WAGO

Western Association of Gynecologic Oncology

ASCO Annual Meeting 2025
Ovarian Cancer

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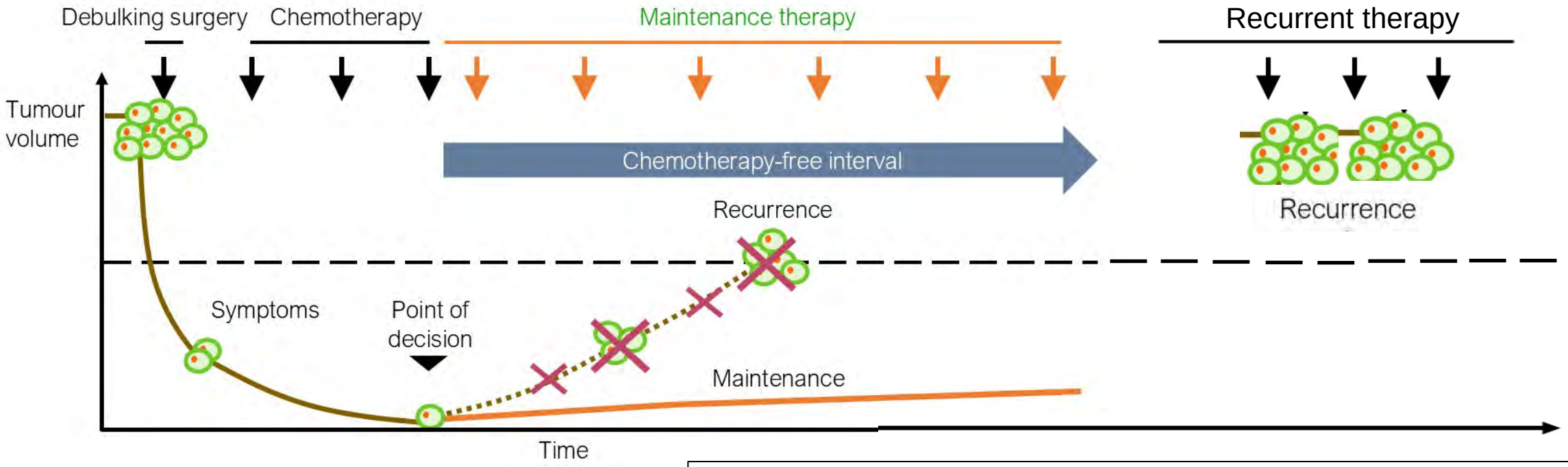
Clinical Presentation: Timing of Surgery, Maintenance, Resistant Treatment

TRUST (Trial of Radical Upfront Surgical Therapy) ENGOT ov3/AGO-OVAR

OVATION-2 Trial: Phase I/II IP IMNN-001 with NACT

FIRST: Dostarlimab and Niraparib in First-Line Advanced



ROSELLA/GOG 3073: Ph3 Relacorilant + Nab-Pac vs Nab-Pac

Phase 2 Pembro and Lenvatinib in recurrent/persistent OCCC

Phase 1 of INCB123667: CDK2 inhibitor in PROC refractory OC

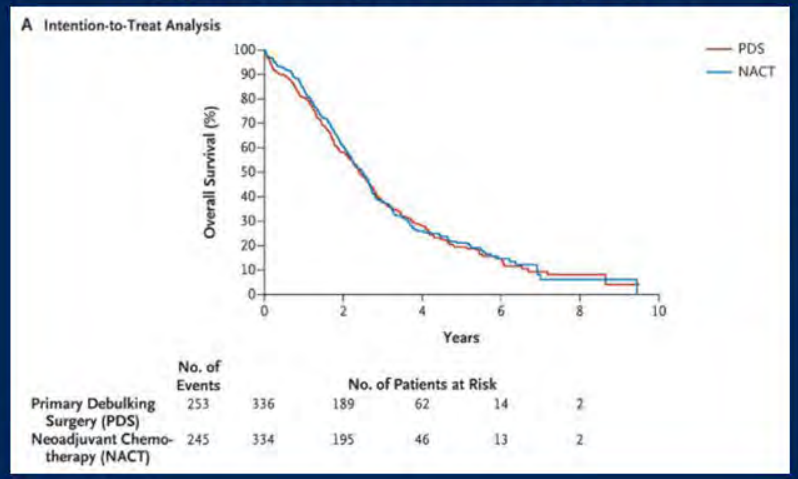
Summary of ASCO Annual Meeting 2025 Ovarian Cancer Plenary

- TRUST (Trial of Radical Upfront Surgical Therapy) ENGOT ov3/AGO-OVAR
  - Primary endpoint – OS. OS improvement was not seen. First Ph3 RCT to show improved median PFS for PDS compared to ICS particularly in Stage III
- OVATION-2 Trial: Phase I/II IP NACT +/- IMNN-001 (IL-12 gene lipopolymer nanoparticle)
  - Primary Endpoint: Safety and PFS. Increased activity in HRD patients. Confirmatory Ph3 underway
- FIRST: Carbo/pac +/- Dostarlimab +/- Bev followed by maintenance niraparib +/- dostarlimab in first-line
  - Primary Endpoint PFS in the ITT. Dostarlimab + maintenance niraparib was statistically significant though clinically modest
- ROSELLA/GOG 3073: Phase III Nab-Pac +/- Relacorilant
  - Primary Endpoint PFS and OS. Met PFS endpoint. Interim OS showed clinically meaningful 16 vs. 11.5 months
- Phase 2 Pembro and Lenvatinib in recurrent/persistent OCCC
  - Primary Endpoint of ORR (25%) and PFS at 6 months (30%). Met ORR with 37% and 56% are PFS at 6 months
- Phase 1 of INCB123667: CDK2 inhibitor in PROC refractory OC
  - Primary Endpoint: Safety. Secondary ORR. Safe with most common TEAEs hematologic and GI grade $\leq$ 2. ORR of 33%

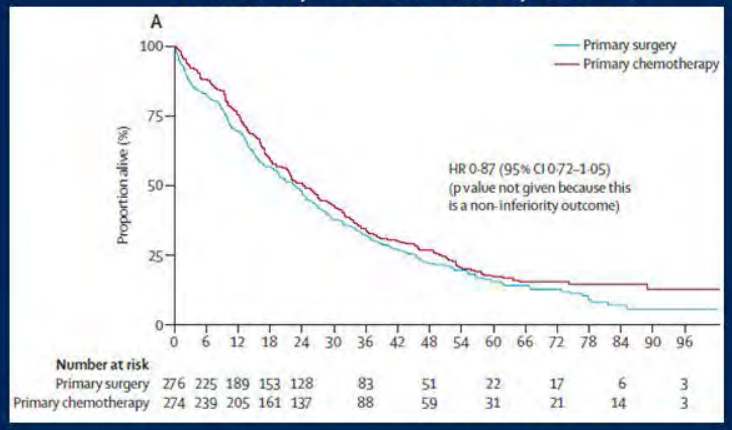
PDS versus NACT for Stage III/IV Ovarian Cancer

- Primary debulking surgery traditional preferred treatment strategy
- 4 prior RCTs

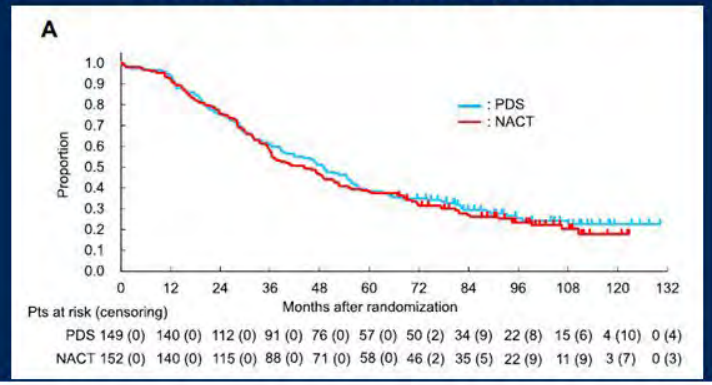
Vergote, EORTC 55971, 2010



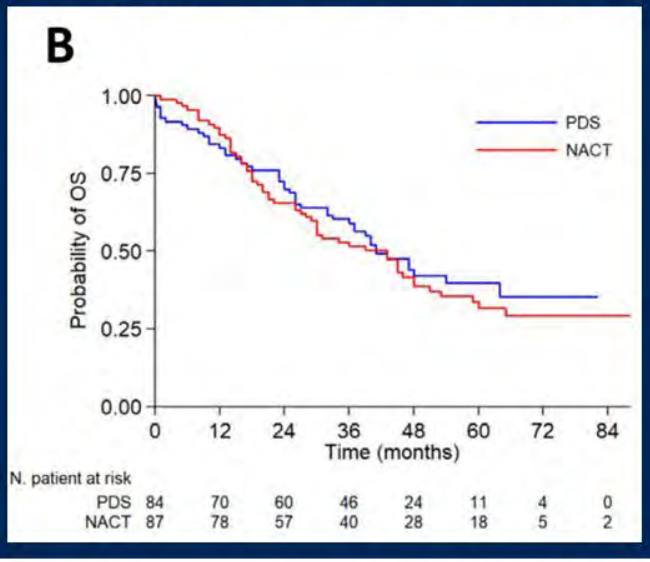
Kehoe, CHORUS, 2015



Onda, JGOG0602, 2020



Fagotti, SCORPION, 2020



TRUST Study Design

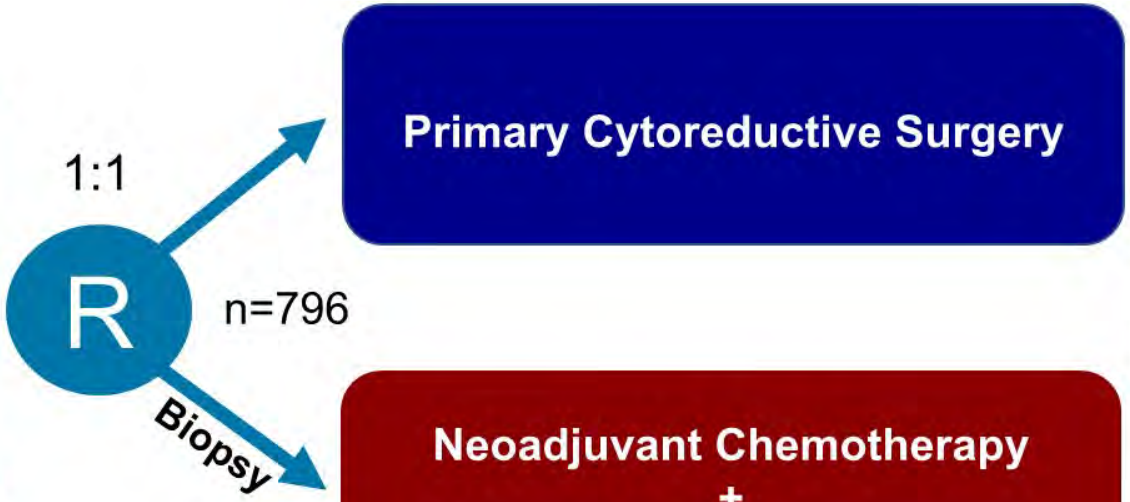
Main Inclusion Criteria

- Epithelial ovarian, fallopian tube or peritoneal cancer
  - FIGO stage IIIB/C, IVA/B
  - Considered resectable
- Fit enough to tolerate radical surgery

Stratification factors

- Center
- Age-ECOG-combination
  ECOG0 and age ≤65y vs.
  ECOG>0 or age >65y

Qualification process for participating centers to ensure surgical quality



Recommended systemic treatment:

- Carboplatin AUC5, Paclitaxel 175mg/m² q3w
- Bevacizumab 15mg/kg q3w as indicated
- PARPi as indicated
- Study participation or any other treatment as long as applicable for both study arms

Primary endpoint

- Overall survival

Key secondary endpoints

- Progression-free survival
- Complete resection rate
- Surgical procedures
- Surgical morbidity
- Quality of life

Predefined exploratory and translational endpoints

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TRUST Baseline Characteristics

	PCS (n=345)	NACT-ICS (n=343)	Total (n=688)
Median age, years (range)	**63** (34-83)	**64** (32-83)	**63.5** (32-83)
Median BMI, kg/m^2 (range)	**24.6** (15.6-50.1)	**24.9** (15.9-47.2)	**24.8** (15.6-50.1)
ECOG, n (%)			
0	267 **(77%)**	263 **(77%)**	530 **(77%)**
1	78 **(23%)**	80 **(23%)**	158 **(23%)**
Confirmed FIGO stage (highest), n (%)			
IIIB	30 **(8.7%)**	18 **(5.3%)**	48 **(7.0%)**
IIIC	203 **(59%)**	217 **(63%)**	420 **(61%)**
IVA	31 **(9.0%)**	35 **(10%)**	66 **(9.6%)**
IVB	79 **(23%)**	68 **(20%)**	147 **(21%)**
Not reported	2 **(0.6%)**	5 **(1.5%)**	7 **(1.0%)**
Histological subtype, n (%)			
High grade serous	320 **(93%)**	312 **(91%)**	632 **(92%)**
Low grade serous	18 **(5.2%)**	23 **(6.7%)**	41 **(6.0%)**
Other*	4 **(1.2%)**	4 **(1.2%)**	8 **(1.2%)**
Not reported	3 **(0.9%)**	4 **(1.2%)**	7 **(1.0%)**

*Other: PCS: 3 endometrioid, 1 seromucinous; NACT-ICS: 2 clearcell, 1 seromucinous, 1 mucinous,

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TRUST Results: Surgical Effort and Procedures

Procedure, n* (%)	PCS (n=331)	NACT-ICS (n=328)
Median duration of surgery, minutes (IQR)	**331** (253-432)	**284** (213-360)
Median blood loss, mL (IQR)	**500** (300-800)	**400** (200-600)
Mean number of RBC units transfused (SD)	**0.9** (1.5)	**0.6** (1.1)
Upper abdominal procedures	263 **(79%)**	221 **(67%)**
Splenectomy	91 **(27%)**	42 **(13%)**
Intestinal resections	224 **(68%)**	123 **(38%)**
Colorectal resection	187 **(56%)**	95 **(29%)**
Large bowel resection	135 **(41%)**	74 **(23%)**
Small bowel resection	70 **(21%)**	33 **(10%)**
Stoma formation	66 **(20%)**	27 **(8.2%)**
Lymph node dissection	197 **(60%)**	156 **(48%)**
Pelvic nodes	166 **(50%)**	135 **(41%)**
Paraaortic nodes	172 **(52%)**	134 **(41%)**
Chest procedures	63 **(19%)**	35 **(11%)**
Pericardiophrenic nodes	33 **(10%)**	15 **(4.6%)**
Open assessment of the pleura	47 **(14%)**	23 **(7.0%)**
Pleurectomy	15 **(4.5%)**	5 **(1.5%)**

* patients with documented debulking surgery; analyzed as treated;

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TRUST Results: Surgical Outcome

	PCS (n=345)	NACT-ICS (n=343)	Total (n=688)
Residual disease, n (%)			
complete gross resection	235 **(68%)**	271 **(79%)**	506 **(74%)**
macroscopic residual disease	99 **(29%)**	49 **(14%)**	148 **(22%)**
0.1-0.5 cm	*39 **(11%)***	*29 **(8.5%)***	*68 **(9.9%)***
0.6-1 cm	*25 **(7.3%)***	*7 **(2.0%)***	*32 **(4.7%)***
> 1 cm	*35 **(10%)***	*13 **(3.8%)***	*48 **(7.0%)***
not operated / not reported	11 **(3.2%)**	23 **(6.7%)**	34 **(4.9%)**
Documented complete resections in operated patients, n (%)	235/334 **(70%)**	271/320 **(85%)**	506/654 **(77%)**

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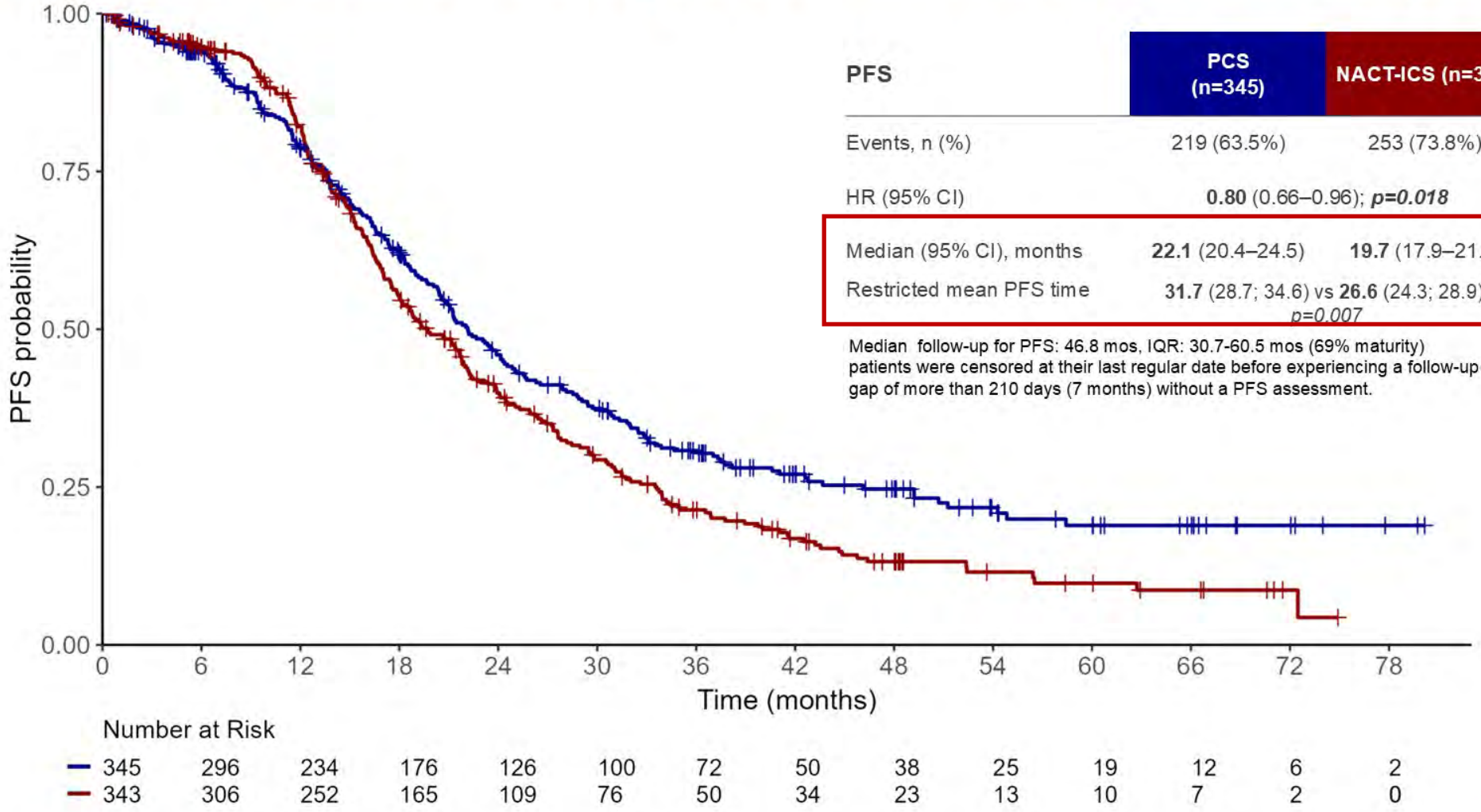
TRUST Results: Progression-free Survival (ITT)



PFS	PCS (n=345)	NACT-ICS (n=343)
Events, n (%)	219 (63.5%)	253 (73.8%)
HR (95% CI)	**0.80** (0.66–0.96); ***p=0.018***	
Median (95% CI), months	**22.1** (20.4–24.5)	**19.7** (17.9–21.9)
Restricted mean PFS time	**31.7** (28.7; 34.6) vs **26.6** (24.3; 28.9); *p=0.007*	

Median follow-up for PFS: 46.8 mos, IQR: 30.7-60.5 mos (69% maturity)
patients were censored at their last regular date before experiencing a follow-up gap of more than 210 days (7 months) without a PFS assessment.

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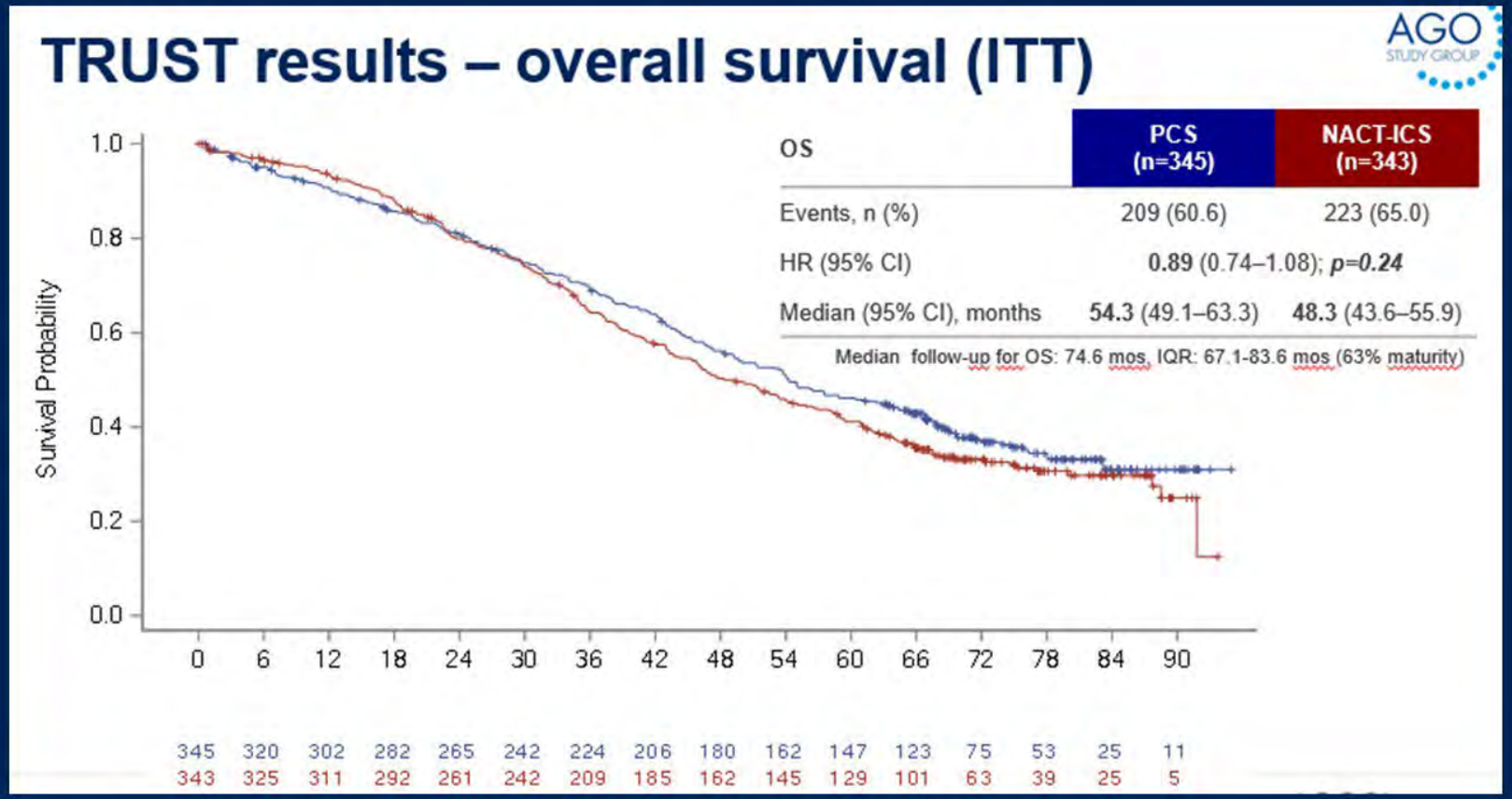
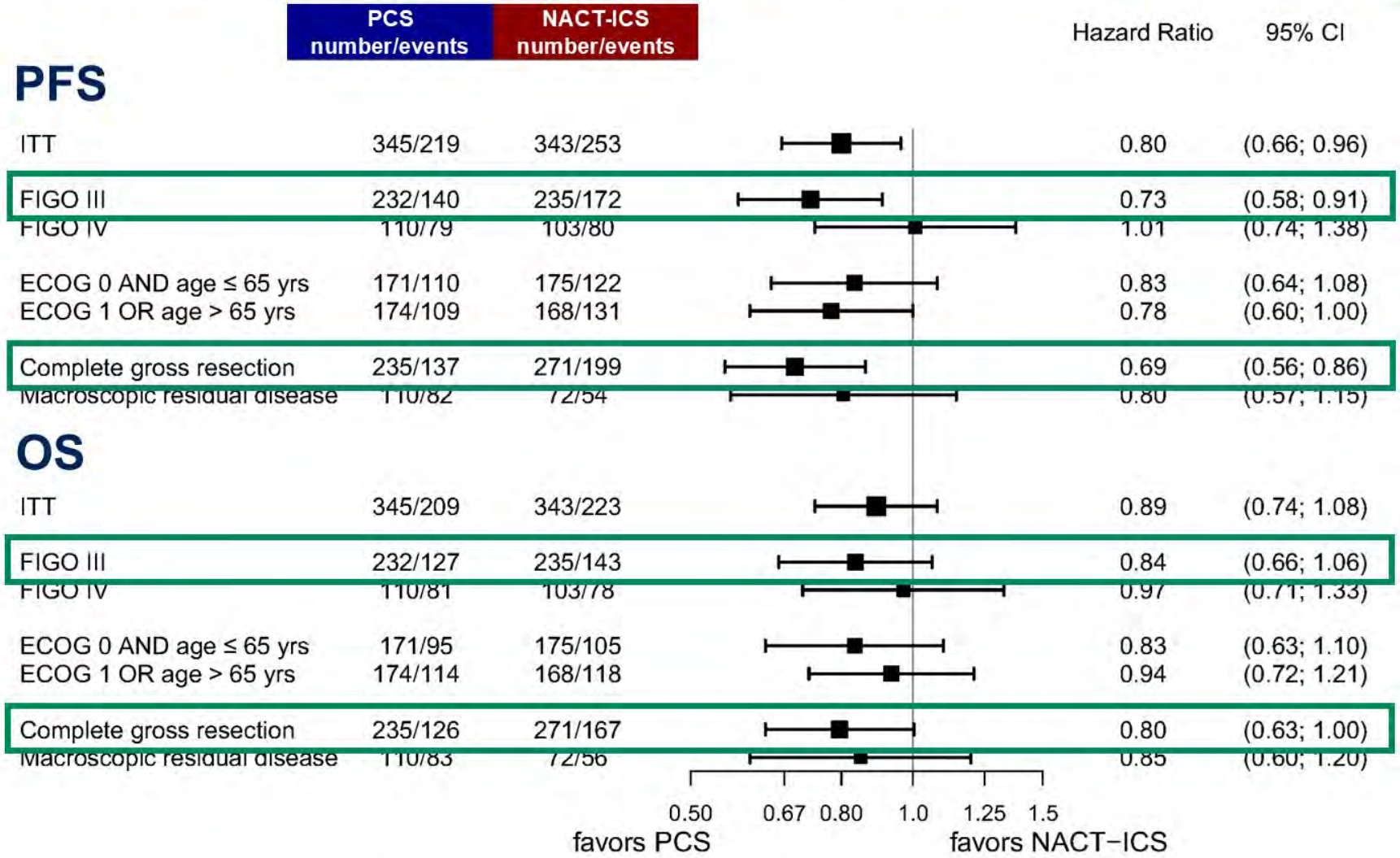
Primary Endpoint: Overall Survival

- Appropriate primary endpoint
- Original power calculations: HR 0.75, PDS 60 months versus NACT 45 months



TRUST Results: Treatment Effects According to Subgroups



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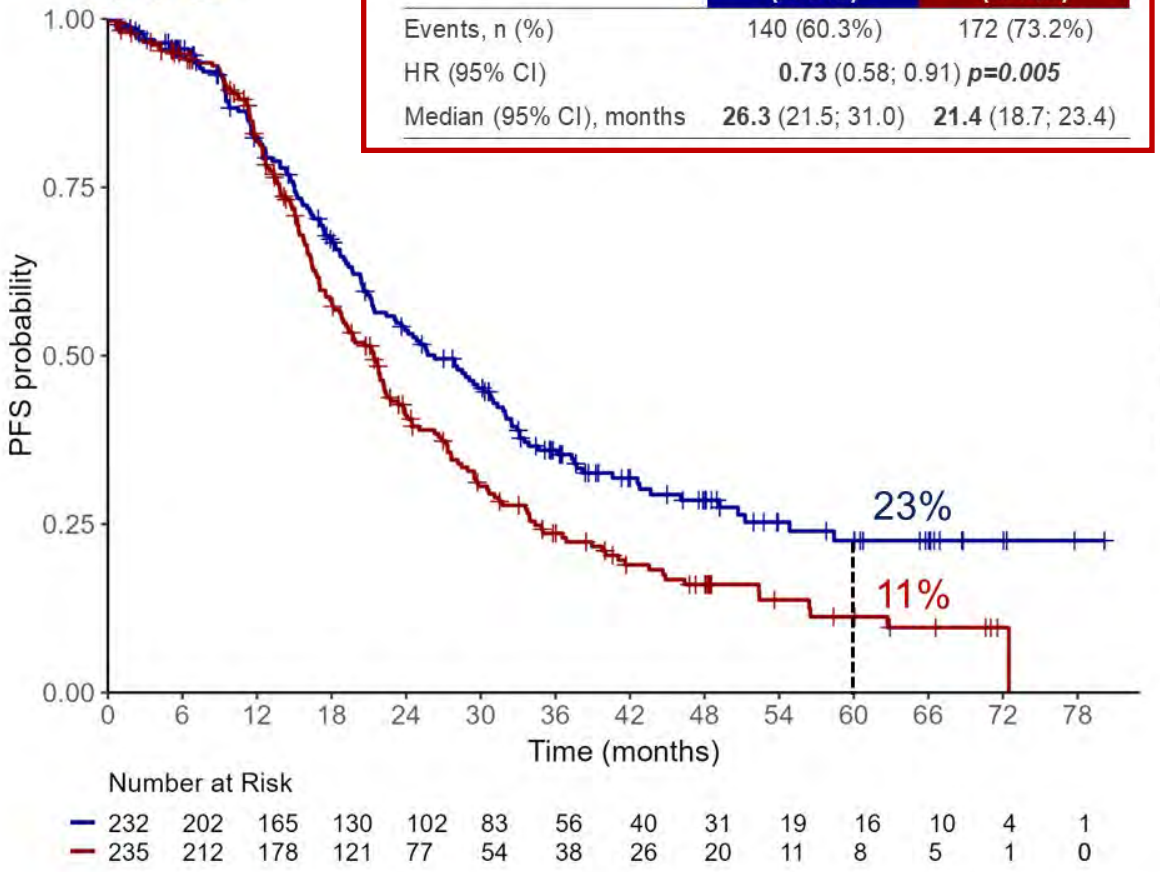
TRUST Results: Prespecified Exploratory Subgroup Analysis
FIGO Stage III

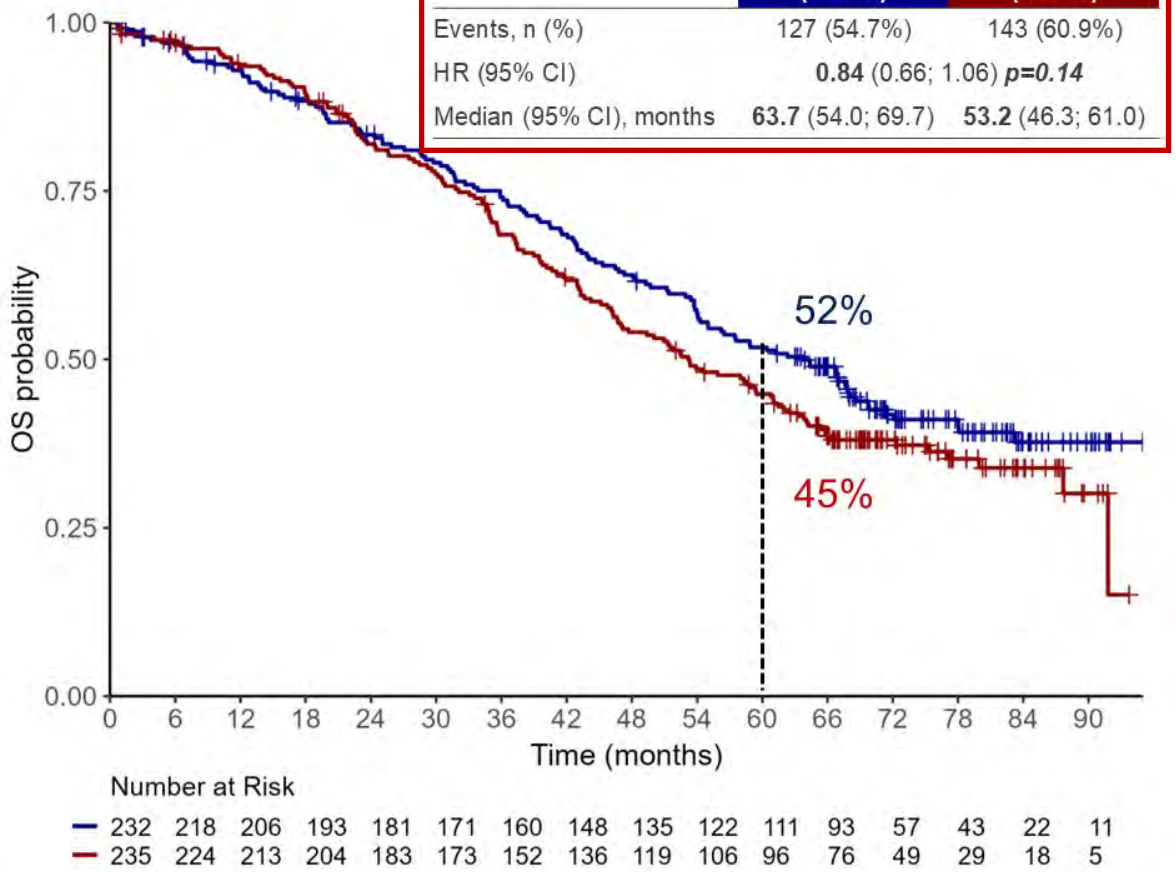
PFS

PFS	PCS (n=232)	NACT-ICS (n=235)
Events, n (%)	140 (60.3%)	172 (73.2%)
HR (95% CI)	**0.73** (0.58; 0.91) ***p=0.005***	
Median (95% CI), months	**26.3** (21.5; 31.0)	**21.4** (18.7; 23.4)



OS

OS	PCS (n=232)	NACT-ICS (n=235)
Events, n (%)	127 (54.7%)	143 (60.9%)
HR (95% CI)	**0.84** (0.66; 1.06) ***p=0.14***	
Median (95% CI), months	**63.7** (54.0; 69.7)	**53.2** (46.3; 61.0)



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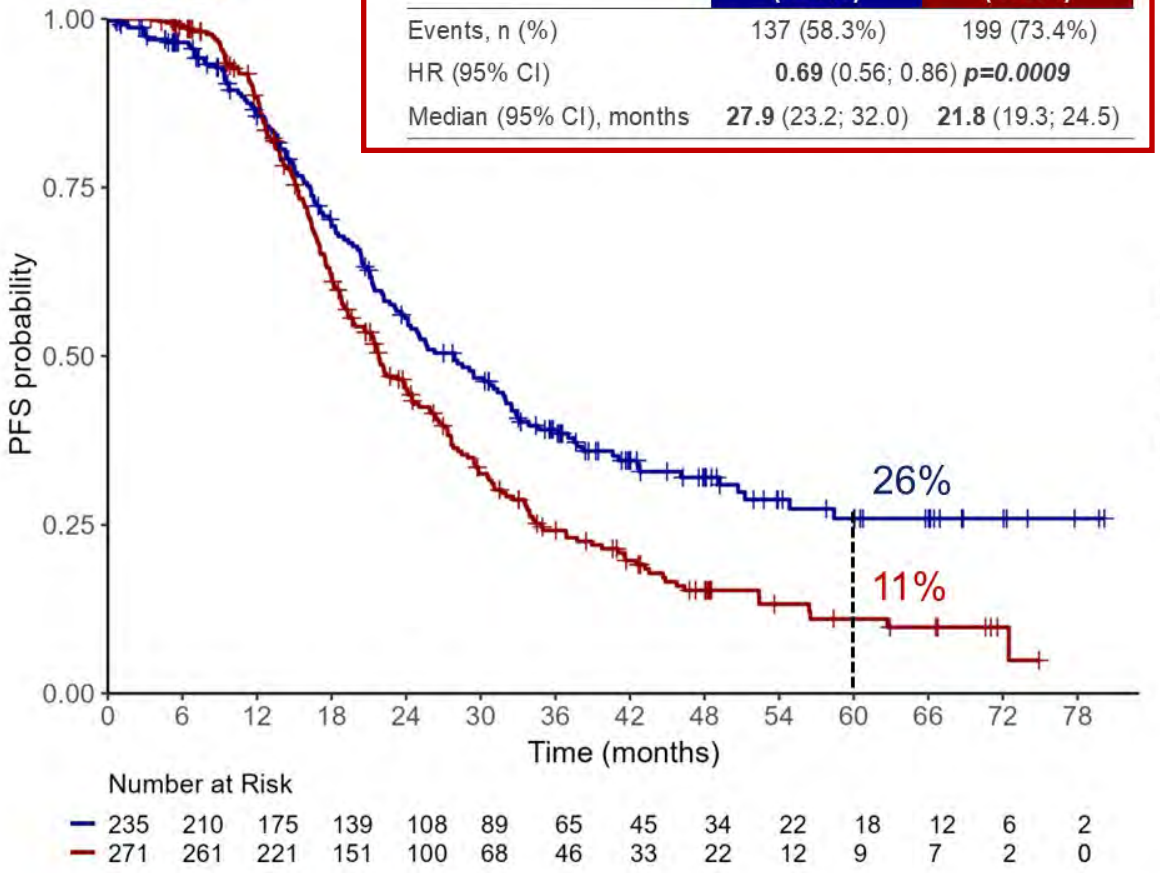
TRUST Results: Prespecified Exploratory Subgroup Analysis
Complete Gross Resection in All FIGO Stages

AGO STUDY GROUP

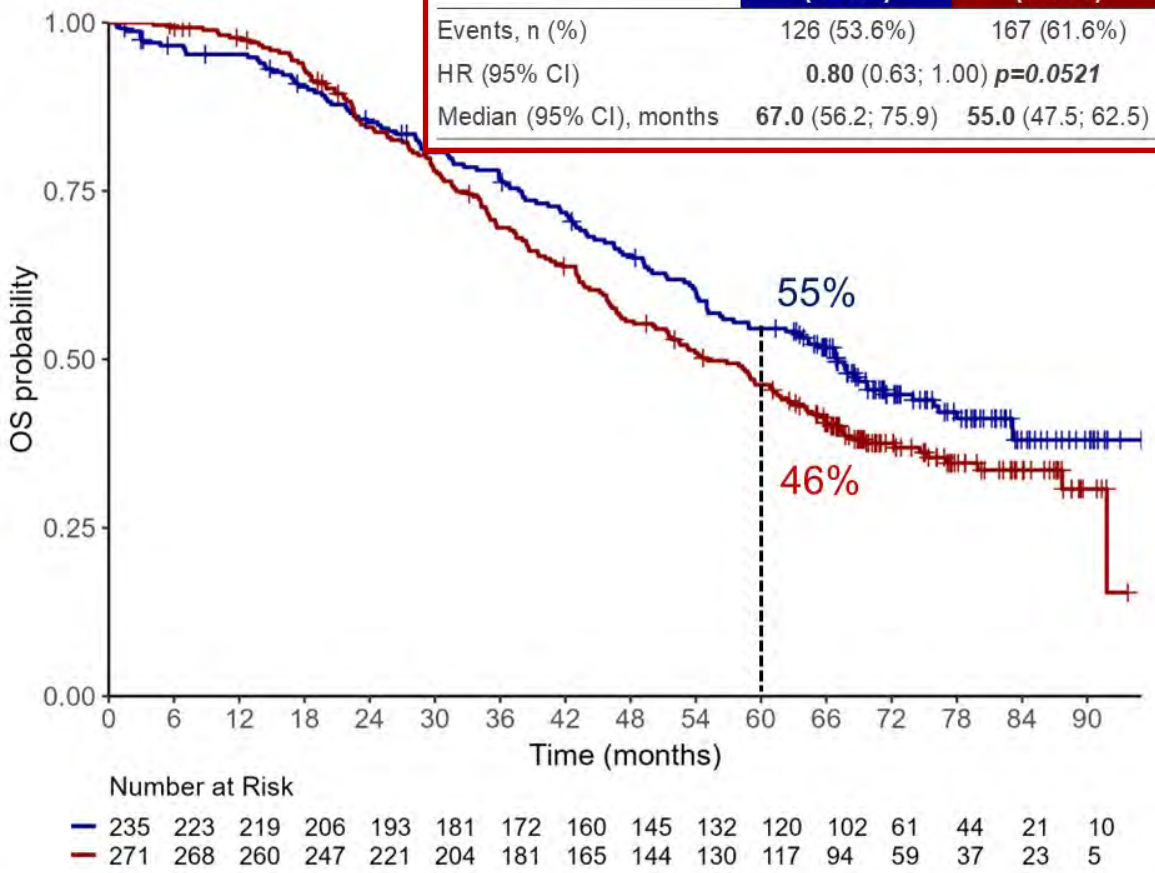
PFS

PFS	PCS (n=235)	NACT-ICS (n=271)
Events, n (%)	137 (58.3%)	199 (73.4%)
HR (95% CI)	**0.69** (0.56; 0.86)	***p=0.0009***
Median (95% CI), months	**27.9** (23.2; 32.0)	**21.8** (19.3; 24.5)



OS

OS	PCS (n=235)	NACT-ICS (n=271)
Events, n (%)	126 (53.6%)	167 (61.6%)
HR (95% CI)	**0.80** (0.63; 1.00)	***p=0.0521***
Median (95% CI), months	**67.0** (56.2; 75.9)	**55.0** (47.5; 62.5)



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A Surgical Trial with Robust Surgical Quality

- Overcomes a key criticism of previous studies
- High-volume centers and high-volume surgeons
- High quality surgery performed with high rates of resection to R0 among those who underwent surgery
  - 70% PDS
  - 85% NACT
- Surgical centers of excellence
  - High ability to rescue and support through radical surgery and complications
  - Generalizability limited to these centers

Surgical Procedures and Morbidity with PDS

- Any 28-day complication
  - 18.1% versus 11.9% (RR 1.5, p=0.03)
- Stoma formation
  - 19.9% versus 8.2% (RR 2.4, p<0.001)
- No difference 28-day mortality
  - 0.9% versus 0.6% (p=1.0)
- No difference in EORTC QLQ-C30 Global Health Status
  - Some variability in response rates especially at 3-month time point with lower survey return in the PDS patients

Where to Position These Results in NACT Literature

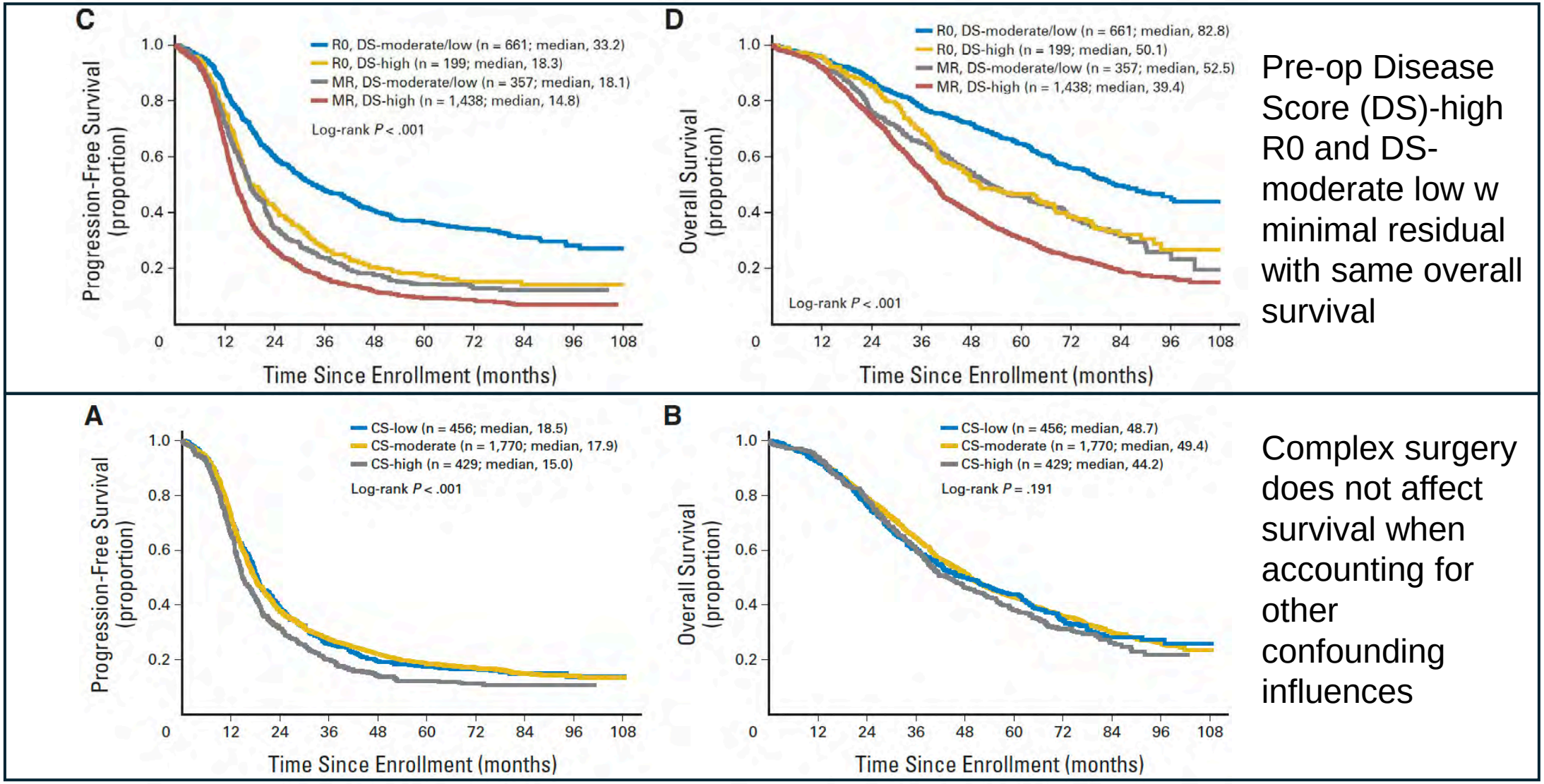
	TRUST 2025	EORTC 2010	CHORUS 2015	SCORPION 2020	JGOG0602 2020	PAOLA1 2019	PRIMA 2019
Study Design	super PDS	noninfer NACT	noninfer NACT	super NACT	noninfer NACT		
Median Age	63yo	62yo	65yo	56yo	60yo	61yo	60yo
Stage IV	31%	23%	25%	12%	31%	30%	35%
Complete Gross Resection PDS	70%	19%	17%	48%	31%		67%
Complete Gross Resection IDS	85%	51%	39%	77%	64%		NACT
Major Complications PDS	18%	19%	24%	26%	15%		
Major Complications IDS	12%	6%	14%	8%	5%		
30d death PDS	0.9%	2.5%	6%	1.7%	0.7%		
30d death IDS	0.6%	0.7%	<1%	0%	0%		
OS PDS	54 mo	29 mo	23 mo	41 mo	49 mo	57 mo	47 mo
OS IDS	48 mo	30 mo	24 mo	43 mo	44 mo	52 mo	49 mo
OS HR	HR 0.89	HR 1.02	HR 1.15	HR 1.12	HR 0.95		

Key Takeaway Points: TRUST Trial

Primary debulking surgery was not associated with improved overall survival compared to neoadjuvant chemotherapy.

Differential effects of primary debulking surgery on progression free and overall survival were noted in some sub-groups.

Initial disease burden as a significant prognostic indicator despite R0



Pre-op Disease Score (DS)-high R0 and DS-moderate low w minimal residual with same overall survival

Complex surgery does not affect survival when accounting for other confounding influences

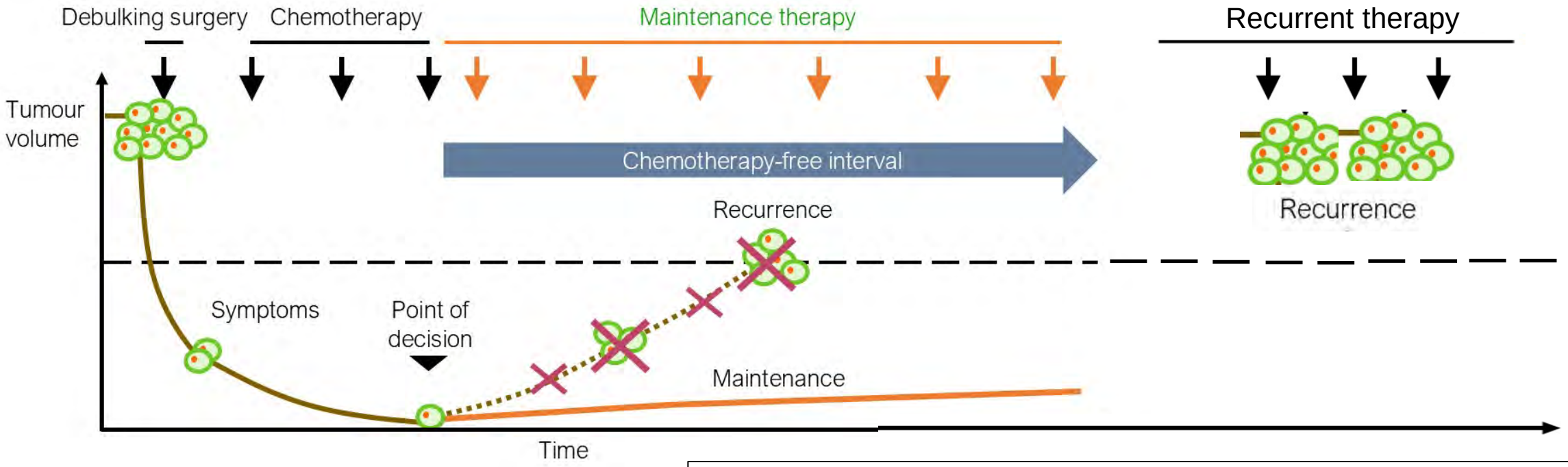
Horowitz et al. GOG 182 analysis JCO 2015

Clinical Presentation of Ovarian Cancer

TRUST (Trial of Radical Upfront Surgical Therapy) ENGOT ov3/AGO-OVAR OP.7

OVATION-2 Trial: Phase I/II IP IMNN-001 with NACT

FIRST: Dostarlimab and Niraparib in First-Line Advanced



ROSELLA/GOG 3073: Ph3 Relacorilant + Nab-Pac vs Nab-Pac

Phase 2 Pembro and Lenvatinib in recurrent/persistent OCCC

Phase 1 of INCB123667: CDK2 inhibitor in PROC refractory OC

2025 ASCO ANNUAL MEETING

A Phase I/II study of the Safety and Efficacy of IP IMNN-001 in combination with N/ACT in patients newly-diagnosed with advanced EOC:

Updated Survival Analysis from OVATION-2 Trial

P. Thaker, D. Richardson, A. Hagemann, R. Holloway, M. Reed, M. Bergman, B. Pothuri, S. DePasquale, J. Scalici, A. Begar, C. Darus, K. Finkelstein, C. Leath III, M. Bell, D. Warshal, R. Agajanian, M. Indermaur, A. Mendivil, D. Provencher, LJ Wei, L. Musso, S. Lindborg, D. Faller, K. Anwer, W. Bradley.

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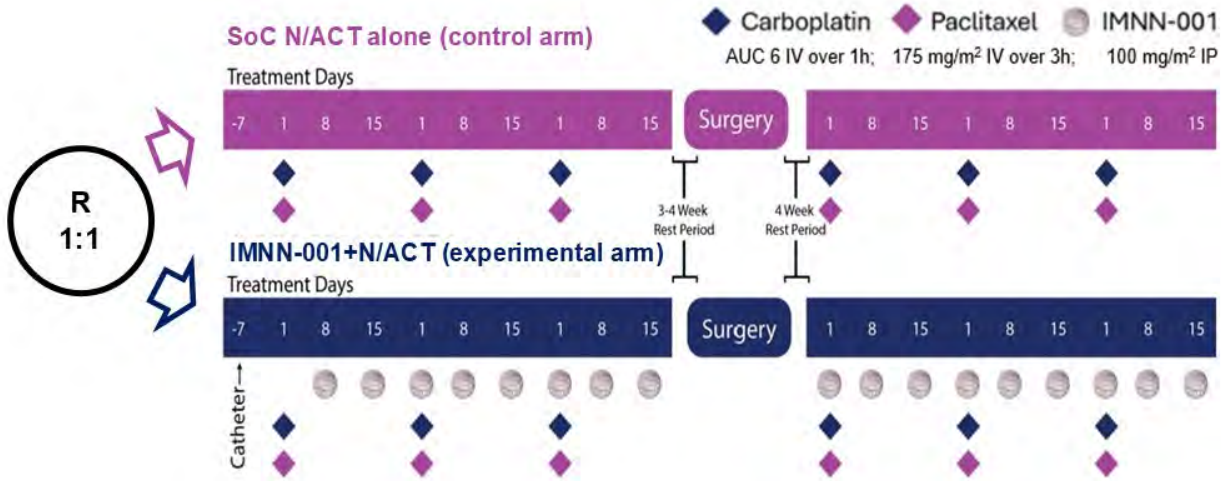
Chief of Gynecologic Oncology, Interim. Director of Gynecologic Oncology Clinical Research. Professor in Gynecologic Oncology.
Washington University School of Medicine

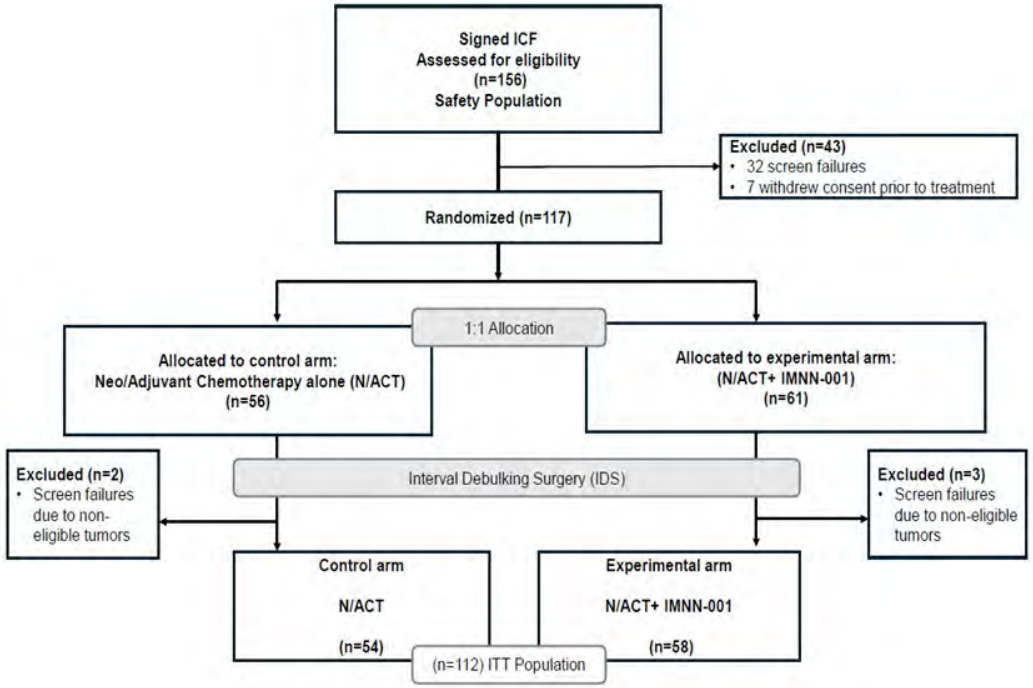
OVATION-2 Phase I/II Study in EOC N/ACT +/- IMNN-001

Study Schema (NCT03393884)



- A 15-patient **safety lead-in phase 1** monitored a 100 mg/m^2 dose of IMNN-001 given IP in combination with N/ACT SoC before opening the phase 2 recruitment
- **Ph2 Endpoints**: Primary: Safety and PFS
  Secondary: OS, ORR, Surgical response, Chemotherapy Response Score, Serologic response rates
- **No** endpoints were **powered for statistical significance**

Consort Diagram

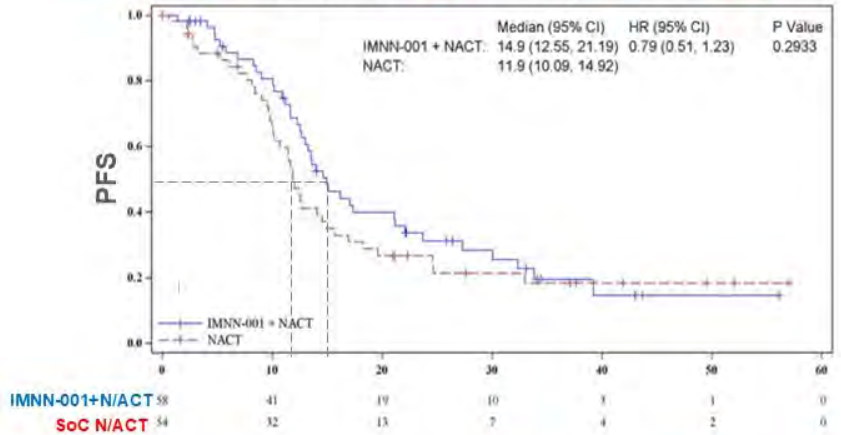


IMNN-001 is a nanoparticle encased gene therapy: IL-12 gene therapy

Results Efficacy: PFS (Primary endpoint) and Response

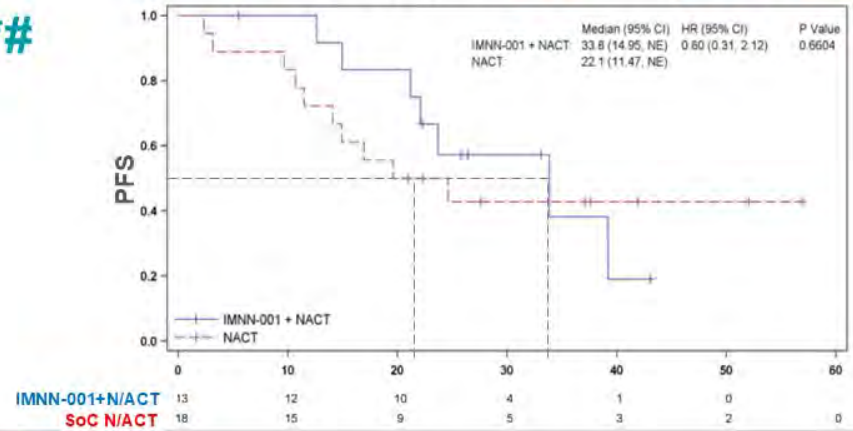
ITT

- **IMNN-001 Δ3 mo** to **SoC** PFS (**14.9** vs **11.9**) HR: 0.79



PARPi Treated*#

- **IMNN-001 Δ3 11.7mo** to **SoC** PFS (**33.8** vs **22.1**) HR:0.8



Response, ITT

- **IMNN-001** increased **R0** and **CRS 3**

Endpoint	N/ACT n=54	IMNN-001 + N/ACT N=59
Objective Response Rate n (%) (ORR=CR+PR) prior surgery	31 (57.4)	31 (53.4)
Best Overall Response n (%)		
CR	1 (1.9)	1 (1.7)
PR	30 (55.6)	30 (51.7)
SD	12 (22.2)	12 (20.7)
PD	4 (7.4)	0
NE	1 (1.9)	2 (3.4)
Serologic response n (%)		
Yes	43 (79.6)	44 (75.9)
No	6 (11.1)	10 (17.2)
NA	5 (9.3)	4 (6.9)
Surgical response* n (%)		
R0	25 (52.1)	31 (64.6)
R1	14 (29.2)	5 (10.4)
R2	9 (18.8)	12 (25.0)
CT Response score* n (%)		
CRS3	6 (13.0)	12 (26.1)
CRS2	24(52.2)	18 (39.1)
CRS1	16 (34.8)	16 (34.8)

(*) PARPi treated in first line maintenance before first PD
(#) in Non-PARPi treated subgroup (n=81): PFS was 13.3 vs 10.2 mo HR 0.63 no statistically significant (ss)

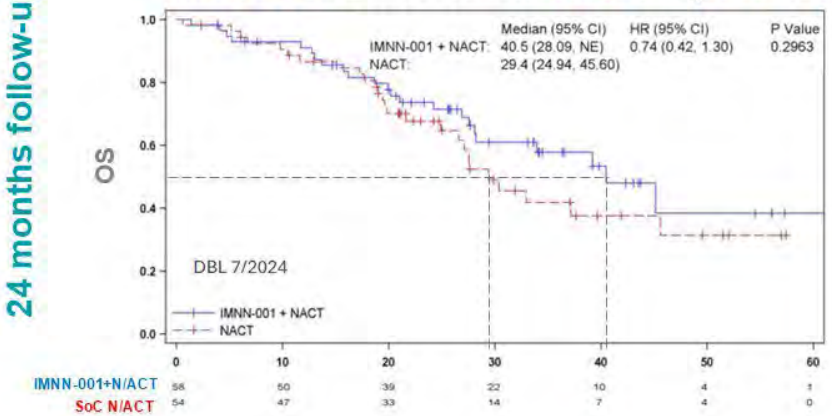
Results Efficacy: OS (13 mo benefit at 31 mo FU)

ITT

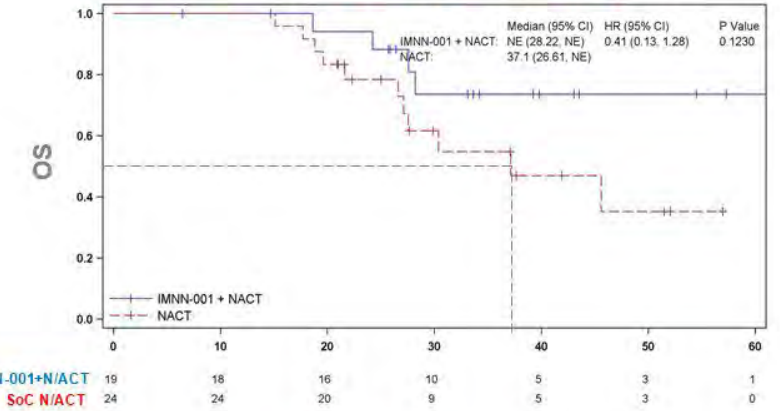
PARPi treated#$

24 months follow-up

- IMNN-001 Δ 11.1 mo to SoC OS (40.5 vs 29.4) HR:0.74

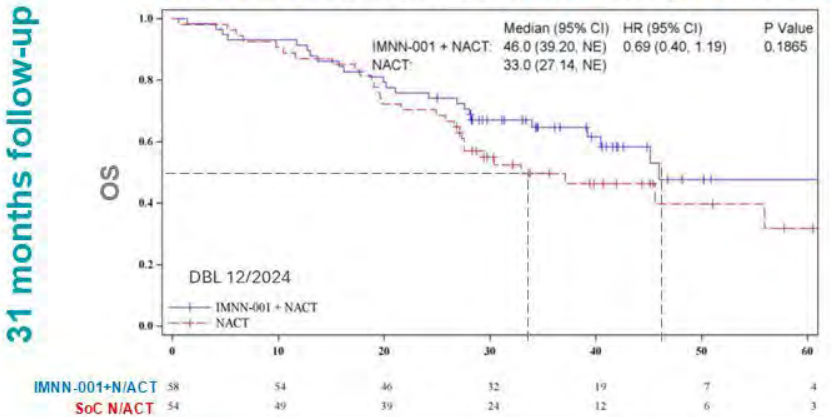


- IMNN-001 vs SoC (NE vs 37.1) HR:0.41

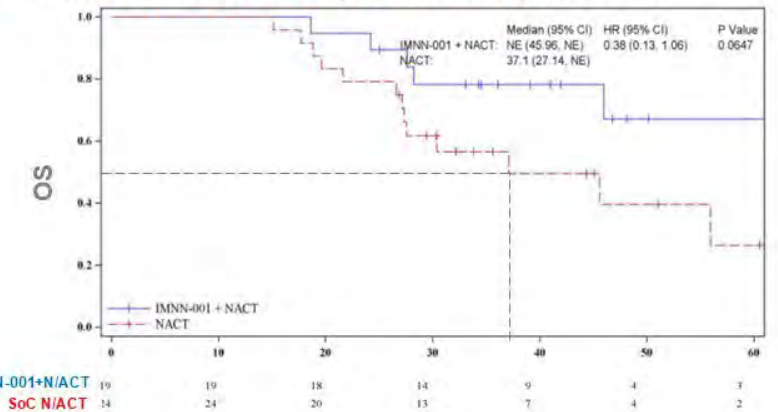


31 months follow-up

- IMNN-001 Δ 13 mo to SoC OS (46.0 vs 33.0) HR:0.69



- IMNN-001 vs SoC (NE vs 37.1) HR:0.38



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(#) 31 mo Follow-up for Non-PARPi treated subgroup (n=69): OS was 40.5 vs 29.4 mo HR 0.83 no statistically significant (ss)
($) 31 mo Follow-up for BRCAm/HRD subgroup (n=34): OS was NE vs NE mo HR 0.49 no ss

Conclusions

- OVATION-2, a randomized controlled Phase I/II study of IMNN-001, an IL-12 gene immunotherapy, delivered intraperitoneally in combination with neo/adjuvant chemotherapy in newly-diagnosed advanced epithelial ovarian cancer (EOC), was safe and yielded clinically meaningful benefits to patients over the SoC in terms of PFS, OS, Surgical Response and Chemotherapy Response score

- The IMNN-001 nanoparticle-encased gene delivery system allows safe and tolerable repeated delivery of tumor-localized IL-12, avoiding immune-related adverse events associated with systemic IL-12 exposure

- After 31-month follow-up, the addition of IMNN-001 to SoC neo/adjuvant chemotherapy (N/ACT) provided a 3-month numerical PFS and a 13-month OS advantage over N/ACT alone (46 vs 33 months)

- Increased activity is observed in HRD patients and for those who received maintenance PARPi (the median OS not yet reached in the IMNN-001 arm vs 37.1 months in the control arm)

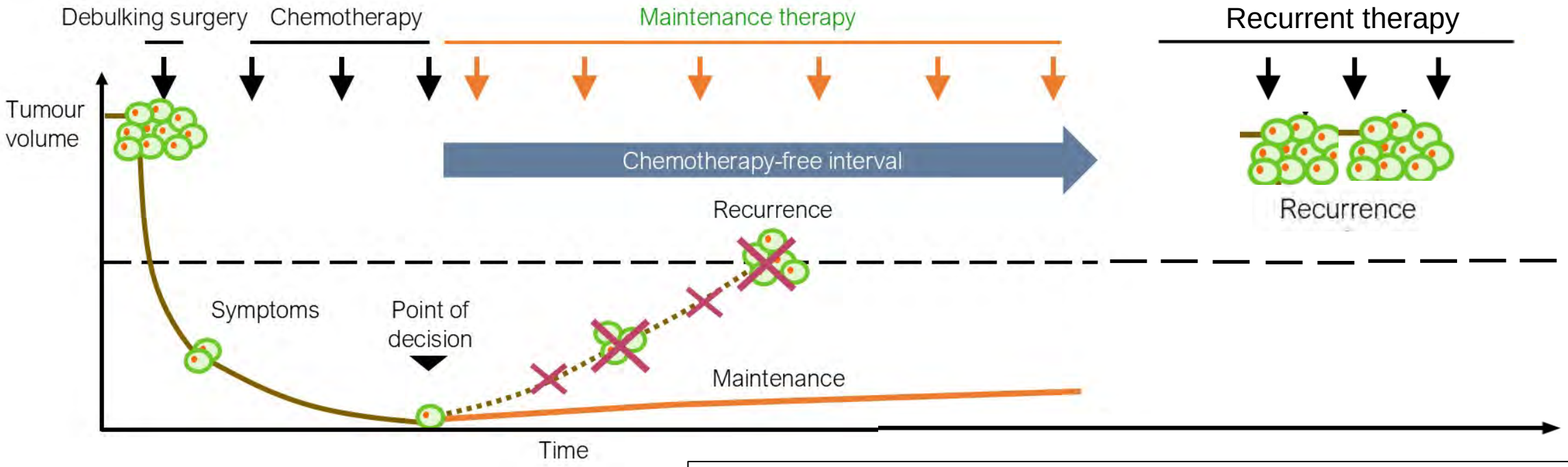
- A confirmatory randomized phase 3 study (NCT06915025) is underway to evaluate the safety and efficacy of IMNN-001 plus N/ACT compared to N/ACT alone and will further explore the contribution of BRCA/HRD status to IMNN-001 efficacy

Clinical Presentation of Ovarian Cancer

TRUST (Trial of Radical Upfront Surgical Therapy) ENGOT ov3/AGO-OVAR OP.7

OVATION-2 Trial: Phase I/II IP IMNN-001 with NACT

FIRST: Dostarlimab and Niraparib in First-Line Advanced



ROSELLA/GOG 3073: Ph3 Relacorilant + Nab-Pac vs Nab-Pac

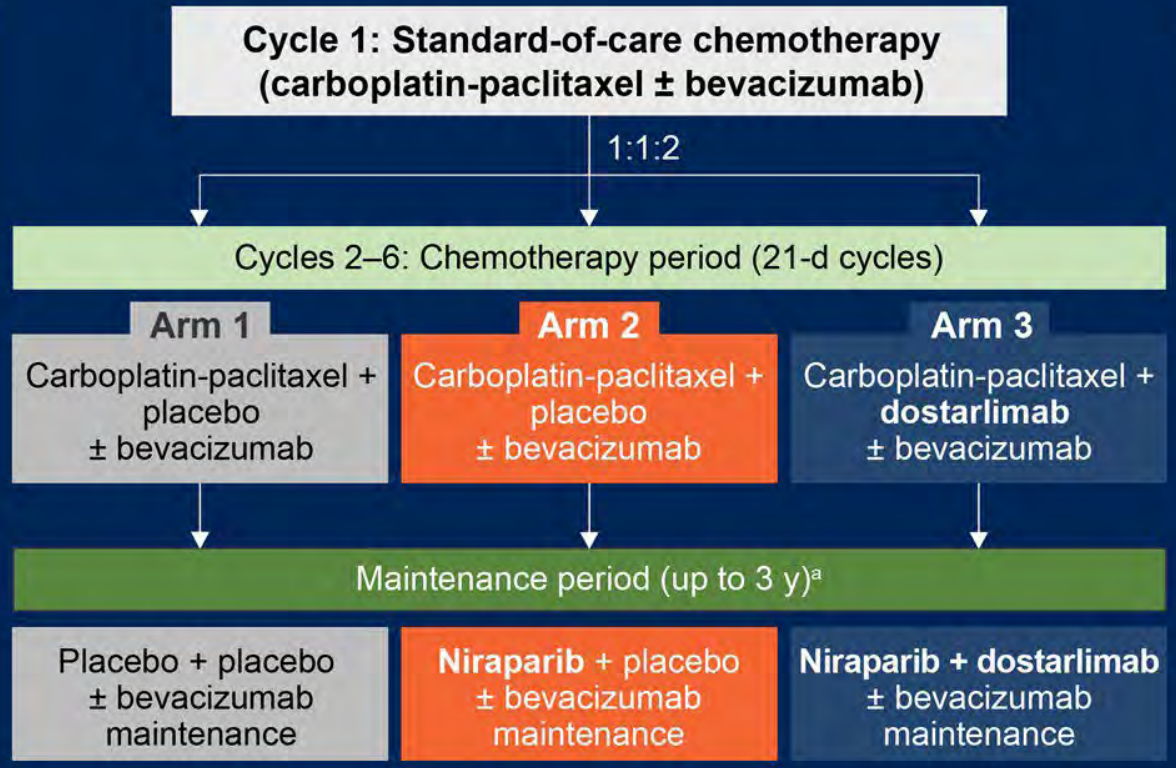
Phase 2 Pembro and Lenvatinib in recurrent/persistent OCCC

Phase 1 of INCB123667: CDK2 inhibitor in PROC refractory OC

FIRST Trial Design

Key inclusion criteria

- Aged ≥18 y
  - High-grade nonmucinous epithelial OC
  - Stage IV disease
  - Stage III disease if
    - Stage IIIC with CC0 resection during PDS if aggregate ≥5-cm extrapelvic disease
    - Inoperable disease
    - Macroscopic residual tumor after PDS
    - Planned neoadjuvant chemotherapy
  - PDS, IDS, and inoperable were all included



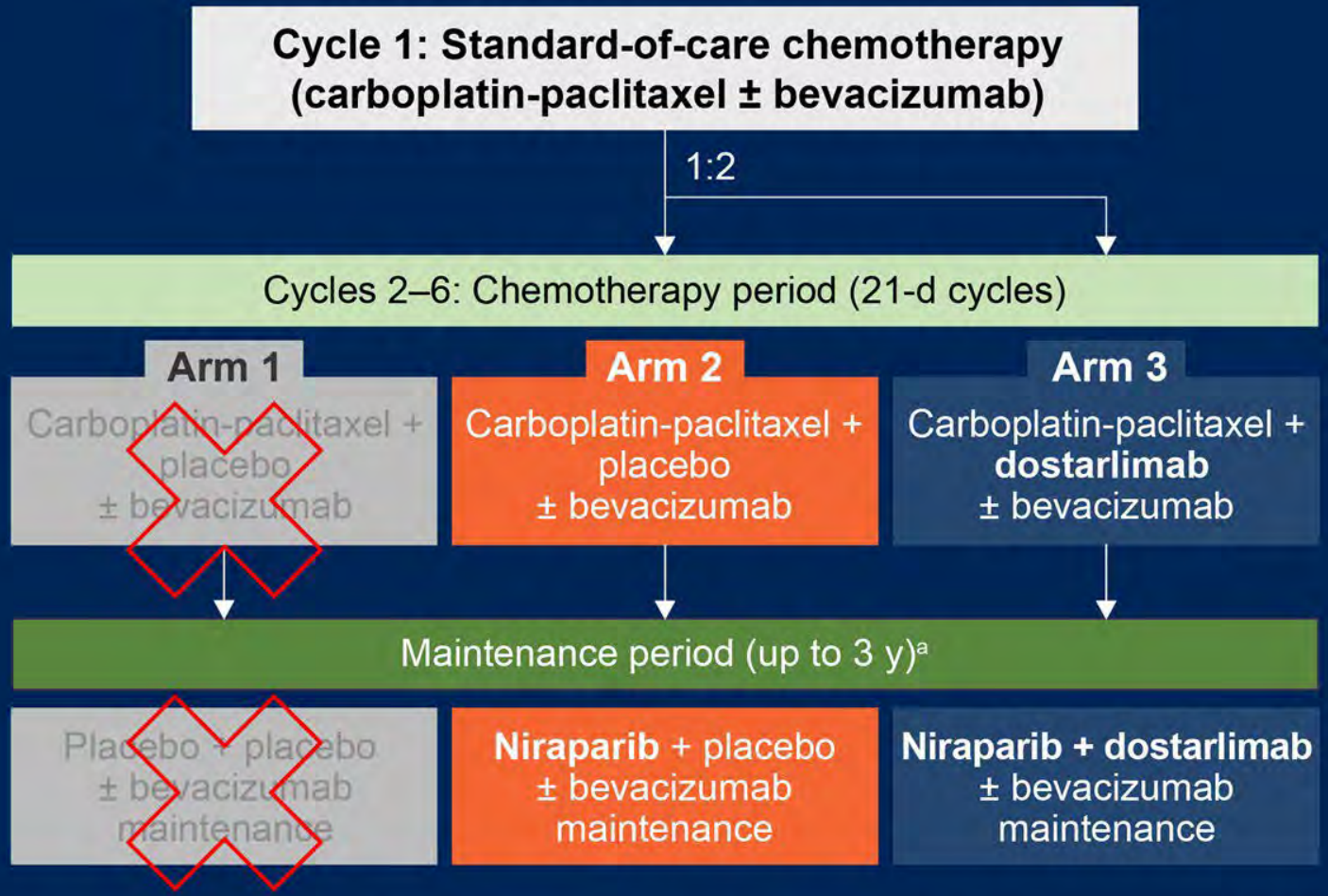
Stratification factors

- Intended bevacizumab use
- HRR mutation status (*BRCA*m, *BRCA*wt/HRRpos, and *BRCA*wt/HRRneg/ not determined)
- Disease burden: Stage III with residual burden <1 cm (yes or no)

[a]May continue treatment beyond 3 years in consultation with the medical monitor. *BRCA*m, *BRCA*-mutated; *BRCA*wt, *BRCA* wild-type; CC0, complete resection; HRR, homologous recombination repair; IDS, interval debulking surgery; neg, negative; OC, ovarian cancer; PDS, primary debulking surgery; pos, positive.

FIRST Trial Design

- 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,[1,2] enrollment into arm 1 was terminated



[a]May continue treatment beyond 3 years in consultation with the medical monitor. PARPi, poly(ADP-ribose) polymerase inhibitor. 1. González-Martín A, et al. *N Engl J Med* 2019;381(25):2391–2402. 2. Ray-Coquard I, et al. *N Engl J Med* 2019;381(25):2416–2428.

Endpoints and Statistical Testing Strategy

- The primary endpoint was PFS per RECIST v1.1 by investigator assessment in the ITT population (arms 2 and 3)
  - A hierarchical testing strategy was used to control the type I error at 2-sided 0.05 level
  - If PFS results were statistically significant, testing would continue to OS
- Patients with PD-L1–positive or HRd tumors and those with concurrent bevacizumab were specified *a priori* as clinically plausible groups to have differentiated results

This slide presents the endpoints and statistical testing strategy for the final protocol. HRd, homologous recombination-deficient; ITT, intention-to-treat; OS, overall survival; PD-L1, programmed cell death-ligand 1; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Baseline Demographic and Clinical Characteristics

Characteristic	ITT population	
	Niraparib (n=385)	Dostarlimab + niraparib (n=753)
Age, median (IQR), y	64.0 (56.0–70.0)	63.0 (54.0–70.0)
Race		
White	348 (90.4)	666 (88.4)
Black or African American/other/not reported	37 (9.6)	87 (11.6)
FIGO stage at initial diagnosis		
III	247 (64.2)	466 (61.9)
IV	138 (35.8)	287 (38.1)
Predominant histological subtype		
Serous	344 (89.4)	681 (90.4)
Nonserous[a]	43 (11.2)	69 (9.2)
Planned surgical status at time of screening		
PDS	132 (34.3)	273 (36.3)
IDS	217 (56.4)	404 (53.7)
Inoperable	36 (9.4)	76 (10.1)
Macroscopic residual disease after PDS[b]		
Yes	92 (23.9)	178 (23.6)
No	42 (10.9)	100 (13.3)
Not applicable[c]	251 (65.2)	475 (63.1)
Intended bevacizumab use		
Yes	198 (51.4)	397 (52.7)
No	187 (48.6)	356 (47.3)

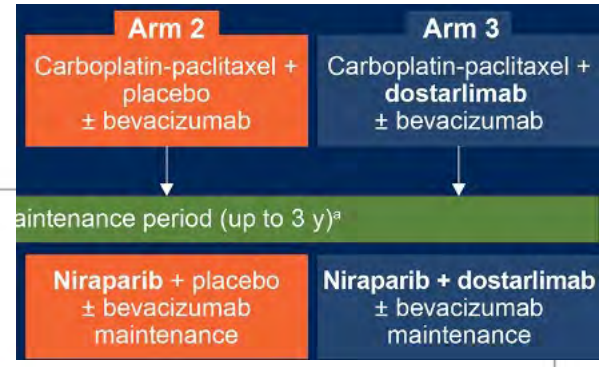
Data cutoff date: October 31, 2024. Values shown are n (%) unless otherwise noted. [a]Nonserous includes endometrioid, carcinosarcoma, clear cell, nonmucinous, and mixed histologies. [b]Some patients did not have PDS planned at time of screening, but investigators subsequently recorded data for macroscopic residual disease after PDS, based on a surgical procedure. [c]Includes patients who had inoperable disease or had IDS. FIGO, International Federation of Gynecology and Obstetrics; IDS, interval debulking surgery; IQR, interquartile range; ITT, intention-to-treat; PDS, primary debulking surgery.

Biomarker Status

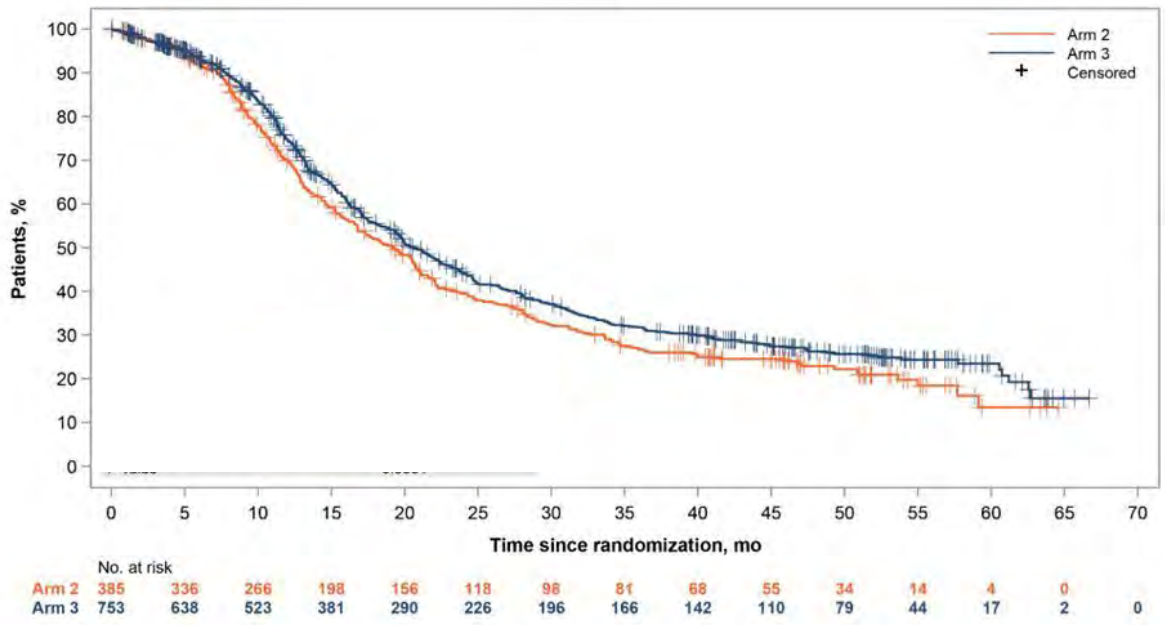
	Characteristic, n (%)	ITT population Niraparib (n=385)	ITT population Dostarlimab + niraparib (n=753)
Tumor tissue	PD-L1 status[a]		
	Positive (TAP ≥5%)	92 (23.9)	226 (30.0)
	Negative (TAP <5%)	230 (59.7)	403 (53.5)
	Unknown	63 (16.4)	124 (16.5)
ctDNA	HRR status[b] (ResBio assay)		
	*BRCA*m	74 (19.2)	143 (19.0)
	*BRCA*wt/HRR-positive	26 (6.8)	45 (6.0)
	*BRCA*wt/HRR-negative/not determined	282 (73.2)	560 (74.4)
	Missing	3 (0.8)	5 (0.7)
Tumor tissue	HRD status[c] (Myriad MyChoice® assay)		
	HRd	146 (37.9)	298 (39.6)
	HRp	164 (42.6)	312 (41.4)
	Unknown	75 (19.5)	143 (19.0)
	BRCA status[c] (Myriad MyChoice® assay)		
	*BRCA*m	81 (21.0)	151 (20.1)
	*BRCA*wt	253 (65.7)	513 (68.1)
	*BRCA*wt HRd	65 (16.9)	147 (19.5)
	Unknown	51 (13.2)	89 (11.8)

Data cutoff date: October 31, 2024. [a]Determined retrospectively, from tumor samples collected at prescreening or screening, using the SP263 immunohistochemistry assay (Ventana Medical Systems, Inc). PD-L1 positivity defined as TAP score ≥5%. Unknown includes invalid and not tested. [b]Determined based on circulating tumor DNA evaluation of HRR deficiency from blood samples collected at prescreening or screening, using the ResBio ctDx-HRR assay (Resolution Bioscience, Inc). Actual values rather than those entered in the randomization system are presented. [c]Determined retrospectively, from tumor samples collected at prescreening or screening, using the Myriad MyChoice® HRD plus CDx assay (Myriad Genetics, Inc). Unknown includes inconclusive and not tested. *BRCA*m, *BRCA*-mutated; *BRCA*wt, *BRCA* wild-type; HRd, homologous recombination-deficient; HRD, homologous recombination deficiency; HRp, homologous recombination-proficient; HRR, homologous recombination repair; ITT, intention-to-treat; PD-L1, programmed cell death-ligand 1; TAP, tumor area positivity.

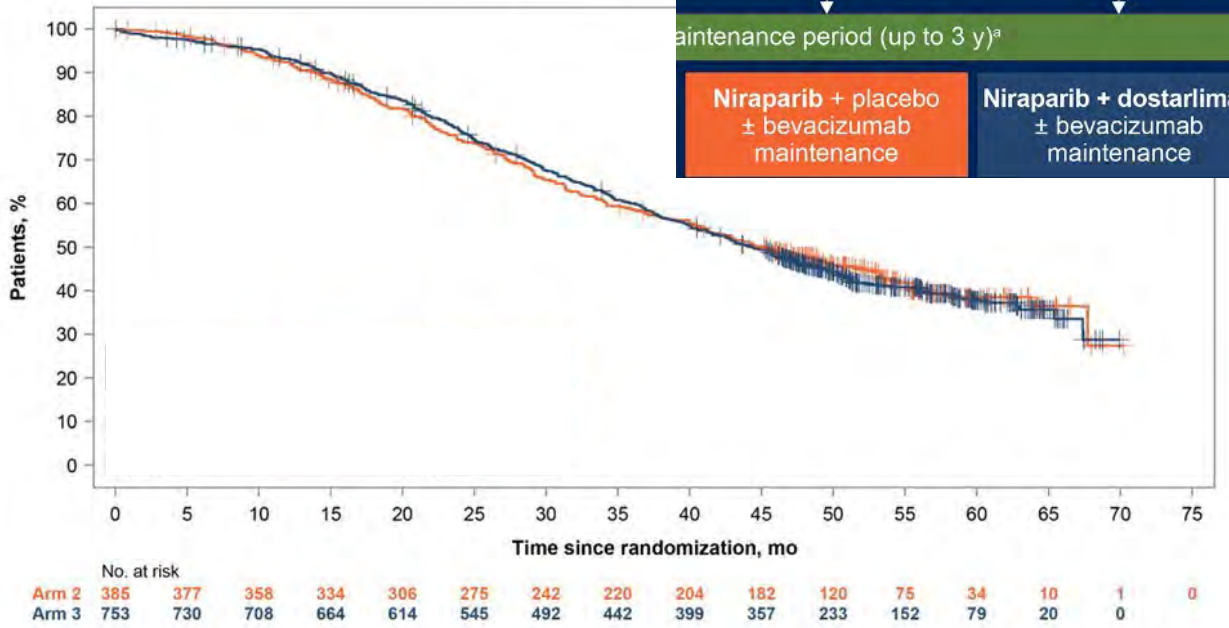
FIRST Trial: Improved PFS with addition of CPI to PARPi compared to PARPi



PFS



OS



	Arm 2 (n=385)	Arm 3 (n=753)
Events, n (%)	260 (67.5)	443 (58.8)
Median (95% CI), mo	19.2 (16.6–21.0)	20.6 (19.2–22.8)
Hazard ratio (95% CI)	0.85 (0.73–0.99)	
P value	0.0351	

Here the addition of CPI to PARPi is compared to PARPi and PFS is modestly improved – no OS improvement

	Arm 2 (n=385)	Arm 3 (n=753)
Events, n (%)	215 (55.8)	434 (57.6)
Median (95% CI), mo	45.4 (40.3–52.2)	44.4 (41.2–47.5)
Hazard ratio (95% CI)	1.01 (0.86–1.19)	
P value	0.9060	

2025 ASCO ANNUAL MEETING

#ASCO25

Hardy ASCO 2025

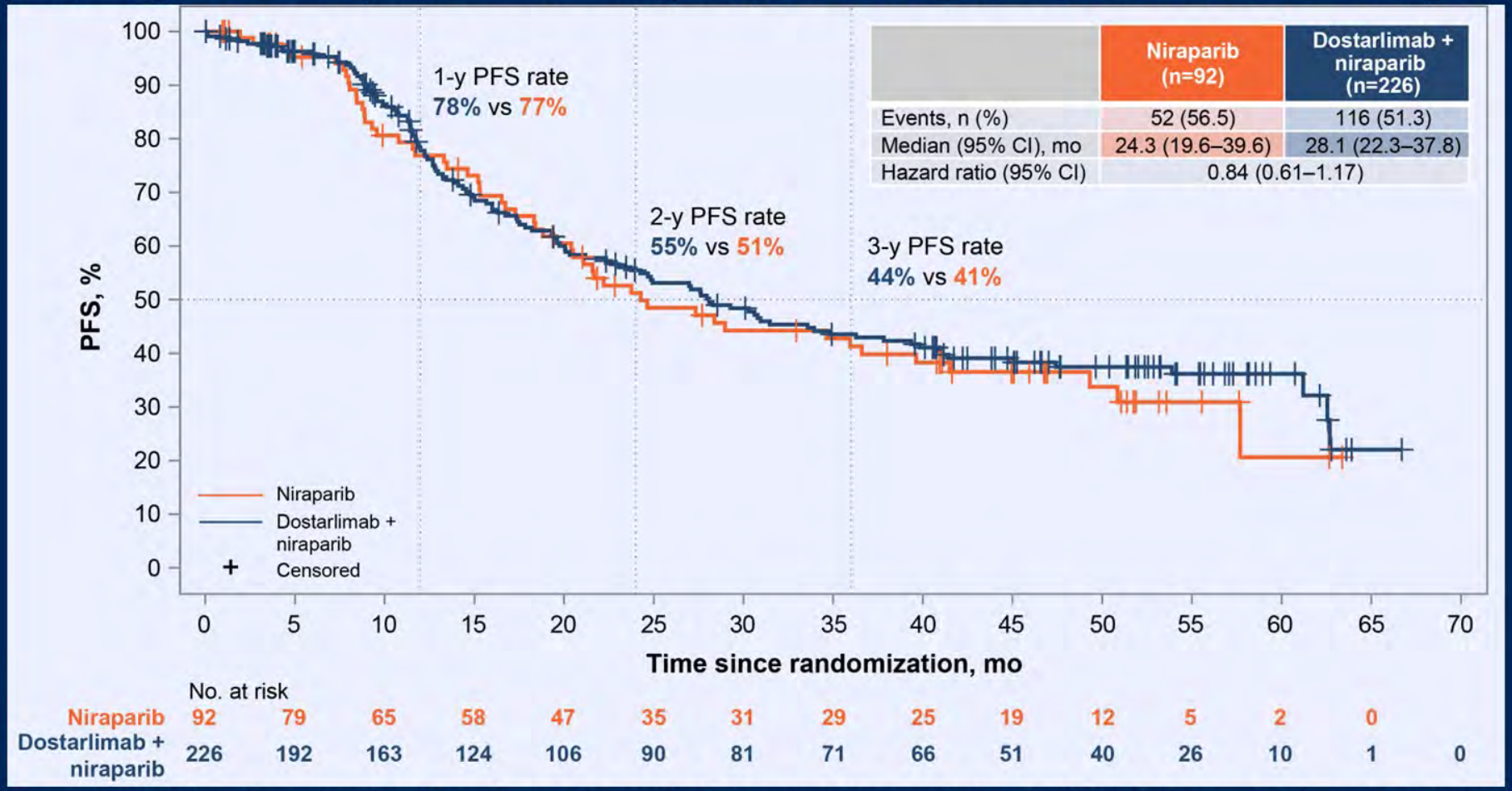
PRESENTED BY: Kathleen N. Moore, MD, MS, FASCO

@DrKatyMoore

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

PFS per RECIST v1.1 in the PD-L1+ Population

In arm 2 (niraparib) and arm 3 (dostarlimab + niraparib), 27.9% of patients had PD-L1+ tumors (TAP ≥5%).



	Niraparib (n=92)	Dostarlimab + niraparib (n=226)
Events, n (%)	52 (56.5)	116 (51.3)
Median (95% CI), mo	24.3 (19.6–39.6)	28.1 (22.3–37.8)
Hazard ratio (95% CI)	0.84 (0.61–1.17)	

Data cutoff date: October 31, 2024. Curves estimated with Kaplan–Meier analyses. Hazard ratio and *P* value are from a stratified Cox proportional hazards model and log-rank test (2-sided), with treatment as only covariate, adjusted for randomization stratification factors. Reasons for nonadministrative censoring included no baseline/postbaseline tumor assessments, early study discontinuation without event, initiation of subsequent anticancer therapy before or without event, or 2 consecutive missed tumor assessments before event. The main contributor to nonadministrative censoring was initiation of subsequent anticancer therapy before or without event. CI, confidence interval; PD-L1,+ programmed cell death-ligand 1-positive; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TAP, tumor area positivity.

PRESENTED BY: Anne-Claire Hardy-Bessard, MD

Conclusions

- 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 ≥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

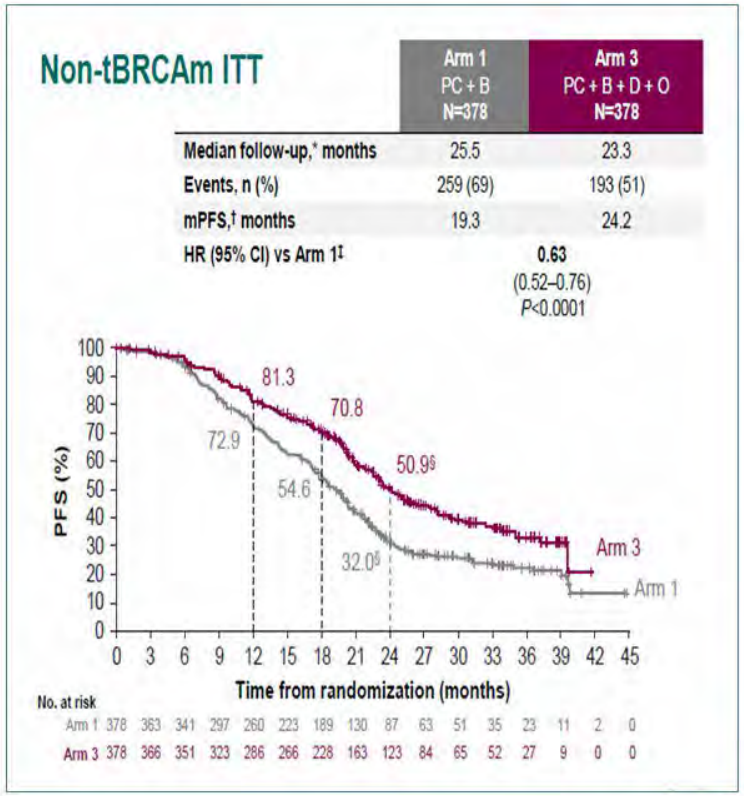
aOC, advanced ovarian cancer; EORTC-QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EQ VAS, European Quality of Life Visual Analogue Scale; OS, overall survival; PD-L1, programmed cell death-ligand 1; PFS, progression-free survival.; TAP, tumor area positivity.

	DUO-O	KEYLINK	ATHENA COMBO	FIRST
Control arm	Bevacizumab x 15 months	Placebo +/- bevacizumab x 15 mo	Rucaparib x 25 mo	Niraparib x 36 mo +/- bevacizumab x 15 mo
Experimental arm maintenance	Olaparib x 24 months Durvalumab x 24 months Bevacizumab x 15 months	Olaparib x 24 mo Pembrolizumab x 29 cycles (21 mo) +/- Bevacizumab x 15 mo	Rucaparib x 25 mo Nivolumab x 24 mo	Niraparib x 36 mo Dostarlimab x 36 mo +/- Bevacizumab x 15 mo
PDS vs IDS	60% vs 40%	63% vs 37%	49% vs 51%	35% vs 55%, 10% inoperable
BRCAm	Independent, single arm	Not eligible	21%	19%
Intended bev use	100%	45% vs 55%	None	52% v 48%
PD-L1 positive	TAP ≥ 5% 37%	CPS ≥10 50%	≥1% 46%	TAP ≥ 5% 28%
Primary outcome	PFS- investigator assessed, Arm 3 v Arm 1, both nontBRCAm HRD and ITT	PFS- investigator assessed, both ITT and CPS ≥ 10	PFS- investigator assessed	PFS- investigator assessed
Stage III vs IV	66% vs 34%	60% vs 40%	75% vs 25%	63% vs 37%
Median PFS (ITT)	25.1 vs 20.6 vs 19.3 mo, HR 0.61 (0.51-0.73)	22.2 vs 15.2 vs 14.6, HR 0.71 (0.61-0.84)	15 vs 20.2 mo, HR 1.29 (1.08-1.53)	20.6 vs 19.2 mo, HR 0.85 (0.73-0.99)
Median OS (ITT)	47.7 vs 47.1 mo, HR 1.04 (0.87-1.25)	48.5 vs NR vs 48 mo, HR 0.95 (0.76-1.2)	49.4 vs 58 mo, HR 1.13 (0.93-1.38)	44.4 vs 45.4 mo HR 1.01 (0.86-1.19)

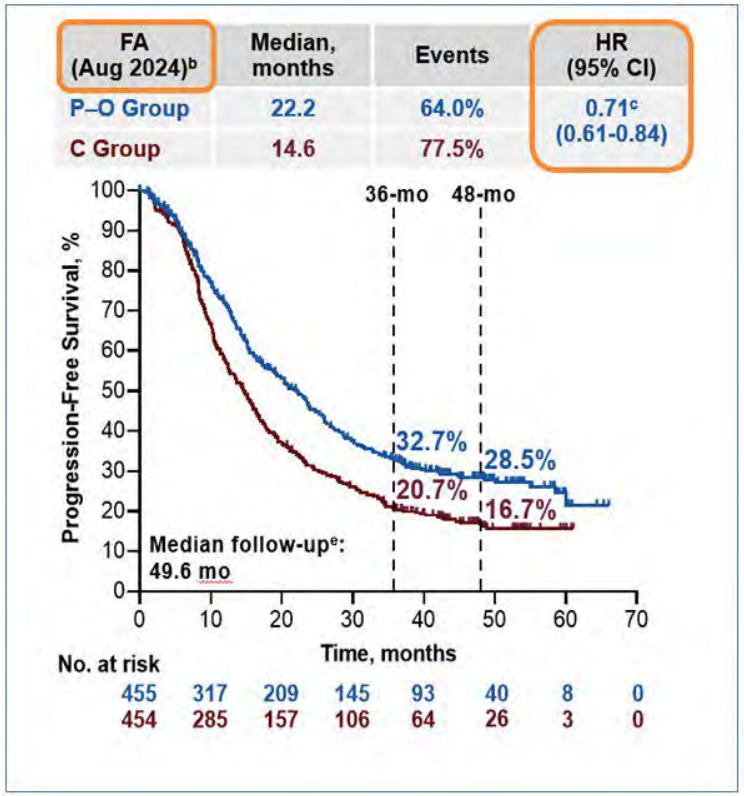
Harter ASCO 2023, Powell SGO 2025, Monk ESMO 2024, Hardy-Bessard ASCO 2025

One of these trials is not like the others

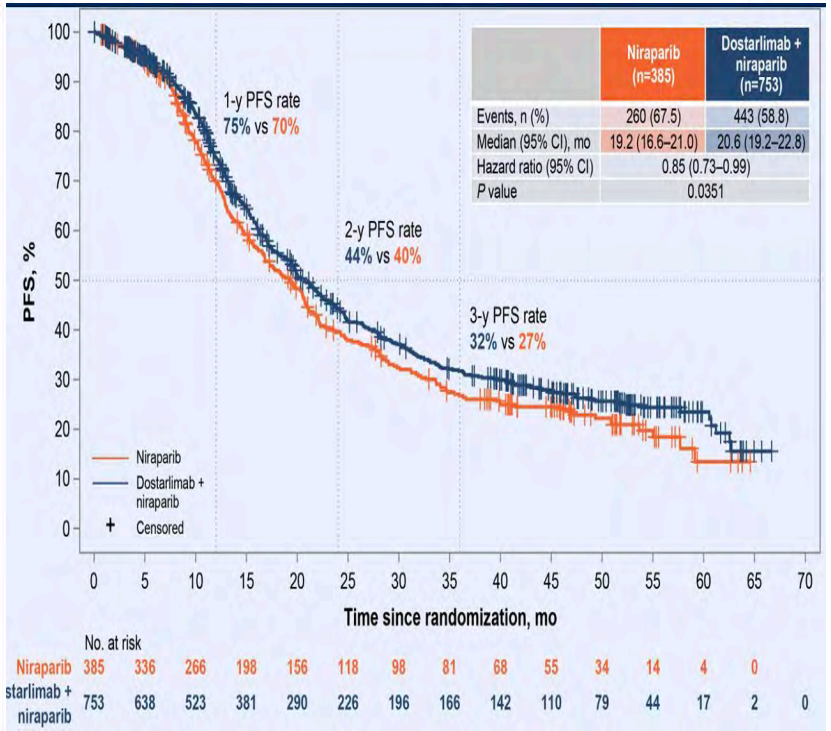
DUO-O: Control arm is bevacizumab maintenance



KEYLINK: Control is +/- bevacizumab maintenance



FIRST: Control is niraparib +/- bevacizumab maintenance

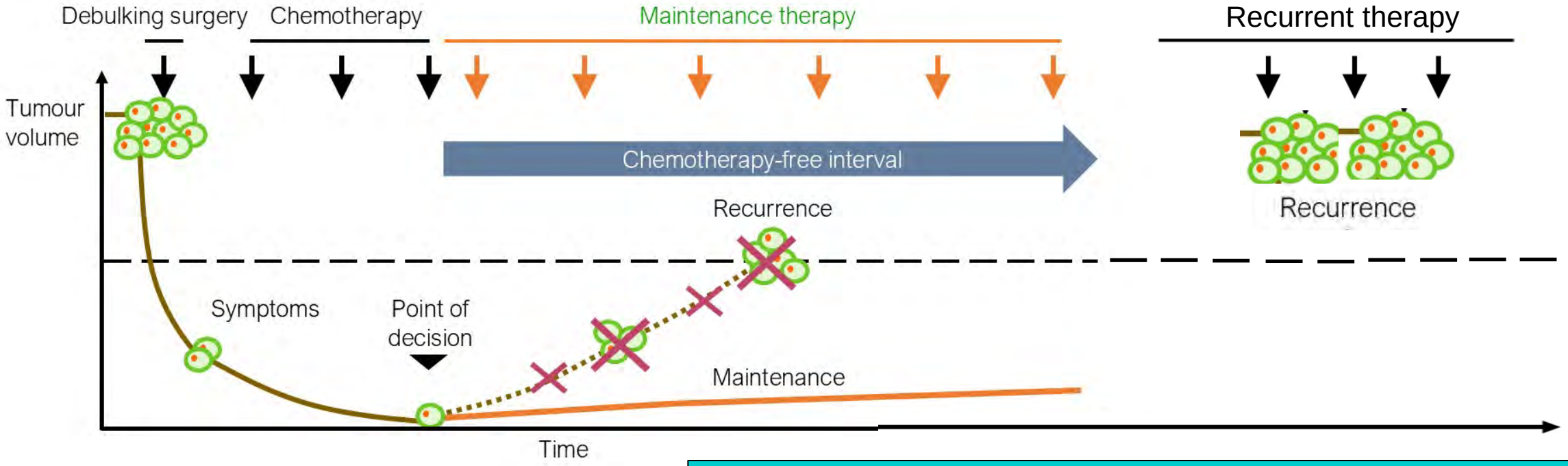


PRESENTED BY: Debra L. Richardson, MD

Harter SGO 2024, Powell SGO 2025, Hadry-Bessard ASCO 2025

Clinical Presentation of Ovarian Cancer

TRUST (Trial of Radical Upfront Surgical Therapy) ENGOT ov3/AGO-OVAR OP.7
OVATION-2 Trial: Phase I/II IP IMNN-001 with NACT
FIRST: Dostarlimab and Niraparib in First-Line Advanced



ROSELLA/GOG 3073: Ph3 Relacorilant + Nab-Pac vs Nab-Pac
Phase 2 Pembro and Lenvatinib in recurrent/persistent OCCC
Phase 1 of INCB123667: CDK2 inhibitor in PROC refractory OC

2025 ASCO® ANNUAL MEETING

ROSELLA: A Phase 3 Study of Relacorilant in Combination with Nab-Paclitaxel versus Nab-Paclitaxel Monotherapy in Patients with Platinum-Resistant Ovarian Cancer

(GOG-3073, ENGOT-ov72, APGOT-Ov10, LACOG-0223, and ANZGOG-2221/2023)

Alexander Olawaiye,[1] Laurence Gladieff, Lucy Gilbert, Jae-Weon Kim, Mariana Scaranti, Vanda Salutari, Elizabeth Hopp, Linda Mileshkin, Alix Devaux, Michael McCollum, Ana Oaknin, Aliza L. Leiser, Nicoletta Colombo, Andrew Clamp, Boglárka Balázs, Giuseppa Scandurra, Emilie Kaczmarek, Hristina I. Pashova, Sachin G. Pai, and Domenica Lorusso

[1]University of Pittsburgh School of Medicine and UPMC Magee-Women's Hospital, Gynecologic Oncology Group, Pittsburgh, PA, USA.

In collaboration with:

GOG FOUNDATION® Transforming the standard of care™

ENGOT European Network of Gynaecological Oncological Trial groups

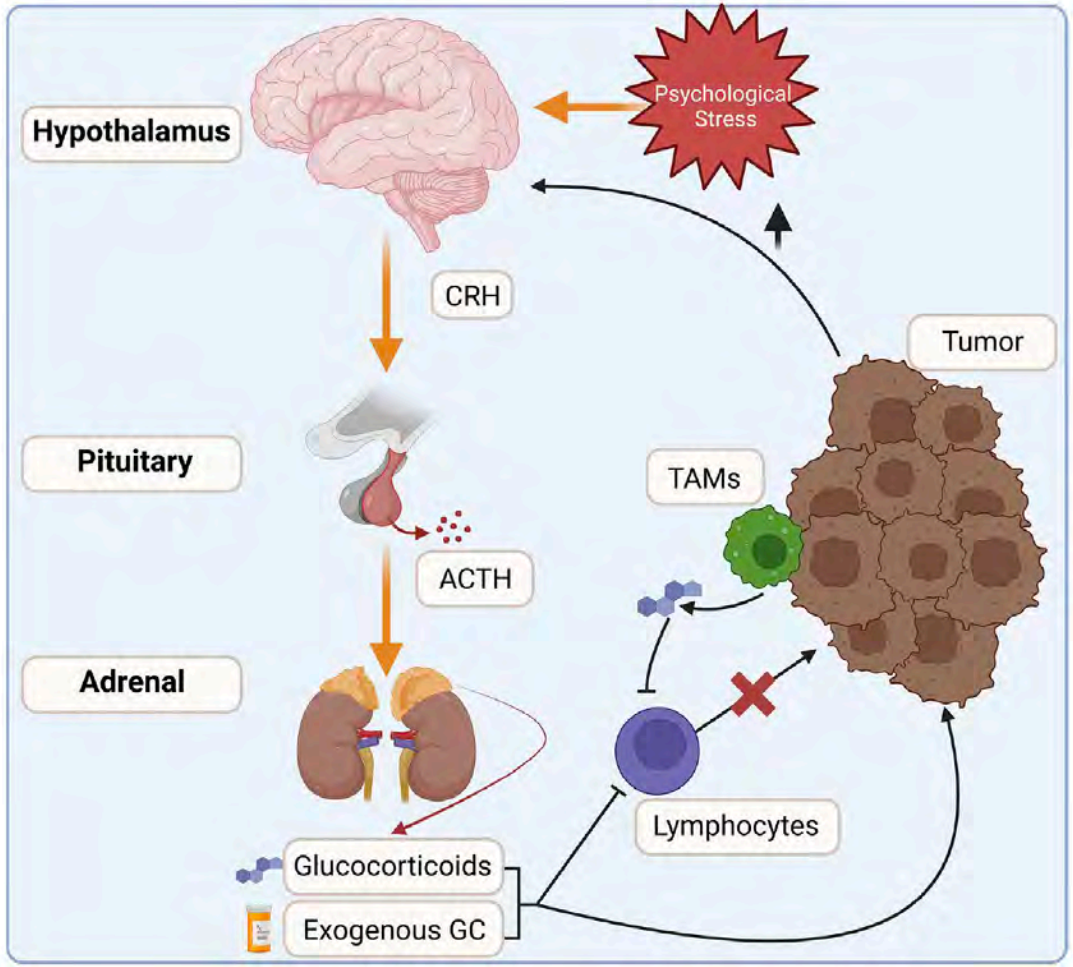
APGOT Asia-Pacific Gynecologic Oncology Trials Group

LACOG LATIN AMERICAN COOPERATIVE ONCOLOGY GROUP

ANZGOG

Targeting glucocorticoid receptor signaling: Tumors produce glucocorticoids to evade immunity

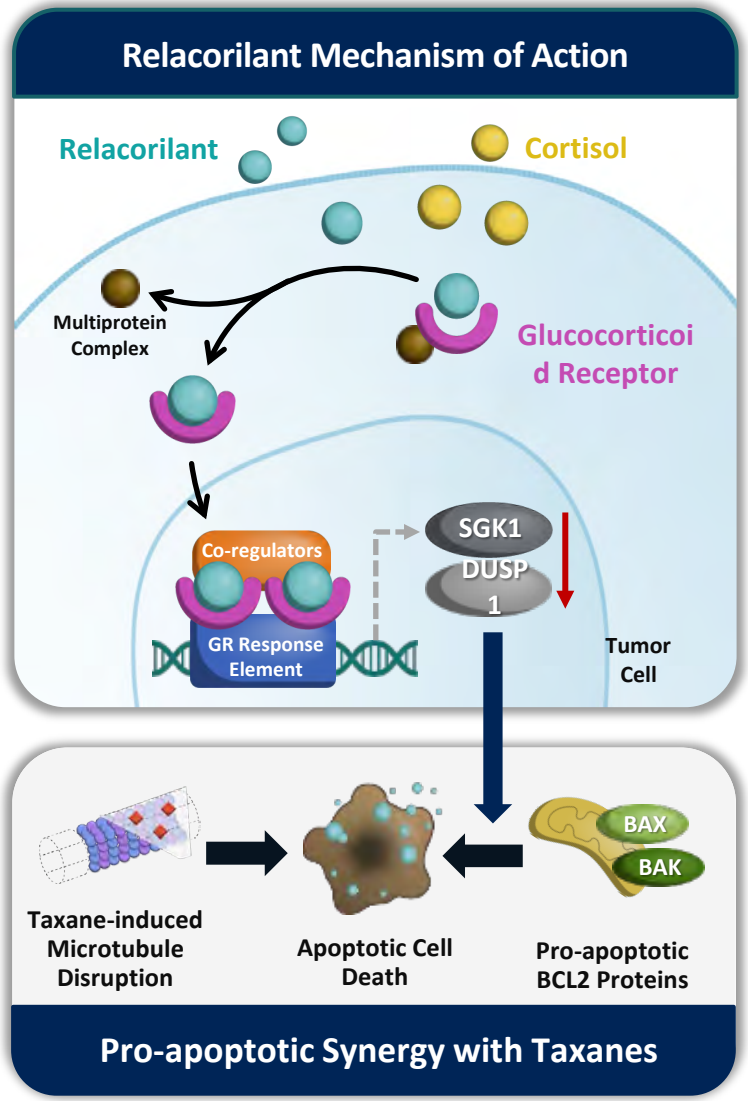
- Increased glucocorticoid signaling is commonly associated with cancers
- Glucocorticoids exert immunosuppressive effects --> suppresses cytotoxic T cells & increases M2 suppressive macrophages
- Tumors and TAMs can induce de novo steroid biosynthesis and increase glucocorticoid conc to affect T cells to evade immunity (Mahata et al Nat Comm 2020)
- **GR** is abundantly expressed in ovarian tumors, and high GR expression is associated poor outcomes[2]



[1] Luvero et al. 2014; [2] Veneris et al. 2017; Munster et al. 2019

Relacorilant binds to the Glucocorticoid Receptor and prevents cortisol from binding and activating

- Relacorilant is a novel, selective GR antagonist (SGRA) that restores the sensitivity of cancers to cytotoxic chemotherapy[3,5,6]
- Relacorilant binds to glucocorticoid receptor with high affinity and prevents cortisol from exerting its effects
- Acts like an antagonist since it prevents cortisol from binding and activating the glucocorticoid receptor
- Combined with nab-paclitaxel since it does not require steroid premedication and thus does not risk impairing the efficacy of relacorilant



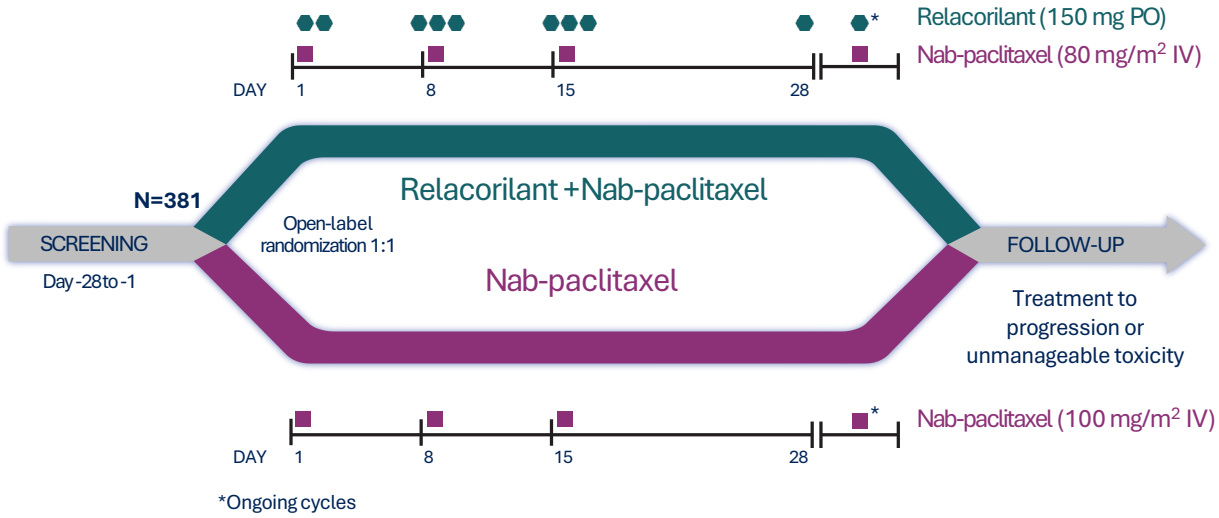
1. Martorana, et al. Int J Gynecol Cancer. 2025;35(1):100009. 2. Veneris, et al. Gynecol Oncol. 2017;146(1):153-60. 3. Greenstein, et al. Oncotarget. 2021;12(13):1243-55. 4. Melhelm, et al. Clin Cancer Res. 2009;15(9):3196-3204. 5. Stringer-Reasor, et al. Gynecol Oncol. 2015;138(3):656-62. 6. Munster, et al. Clin Cancer Res. 2022;28(15):3214-24. 7. Colombo, et al. J Clin Oncol. 2023;41(30):4779-89.

ROSELLA | Study Schema

Population

- Epithelial ovarian, primary peritoneal or fallopian tube cancer
- ECOG performance status 0 or 1
- Progression <6 months after the last dose of platinum therapy (excluding no response to, or progression in <1 month of primary platinum)
- 1–3 prior lines of therapy
- Prior bevacizumab required

NCT05257408



Stratification Factors

- Prior lines of therapy (1 vs >1)
- Region (North America vs Europe vs Korea, Australia, & Latin America)

Dual Primary Endpoints

- Progression-free survival (PFS) by RECIST v1.1 per blinded independent central review
- Overall survival

Secondary Endpoints

- PFS by RECIST v1.1 per Investigator
- ORR, DoR, CBR (RECIST v1.1)
- Response by CA-125 GCIG criteria
- Combined response (RECIST v1.1 and CA-125 GCIG criteria)
- Safety

First patient enrolled: 5th January 2023
Last patient enrolled: 8th April 2024
Data cutoff: 24th February 2025
Conducted at 117 sites in 14 countries.

CA, cancer antigen; CBR, clinical benefit rate; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; GCIG, Gynecologic Cancer Intergroup; IV, intravenous; ORR, objective response rate; PFS, progression-free survival; PO, by mouth; RECIST, Response Evaluation Criteria in Solid Tumors.

ROSELLA | Baseline Characteristics Were Well Balanced

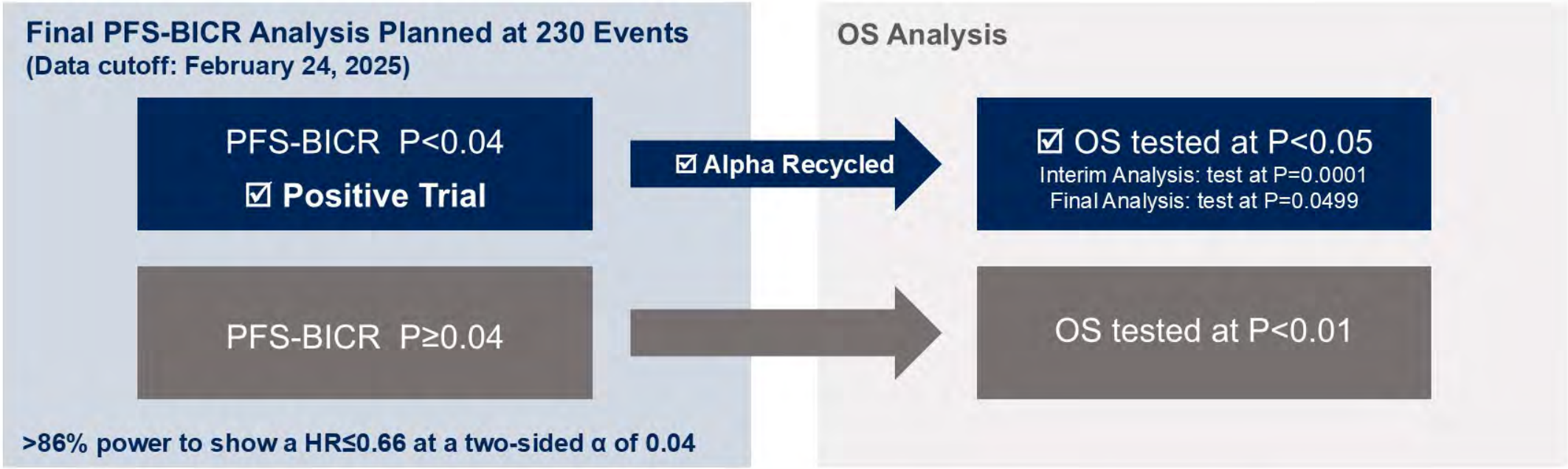
		Relacorilant + Nab-paclitaxel (N=188)	Nab-paclitaxel (N=193)
Age, median (range), years		**61** (26–85)	**62** (33–86)
Race, n (%)	White Black or African-American Asian (92% Korean) Other / Not Reported	136 **(72.3)** 3 **(1.6)** 22 **(11.7)** 27 **(14.4)**	135 **(69.9)** 2 **(1.0)** 26 **(13.5)** 30 **(15.5)**
Ethnicity, n (%)	Hispanic	16 **(8.5)**	17 **(8.8)**
Region	North America Europe Korea, Australia, and Latin America	45 **(23.9)** 107 **(56.9)** 36 **(19.1)**	45 **(23.3)** 109 **(56.5)** 39 **(20.2)**
ECOG Performance Status, n (%)*	1 or 2	53 **(28.2)**	63 **(32.6)**
BRCA1/2 Mutation, n (%)	Yes	23 **(12.2)**	24 **(12.4)**
Prior Lines of Therapy, n (%)	1 2 3	15 **(8.0)** 92 **(48.9)** 81 **(43.1)**	18 **(9.3)** 89 **(46.1)** 86 **(44.6)**
Primary Platinum Refractory, n (%)†	Yes	13 **(6.9)**	13 **(6.7)**
Prior Lines of Therapy in the Platinum-resistant Setting, n (%)	≥1	67 **(35.6)**	82 **(42.5)**
Prior Taxane in the Platinum-resistant Setting, n (%)	Yes	8 **(4.3)**	7 **(3.6)**
Prior Therapies, n (%)	Bevacizumab Taxanes Pegylated Liposomal Doxorubicin PARP Inhibitor	188 **(100)** 187 **(99.5)** 121 **(64.4)** 114 **(60.6)**	193 **(100)** 192 **(99.5)** 125 **(64.8)** 120 **(62.2)**

*In the nab-paclitaxel monotherapy arm, 1 patient had an ECOG performance status of 2. †Progressed within 3 months of the last dose of platinum from their first line platinum regimen. 97% of patients had high-grade serous carcinoma; 8 patients had high-grade endometrioid carcinoma and 2 patients had carcinosarcoma. BRCA, Breast Cancer Gene; ECOG, Eastern Cooperative Oncology Group.

Data cutoff: Feb 24, 2025

ROSELLA | Statistical Plan for Dual Primary Endpoints

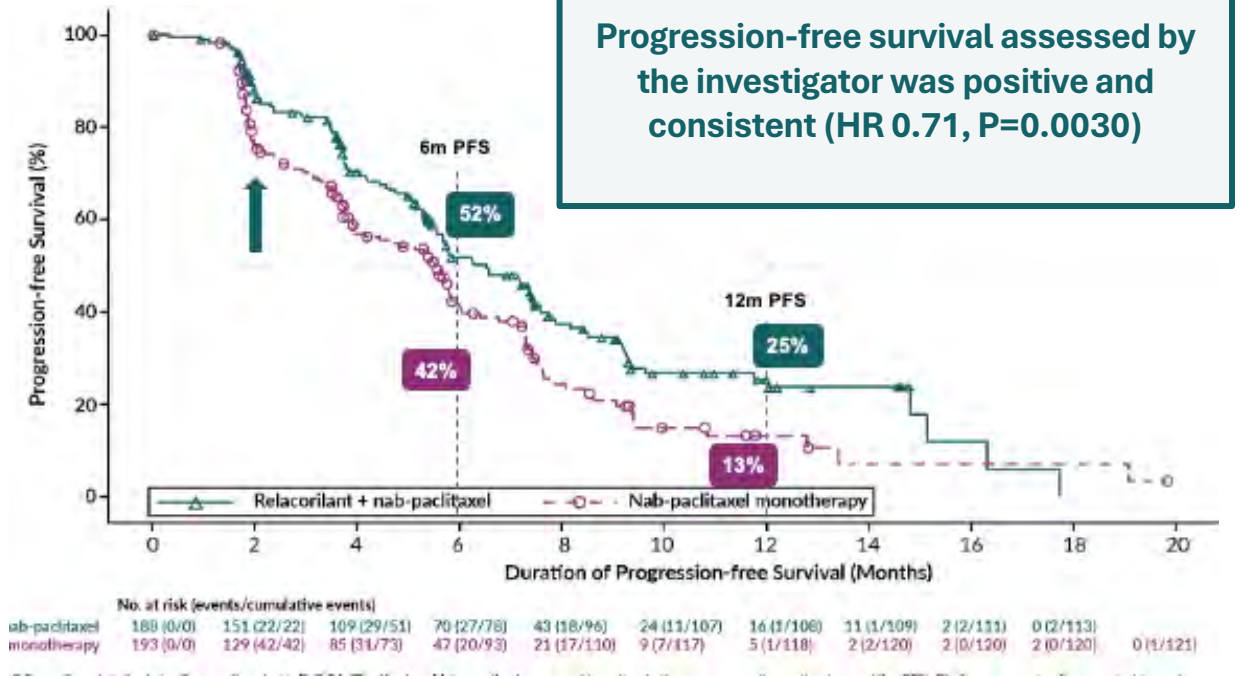
If the P-value (stratified log-rank test) for either PFS-BICR (α=0.04) or OS (α=0.01) is less than the respective, pre-specified alpha boundary, the trial is positive.



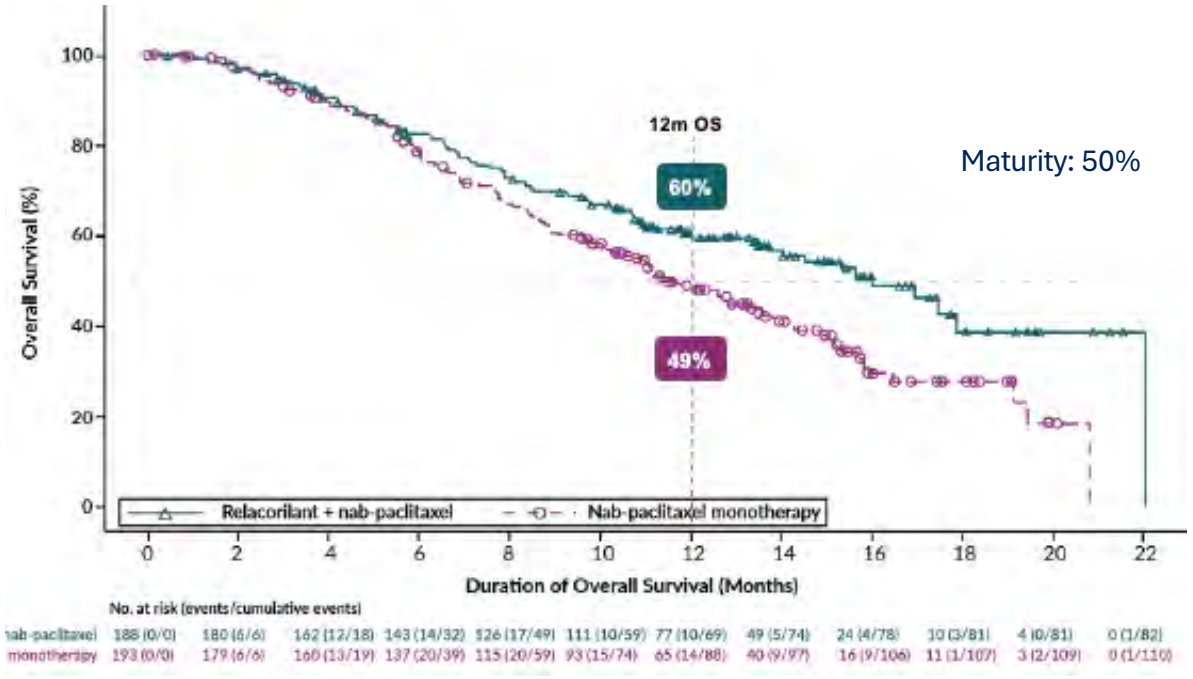
Efficacy endpoints were assessed in the intent-to-treat population (all randomized patients). A group-sequential weighted Holm procedure was used for the dual primary endpoints PFS and OS.
BICR, blinded independent central review; HR, hazard ratio; OS, overall survival; PFS, progression-free survival.

ROSELLA | Relacorilant Significantly Improved Progression-Free Survival Assessed by Blinded Review

Progression-free survival assessed by the investigator was positive and consistent (HR 0.71, P=0.0030)



	Relacorilant + Nab-paclitaxel N=188	Nab-paclitaxel N=193
Events, n (%)	113 (60.1)	121 (62.7)
Median PFS, m (95% CI)	**6.54** (5.55–7.43)	**5.52** (3.94–5.88)
HR (95% CI)	**0.70** (0.54–0.91)	
	P=0.0076 (Log-rank Test)	

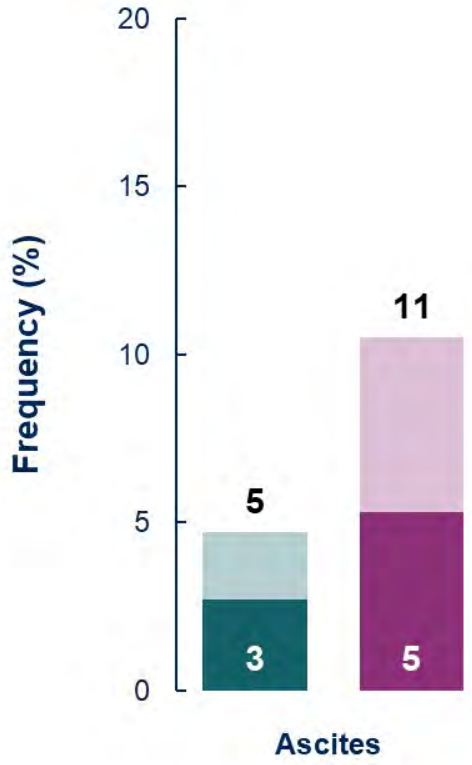


Maturity: 50%

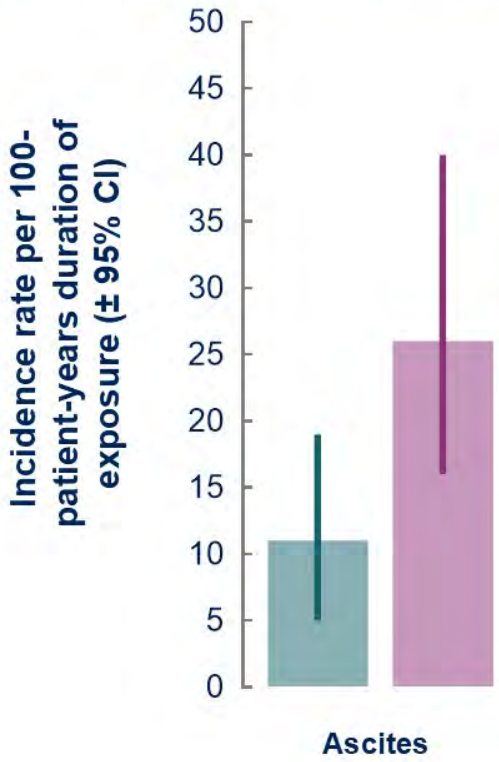
	Relacorilant + Nab-paclitaxel N=188	Nab-paclitaxel N=193
Events, n (%)	82 (43.6)	110 (57.0)
Median OS, m (95% CI)	**15.97** (13.47–NR)	**11.50** (10.02–13.57)
HR (95% CI)	**0.69** (0.52–0.92)	
	Nominal P=0.0121 (Log-rank Test)	

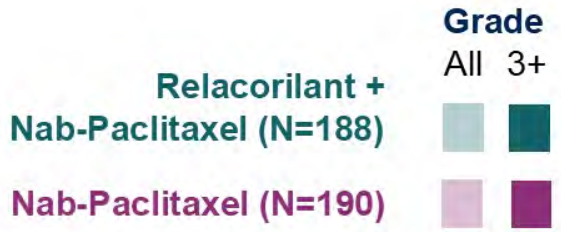
ROSELLA | Lower Incidence of Ascites with Relacorilant + Nab-paclitaxel

Unadjusted Incidence Rate



Exposure-Adjusted Incidence Rate
(Incidence normalized to the duration of exposure)



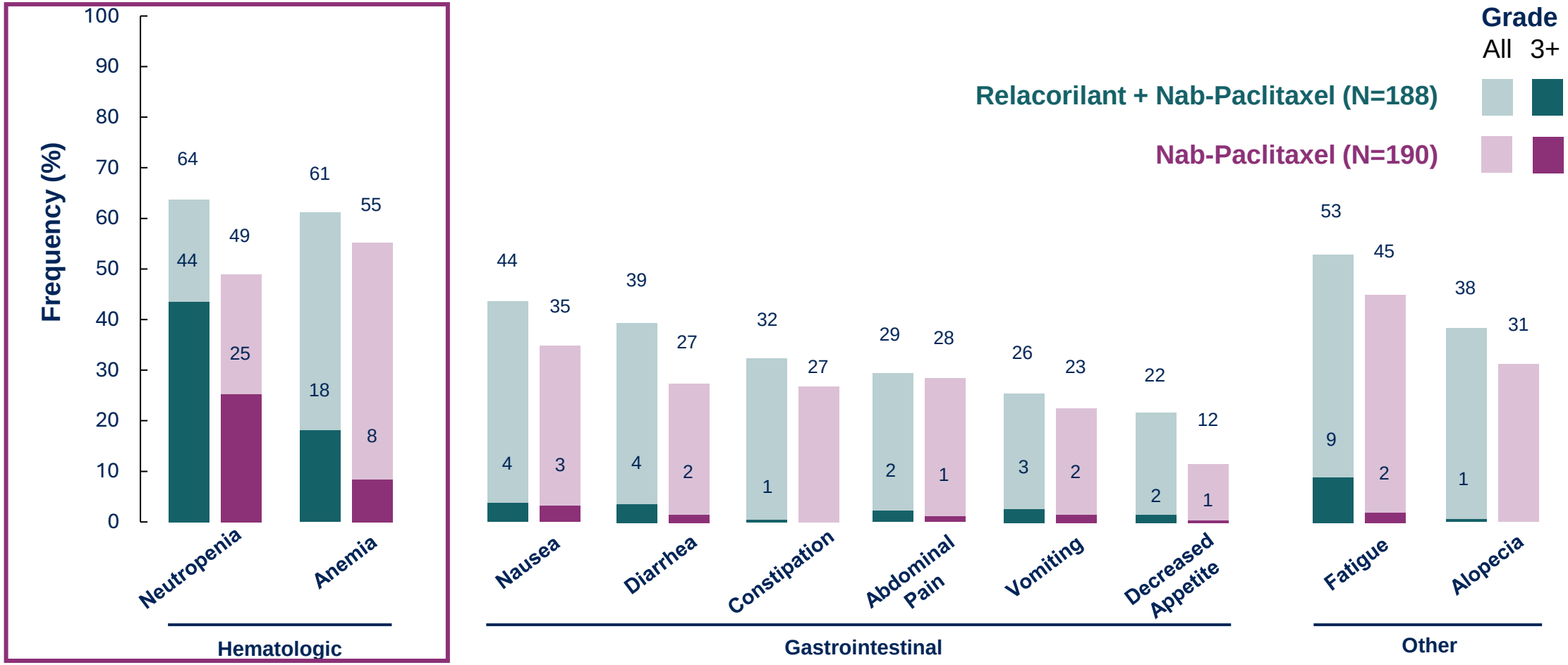


Ascites was less common in patients who received relacorilant.

Abdominal paracenteses were also less common in patients receiving the relacorilant combination compared to nab-paclitaxel monotherapy: 7.4% vs 13.2%.

Data cutoff: Feb 24, 2025

ROSELLA | Common (>20%) Adverse Events



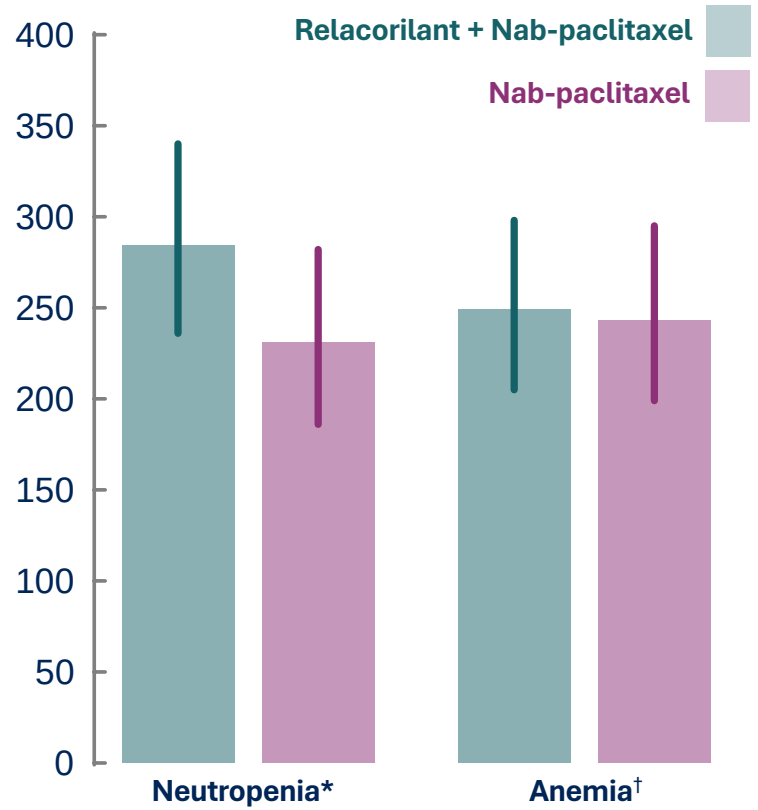
Peripheral neuropathy occurred with similar frequency in both arms (19.1% and 17.4%).
5 SAEs of febrile neutropenia were reported, 4 (2.1%) with relacorilant + nab-paclitaxel and 1 (0.5%) with nab-paclitaxel monotherapy.
5 SAEs of sepsis were reported, 3 (1.6%) with relacorilant + nab-paclitaxel and 2 (1.1%) with nab-paclitaxel monotherapy.

TEAEs that occurred in >20% of patients. Assessed in the safety population of patients who received at least one dose of study drug, N=378. Combined terms are presented for neutropenia (neutropenia, reduced neutrophil count, and febrile neutropenia), anemia (anemia, reduced hemoglobin, and reduced red blood cell count) and fatigue (fatigue and asthenia). SAEs, serious adverse events; TEAEs, treatment-emergent adverse events.

Data cutoff: Feb 24, 2025

ROSELLA | Selected Exposure-Adjusted Adverse Events

Exposure-Adjusted Incidence Rate
(AE incidence normalized to the duration of exposure)



When adjusted for duration of exposure, the incidence rates of neutropenia and anemia were comparable between study arms.

*Combined term including anemia, decreased red blood cell count, and decreased hemoglobin. †Combined term including neutropenia, decreased neutrophil count, and febrile neutropenia. Assessed in the safety population of patients who received at least one dose of study drug, N=378. AE, adverse event; CI, confidence interval. Exposure-Adjusted Incidence Rate (EAIR) is defined as Event Incidence rate per 100 patient-years-exposure (PYE): (Total number of patients with an event/Total PYE)*100. Exact 95% confidence interval based on Poisson distribution for EAIR. The total PYE to a treatment is the sum of individual patient's PYE within the treatment exposure period and is defined as: (i) For patients with an event within the exposure period: (First event start date-first dose date+1)/365.25; (ii) For patients with no event within the exposure period: (Study participation end date- first dose date +1)/365.25.
EAIR difference: [(Relacorilant + Nab-paclitaxel) - Nab-paclitaxel Monotherapy]. The exact confidence interval for difference of EAIR between two treatment arms is based on two independent Poisson distributions.

Data cutoff: Feb 24, 2025

ROSELLA | Conclusions

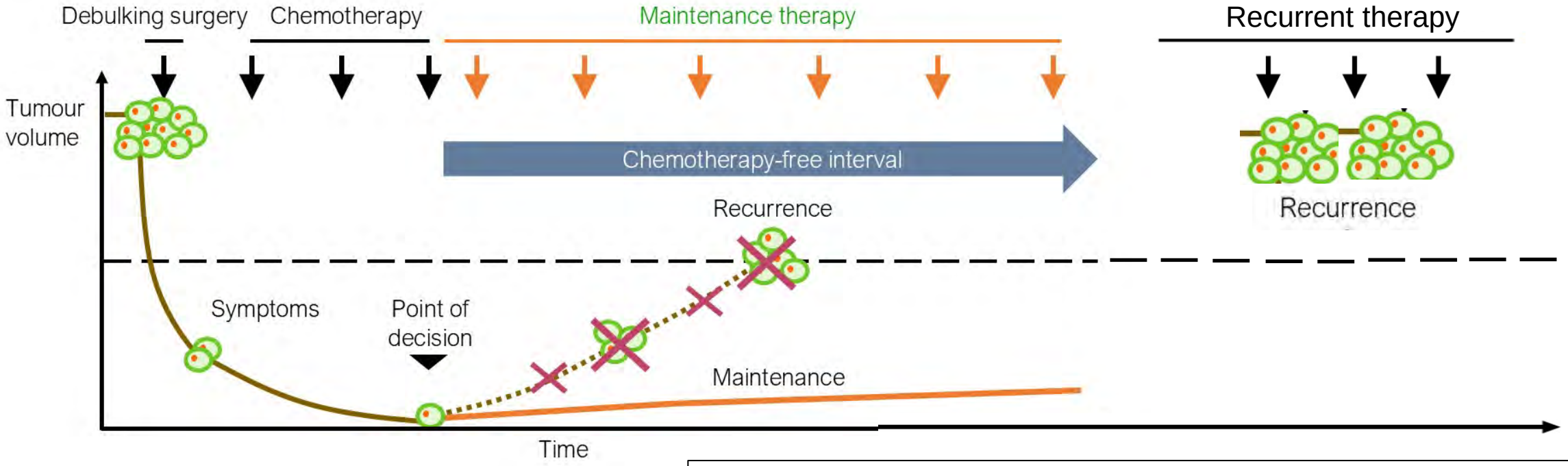
1 **ROSELLA met its primary endpoint of improving PFS**	Relacorilant, **a first-in-class, oral, SGRA, extended progression-free survival** by BICR (log-rank test P=0.0076, HR 0.70) compared to nab-paclitaxel monotherapy in patients with platinum-resistant ovarian cancer, in a population including patients who progressed within 1–3 months after their primary platinum regimen
2 **Median survival prolonged by 4.5 months**	**At this interim overall survival analysis, the addition of relacorilant to nab-paclitaxel showed a clinically meaningful improvement in overall survival** (nominal log-rank test P=0.0121, HR 0.69, median 16.0 vs 11.5 months)
3 **Well-tolerated, favorable safety profile**	Relacorilant plus nab-paclitaxel was well-tolerated, with a favorable safety profile that was comparable between treatment arms when adjusted for duration of exposure. The safety profile was consistent with previously reported data; no new signals were identified
4 **A new standard for PROC**	Intermittently dosed relacorilant plus nab-paclitaxel offers an efficacious treatment regimen for women with platinum-resistant ovarian cancer, without the need for a biomarker

BICR, blinded independent central review; PFS, progression-free survival; PROC, platinum-resistant ovarian cancer; SGRA, selective glucocorticoid receptor antagonist.

Data cutoff: Feb 24, 2025

Clinical Presentation of Ovarian Cancer: Recurrence is typical

TRUST (Trial of Radical Upfront Surgical Therapy) ENGOT ov3/AGO-OVAR OP.7
OVATION-2 Trial: Phase I/II IP IMNN-001 with NACT
FIRST: Dostarlimab and Niraparib in First-Line Advanced



ROSELLA/GOG 3073: Ph3 Relacorilant + Nab-Pac vs Nab-Pac
Phase 2 Pembro and Lenvatinib in recurrent/persistent OCCC
Phase 1 of INCB123667: CDK2 inhibitor in PROC refractory OC

2025 ASCO ANNUAL MEETING

A phase II trial of pembrolizumab and lenvatinib in recurrent or persistent clear cell ovarian carcinoma (NCT05296512)

Elizabeth K. Lee[1], Yinglu Zhou[1], Andrea E. Wahner Hendrickson[2], Gini F. Fleming[3], Carolyn Krasner[1], Panagiotis A. Konstantinopoulos[1], Elizabeth H. Stover[1], Neil S. Horowitz[1], Rebecca L. Porter[1], Alexi A. Wright[1], Ursula A. Matulonis[1], Niya Xiong[1], Hannah Sawyer[1], Nabihah Tayob[1], **Joyce F. Liu[1]**

[1]Dana-Farber Cancer Institute, Boston, MA; [2]Mayo Clinic, Rochester, Minnesota; [3]University of Chicago, Chicago, IL

Study Design

- Phase 2 multi-center study with Simon two-stage design
- All patients received combination lenvatinib and pembrolizumab
  - Starting dose lenvatinib 20mg daily; pembrolizumab 200mg IV q3weeks
- Treated until disease progression
- Co-primary endpoints: objective response rate (ORR) and rate of PFS at 6 months (PFS6)
  - ORR: H_0 5%, H_1 25%
  - PFS6: H_0 10%, H_1 30%
- At least 90% power to reject null hypothesis with a type 1 error rate of ≤10%

Key Inclusion/Exclusion Criteria

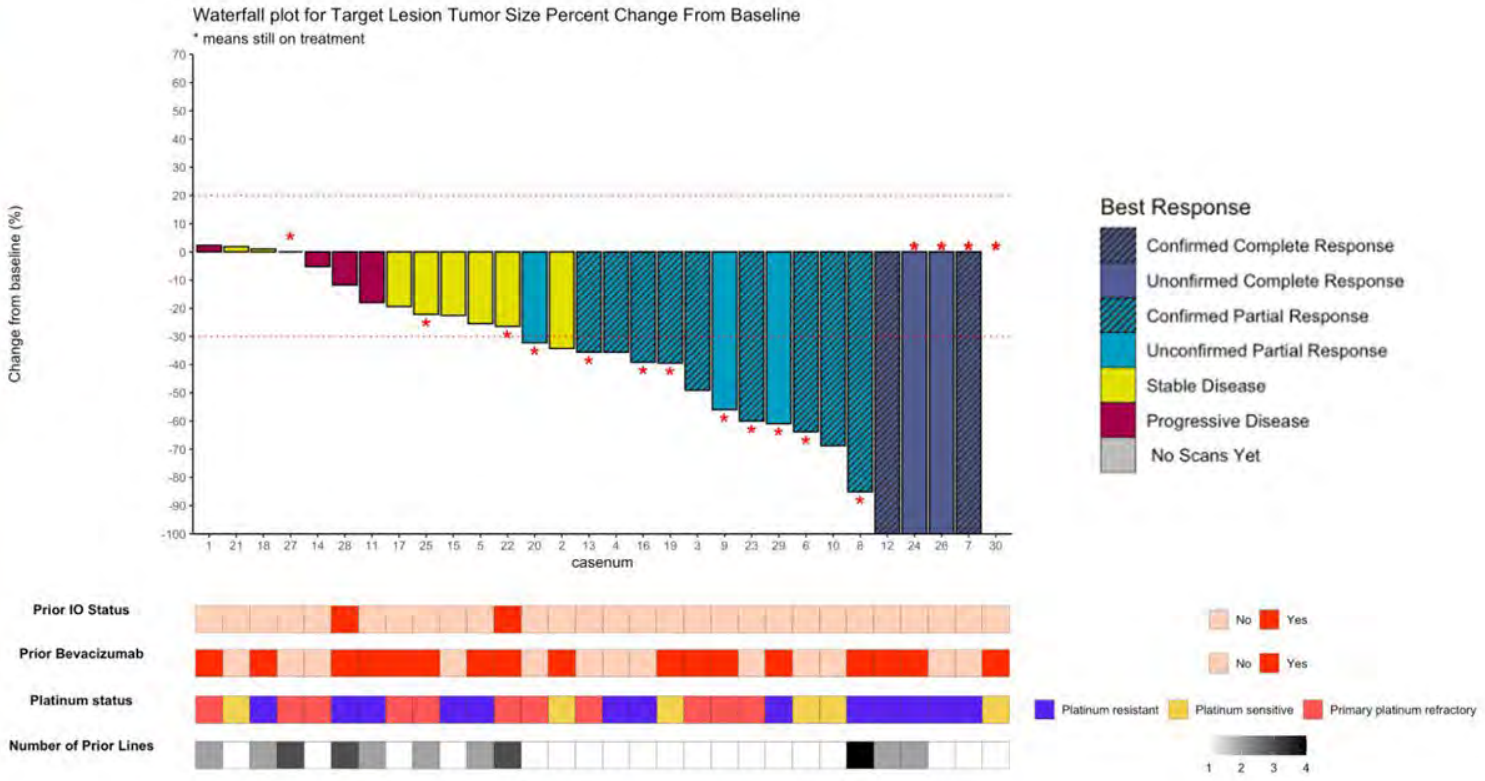
- Pathologically confirmed clear cell ovarian cancer
  - Mixed histology allowed as long as ≥ 50% clear cell histology
- Measurable disease by RECIST 1.1
- At least one prior platinum-based therapy
- No prior use of lenvatinib; prior bevacizumab use allowed
- No evidence of bowel involvement by malignancy
- No GI disorders that could interfere with normal swallowing, passage, or absorption of oral medication

Patient Characteristics

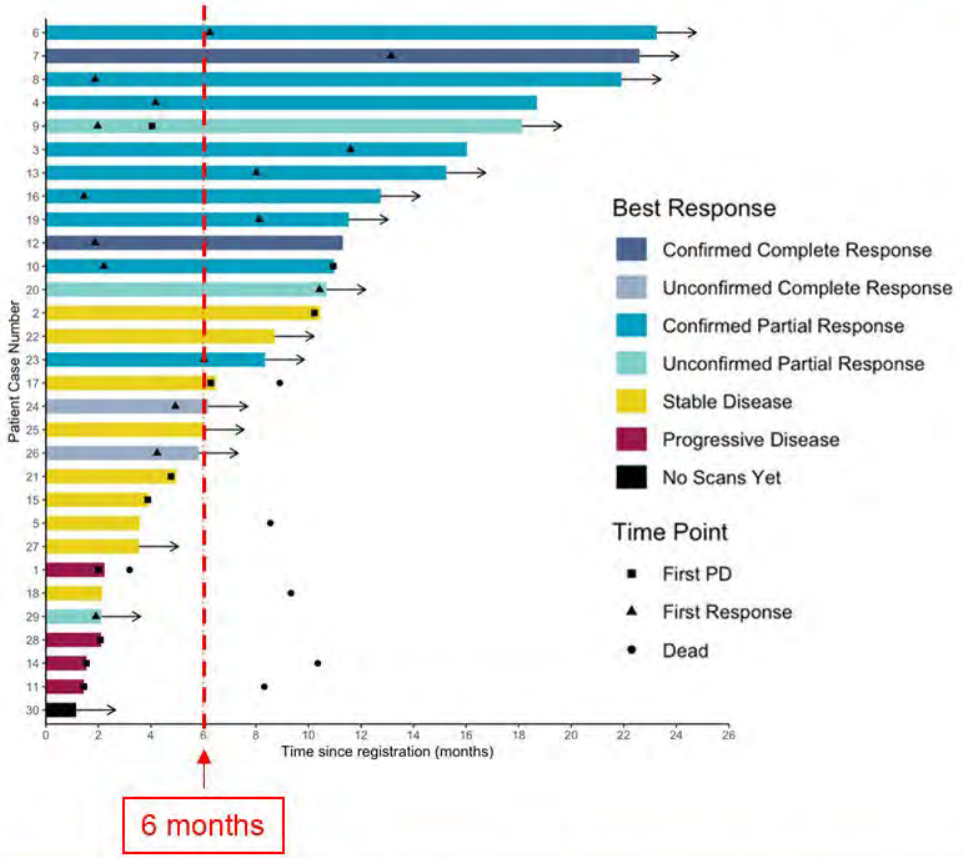
	Total (N=30)
Age (years)	
Median [Min, Max]	54.2 [35.1, 72.4]
Race	
White	25 (83.3%)
Black or African American	0 (0%)
Asian	4 (13.3%)
Other	1 (3.3%)
ECOG Performance Score	
0	19 (63.3%)
1	11 (36.7%)
Mismatch Repair Status	
pMMR/MSS	29 (96.7%)
Unknown	1 (3.3%)
Number of Prior Lines	
Median [Min, Max]	1 [1, 4]
Prior Immune Checkpoint Inhibition	
No	28 (93.3%)
Yes (Ipilimumab/Nivolumab)	2 (6.7%)
Platinum Sensitivity Status	
Primary platinum refractory (PFI <1 mo)	11 (36.7%)
Platinum resistant	13 (43.3%)
Platinum sensitive (PFI ≥6 mo)	6 (20%)

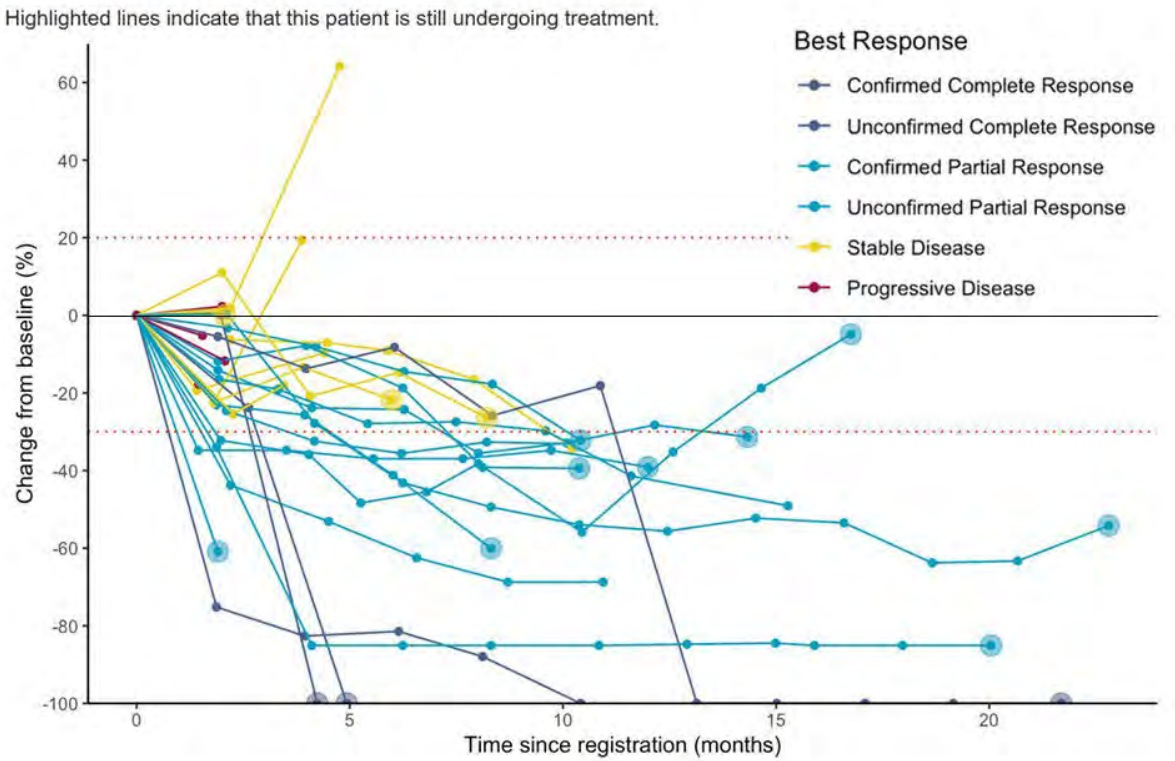
Co-primary endpoint: Objective response rate

Best Overall Response	Overall N=30
Complete response	
Confirmed	2 (6.7%)
Unconfirmed	2 (6.7%)
Partial response	
Confirmed	9 (30.0%)
Unconfirmed	3 (10.0%)
Stable disease	
≥ 6 months	3 (10.0%)
< 6 months	6 (20.0%)
Progressive disease	4 (13.3%)
Unevaluable (no scans yet)	1 (3.3%)
Objective response rate (confirmed CR and PR)	**11 (36.7%)**



Progression-free survival at 6 months





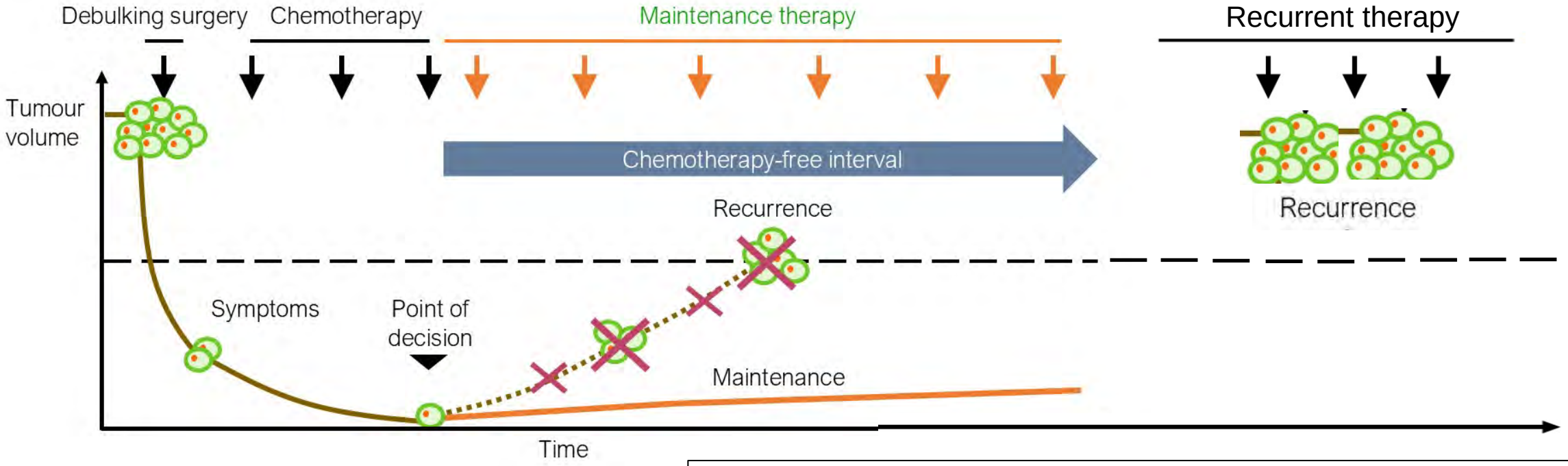
- **17 patients alive and progression-free at 6 months (median f/u time 10.2 months)**
- **Median PFS estimated at 10.9 months**

Key Takeaway Points/Conclusions

- Combination lenvatinib and pembrolizumab demonstrated promising clinical activity in clear cell ovarian cancer
- The study met both primary endpoints of objective response rate and proportion of patients alive and progression-free at 6 months.
  - **Eleven of 30 patients had a confirmed response (ORR 37%)**, with four additional patients with unconfirmed responses not yet having received a confirmatory scan.
  - **17 patients were alive and progression-free at 6 months**.
  - **Median PFS was estimated at 10.9 months**.
- The safety profile was consistent with that previously described with lenvatinib/pembrolizumab.

Clinical Presentation of Ovarian Cancer: Recurrence is typical

TRUST (Trial of Radical Upfront Surgical Therapy) ENGOT ov3/AGO-OVAR OP.7
OVATION-2 Trial: Phase I/II IP IMNN-001 with NACT
FIRST: Dostarlimab and Niraparib in First-Line Advanced

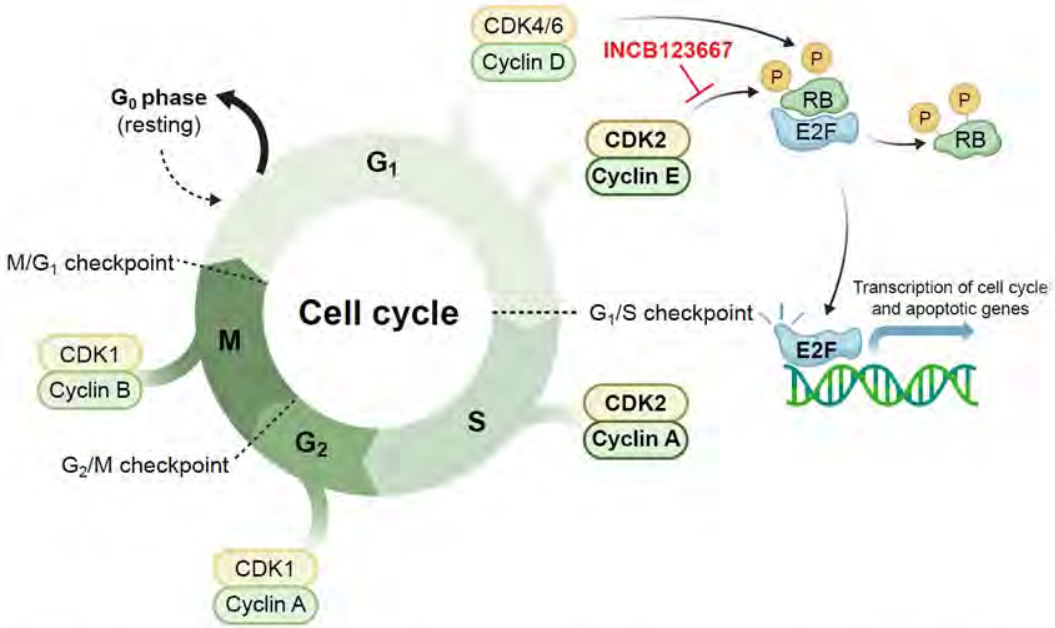


ROSELLA/GOG 3073: Ph3 Relacorilant + Nab-Pac vs Nab-Pac
Phase 2 Pembro and Lenvatinib in recurrent/persistent OCCC
Phase 1 of INCB123667: CDK2 inhibitor in PROC refractory OC

Introduction

- The cyclin-dependent kinase 2 (CDK2)/cyclin E1 (*CCNE1*) complex is crucial for DNA replication and cell cycle progession[1-4]
- *CCNE1* amplification or overexpression results in premature entry into S phase, leading to double-strand DNA breaks, stress replication forks, and genomic instability[5-8]
- *CCNE1* amplification and cyclin E1 overexpression is associated with poor prognosis[9]
- Approximately 50% of ovarian cancers overexpress cyclin E1[10,11]
- In this ongoing phase 1 study, INCB123667, a potent and selective CDK2 inhibitor, demonstrated manageable safety and preliminary efficacy in patients with advanced solid tumors (NCT05238922)[12]

Role of CDK2/Cyclin E Complex in the Cell Cycle



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1. Malumbres M. *Genome Biol.* 2014;15:122. 2. Sherr CJ. *Science.* 1996;274:1672-1677. 3. Karst AM, et al. *Cancer Res.* 2014;74:1141-1152. 4. Siu KT, et al. *Cell Cycle.* 2012;11:57-64.
5. da Costa A, et al. *Nat Rev Drug Discov.* 2023;22:38-58. 6. Xu H, et al. *Cell Rep Med.* 2021;2:100394. 7. Matson JP, et al. *eLife.* 2017;6:e30473. 8. Zeng J, et al. *Cell.* 2023;186:528-542.
9. Nakayama K, et al. *Int J Oncol.* 2016;48:506-516. 10. Gorski JW et al. *Diagnostics (Basel).* 2020;10:279. 11. MSK-IMPACT panel data from AACR Genie v16 public database. 12. Simonelli M, et al. *Ann Oncol.* 2024;35(Suppl 2):S482-S535.
CDK2, cyclin-dependent kinase 2; CCNE1, cyclin E1.

Study Design

Part 1A Dose Escalation (N=84)

- Advanced or metastatic solid tumors
- Disease progression on prior standard treatment
- Documented *CCNE1* amplification (local laboratory) was preferred but not mandatory
- ECOG PS 0 or 1

Part 1B Ovarian Cancer Cohort (N=45)

- Platinum-resistant or -refractory epithelial ovarian/fallopian/primary peritoneal carcinoma
- Up to 4 prior lines of systemic therapy
- *CCNE1* amplification (local laboratory) or central cyclin E1 overexpression
- ECOG PS 0 or 1

- Starting at 50 mg qd; escalated to
  - 50 mg bid
  - 75 mg qd/bid
  - 125 mg qd
  - 150 mg qd*

Identification of RDEs

- RDEs
  - 50 mg bid
  - 100 mg qd
  - 125 mg qd

Objectives

- Primary: Safety, tolerability, and determine MTD and RDEs of INB123667 monotherapy
- Secondary: Preliminary efficacy of INCB123667 as monotherapy in terms of ORR, DCR, and DOR
- Exploratory: Biomarkers that predict pharmacologic activity and/or correlate with clinical safety or efficacy

*Continuous or intermittent dosing.
bid, twice daily; CCNE1, cyclin E1; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; MTD, maximum tolerated dose; ORR, overall response rate; qd, daily; RDE, recommended dose for expansion.

Patients and Disease Characteristics

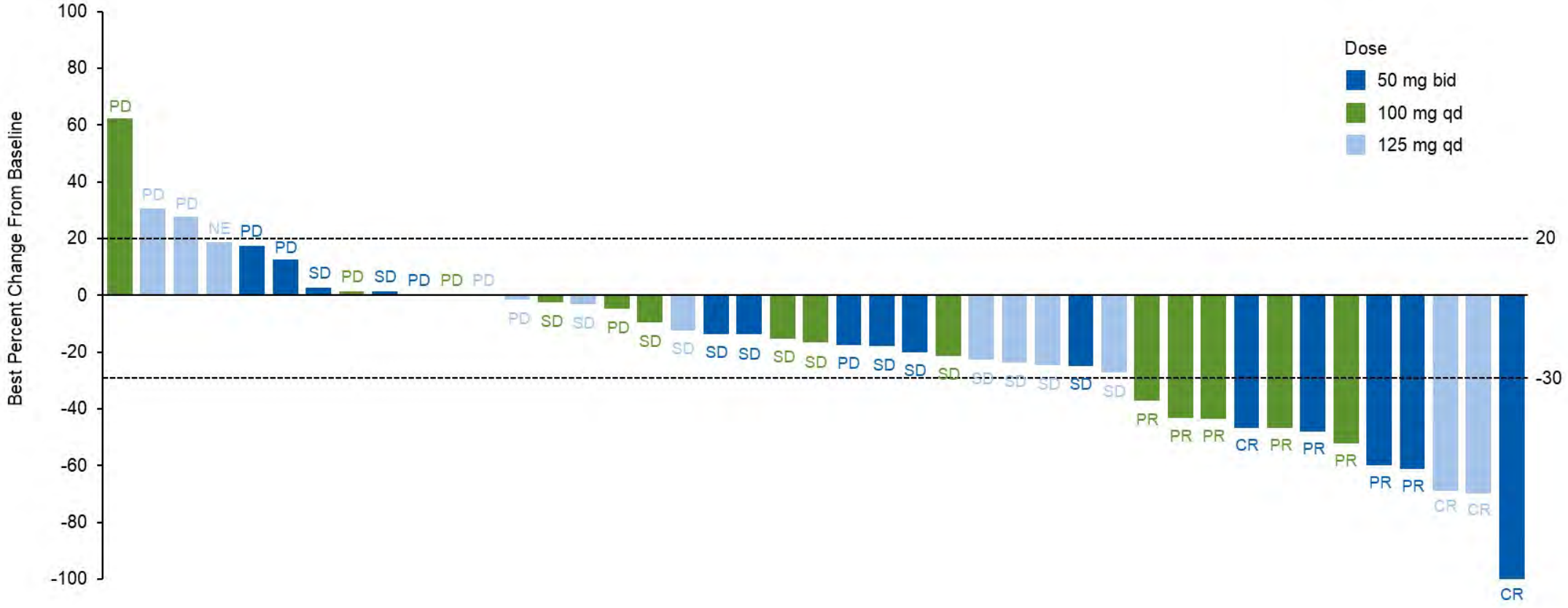
- 90 patients with ovarian cancer were enrolled and received INCB123667 (45 in Part 1A and 45 in Part 1B)
- As of the data cutoff (March 10, 2025), treatment was ongoing in 8 patients (8.9%)
- 82 patients (91.1%) discontinued, primarily for disease progression (n=70; 77.8%)
  - 3 patients (3.3%) discontinued for AEs
- **Here we report safety and efficacy data of Part 1B**

Baseline Characteristic	Total (N=90)
Age, median (range), years	62.0 (37.0-80.0)
≥65 years, n (%)	31 (34.4)
Race, n (%)	
White	64 (71.1)
Asian	8 (8.9)
Not reported/unknown/missing	18 (20.0)
ECOG PS, n (%)	
0	68 (75.6)
Histology, n (%)	
Serous	72 (80.0)
Clear cell	5 (5.6)
Endometrioid	1 (1.1)
Other*	12 (13.3)
Cyclin E1 overexpression,† n (%)	83 (92.2)
CCNE1 amplification,† n (%)	51 (56.7)
Prior systemic therapies, median (range)	4 (1-12)
Prior PARPi, n (%)	62 (68.9)
Prior bevacizumab, n (%)	69 (76.7)

*Mucinous, carcinosarcoma, neuroendocrine and adenocarcinoma-NOS.
†Overexpression as determined by central testing; CCNE1 amplification determined by either local results or central testing.
AE, adverse event; CCNE1, cyclin E1; ECOG PS, Eastern Cooperative Oncology Group performance status; NOS, not otherwise specified; PARPi, poly-ADP ribose polymerase inhibitor.

Best Percent Change in Target Lesions From Baseline

- Over 70% of patients had a reduction in tumor size compared with baseline



bid, twice daily; CR, complete response; PD, progressive disease; PR, partial response; qd, daily; SD, stable disease.

Efficacy (Part 1B)

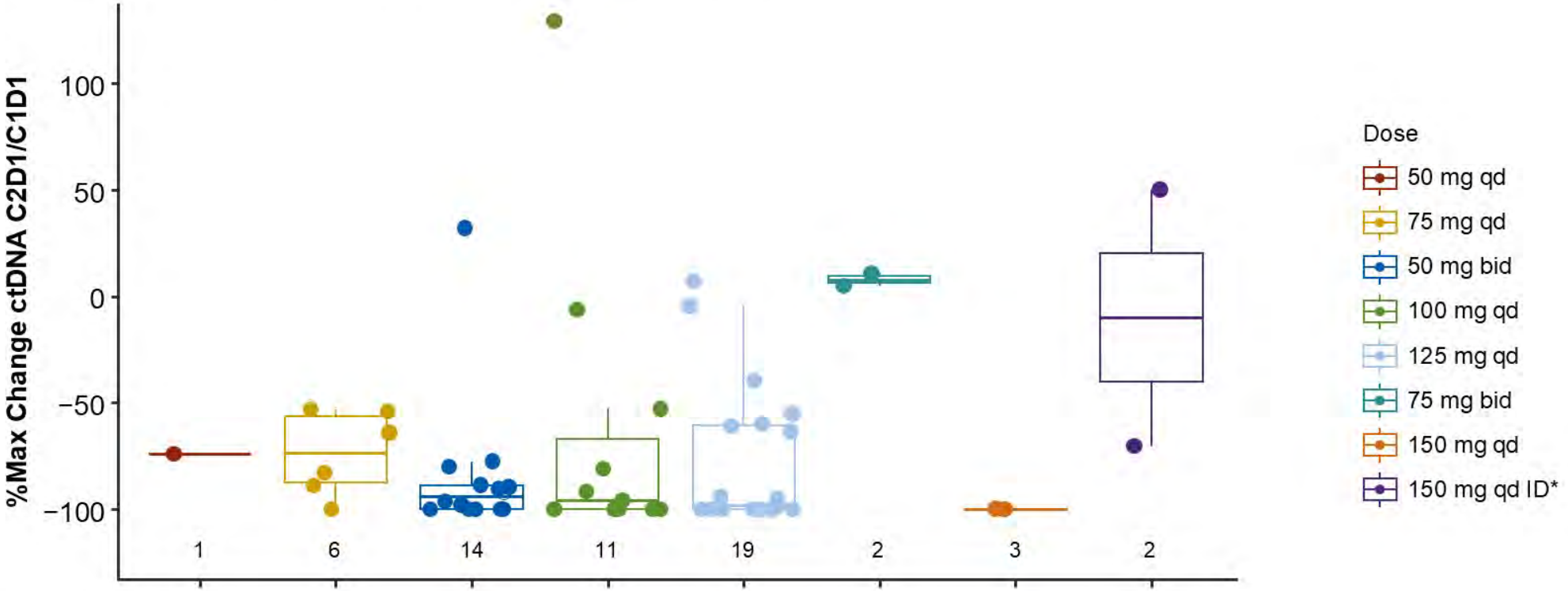
- Best response rate was achieved at 100 mg daily
  - In the combined dataset (50 mg bid and 100 mg qd), ORR was 33.3%, median DOR 3.6 months, and median PFS 5.3 months
- Cyclin E1 overexpression was noted in all but 1 responder (11/12), whose status was unknown due to limited tissue
- Responses were observed in patients with *CCNE1* amplification (7/29) and in patients without *CCNE1* amplification but with cyclin E1 overexpression (5/16)

Variable	50 mg bid (n=16)	100 mg qd (n=14)	125 mg qd (n=15)
Overall response rate, n (%) [95% CI]	5 (31.3) [11.0, 58.7]	5 (35.7) [12.8, 64.9]	2 (13.3) [1.7, 40.5]
Complete response	2 (12.5)	0 (0)	2 (13.3)
Partial response	3 (18.8)	5 (35.7)	0 (0)
Stable disease	7 (43.8)	5 (35.7)	6 (40.0)
Progressive disease	4 (25.0)	4 (28.6)	4 (26.7)
Not evaluable/missing, n (%)	0 (0)	0 (0)	3 (20.0)
Disease control rate, n (%) [95% CI]	12 (75.0) [47.6, 92.7]	10 (71.4) [41.9, 91.6]	8 (53.3) [26.6, 78.7]
Duration of response, median (95% CI), months	4.5 (1.7, NE)	3.6 (1.9, NE)	-
Progression-free survival, median (95% CI), months	5.5 (2.0, 7.3)	4.5 (2.0, 6.2)	5.4 (1.8, 9.0)

Median follow-up of 9.4 months.
bid; twice daily; CCNE1, cyclin E1; CI, confidence interval; DOR, duration of response; NE, not evaluable; ORR, overall response rate; PFS, progression-free survival; qd, daily.

Pharmacodynamics: ctDNA

- A decrease in ctDNA was observed on treatment (C2D1) compared with baseline (C1D1), consistent with the cell growth arrest mechanism of action of CDK2 inhibition



*5 days on/2 days off.
% max change in ctDNA determined by using PredicineSCORE™.
bid, twice daily; ctDNA, circulating tumor deoxyribonucleic acid; ID, intermittent dose; qd, daily.

Conclusions

- In patients with recurrent platinum-resistant or refractory ovarian cancer, single agent INCB123667 at the dose of 100 mg daily achieved
  - ORR of 33.3% (31.3% at 50 mg bid and 35.7% at 100 mg qd)
  - Median DOR of 3.6 months (4.5 months at 50 mg bid and 3.6 months at 100 mg qd)
  - Median PFS of 5.3 months (5.5 months at 50 mg bid and 4.5 months at 100 mg qd)
- All responders had cyclin E1 overexpression except 1 with unknown status
- INCB123667 showed manageable safety and tolerability
  - Most common TEAEs were hematologic and gastrointestinal, predominantly grade ≤2
  - Few (2.2%) patients discontinued due to TEAEs
- The observed safety, tolerability, and encouraging antitumor activity of single agent INCB123667 provides proof of concept and supports the advancement of INCB123667 into pivotal studies in patients with advanced or recurrent ovarian cancer

bid, twice daily; DOR, duration of response; ORR, overall response rate; PFS, progression-free survival; qd, daily; TEAE, treatment-emergent adverse event.

Assessment of Homologous Recombination Deficiency and *BRCA* Status in Ovarian Cancer: Analytical Performance and Relevance of a Decentralized NGS Assay for Comprehensive Genomic Profiling

Mohit Gupta*[1], Michael Rozas[1], Vinay Kumar Mittal[1], Xiaoping Duan[1], Michael Allen[1], Cheng-Zong Bai[1], Jim Veitch[1], Jose Luis Costa[1], Philip Jermann[1], Seth Sadis[1], Elaine Wong-Ho[1], Luca Quagliata[1], Julia Welz[2], Domenica Lorusso[3], Maria Jesús Rubio[4], Regina Berger[5], Sakari Hietanen[6], Guillaume Bataillon[7], Eric Pujade-Lauraine[8], Isabelle Ray-Coquard[9].

[1]Thermo Fisher Scientific, South San Francisco, CA; Carlsbad, CA; Ann Arbor, MI; Reinach, Switzerland; Porto, Portugal. [2]Department of Gynecology & Gynecologic Oncology, Kliniken Essen-Mitte, Essen, and AGO Studiengroup, Germany. [3]Humanitas San Pio X and Humanitas University, Milan, and MITO, Italy. [4]Hospital Universitario Reina Sofia, Córdoba, and GEICO, Spain. [5]Medical University Innsbruck, Department for Gynecology and Obstetrics, Innsbruck, and AGO Austria Study Center, Austria. [6]Turku University Hospital, Turku, Finland, and NSGO-CTU. [7]Department of Pathology, IUCT-Oncopole Toulouse, Toulouse, France. [8]ARCAGY Research, Paris, France. [9]Centre Léon Bérard, Lyon, and GINECO, France.

*Corresponding author: Mohit Gupta, mohit.gupta@thermofisher.com

Key Takeaways

1. **OCA Plus is a distributable NGS assay that allows CGP for solid tumors including HRD evaluation with only 20 ng DNA input and very high sequencing success rate.**
2. **GI is characterized using a proprietary algorithm that generates a quantitative score, GIM, summarizing different unbalanced copy number events across the autosomes.**
3. **GIM status is combined with *BRCA1/2* mutational status to provide overall HRD status that has high overall percent agreement of 91% with the reference method.**
4. **PFS analysis demonstrated clinical research relevance for HRD assessment using OCA Plus with a significantly improved hazard ratio for the HRD positive cases (HR: 0.37, p < 0.005) compared to the HRD negative cases (HR: 0.91, p=0.78).**

	BRCA1/2 mutational status (n = 125)	GIM status (n = 125)	HRD status (*BRCA1/2* + GIM) (n = 125)
Positive Percent Agreement	95.5	78.4	92.4
Negative Percent Agreement	100	88.4	89.1
Overall Percent Agreement	98.4	86.4	91.2

Retrospective Study Results

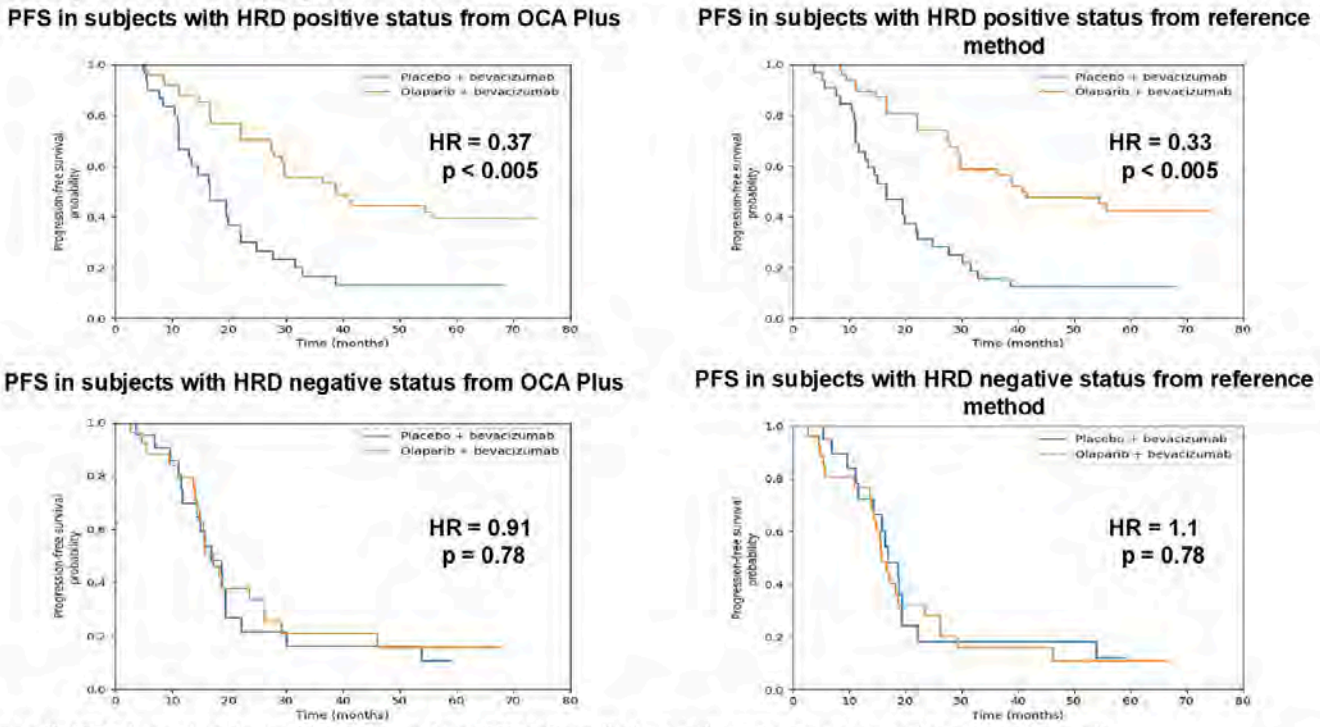


Figure 2. PFS for subjects by HRD status from OCA Plus (left panel) and reference method (right panel).

PFS for subjects taking olaparib + bevacizumab or placebo + bevacizumab was assessed and analyzed for subjects **stratified according to overall HRD status from OCA Plus** and reference method respectively (Figure 2). The **stratification with only *BRCA1/2* mutation status or only GI status from HRD assessment using OCA Plus also demonstrates significantly better hazard ratio** by itself as shown in Table 2.

Summary of ASCO Annual Meeting 2025 Ovarian Cancer Plenary

- TRUST (Trial of Radical Upfront Surgical Therapy) ENGOT ov3/AGO-OVAR
  - Primary endpoint – OS. OS improvement was not seen. First Ph3 RCT to show improved median PFS for PDS compared to ICS particularly in Stage III
- OVATION-2 Trial: Phase I/II IP NACT +/- IMNN-001 (IL-12 gene lipopolymer nanoparticle)
  - Primary Endpoint: Safety and PFS. Increased activity in HRD patients. Confirmatory Ph3 underway
- FIRST: Carbo/pac +/- Dostarlimab +/- Bev followed by maintenance niraparib +/- dostarlimab in first-line
  - Primary Endpoint PFS in the ITT. Dostarlimab + maintenance niraparib was statistically significant though clinically modest
- ROSELLA/GOG 3073: Phase III Nab-Pac +/- Relacorilant
  - Primary Endpoint PFS and OS. Met PFS endpoint. Interim OS showed clinically meaningful 16 vs. 11.5 months
- Phase 2 Pembro and Lenvatinib in recurrent/persistent OCCC
  - Primary Endpoint of ORR (25%) and PFS at 6 months (30%). Met ORR with 37% and 56% are PFS at 6 months
- Phase 1 of INCB123667: CDK2 inhibitor in PROC refractory OC
  - Primary Endpoint: Safety. Secondary ORR. Safe with most common TEAEs hematologic and GI grade $\leq$ 2. ORR of 33% in CCNE1 amp/OE tumors

Thank you!