



STANDARD TREATMENTS AND NEW DIRECTIONS IN GYNAECOLOGICAL CANCERS

MILANO June 26th-29th, 2025

Responsabili Scientifici:
NICOLETTA COLOMBO, FRANCESCO RASPAGLIESI



OVARIAN CANCER TRIALS

Short summary on ongoing studies

Elena Biagioli, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Milano

OVARIAN CANCER TRIALS SUMMARY

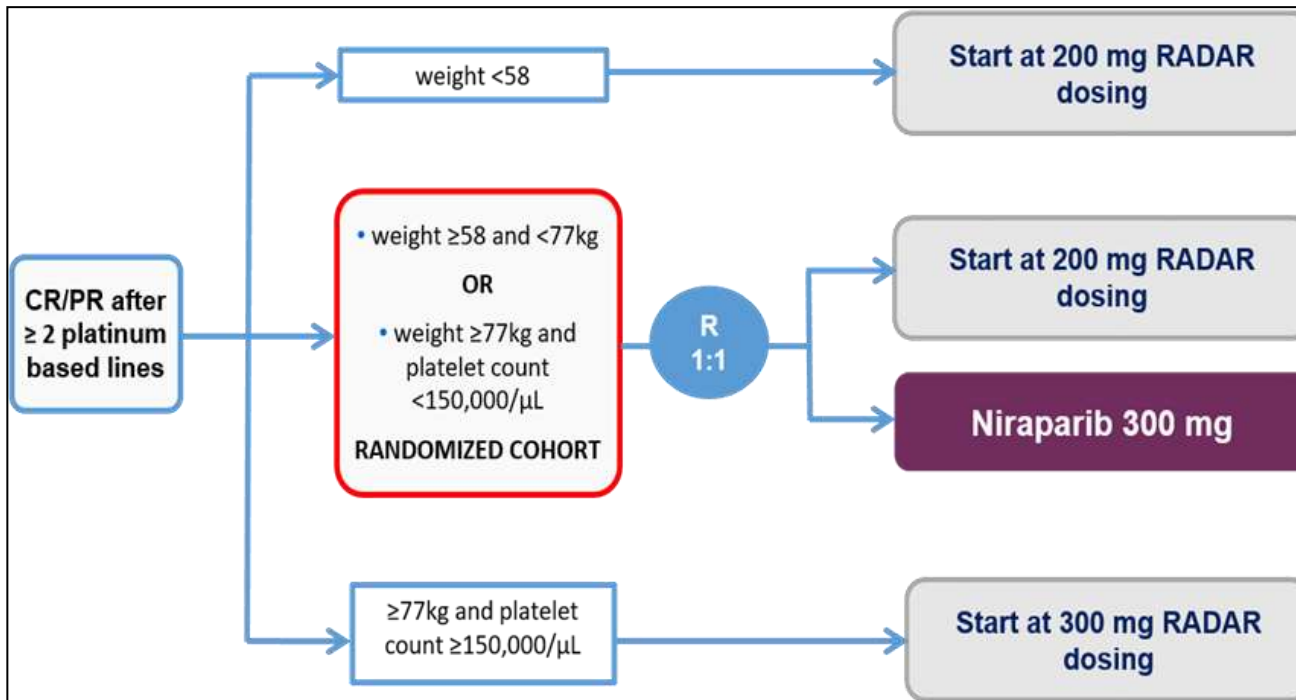
Accrual closed

- ENGOT-ov49 / NEWTON
- ENGOT-ov51 / MITO 33 / NITCHE
- ENGOT-ov65 / KEYNOTE-B96

Ovarian cancer trials summary – Accrual closed **NEWTON**

NEWTON study: NEW dosing maintenance therapy Ovarian cancer

A multicenter, open-label phase II trial of a new customized dosing (Rational Adjustment of Dose to reduce Adverse Reactions “RADAR” dosing) of niraparib as maintenance therapy in platinum sensitive ovarian, fallopian tube or primary peritoneal recurrent cancer patients



ENGOT model: A

Sponsor: MaNGO

PI: Nicoletta Colombo (IEO Milano)

Two primary objectives:

- 1) comparison of RADAR vs 300 mg in the randomized cohort in terms of severe thrombocytopenia during the first 3 cycles
- 2) evaluation of RADAR safety in the entire RADAR cohort in terms of severe thrombocytopenia during the first 3 cycles

Sample-size 105 patients:

35 pts no random cohort > accrual reached
70 pts randomized cohort > **accrual not reached:**
48 pts randomized

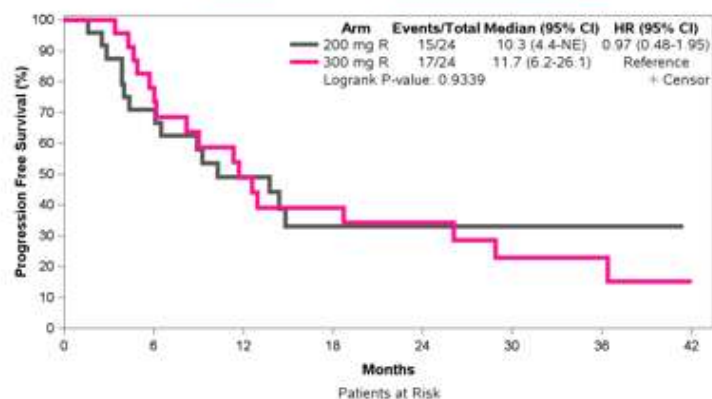
Poster with results presented at ESMO gynecological cancers 19-21 June 2025

85P Niraparib customized dosing regimen (RADAR) to manage thrombocytopenia events in platinum-sensitive recurrent ovarian cancer patients.

The NEWTON trial /ENGOT-ov49



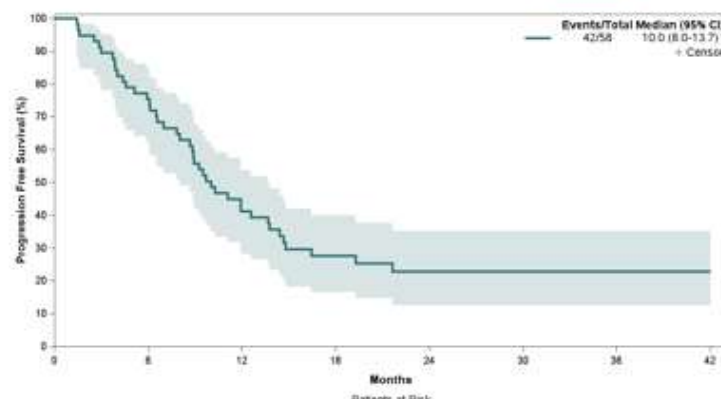
Kaplan-Meier curves of PFS of randomized arms



Months	24	17	10	4	3	2	2	0
200 mg R	24	17	10	4	3	2	2	0
300 mg R	24	17	10	8	6	4	3	2

No differences were found in PFS between the randomized arms.

Kaplan-Meier curve of PFS of RADAR cohort



Median PFS in the entire RADAR cohort was 10.0 [8.0-13.7] months.

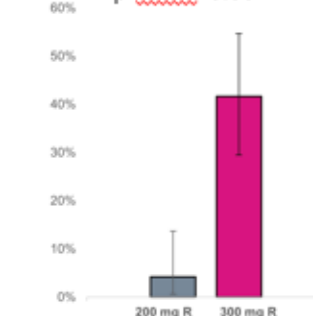
E-mail: nicoletta.colombo@ieo.it; mango@marionegri.it

Galli³, M. Lapresa¹, G. Doria¹¹, S. Ficarelli⁴, S. Canova⁵, S. Derio¹, E. Biagioli³.

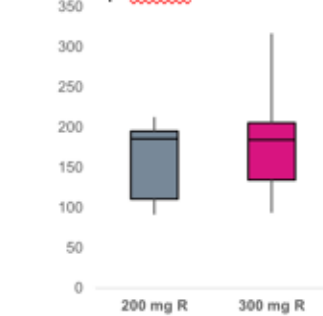
¹UO Ostetricia e Ginecologia, ASST Spedali Civili di Brescia, Brescia, Italy; ²Medical Oncology, IRCCS, Regio Emilia, Italy; ³Gynecologic Oncology dept., Fondazione IRCCS-Istituto Nazionale dei Tumori, Milan, Italy; ⁴UO Ostetricia e Ginecologia, ASST Spedali Civili di Brescia, Brescia, Italy; ⁵Medical Oncology, IRCCS, Regio Emilia, Italy; ⁶Gynecologic Oncology dept., Fondazione IRCCS-Istituto Nazionale dei Tumori, Milan, Italy; ⁷UO Ostetricia e Ginecologia, ASST Spedali Civili di Brescia, Brescia, Italy; ⁸Medical Oncology, IRCCS, Regio Emilia, Italy; ⁹Gynecologic Oncology dept., Fondazione IRCCS-Istituto Nazionale dei Tumori, Milan, Italy; ¹⁰UO Ostetricia e Ginecologia, ASST Spedali Civili di Brescia, Brescia, Italy; ¹¹UO Ostetricia e Ginecologia, ASST Spedali Civili di Brescia, Brescia, Italy.

across 9 sites (8 sites were prematurely closed). Non-randomized cohort

G₃ thrombocytopenia rates
p-value=0.0044



Niraparib (mg) dose intensity
p-value=0.2700



Arm	300mg NR
200 mg R	60 (46-85)
300 mg R	82 (77-97)
300 mg R	17 (100.0)

Conclusions

Niraparib RADAR dosing seems to be a valid schedule to reduce severe thrombocytopenia, with no apparent detrimental impact on PFS.

References

1. Mansoor R. M., et al. N Engl J Med 2016; Volume 375(22):2154-2164;
2. Josep M.d.C., et al. J Clin Oncol 2019; Volume 37, no. 22;
3. Sandhu SK et al. Lancet Oncol 14:882-92, 2013

Acknowledgements

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Disclosures

N. Colombo: Advisory Board: AbbVie, Gilead, BioNTech, Novocure, Onxerna, Eisai, Immunogen, GSK, MSD/Merck, AstraZeneca, Roche
Invited Speaker: GSK, MSD/Merck, AstraZeneca

Ovarian cancer trials summary – Accrual closed **NItCHE**

ENGOT-ov51/ MITO 33 A Randomized phase III trial on Niraparib-dostarlimab vs physician's choice CHEmotherapy in recurrent, platinum resistant ovarian, fallopian tube or primary peritoneal cancer: NItCHE trial

- ENGOT Model: B
- Sponsor: MITO Group
- Lead Group: MaNGO
- Participating Groups: MaNGO, MITO, GINECO, NOGGO, CEEGOG
- Participating MaNGO sites **IEO / Nicoletta Colombo (MaNGO PI) , Spedali Civili/Germana Tognon, Ospedale S. Anna /Dionyssios Katsaros, Ospedale Manzoni /Federica Villa**

MaNGO sites & study updates

The study has currently closed the recruitment

- N° enrolled patients :**586**
- N° total screening failure :**133**
- N° randomized patients : **441**
- N° death events: **192 (a total number of 247 events are required)**

Take home messages:

To complete eCRF & solve pending queries

Ovarian cancer trials summary – Accrual closed **ENGOT-ov65 / KEYNOTE-B96**

ENGOT-ov65 / MK-3475-B96 / KEYNOTE-B96: A Phase 3, Randomized, Double-Blind Study of Pembrolizumab Versus Placebo in Combination With Paclitaxel With or Without Bevacizumab for the Treatment of Platinum-resistant Recurrent Ovarian Cancer (KEYNOTE-B96/ENGOT-ov65)



Key Eligibility Criteria

- Platinum Resistant OC patients (refractory excluded)
- Up to 2L of prior therapy
- ECOG PS 0, 1
- Prior immune oncology allowed
- Prior PARPi allowed
- Prior bevacizumab allowed

Randomization
1:1
N=600

Stratification factors for randomization

- Bevacizumab use
- PD-L1 status
- Prior IO

Pembrolizumab
+
Paclitaxel
+/- bevacizumab

Pembrolizumab
placebo
+
Paclitaxel
+/- bevacizumab

Statistical Considerations

- Primary endpoints:

- PFS in CPS \geq 1 ($\alpha=0.02$ 1-sided)
- PFS in all population ($\alpha=0.005$ 1-sided) with roll-over of alpha from PFS in CPS1 if positive

- Key secondary endpoints:

- OS in CPS \geq 1
- OS in all population

Hierarchical approach:

- ❖ OS in CPS1 can be tested only if both PFS analyses are positive
- ❖ OS in all pts can be tested only if OS in CPS1 will be positive

- ENGOT Model: C
- Sponsor: Merck Sharp & Dohme Corp.
- **Lead Group: MaNGO**
- **PI ENGOT: Nicoletta Colombo**

- **LPLV:** 05/03/2025 >> Interim Analysis 2 / abstract sent to ESMO 2025

Pembrolizumab Combo Improves PFS in Platinum-Resistant Ovarian Cancer

May 21, 2025

By Russ Conroy

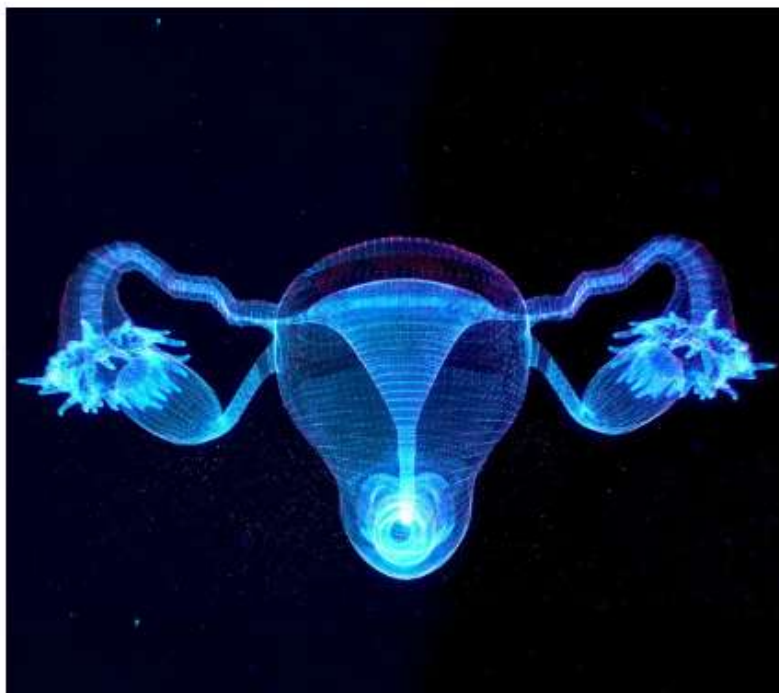
Fact checked by Ariana Pelosci

News

Article



KEYNOTE-B96 showed pembrolizumab-based therapy improved PFS and OS in PD-L1–positive platinum-resistant ovarian cancer.



The phase 3 KEYNOTE-B96/ENGOT-ov65 trial (NCT05116189) found that pembrolizumab (Keytruda) plus paclitaxel with or without bevacizumab (Avastin) significantly improved progression-free survival (PFS) in patients with platinum-resistant ovarian cancer, including those with PD-L1–positive tumors, meeting the trial’s primary end point, according to a press release from Merck.¹

After an independent data monitoring committee conducted prespecified interim analyses, data showed that pembrolizumab-based treatment produced a clinically meaningful and statistically significant PFS improvement vs placebo plus chemotherapy with or without bevacizumab, regardless of

OVARIAN CANCER TRIALS SUMMARY

Accrual ongoing trials

- ENGOT-ov63 / NIRVANA-1 (first line)
- IOLANTHE (first line)
- ENGOT-ov76 / GLORIOSA (platinum sensitive)
- ENGOT-ov77 / DS6000-109 (platinum resistant)

Ovarian cancer trials – Accrual ongoing **ENGOT-ov63/NIRVANA-1**

ENGOT-ov63 / NIRVANA-1 A Randomized Study of Paclitaxel-Carboplatin followed by maintenance Niraparib compared to Paclitaxel-Carboplatin-Bevacizumab followed by maintenance Niraparib+Bevacizumab in Patients With Advanced Ovarian Cancer Following a Front-Line Complete Cytoreductive Surgery

Site and PI	Patients
Istituto Nazionale dei Tumori - PI Francesco Raspagliesi (MaNGO PI)	13 patients randomized, 2 screen-failed
AOU Careggi – PI Maria Cristina Petrella	2 patients randomized,
Ospedale di Sondrio - PI Alessandro Bertolini	Open not yet recruited
Ospedale S. Gerardo - PI Andrea Alberto Lissoni	6patients randomized
Istituto Europeo di Oncologia – PI Nicoletta Colombo	10 patients randomized
Ospedale Croce e Carle - PI Marcella Occelli	Open not yet recruited
Ospedale Sant’Anna – PI Dionyssios Katsaros	Agreement not yet negotiated

ENGOT Model: A

Sponsor: ARCAGY GINECO

- The recruitment is currently ongoing
- 271 patients randomized (target 380 pts)
- Last randomized patient : Q1 2026 (estimated)
- Last patient last treatment: Q2 2028 (planned)
- Last patient last visit : Q1 2031 (planned)

Take home message:

- to identify new potential patients
- to complete eCRF & solve pending queries



NEW DIRECTIONS IN GYNAECOLOGICAL CANCERS



Ovarian cancer trials – Accrual ongoing IOLANTHE

IOLanTHE A phase IIIb-IV trial testing Olaparib and Bevacizumab as maintenance frontline Treatment of HRD positive ovarian tumours

Sponsor: Ymagine

PI: Federica Tomao (Sapienza Roma)

No. of sites involved: 13

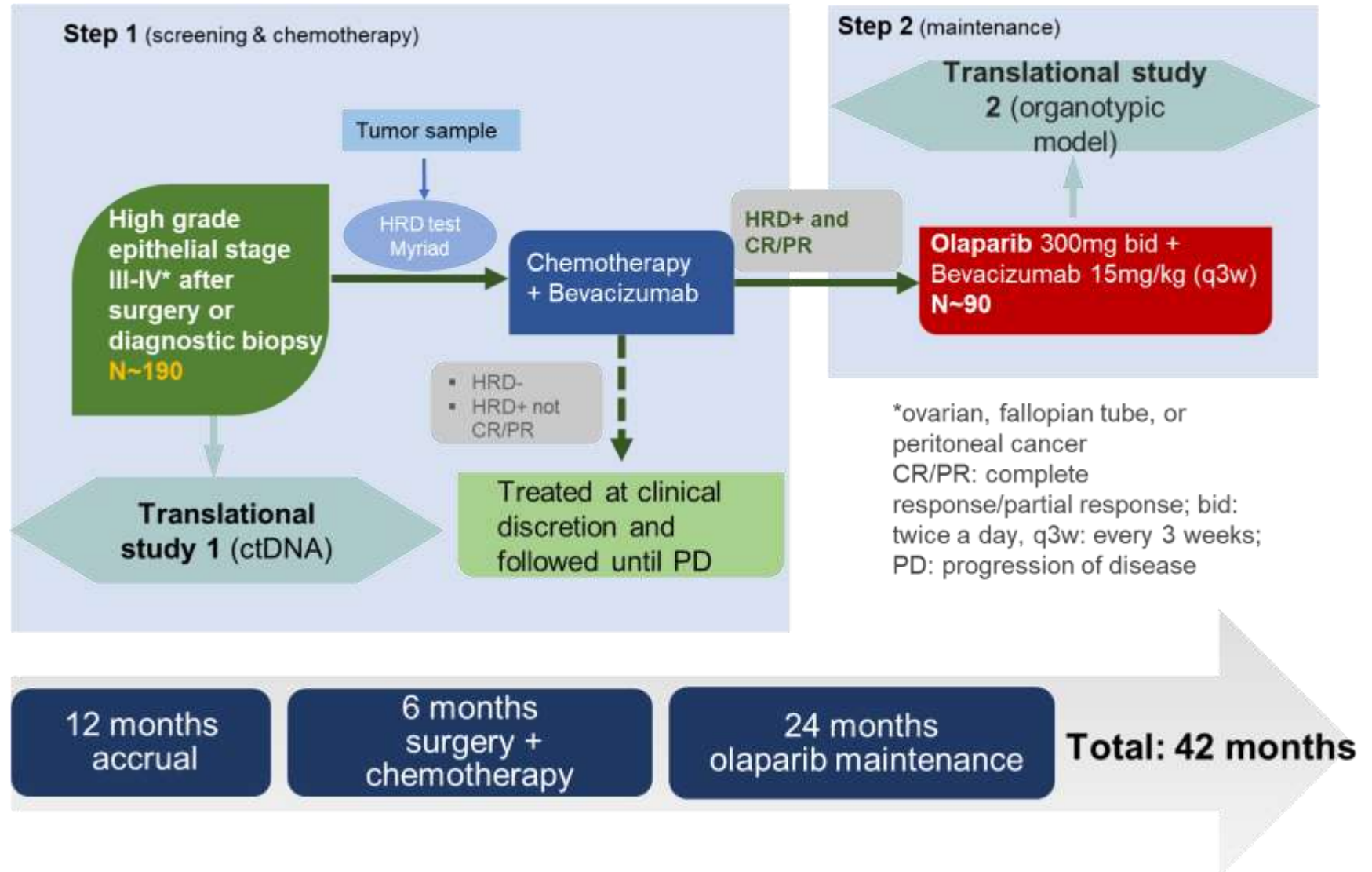
First patient-in: 15-Sep-2023

No. of pts registered: 198

No. of screening failures: 25

No. of pts eligible for step 1: 134

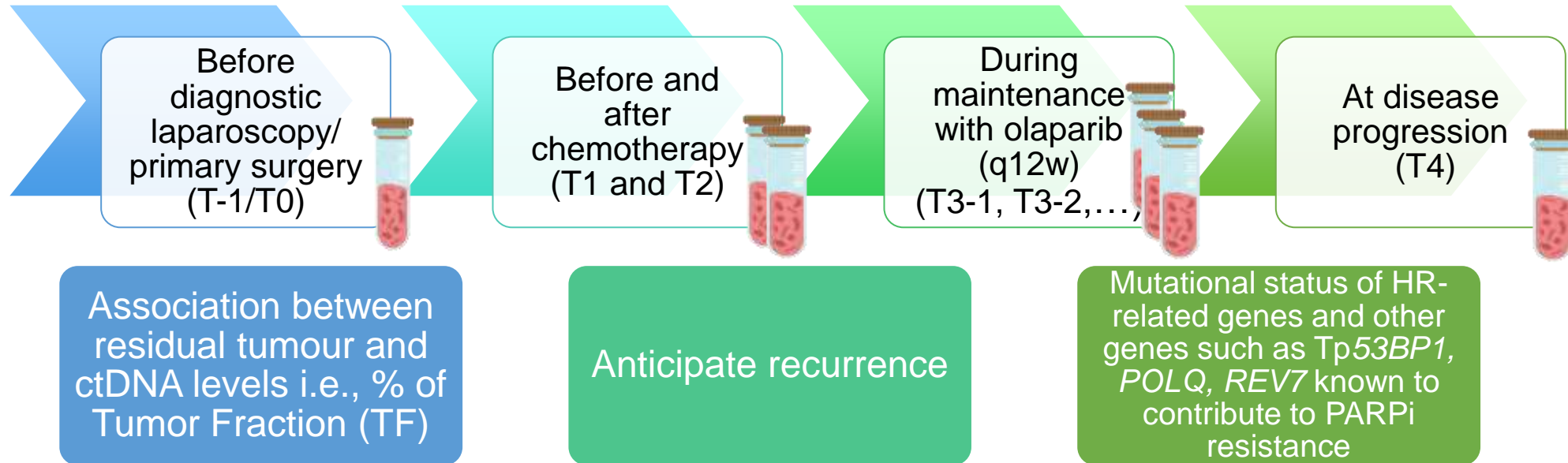
Closure of enrolment: end of Sep. 2025



Translational study no. 1 - aims

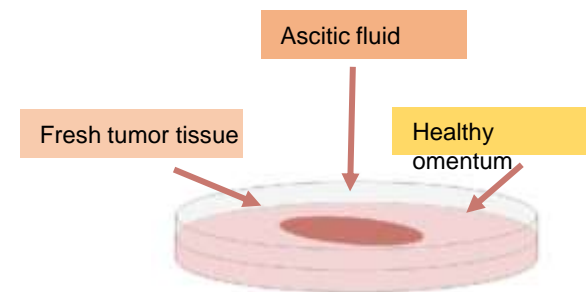
Plasma collection at specific timepoints for ctDNA longitudinal monitor

Cancer
Pharmacology group
Prof. Maurizio
D'Incalci



Translational study no. 2 - aims

Organotypic model



Ugo Cavallaro
Unit of Gynecological
Oncology Research

The patients' response to olaparib and bevacizumab will be evaluated in terms of **24 month PFS**



The **cancer cells' response** is defined as the **percentage of either bulk or cancer stem cells** which **survive after 72-hour** exposure to olaparib.

Exploratory aims:

Primary tumor tissues will be analysed with different in-house assays aimed at predicting the response to platinum and olaparib.

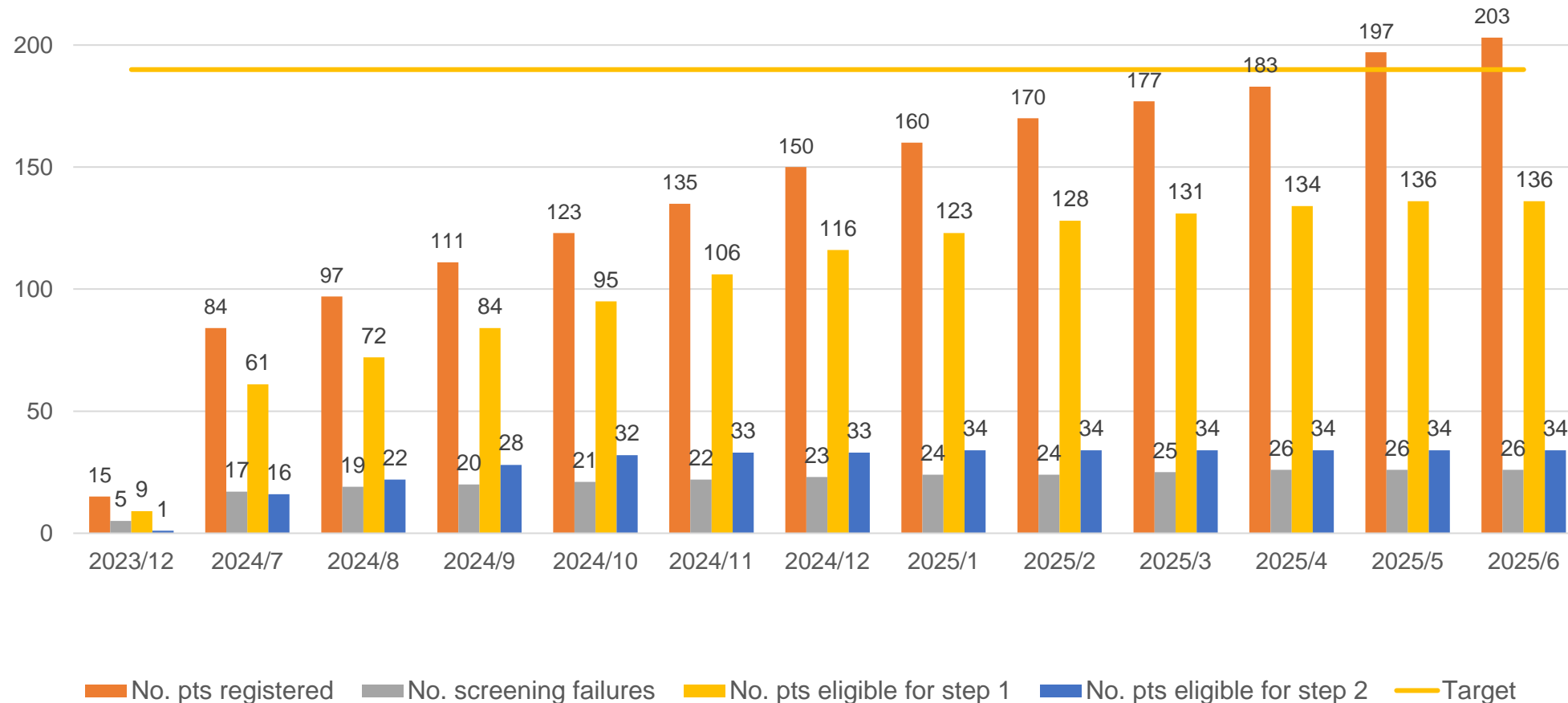
The agreement between these assays and the commercial one (Myriad Mychoice CDxPlus) will be evaluated.

These assays will include:

- the quantification by an immunofluorescence-based assay of number of RAD51/Gemin positive cells (RAD51 score) - Evaluation performed at Mario Negri by Giovanna Damia group
- An academic HRD - Test developed by Humanitas/ D'Incalci group

Ovarian cancer trials – Accrual ongoing IOLANTHE

Enrolment Status as of Jun 26, 2025



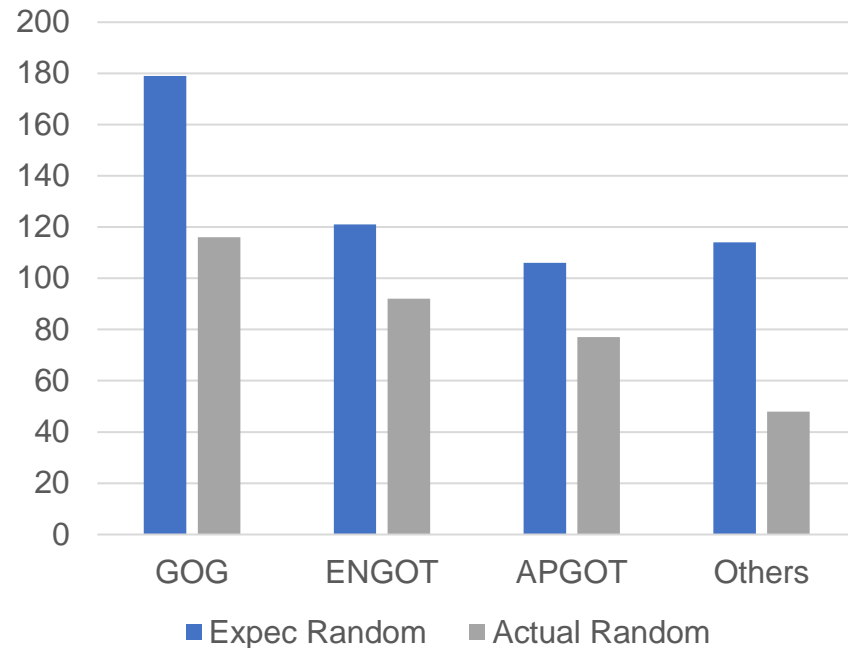
ENGOT-ov76/GLORIOSA Randomized, multicenter, open-label, Phase 3 study of mirvetuximab soravtansine in combination with bevacizumab versus bevacizumab alone as maintenance therapy for patients with FR α -high recurrent platinum-sensitive epithelial ovarian, fallopian tube, or primary peritoneal cancers who have not progressed after second-line platinum-based chemotherapy plus bevacizumab

- ENGOT model: C
- Sponsor: AbbVie
- Lead Group ENGOT: MITO

GLORIOSA

Ovarian cancer trials – Accrual ongoing ENGOT-ov76/GLORIOSA

Enrolment Global



Total expected: 520

Total random: 333

Total screening failure: 1064
due to negative FRα: 808

Enrolment updates MaNGO sites

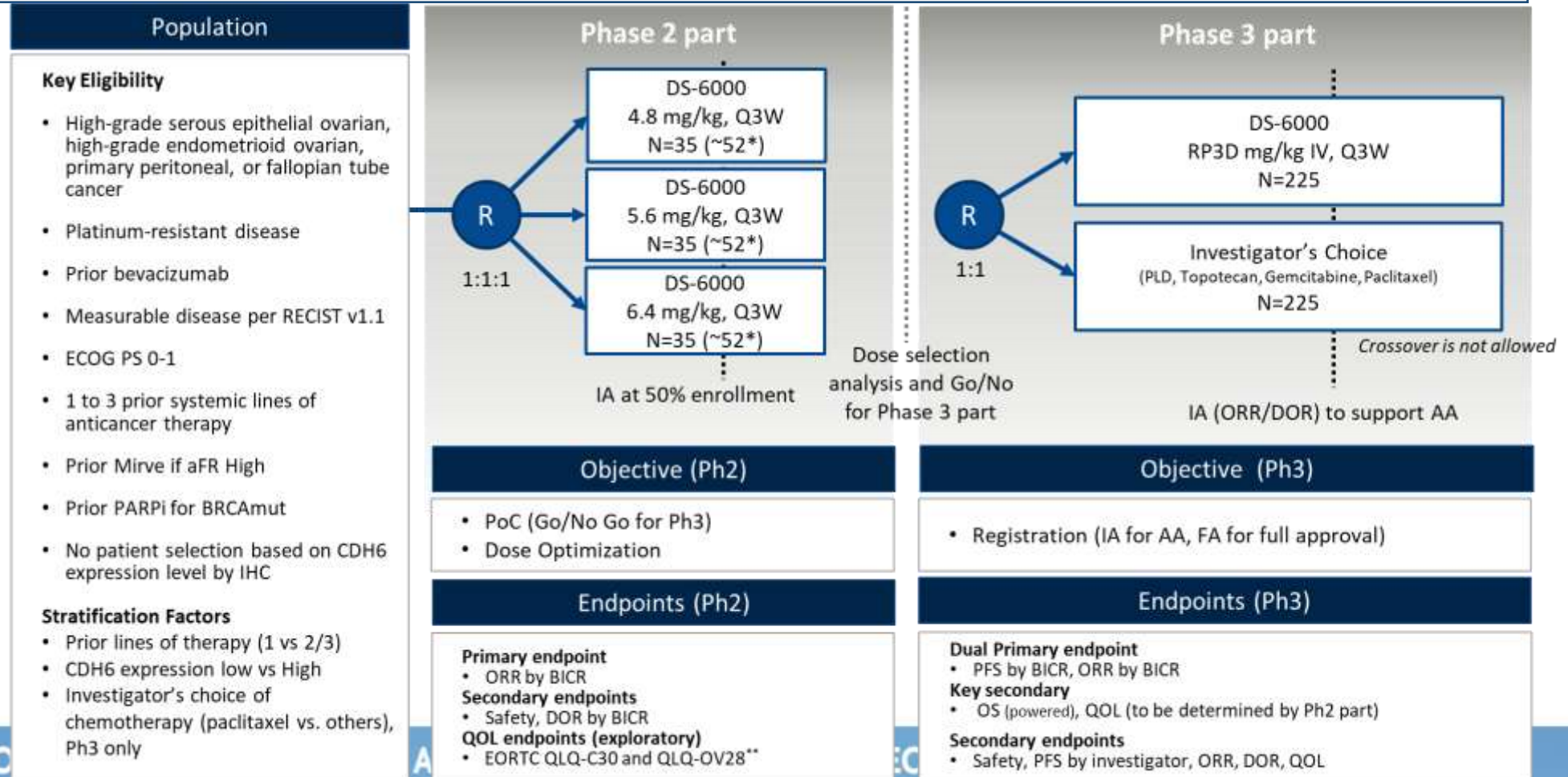
@11 June 2025

PI	Hospital/Institution Name	Maintenance Enrolled	Run In Enrolled	Screening failure
Petrella Maria Cristina (MaNGO PI)	AOU Careggi	1	0	6
Sikokis Angelica	AOU di Parma	0	0	0
Tomao Federica	AOU Policlinico Umberto I	0	0	0
Villa Federica	ASST Ospedale Alessandro Manzoni	1	0	2
Porzio Rosa	AUSL Piacenza Ospedale Guglielmo da Saliceto	1	0	0
Bologna Alessandra	AUSL RE Arcispedale Santa Maria Nuova	0	1	0
Baldini Editta	Azienda USL Toscana Nord Ovest Ospedale San Luca	0	0	1
Raspagliesi Francesco	Fondazione IRCCS Istituto Nazionale dei Tumori	5	1	6
Mammoliti Serafina	IRCCS AOU San Martino	1	1	3

Ovarian cancer trials – Accrual ongoing ENGOT-ov77 /DS6000-109

ENGOT-ov77 / DS6000-109 A Phase 2/3, Multicenter, Randomized Study of Raludotatug Deruxtecan (R-DXd), a CDH6-directed Antibody-drug Conjugate, in Subjects with Platinum-resistant, High-grade Ovarian, Primary Peritoneal, or Fallopian Tube Cancers

- ENGOT model: C
- Sponsor: Daiichi Sankyo, Inc
- Lead Group ENGOT: GINECO



Ovarian cancer trials – Accrual ongoing ENGOT-ov77 /DS6000-109

Study Timelines & MaNGO Sites status

Phase II (Optimization dose)

- First Patient In (ENGOT): 19-Jun-2024
- Last Patient In: 14-Oct-2024
- Phase II expansion: for all site starting since Aug-2025 (Italy will join only in case of remaining slots from US)

Results Optimization dose
(107 pts) will be
presented at ESMO 2025

Phase III

- First Patient In expected: Q4 2025

SITE_ID	SITE_NAME	SITE_STATUS	FIRST_NAME	LAST_NAME	SIV Date	Site Activation Date	# Patient in screening	# Patient enrolled	# Patient Screen failed	TOTAL # Patient	Next Steps
3901	Ospedale San Gerardo Monza	1. Not open	Andrea Alberto	LISSONI							Phase 3
3903	AOU Careggi	3. Open - Active	Maria Cristina	PETRELLA	19-Jul-24	01-Aug-24	0	5	2	7	
3904	Istituto Europeo di Oncologia	3. Open - Active	Nicoletta	COLOMBO	15-Jul-24	17-Jul-24	0	19	10	29	
3907	Ospedale Mauriziano	3. Open - Active	Annamaria	FERRERO	11-Jul-24	11-Jul-24	0	4	1	5	

Grazie per l'attenzione