NSGO-CTU
Nordic Society of Gynaecological Oncology - Clinical Trial Unit

Is There a Need for the Real-World Evidence Studies

Mansoor Raza Mirza

ENGOT
European Network of Gynaecological Oncological Trial groups

Declaration of Interests
Mansoor Raza Mirza

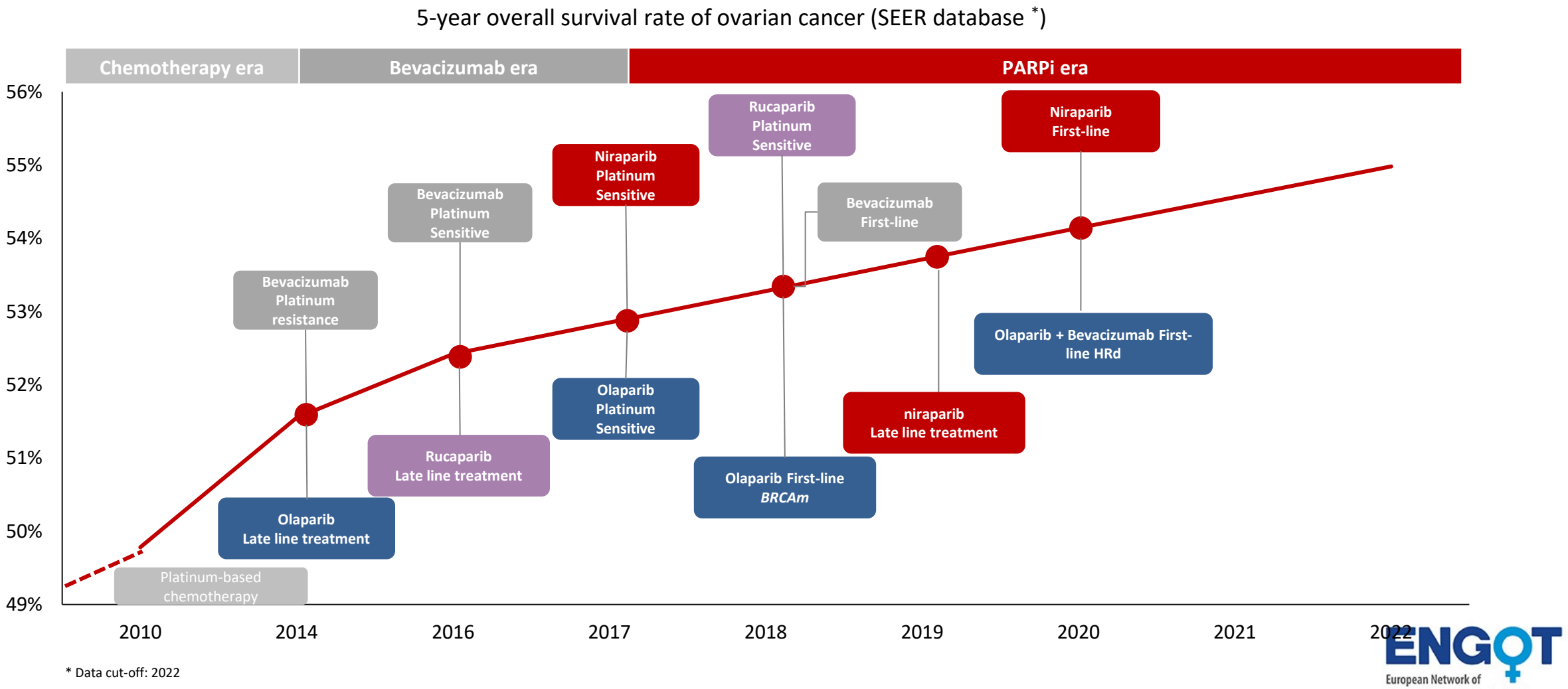
Personal:

Chief Oncologist	Dept. of Oncology, Rigshospitalet, Copenhagen University Hospital, Denmark.
Medical Director	NSGO-CTU (Nordic Society of Gynaecological Oncology)
Chairman$_{2020\text{-}2022}$	ENGOT (European Network of Gynaecological Oncology Trials group)
Vice-President$_{2020\text{-}2024}$	ESGO (European Society of Gynaecological Oncology)
Faculty	ESMO (European Society of Medical Oncology)
Scientific Chair	IGCS Congress 2024
Congress Chair	ESGO Congress 2026
Prix Galien Foundation	Jury member
Advisory board:	AbbVie, Allarity Therapeutics, Astra Zeneca, Biocad, Biontech, Daiichi-Sankyo, Eisai, Genmab, GSK, Immunogen, Incyte, Karyopharm, Merck/MSD, Mersana, Regeneron, Takeda, Zailab
Member of board of directors, stocks/shares:	Karyopharm Therapeutics, Sera Prognostics

Institutional (no personal financial interest)

Research grant:	Allarity, Apexigen, Astra Zeneca, Boehringer Ingelheim, Clovis, GSK, Novartis, Tesaro, Ultimovacs
Trial chair:	AstraZeneca, Boehringer Ingelheim, Deciphera, Daiichi-sankyo, GSK, Merck, Mersana, NuvationBio, Tesaro

The 5-Year Overall Survival Rate of Ovarian Cancer is Increasing Annually



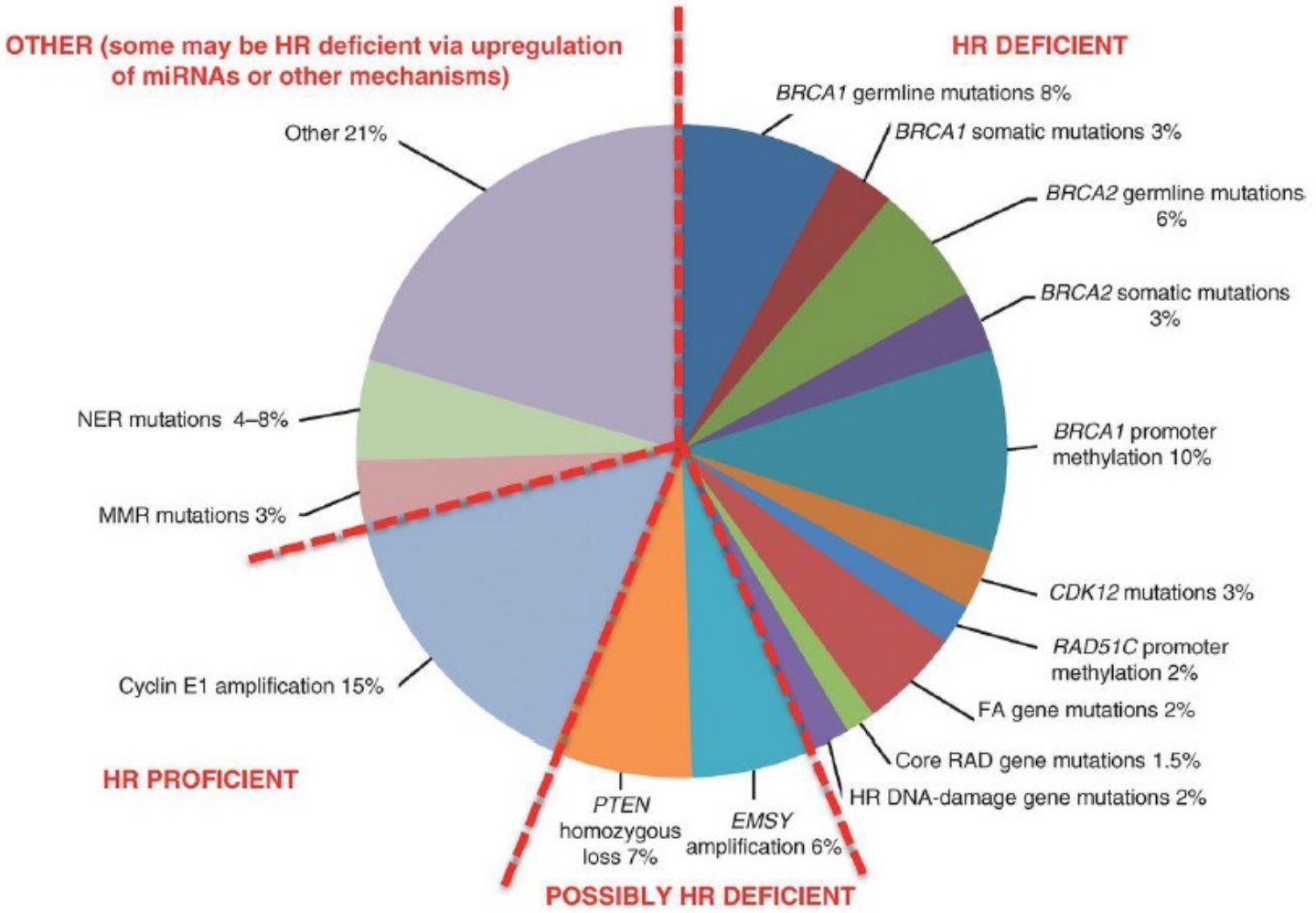
* Data cut-off: 2022

https://seer.cancer.gov/statfacts/html/ovary.html

Homologous Recombination Defects in High-Grade Serous Ovarian Cancer

- Ovarian Cancer is a genetically heterogeneous disease

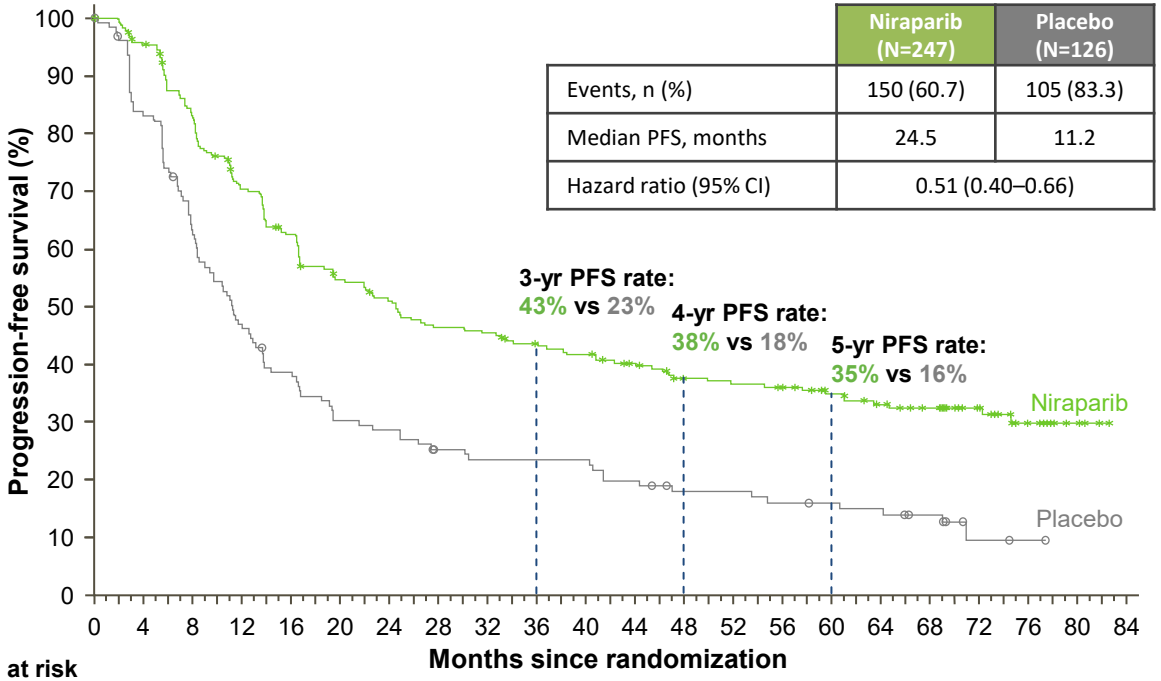
- *BRCA*1/2 deleterious mutations or chromosomal damage result in similar biology



Levine D. *The Cancer Genome Atlas, 2011*
Konstantinopoulos et al. *Cancer Discov 2015*

PRIMA Final Analysis: PFS in the overall and HRd populations

PFS in HRd

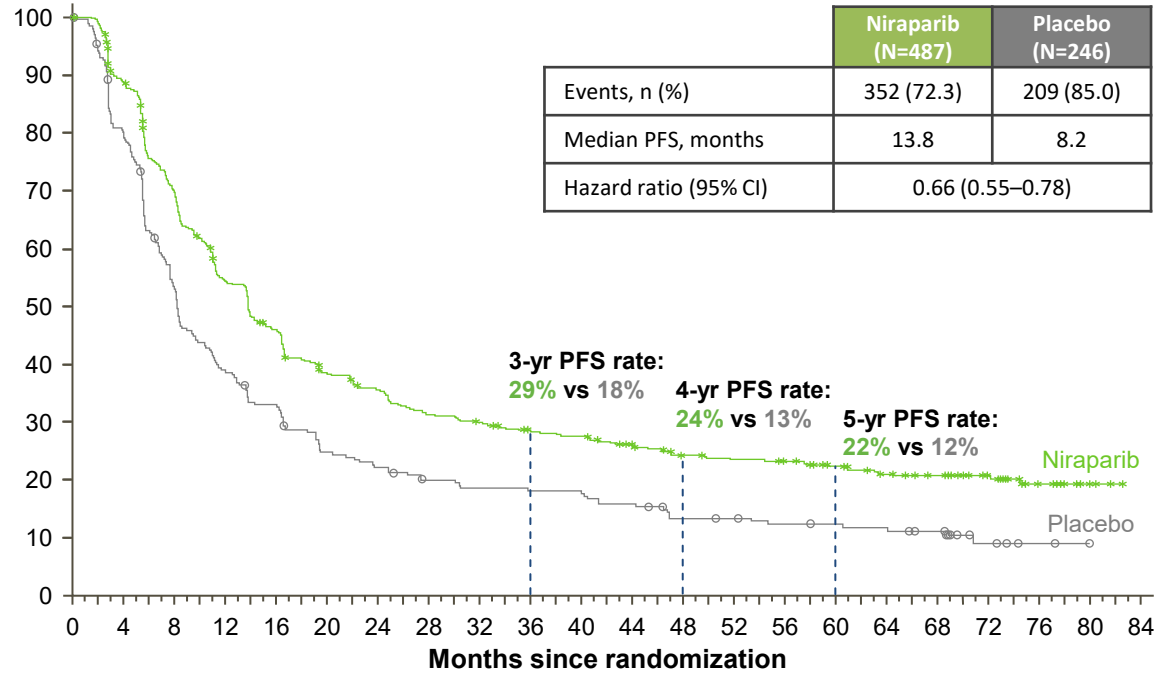


	Niraparib (N=247)	Placebo (N=126)
Events, n (%)	150 (60.7)	105 (83.3)
Median PFS, months	24.5	11.2
Hazard ratio (95% CI)	0.51 (0.40–0.66)	

No at risk

Niraparib	247	221	189	158	138	119	110	100	98	91	87	79	69	67	64	58	52	46	29	15	8	0
Placebo	126	102	76	57	46	36	34	28	26	26	26	22	18	18	16	15	14	11	3	2		

PFS in ITT



	Niraparib (N=487)	Placebo (N=246)
Events, n (%)	352 (72.3)	209 (85.0)
Median PFS, months	13.8	8.2
Hazard ratio (95% CI)	0.66 (0.55–0.78)	

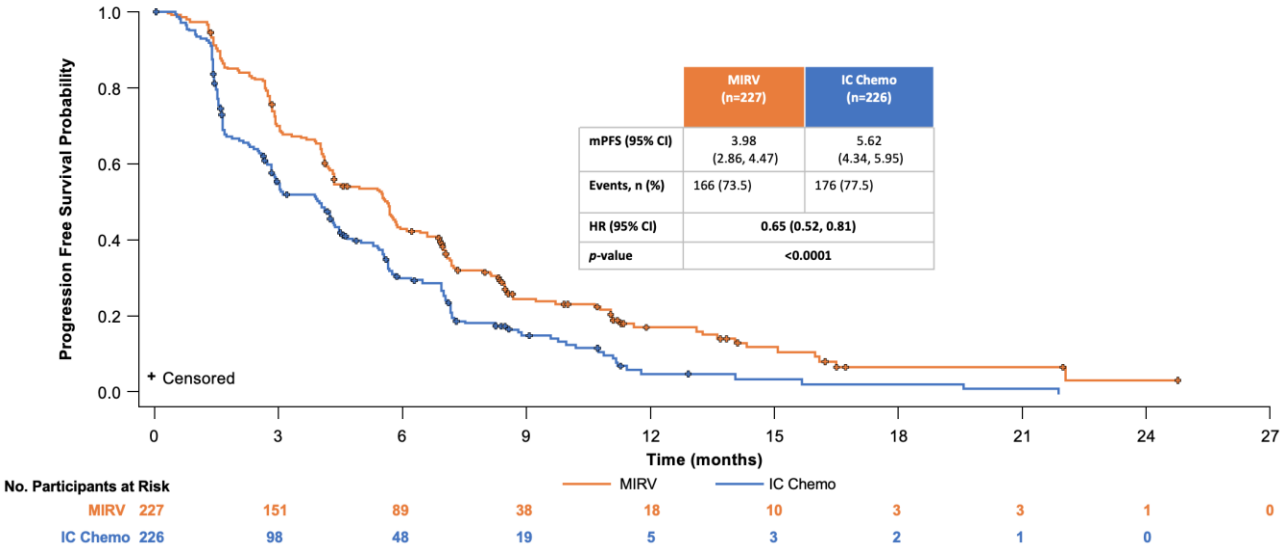
Niraparib	487	406	316	243	204	168	153	135	128	118	114	103	89	85	82	74	66	60	35	16	8	0
Placebo	246	191	125	92	77	57	51	43	40	39	39	34	27	26	23	22	21	18	6	3	1	

- The 5-year PFS rate **numerically favored niraparib** in the ITT and HRd populations
- Among patients alive at 5 years in the HRD and ITT populations, niraparib-treated patients were ~twice as likely to be progression free compared with placebo (35% vs 16% and 22% vs 12% respectively).

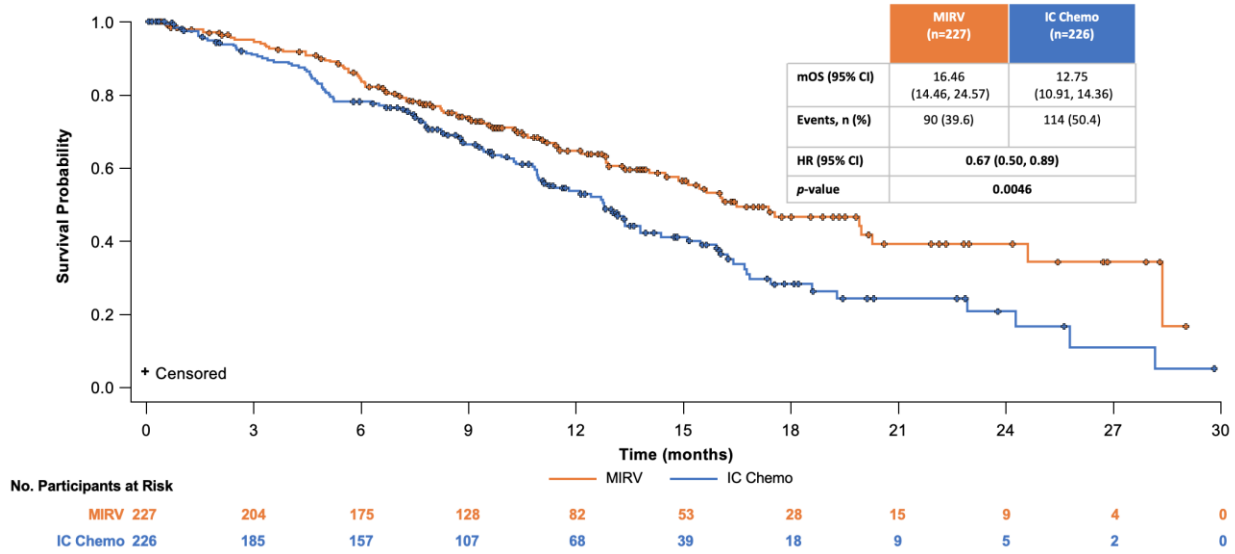
Data cut-off date: 8 April 2024; median duration of follow-up: 6.2 years. Data are investigator-assessed PFS.; HRd = homologous recombination deficient; ITT = intention-to-treat; PFS = progression-free survival; yr = year.

Monk BJ …Mirza MR et al. Ann Oncol. 2024

MIRASOL: Progression-Free and Overall Survival with Mirvetuximab Soravtansine



	MIRV (n=227)	IC Chemo (n=226)
mPFS (95% CI)	3.98 (2.86, 4.47)	5.62 (4.34, 5.95)
Events, n (%)	166 (73.5)	176 (77.5)
HR (95% CI)	0.65 (0.52, 0.81)	
p-value	<0.0001	



	MIRV (n=227)	IC Chemo (n=226)
mOS (95% CI)	16.46 (14.46, 24.57)	12.75 (10.91, 14.36)
Events, n (%)	90 (39.6)	114 (50.4)
HR (95% CI)	0.67 (0.50, 0.89)	
p-value	0.0046	

Moore et al ASCO 2023

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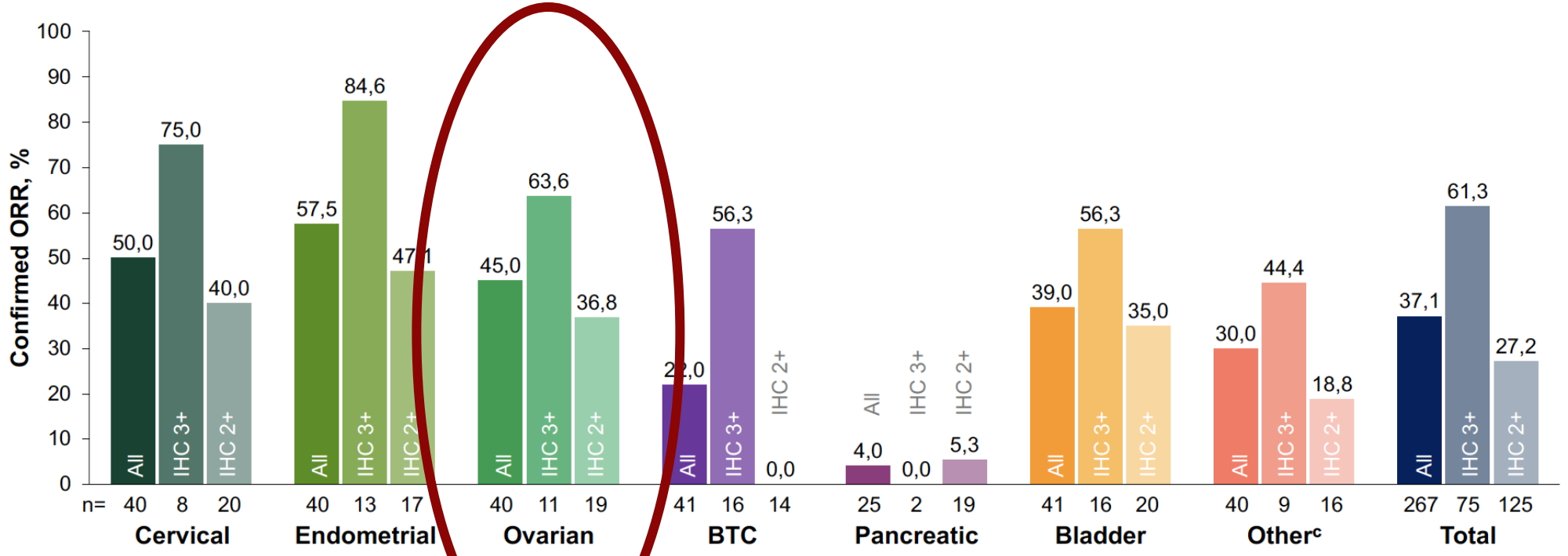
Objective Response Rate by HER2 status

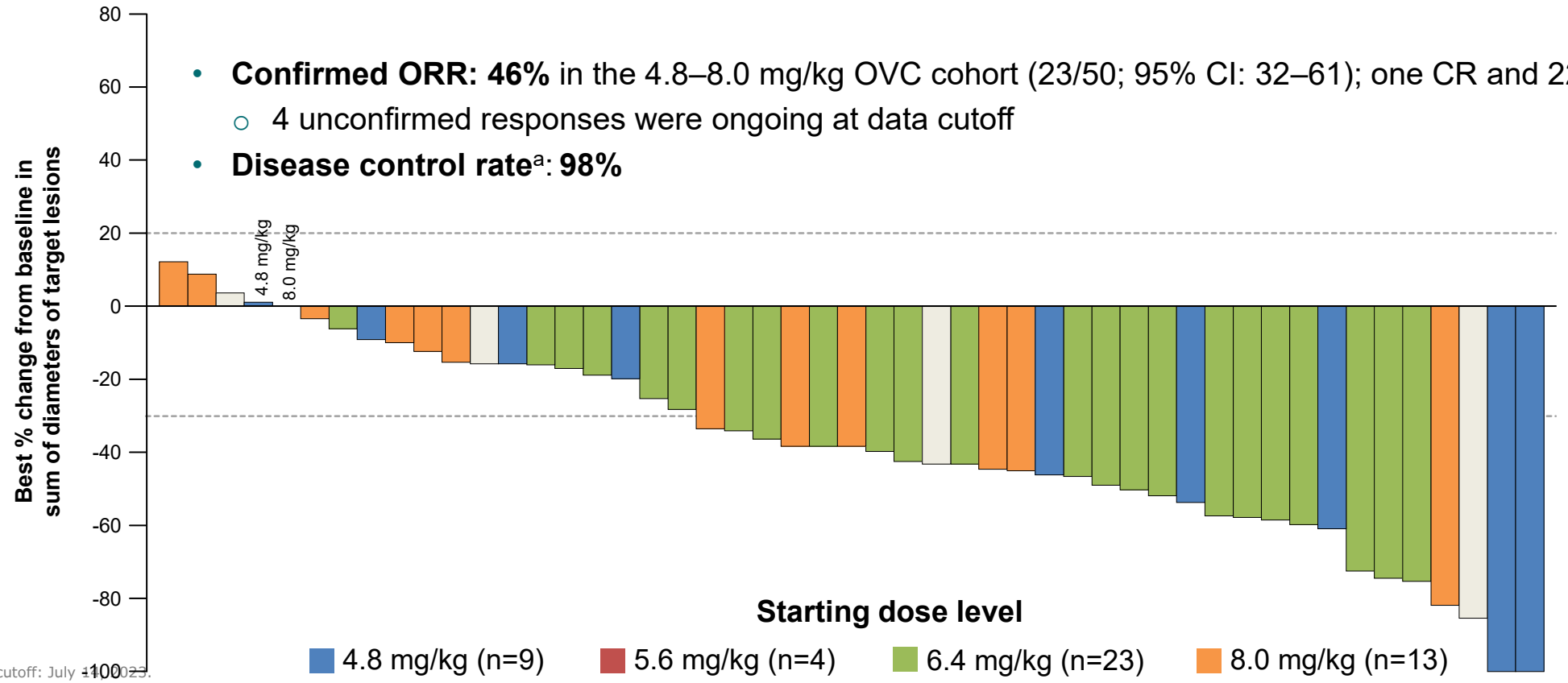


	All patients (N=99)	IHC 3+ (n=46)	IHC 2+ (n=34)
Median DOR, months (95% CI)	11.8 (9.8–NE)	22.1 (9.3–NE)	9.8 (4.2–12.6)

Analysis of ORR was performed in patients who received ≥1 dose of T-DXd; all patients (n=267; including 67 patients with IHC 1+ [n=25], IHC 0 [n=30], or unknown IHC status [n=12] by central testing) and patients with centrally confirmed HER2 IHC 3+ (n=75) or IHC 2+ (n=125) status. Analysis of DOR was performed in patients with objective response who received ≥1 dose of T-DXd; all patients (n=99; including 19 patients with IHC 1+ [n=6], IHC 0 [n=9], or unknown IHC status [n=4] by central testing) and patients with centrally confirmed HER2 IHC 3+ (n=46) or IHC 2+ (n=34) status. [a]Responses in extramammary Paget's disease, head and neck cancer, oropharyngeal neoplasm, and salivary gland cancer.
BTC, biliary tract cancer; CI, confidence interval; DOR, duration of response; IHC, immunohistochemistry; NE, non-estimable; ORR, objective response rate.

Preliminary efficacy data for R-DXd are promising in pretreated OVC patients

- **Confirmed ORR: 46%** in the 4.8–8.0 mg/kg OVC cohort (23/50; 95% CI: 32–61); one CR and 22 PRs
  - 4 unconfirmed responses were ongoing at data cutoff
- **Disease control rate**[a]: **98%**



- Data cutoff: July 4, 2023.
  [a]CR + PR + stable disease.
- The efficacy evaluable population included patients who received ≥1 dose of study treatment and completed ≥1 post-baseline tumor assessment or discontinued treatment for any reason. Change from baseline in target tumor size was assessed per RECIST v1.1.
  Two patients with no measurable lesions at baseline and one patient who discontinued and did not have a post-baseline tumor assessment were not included in the waterfall plot.
- CI, confidence interval; CR, complete response; ORR, objective response rate; OVC, ovarian cancer; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

ADC´s at ESMO 2024 *(posters not included...)*

Authors/Study	Target/drug	Cancer type	N	ORR (%)	DOR (median, months)	PFS (months)
Oaknin et al. TROPION-PanTumor03	TROP-2/Dato-DXd	**Ovarian cancer**	35	42.9	5.7	5.6
		Endometrial cancer	40	27.5	16.4	6.3
Wang et al. ´	TROP-2/ sacituzumab tirumotecan	**Ovarian cancer**	40	40	5.3	6.0
		Endometrial cancer	44	34.1	5.7	5.7 46.5%@6 months
Wu et al.	TROP-2/ sacituzumab tirumotecan+pembro	Cervical cancer	38	57.9	82.1%@6monts	65.7% @6 months
Tang et al. PRO1184-001	TROP-2/SHR-A1921	**Ovarian cancer**	46	48.8	6.4	7.2
Lee et al.	FRalphα/Rina-S	**Ovarian cancer**	12*	50	NR	Not reported
		Endometrial/ **ovarian cancer**	11	30.8	35	Not reported
Alvarez-Secord et al. PICCOLO	FRalphα/ mirvetuximab soravtansine	**Ovarian cancer**	79	51.9	8.3	6.9
Shu et al.	HER-2/IBI354	**Ovarian cancer**	129	40-52	Not reached*	6.5
Konecny et al.	Claudin-6/TORL-1-23	**Ovarian cancer**	32**	21-67	Not reported	Not reported

Ovarian cancer

Primary disease

HRD | HRP

BRCA mut | BRCA wt

Ovarian cancer

Primary disease

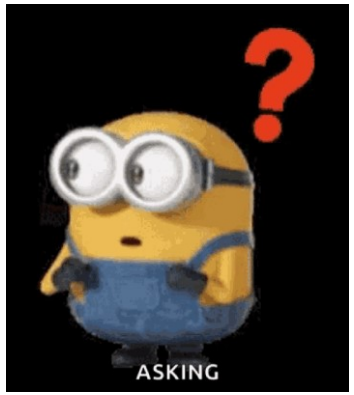
HRD | HRP

BRCA mut | BRCA wt

ENGOT-OV85/MK2870-021 TROP-2 ADC Maintenance

ENGOT-OV89/DESTINY OVARIAN-01 *HER2 pos*
T-Dxd Maintenance

FRα **HER2** **TROP-2** **PD-L1 …….**



Ovarian cancer

Primary disease

HRD

HRP

BRCA mut

BRCA wt

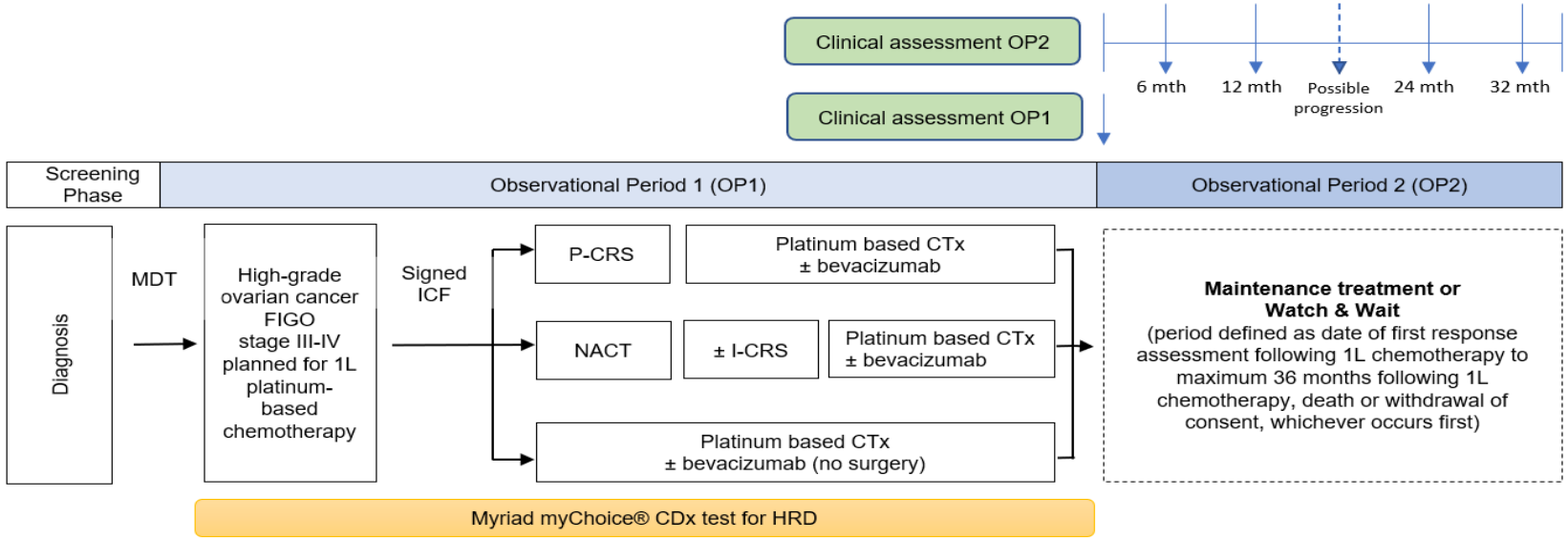
ENGOT-OV85/MK2870-021 TROP-2 ADC Maintenance

ENGOT-OV89/DESTINY OVARIAN-01 *HER2 pos*
T-Dxd Maintenance

HERO

NSGO-CTU-HERO

Characterization of High-grade Serous Ovarian Cancer Patients in Terms of Homologous Recombination Phenotype – A Prospective Observational Study



ENGOT model: A
Status: Recruiting
Planned number of patients: 1000
Sponsor: NSGO-CTU
NSGO-CTU Lead PI: Mansoor Raza Mirza
NSGO-CTU Contacts: Henriette Watson Hansen, Line Jensen, Kristine Madsen and Mansoor Raza Mirza
Primary Endpoint: OP1: Number of HR deficient patients; OP2: Progression at 6 months in subgroups

NSGO-CTU-HERO

Key Inclusion criteria

- Histologically confirmed epithelial ovarian cancer
  - FIGO stage I-II with a known *BRCA1/2* mutation (gBRCA or tBRCA)
  - FIGO stage III-IV of any histology

- Intended for platinum-based doublet chemotherapy
- Patients consent to provide archival tumor tissue sample

Key Exclusion criteria

- Non-epithelial ovarian cancer, borderline tumors, low-grade tumors, or mucinous histology
- Patients with FIGO stage I-II, *BRCA*wt ovarian cancer

NSGO-CTU-HERO

Characterization of High-Grade Ovarian Cancer Patients in Terms of Homologous Recombination Phenotype – A Prospective Observational Study

AMENDMENT

A: Increase follow-up from 36 months to 60 months

B: Increase sample size to 1000 patients

C: Publish Annual report *(possibility to share data with the grant provider)*

D: Initiate translational research

1: HRD tested in all patients

2: Tumour tissue blocks/slides are stored, and patients are consented: Exploratory translational analyses will be performed on the collected archival tumour tissue. This will include but is not limited to **FRα, HER2, TROP-2, PD-L1 (including interplay of 22C3 and SP263) -these are potential drug targets for the future - but also molecular profiling (panel), histology**.

Date: 26-11-2024

NSGO-CTU-HERO

Characterization of High-Grade Ovarian Cancer Patients in Terms of Homologous Recombination Phenotype – A Prospective Observational Study

STUDY STATUS AND EXPECTED ENROLLMENT

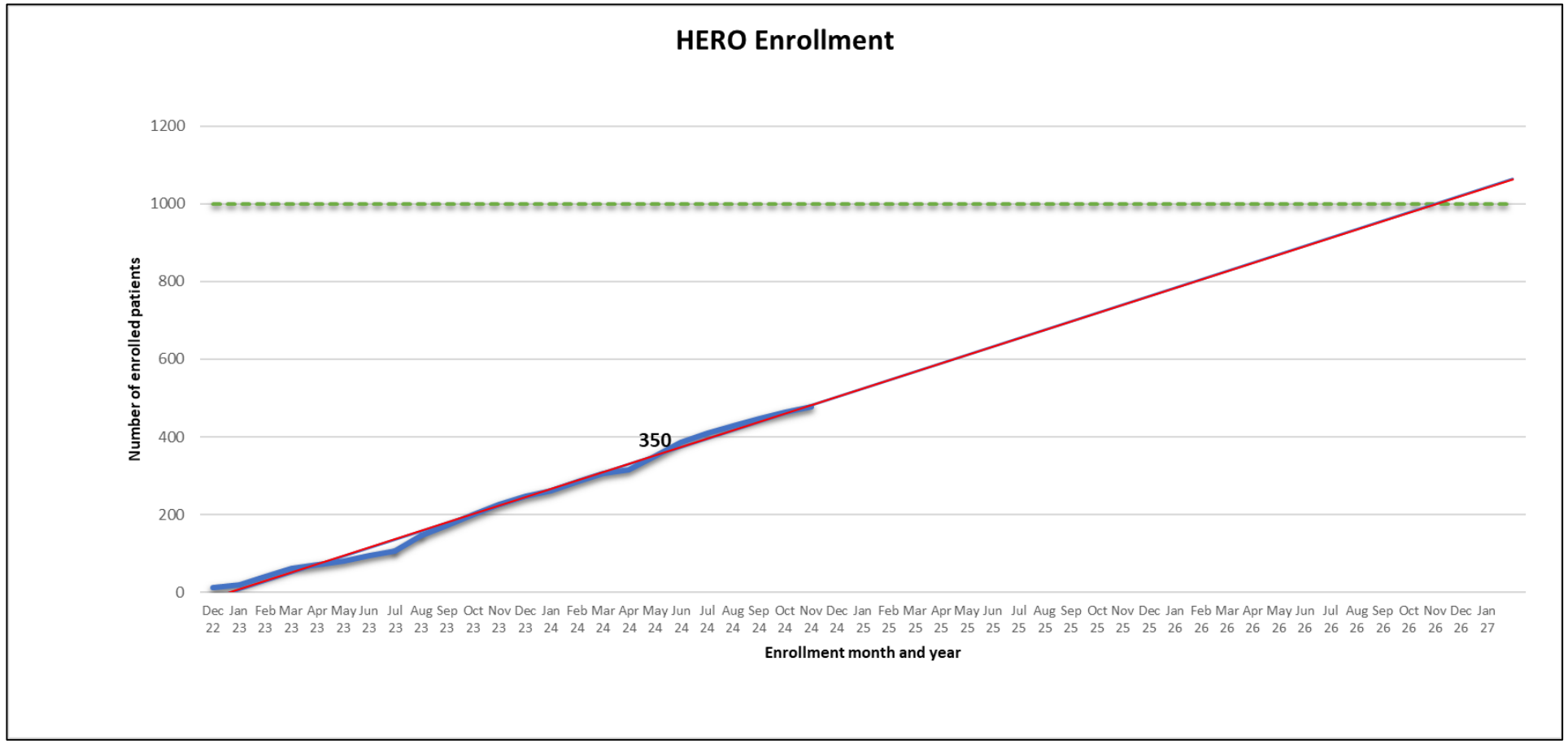
Country/Site	HERO	
	PI and NC	Inclusion
NORWAY		
Oslo	Elstrand	55
Kristiansand	Vistad	10
Tromsø	Ingebrigtsen	22
Trondheim	Aune	32
Stavanger	Nilsen	17
Bergen	Björke	0
TOTAL		**136**
SWEDEN		
Lund	Malander (NC)	88
Uppsala	Dimoula	7
Linköping	Lindahl	8
TOTAL		**103**
DENMARK		
Rigshospitalet	Mirza (NC)	73
Vejle	Adimi	39
Odense	Knudsen	18
Gødstrup	Hæe	6
TOTAL		**136**
FINLAND		
Kuopio	Sopo	19
Helsinki	Lassus (NC)	57
Oulu	Simojoki	7
Tampere	Staff	19
TOTAL		**102**
NSGO-CTU TOTAL		**477**

NSGO-CTU-HERO

Characterization of High-Grade Ovarian Cancer Patients in Terms of Homologous Recombination Phenotype – A Prospective Observational Study

STUDY STATUS AND EXPECTED ENROLLMENT

Last patient in expected in Q4 2026



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Thank You !

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