OVARIAN CARCINOMA
PLATINUM RESISTANT RELAPSE

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- ENGOT OV55 – MIRASOL (RESULTS AVAILABLE)
- ENGOT OV50 – INNOVATE-3 (ACCRUAL CLOSED)
- ENGOT OV61 – EPIK-O (ACCRUAL CLOSED)
- ENGOT OV66 – AXLERATE-OC (ACCRUAL CLOSED)
- ENGOT OV65 - KEYNOTE-B96 (ACCRUAL CLOSED)
- ENGOT OV51 – NITCHE (ONGOING)
- ENGOT OV68-ARTISTRY-7 (NEW)
- ENGOT-OV79/GEICO 134-O/STRO-002-GM3 (NEW)

MaNGO
Mario Negri Gynecologic Oncology

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

ENGOT Model: C
Sponsor: Immunogen
Lead group: BGOG

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

Planned No. of patients: 430

ENROLLMENT CLOSED July 2022

ENGOT Groups

- 11 participating ENGOT groups
- 1004 patients screened
- **235 patients randomized**

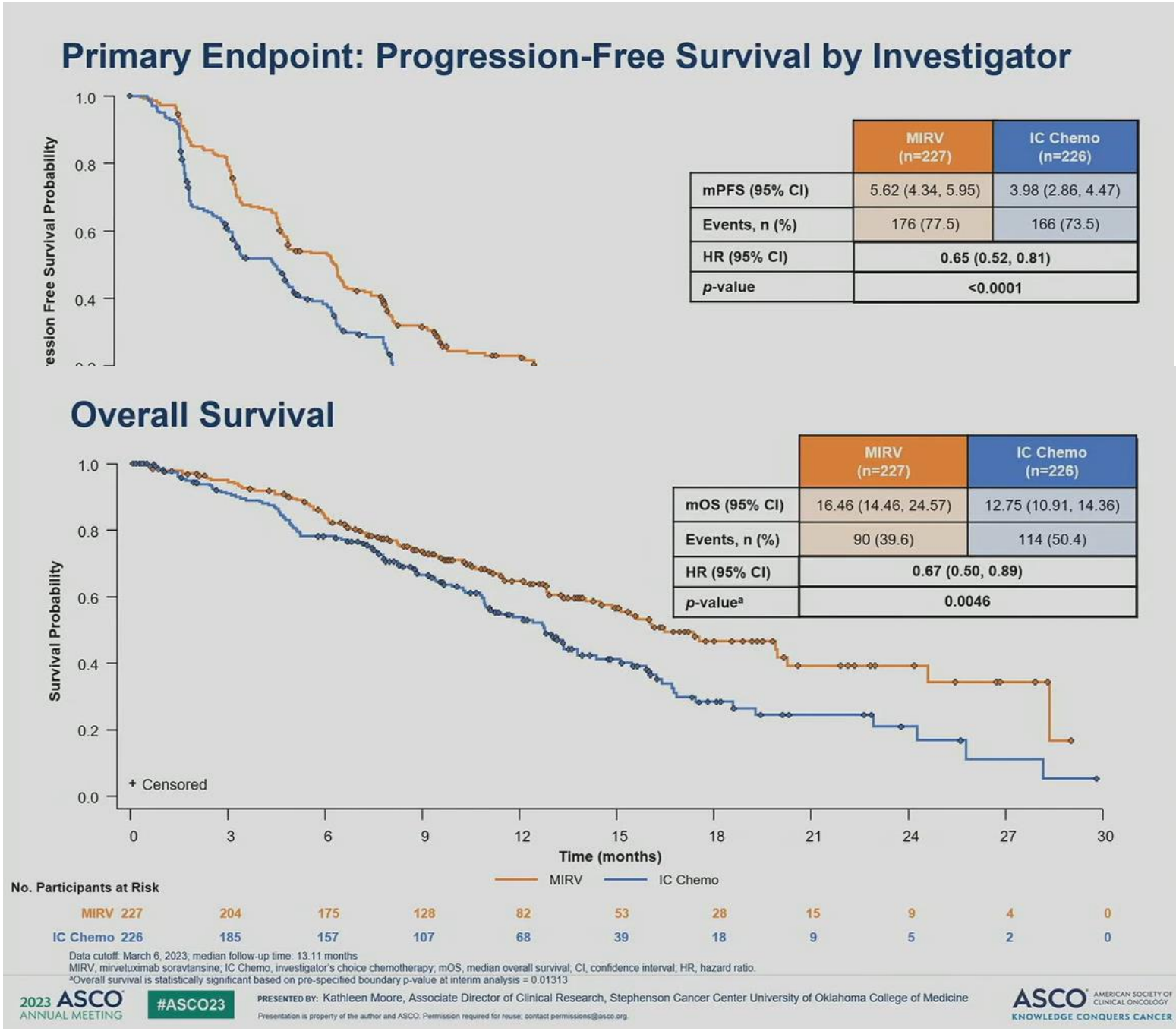
ENGOT-ov55/MIRASOL: Final accrual

MaNGO (Italy)

Site number		PI	Total Screened	Total Randomized
502	IRCCS - Istituto Europeo di Oncologia	Dr. Colombo	73	16
519	Azienda Socio Sanitaria Territoriale degli Spedali Civili di Brescia	Dr. Tognon	4	0
520	Ospedale Mauriziano Umberto I	Dr. Ferrero	7	0
522	Servizio Sanitario Regionale Emilia-Romagna	Dr. Bologna	2	1
525	Azienda Ospedaliera di Lecco	Dr. Ardizzoia	7	0
526	IOV Istituto Oncologico	Dr. Tasca	5	1
527	Azienda Ospedaliera Città della Salute e della Scienza di Torino	Dr. Zola	0	0
			98	18

MIRASOL Results: Final PFS

(ASCO 2023)



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

ENGOT model C

Sponsor: Novocure

Lead group: BGOG

Primary endpoint: OS

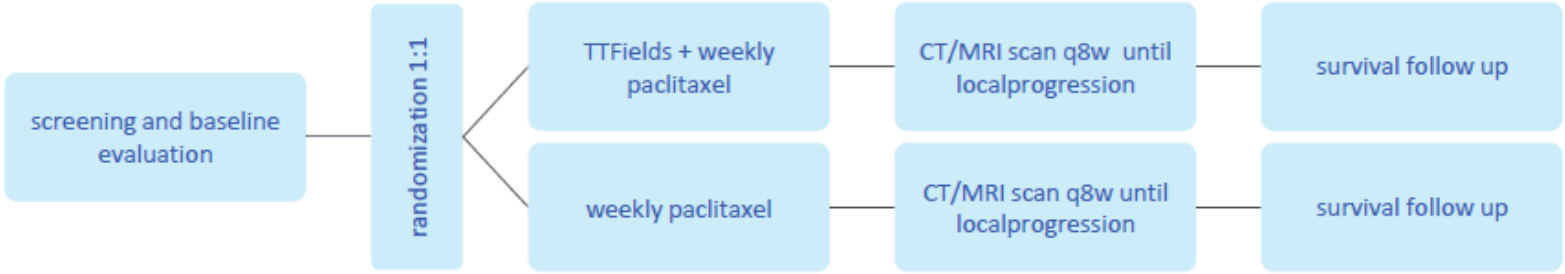
Secondary endpoints: PFS, ORR, severity and frequency of adverse events, QOL, time to undisputable deterioration in health-related QoL / death

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



Accrual closed oct 2021

MaNGO enrolled 33 patients from 3 MaNGO sites

OS results expected soon

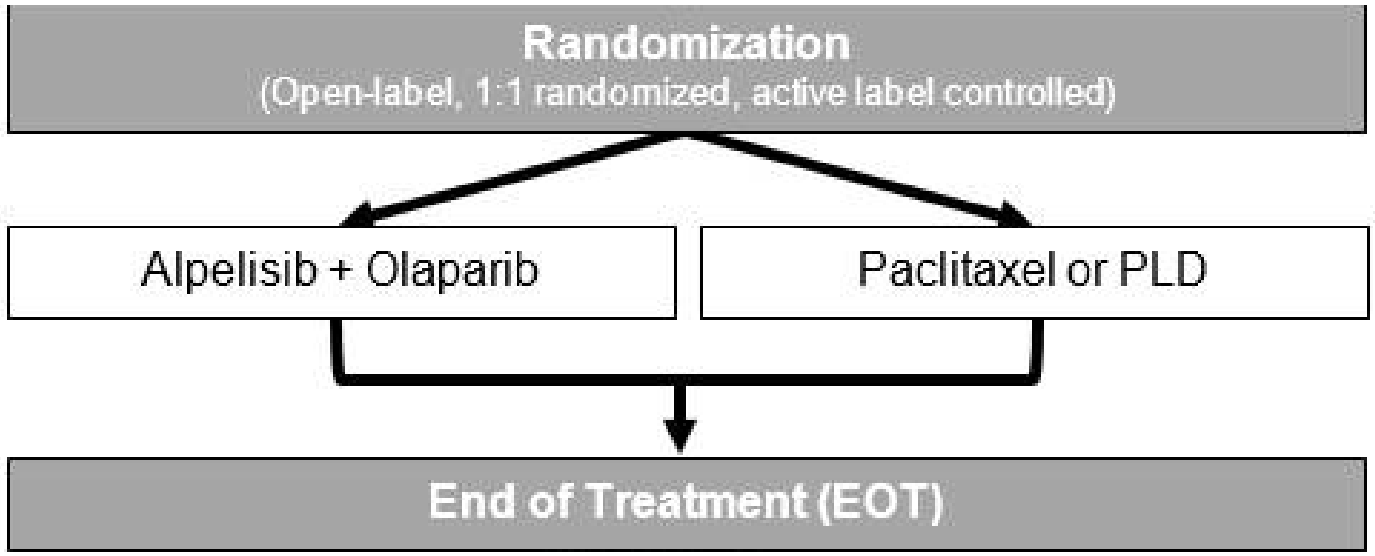
A Phase III, multi-center, randomized (1:1), openlabel, active-controlled study to assess the efficacy and safety of alpelisib (BYL719) in combination with olaparib as compared to single agent cytotoxic chemotherapy, in participants with no germline BRCA mutation detected, platinum-resistant or refractory, high-grade serous ovarian cancer

ENGOTov61 – EPIK-O Study Design

Study Design

ENGOT Model: C
Sponsor: Novartis
Lead group: GEICO

Patients with platinum-resistant or refractory, gBRCAnm HGSOC



Previous PARPi and Bevacizumab treatment allowed

Primary Endpoint PFS

- HR: 0.60 (which corresponds to an increase in median PFS to 5.7 months)

Target: 380 pts

Update as of June 2023

Accrual Closed

Grupo Español de Investigación en Cáncer de Ovario

Italy- MANGO

MaNGO Mario Negri Gynecologic Oncology

ENGOT ESGO European Network of Gynaecological Oncological Trial groups

Country	nº sites planned	nª sites activated	Targeted nº of randomized patients	% Allocation Met
Italy- MANGO	4	4	12	175%

Site Number	Investigator	Pre-Screened	In Pre-Screenin	Pre-Screen Failed	Screen	In Screening	Screen Failed	Randomi
TOTAL		**33**	**2**	**2**	**29**	**0**	**8**	**21**
4300	Nicoletta Colombo	14	0	0	14	0	5	9
4303	Claudio Zamagni	8	1	0	7	0	1	6
4304	Lorenzo Antonuzzo	4	0	1	3	0	0	3
4306	Francesco Raspagliesi	7	1	1	5	0	2	3

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

ENGOTov66/GEICO104-O AXLerate-OC AVB500-OC-004

ENGOT Model: C
Sponsor: Aravive
Lead group: GEICO

PROC 1-4 lines
ECOG 0 or 1
N=300-500

1:1 randomization

AVB-500 + PAC

Placebo + PAC

First Interim
~64 PFS events
PFS conditional power in prior bevacizumab stratum

Second Interim and ORR Final
~116 PFS events
PFS conditional power overall and for biomarker enrichment

PFS Final
~235 PFS events
OS Interim

OS Final
~230 OS events

|----- ~Months 1-11 ------| |--- ~Months 12-15 ----| |------- ~Months 16-26 -------| |---- ~Months 23-45 -----|

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

Legend: PAC cisplatin, doxorubicin and cyclophosphamide

FPI: 21 April 2021;
LPI: 09 Jan 2023 (Accrual closed)
Primary analysis PFS: Q3 2023 (DB lock July 2023)
Primary analysis OS expected: Q2 2024

ENGOTov66/GEICO104-O
AXLerate-OC AVB500-OC-004

ENGOT OV66 / GEICO 104-O

AXLerate-OC /AVB500-OC-004

Enrollment By Country (as per 21 February 2023)

Country	Active Sites	Screened	In Screen	Screen Failed	Random	Active	Bev	No Bev
USA	84	262	0	60	202	39	119	82
Canada	3	11	0	0	11	6	2	9
Belgium	8	11	0	1	10	1	6	4
Czechia	4	7	0	0	7	2	4	3
France	1	8	0	1	7	0	7	0
Georgia	6	21	0	4	17	11	2	15
Greece	1	3	0	2	1	1	0	1
Italy	8	29	0	5	24	11	11	13
Poland	5	13	0	3	10	5	4	6
Spain	11	55	0	6	49	14	29	20
UK	5	14	0	3	11	2	1	10
China	14	26	2	10	14	6	2	12
Study Totals	**150**	**460**	**2**	**95**	**363**	**98**	**187**	**175**

Country	Active Sites	Screened	In Screening	Screen Failed	Random	Active	Bev	No Bev
ENGOT	49	161	0	25	136	47	64	72
NO ENGOT	101	299	2	70	227	51	123	103

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Total MaNGO sites acivated 4

- IEO, Milano
- Ospedale San Luca, Lucca
- Ospedale Santo Stefano, Prato
- Policlinico S. Orsola-Malpighi, Bologna

- 4 patients randomized by MaNGO sites

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

ENGOT Model C
Sponsor: Merck/MSD
ENGOT lead group: MaNGO
PI: Nicoletta Colombo (IEO, Milano)

KEYNOTE-B96/ ENGOT-ov65 Study design

Key Eligibility Criteria

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

Stratification factors for randomization

- Bevacizumab use
- PD-L1 status
- Prior IO

Randomization 1:1 **N=600**

Pembrolizumab + Paclitaxel +/- bevacizumab

Pembrolizumab placebo + Paclitaxel +/- bevacizumab

Statistical Considerations

- **Primary endpoints:**
  - PFS in CPS>=1 (α=0.02 1-sided)
  - PFS in all population (α=0.005 1-sided) with roll-over of alpha from PFS in CPS1 if positive
- **Key secondary endpoints**:
  - OS in CPS>=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

Study Milestones

Expected Final Database Lock: **Q3 2027**
Expected final PFS analysis: **Q4 2027**

KEYNOTE-B96 / ENGOT-ov65 trial updates as of 07 June 2023 (final)

ENGOT sites

Group	Country	Sites involved	First Site Ready*	Screened	Randomized
MaNGO	Italy	7 (7 active)	29 Mar 2022	83	71
BGOG	Belgium	4 (4 active)	23 May 2022	18	15
GINECO	France	6 (6 active)	28 Mar 2022	53	45
NOGGO	Germany	9 (9 active)	04 May 2022	23	14
DGOG	Netherlands	4 (4 active)	15 Mar 2022	32	22
NCRI	UK	8 (8 active)	18 Feb 2022	39	28
CTI	Ireland	2 (1 active)	04 Jul 2022	6	3
ISGO	Israel	7 (7 active)	09 Dec 2021	37	28
TSRGO	Turkey	8 (8 active)	13 Apr 2022	34	26
PGOG	Poland	8 (8 active)	23 Dec 2021	49	34
NSGO	Denmark	1 (active)	05 Apr 2022	5	4
	Finland	1 (active)	03 Feb 2022	6	4
	Norway	1 (active)	21 Feb 2022	2	2
ENGOT TOTAL:		**65/66 activated**		**387**	**296**

*Activation date of the first site

KEYNOTE-B96 / ENGOT-ov65 MaNGO sites as of 16 June 2022 (final)

Principal Investigator	Institution name	Site ready	Screened	Randomized
Nicoletta Colombo	Istituto Europeo di Oncologia Milano	29 Mar 2022	38	33
Claudio Zamagni	Azienda Ospedaliero-Universitaria di Bologna IRCCS	26 Apr 2022	15	12
Francesco Raspagliesi	Fondazione Istituto Nazionale Tumori Milano	21 Apr 2022	13	11
Annamaria Ferrero	Ospedale Mauriziano Torino	31 May 2022	5	5
Germana Tognon	ASST Spedali Civili Brescia	15 Apr 2022	4	4
Schiavetto Ilaria	Ospedale Niguarda Milano	03 May 2022	4	4
Stefania Canova	Ospedale San Gerardo Monza	23 Jun 2022	4	2

NItCHE Clinical Trial
ENGOT OV51 / MITO 33

ENGOT Ov51-MITO 33: NItCHE trial

ENGOT model B

Sponsor: MITO

Supporter: GSK

-Epithelial ovarian, 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**;
- **Weekly Paclitaxel**
- **Gemcitabine**
- **Topotecan**
-**+/- 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

Primary Objective OS

NItCHE Clinical Trial
ENGOT OV51 / MITO 33

STUDY STATUS UPDATE

Country	CA approval	Coordinating EC approval	Status	Open sites
Italy	09/10/2020	25/11/2020	Study start: 1/12/2020	12/13
France	07/05/2021	04/05/2021	Study start: 19/08/2021	6/9
Germany	19/04/2021	25/02/2021	Study start: 12/10/2021	6/6
Czech Republic	24/09/2021	24/09/2021	Study start: 24/11/2021	3/3
Greece	24-10-2022	21/10/2022	Study start: 15/03/202	1/1
Instituto Médico Especializado Alexander Fleming- Argentina	-	-	Submission in progress	0/1

NItCHE Clinical Trial
ENGOT OV51 / MITO 33

RECRUITMENT STATUS

Group	Total Screened	Total Screen Failed	Total randomized	Total Treatment Discontinuation
MITO	120	17	102	83
MaNGO	**25**	**6**	**17**	**9**
GINECO	59	18	36	20
NOGGO	13	5	6	3
HeCOG	-	-	-	-
CEEGOG	11	0	10	6
TOTAL study	**228**	**44**	**171**	**121**

NItCHE Clinical Trial
ENGOT OV51 / MITO 33

ENGOT Ov51-MITO 33/ NItCHE trial UPDATE as of 06Jun 2023

Total subjects randomized: 171/427
Total number of sites open to enrollment: 28/33

Italy: MaNGO

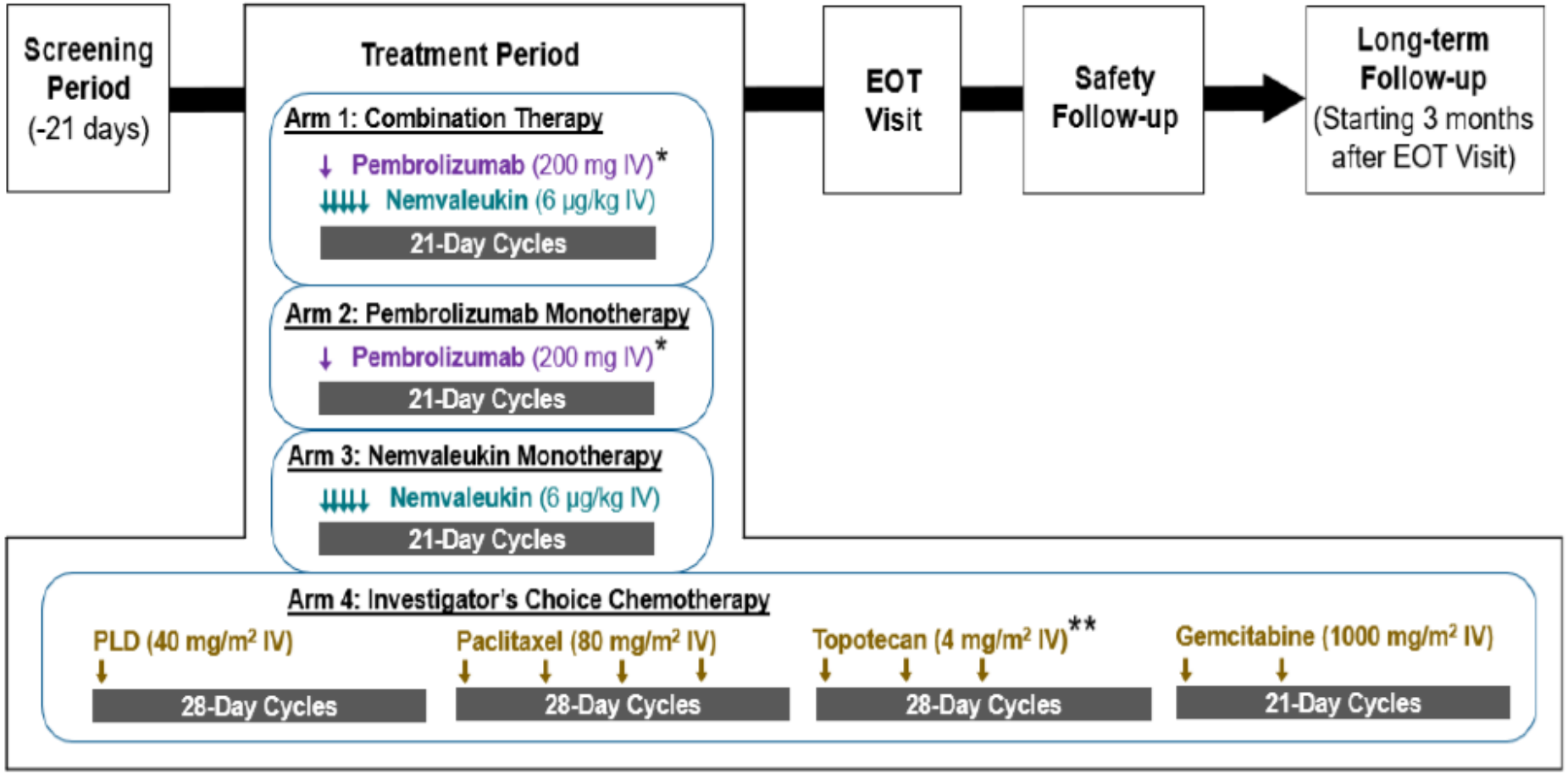
Site Number/Name	SIV Date	last screened	Screened	Screening failure	Randomized	last randomized	EOT	Open queries
IEO - MILANO	27 Jul 2021	20 Mar 2023	6	3	3	22 Feb 2023	1	18
Spedali Civili di Brescia - BRESCIA	18 May 2021	31 May 2022	5	0	5	28 Jun 2022	5	16
Ospedale Sant'Anna (Torino)	22 Feb 2022	15 May 2023	10	1	8	28 Mar 2023	2	166
ASST Lecco	17 Feb 2022	29 Nov 2022	4	3	1	14 Sep 2022	1	31
Total			**25**	**7**	**17**		**9**	**231**

ALKS 4230-007 / ENGOT-ov68

A Phase 3, Multicenter, Open-Label, Randomized Study of Nemvaleukin Alfa in Combination With Pembrolizumab Versus Investigator's Choice Chemotherapy in Patients With Platinum-Resistant Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer (ARTISTRY-7)

- ENGOT model: C
- Sponsor(s): Alkermes, Inc.
- Cooperating groups: GOG Foundation + 10 interested ENGOT groups
- No. of already recruited patients: 20
- Planned No. of patients: 376
- Status: Recruiting
- Other important information: 147 sites selected; 39 sites active in US, Canada, Spain, South Korea, Australia
- Enrollment is expected to end in late Q1 2024

Study Design



Abbreviations: EOT=end of treatment, IV=intravenous, PLD=pegylated liposomal doxorubicin.
*Treatment with pembrolizumab (Arms 1 and 2) is allowed for up to a maximum of 35 cycles (approximately 2 years).
**Alternatively, topotecan may be administered at 1.25 mg/m^2 on Days 1 through 5 of 21-day cycles.

ARTISTRY-7 Update May 2023

- MaNGO participation was recently considered
- MaNGO sites are currently not yet active

Global:

We currently have globally **65 active sites out of 147 selected sites**, and **95 patients** have been randomized.

Region/country	# of sites
North America	32
Asia Pacific	10
ENGOT	19

Overall	Total number
Total # Subjects	243
Total # Screen Fail Subjects	72
Total # of randomized subjects	**95**
Total # Screening	**76**

Europe:

We currently have 19 active ENGOT sites, and 12 patients have been randomized.

Region/country	# of sites	# of randomized patients
Total	**19**	**12**
Austria	3	
Belgium		
Czech Republic		
Denmark		
France		
Germany		
Israel		
Italy	4	4
Lithuania		
Norway		
Poland		
Spain	11	8
United Kingdom	1	

ARTISTRY-7 / MaNGO sites

City	Hospital	PI
Milano	Ist. Europeo di Oncologia	Nicoletta Colombo
Milano	Istituto Naz. dei Tumori	Francesco Raspagliesi
Padova	Ist. Oncologico Veneto	Giulia Tasca
Reggio Emilia	Arcispedale S. Maria N.	Alessandra Bologna

28 June 2023: The participation of MaNGO is currently on-hold.

SRTO-002- GM3. Phase 3 study of Luvelta vs. Standard chemotherapy in Platinum Resistant Ovarian Cancer study

- New study proposed by ENGOT Model C ENGOT
- GEICO lead group
- This will be circulated for interest in the next months