

ASGO Webinar #62  
First-Half 2025 Breakthroughs & Highlights  
Ovarian Cancer

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07/24/2025



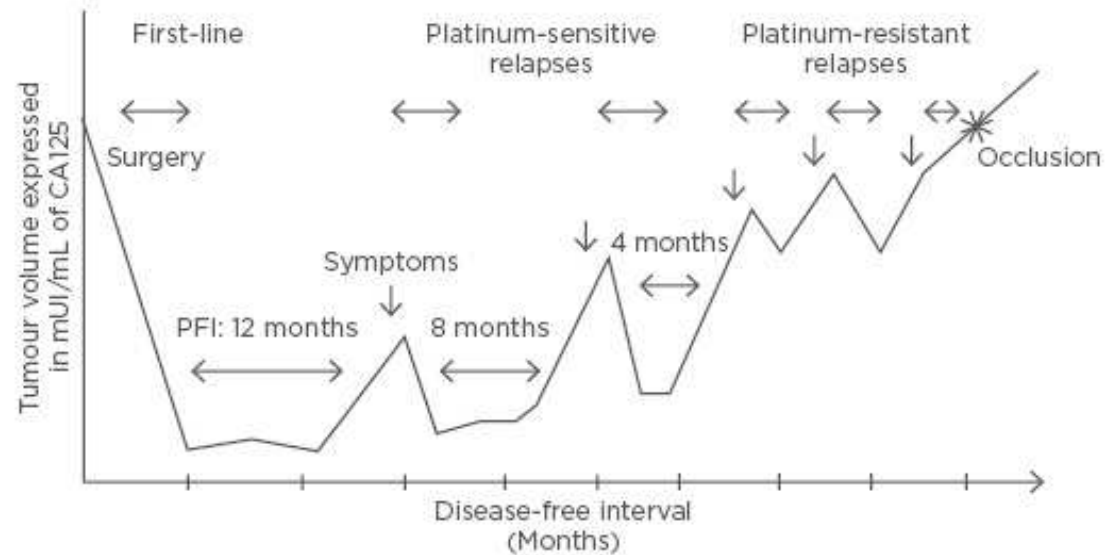
# Ovarian Cancer

- Over 70% Ovarian cancer are diagnosed with advanced stages
- Disease recurrence is typical
- >70% of patients with advanced OC will recur in 3-5 years
- When it recurs, it will eventually become platinum refractory recurrence

Maintenance therapy



Advanced ovarian cancer is characterized by multiple relapse



# Goals of Maintenance Therapy

- Prolong remission after successful initial treatment
- Extend treatment-free intervals, improve PFS1, hopefully OS
- Balance efficacy with tolerability with manageable toxicity
- Better QoL after surgery and chemotherapy



**BETTER SURVIVAL**



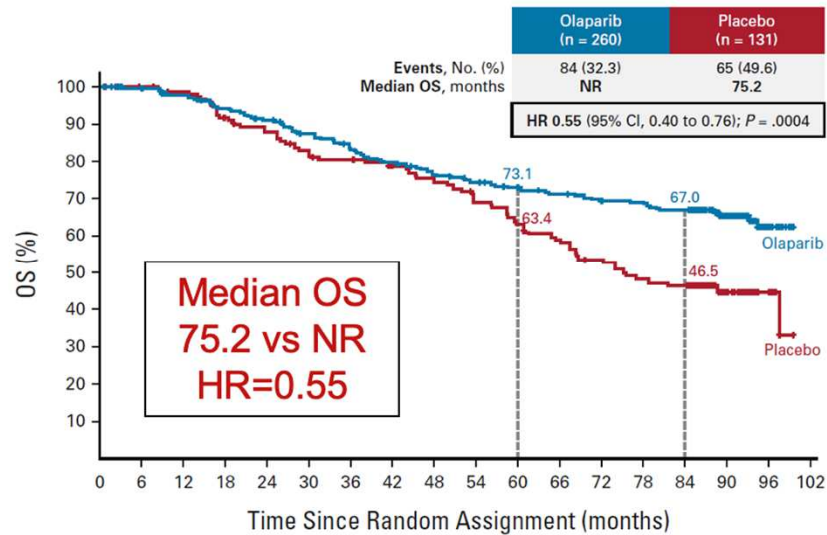
# RCTs of Maintenance Therapy

	PARPi monotherapy	PARPi+bevacizumab	PARPi+IO
BRCAm	SOLO-1(Olaparib) PRIMA(Niraparib) ATHENA-MONO(Rucaparib)	PAOLA-1 (Olaparib+bevacizumab)	ATHENA-COMBO (Rucaparib+nivolumab) FIRST (niraparib+dostarlimab)
BRCAct; HRD pos	PRIMA(Niraparib) ATHENA-MONO(Rucaparib)	PAOLA-1 (Olaparib+bevacizumab)	ATHENA-COMBO (Rucaparib+nivolumab) DUO-O (Olaparib+bev+durvalumab) FIRST (niraparib+dostarlimab) KEYLYNK-001 (Olaparib+Pembro+/-bev)
BRCAct; HRD neg	PRIMA(Niraparib) ATHENA-MONO(Rucaparib)	PAOLA-1 (Olaparib+bevacizumab)	ATHENA-COMBO DUO-O (Olaparib+bev+durvalumab) FIRST (niraparib+dostarlimab) KEYLYNK-001 (Olaparib+Pembro+/-bev)

# PARPi maintenance demonstrates long-term survival benefit in patients with BRCAm OC

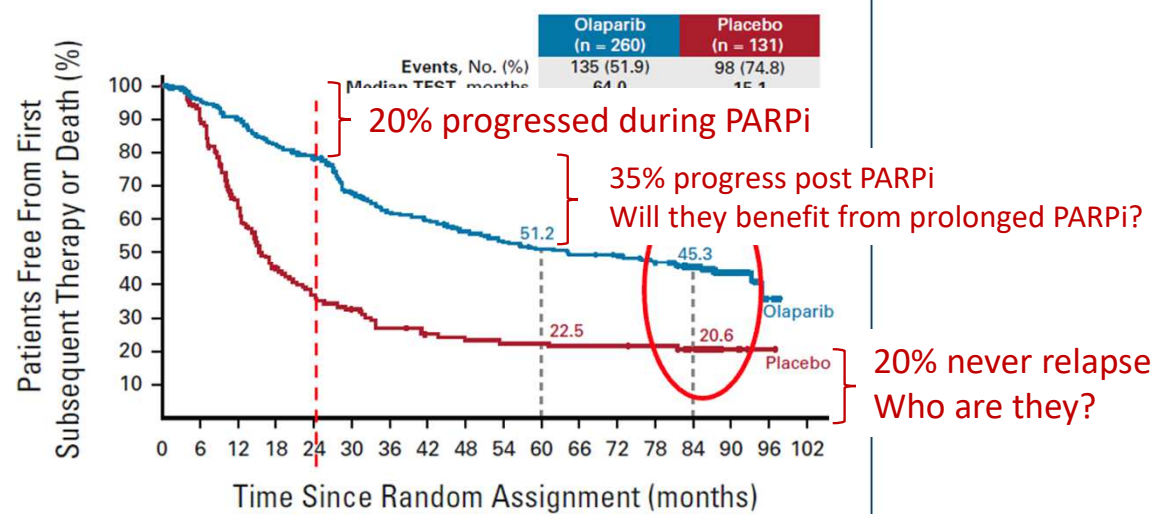
Time to First Subsequent Therapy  $\approx$  Long Term Survival

## Overall Survival



No. at risk:	0	6	12	18	24	30	36	42	48	54	60	66	72	78	84	90	96	102
Olaparib	260	252	246	236	227	214	203	194	185	177	170	165	159	157	153	79	21	0
Placebo	131	128	125	114	108	100	97	92	87	80	73	67	60	54	52	21	6	0

## Time to First Subsequent Therapy

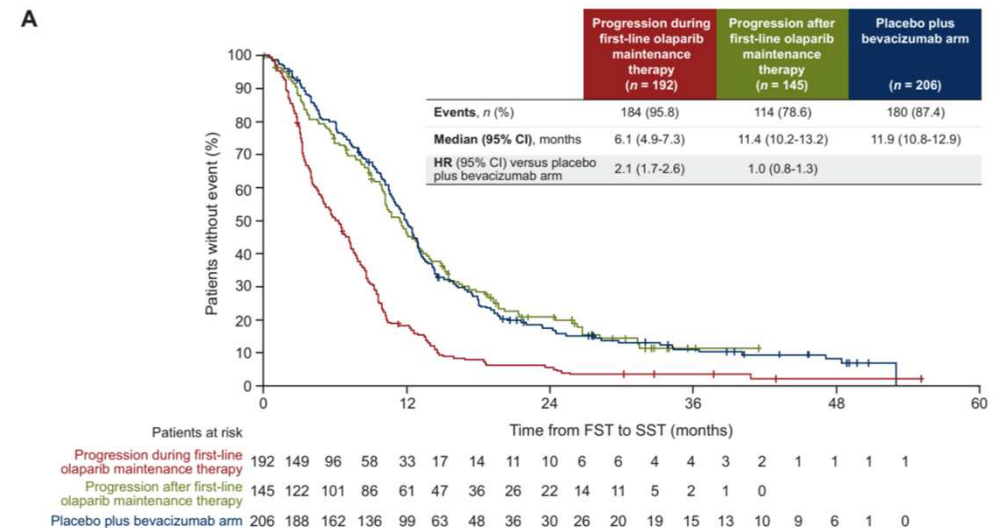
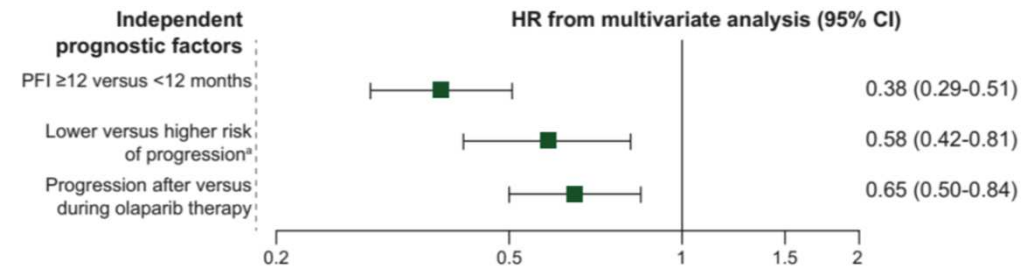


No. at risk:	0	6	12	18	24	30	36	42	48	54	60	66	72	78	84	90	96	102
Olaparib	260	240	223	203	190	160	147	141	132	125	119	115	111	102	75	31	5	0
Placebo	131	114	79	55	45	39	32	28	26	25	25	24	24	23	18	4	1	0

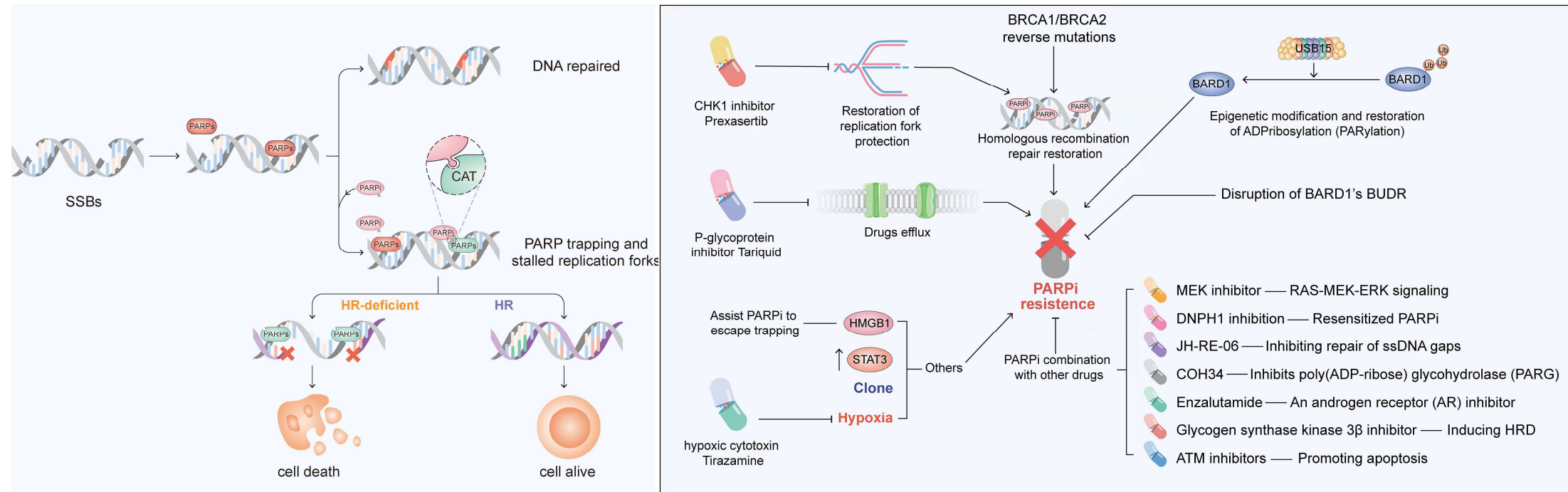
# PAOLA-1 post-hoc analysis

Is PARPi doing benefit in OS?

- Patients progressing during first-line olaparib maintenance had significantly shorter time to second progression after starting subsequent therapy.
- Progression timing was an independent prognostic factor
- Patients rechallenged with platinum chemo + PARP inhibitor as first subsequent therapy: progressing after maintenance is comparable to PARP-naïve patients (18.5 vs 17.4 months)



# PARPi resistance mechanism



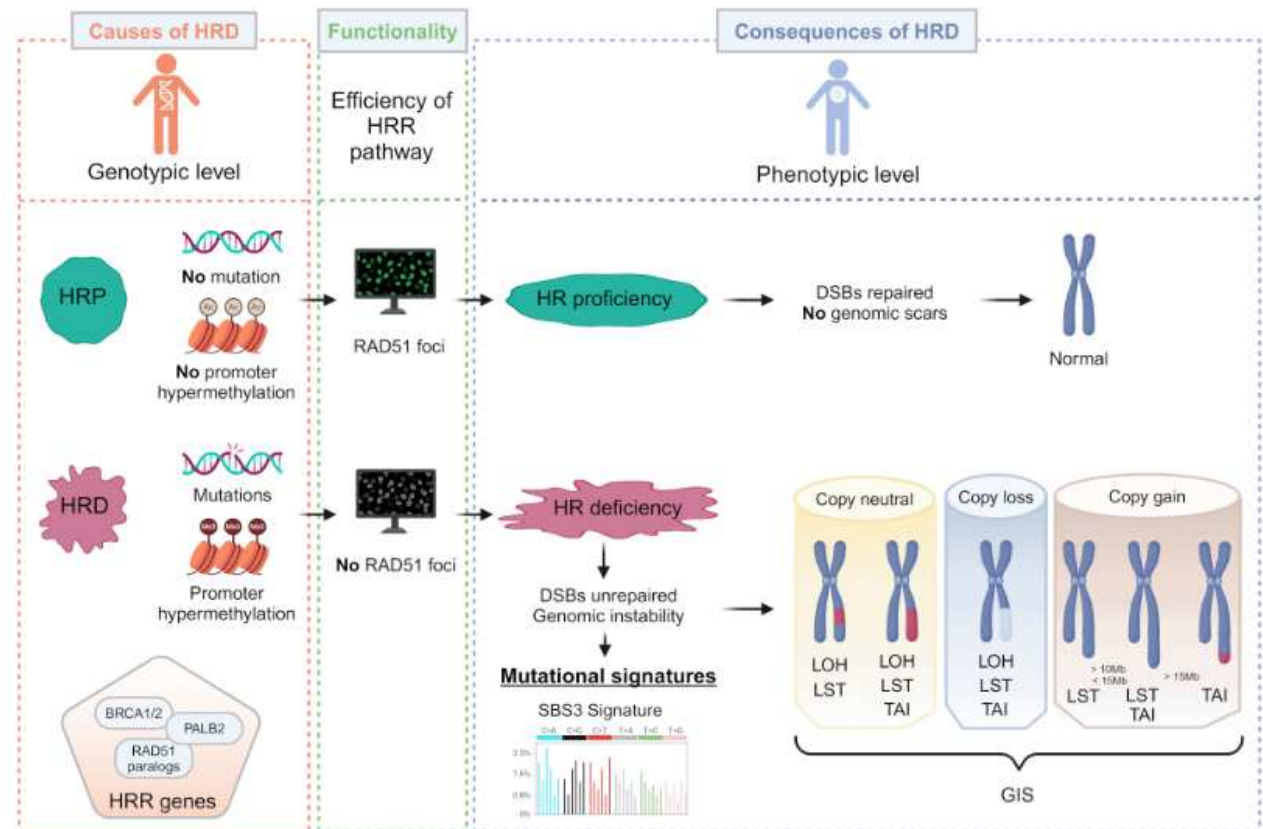
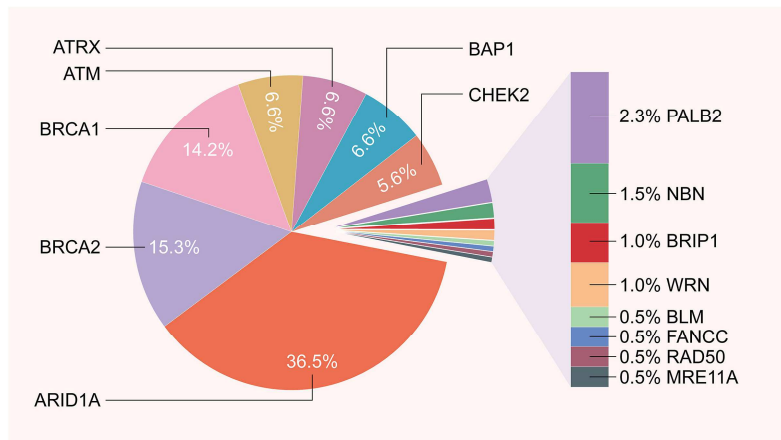
Relation with platinum resistance?

# Factors influencing sensitivity and resistance

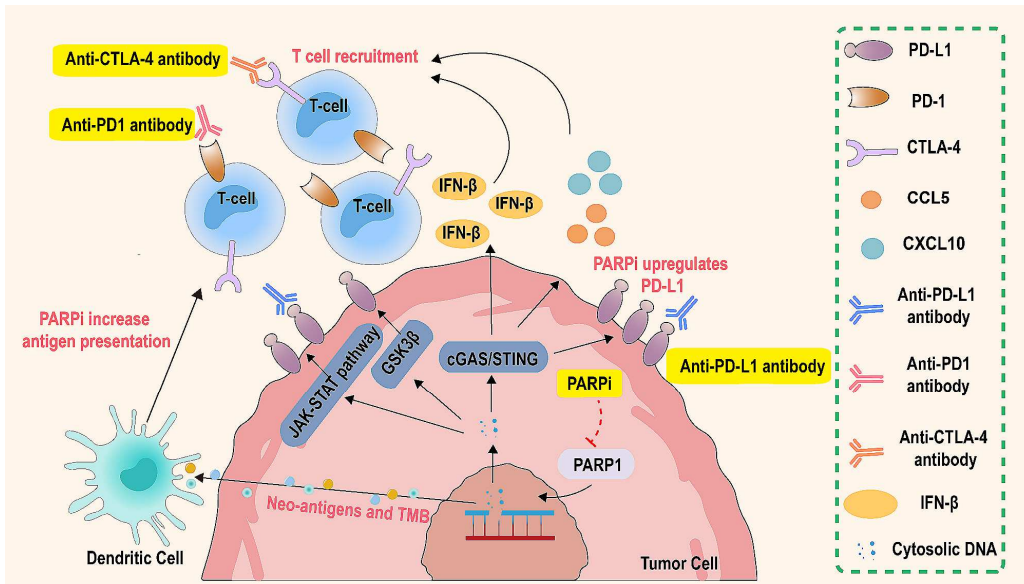
- **Mutation location:**
  - DNA binding domain (DBD) of BRCA1 and BRCA2 - significant benefit from PARPi
  - C-terminal BRCT domain of BRCA1 - less significant benefit
- **Reversion mutations:**
  - Common mechanism of acquired resistance
- **PARP1 alterations:**
  - Reduced PARP1 trapping
- **Replication fork protection:**
  - The restoration of replication fork stability protects DNA from damage during replication stress caused by PARP inhibitors.
- **Drug efflux:**
  - Eg. P-glycoprotein (MDR1), can decrease the intracellular concentration of PARPi

# HRD(Homologous Recombination Deficiency)

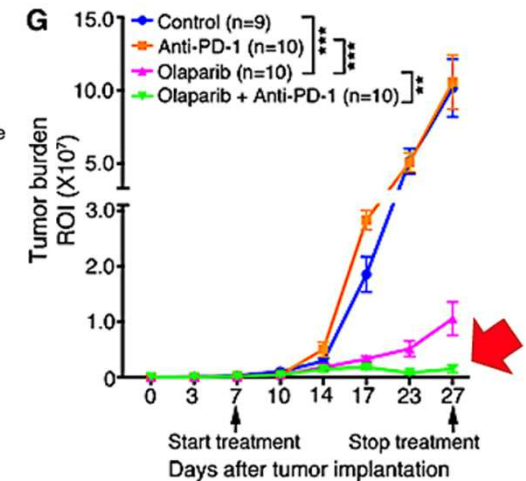
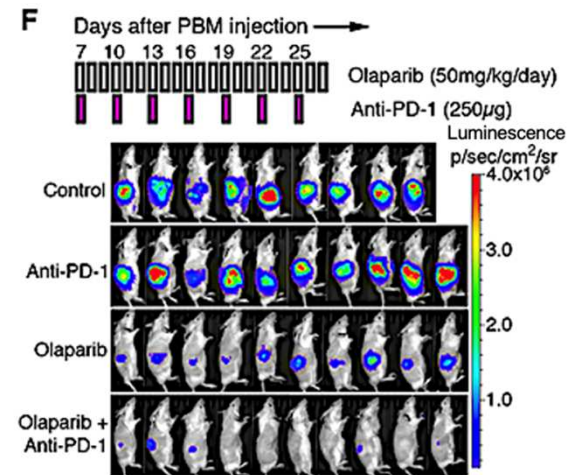
- HRD clinical detection relies on surrogate markers. (Gene scars: LOH, LST, TAI)
- HRD status can vary between tumor regions (spatial) and over time (temporal).
- PARPi efficacy correlates better with functional HRD than scars alone.



# PARPi + immunotherapy



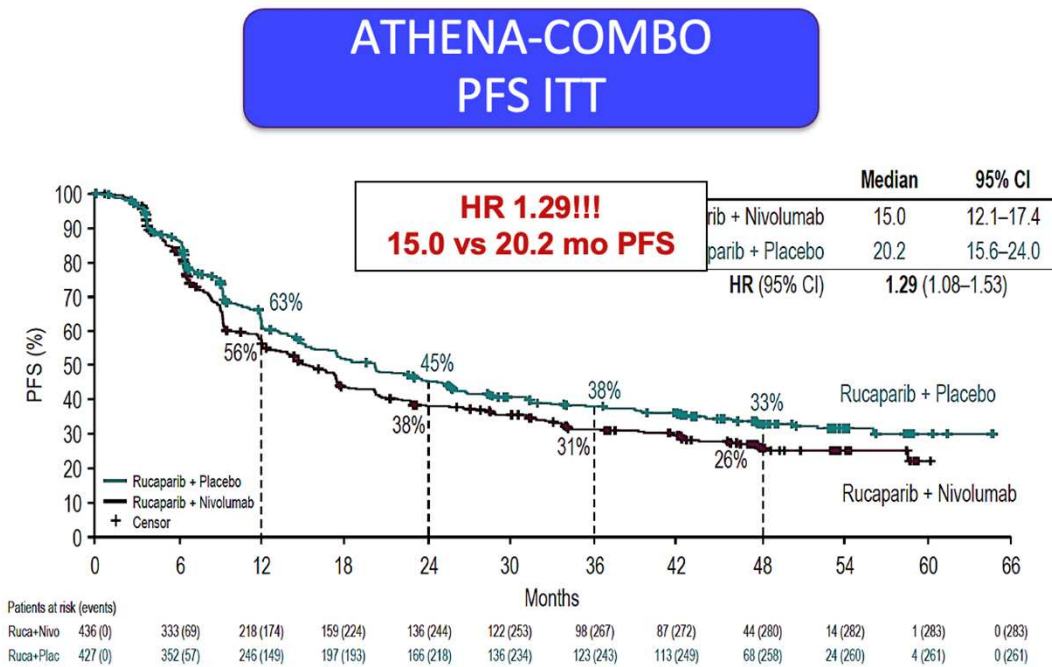
Xiao F et al, J Trans Res. 2024



Ding L et al., Cell Rep. 2018

- PARP inhibitors enhance tumor immunogenicity and the presentation of neoantigens in the tumor microenvironment (TME) by increasing antigen presentation and upregulating PD-L1 expression.
- The combination promotes the secretion of IFN- $\beta$  through the JAK-STAT and GSK3 $\beta$  pathways, further enhancing the immune system's attack on tumor cells

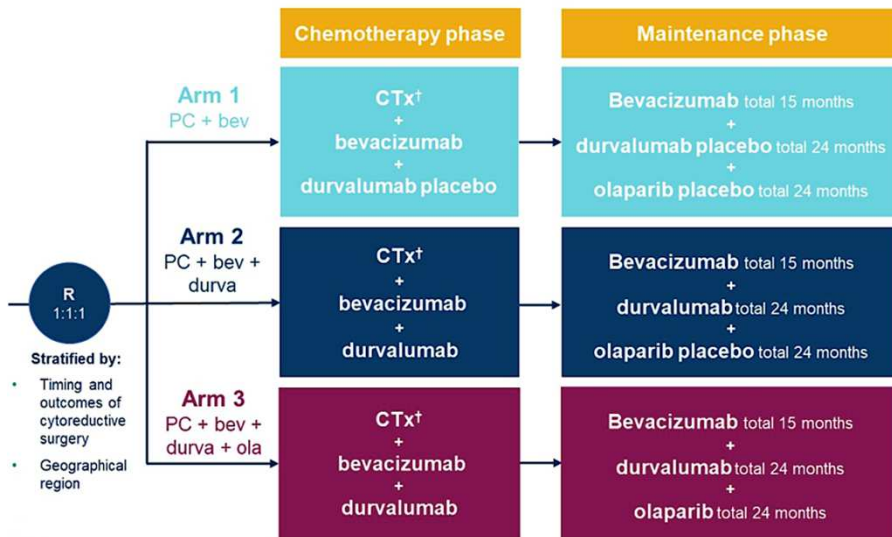
# ATHENA-COMBO: Rucaparib+nivolumab



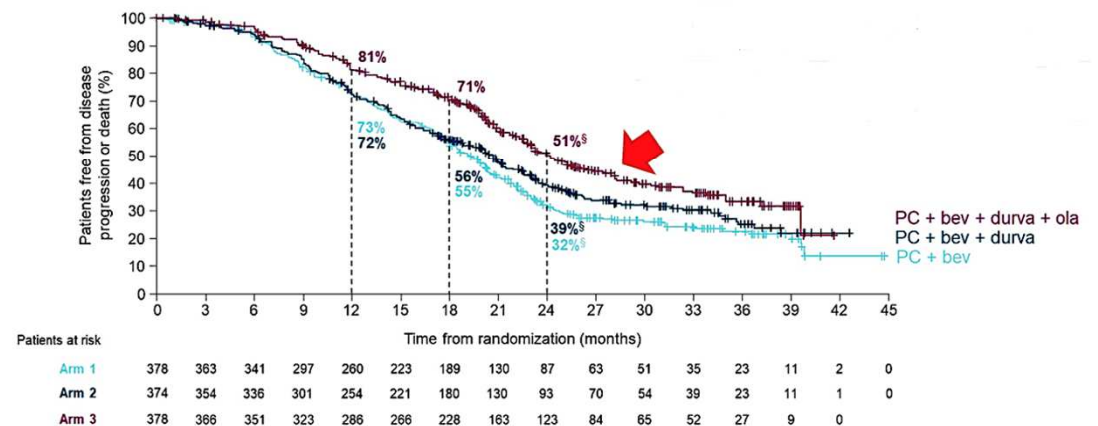
	Rucaparib/ Nivolumab (N=410)	Rucaparib/ Placebo (N=448)
Oral drug interruption and/or dose reduction for TEAE	321 (78.3)	283 (63.2)
Oral drug d/c for TEAE	104 (25.4)	66 (14.7)
IV drug d/c for TEAE	145 (35.4)	43 (9.6)
Oral and IV drug d/c for TEAE	63 (15.4)	19 (4.2)

# DUO-O: Olaparib+durvalumab+bevacizumab

Interim OS is not significant.

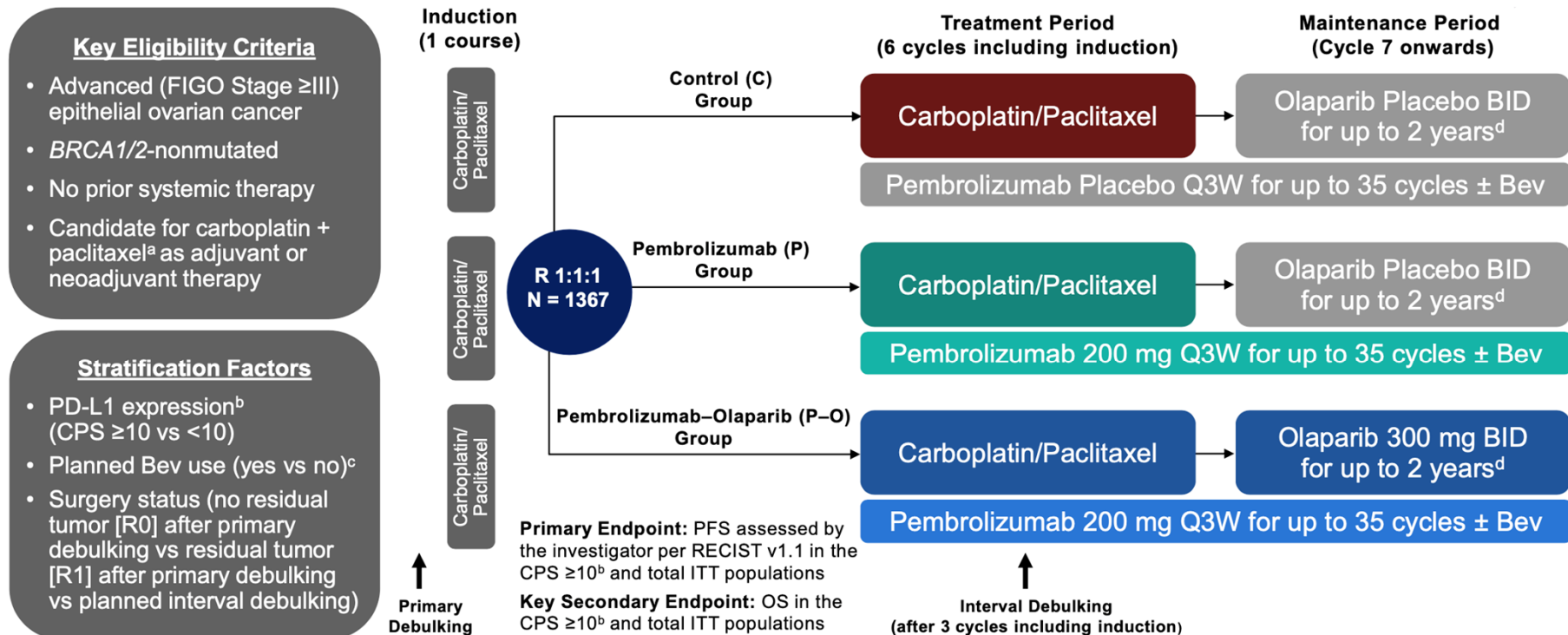


	Arm 1 PC + bev N=378	Arm 2 PC + bev + durva N=374	Arm 3 PC + bev + durva + ola N=378
<b>Median follow-up,* months</b>	25.5	23.1	23.3
<b>Events, n (%)</b>	259 (69)	226 (60)	193 (51)
<b>Median PFS,† months</b>	19.3	20.6	24.2
<b>HR (95% CI) vs Arm 1</b>		<b>0.87</b> (0.73–1.04)† P=0.13	<b>0.63</b> (0.52–0.76)† P<0.0001
			<b>HR 0.63</b>



But, the control arm does not include a PARP inhibitor – we do not know if it is benefit from Olaparib.

# KEYLYNK-001: Olaparib+Pembro

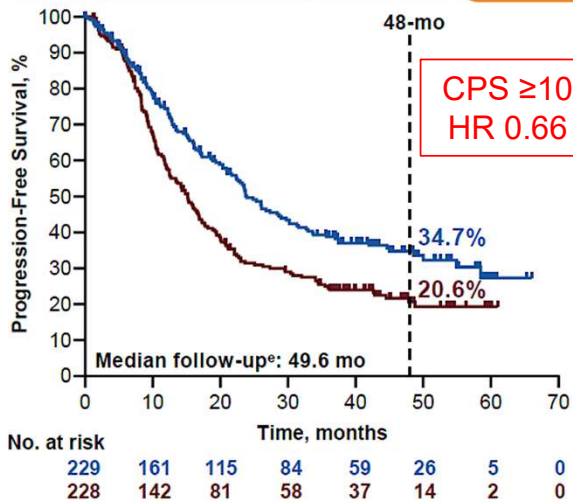


<sup>a</sup>Docetaxel may be considered for participants who experience either a severe hypersensitivity reaction to paclitaxel or an adverse event requiring discontinuation of paclitaxel. <sup>b</sup>Assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx and measured using the combined positive score (CPS; number of PD-L1-positive tumor cells, lymphocytes, and macrophages divided by total number of tumor cells x 100). <sup>c</sup>Bevacizumab (Bev) administered per investigator discretion as part of upfront therapy according to local standard of care; Bev was supplied by the Sponsor. <sup>d</sup>Only participants with no evidence of disease at start of maintenance and no progression stopped after 2 years.

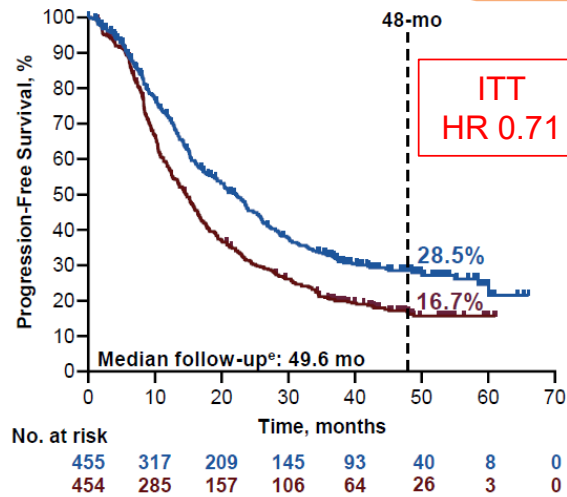
we still do not have the control arms of olaparib

# KEYLYNK-001: Olaparib+Pembro

FA (Aug 2024) <sup>b</sup>	Median, months	Events	HR (95% CI)
P-O Group	23.9	58.5%	0.66 <sup>c</sup> (0.53-0.83)
C Group	15.2	72.4%	



FA (Aug 2024) <sup>b</sup>	Median, months	Events	HR (95% CI)
P-O Group	22.2	64.0%	0.71 <sup>c</sup> (0.61-0.84)
C Group	14.6	77.5%	

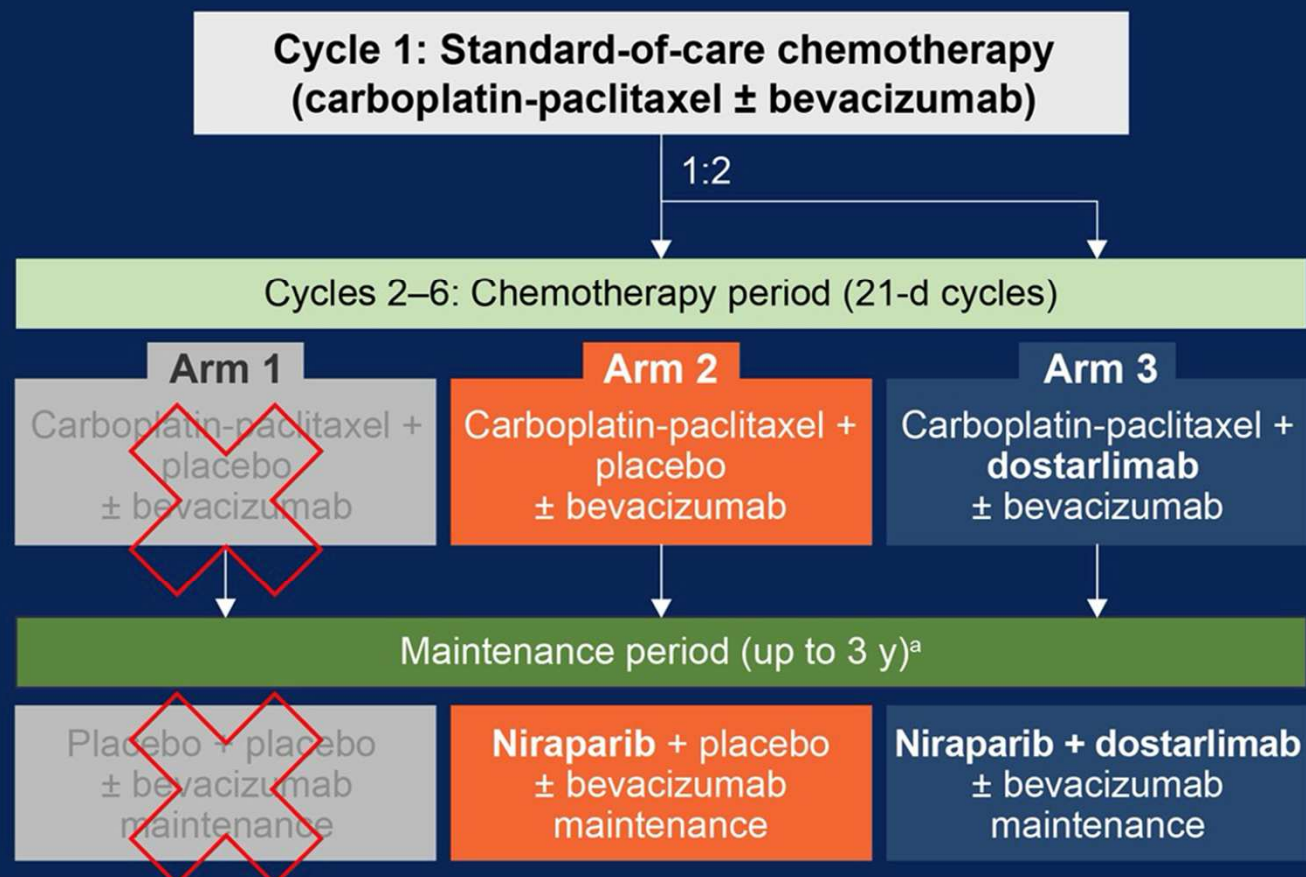


Overall Survival	P-O Group	C Group
<b>CPS ≥ 10 Population</b>		
Median, mo	50.2	51.6
HR (95% CI)	0.98 (0.75-1.27)	
<b>Total ITT Population</b>		
Median, mo	47.7	47.1
HR (95% CI)	1.04 (0.87-1.25)	

We still do not have the control arms of PARPi

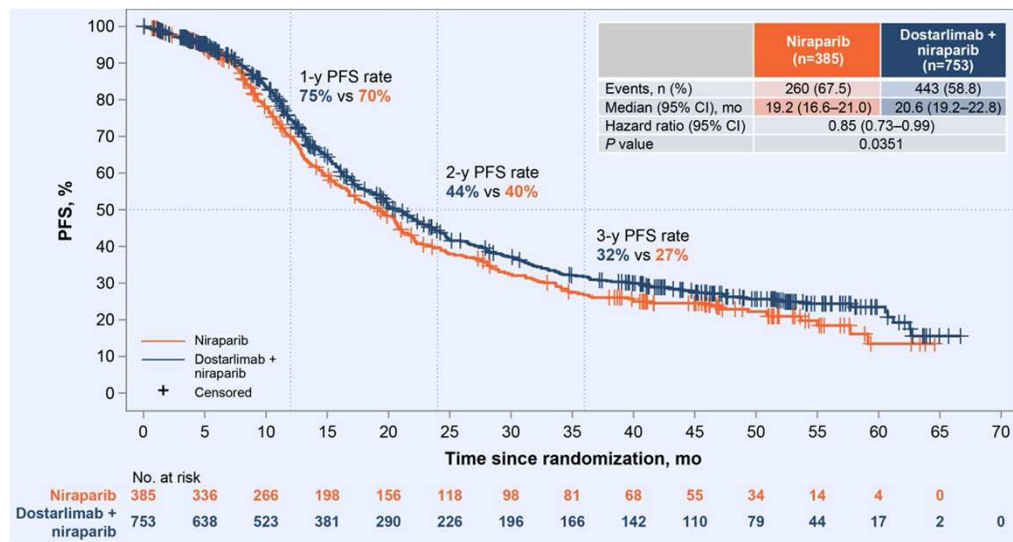
# FIRST: Niraparib + dostarlimab

- Given ongoing PARPi maintenance clinical trials during the design of FIRST, it was an *a priori* intention to amend the protocol to redefine the control arm if emerging evidence supported the incorporation of PARPis during the maintenance period
- Following approvals of olaparib and niraparib as first-line maintenance therapy,<sup>1,2</sup> enrollment into arm 1 was terminated

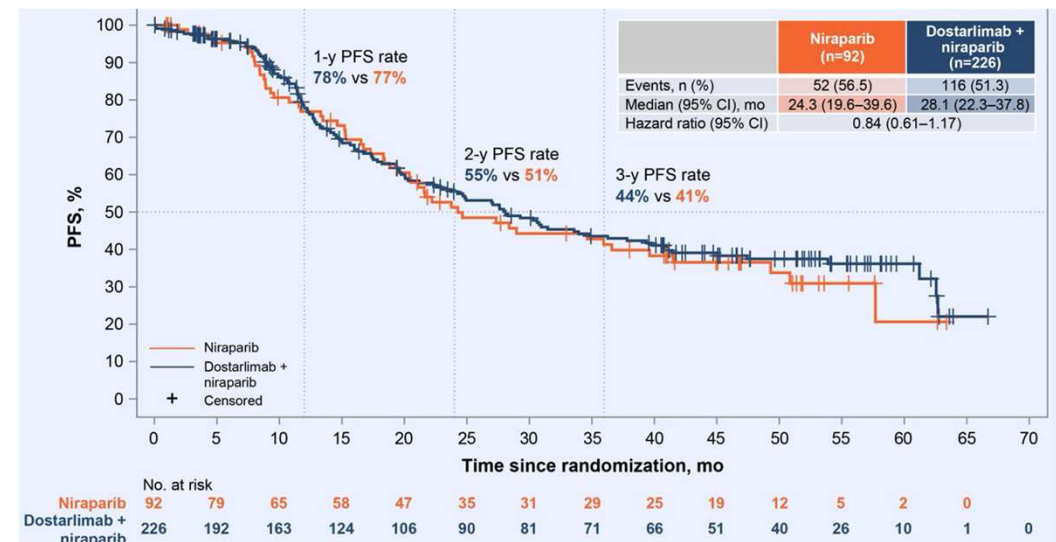


# FIRST: Niraparib + dostarlimab

PFS in ITT population



PFS in PD-L1 population

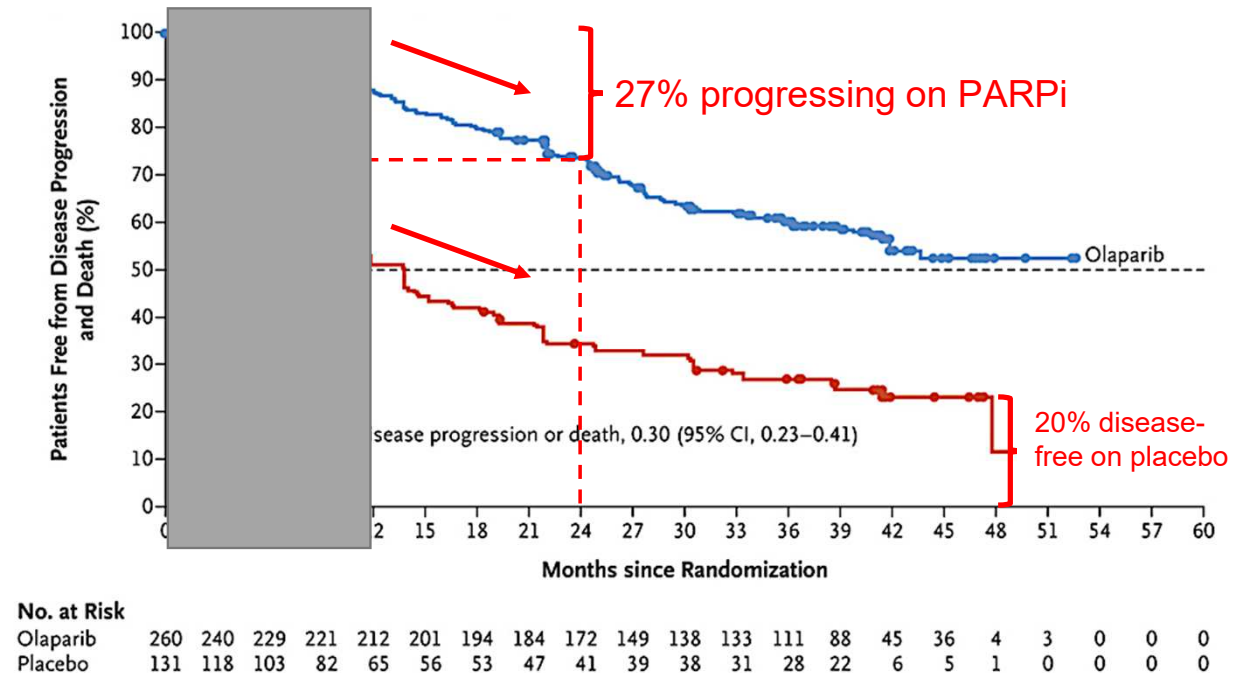


- The addition of dostarlimab to first-line platinum-based chemotherapy and maintenance niraparib was associated with a statistically significant, though clinically modest, improved PFS for patients with newly diagnosed aOC.
- PD-L1 positivity (TAP  $\geq 5\%$ ) did not differentiate dostarlimab effect.
- There was no observed difference in OS.
- Safety results were consistent with known individual profiles of the agents used in the study.
- There were no meaningful differences in patient-reported outcomes of the EQ VAS or the EORTC-QLQ-C30.

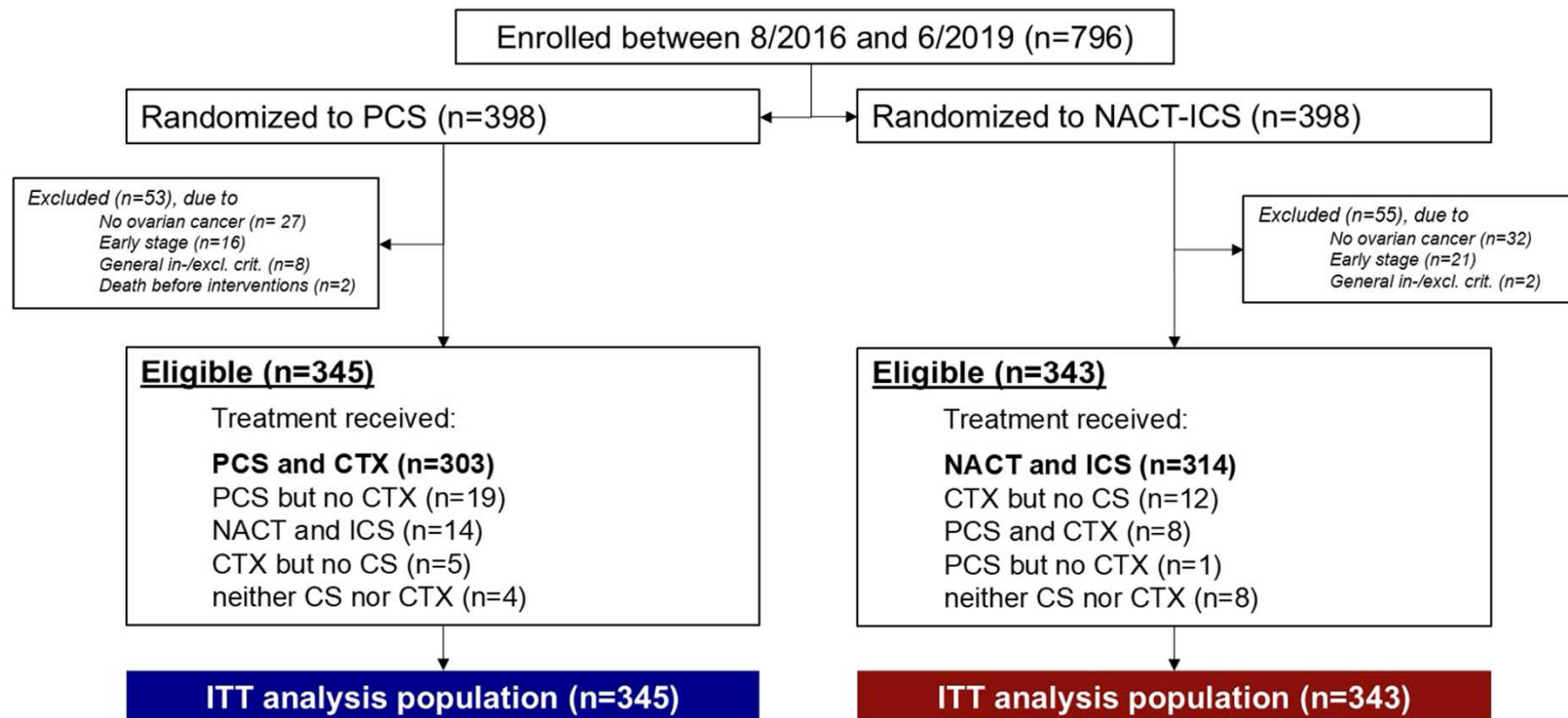


# What's still ahead?

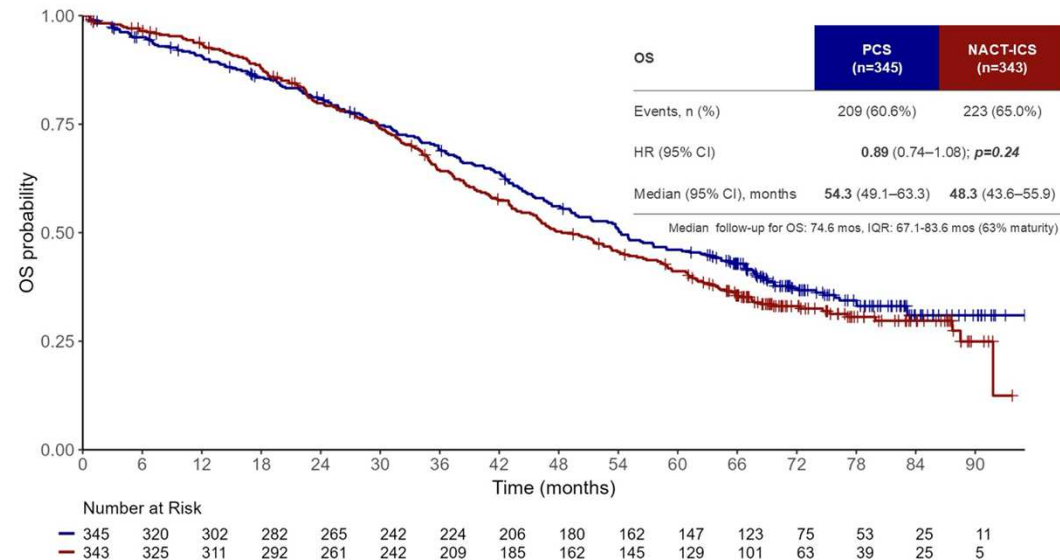
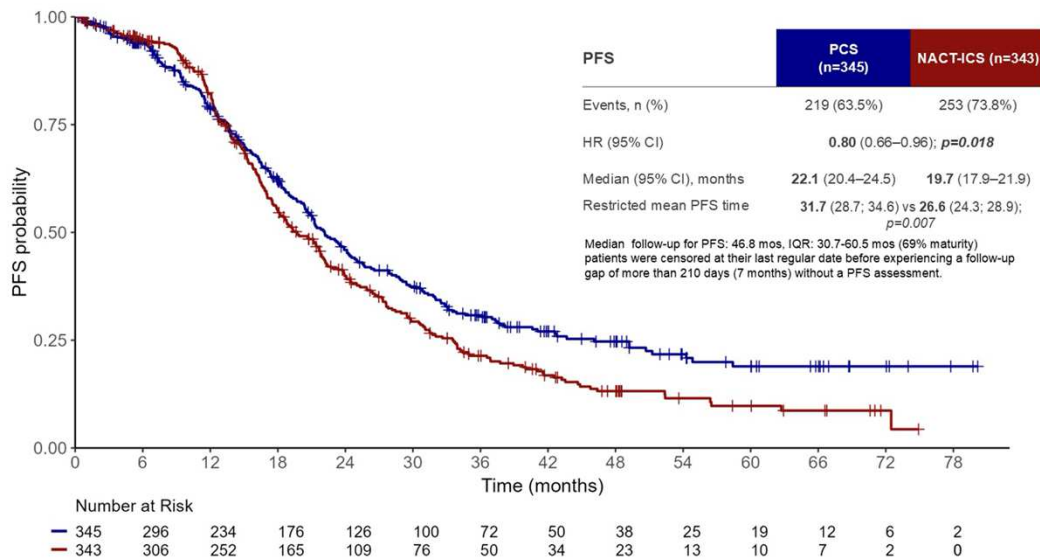
- Stratification
  - Risk for progression with PARPi
  - Exceptional prognosis
- Optimal duration of therapy
  - NRG-GY036: One vs. two years of maintenance olaparib
- Patient with HRP tumors
  - ADC?
- Ultra radical surgery
  - Diaphragm LN dissection?



# TRUST: Radical upfront surgery vs NACT+ICS

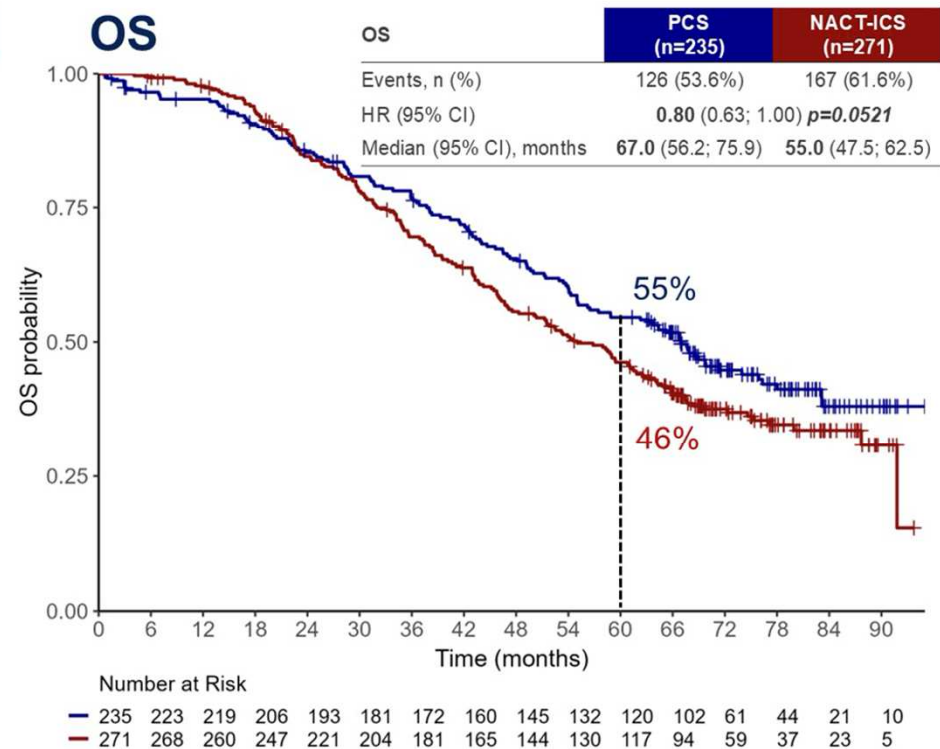
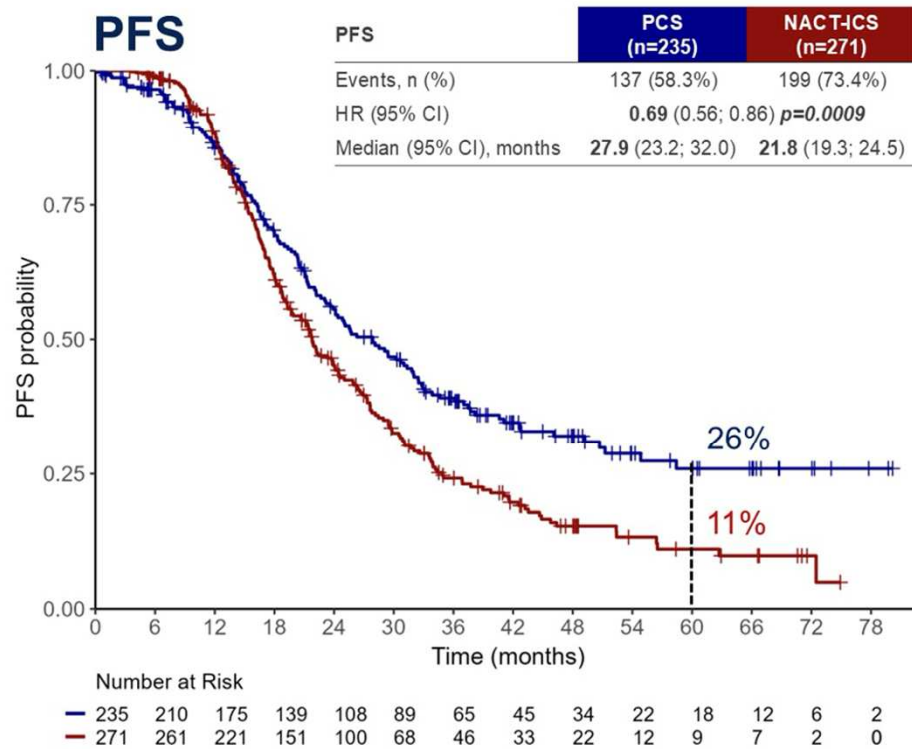


# TRUST: Radical upfront surgery vs NACT+IDS



# TRUST: Radical upfront surgery vs NACT+IDS

## TRUST Results: Prespecified Exploratory Subgroup Analysis **Complete Gross Resection in All FIGO Stages**



# TRUST: Radical upfront surgery vs NACT+IDS

**Patients with advanced ovarian cancer in TRUST had excellent PFS and OS after maximal effort cytoreductive surgery. Complete resection rates were high and morbidity and mortality were low.**

**A statistically significant OS improvement for primary compared to interval cytoreductive surgery was not observed.**

**TRUST is the first randomized phase III trial to show improved median PFS for primary compared to interval cytoreductive surgery without compromising short- or long-term quality of life.**

Thank you!

The poster features a dark blue background on the left side with white and colorful text. On the right, there is a photograph of a cityscape, likely Shanghai, with a prominent tower and a river. A large, stylized blue graphic element, resembling a ribbon or a wave, curves across the bottom and right side of the poster.

**ASGO** 2026

Annual Meeting of  
Asian Society of  
Gynecologic Oncology

December 4-6, 2026  
Shanghai International Convention Center  
Shanghai, China

ASGO