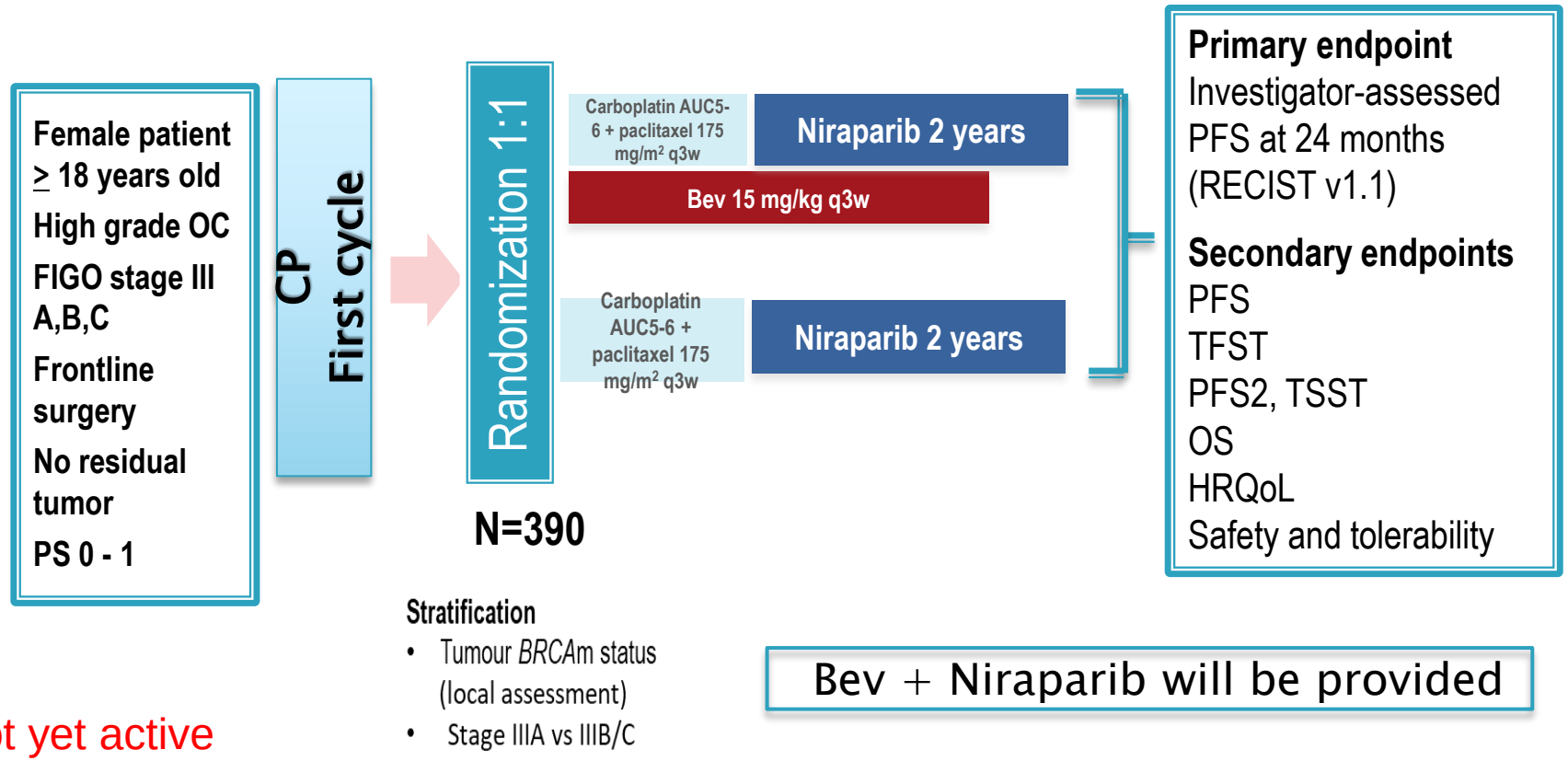
NIRaparib with or without be**V**acizumab in m**A**intenance after complete cytoreductio**N** in patients with ov**A**rian cancer

NIRVANA-1-ENGOTov63

Study model A

THE NIRVANA STUDY

Newly diagnosed FIGO stage III high-grade serous/endometrioid ovarian, fallopian tube or primary peritoneal cancer



Stratification

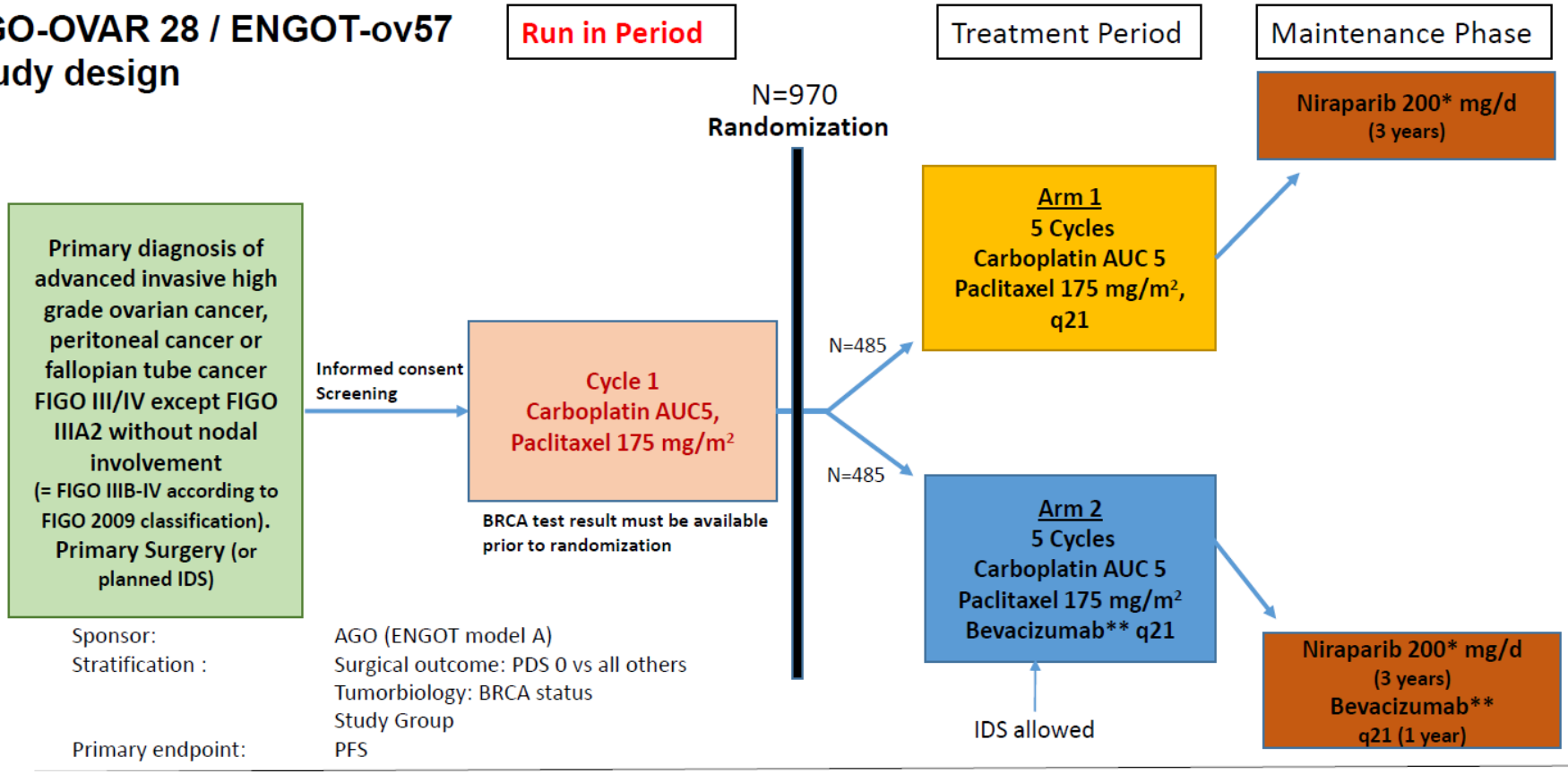
- Tumour *BRCA*m status (local assessment)
- Stage IIIA vs IIIB/C

Bev + Niraparib will be provided

Not yet active
6 MaNGO sites interested

GINECO

AGO-OVAR 28 / ENGOT-ov57 Study design



Not yet active

9 MaNGO sites interested

Ovaio 1° linea

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- ENGOT ov46 - DUO-O
- ENGOT ov43
- ENGOT ov63 NIRVANA (new)
- ENGOT ov57 AGO-OVAR 28 (new)

Ovaio recidiva platino sensibile

- ENGOT ov38 - OReO
- ENGOT ov41 - ANITA

Ovaio recidiva platino resistente

- ENGOT ov51 - NiTChe
- ENGOT ov50
- ENGOT ov55 - MIRASOL
- EPIK-O
- ENGOT-ov66 (ARAVIVE)

Carcinoma ovarico di basso grado

- ENGOT-ov60

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•ENGOT ov38 – OReO
•ENGOT ov41 - ANITA

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•OBIETTIVI:

•Utilità di mantenere PARPi oltre una progressione occorsa durante PARPi – 230 pazienti

•Efficacia di IO in aggiunta a Chemio+PARPi - 400 pazienti

ENGOT Ov38/OReO

OReO design

Total sample size: 416 pts

Eligible patients

- Relapsed non-mucinous EOC
- **Treatment with one course of PARPi maintenance therapy**
- **PR/CR after≥4 cycles of platinum-based chemo**
- Documented *BRCA1/2* status

Cohort 1 *BRCAm*

120 patients
with a germline or somatic mutation in *BCRA1/2*

Exposure for ≥18 months after first-line chemotherapy or ≥12 months after second-/later-line chemotherapy

Cohort 2 non-*BRCAm*

108 patients

Exposure for ≥12 months after first-line chemotherapy or ≥6 months after second-/later-line chemotherapy

PR or CR to most recent course of platinum-based chemotherapy (no bevacizumab)

RANDOMIZATION 2:1

Olaparib tablets

300 mg bid or last tolerable dose

Placebo

PFS
Primary endpoint
(RECIST 1.1)

PFS, OS, TTP ‡, TDT, TFST, TSST, HRQoL, Safety

Stratification factors:
- Prior bevacizumab
- ≤3 vs ≥4 prior lines of chemotherapy

ENGOT Model C; Lead Group GINECO

OReO status May 2021

Cohort	Subjects Screened	Subjects in Screening	Subjects Screen Failed	Subjects Randomised	Subjects On Treatment	Subject Discontinued from the study	Progressions	Deaths
BRCA+ve	149	0	37	112	5	107	102	61
BRCA-ve	149	0	41	108	19	89	81	24
	298	**0**	**78**	**220**	**24**	**193**	**183**	**85**

Cohort	First patient Screened	First Patient randomised	Last patient screened	Last patient randomised	Recruitement period in days (First patient screened to last patient randomised)	Recruitement period in months (FPS to LPR)	Recruitement period in years (FPS to LPR)
BRCA+ve	12-Sep-17	3-Oct-17	6-Apr-20	15-Apr-20	946	31.1	2.6
BRCA-ve	8-Jun-17	28-Jun-17	15-Jan-21	10-Feb-21	1343	44.2	3.7

Data Cut Off	Mon, 15-Feb-2021
Database Lock	**Tue, 12-May-2021**
High Level Delivery to AZ/GINECO	Tue, 18-May-21
Final TFLs	Wed, 07-Jul-2021
Result Interpretation Meeting	Mon, 19 – Jul -2021
AZ Approve and sign off CSR	Tue, 14 – Sep - 2021

OReO Recruitment status per ENGOT groups (30 Apr 21)

ENGOT/GCIG	Country	Sites Initiated	Closed Sites	Sites Active (1 patient screened at least)	Subjects Screened	Subjects in Screening	Subjects Screen Failed	Subjects Randomized	Patients in treatment	Subjects Withdrawn	# BRCA Positive Subjects Randomized	# BRCA Negative Subjects Randomized
BGOG	Belgium	3	1	2	7	0	1	6	2	4	3	3
PMC	Canada	3	2	2	5	0	3	2	0	2	0	2
NSGO	Denmark	3	0	3	5	0	0	5	0	5	3	2
	Norway	1	0	1	5	0	0	5	0	5	0	5
GINECO	France	20	1	19	75	0	17	58	3	55	33	25
AGO	Germany	20	11	12	45	0	19	26	3	23	9	17
ISGO	Israel	7	4	5	8	0	4	4	0	4	2	2
MANGO	**Italy**	**7**	**2**	**4**	**14**	**0**	**4**	**10**	**1**	**9**	**8**	**2**
MITO	Italy	11	3	8	47	0	7	40	8	32	21	19
PGOG	Poland	6	1	5	12	0	2	10	0	10	9	1
GEICO	Spain	13	1	13	62	0	16	46	5	41	23	23
NCRI	UK	8	1	7	13	0	5	8	1	7	1	7
	Totals	**102**	**27**	**81**	**298**	**0**	**78**	**220**	**23**	**197**	**112**	**108**
								BRCA+	**5**	**107**	Missing BRCA-	**0**
								BRCA-	**18**	**90**		

ITALY - MaNGO

Site Recruitment status:

Country	PI Name	Centre Number	Centre Status	Subjects Enrolled	Subjects in screening	Subjects Screen Failed	Subjects Randomised	Subjects Withdrawn
Italy	Colombo,Nicoletta	4102	Active	8	0	3	5	5
Italy	Zola,Paolo	4120	Active	2	0	0	2	2
Italy	Tognon,Germana	4121	Active	2	0	1	1	0
Italy	Bologna,Alessandra	4122	Active	2	0	0	2	2
Italy	Conte,Pierfranco	4103	Activated	0	0	0	0	0
Italy	Ferrero,Annamaria	4124	Activated	0	0	0	0	0
Italy	Gadducci,Angiolo	4131	Activated	0	0	0	0	0

ENGOT-Ov41 / GEICO 69-O / ANITA

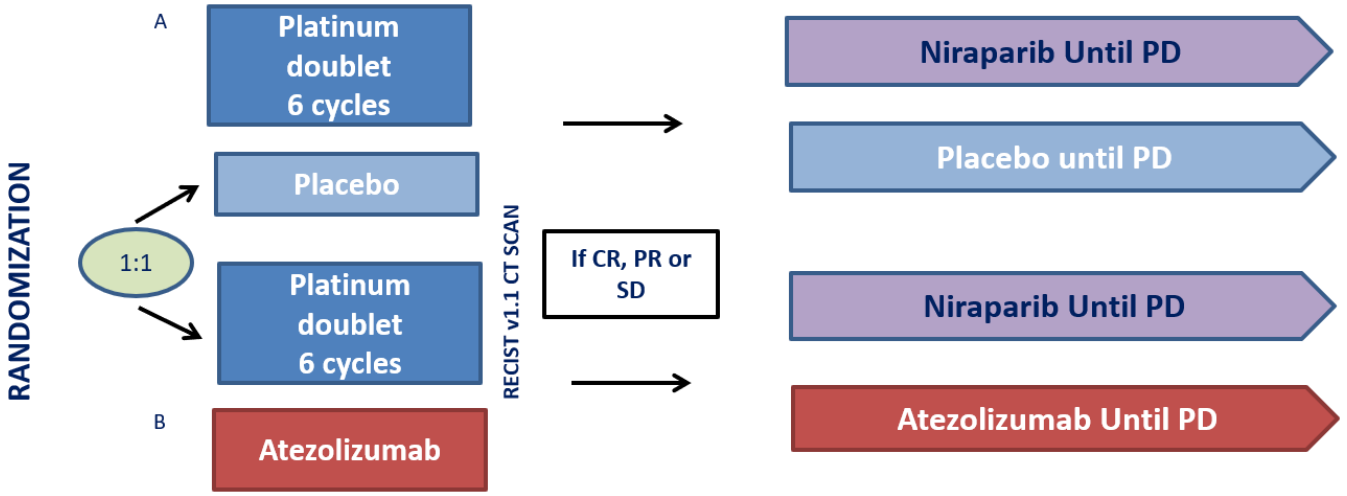
(Atezolizumab and Niraparib Treatment Association)

ENGOT Model B: Lead Group GEICO

N= 414 patients

- Recurrent high- grade serous or endometrioid, or undifferentiated
- TFIp >6 months
- ≤ 2 prior lines
- Measurable disease
- ECOG≤ 1

IP: A. González



Stratification factors:

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

Primary Endpoint:

- PFS by RECIST v.1.1

Secondary endpoints:

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

ENGOT-Ov41 / GEICO 69-O / ANITA

(Atezolizumab and Niraparib Treatment Association)

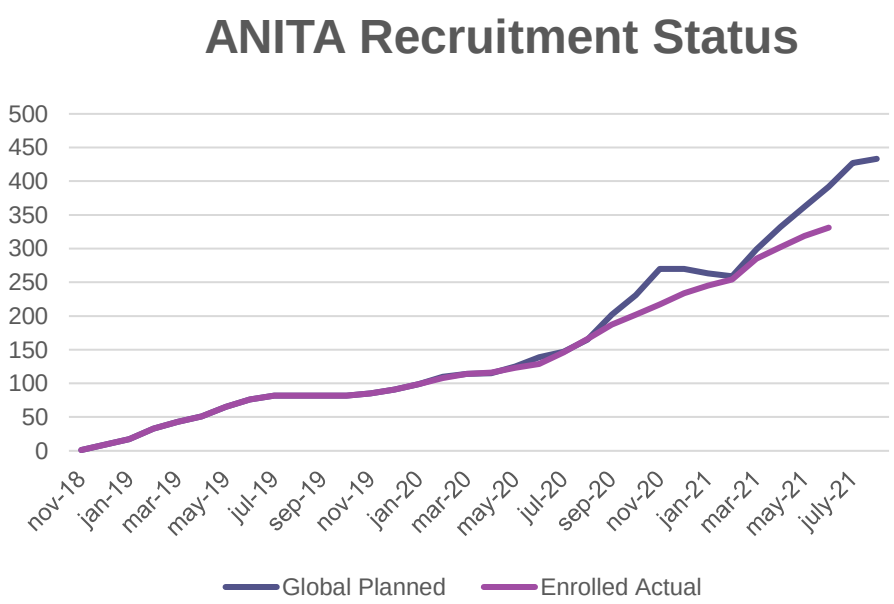
Patients Randomized:335/414 patients

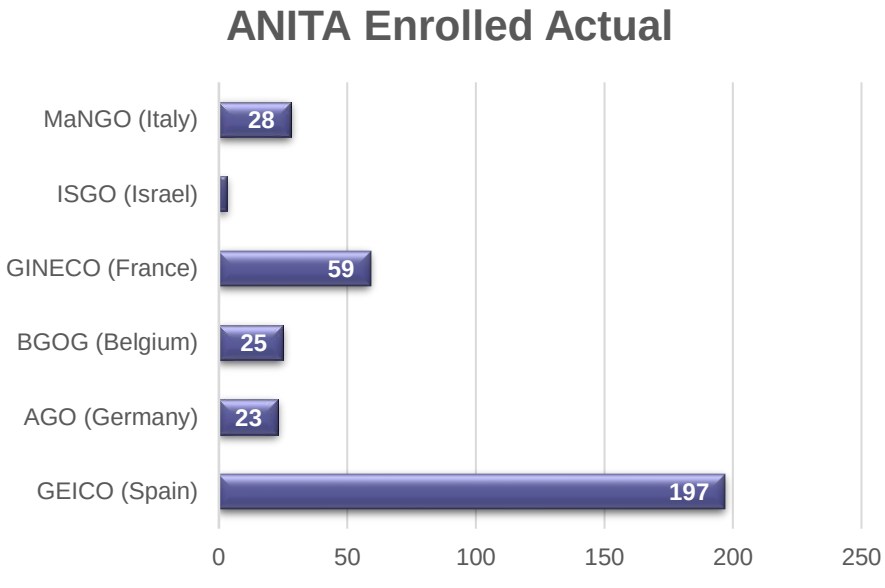
Patients in Screening: 13 patients

Group	Patients in screening	Randomized patients
GEICO	3	197
GINECO	7	59
MaNGO	2	28
BGOG	1	25
AGO	0	23
ISGO	0	3
Total	**13**	**335**

ENGOT-Ov41 / GEICO 69-O / ANITA

(Atezolizumab and Niraparib Treatment Association)





ENGOT-Ov41 / GEICO 69-O / ANITA

(Atezolizumab and Niraparib Treatment Association)

Site	Principal Investigator	Total Screened	Screening Failure	In Screening Actual	Enrolled Actual
IEO Milano	**Colombo**	**21**	**3**	**1**	**17**
Spedali Civili Brescia	**Tognon**	**3**	**0**	**0**	**3**
Ospedale Mauriziano Torino	**Ferrero**	**4**	**0**	**1**	**3**
IRCCS Arcispedale Reggio Emilia	**Bologna**	**2**	**0**	**0**	**2**
IOV-IRCCS Padova	**Tasca**	**2**	**1**	**0**	**1**
ASST-Lecco	**Ardizzoia**	**1**	**0**	**0**	**1**
Ospedale Sant'Anna Torino	**Zola**	**2**	**1**	**0**	**1**
TOTAL		**35**	**5**	**2**	**28**

Actual commitment 40 patients

ENGOT-Ov41 / GEICO 69-O / ANITA

(Atezolizumab and Niraparib Treatment Association)

Protocol Amendment 2.0 Submitted on 30 Jun 2021

- IB Niraparib Version 11.0
- Atezolizumab DIL: Severe Cutaneous Adverse Reactions (SCARs)
- Atezolizumab Version 17
- Recruitment Extension: August 2021
- **<u>Allow Archival biopsy for patient randomization</u>** if the novo is not technically possible or failed to produce enough representative tumor tissue, after GEICO approval.

Ovaio 1° linea

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- ENGOT-ov60

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- **ENGOT ov50**
- **ENGOT ov55 – MIRASOL**
- **EPIK-O**
- **ENGOT-ov66 (ARAVIVE)**

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OBIETTIVI:

- **Efficacia di IO+PARPi verso chemio - 420 pazienti**
- **Efficacia di TTFields in aggiunta a chemio - 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 inibitore della chinasi PI3K + PARPi verso chemio - 322 pazienti wtBRCA**
- **Efficacia di inibitore della via GAS6/AXL in aggiunta a chemio – 300 pazienti**

NItCHE Clinical Trial
ENGOT OV51 / MITO 33

ENGOT Ov51-MITO 33: NItCHE trial

Randomized phase III trial on **NI**raparib-**T**SR 042 (dostarlimab) vs physiscian's choice **CHE**motherapy in recurrent, platinum resistant ovarian, fallopian tube or primary peritoneal cancer: NItCHE trial (MITO 33)

ENGOT model: B

Sponsor: Fondazione Policlinico Universitario A. Gemelli IRCCS of Rome (FPG)

Status: recruiting

Planned No. of patients: 427

Trial setting: platinum resistant ovarian, fallopian tube or primary peritoneal cancer

Study Design: multicenter, phase III, open labeled, randomized, controlled study

NItCHE Clinical Trial
ENGOT OV51 / MITO 33

STUDY DESIGN

-Epithelial ovarian, primary peritoneal and / or fallopian-tube cancer
-Patients unfit for platinum treatment
-No more than 2 previous CHT lines
- Measurable or Evaluable disease

N= 427

1:1

RANDOMIZATION

ARM A
Chemotherapy
(physician choice):
- **PLD** 40 mg/mq d1 q28;
- **Weekly Paclitaxel** 80 mg/mq d1,8,15 q28
- **Gemcitabine** 1000 mg/mq gg1,8,15 q28
- **Topotecan** 1.25 mg/mq gg1-5 q 21
-**+/- Bevacizumab**

ARM B: TSR 042 (**Dostarlimab**) 500 mg q 3W for the first 4 cycles, 1000 mg q 6W thereafter + **Niraparib** 200 mg or 300 mg (according to weight e platelets number) QD q 4W

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

Primary Objective:
- Overall survival (OS)

Secondary Objectives:
- PFS
- TFST
- ORR

NItCHE Clinical Trial
ENGOT OV51 / MITO 33

ACTIVATION STATUS

Country	CA approval	Coordinating EC approval	Status	Open sites
ITALY	09/10/2020	25/11/2020	Study start: 1/12/2020	4
FRANCE	07/05/2021	04/05/2021	Contracts negotiation in progress	-
GERMANY	19/04/2021	25/02/2021	Waiting for German Federal office for radiation protection approval	-
GREECE	-	-	Submission in progress	-
CZECH REPUBLIC	-	-	Waiting for EC and CA approval	-

NItCHE Clinical Trial
ENGOT OV51 / MITO 33

ENGOT
European Network of Gynaecological Oncological Trial groups

Multicentre Italian Trials in Ovarian cancer
MITO

CEEGOG
Central and Eastern European Gynecologic Oncology Group

HeCOG
Hellenic Cooperative Oncology Group

MaNGO

ARCAGY - GINECO

NOGGO e.V.

RECRUITMENT STATUS

Group	Total Screened	Total Screen Failed	Total randomized	Total Treatment Discontinuation
MITO	25	2	19	7
MaNGO	-			
GINECO	-			
NOGGO	-			
HeCOG	-			
CEEGOG	-			
TOTAL study	25	2	19	7

NItCHE Clinical Trial
ENGOT OV51 / MITO 33

MaNGO SITE STATUS

Site	Principal Investigator	Site Status	Total randomized
Istituto Europeo di Oncologia IEO-Milano	Nicoletta Colombo	Contract finalised	-
Spedali Civili Brescia	Germana Tognon	Active	-
IOV IRCCS Padova	Pierfranco Conte	Contract negotiation	-
ASST Lecco	Federica Villa	CE evaluation	
Ospedale Sant'Anna Torino	Dionyssios Katsaros	CE evaluation	-

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

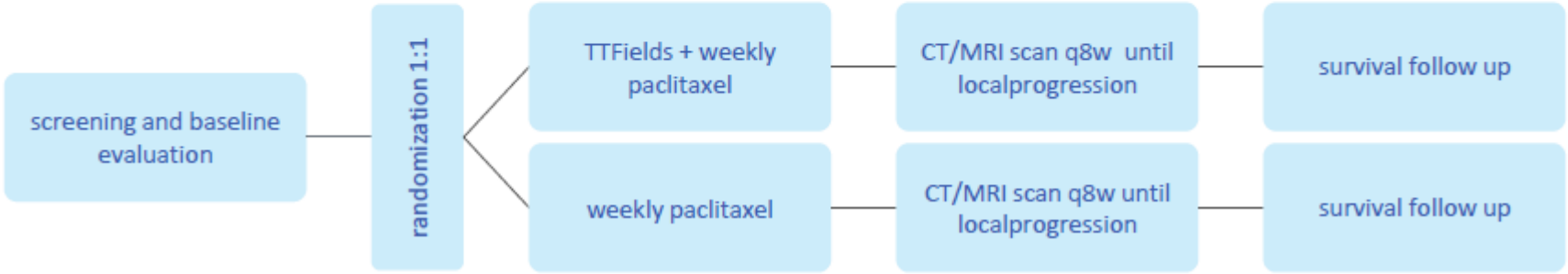
Secondary endpoints: PFS, ORR, severity and frequency of adverse events, QOL, time to undisputable deterioration in health-related QoL / death

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-ov50/
INNOVATE-3
Ovarian Cancer

ENGOT
European Network of Gynaecological Oncological Trial groups

BGOG

novocure | clinicaltrials

GOG FOUNDATION

Enrollment status (as of 31Mar2021)

ENGOT Group/Country	Sites open	Patients enrolled
A-AGO/Austria	4	9
BGOG/Belgium	8	76
ISGO/ Israel	4	19
DGOG/ The Netherlands	0	0
CEEGOG/ Czechia, Hungary	7	42
NOGGO/ Germany	3	17
PGOG/Poland	3	1
MANGO/Italy	3	26
MITO/Italy	5	61
SAKK/Switzerland	4	15
GEICO/Spain	7	17
Canada	0	0
GOG Partners/USA	41	102
TOTAL	**89**	**385**

	31-Jan-2021	31-Mar-2021
Enrollment	312 (58%)	385 (71%)
ENGOT	238	283
GOG	74	102

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

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*

Primary Endpoint

Progression-free survival by INV
BICR for sensitivity analysis*

Secondary Endpoints

Overall response rate by INV
Overall survival
Patient reported outcomes

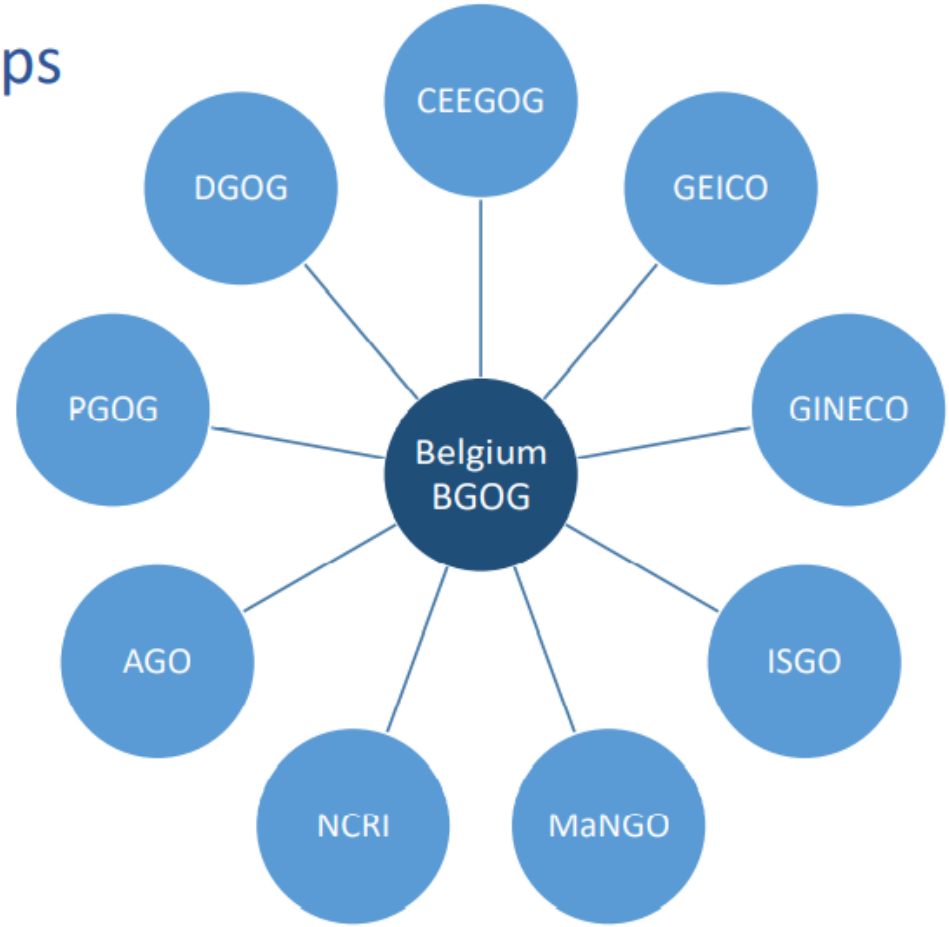
*BICR: Blinded Independent Central Review
†PLD: pegylated liposomal doxorubicin

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

MIRASOL- Update june 2021

ENGOT Groups

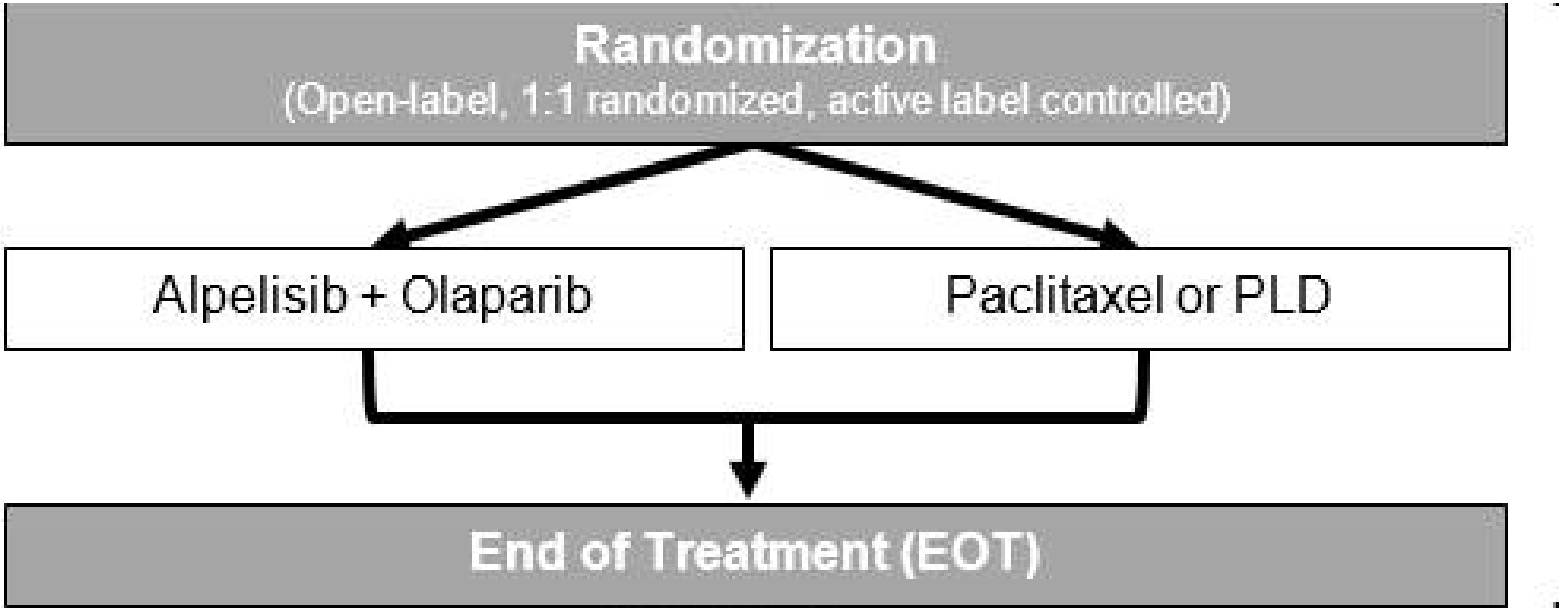
- 10 participating ENGOT groups
- 47 sites activated
- 236 patients screened
- **38 patients enrolled**



MaNGO (Italy)

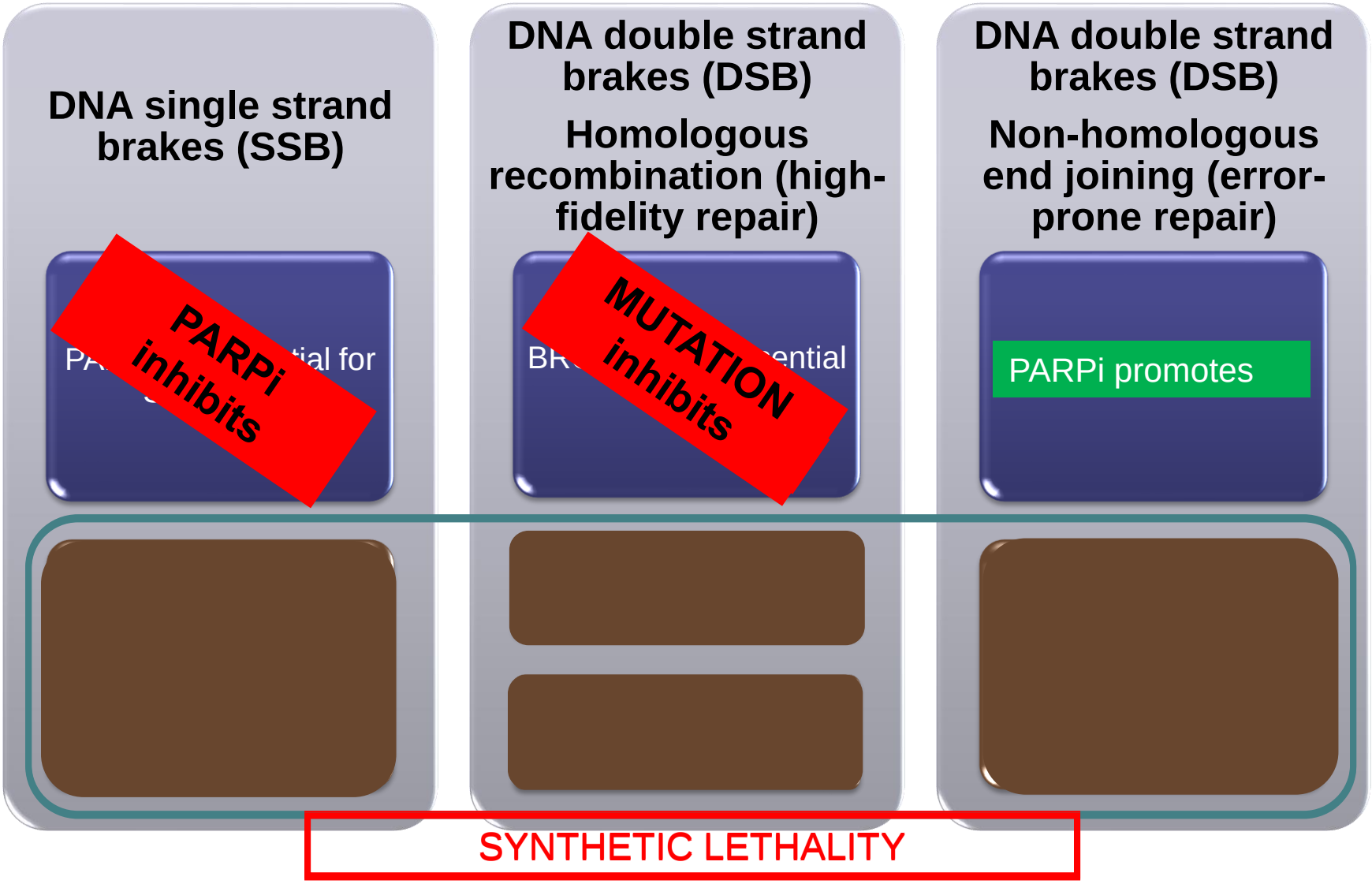
Site	Activation status	Total screened	Total Randomized	Comments
IRCCS - Istituto Europeo di Oncologia (The European Institute of Oncology) (IEO)	Activated	24	3	
Azienda Socio Sanitaria Territoriale degli Spedali Civili di Brescia	Activated	1	0	
Ospedale Mauriziano Umberto I	Activated	0	0	
Servizio Sanitario Regionale Emilia-Romagna	Activated	0	0	
Azienda Ospedaliera di Lecco	SIV: 10-Jun-2021			
IOV Istituto Oncologico	SIV: 7-Jun-2021			
Azienda Ospedaliera Città della Salute e della Scienza di Torino	SIV: 22-Jun-2021			
Total: 7		**25**	**3**	

Epik-o



322 Pazienti wtBRCA; ammesso precedente PARP e bev; endpoint pirmario PFS

PARPi and PI3Ki



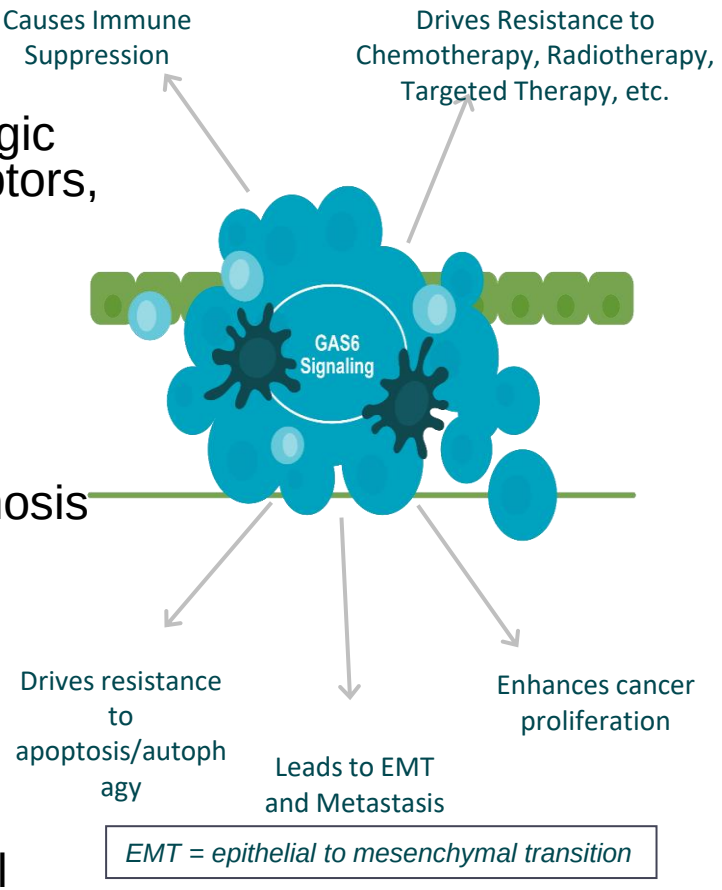
A Phase 3, Randomized, Double-Blind, Adaptive, Placebo/Paclitaxel-Controlled Study of AVB-S6-500 in Combination with Paclitaxel in Patients with Platinum-Resistant Recurrent Ovarian Cancer

ENGOT-ov66 ARAVIVE

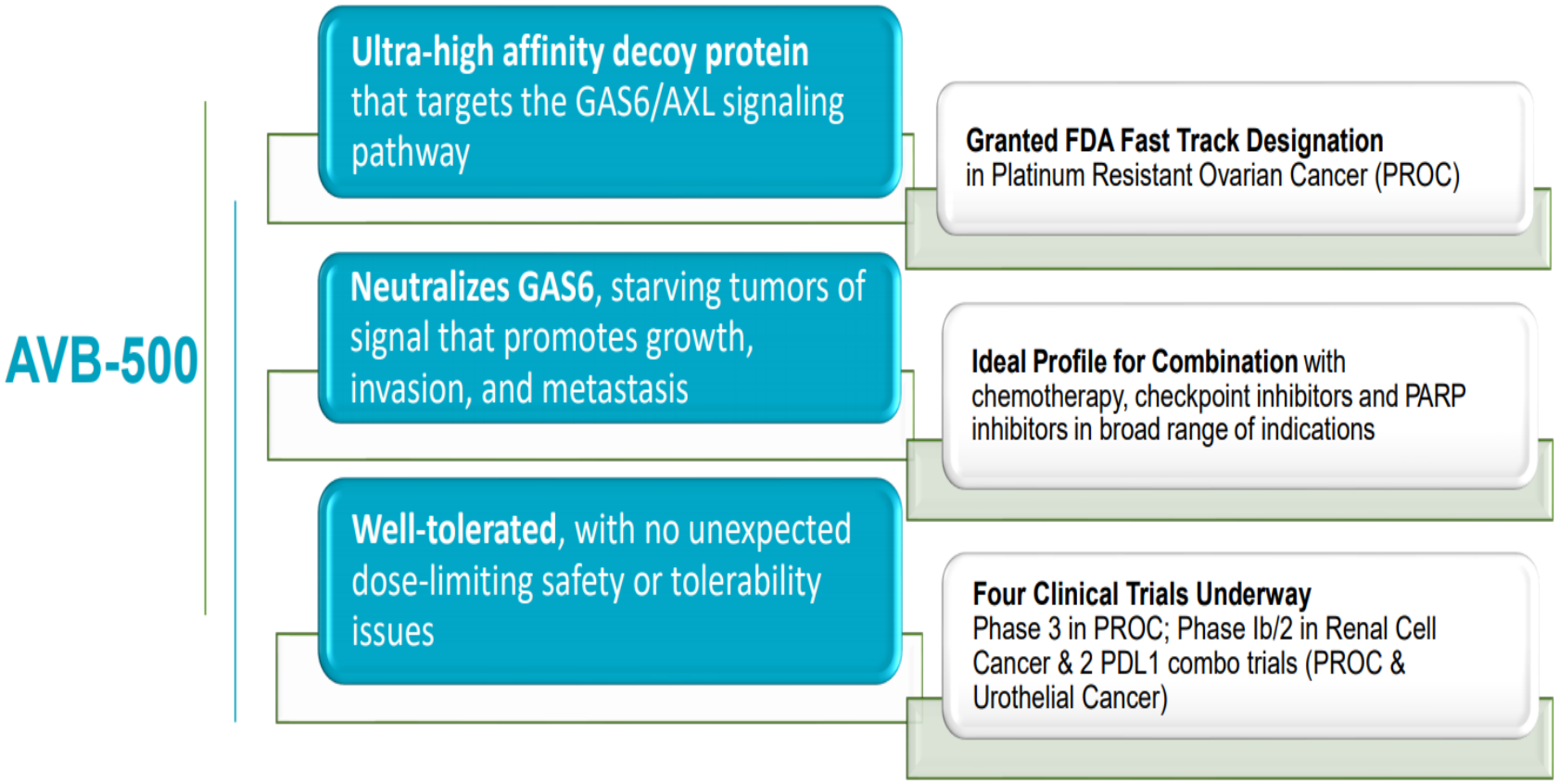
GAS6/AXL Signaling Pathway

GAS6 and AXL are overexpressed in many cancers and associated with tumor growth, metastasis, drug resistance, and poor overall survival

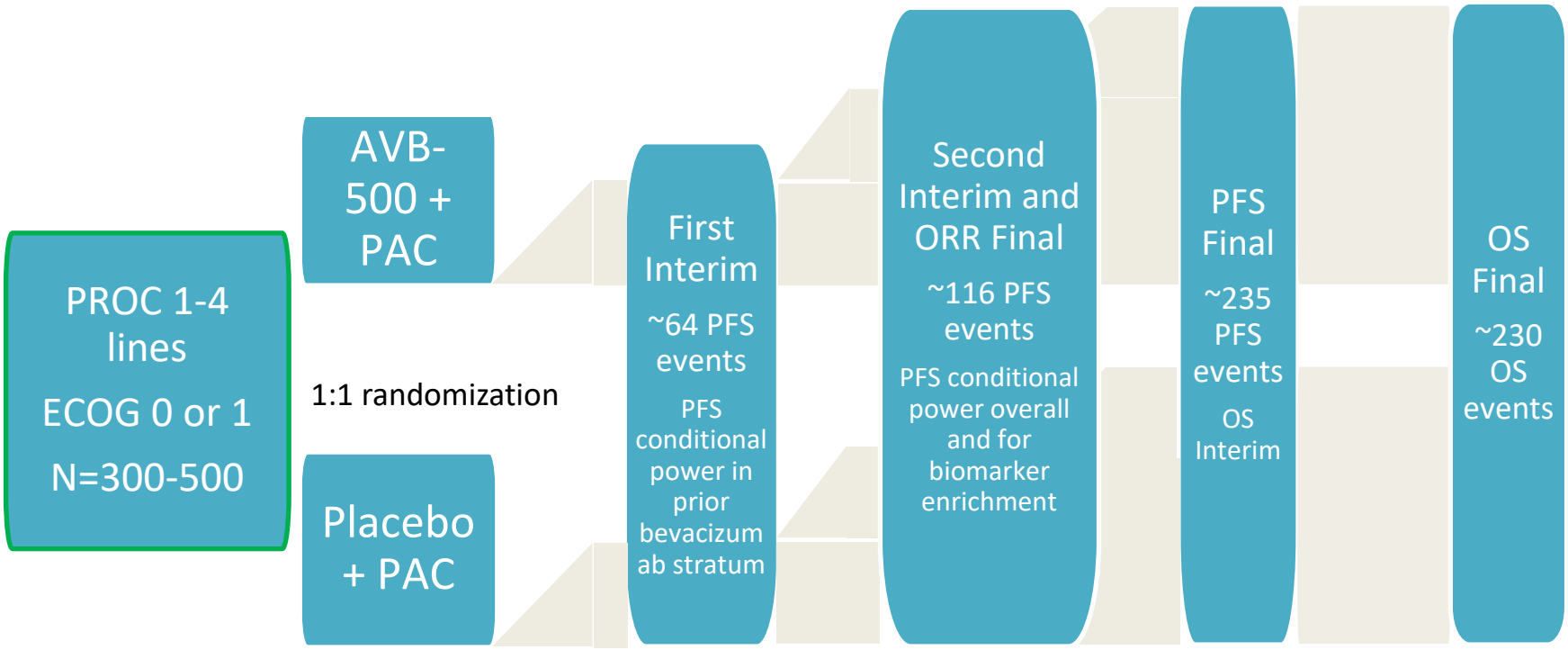
- GAS6 is growth factor that regulates several biologic processes in cells through interaction with its receptors, including AXL, Tyro3, and Mer
- GAS6 is the sole activating ligand of AXL
- GAS6/AXL signaling is key driver of cell migration/invasion, and associated with poor prognosis in cancer/fibrosis
- Pathway associated with acquired resistance to chemo, platinum-containing therapy, and targeted agents
- Inhibition of GAS6 & AXL has no toxicity to normal tissue



AVB-S6-500



AVB500-OC-004 Study Design – Current



<u>Stratification</u>
- Time since recurrence (<3m, ≥ 3m)
- Prior lines (1-2, 3-4)
- Prior bevacizumab (yes, no)

- First interim addresses unknowns about treatment effect in prior bevacizumab subjects
- Second interim addresses unknowns about treatment effect in biomarker enriched subjects
- Adaptive Design Goal: PFS Final analysis with at least 97% power to detect HR ≤ 0.60 at 1-sided α=0.025, median PFS of 3.9m in placebo group, ≤ 2% LTFU, 18 months accrual of 300 subjects from final target population, where HR=0.60 is expected to correspond to median difference of 2.6m

Ovaio 1° linea

- ENGOT ov33 - TRUST
- ENGOT ov46 - DUO-O
- ENGOT ov43
- ENGOT ov63 NIRVANA (new)
- ENGOT ov57 AGO-OVAR 28 (new)

Ovaio recidiva platino sensibile

- ENGOT ov38 - OReO
- ENGOT ov41 - ANITA

Ovaio recidiva platino resistente

- ENGOT ov51 - NiTChe
- ENGOT ov50
- ENGOT ov55 - MIRASOL
- EPIK-O
- ENGOT-ov66 (ARAVIVE)

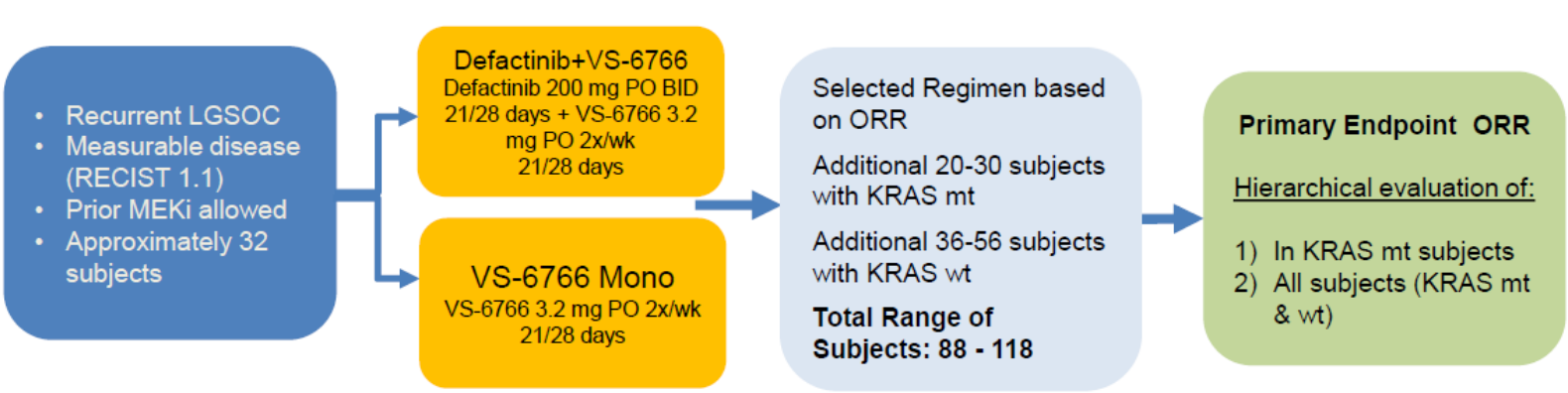
Carcinoma ovarico di basso grado

- ENGOT-ov60

MaNGO
Mario Negri Gynecologic Oncology

VS-6766-201
(ENGOT-ov60/NCRI; GOG-3052)

International CI/ENGOT lead: Susana Banerjee
GOG Foundation lead: Rachel Grisham



*Selection Phase – KRAS mt only

**Expansion Phase – final sample size to be adjusted based on adaptive design