OVARIAN CARCINOMA
PLATINUM SENSITIVE RELAPSE

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MaNGO
Mario Negri Gynecologic Oncology

- ENGOT-OV41 – ANITA (ACCRUAL CLOSED)
- ENGOT-OV49 – NEWTON (ONGOING)
- ENGOT-OV71 – UP-NEXT (ONGOING)
- ENGOT-OV73 – LUPPA (NEW PROPOSAL)
- ENGOT-OV76 - GLORIOSA (NEW PROPOSAL)

MaNGO
Mario Negri Gynecologic Oncology

ENGOT-Ov41 / GEICO 69-O / ANITA (Atezolizumab and Niraparib Treatment Association)

ENGOT Model B
Lead Group and Sponsor: GEICO
Supporter: ROCHE

N= 414 patients

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

IP: A. González

RANDOMIZATION

1:1

A
Platinum doublet 6 cycles
Placebo

B
Platinum doublet 6 cycles
Atezolizumab

RECIST v1.1 CT SCAN

If CR, PR or SD

Niraparib Until PD
Placebo until PD
Niraparib Until PD
Atezolizumab Until PD

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)

Site	PI	Total Screened	Screening Failure	Enrolled
IEO Milano	Colombo	21	3	18
Spedali Civili Brescia	Tognon	5	0	5
Ospedale Mauriziano Torino	Ferrero	4	0	4
IRCCS Arcispedale Reggio Emilia	Bologna	3	0	3
Ospedale Sant'Anna Torino	Zola	3	1	2
IOV-IRCCS Padova	Tasca	2	1	1
ASST-Lecco	Ardizzoia	1	0	1
TOTAL		**39**	**5**	**34**

417 patients randomized

Accrual closed on Q4 2021

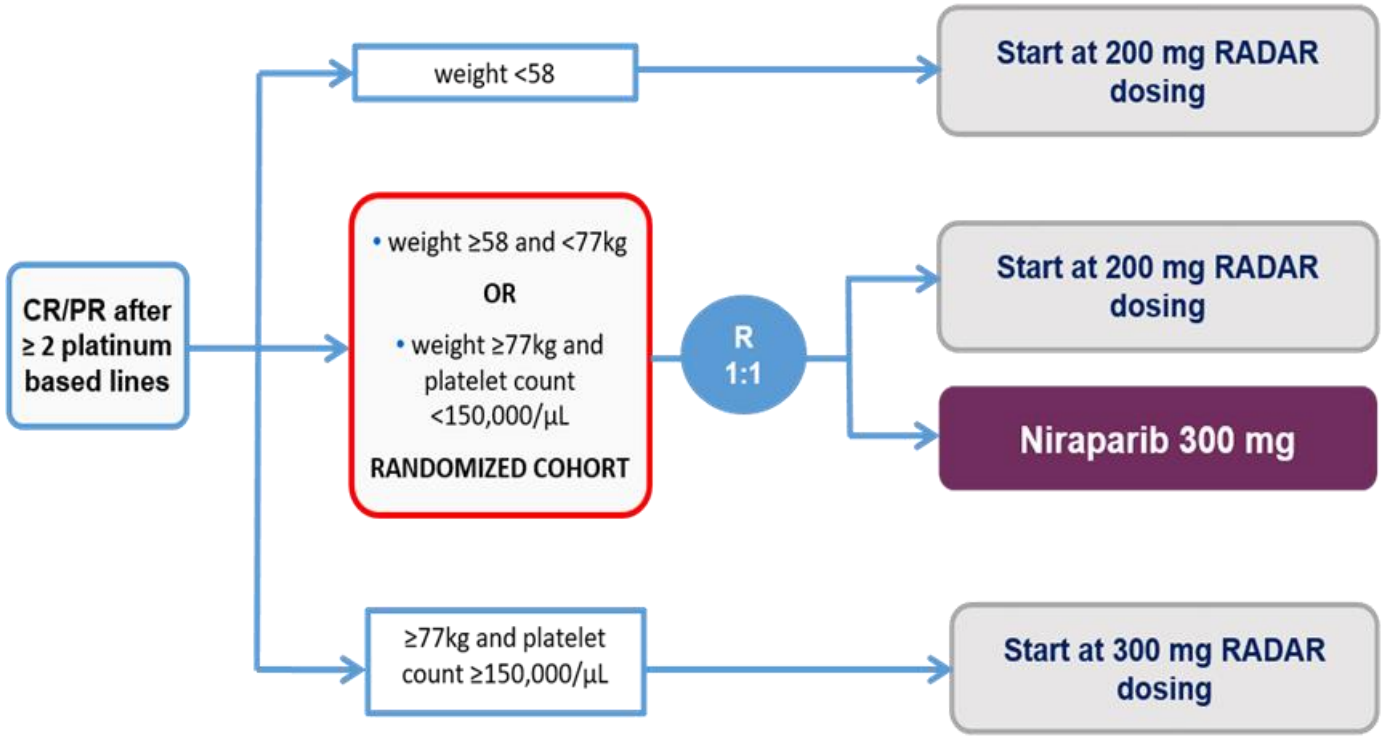
34 patients included by 7 MaNGO sites

332 PFS events (needed for the primary endpoint analysis) has been reached.

The cut off for data cleaning took place on 15th April 2023 and the data base lock will be on 1st July 2023

ENGOT-ov49 / MaNGO / NEWTON

(NEWTON study: NEW dosing maintTenance therapy Ovarian cancer)



ENGOT model: A
Sponsor: MaNGO
PI: Nicoletta Colombo (IEO Milano)

Accrual length: 18 months
Follow-up: 24 months

Sample-size: 105 patients
35 pts no random cohort
70 pts randomized cohort

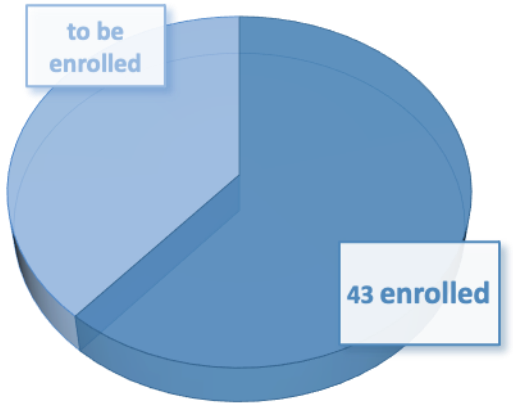
Two primary objectives:
1)comparison of RADAR vs 300 mg *in the* ***randomized cohort*** *in terms of* ***severe thromobocytopenia during the first 3 cycles***

2)evaluation of RADAR safety *in the* ***entire RADAR*** *cohort in terms of* ***severe thromobocytopenia during the first 3 cycles***

ENGOT-ov49/MaNGO/NEWTON

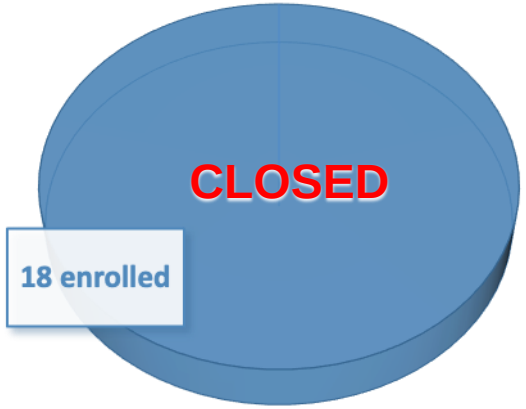
Accrual update by study cohort (at June 15th 2023)

Random Cohort / target 70 pts



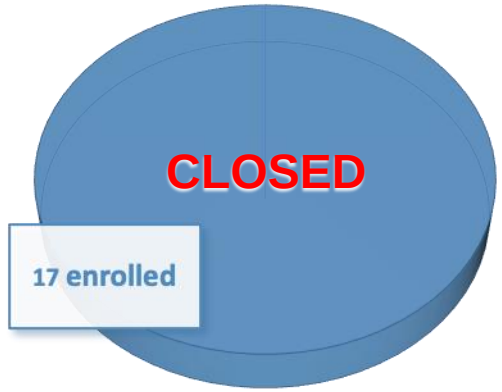
23 pts are missing!!!

Not-Random Cohort
<58 kg - 200 mg / target 18 pts



The number of patients as per sample size was reached!

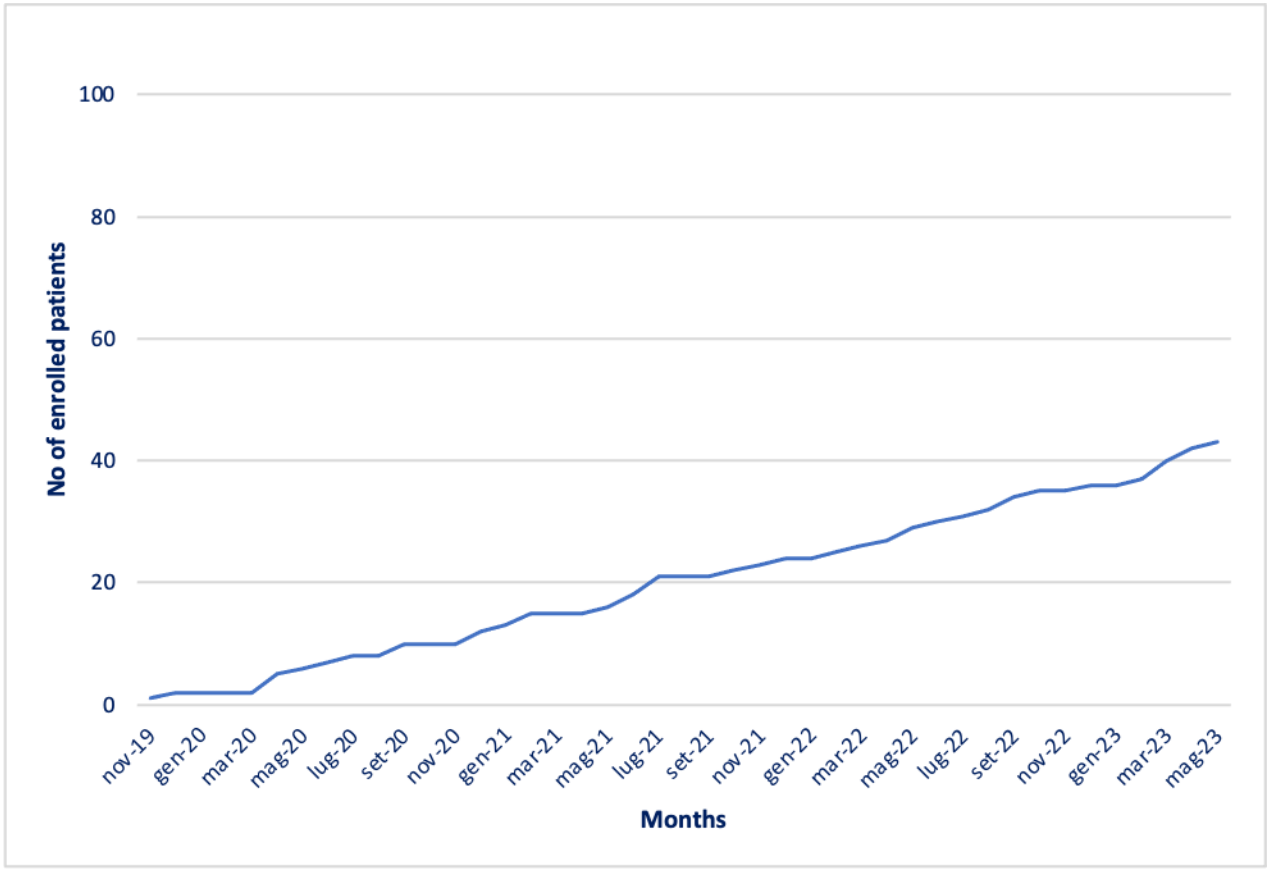
Not-Random Cohort
≥77kg and platelet ≥150,000/μL
300 mg / target 17 pts



The number of patients as per sample size was reached!

ENGOT-ov49/MaNGO/NEWTON

Trend of accrual ONLY in RANDOMIZED COHORT



An average number of 1 pt per month
Accrual under performing!!!!!

ENGOT-ov49/MaNGO/NEWTON

Enrollment by site

Site and PI	Activation date	Enrolled patients	Registered/ Randomized patients	Date of last registration/ randomization	Average time between registrations/ randomizations (days)
Milano IEO - PI Colombo	30-10-2019	39	34	06-03-2023	39
IOV Padova – PI Tasca	10-09-2020	14	13	29-05-2023	78
Spedali Civili -Brescia – PI Tognon	28-02-2020	14	12	24-05-2022	100
ASST - Monza – PI Lissoni	30-07-2020	9	8	05-12-2022	131
Mauriziano - Torino – PI Ferrero	15-09-2020	3	3	21-02-2022	335
INT – Milano – PI Raspagliesi	28/06/2022	1	1	28-04-2023	353
Policlinico Umberto I - Roma – PI Perniola	14/06/2022	1	1	17-04-2023	367
Sant'Anna - Torino - PI Katsaros	01-12-2020	2	2	14 -05-2021	464
Universitätsklinikum Carl Gustav Carus Dresden – PI Wimberger	10-11-2020	2	2	27-06-2022	474
IRCCS Arcispedale - Reggio Emilia - PI Bologna	27-01-2021	2	2	01-03-2023	884
Kliniken Essen Mitten – PI Heitz	23-02-2021	1	0	-	-
Charitè - Berlin – PI Chekerov	07-04-2022	0	0	-	-

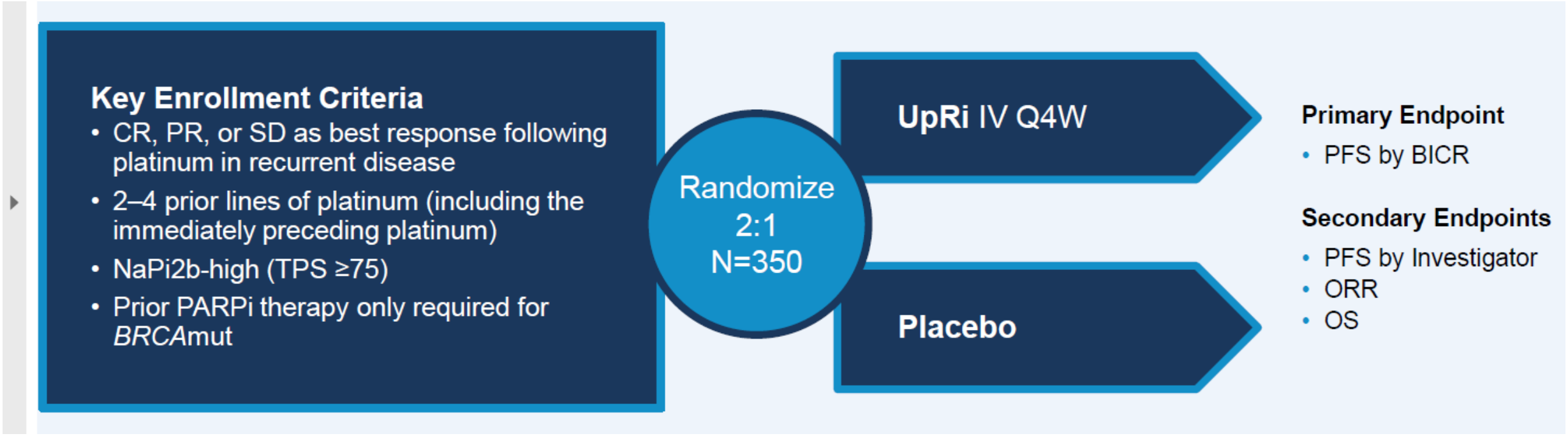
NSGO-CTU
Nordic Society of Gynaecological Oncology - Clinical Trial Unit

ENGOT
European Network of Gynaecological Oncological Trial groups

ENGOT Model C
Lead Group: NSGO-CTU
Sponsor: Mersana Therapeutics

ENGOT-OV71/NSGO-CTU/UP-NEXT
/GOG-3049

A Phase 3, Randomized, Placebo-controlled, Multicenter Study of Upifitamab Rilsodotin as Post-Platinum Maintenance Therapy for Participants with Platinum-Sensitive Recurrent Ovarian Cancer



ENGOT-ov71/UP-NEXT update as June 2023

Milestone	Updated Timelines
First Patient First Visit	Actual: 12 October 2022
Last Patient First Visit	September 2024
Last Patient Last Visit	September 2025
Primary Endpoint Analysis	Q4 2025
Study Closure	Q4 2025
Final Clinical Study Report	Q1 2026

Sponsor comment: *"We have encountered some delays in activities and have shifted our timelines, however, we do hope we are able activate sites and speed enrollment to achieve these milestones earlier"*

Study Status as of 26 Jun 2023:

- 73 sites active total (67 sites activated in North America, 5 sites activated in APAC, 1 site in Israel)

- 275 pre-screened, 52 screened,
- **20 randomized patients**

ENGOT-ov71/UP-NEXT update as June 2023: MaNGO sites

Italy (MITO/MaNGO)

- CA Approval received 07Dec2022
- EC Approval received 10Jan2023
  - EC approval for additional sites received 11May2023
- Amendment
  - RA submission occurred on 10Feb2023, pending approval
  - **Lead EC approved received 28Mar23**

Site Name	PI	Selection complete?	Agreeement status
Ospedale Sant'Anna, Torino. Day Hospital Oncologico	Dyonissios Katsaros	Yes	Under revision
Spedali Civili, Brescia. Ostetricia e Ginecologia	Rossella Franzini	Yes	Finalized
Ospedale Manzoni, Lecco. Oncologia	Alessandra Crippa	Yes	Finalized
Istituto Europeo di Oncologia, Milano. Ginecologia Oncologica	Nicoletta Colombo	Yes	Under revision
Istituto Nazionale dei Tumori, Milano. Ginecologia Oncologica	Francesco Raspagliesi	Yes	Finalized
Ospedale San Gerardo, Monza. Oncologia Ginecologica	Andrea A. Lissoni	Yes	Under revision
Veneto Oncology Institute (IOV), IRCCS	Valentina Guarneri	Yes	Finalized

Activation of MaNGO sites will start soon

Phase III trial

Lurbinectedin – Paclitaxel in platinum sensitive ovarian cancer relapsed to prior PARPi and Bevacizumab (LUPPA-1 study)

Study design

2022

ENGOT-ov73/LUPPA-1 study

Adaptive Study Design:

N=250 to 375 patients

- High grade serous ovarian cancer
- ECOG-PS: 0-1
- 2-3 prior lines
- (at least one platinum-paclitaxel based combination)
- Platinum sensitive disease
- Prior bevacizumab
- Prior PARPi
- Measurable disease (RECIST v1.1)

Randomization 1:1

3rd / 4th line of treatment

- **Lurbinectedin** (2.2 mg/m² D1 q3wk) + **Paclitaxel** (80 mg/m² D1, D8 q3wk)

N=125

Lurbinectedin (3.2 mg/m² D1 q3wk)
In case PAC discontinuation due to tox

- **Platinum combo** (PLD, Gem or Paclitaxel)
- **Weekly Paclitaxel** (a mín of 30% of pts needed)

N=125

Primary endpoint: PFS

Until PD or toxicity

Planned enrolment period: 26 months

Stratification:

1. BRCA status (wild/mut)
2. PFI (6-12 vs > 12 m)
3. TTP to PARPi (≤18 vs >18 m)
4. Inv Preference

Interim analysis 12wks after pt 60*

SSR (Sample Size Reassessment) At the end of Recruitment

Final PFS analysis

- **Interim analysis based on ORR:** (H0) that 15% or less patients responded ($p \leq 0.15$) *versus* the alternative hypothesis (H1) that 40% or more patients are responders ($p \geq 0.40$). *At least 10 responses out of 30 pts and no detrimental difference in ORR are needed to continue recruitment.
- **SSR (Sample Size Reassement) based on PFS**

LUPPA-1 Update as June 2023: MaNGO sites involved

City	Hospital	Principal Investigator	Commitment*
Torino	Ospedale Mauriziano	Annamaria Ferrero	10 pts/year
Brescia	Spedali Civili	Germana Tognon	6 pts/year
Lecco	Ospedale Manzoni	Federica Villa	4 pts/year
Milano	Istituto Naz. dei Tumori (INT)	Francesco Raspagliesi	10 pts/year
Genova	Osp. San Martino	Serafina Mammoliti	10 pts/year
Padova	Ist. Oncologico Veneto	Valentina Guarnieri	4 pts/year
Reggio E.	Arcispedale S. M. Nuova	Alessandra Bologna	20 pts/year

*according to the feasibility questionnaire

The MaNGO feasibility was presented to the lead group/we are waiting indication

GLORIOSA

RANDOMIZED PHASE 3 TRIAL OF MIRVETUXIMAB + BEVACIZUMAB MAINTENANCE IN FRα-HIGH PSOC PATIENTS

ENGOT Model C

Sponsored by **ImmunoGen**

Lead in ENGOT by **MITO**

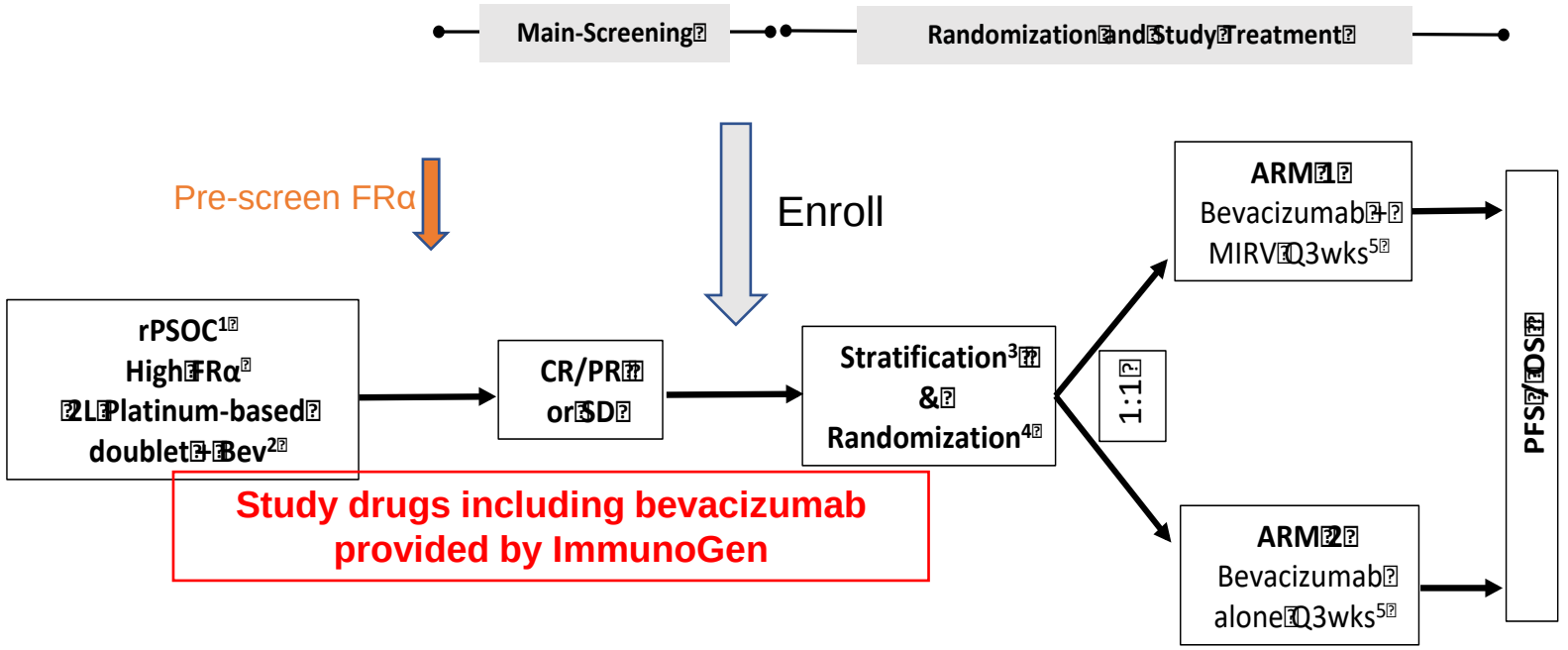
GLORIOSA: Schema (Maintenance only)

There are two different ways to enter the study: as maintenance only (after chemo; option 1) OR before chemo (chemo is given on study; option 2)

OPTION 1:

Enrollment after completion of triplet chemotherapy

- Chemotherapy per standard practice
  - Carboplatin
  - Bevacizumab
  - Inv Choice: Pac, PLD, or Gem
- Enroll patient after response to chemotherapy prior to maintenance
- Pre-screen for FRα at any time prior to consenting



[1] High-grade epithelial ovarian, primary peritoneal, or fallopian tube cancers

[2] Platinum + chemo + bevacizumab for planned 6 cycles (minimum of 4 and maximum of 8 cycles) including at least 3 cycles of bevacizumab

[3] Stratification factors: prior PARP inhibitor: Yes vs No; CR or PR or SD; prior bevacizumab: Yes vs. No.

[4] Enrollment into Trial for Randomization will require documented radiographic confirmed CR, PR or SD

[5] Maintenance treatment must begin 12 weeks or less from last dose of triplet therapy and w/in 30 days of randomization. Treatment continued until progressive disease, unacceptable toxicity, withdrawal of consent, death, or Sponsor terminates the study

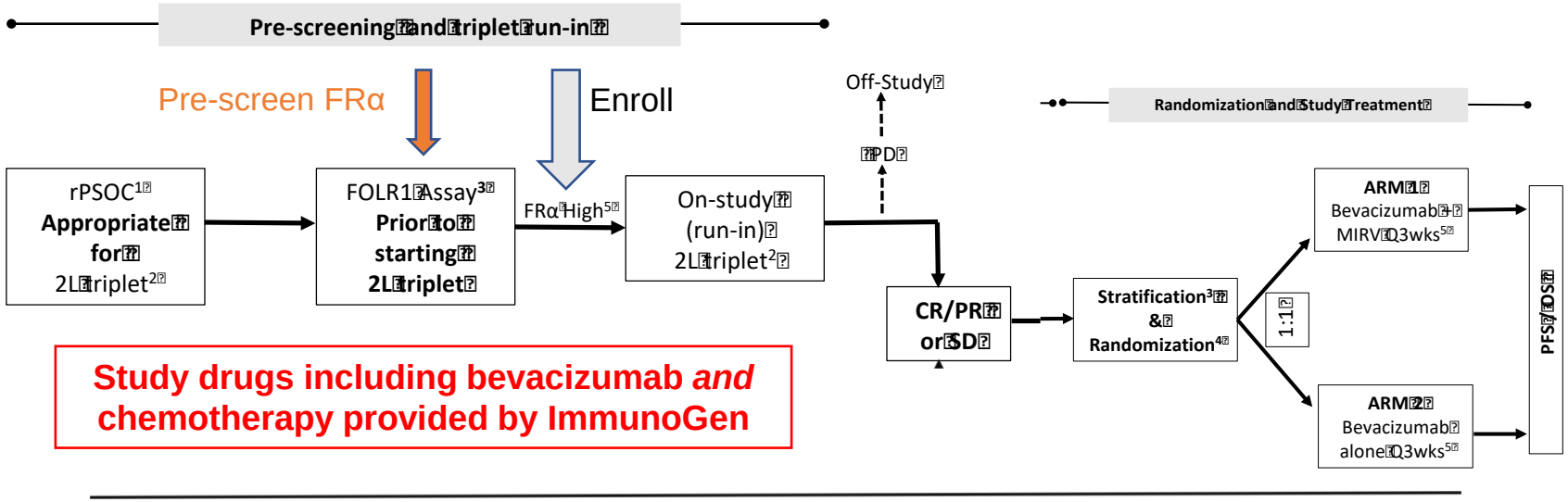
Abbreviations: CR: complete response; PR: partial response; SD: stable disease; MIRV: mirvetuximab soravtansine; PFS: progression free survival; OS: overall survival

GLORIOSA: Schema (Run-In Option)

OPTION 2:

Enrollment prior to triplet chemotherapy "Run-In"

- Chemotherapy dosing as per protocol
  - Carboplatin
  - Bevacizumab
  - Inv Choice: Pac, PLD, or Gem
- Plan 6 cycles of treatment
- Pre-screen for FRα prior to treatment and consenting
- Enroll patient prior to chemotherapy for recurrence
- **Patients will receive their triplet therapy on study (provided by Immunogen)**



[1] High-grade epithelial ovarian, primary peritoneal, or fallopian tube cancers
[2] Triplet = Platinum + chemo + bevacizumab for planned 6 cycles (minimum of 4 and maximum of 8 cycles) including at least 3 cycles of bevacizumab
[3] Patients pre-screened by FOLR1 Assay **prior to initiation of 2L triplet**. FRα high patients receive 2L triplet on-study (run-in). Upon completion of triplet, patients determined to have PD will not proceed to randomization and will come off study.
[4] Patients pre-screened by FOLR1 Assay **during or upon completion of their ongoing triplet.** FRα high patients determined to have PDs after completion of triplet are screen failures.
[5] Patients who are FRα negative by FOLR1 Assay will be considered screen failures.
Abbreviations - 2L Second Line; CR complete response; FOLR1 Folate Receptor 1; FRα Folate Receptor alpha; PD progressive disease; PR partial response; SD stable disease.

GLORIOSA UPDATE June 2023:

the submission of the study through the new EU platform completed on June 2023

MaNGO selected sites

PI Surname	PI Forename	Hospital/Institution Name	Status of the site
Petrella	Maria Cristina	AOU Careggi	Ready for the submission
Sikokis	Angelica	AOU di Parma	This site will be submitted with the next amendment
Tomao	Federica	AOU Policlinico Umberto I	This site will be submitted with the next amendment
Villa	Federica	ASST Ospedale Alessandro Manzoni	Ready for the submission
Porzio	Rosa	AUSL Piacenza Ospedale Guglielmo da Saliceto	Ready for the submission
Bologna	Alessandra	AUSL RE Arcispedale Santa Maria Nuova	This site will be submitted with the next amendment
Baldini	Editta	Azienda USL Toscana Nord Ovest Ospedale San Luca	This site will be submitted with the next amendment
Raspagliesi	Francesco	Fondazione IRCCS Istituto Nazionale dei Tumori	This site will be submitted with the next amendment
Mammoliti	Serafina	IRCCS AOU San Martino	This site will be submitted with the next amendment

GRAZIE

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