ENDOMETRIAL CANCER TRIALS

Short summary on ongoing studies

Elisa Piovano

SC Ostetricia e Ginecologia 2U - AOU Città della Salute e della Scienza di Torino – Presidio Sant'Anna, Direttore Prof Alberto Revelli

Endometrial cancer trials summary – Accrual closed

First line:

- ENGOT-en2
- ENGOT-en7/AtTEnd
- ENGOT-en11 – KEYNOTE-B21

Relapse:

- EN12/Podium
- ENGOT-en15 – KEYNOTE-C93

ENGOT-en2: A phase II Trial of postoperative chemotherapy or no further treatment for patients with node-negative stage I-II intermediate or high risk endometrial cancer (ENGOT-en2/DGCG)

Design: 1:1 randomization

n=240

Lymphnodes negative

Endometrioid Stage I (Grade 3) and Stage II

Non-endometrioid: Stage I-II

Chemotherapy

Carboplatin AUC5 IV q21d
Paclitaxel 175mg/m2 IV q21d 6 courses

+/- Brachytherapy

Observation

+/- Brachytherapy

Primary Endpoint
Overall survival in the subgroup of endometrioid adenocarcinoma

Secondary Endpoints
Overall survival of whole study population
Descriptive analysis of overall survival in non-endometrioid adenocarcinoma
Disease Specific Survival (DSS)
Progression-Free Survival (PFS)

Toxicity
Quality of Life (QOL) EORTC QLQ-C30 and EORTC-QLQ-EN24

Rate of isolated pelvic relapse (central and/or pelvic wall)
Rate of isolated distant relapse
Rate of mix local and distant relapse

Adjuvant vaginal brachytherapy is permitted in both arms.
In chemotherapy arm, timing of VBT should not cause delay in chemotherapy schedule.

A phase II trial of postoperative chemotherapy or no further treatment for patients with node-negative stage I-II intermediate or high risk endometrial cancer (ENGOT-en2/DGCG)

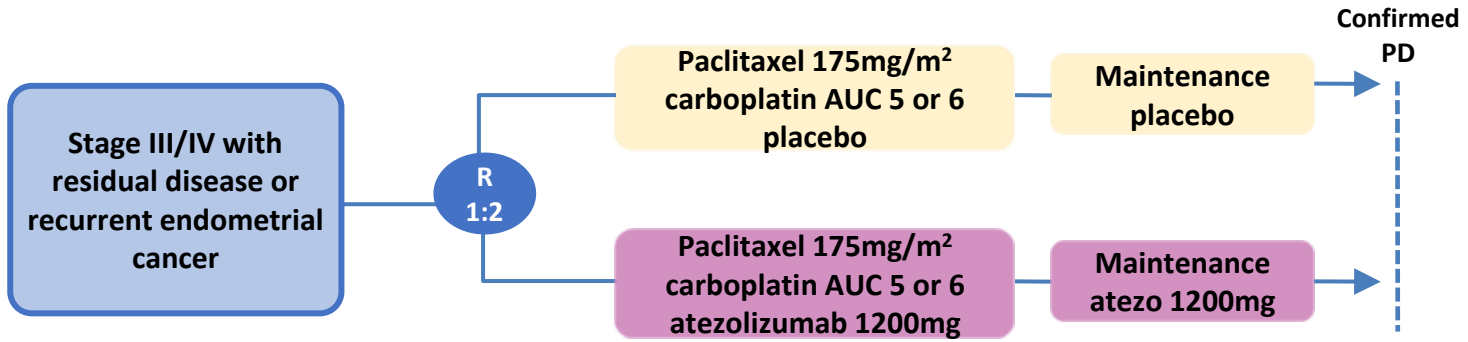
- **ENGOT Model: A**
- **Sponsor : Danish Gynecological Cancer Group**
- Status: accrual closed
- Primary Completion (Estimated): 15 April 2024 (Last Patient Last Visit)
- Study Completion (Estimated): 15 January 2025
- Enrollment (Actual): 244
- Results expected soon

ENGOT-en7/AtTEnd: A phase III double-blind randomized placebo-controlled trial of atezolizumab in combination with paclitaxel and carboplatin in women with advanced/recurrent endometrial cancer

- **ENGOT Model: A**
- **Sponsor: Istituto Mario Negri /MaNGO**
- **PI: Nicoletta Colombo**, European Institute of Oncology (EIO), Milano
- Status: accrual closed
- Last Patient Last visit: 20 January 2025
- **Study Completion (Database lock for OS): 24 March 2025**

Endometrial cancer trials summary First line – Accrual closed **AtTEnd**

AtTEnd study: Atezolizumab Trial in Endometrial Cancer
ENGOT-en7/MaNGO/AtTEnd



Primary Endpoints:

- PFS on MSI and all-comers with a hierarchical approach
- OS in all-comers

Cooperating groups: ENGOT (AGO, AGO-A, GEICO, NCRI, SAKK) non-ENGOT (ANZGOG, JGOG, TGOG, KGOG)

Final No. of patients: 551
70% from ENGOT sites and 43% from MaNGO sites!

- ***Manuscript with Primary PFS published on Lancet Oncology on July 2024***
- ***Manuscript focused on Asia population post-hoc published on Journal of Gynecologic Oncology on May 2025***
- ***Translational analyses ongoing***
- ***OS analysis ongoing to be presented at ESMO 2025***

Atezolizumab and chemotherapy for advanced or recurrent endometrial cancer (AtTEnd): a randomised, double-blind, placebo-controlled, phase 3 trial

*Nicoletta Colombo, Elena Biagioli, Kenichi Harano, Francesca Galli, Emma Hudson, Yoland Antill, Chel Hun Choi, Manuela Rabaglio, Frederic Marmé, Christian Marth, Gabriella Parma, Lorena Fariñas-Madrid, Shin Nishio, Karen Allan, Yeh Chen Lee, Elisa Piovano, Beatriz Pardo, Satoshi Nakagawa, John McQueen, Claudio Zamagni, Luis Manso, Kazuhiro Takehara, Giulia Tasca, Annamaria Ferrero, Germana Tognon, Andrea Alberto Lissoni, Mariacristina Petrella, Maria Elena Laudani, Eliana Rulli, Sara Uggeri, M Pilar Barretina Ginesta, and AtTEnd study group**

Summary

Background At the time of AtTEnd trial design, standard treatment for advanced or recurrent endometrial cancer included carboplatin and paclitaxel chemotherapy. This trial assessed whether combining atezolizumab with chemotherapy might improve outcomes in this population.

Methods AtTEnd was a multicentre, double-blind, randomised, placebo-controlled, phase 3 trial done in 89 hospitals in 11 countries across Europe, Australia, New Zealand, and Asia. Enrolled patients were aged 18 years or older, and had advanced or recurrent endometrial carcinoma or carcinosarcoma, an Eastern Cooperative Oncology Group performance status of 0–2, and received no previous systemic chemotherapy for recurrence. Patients were randomly assigned (2:1) using an interactive web response system (block size of six) to either atezolizumab 1200 mg or placebo given intravenously with chemotherapy (carboplatin at area under the curve of 5 or 6 and paclitaxel 175 mg/m² intravenously on day 1 every 21 days) for 6–8 cycles, then continued until progression. Stratification factors were country, histological subtype, advanced or recurrent status, and mismatch repair (MMR) status. Participants and

Lancet Oncol 2024; 25: 1135–46

Published Online
August 2, 2024
https://doi.org/10.1016/S1470-2045(24)00334-6

*Investigators are listed in the appendix (pp 2–6)

European Institute of Oncology IRCCS, Milan, Italy (Prof N Colombo MD, G Parma MD); **University of Milan-Bicocca, Milan, Italy** (Prof N Colombo); **Istituto di Ricerche Farmacologiche Mario**

Endometrial cancer trials summary First line – Accrual closed **AtTEnd**

J Gynecol Oncol. 2025 Jul;36(4):e117
https://doi.org/10.3802/jgo.2025.36.e117
pISSN 2005-0380·eISSN 2005-0399

JOURNAL OF GYNECOLOGIC ONCOLOGY

Original Article

Check for updates

Phase III double-blind randomized placebo controlled trial of atezolizumab in combination with carboplatin and paclitaxel in women with advanced/recurrent endometrial carcinoma: the Asian cohort of the AtTEnd/ENGOT-EN7 trial

OPEN ACCESS

Received: Feb 5, 2025
Revised: Apr 11, 2025
Accepted: Apr 21, 2025
Published online: Apr 25, 2025

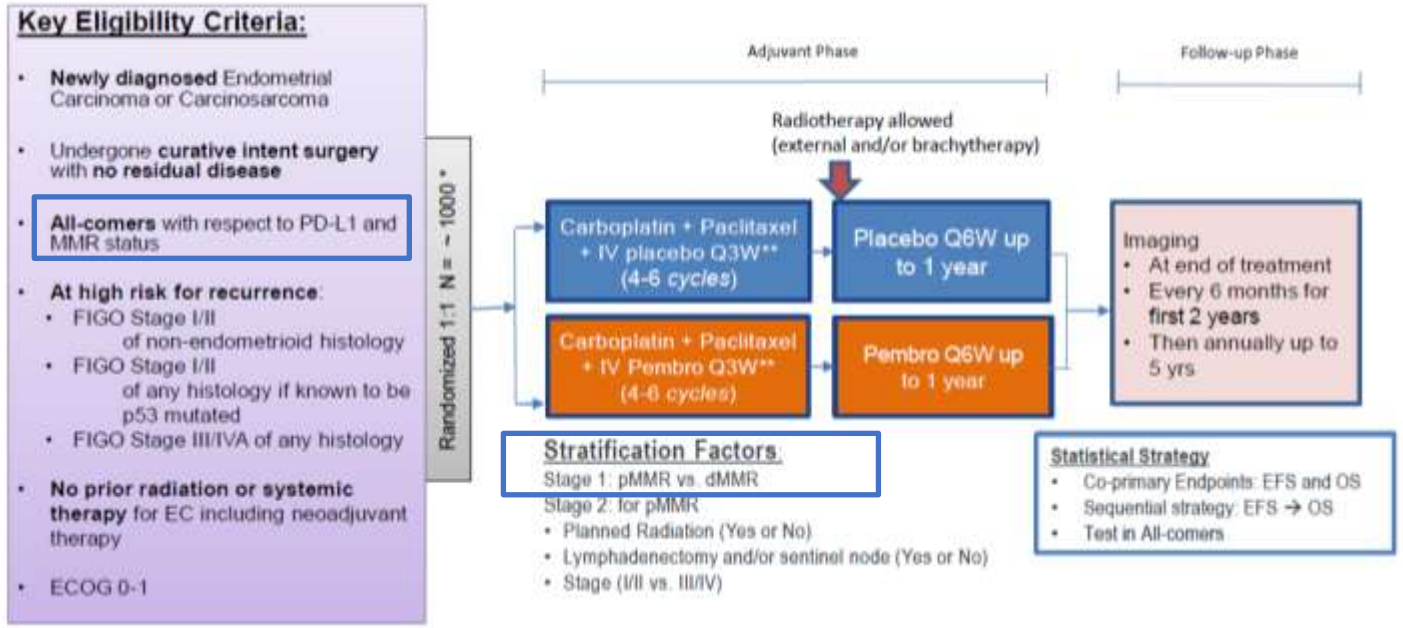
Correspondence to
Sara Uggeri
Clinical Oncology Department, Istituto di Ricerche Farmacologiche Mario Negri, Via Mario Negri, 2, 20156 Milano, Italy.
Email: sara.uggeri@marionegri.itelena.

Kenichi Harano [1], Roldano Fossati [2], Beatriz Pardo [3], Francesca Galli [2], Emma Hudson [4], Yoland Antill [5], Chulmin Lee [6], Manuela Rabaglio [7], Florian Heitz [8], Vassiliki Kolovetsiou-Kreiner [9], Chyong-Huey Lai [10], Elena Biagioli [2], Luis Manso [11], Shin Nishio [12], Karen Allan [13], Yeh Chen Lee [14], Sara Uggeri [2], Andres Redondo [15], Satoshi Nakagawa [16], Eunice Au [13], Janine Lombard [17], Angiolo Gadducci [18], Kazuhiro Takehara [19], Edi Editta Baldini [20], Innocenza Palaia [21], Claudia Casanova [22], Antonio Ardizzoia [23], Alessandra Bologna [24], Maria-Pilar Barretina-Ginesta [25], Nicoletta Colombo [26]

Synopsis

An analysis of the AtTEnd trial in proficient mismatch repair tumors showed no benefit from atezolizumab in Asians. The clinical profile of these populations seems quite different. Asian patients on atezolizumab have a lower cumulative incidence of new lesions but a higher cumulative incidence of primary tumor regrowth than non-Asians.

ENGOT-en11 KEYNOTE-B21 / A Phase 3, Randomized, Double-Blind Study of Pembrolizumab versus Placebo in Combination With Adjuvant Chemotherapy With or Without Radiotherapy for the Treatment of Newly Diagnosed High-Risk Endometrial Cancer After Surgery With Curative Intent (GOG-3053)



- **ENGOT Model: C**
- Sponsor: MSD
- **Lead Group: BGOG**
- Status: accrual closed; accrual start: Jan 2021; accrual end: Dec 2022
- Final DFS results published

Endometrial cancer trials summary First line – Accrual closed **ENGOT-EN11**

ANNALS OF ONCOLOGY DRIVING INNOVATION IN ONCOLOGY

ORIGINAL ARTICLE

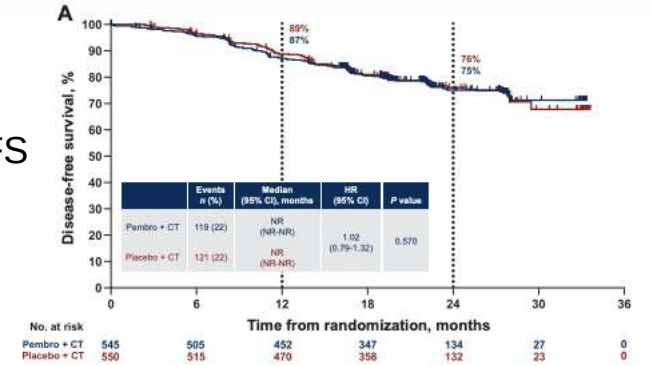
ENGOT-en11/GOG-3053/KEYNOTE-B21: a randomised, double-blind, phase III study of pembrolizumab or placebo plus adjuvant chemotherapy with or without radiotherapy in patients with newly diagnosed, high-risk endometrial cancer☆

T. Van Gorp[1,2*], D. Cibula[3,4], W. Lv[5], F. Backes[6,7], F. Ortaç[8,9], K. Hasegawa[10], K. Lindemann[11,12,13], A. Savarese[14,15], A. Laenen[2,16], Y. M. Kim[17], L. Bodnar[18,19], M.-P. Barretina-Ginesta[20,21], L. Gilbert[22,23,24], B. Pothuri[7,25], X. Chen[26,27], M. B. Flores[28], T. Levy[29], N. Colombo[30,31,32], C. Papadimitriou[33,34], T. Buchanan[7,35], L. C. Hanker[36,37,38], G. Eminowicz[39,40], L. Rob[4,41], D. Black[7,42,43], J. Lichfield[44], G. Lin[45], R. Orlowski[45], S. Keefe[45], A. Lortholary[46,47] & B. Slomovitz[7,48], on behalf of the ENGOT-en11/GOG-3053/KEYNOTE-B21 investigators†

Ann Oncol. 2024 Nov;35(11):968-980.

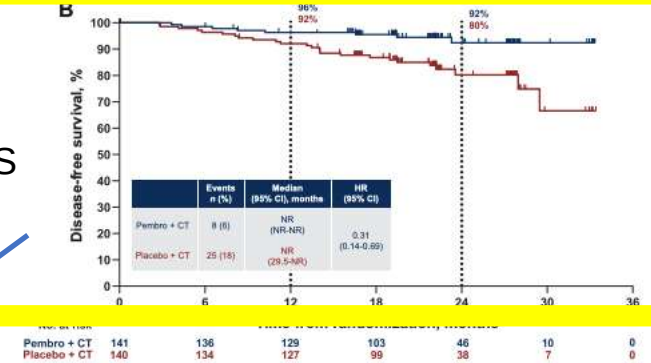
	Events *n* (%)	Median (95% CI), months	HR (95% CI)
Pembro + CT	8 (6)	NR (NR-NR)	0.31 (0.14-0.69)
Placebo + CT	25 (18)	NR (29.5-NR)	

DFS



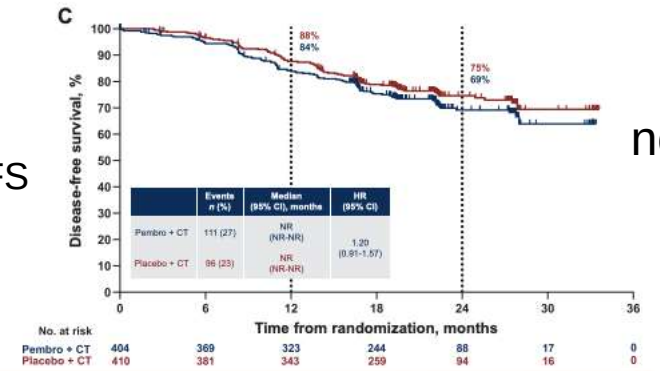
ITT

DFS



dMMR

DFS



nondMMR

ENGOT-en11 / KEYNOTE-B21
Study Update

Groups	Randomized
ENGOT	412
GOG	142
ROW	541
Total	**1095**

ENGOT Groups	Randomized
A-AGO	4
AGO	11
BGOG	20
CEECOG	55
GEICO	29
GINECO	48
HeCOG	14
ISGO	16
MaNGO	14
MITO	48
GTG-UK	11
NSGO	51
PGOG	38
TRSGO	53
Total ENGOT	**412**

Recent Abstracts

ESGO 2025: Exploratory analysis of Disease-Specific Free Survival (DSFS)

ASTRO 2025: Exploratory analysis of Disease-Specific–Free Survival (DSFS) and Safety by Radiation Usage

Study extension for 2 additional years
→ To confirm the improved DFS with pembrolizumab in dMMR subjects after a longer FU time.

ENGOT
European Network of Gynaecological Oncological Trial groups

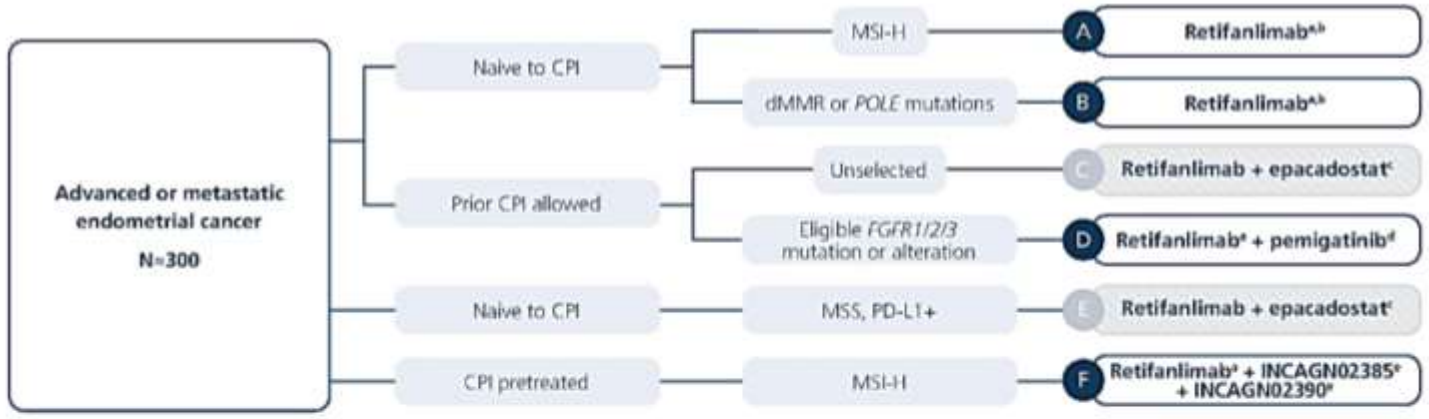
Retifanlimab

ENGOT-en12/POD1UM-204 An Umbrella Study of INCMGA00012 Alone and in Combination With Other Therapies in Participants With Advanced or Metastatic Endometrial Cancer Who Have Progressed on or After Platinum-Based Chemotherapy

- **ENGOT Model: C**
- SPONSOR: Incyte Corporation
- **Lead ENGOT group: NOGGO**
- Planned No. of patients: 267
- No. of recruited patients at end of recruitment: 206

Endometrial cancer trials summary First line – Accrual closed **ENGOT-EN12**

ENGOT-EN12 / POD1UM-204: STUDY DESIGN



Key Inclusion Criteria

- Women ≥18 years of age (or as applicable per local country requirements)
- Histologically confirmed diagnosis of advanced or metastatic endometrial cancer
- Disease progression on or after treatment with ≥1 platinum-containing regimen for advanced or metastatic disease
- ≥1 measurable tumor lesion per RECIST v1.1
- ECOG PS of 0 to 1
- Willingness to provide tumor tissue sample (fresh or archived)

Key Exclusion Criteria

- Histologically confirmed diagnosis of sarcoma of the uterus
- Toxicity of prior therapy that has not recovered to grade ≤1 unless approved by the medical monitor
- Active autoimmune disease requiring systemic immunosuppression with corticosteroids or immunosuppressive drugs within 14 days before the first dose of study treatment
- Groups C, D, and F: Limiting immune-related toxicity during prior CPI therapy

Primary Endpoint

- Group A: ORR (per RECIST 1.1, by ICR)

Secondary Objectives

- Groups A and B: DoR, DCR, PFS, OS
- Groups B-F: ORR
- All groups: Safety and tolerability

For more information search for study NCT04463771 on IncyteClinicalTrials.com, or contact us at clintrials@incyte.com

[a] Patients eligible for retifanlimab monotherapy will first be considered for Group A until fully enrolled, unless they do not meet MSI-H criteria. Retifanlimab administered IV on day 1 of each 28-day cycle for up to 26 cycles. [b] Patients in Groups A or B who experience disease progression on retifanlimab monotherapy may be eligible for further treatment with one of the combination regimens. [c] Enrollment closed. [d] Pemigatinib (FGFR1/2/3 inhibitor) administered orally qd. [e] INCAGN02385 (LAG-3–directed antibody) and INCAGN02390 (TIM-3–directed antibody) administered IV q3w.

Recent information:

- **Last Patient in: 9 July 2024**
- **presentation of data not planned yet**

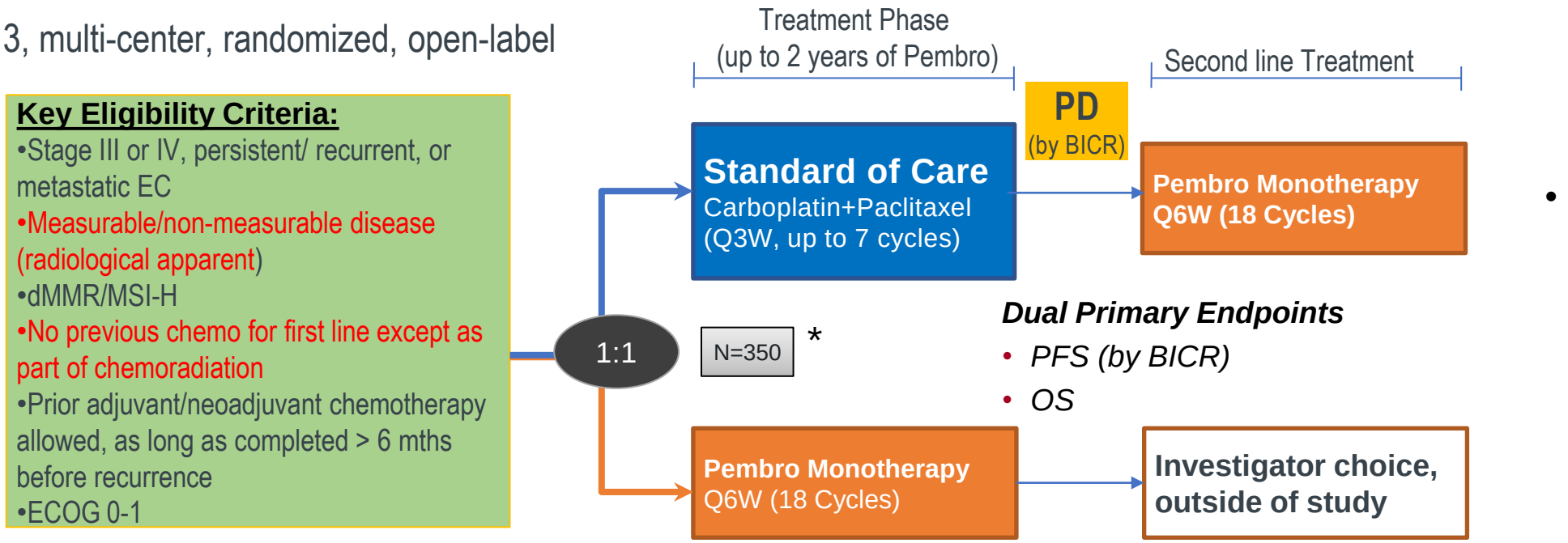
Endometrial cancer trials summary First line – Accrual closed ENGOT-EN15

ENGOT-en15 / MK-3475-C93 / GOG-3064 / KEYNOTE-C93
A Phase 3 Randomized, Open-label, Active-comparator Controlled Clinical Study of Pembrolizumab vs. Platinum Doublet Chemotherapy in Participants With Mismatch Repair Deficient (dMMR) Advanced or Recurrent Endometrial Carcinoma in the First-line Setting

- **ENGOT Model: C**
- Sponsor: Merck Sharp & Dohme LLC
- **Lead Group: MITO**
- Status: recruitment completed on December 12th, 2023

ENGOT-en15 / MK-3475-C93 / GOG-3064 STUDY DESIGN

Phase 3, multi-center, randomized, open-label



- **Target sample size was decreased from 350 to 280 pts through adjustment of assumptions and target HRs for PFS/OS leveraging data from comparator ARM in recent 1L EC trials.**
  Accrual closed in Dec 2023
- **Waiting PFS events: Expected for Q4 2025 or Q1 2026**

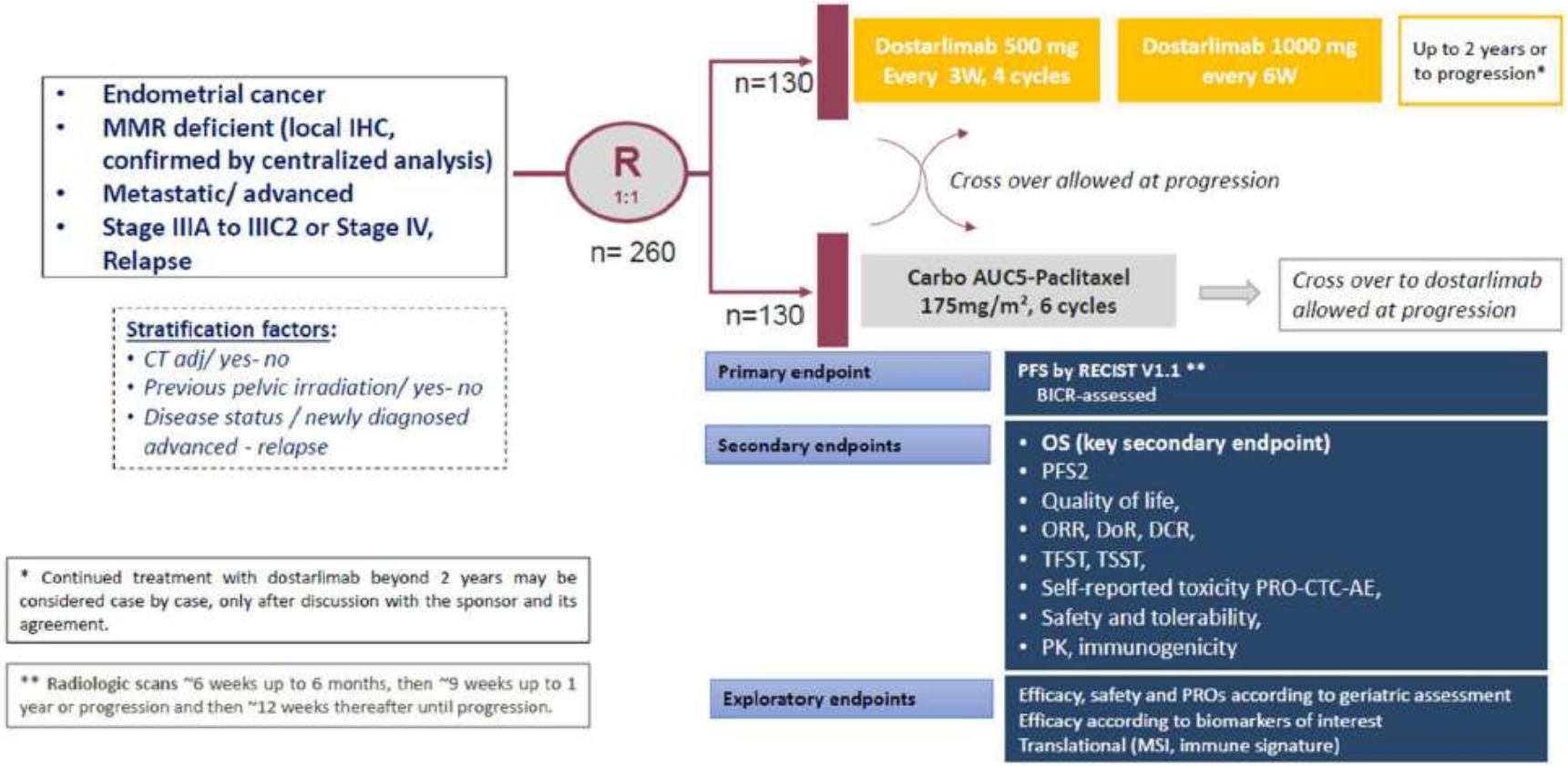
Endometrial cancer trials summary – Accrual Ongoing

Relapse:

- ENGOT-en13/DOMENICA
- ENGOT-en20 – XPORTEC
- ENGOT-en23

Domenica/ENGOT-EN13 Study design

ENGOT study: Model A
Sponsor: GINECO



The accrual will close on Monday 30.06

Screening is already closed

Recruitment status:

(24 June 2025)

263 patients randomized

2 patients in screening

46 patients Screen failed

- 69 cross-over
- 115 PFS1 (44 deaths)

Last randomized patient (planned): **30 June 2025**

MaNGO sites:

- **5 sites** were activated but 2 sites withdrawn after SIV and 1 site (Rome) had short time to recruit, as Sponsor stopped the new screenings by April 2025
- Activated sites: IEO (Milan); Spedali Civili (Brescia); Ospedale Umberto I (Rome).
- MaNGO PI: dott.ssa. Germana Tognon
- Only Site IEO (Milan) has recruited patients: **3 patients randomized**

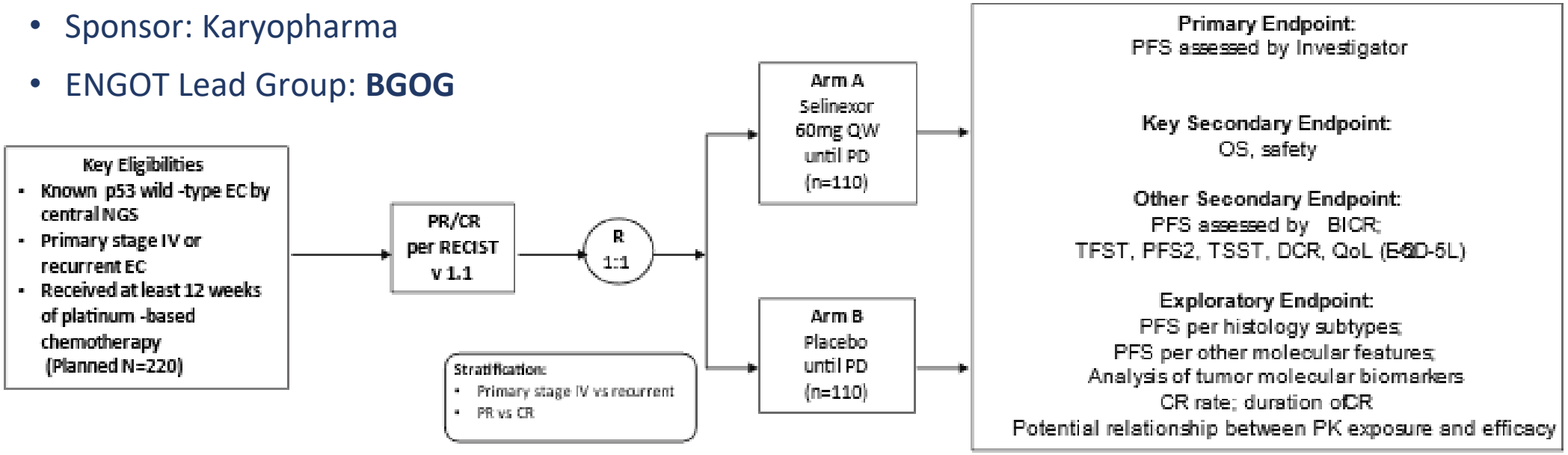
Endometrial cancer trials Relapse – Accrual ongoing **ENGOT-EN20/XPORT-EC**

ENGOT-en20/XPORT-EC A phase III, randomized, placebo-controlled, double-blind, multicenter trial of selinexor in maintenance therapy after systemic therapy for patients with p53 wild-type, advanced or recurrent endometrial carcinoma

inibitore orale dell'esportazione della proteina di esportazione nucleare 1 (XPO1)

Background: Pre-specified exploratory subgroup analyses of the ENGOT-EN5/GOG-3055/SIENDO trial identified p53 wild-type as a potential predictor of efficacy of selinexor, with 10-month PFS improvement over placebo; no benefit for selinexor was seen in patients with p53 mutant/aberrant tumors.

- **ENGOT model: C**
- Sponsor: Karyopharma
- ENGOT Lead Group: **BGOG**



N=220 pts
HR in PFS of 0.55

ENGOT-en20/XPORT-EC - Sites

ENGOT Enrollment update:

- Total in pre-screening: 291 pts
- Total randomized: 89 pts

City	Hospital	PI Name	Status	Total in Pre-Screening	Total Randomized	Total Screened
Milano	**Istituto Europeo di Oncologia**	**Nicoletta Colombo (MaNGO PI)**	**Active (29Jan2024)**	**2 (both WT)**	**0**	**4**
Torino	Ospedale Sant'Anna	Dionyssios Katsaros	Active (13Nov2024)	1 (WT)	0	1
Brescia	Spedali Civili	Valentina Zizioli	Active (23Jan2024)	1 (WT)	1	2
Milano	Istituto Nazionale dei Tumori	Francesco Raspagliesi	Pending activation (SIV 24Jun2025)	-	-	-
Monza	Ospedale San Gerardo	Andrea A. Lissoni	Active (14Mar2024)	1 (WT)	0	4
Padova	Istituto Oncologico Veneto	Valentina Guarneri	Active (16May2024)	-	2	3
Pisa	Università di Pisa	Carmelo Bengala	Active (18Sep2024)	0	0	0
			MaNGO Total	5	3	14

Endometrial cancer trials Relapse– Accrual ongoing ENGOT-en23

ENGOT-en23/GOG-3095/MK-2870-005

A Phase 3, Randomized, Active-controlled, Open-label, Multicenter Study to Compare the Efficacy and Safety of MK-2870 Monotherapy Versus Treatment of Physician's Choice in Participants With Endometrial Cancer Who Have Received Prior Platinum-based Chemotherapy and Immunotherapy

ENGOT Model: C
Sponsor: MSD
Lead Group: MITO
N patients: 710

Enrolment update (23 May 2025):
Total screened : 968 pts
Total randomized: 675 pts

MaNGO sites & study updates at 23 May 2025

Site	PI	Total screened	Screening failure	Total randomized
INT, Milano	Raspagliesi	6		6
IEO, Milano	Colombo	6	3	3
Mauriziano, Torino	Ferrero	3		3
Spedali Civili, Brescia	Tognon	3	1	2
AUSL, IRCCS, Reggio Emilia	Bologna	2		2

NEXT STUDY MILESTONE
Last Subject First visit planned date **26 Sep 2025**
Last Subject Randomized: planned date **24 Oct 2025**
Last Patient Last visit :planned date **10 Jan 2028**
DB LOCK: planned date **14 Feb 2028**