XXII ASSEMBLEA MaNGO MILANO

STANDARD TREATMENTS AND NEW DIRECTIONS IN GYNAECOLOGICAL CANCERS

MILANO June 26th-29th, 2025

Responsabili Scientifici:
NICOLETTA COLOMBO, FRANCESCO RASPAGLIESI

MaNGO

OVARIAN CANCER TRIALS

Opening studies 1st line

Antonio Ardizzoia , ASST Lecco - Ospedale Alessandro Manzoni, Lecco

Disclosure

Relatore:

- GSK
- Servier

OVARIAN CANCER TRIALS - 1st line

Opening and recruiting trials

- ENGOT-ov62 / N-PLUS
- ENGOT-ov78 / SALVOVAR

Opening and planned trials

- ENGOT-ov85 / MK-2870-021
- ENGOT-ov89 / DESTINY Ov-01

- EARLY DIAGNOSIS: EVA TEST study (MaNGO)

OVARIAN CANCER TRIALS - 1st line
Opening and recruiting trials

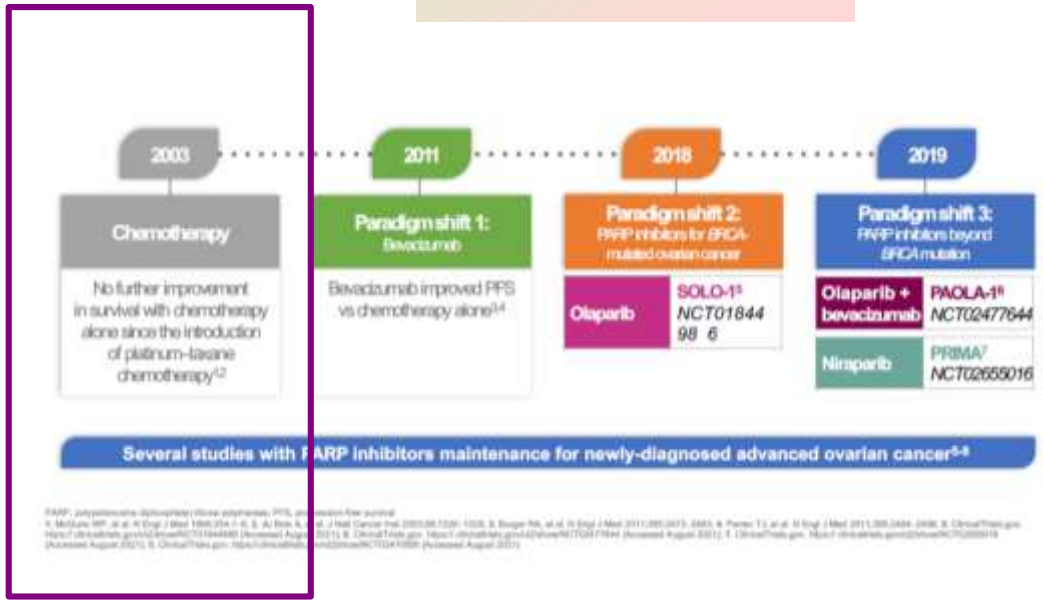
ENGOT-ov62/N-Plus

A Phase II randomized, open-label non-inferiority study of Niraparib maintenance after 3 vs. 6 cycles of platinum-based chemotherapy in completely debulked advanced HRDpositive high-grade ovarian cancer patients in first-line therapy

ENGOT-ov78 / SALVOVAR:

A pragmatic randomized phase III trial to assess the utility of adjusting chemotherapy dose & dosing schedule with the SALVage weekly dose-dense regimen in patients with poor prognostic OVARian cancers based on the tumor unfavorable primary chemosensitivity and incomplete debulking surgery

DESCALATION



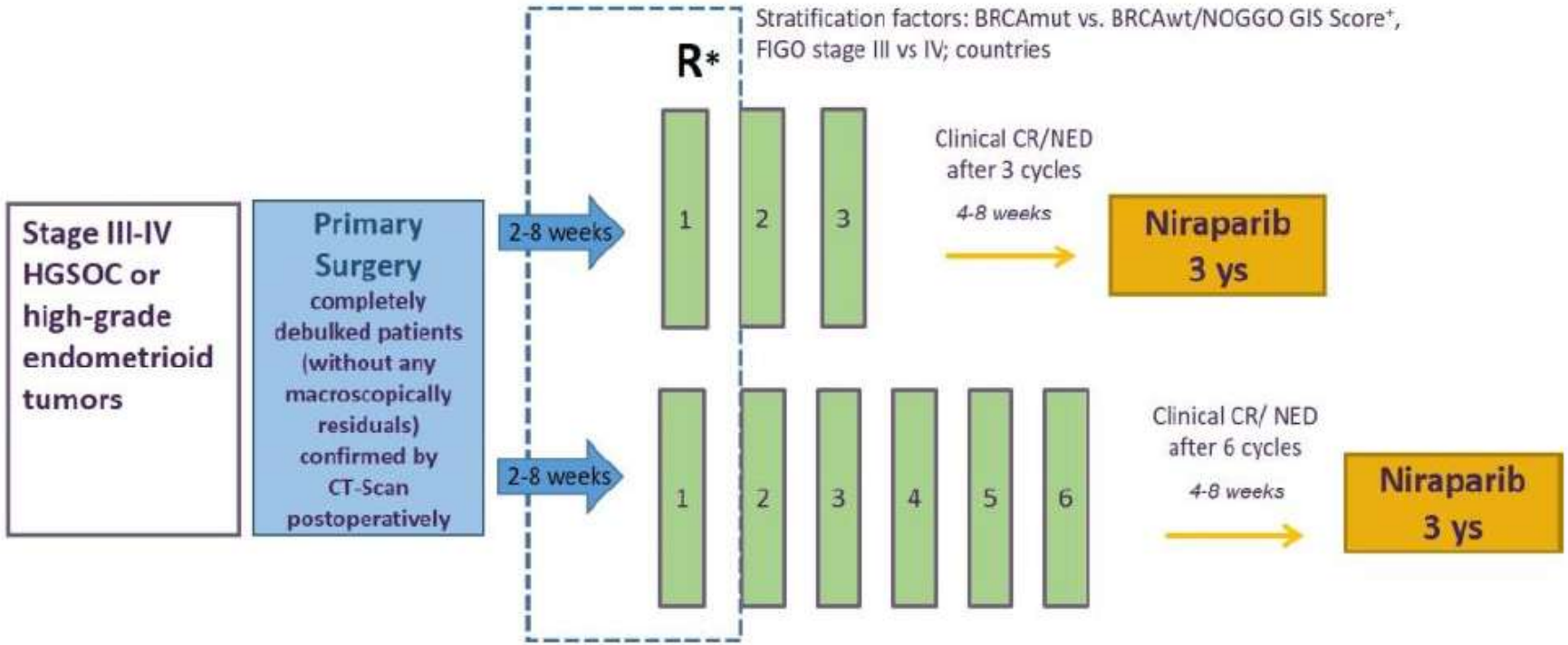
INTENSIFICATION

Ovarian cancer trials 1st line – Opening & recruiting **ENGOT-ov62 / N-PLUS**

ENGOT-ov62 / N-PLUS A Phase II randomized, open label non-inferiority study of NiraParib maintenance after 3 vs. 6 cycles of platinum-based chemotherapy in completeLy debUlked advanced HRDpositive high-grade ovarian cancer patientS in first line therapy

- ENGOT Model: B (academic)
- Sponsor & Lead Group: NOGGO (Germany)
- Participating Groups: MaNGO, CEEGOG, AGO, BGOG, GEICO

Ovarian cancer trials 1st line – Opening & recruiting **ENGOT-ov62 / N-PLUS**



- Standard chemotherapy has to start within 8 weeks after primary surgery and may start before randomization
- Randomization has to take place on C2D1 the latest

Primary Endpoint:

RFS (Recurrence free survival, defined as time from treatment randomization to the earliest date of assessment of first relapse or death by any cause)

Secondary Endpoint:

OS (time to event and rate at 3 and 5 years), TFST, TWIST at baseline, 3, 6, and 12 months, PFS2, PROs (EORTC QLQ-C30 and EORTC QLQ-OV28), Safety assessment, Cost effectiveness

MaNGO sites & study updates (June 2025)

	Hospital	Name & Surname	status
1	Ospedale Sant'Anna, Torino	Dionyssios Katsaros (MaNGO Lead PI)	Agreement final
2	Azienda Ospedaliero Universitaria di Cagliari	Elena Massa	No feed-back on agreement
3	Ospedale Manzoni, Lecco	Antonio Ardizzoia	No feed-back on agreement
4	Policlinico Sant'Orsola, Bologna	Claudio Zamagni	Agreement final
5	Istituto Naz. dei Tumori, Milano	Francesco Raspagliesi	Agreement final
6	Spedali Civili di Brescia	Valentina Zizioli	No feed-back on agreement
7	Azienda Ospedaliera Universitaria Pisana	Carmelo Bengala	SIV done 10 June 2025
8	Istituto Oncologico Veneto, padova	Giulia Tasca	SIV done 21 May 2025
9	Ospedale Mauriziano, Torino	Anna Maria Ferrero	SIV done 20 June 2025
10	IRCCS di Reggio Emilia	Alessandra Bologna	Agreement final

GLOBAL STATUS

- The study is currently active in Austria, Germany, Spain, Belgium, Czechia, Italy
- Planned No. of active sites **46**
- Nº randomized patients (07/06/2025): **11**
- Planned No. of patients: 640 screened / 360 randomized ratio 1:1
- EU FPFV: 30April 2024
- LPO (last patient last visit): 30 Apr 2027
- End of Follow-up: 30 Apr 2032

ITALY STATUS

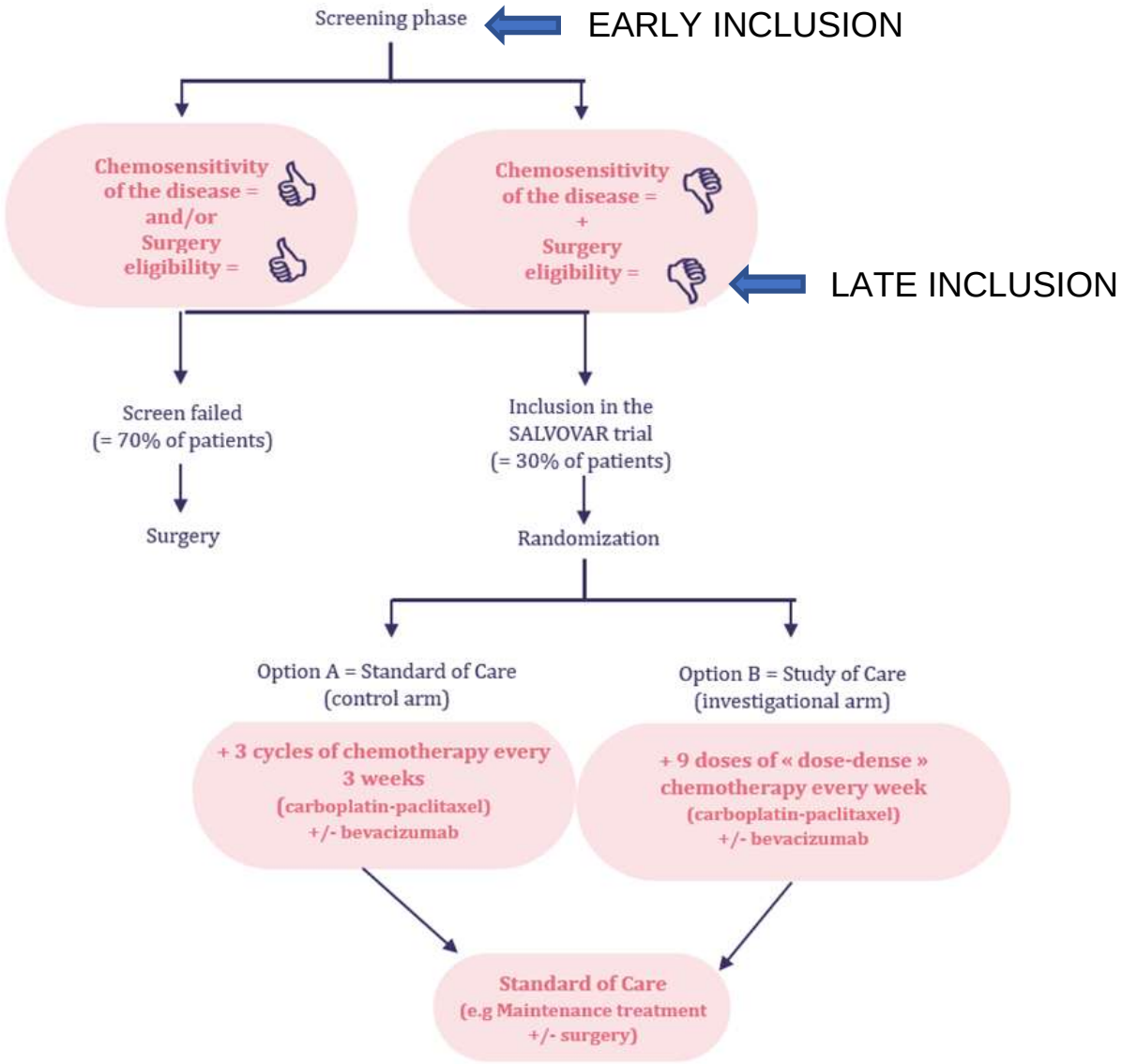
- Active sites: 3/10
- Agreement under negotiation for other sites
- Activation of new sites is ongoing

Ovarian cancer trials 1st line – Opening & recruiting **ENGOT-ov78 / SALVOVAR**

ENGOT-ov78 / SALVOVAR A pragmatic randomized phase III trial to assess the utility of adjusting chemotherapy dose & dosing schedule with the SALVage weekly dose-dense regimen in patients with poor prognostic OVARian cancers based on the tumor unfavorable primary chemosensitivity and incomplete debulking surgery

- ENGOT model A
- Sponsors: ARCAGY-GINECO
- Cooperating groups: CEEGOG, DGOG,GTG-UK, ISGO, JGOG, MaNGO
- ManGO lead PI: Gabriella Parma, IEO

Ovarian cancer trials 1st line – Opening & recruiting **ENGOT-ov78 / SALVOVAR**



- **Primary Objective:**
- To demonstrate the superiority in terms of efficacy of a densification of the chemotherapy with the salvage weekly dose-dense carboplatin-paclitaxel regimen compared to the continuation of the standard 3-weekly carboplatin-paclitaxel, in ovarian cancer patients found to have a poor prognostic disease
- **Co-Primary Endpoints:**
- Percentage of patients operated with late complete debulking surgery (expected increase from 5% to 20%)
- Overall survival improvement by 49% (HR = 0.61) in the whole population translating in an improvement in median OS from 20 months (control arm) to 32.8 months (experimental arm) with a 1:1 randomization

Ovarian cancer trials 1st line – Opening & recruiting ENGOT-ov78 / SALVOVAR

Study Global Updates

- No. of sites: Planned: 98, Active: 26
- No. of recruited patients: GINECO: 29 in screening, 28 randomized & 14 in observational cohort
- Planned no. of patients: 250

MaNGO sites & study updates – June 2025

	Hospital	First Name	Last Name	Status
1	**Istituto Europeo di Oncologia, Milano**	**Gabriella**	**Parma***	*MaNGO PI/ Planned SIV
2	Ospedale SS Antonio e Biagio, Alessandria	Giulia	Galizzi	Contract finalization
3	Ospedale Manzoni, Lecco	Federica	Villa	Contract finalization
4	Policlinico S. Orsola, Bologna	Claudio	Zamagni	Active site since March 2025 – awaiting enrollment
5	Policlinico Careggi, Firenze	Cristina	Petrella	Contract finalization
6	Ospedale di Mirano, Mirano	Alessandra	Baldoni	Contract finalization

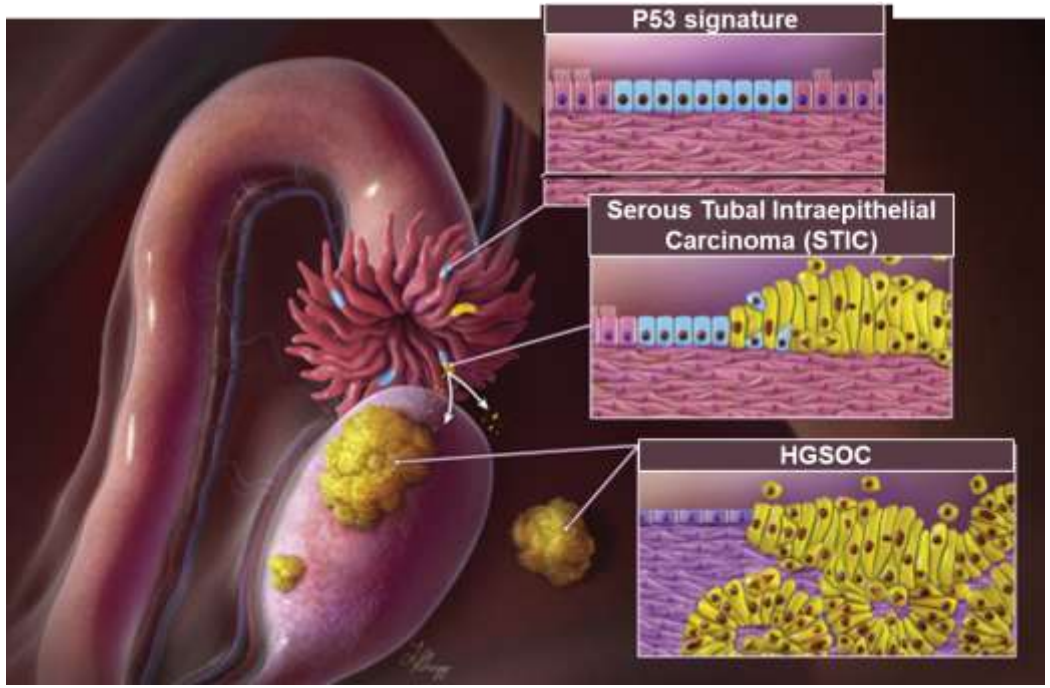
ENGOT-ov85 – MK2870-021

CONFIDENTIAL

ENGOT-ov89 / DESTINY Ov-01

CONFIDENTIAL

RATIONALE FOR A NON-INVASIVE TEST FOR EARLY DIAGNOSIS OF OVARIAN CANCER

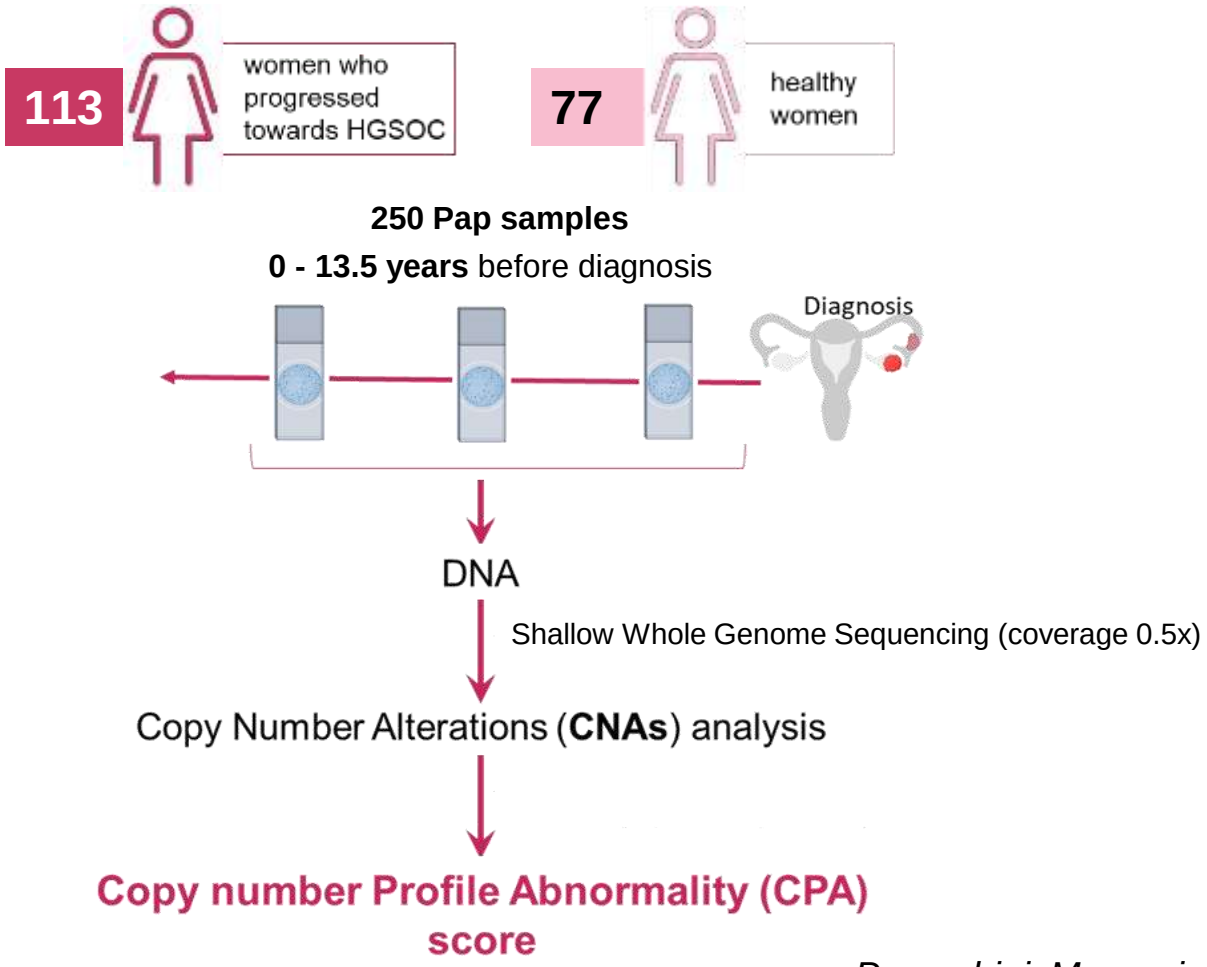


Shih et al. Am J Pathol. 2021

- The **lead time** for the development of high-grade serous OC is estimated to be between **5 to 9 years**.
- Tumor cells can be shed into the uterine cavity, and their components can be **detected in a cervical swab**.
- Some molecular alterations that characterize high-grade serous OC are also present at early stages, including in STIC:
  - **Pathogenic TP53 mutation**
  - **Methylation changes**
  - **Copy number alterations** resulting from genomic instability

Ovarian cancer trials – Opening **EVA TEST STUDY**

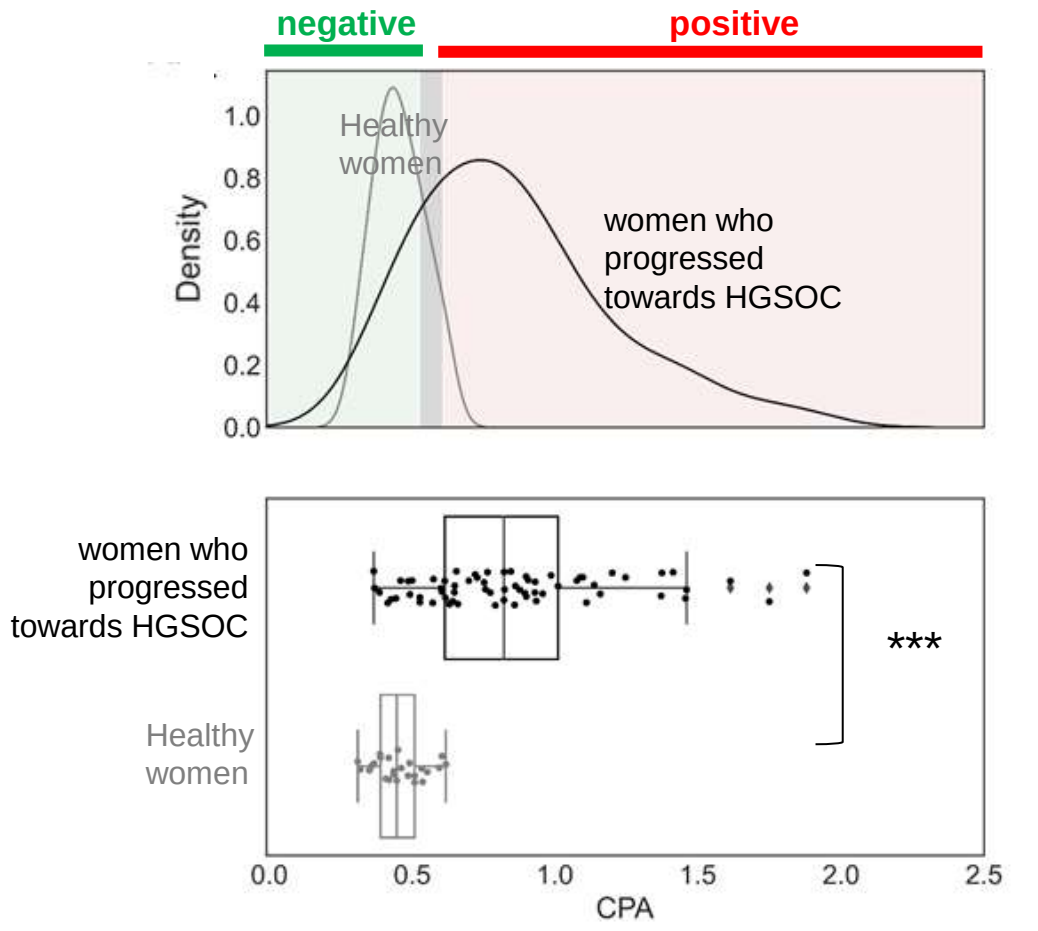
APPROACH



Paracchini, Mannarino, Romualdi et al. Sci Transl Med 2023

Ovarian cancer trials – Opening **EVA TEST STUDY**

Background - RESULTS

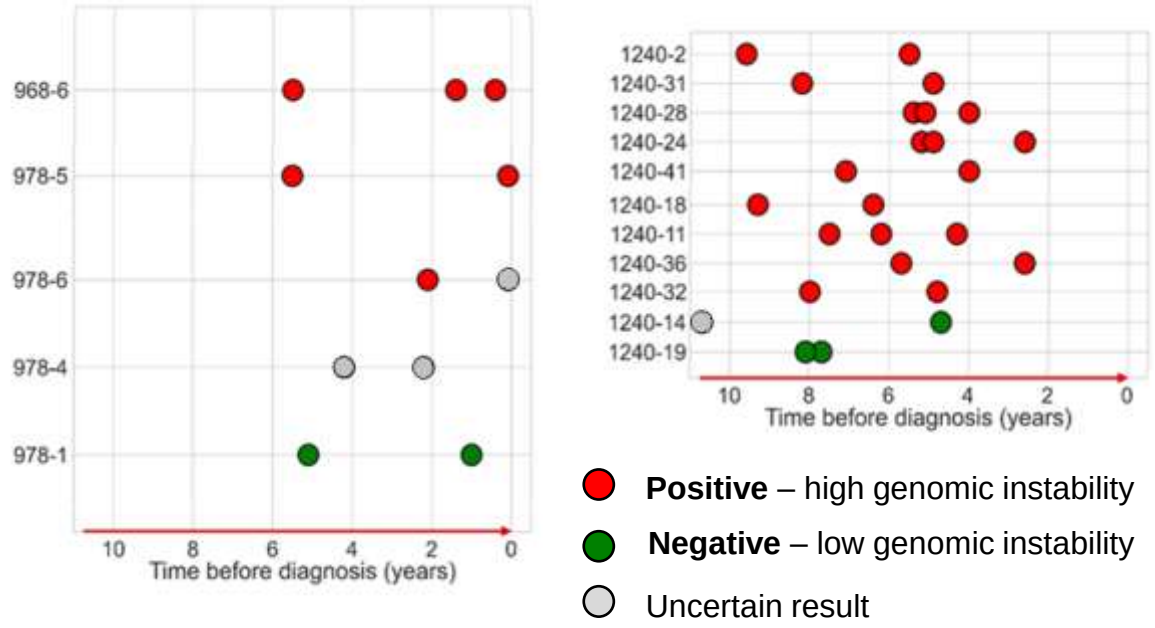


Sensitivity: 75% (95% CI, 65 – 86%)

Specificity: 96% (95% CI, 88 – 100%)

Accuracy: 81%

Longitudinal samples

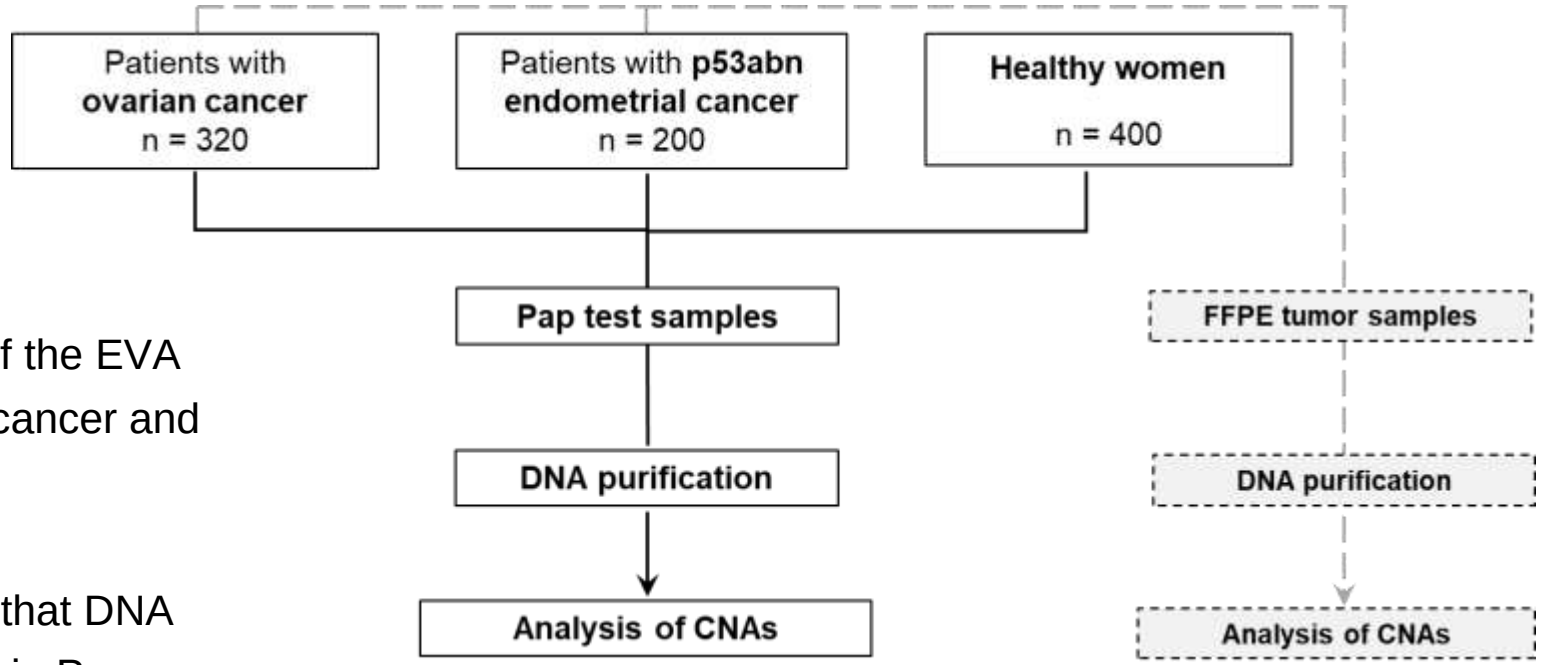


Paracchini, Mannarino, Romualdi et al. Sci Transl Med 2023

Ovarian cancer trials – Opening **EVA TEST STUDY**

Study Design

Early diagnosis of epithelial ovarian cancers and p53 abnormal endometrial cancer by molecular analysis of cervical swab. A retrospective study



Objectives

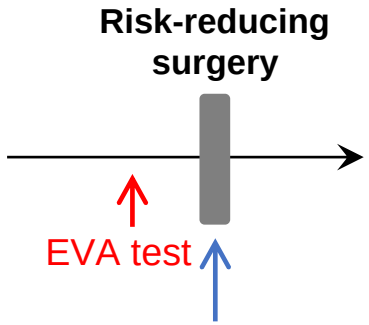
- To assess the **diagnostic accuracy** of the EVA test for the early detection of ovarian cancer and p53abn endometrial cancer
- To **validate** the test by demonstrating that DNA exhibiting chromosomal abnormalities in Pap samples is **derived from primary tumors**

Ovarian cancer trials – Opening **EVA TEST STUDY**

Study Objective

Diagnosis of malignant ovarian cancer precursor lesions through the analysis of DNA derived from Pap samples (EVATEST study)

Women with germline BRCA mutations opting for risk-reducing surgery



Type of study: retrospective + prospective

Objective

To assess the **concordance** between the **histological findings of malignant tubal and ovarian lesions** and the **results of the EVA test** collected before risk-reducing surgery.

Ovarian cancer trials – Opening **EVA TEST STUDY**

Sponsor: IRCCS Istituto Clinico Humanitas

Participating centers: **47** Italian clinical centers

Management and statistical analysis: Istituto di Ricerche Farmacologiche Mario Negri IRCCS

Status: Approved by Comitato Etico Territoriale Lombardia 5

Agreement Mario Negri- Humanitas finalized

Sites will be contacted soon to finalize the activation process