



STANDARD TREATMENTS AND NEW DIRECTIONS IN GYNAECOLOGICAL CANCERS

MILANO June 26th-29th, 2025

Responsabili Scientifici:
NICOLETTA COLOMBO, FRANCESCO RASPAGLIESI



RARE TUMORS

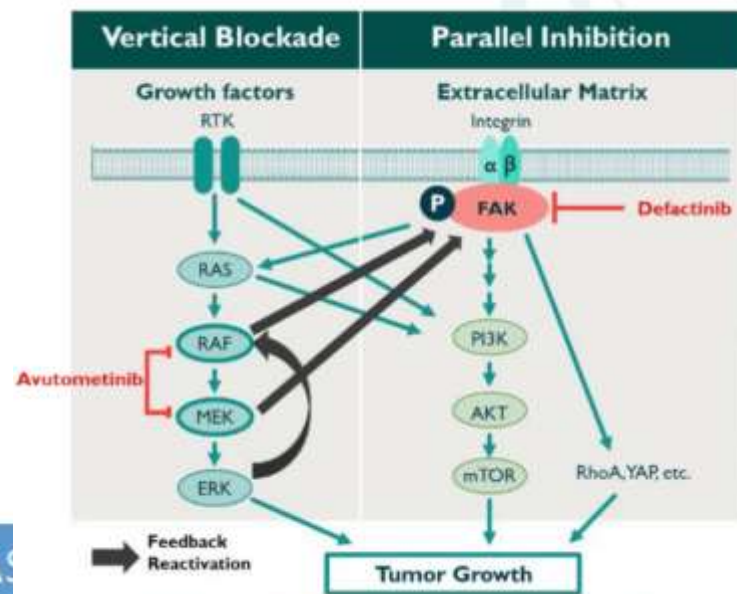
Short summary on ongoing studies

Lorenzo Ceppi, Fondazione IRCCS Istituto Nazionale dei Tumori - INT, Milano

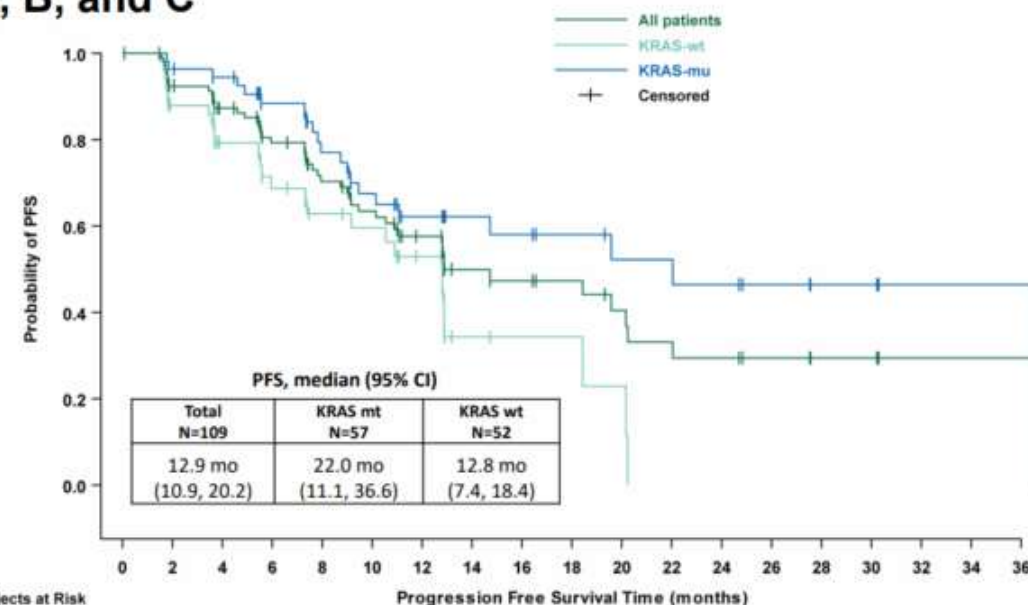
OncoDaily
May 8, 2025

FDA APPROVES Accelerated Approval

Avutometinib + Defactinib for KRAS-Mutated Low-Grade Serous Ovarian Cancer



Progression-Free Survival: Avutometinib + Defactinib: Parts A, B, and C



All patients	109	94	81	66	53	45	32	19	17	15	11	9	8	6	3	3	1	1	1
KRAS-wt	52	41	32	25	20	18	13	4	3	3	2	0							
KRAS-mu	57	53	49	41	33	27	19	15	14	12	9	9	8	6	3	3	1	1	1

KRAS, kirsten rat sarcoma virus; mt, mutant; PFS, progression-free survival; wt, wild type.

Rare tumors ongoing studies summary ENGOT-ov81 / RAMP-301

GOG-3097/ENGOT-ov81/RAMP 301: A Phase 3, Randomized, Open-Label Study of Combination Therapy with Avutometinib plus Defactinib Versus Investigator's Choice of Treatment in Patients with Recurrent Low-Grade Serous Ovarian Cancer (LGSOC)

ENGOT Model: C
Sponsor: VERASTEM
Lead Group: NCRI

North America:

United States, Canada

Europe:

Belgium, France

Denmark, Germany

Italy, Spain

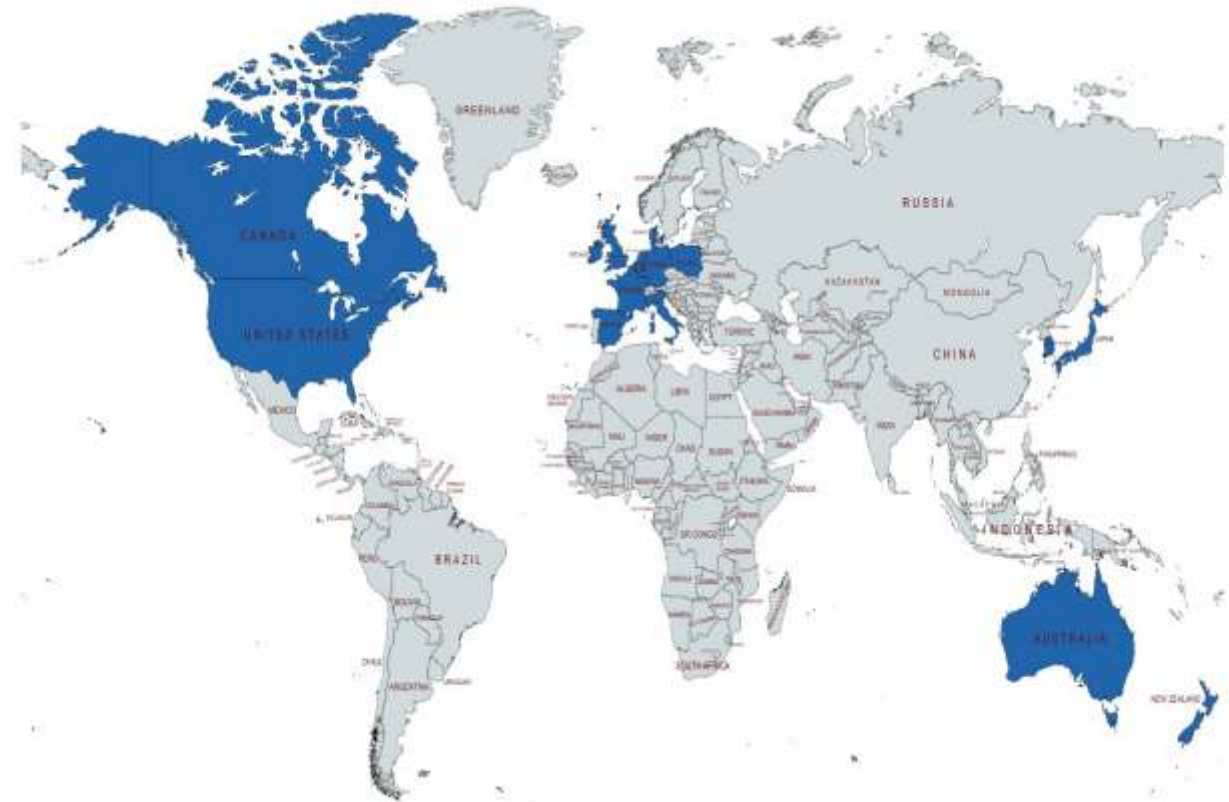
United Kingdom, Poland

Ireland, Netherlands

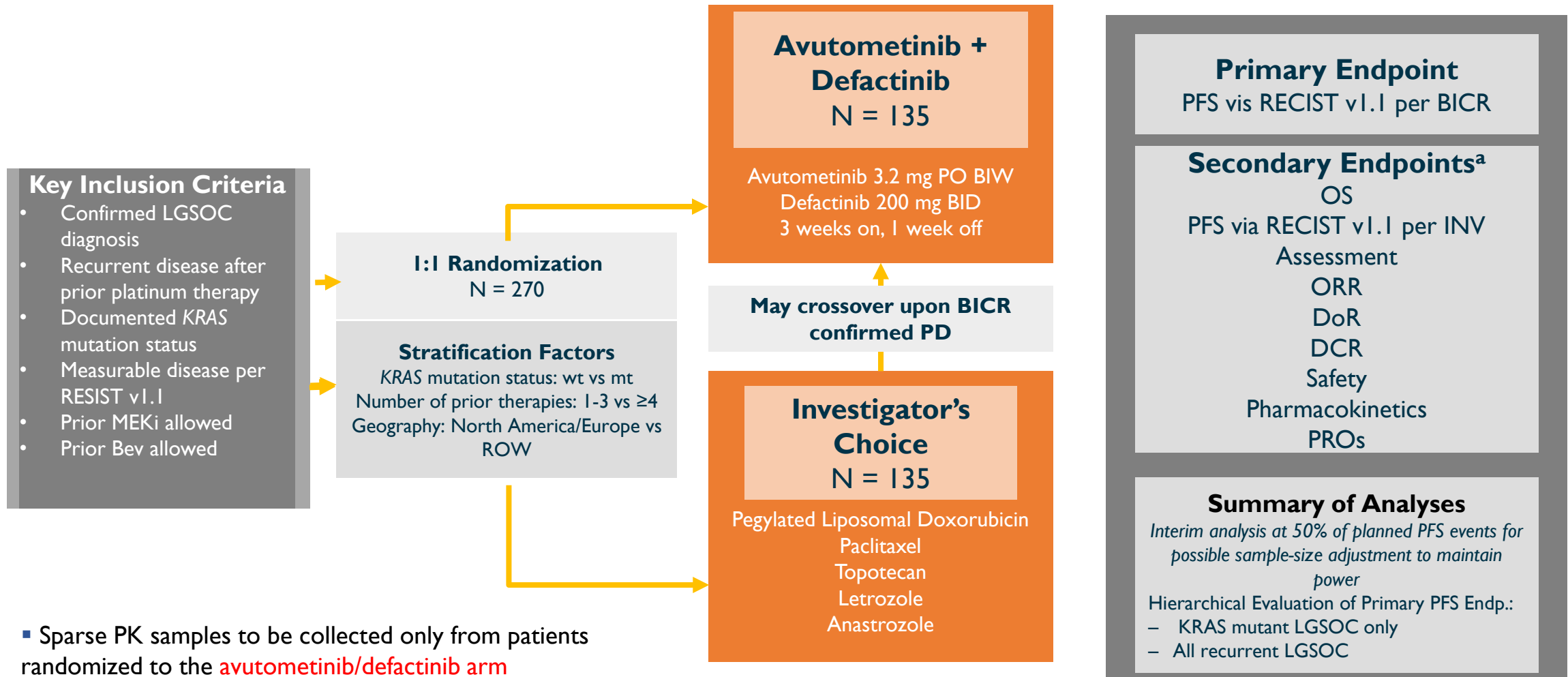
Asia Pacific:

Australia, New Zealand

Republic of Korea, Japan



Rare tumors ongoing studies summary ENGOT-ov81 / RAMP-301



Rare tumors ongoing studies summary ENGOT-ov81 / RAMP-301

RAMP301: Current Enrollment Status

Randomized	216 of 270	
	KRAS-wt (max of 180)	KRAS-mut (min of 90)
as of 28May:	155	61
Overall slots remaining:	54	
KRAS specific slots remaining/needed:	KRAS-wt (25 remaining)	KRAS-mut (29 more needed)

MaNGO sites & study updates

Site name	PI name	# Enrolled
Spedali Civili di Brescia-Brescia	Dr Germana Tognon	0
Istituto Oncologico Veneto - Padova	Dr Valentina Guarneri	0
Istituto Nazionale dei Tumori- Milano	Dr Mara Mantiero	1
Istituto Europeo di Oncologia – Milano	Dr Nicoletta Colombo	16 (↑1)

Effective May 28, 2025, RAMP301 has moved from **open enrollment** to **formal slot request**

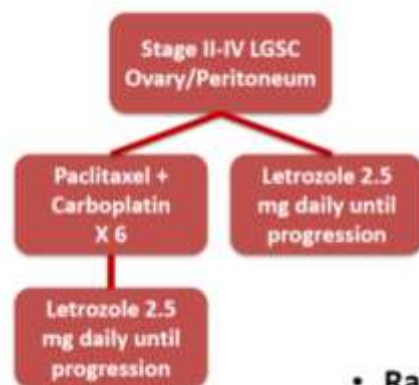
- Decision made to ensure statistical integrity and meet regulatory requirements
- Maintain appropriate balance of:
 - KRAS-wild type (WT): max target of 180 patients
 - KRAS-mutant (MT): minimum target of 90 patients

Update 10-Jun-2025: 233 patients were randomized and there were 23 open slots available: 21 for KRAS-mutant and 2 for KRAS-wild-type.

Competitive recruiting studies within ENGOT and GCIg

NRG-GY-019:

Randomized Phase III Trial of Paclitaxel/Carboplatin Followed by Maintenance Letrozole versus Letrozole Monotherapy in Stage II-IV Low-Grade Serous Carcinoma



- Sponsor: NCI (NRG Oncology)
- International phase III trial
- Primary Objective: PFS
- Target: 450 pts

- Randomization: 1:1
- Sample size: 450 patients
- Non-inferiority design
- Primary objective: PFS

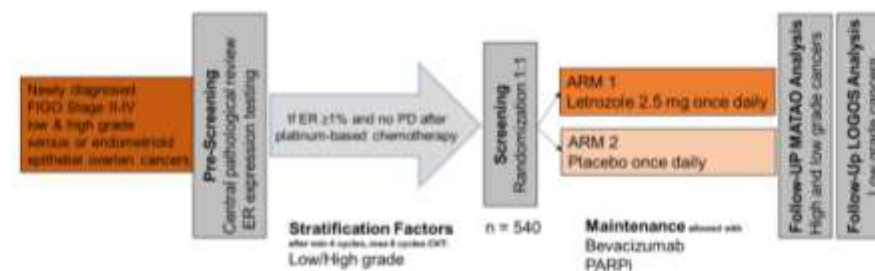
ENGOT-ov54 / Swiss-GO-2/MATAO



MAintenance Therapy with Aromatase inhibitor in epithelial Ovarian cancer: a randomized double-blinded placebo-controlled multi-center phase III Trial (ENGOT-ov54/Swiss-GO-2/MATAO) including LOGOS (Low Grade Ovarian cancer Sub-study)

Trial setting: Newly diagnosed high and low grade serous and endometrioid ovarian cancer FIGO II-IV

Study Design: Randomized double-blinded placebo-controlled multi-center phase III trial
Examining the maintenance therapy with aromatase inhibitor letrozole versus placebo.



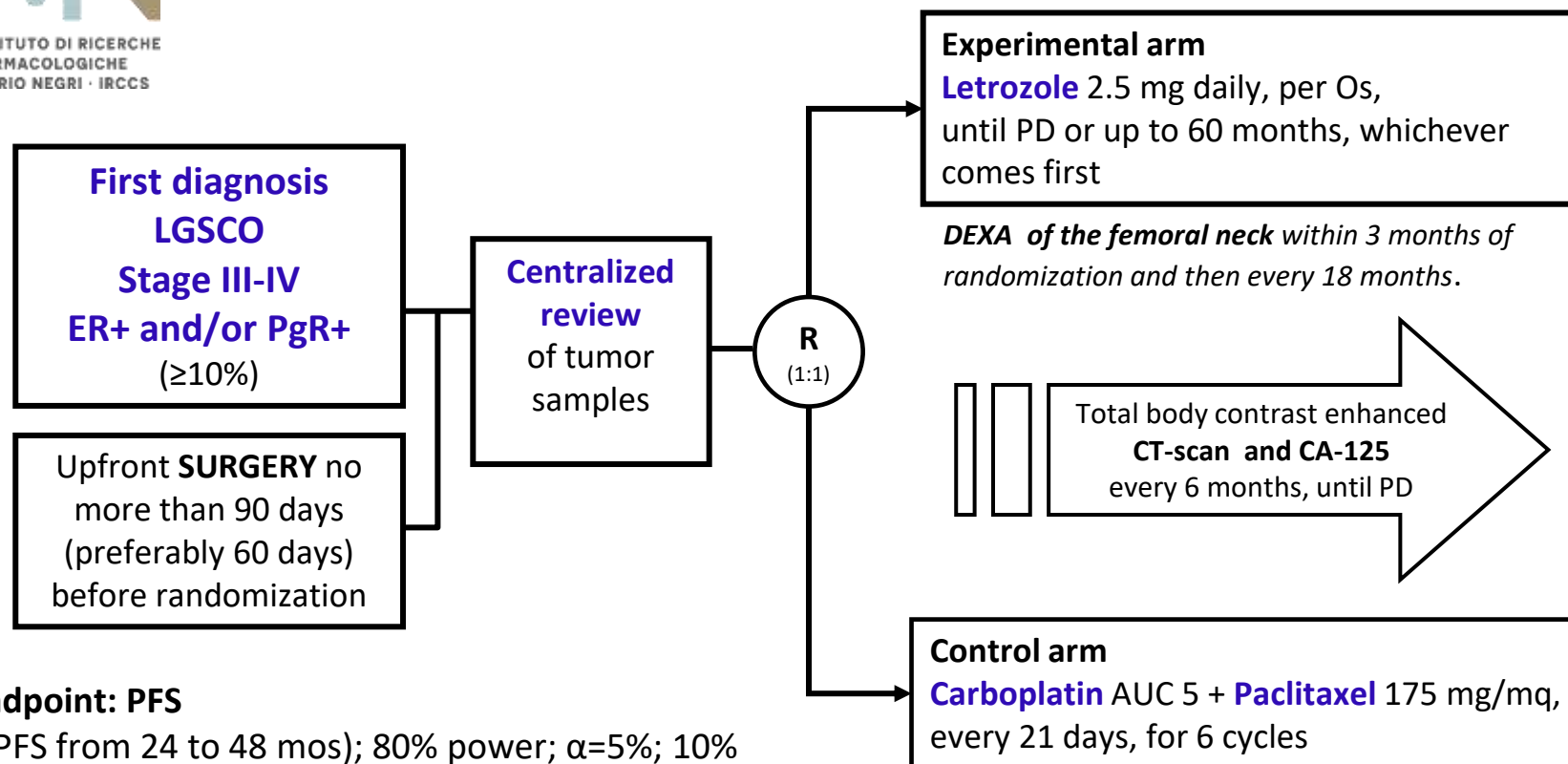
Status: CH recruiting, 20/21 since Q4/2020 (241 pat.)
 • AT recruiting 5/8 since Q2/2022 (17 pat.)
 DE 27 approved/ 4 initiated/ 3 activated/ 1 recruiting since Q1/2023 (2 pat.)

Rare tumors ongoing studies summary **LEPRE Trial**

**Letrozole for Estrogen/Progesterone Receptor
positive low-grade Epithelial serous ovarian cancer.**

A randomized phase III trial

PI: Andrea De Censi
Sponsor: MaNGO



Primary Endpoint: PFS

HR=0.5 (mPFS from 24 to 48 mos); 80% power; $\alpha=5\%$; 10% dropout

Accrual 24 months - Follow-up 30 months

Sample-size: 132 patients

**Supported by AIRC Investigator Grant -
IG 2018**

Rare tumors ongoing studies summary **LEPRE**

Update as of 20 June 2025

First patient enrolled: February 2023

Patient enrolled: 55

No Randomized: 52

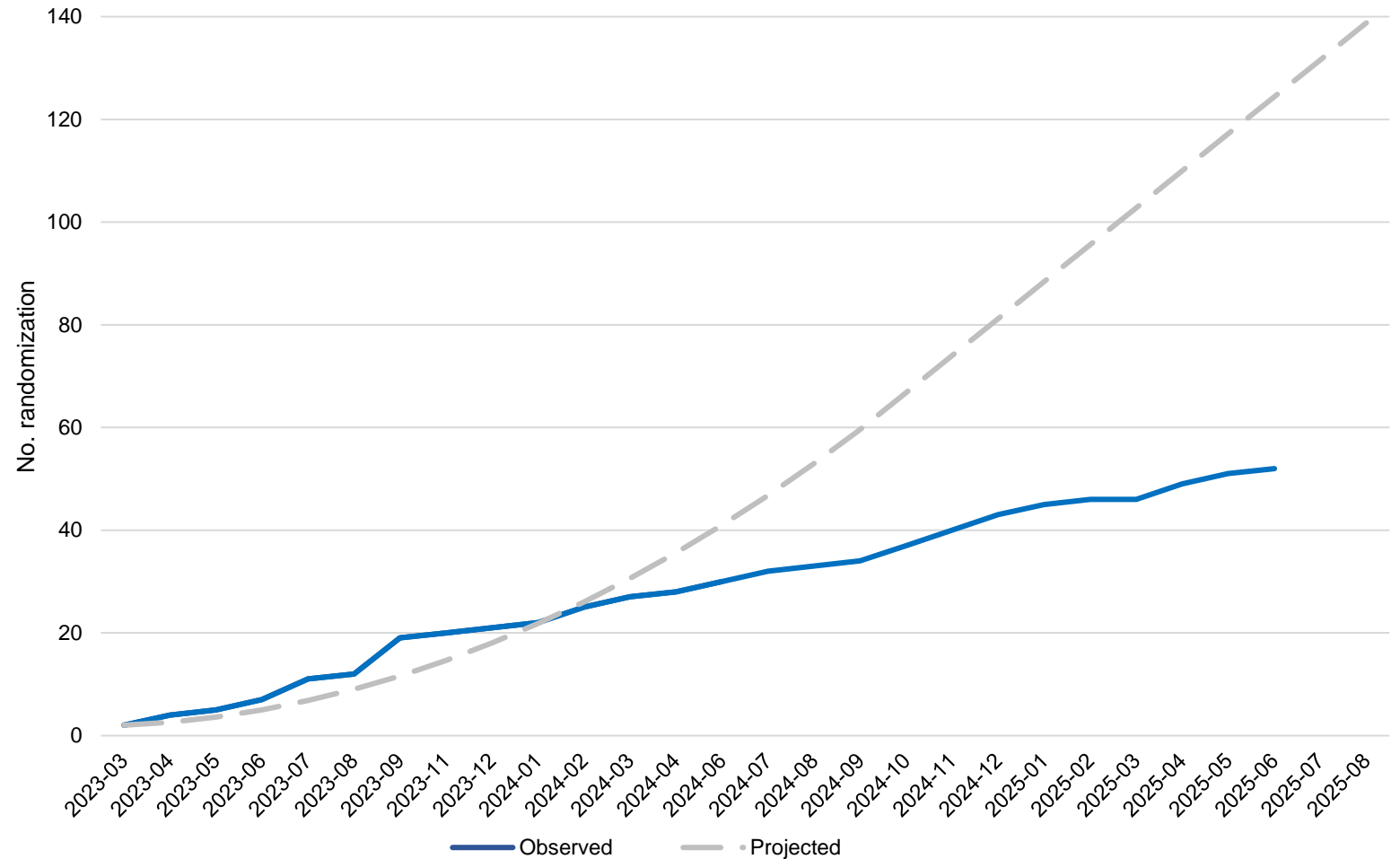
No Screening Failure: 2

No. withdrawal: 5

Total number of sites active: 34

Activation of Central and Eastern
European Gynecologic Oncology Group
(CEEGOG) is ongoing

A paper is under submission to describe
the study protocol, the population
enrolled and safety



Rare tumors ongoing studies summary LEPRE

	Città	Investigatore Principale	Data attivazione	Pazienti arruolate	Screening in corso	Pazienti randomizzate
1	Roma	Vanda Salutari	30/11/2022	15	0	14
2	Milano	Luca Bocciolone	30/08/2023	6	0	6
3	Treviso	Grazia Artioli	23/11/2022	5	0	4
4	Milano	Nicoletta Colombo	13/06/2023	4	0	4
5	Brescia	Chiara Abeni	12/01/2023	4	0	4
6	Meldola	Alberto Farolfi	09/02/2023	3	0	3
7	Padova	Valentina Guarneri	18/11/2022	3	0	3
8	Genova	Andrea De Censi	22/09/2022	3	0	3
9	Pavia	Chiara Cassani	15/01/2024	2	0	2
10	Milano	Domenica Lorusso	30/10/2024	2	0	1
11	Milano	Giovanna Scarfone	18/03/2024	1	0	1
12	Biella	Laura Zavallone	03/04/2023	1	0	1
13	Varese	Nicoletta Donadello	13/03/2023	1	0	1
14	Roma	Violante di Donato	09/02/2023	1	0	1
15	Como	Monica Giordano	20/01/2023	1	0	1
16	Castelfranco V. (TV)	Elvira Scelzi	29/11/2022	1	0	1
17	Brescia	Germana Tognon	15/09/2022	1	0	1

	Città	Investigatore Principale	Data attivazione	Pazienti arruolate	Screening in corso	Pazienti randomizzate
18	Firenze	Maria Cristina Petrella	25/10/2023	1	1	0
19	Pisa	Stefania Cosio	19/02/2025	0	0	0
20	Manerbio (BS)	Anna Rizzi	23/12/2024	0	0	0
21	Reggio Emilia	Alessandra Bologna	28/10/2024	0	0	0
22	Cagliari	Elena Massa	08/10/2024	0	0	0
23	Napoli	Stefania Napolitano	26/07/2024	0	0	0
24	Lecco	Federica Villa	24/06/2024	0	0	0
25	Monza	Andrea Lissoni	08/05/2024	0	0	0
26	Prato	Elena Zafarana	02/11/2023	0	0	0
27	Piacenza	Rosa Porzio	12/09/2023	0	0	0
28	Udine	Claudia Andreetta	06/07/2023	0	0	0
29	Roma	Paola Malaguti	13/06/2023	0	0	0
30	Ferrara	Federica Lancia	15/05/2023	0	0	0
31	Ravenna e Rimini	Claudia Casanova	04/05/2023	0	0	0
32	Belluno	Fable Zustovich	08/02/2023	0	0	0
33	Arezzo	Sabrina Del Buono	19/12/2022	0	0	0
34	Milano	Francesco Raspagliesi	29/11/2022	0	0	0
Totali				55	1	52

Rare tumors ongoing studies summary RARE CANCERS ENGOT REGISTRY

SPONSOR	Each Group is the Sponsor in its own country
MaNGO (YMaGiNe)	Delegated for database implementation
Responsible person for the initiative	Lorenzo Ceppi (MaNGO) Alice Bergamini (MITO)

Study Design

- ✓ **Multi-center, retrospective and prospective observational study** based on the collection of data related to patients with rare gynecological neoplasms
- ✓ The study involves **malignant germinal cell tumors of the ovary, sex cord stromal tumors** and **low grade serous tumors of the ovary**, with complete clinical, surgical and pathology data
- ✓ Data will be collected electronically using an eCRF format shared within the ENGOT network

Objectives

- ✓ To retrospectively and prospectively collect epidemiological, pathological and clinical data on rare gynecological tumors using a shared matrix to standardize this collection among the different existing national databases;
- ✓ Describe the main lines of diagnosis and treatment of these tumors in the centers of European reference;
- ✓ To spread the knowledge about rare tumors;
- ✓ **To promote the collaboration and comparison between the centers involved in the treatment of these tumors.**

Rare tumors ongoing studies summary RARE CANCERS ENGOT REGISTRY

Current status of the study in Italian sites (as of 16th June 2025)

✓ 14/17 sites have received regulatory approval and were activated

✓ The patients currently registered in the database are 264



Site	No of enrolled patients	Low grade serous ovarian carcinoma	Sex cord stromal cell tumors	Malignant germinal cell tumors
Istituto Nazionale dei Tumori - Milano	55	19	23	13
Ospedale Niguarda - Milano	11	2	7	2
Ospedale Galliera - Genova	14	5	6	3
Ospedale Sant'Anna - Como	8	1	6	1
Ospedale Manzoni - Lecco	4	3	1	0
Istituto Europeo di Oncologia - Milano	125	59	47	19
A.O. Ordine Mauriziano - Torino	3	1	2	0
Arcispedale Santa Maria Nuova - Reggio Emilia	5	3	2	0
Spedali Civili - Brescia	22	9	11	2
AOU - Modena	2	1	1	0
Istituto Oncologico Veneto - Padova	12	7	5	0
Ospedale del Ponte - Varese	3	0	3	0
Ospedale San Luca - Lucca	0	0	0	0
Total	264	110	114	40

For more information: <http://www.mango-group.it/studi/recruiting-planned/other-studies>

Rare tumors ongoing studies summary RARE CANCERS ENGOT REGISTRY

Groups involvement

Interested Groups	Status	Submission timeline
EORTC	Data transfer request submitted in June 2025 – participation in retrospective part	
G-AGO	Participation in the retrospective part – pending point from ethical committee	Submission performed
A- AGO	Full participation	Submission under preparation
BGOG	Full participation	Submission under preparation
CEECOG	Full participation	Expected for autumn 2025
UK	Participation within the national databases (RANGO registry) that foreseen a collaboration with international registries. 18 sites. Now they are rebuilding the national registry to be aligned with ENGOT initiative	NA
PGOG	Recently expressed interest. Participation to be confirmed	
SWISS-GO	Recently expressed interest. Participation to be confirmed	
GINECO	Recently expressed interest. Participation to be confirmed	
ISGO	Participation to be confirmed	
DGOG	Participation to be confirmed	
GEICO	Declined the participation due to the lack of funding	
SAKK	Declined the participation due to the lack of funding	

Rare tumors ongoing studies summary RARE CANCERS ENGOT REGISTRY

Description of low-grade serous ovarian cancer, an early report from the ENGOT rare cancers registry, the MaNGO Cohort



L. Ceppi¹, F. Multini², M. Polignano³, M.F. Alvisi⁴, N. Provinciali⁵, C. Quatrali⁶, G. Tasca⁷, M. Giordano⁸, A. Ardizzone⁹, A. Bologna¹⁰, A. Ferrero¹¹, G. Schivardi¹², F. Calazzo¹³, M. C. Caudana¹⁴, N. Colombo¹⁵, F. Raspagliesi¹⁶, E. Biagioli¹⁷, A. Bergamini¹⁸, I. Ray-Coquard¹⁹, S. Pignata²⁰

¹Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy; ²European Institute of Oncology, Milano, Italy; ³Istituto Nazionale dei Tumori, Milano, Italy; ⁴Istituto di Ricerche Farmacologiche Mario Negri, Milano, Italy; ⁵Ospedali Galliera, Genova, Italy; ⁶ASST Niguarda, Milano, Italy; ⁷IOV Padova, Padova, Italy; ⁸ASST Lariana Ospedale Sant'Anna di Como, Como, Italy; ⁹ASST di Lecco, P.O. A. Manzoni, Lecco, Italy; ¹⁰Azienda USL IRCCS Reggio Emilia, Reggio Emilia, Italy; ¹¹Academic Division Obstetrics and Gynecology Maurizio Hospital, Department of Surgical Sciences University of Torino, Torino, Italy; ¹²European Institute of Oncology, University Milan-Bicocca, Milano, Italy; ¹³Department of Obstetrics and Gynecology, San Raffaele Hospital, Milano, Italy; ¹⁴Centre Leon-Berard, Lyon, France; ¹⁵Department of Urology and Gynecology, Istituto Nazionale Tumori IRCCS Fondazione G. Pascale, Napoli, Italy

INTRODUCTION

Low-grade serous ovarian cancer (LGSOC) is considered among rare gynecological diseases, and its presentation is often in advanced stage and associated with serous borderline ovarian tumor¹⁰. This is an international, observational study on rare gynecological neoplasms including LGSOC in centers of the European Network of Gynecological Oncological Trial Group (ENGOT).

AIM

Here we report a description of LGSOC cases included by Italian sites part of the Mario Negri Gynecology Oncology (MaNGO) network.

METHOD

Eligible patients were prospectively and retrospectively registered in RedCap collecting clinical, pathological, surgical data and treatment details of first diagnosis and relapses. Descriptive analysis were conducted, and survival curve of relapse free survival (RFS) was described with the Kaplan-Meier (KM) method. Univariable Cox regression models were used to assess associations with RFS and clinical-biological features.

Figure 1



Rare Cancers In Gynecologic Oncology, ENGOT Initiative For A European Registry: Update Of The European Activation In 2024

Lorenzo Ceppi¹, Alice Bergamini², Elena Biagioli³, Serena Giolitto³, Olesya Solheim⁴, Antonio Gonzalez-Martin⁵, Nelleke Ottevanger⁶, Els Van Nieuwenhuysen⁷, Annette Hasenburger⁸, Karen Cadoo⁹, Elena Ioana Braicu¹⁰, Stefanie Aust¹¹, Rosalind Glasspool¹², Christianne A R Lok¹³, David Cibula¹⁴, Viola Heinzlmann-Schwarz¹⁵, Sandro Pignata¹⁶, Isabelle Ray-Coquard¹⁷

¹Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; ²IRCCS San Raffaele Hospital, Milan, Italy; ³Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Milan, Italy; ⁴Department of Gynecological Oncology, Oslo University Hospital, Oslo, Norway; ⁵Medical Oncology Department Cancer Center, Clinica Universidad de Navarra, Madrid, and Program in Solid Tumours CIMA, Pamplona, Madrid, Spain; ⁶Radboud UMC, Nijmegen, The Netherlands; ⁷UZ Leuven, Leuven, Belgium; ⁸University Medical Center of Mainz, Mainz, Germany; ⁹The Haematology, Oncology and Palliative Care (HOPE) Directorate, St James's Hospital, Dublin, Ireland; ¹⁰Department of Gynecology European Competence Center for Ovarian Cancer, Campus Virchow-Klinikum, Charité Medical University, Berlin, Germany; ¹¹Department of Obstetrics and Gynecology, Division of General Gynecology and Gynecologic Oncology, Gynecologic Cancer Unit, Comprehensive Cancer Center (CCC), Medical University of Vienna, Vienna, Austria; ¹²Beatson West of Scotland Cancer Centre, NHS Greater Glasgow and Clyde and University of Glasgow, Glasgow, United Kingdom; ¹³Centre of Gynecologic Oncology, Amsterdam, The Netherlands; ¹⁴First Faculty of Medicine, Charles University and General University Hospital, Prague, Czech Republic; ¹⁵Gynaecological Cancer Centre, University Hospital Basel, Basel, Switzerland; ¹⁶Department of Urology and Gynecology, Istituto Nazionale Tumori IRCCS Fondazione G. Pascale, Napoli, Italy; ¹⁷Centre Leon-Berard, Lyon, France

INTRODUCTION

Rare diseases are difficult to managed properly, reasons are several including lack of experience, low referral rates to oncological centers, and treatments based on experts' opinions. The European Commission has highlighted the need for treatment standardization in rare cancers, suggesting the creation of international networks that would allow collection and sharing of knowledge on these neoplasms. In Europe, currently there are no comprehensive databases that deal with rare gynecological cancers. The need to have multicentric databases is supported by the results obtained with both retrospective and prospective studies. Many retrospective studies published from national and international collaborating groups have led to significant changes in some of the available guidelines.

METHOD

This is a multi-center, international, retrospective and prospective observational study collecting data of patients with rare gynecological neoplasms in centers part of the European Network of Gynecological Oncological Trial Group (ENGOT). The study includes patients with malignant germ cell tumors, sex-cord stromal tumors, and low-grade serous tumors of the ovary but can be possibly expanded to other rare gynecological cancers. The follow-up of patients will continue for up to 20 years. REDCap (Research Electronic Data Capture) web application is used for data collection. The groups have the option of two ways of participation: they could receive the database structure (xml file) to be imported

Figure 1



Bandi di Ricerca Indipendente 2025

AIFA pubblica il Bando Ricerca Indipendente 2025 sulle Malattie Rare che destina 17.800.000 euro alla ricerca scientifica indipendente per la promozione di studi su patologie a bassa prevalenza che spesso non attraggono investimenti commerciali significativi.

Il bando è rivolto a tutti i ricercatori italiani di enti e istituzioni che intendano condurre studi non a fini commerciali ed è finanziato con una quota derivante dall'art. 11 del Testo Unico Malattie Rare (Legge 175/2021) che ha previsto un incremento del 2% del Fondo costituito dal contributo delle spese promozionali sostenute annualmente dalle aziende farmaceutiche.

L'obiettivo principale è quello di incentivare lo sviluppo di terapie farmacologiche efficaci per le malattie rare per migliorare la salute e la qualità di vita dei pazienti.

Il presente Bando, tenendo conto del Testo Unico Malattie Rare, prevede che la proposta di studio ricada in una delle seguenti linee di indagine: