Gynecologic Oncology
Best of ASCO

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Disclosure

I have no relevant financial relationships or conflicts of interests to disclose

CERVIX CANCER

RTOG 0724/GOG-0724

Adjuvant Chemotherapy following Concurrent Chemoradiation (CRT) in High-Risk Early-Stage Cervical Carcinoma Patients Following Radical Hysterectomy: Results of NRG Oncology/RTOG 0724/GOG-0724

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Schema

- Clinical stage IA2, IB, or IIA with high risk factors after surgery
- Radical hysterectomy – positive nodes and/or positive parametrium

STRATIFY		RANDOMIZE	
	Intention To Use Brachytherapy 1. No 2. Yes RT Modality 1. Standard RT 2. IMRT Radiation Therapy Dose 1. 45 Gy 2. 50.4 Gy		<u>Arm 1</u> Concurrent weekly cisplatin and RT ± brachytherapy Versus <u>Arm 2</u> Concurrent weekly cisplatin and RT ± brachytherapy FOLLOWED BY Carboplatin and paclitaxel

RTOG 0724/GOG-0724

Results: Enrollment

- Enrollment: 9/16/2009 - 3/2/2022
- 236 patients randomized - 212 eligible
  - 109 Cisplatin-RT (Arm 1)
  - 103 Cisplatin-RT + Chemo (Arm 2)
- Median age 46 years (min-max: 25 -77)
- Median follow-up for all patients – 4.5 years (min-max: 0.02-12.8)

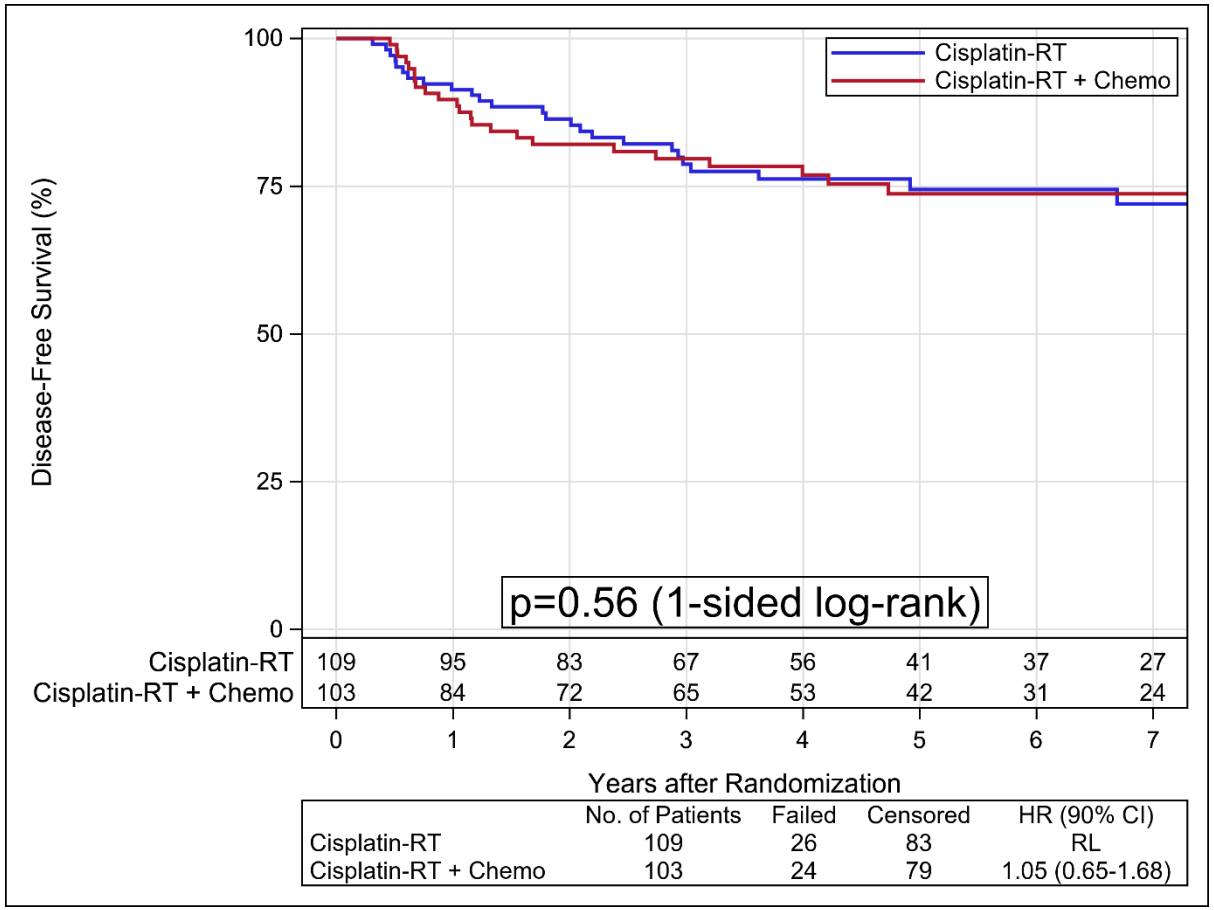
	Cis + RT (n=109)	Cis + RT + chemo (n=103)	Total (n=212)
Race			
White	60 (55%)	49 (48%)	109 (51%)
Asian	42 (39%)	40 (39%)	82 (39%)
Other	7 (6%)	14 (14%)	21 (10%)
Hysterectomy			
Open	64 (59%)	54 (52%)	118 (56%)
Laparoscopic/Robotic	45 (41%)	49 (48%)	94 (44%)
Histological type			
Squamous cell	88 (81%)	74 (72%)	162 (76%)
Adenosquamous	6 (6%)	5 (5%)	11 (5%)
Adenocarcinoma	15 (14%)	24 (23%)	39 (18%)

	Cis + RT (n=109)	Cis + RT + chemo (n=103)	Total (n=212)
Stage			
IA2	3 (3%)	6 (6%)	9 (4%)
IB	97 (89%)	88 (85%)	185 (87%)
IIA	9 (8%)	9 (9%)	18 (8%)
Positive pelvic nodes			
No	33 (30%)	23 (22%)	56 (26%)
Yes	76 (70%)	80 (78%)	156 (74%)
Positive para-aortic nodes			
No	54 (50%)	43 (42%)	97 (46%)
Yes	3 (3%)	5 (5%)	8 (4%)
Not dissected	52 (48%)	55 (53%)	107 (50%)

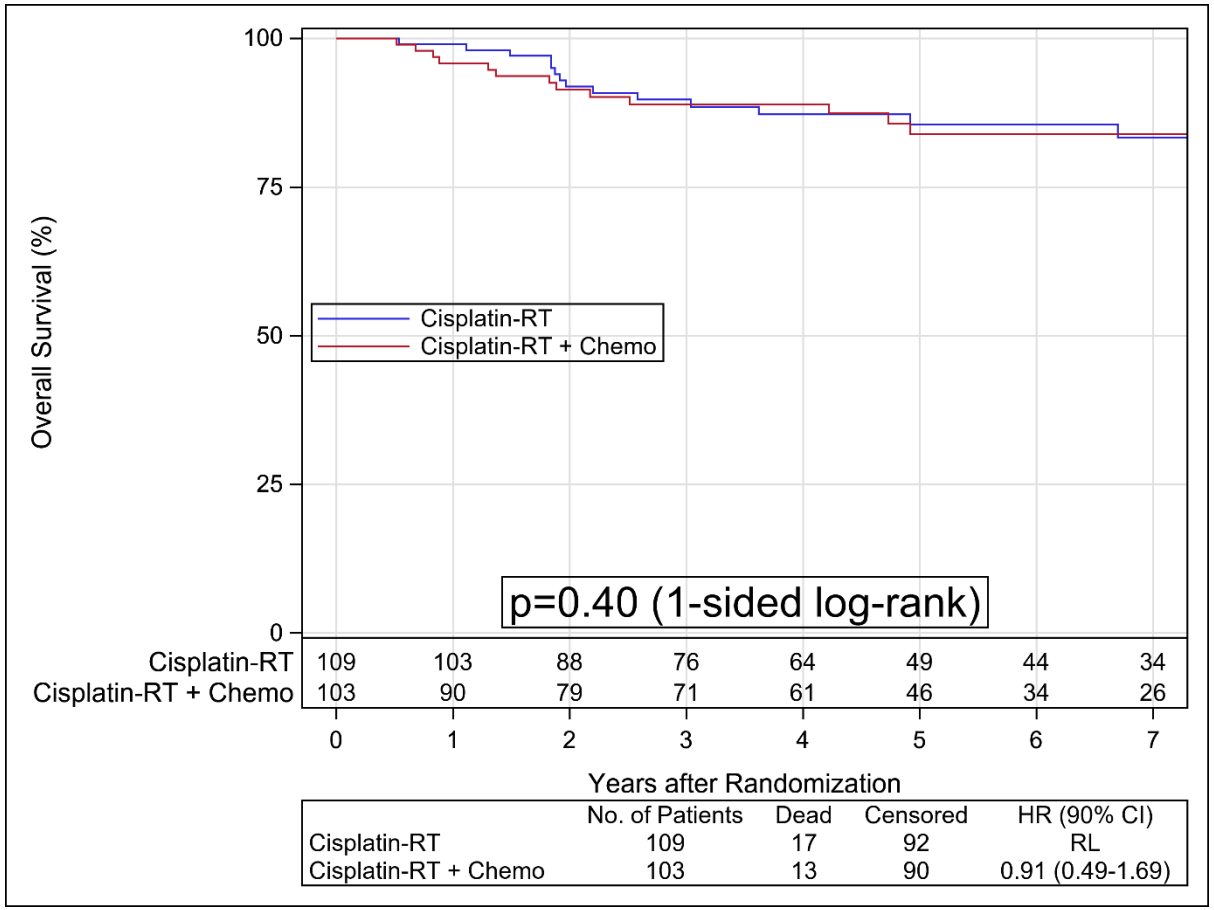
	Cis + RT (n=109)	Cis + RT + chemo (n=103)	Total (n=212)
Intention to use Brachytherapy			
No	61 (56%)	58 (56%)	119 (56%)
Yes	48 (44%)	45 (44%)	93 (44%)
RT modality			
Standard RT	46 (42%)	41 (40%)	87 (41%)
IMRT	63 (58%)	62 (60%)	125 (59%)
RT dose			
45 Gy	35 (32%)	30 (29%)	65 (31%)
50.4 Gy	74 (68%)	73 (71%)	147 (69%)

RTOG 0724/GOG-0724

Disease-Free Survival



Overall Survival



RTOG 0724/GOG-0724

Conclusion and Key Takeways

- The addition of systemic chemotherapy to CRT did not improve DFS or OS in patient with high-risk cervical cancer after radical hysterectomy.

- There is no role for chemotherapy following CRT in the treatment of cervical cancer.

ENDOMETRIAL CANCER

SIENDO-LONG TERM FOLLOW UP UPDATE

Long-term Follow-up of Selinexor Maintenance for Patients With *TP53*wt Advanced or Recurrent Endometrial Cancer: A Prespecified Subgroup Analysis From the Phase 3 ENGOT-EN5/GOG-3055/SIENDO Study

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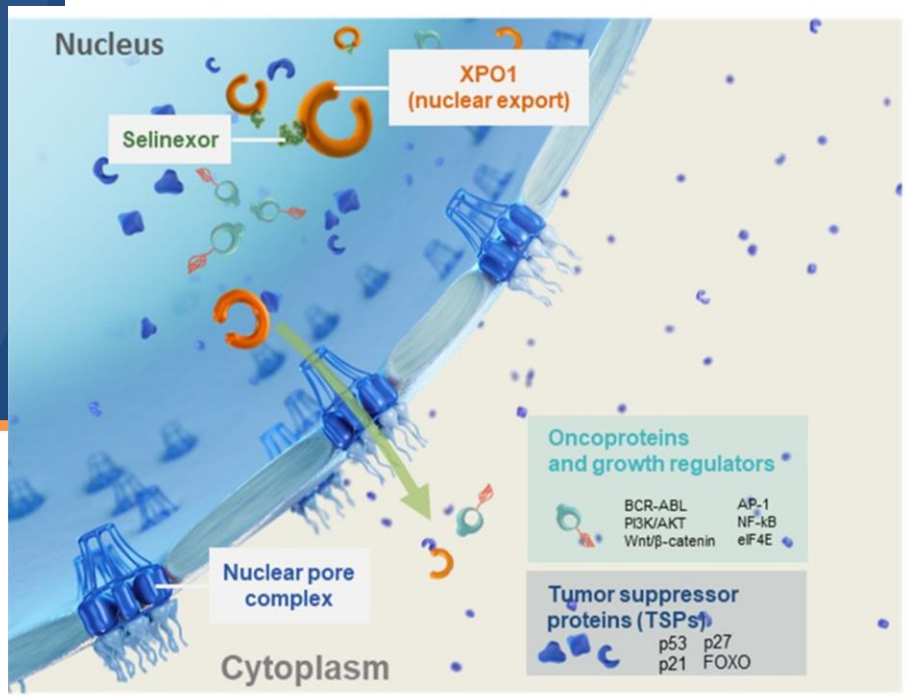


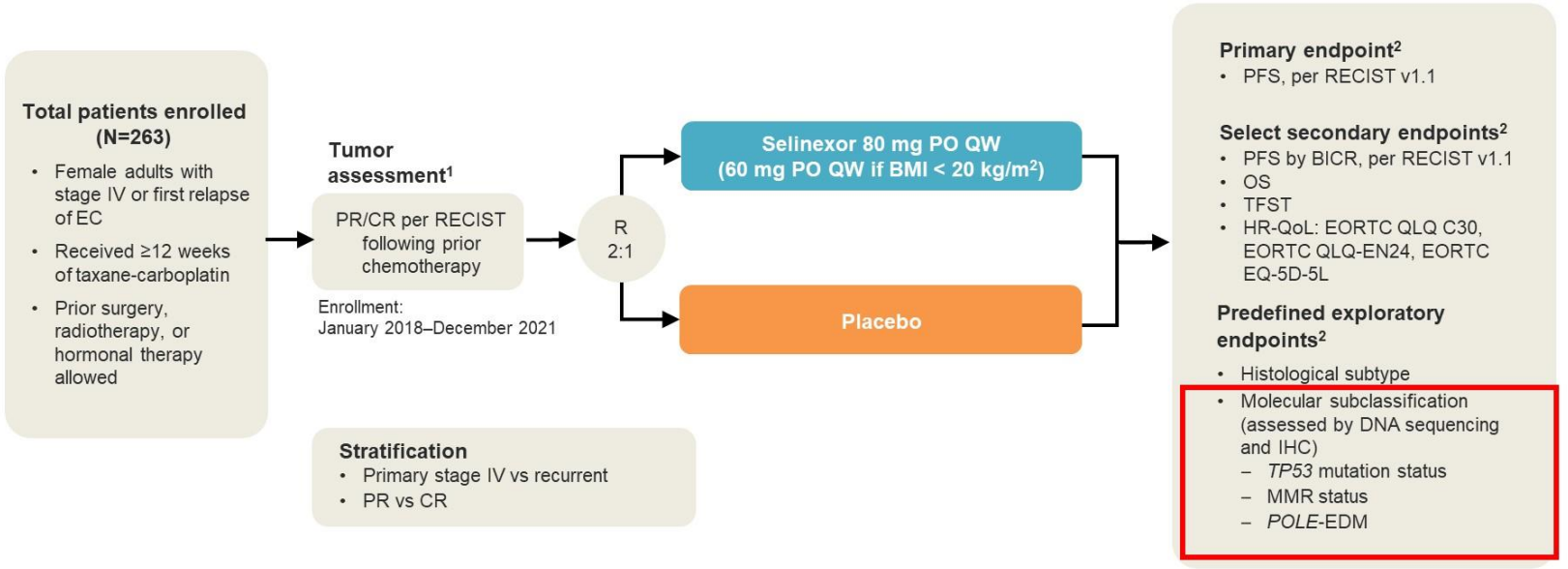
Selinexor prevents the XPO1-mediated export of several TSPs, including wild-type p53[1]

ENGOT European Network of Gynaecological Oncological Trial groups

GOG FOUNDATION Transforming the standard of care

SIENDO-LONG TERM FOLLOW UP UPDATE

ENGOT-EN5/GOG-3055/SIENDO (NCT03555422): A Randomized Double-Blind, Phase 3 Trial of Maintenance With Selinexor/Placebo After Combination Chemotherapy for Patients With Advanced or Recurrent Endometrial Cancer[1,2]



BICR, blinded independent central review; CR, complete response; EDM, exonuclease domain mutation; EORTC, European Organisation for Research and Treatment of Cancer; EQ-5D-5L, Quality of Life Questionnaire EuroQol-5 Dimensions-5 Levels; HR-QoL, health-related quality of life; MMR, mismatch repair; OS, overall survival; PD, progressive disease; PO, by mouth; POLE, polymerase epsilon; PR, partial response; PROs, patient-reported outcomes; QLQ, quality of life questionnaire; QW, once weekly; R, randomized; RECIST, Response Evaluation Criteria in Solid Tumors; TFST, time to first subsequent therapy

1. ClinicalTrials.gov. NCT03555422. https://www.clinicaltrials.gov/study/NCT03555422?term=NCT03555422. Accessed April 1 2024. **2.** Vergote I, *et al.* Presentation at: European Society for Medical Oncology Virtual Plenary; March 17-18, 2022; Abstract VP2-2022.
Primary study results previously published in Vergote I, et *al J Clin Oncol*. 2023;41(35):5400-5410.

Makker, ASCO 2024

SIENDO-LONG TERM FOLLOW UP UPDATE

Long-term mPFS of 28.4 Months in *TP53*wt Subgroup

Data cutoff date: April 1, 2024
HR, hazard ratio; NR, not reached.
*Molecular status determined by sequencing (*TP53*wt, n=99; *TP53* mutant, n=97) and if NGS not available, by immunohistochemistry (*TP53*wt, n=14; *TP53* mutant, n=29).

5 | Presented by Vicky Makker, MD

These Results Further Support The Ongoing Phase 3 ENGOT-EN20/GOG-3083/XPORT-EC-042 Trial of Selinexor 60 mg QW as Maintenance Therapy in Patients With Advanced or Recurrent *TP53*wt EC

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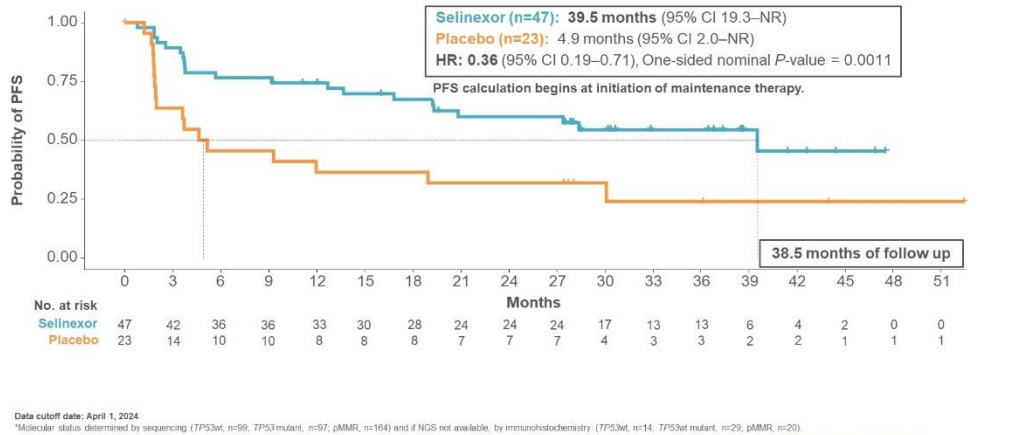
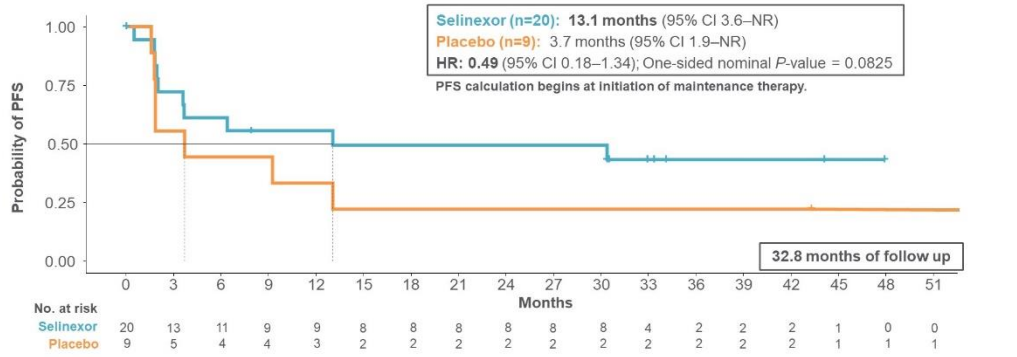
Long-term mPFS of 39.5 Months in *TP53*wt/pMMR* Subgroup



Data cutoff date: April 1, 2024
*Molecular status determined by sequencing (*TP53*wt, n=99; *TP53* mutant, n=97; pMMR, n=164) and if NGS not available, by immunohistochemistry (*TP53*wt, n=14; *TP53*wt mutant, n=29; pMMR, n=20).

6 | Presented by Vicky Makker, MD

Long-term mPFS of 13.1 Months in *TP53*wt/dMMR* Subgroup



Data cutoff date: April 1, 2024
*Molecular status determined by sequencing (*TP53*wt, n=99; *TP53* mutant, n=97; pMMR, n=164) and if NGS not available, by immunohistochemistry (*TP53*wt, n=14; *TP53*wt mutant, n=29; pMMR, n=20).

7 | Presented by Vicky Makker, MD

SIENDO-LONG TERM FOLLOW UP UPDATE

Preliminary OS

	No. w/ events (%)	Median, months (95% CI)	Overall maturity (%)	HR (95% CI)	Nominal one-sided *P*-value	Median follow up (months)
***TP53*wt**						
Selinexor (n=77)	24.7%	NR (45.4–NR)	29.2%	**0.65** (0.32–1.29)	0.11	36.8
Placebo (n=36)	38.9%	NR (35.2–NR)				
***TP53*wt/pMMR**						
Selinexor (n=47)	25.5%	NR (45.4–NR)	34.3%	**0.48** (0.22–1.07)	0.03	38.5
Placebo (n=23)	52.2%	35.19 (26.9–NR)				
***TP53*wt/dMMR**						
Selinexor (n=20)	10.0%	NR (NR–NR)	10.3%	**0.62** (0.06–6.81)	0.35	32.8
Placebo (n=9)	11.1%	NR (NR–NR)				

OS calculation begins at time of randomization and does not include duration of previous systemic chemotherapy.

Data cutoff date: April 1, 2024

Molecular status determined by sequencing (*TP53*wt, n=99; *TP53* mutant, n=97; pMMR, n=164) and if NGS not available, by immunohistochemistry (*TP53*wt, n=14; *TP53*wt mutant, n=29; pMMR, n=20).

8 | Presented by Vicky Makker, MD

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GOG FOUNDATION Transforming the standard of care

These Results Further Support The Ongoing Phase 3 ENGOT-EN20/GOG-3083/XPORT-EC-042 Trial of Selinexor 60 mg QW as Maintenance Therapy in Patients With Advanced or Recurrent *TP53*wt EC

Makker, ASCO 2024

FULVESTRANT/ABEMACICLIB

A Phase II Study of Fulvestrant plus Abemaciclib in Hormone-Receptor Positive Advanced or Recurrent Endometrial Cancer

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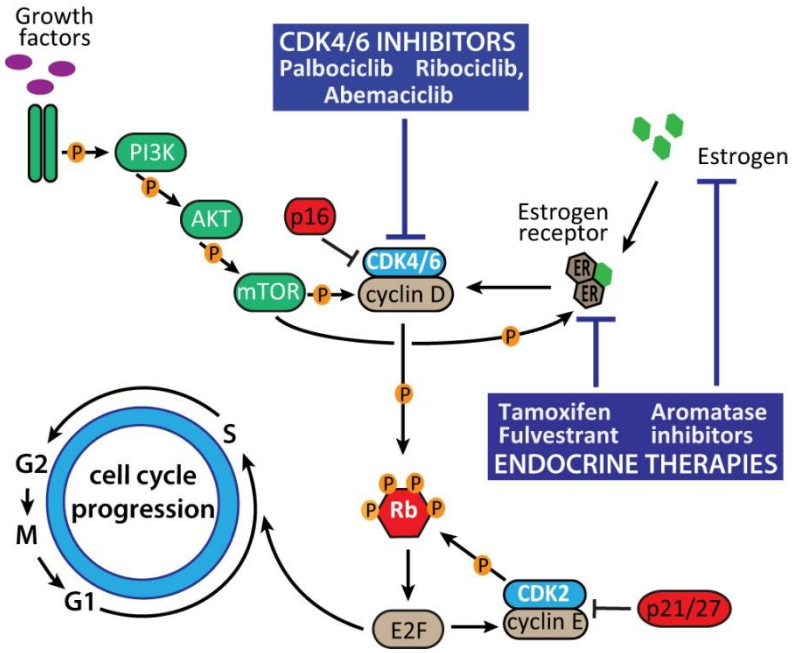


Endocrine-Related Cancer 26, 1; 10.1530/ERC-18-0317

FULVESTRANT/ABEMACICLIB

Study Design

Eligibility
- Advanced or recurrent EC
- Measurable disease
- 0-2 prior lines of chemotherapy
- 0-1 prior line of hormonal therapy
- ER or PR expression ≥ 1% by IHC

Abemaciclib 150 mg oral twice daily
+
Fulvestrant 500 mg IM monthly with 2 week loading dose

Primary endpoint
- ORR by RECIST v1.1

Key Secondary endpoints
- DOR
- CBR
- PFS
- OS
- Safety and tolerability

Exploratory endpoints
- Biomarkers of resistance and response

Exact one-sample test for binomial proportion
H_a: ORR ≥ 30%
H_o: ORR ≤ 10%
Sample size 25 patients → 90% power
If ≥ 5/25 responses observed, consider promising

IM=intramuscularly; ORR=Objective response rate; DOR=Duration of response; CBR=Clinical Benefit Rate; PFS=Progression Free Survival; OS=Overall survival

	Overall (N = 27)
Age, years, median (range)	66 (49-83)
Histology, number (%)	
Endometrioid	24 (88.9)
Grade 1	10 (41.7)
Grade 2	10 (41.7)
Grade 3	4 (16.7)
Serous	1 (3.7)
Mixed Endometrioid/Serous	2 (7.4)
Estrogen Receptor IHC, number (%)	
Positive	26 (96.3)
Negative	1 (3.1)
Progesterone Receptor IHC, number (%)	
Positive	19 (70.4)
Negative	1 (3.1)
Unknown/missing	7 (25.9)
Number of prior lines of systemic therapy	
1	13 (48.1)
2	14 (51.9)
Prior hormone therapy	
Yes	11 (40.7)
No	16 (59.3)

Green, ASCO 2024

FULVESTRANT/ABEMACICLIB

Results – Objective Response Rate

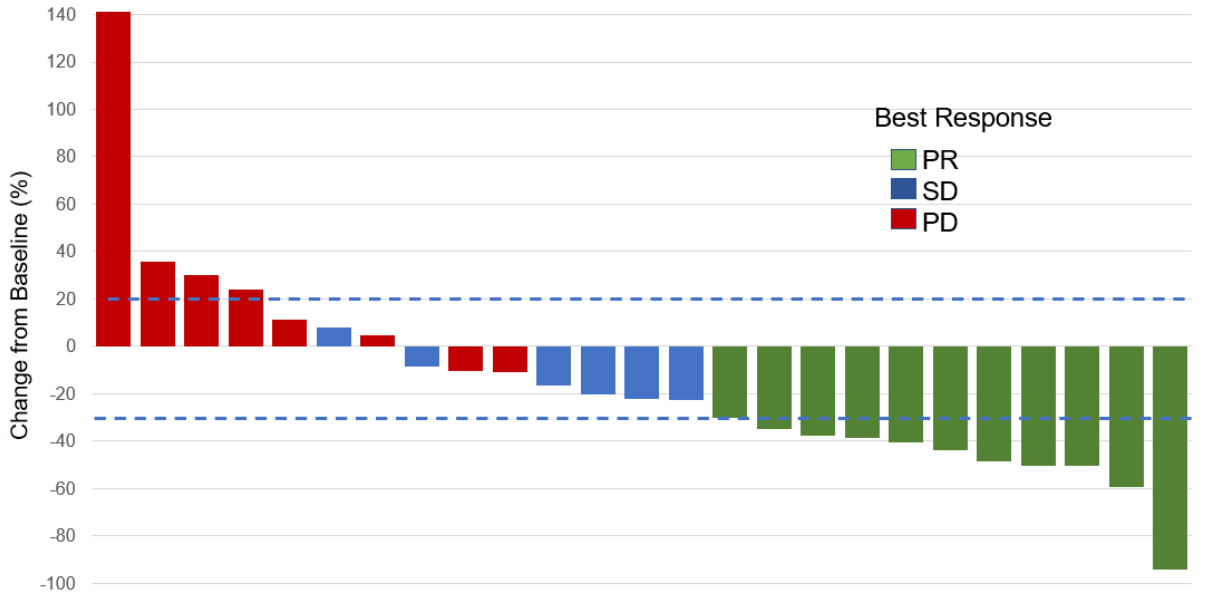
- Data Cutoff: October 7, 2023

Response	Evaluable Patients* (N = 25) n (%)
Best Overall Response	
Complete Response	0
Partial Response	11 (44%)
Stable Disease	6 (20%)
Progressive Disease	8 (32%)
ORR % (90% CI)	**44% (27% to 62%)**

Median Duration of Response = 15.6 months

*Two of 27 total patients enrolled were non-evaluable for response

Best Change in Target Lesions from Baseline (N=25)



Green, ASCO 2024

FULVESTRANT/ABEMACICLIB

Responses by Clinical Characteristics

- **Grade**
  - All responses in endometrioid tumors
    - G1 endometrioid (7/8, ORR=87.5%)
    - G2 endometrioid (4/10, ORR=40%)
    - *1 subsequent PR post data cutoff in G3 endometrioid tumor (1/4, ORR=25%)*
- **PR status**
  - PR positive (8/17, ORR=47%)
  - PR negative (0/1, ORR=0%)
  - 7 with unknown PR status
- **Hormonal therapy**
  - No prior hormonal (8/16, ORR=50%)
  - Prior hormonal (3/9, ORR=33%)
- **Prior systemic therapy (non hormonal)**
  - 1 prior (5/13, ORR 38%)
  - 2 prior (6/14, ORR 43%)

Responses across EC Molecular Subtypes

- CN-L/NSMP more likely to have a response than other molecular subtypes (ORR 59% v 13%, p=0.042)
- Among 4 patients with MSI-H tumors, 1 had PR, 3 derived no clinical benefit.

Characteristic	Evaluable Patients, N=25	OR		p-value
Molecular Subtype		Yes	No	0.090
CN-L/NSMP	17	10(59)	7(41)	
CN-H/*TP53*abn	4	0(0)	4(100)	
MSI-H	4	1(25)	3(75)	
POLE	0	-	-	

Characteristic	Evaluable Patients, N=25	OR		p-value
Molecular Subtype		Yes	No	0.042
CN-L/NSMP	17	10(59)	7(41)	
CN-H+MSI-H	8	1(13)	7(88)	

No association between presence of PI3K pathway gene (*PTEN, PIK3CA* and *PIK3R1)*, *KRAS*, or *CTNNB1* mutations, respectively, with response to abemaciclib/fulvestrant

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BrUOG 354

2024 ASCO ANNUAL MEETING

LEGORRETA CANCER CENTER BROWN UNIVERSITY

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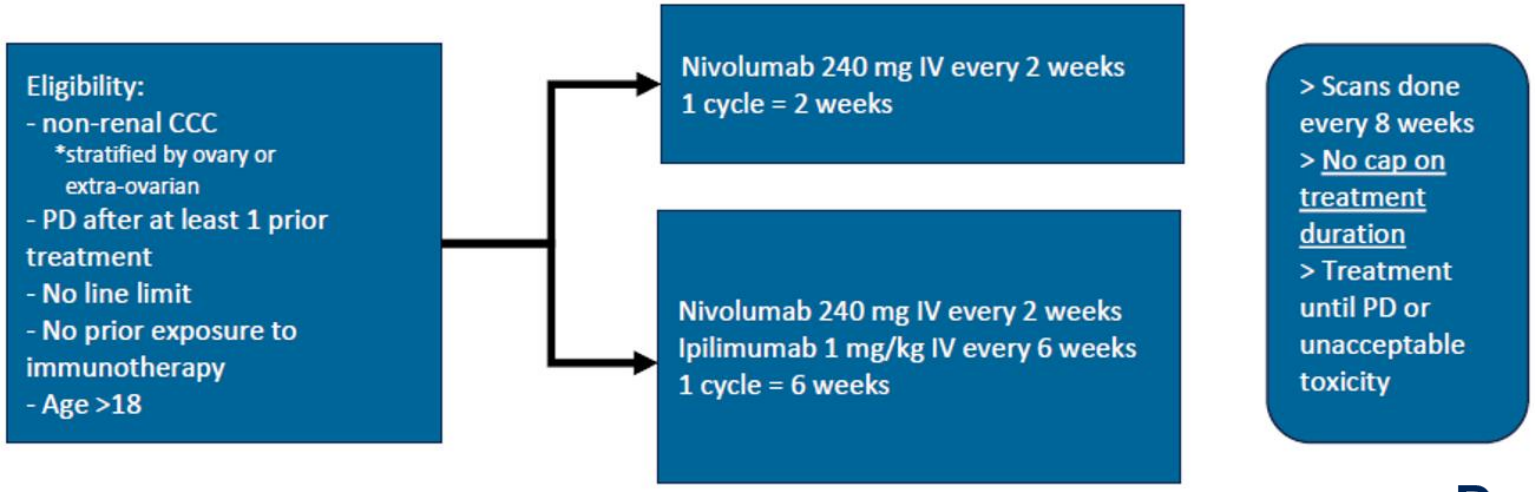
Final results of BrUOG 354:

A randomized phase II trial of nivolumab alone or in combination with ipilimumab for people with ovarian and other extra-renal clear cell carcinomas

Don S. Dizon, Cara Amanda Mathews, Shannon MacLaughlan David, Jason T Machan, Matthew James Hadfield, Eric I Marks, Rani Bansal, Christine McGinn, Faith Hassinger, Denise Luppe, Janine Grigelevich, Kelly A Mitchell, Adam Braga, Ashlee Sturtevant, Roxanne Wood, Ursula A. Matulonis, Alexi A. Wright, Susana M. Campos, Michael J. Birrer

Brown University Oncology Group; Lifespan Cancer Institute, Rhode Island Hospital, Providence, RI; Women and Infants Hospital, Providence, RI; University of Illinois at Chicago, Chicago, IL; Rhode Island Hospital/Alpert Medical School of Brown University, Providence, RI; Rhode Island Hospital, Brown University, Providence, RI; Boston University Medical Campus, Boston, MA; Duke Cancer Institute, Durham, NC; Lifespan Cancer Institute, Providence, RI; Lifespan, Providence, RI; Brown University Oncology Research Group, Providence, RI; Dana-Farber Cancer Institute, Boston, MA; University of Arkansas for Medical Sciences, Little Rock, AR

BrUOG 354



Data cut-off: December 31, 2023
Median Follow-up: 11.3 months (range, 1.6 to 46.4 months)

Randomized, non-comparative, phase 2

Primary Objective: Overall Response Rate (ORR)
Secondary Objectives: PFS and OS, Adverse Events
Exploratory: Molecular characteristics for response or non-response

Dizon, ASCO 2024

Demographics, n=44

	Nivolumab (n=14)	Nivolumab/Ipilimumab (n=30)	Total (n=44)
Age (median, range)	54.5 (18-74)	58 (22-75)	57 (18-75)
Diagnosis (n,%)			
Ovarian	11 (78.6)	25 (83.3)	36 (81.2)
Uterine	3 (21.4)	3 (10)	6 (13.6)
Other	0	2 (6.7)	2 (4.5)
Race (n, %)			
White	12 (85.7)	21 (70)	33 (75)
Black	1 (7.1)	3 (10)	4 (9)
Asian	1 (7.1)	1 (3.3)	2 (4.5)
Not Answered	0	5 (16.6)	5 (11.4)
Ethnicity (n,%)			
Hispanic	1 (7.1)	4 (13.3)	5 (11.4)
Not Hispanic	12 (85.7)	22 (73.3)	34 (77.3)
Not Answered	1 (7.1)	4 (13.3)	5 (11.4)
Prior lines (median, range)	1 (1-7)	1.5 (1-4)	

BrUOG 354

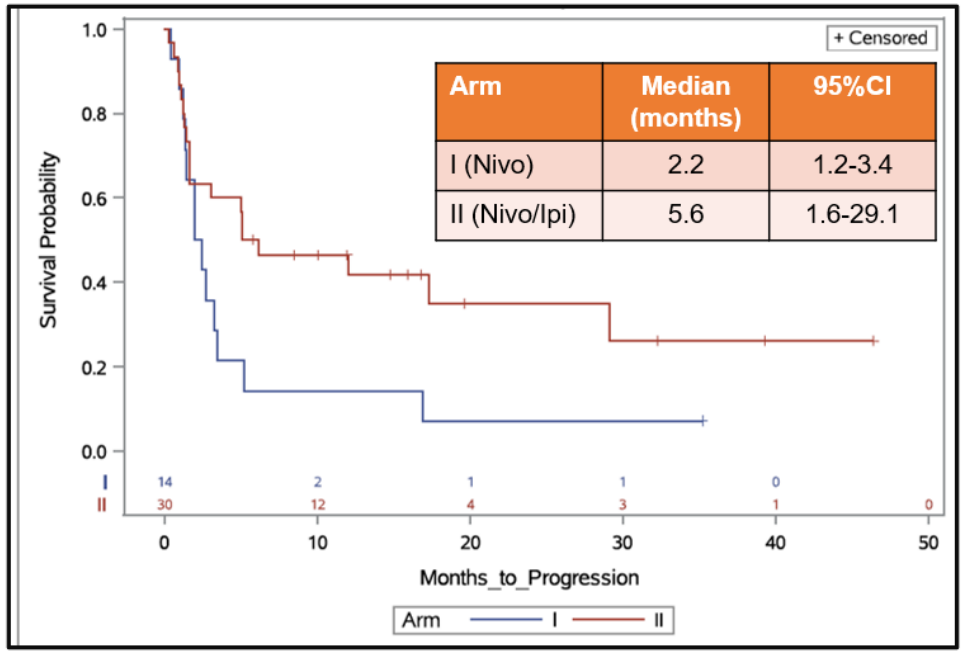
Response Data

	Nivolumab n=14	Nivolumab/Ipilimumab n=30
Complete Response (n, %)	**0**	**5 (16.7)**
Partial Response (n,%)	**2 (14.3)**	**5 (16.7)**
Complete + Partial Response	**2 (14.3)**	**10 (33.3)**
Stable Disease	5 (35.7)	10 (33.3)
Progression	7 (50)	10 (33.3)
Duration of Response (months, median ± SD)	30.6 ± 4.5	22.4 ± 11.8

Dizon, ASCO 2024

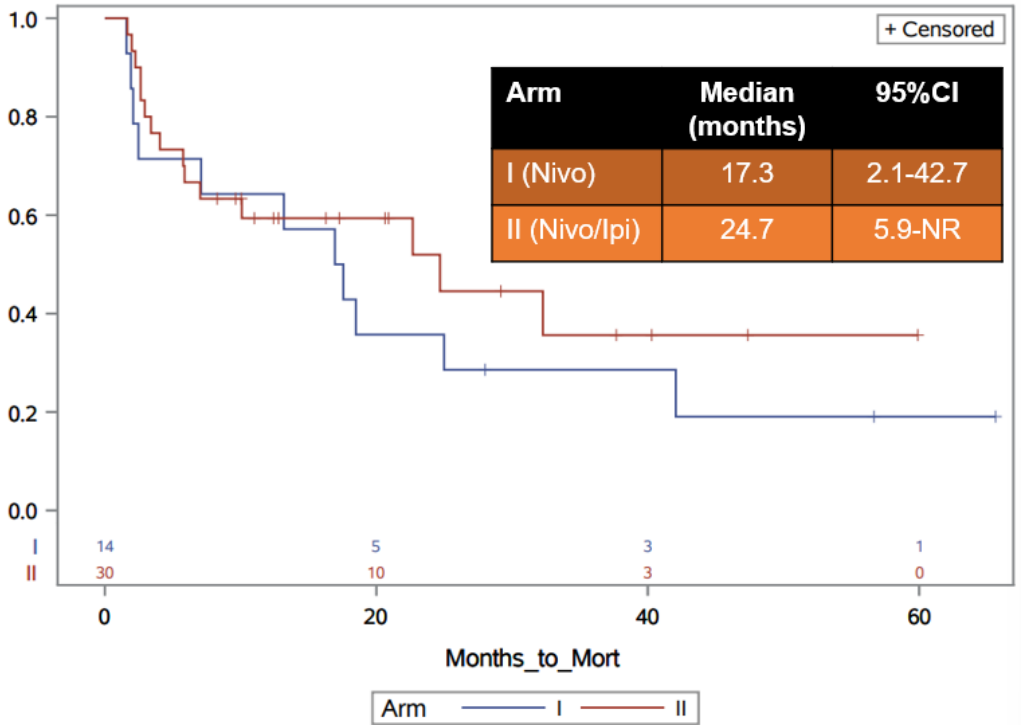
BrUOG 354

Progression-Free Survival



Arm	Median (months)	95%CI
I (Nivo)	2.2	1.2-3.4
II (Nivo/Ipi)	5.6	1.6-29.1

Overall Survival



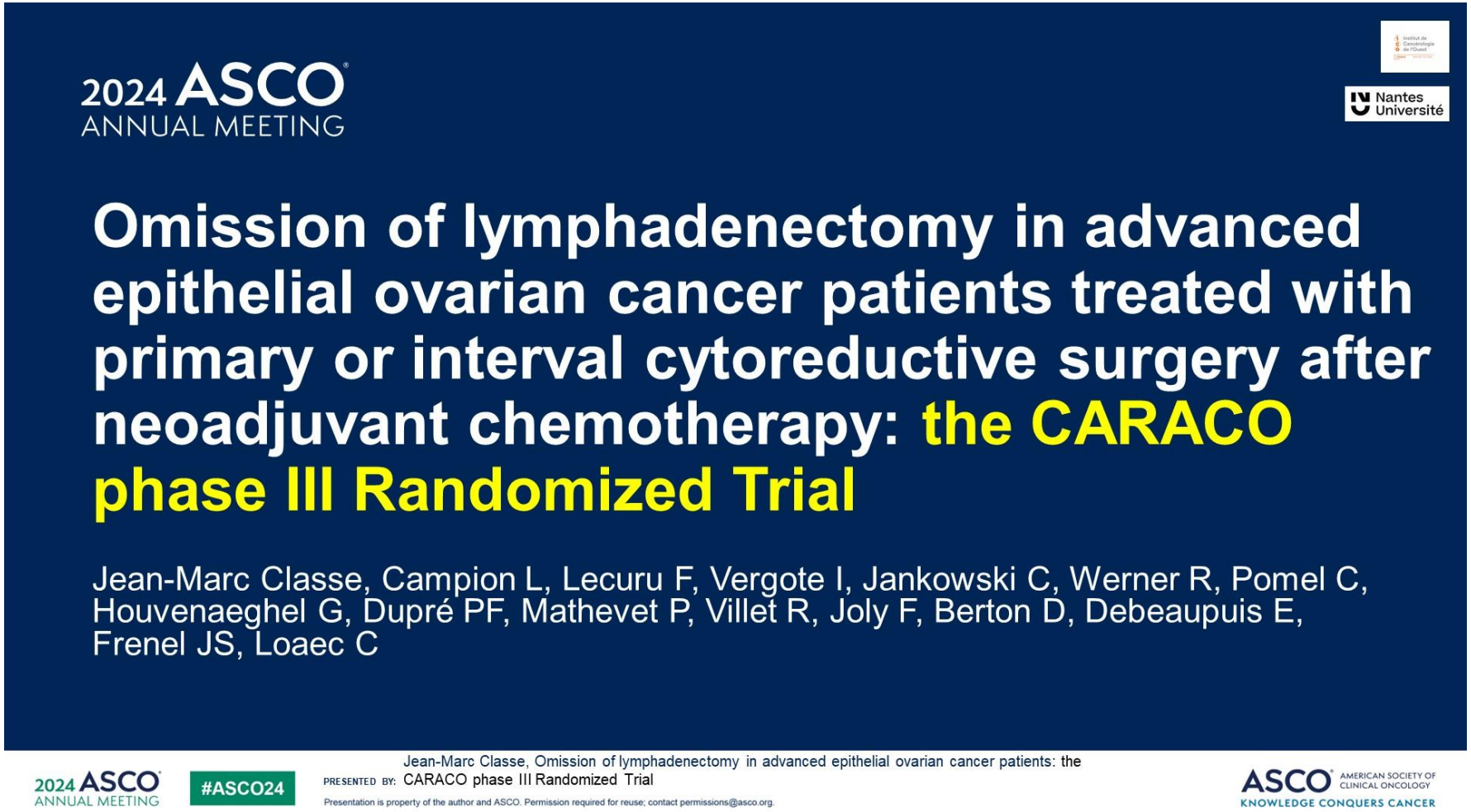
Arm	Median (months)	95%CI
I (Nivo)	17.3	2.1-42.7
II (Nivo/Ipi)	24.7	5.9-NR

- For people with ovarian or gynecologic clear cell carcinoma, the clinical activity and survival outcomes are greater when nivolumab is given with ipilimumab vs. as a single agent.
- There were no new safety signals identified among volunteers with gynecologic clear cell cancer treated with immunotherapy.

Dizon, ASCO 2024

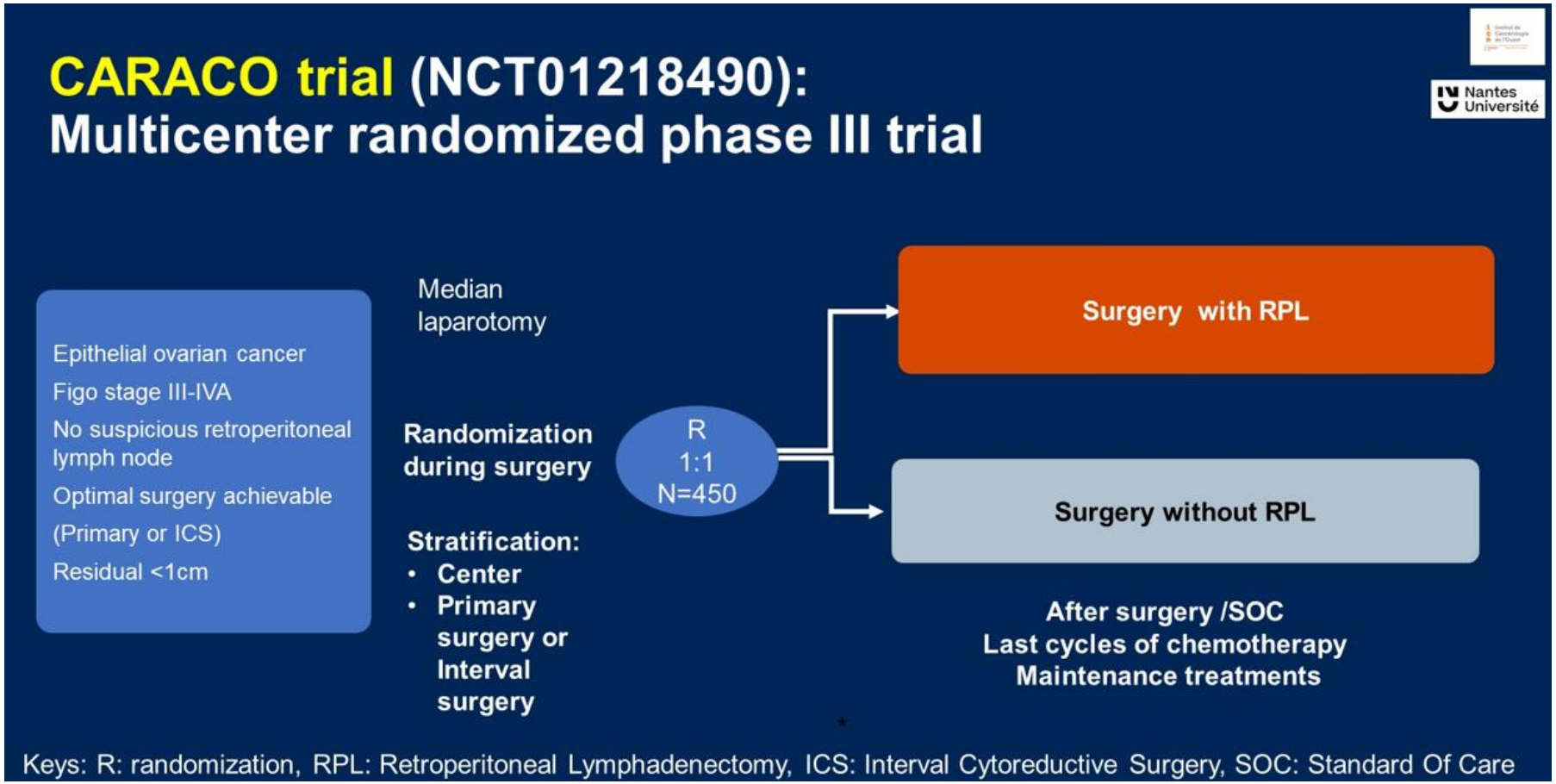
OVARIAN CANCER

CARACO



Classe, ASCO 2024

CARACO



- A superiority, randomized trial
- Primary endpoint: Progression Free Survival
- Secondary endpoints: OS, safety, surgical outcome, QoL

Classe, ASCO 2024

CARACO

Characteristics	No RPL (n=193)	RPL (n=186)
Surgery to not any residual, n (%)	161 (85.6)	158 (88.3)
Resected lymph nodes total (median IQR) Para aortic LN (median IQR) Pelvic LN (median IQR)		28 (19-36) 12 (7-18) 13 (9-19)
Patients with ≥1 involved LN		81(43%)
Median duration of surgery (minutes)	240 (180-290)	300 (240-360)
Maintenance with Bevacizumab after surgery	46 (23.8)	44 (23.7)
Surgical strategy	PS: 50/ ICS: 143	PS: 40/ICS:146

Keys:RPL: Retroperitoneal Lymphadenectomy IQR: Inter Quartile Range, LN: Lymph Node, PS: Primary Surgery, ICS: Interval Cyrtoreductive Surgery

CARACO: Severe morbidity and mortality (within 30 days after surgery)*

No. of patients (%)	No RPL (n=193)	RPL (n=186)	p
Transfusion or blood loss	57 (29.7)	72 (39.3)	**P=0.049**
Re intervention	6 (3.1)	15 (8.3)	**P=0.031**
Urinary injury	0 (0.0)	7 (3.8)	**P=0.006**
Digestive fistula	2 (1.1)	4 (2.2)	NS
Phlebitis – Pulmonary embolism	7 (3.7)	3 (1.6)	NS
Mortality	1 (0.5)	2 (1.1)	NS

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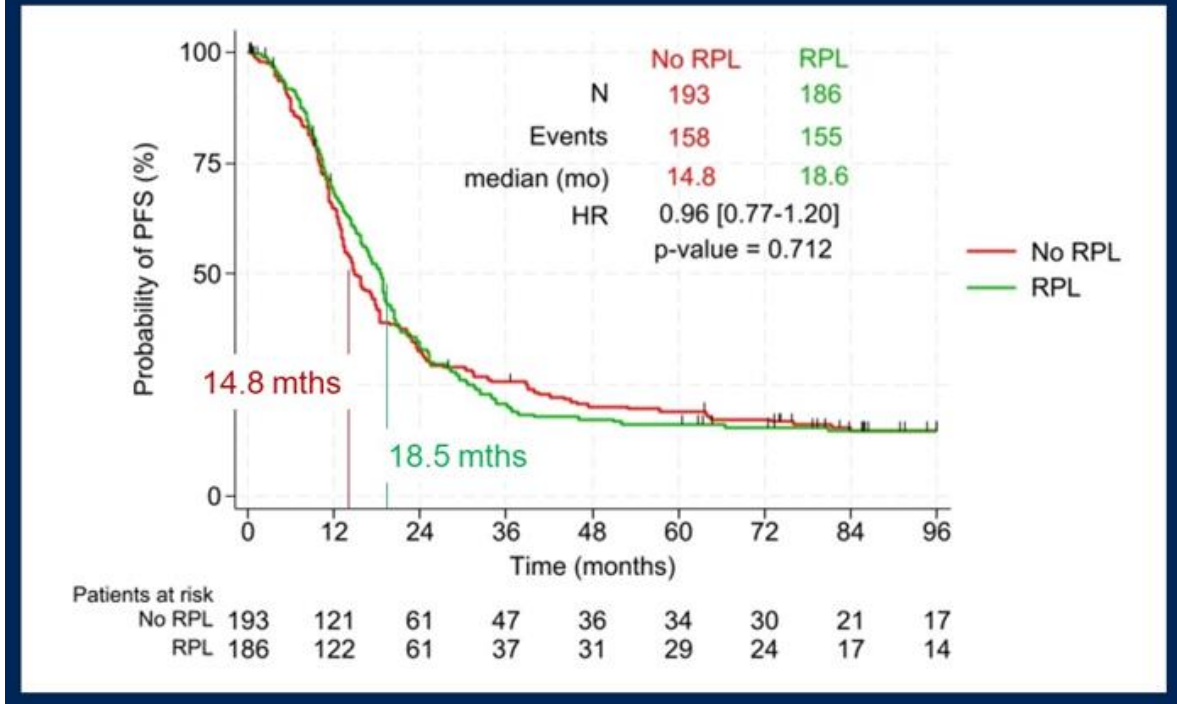
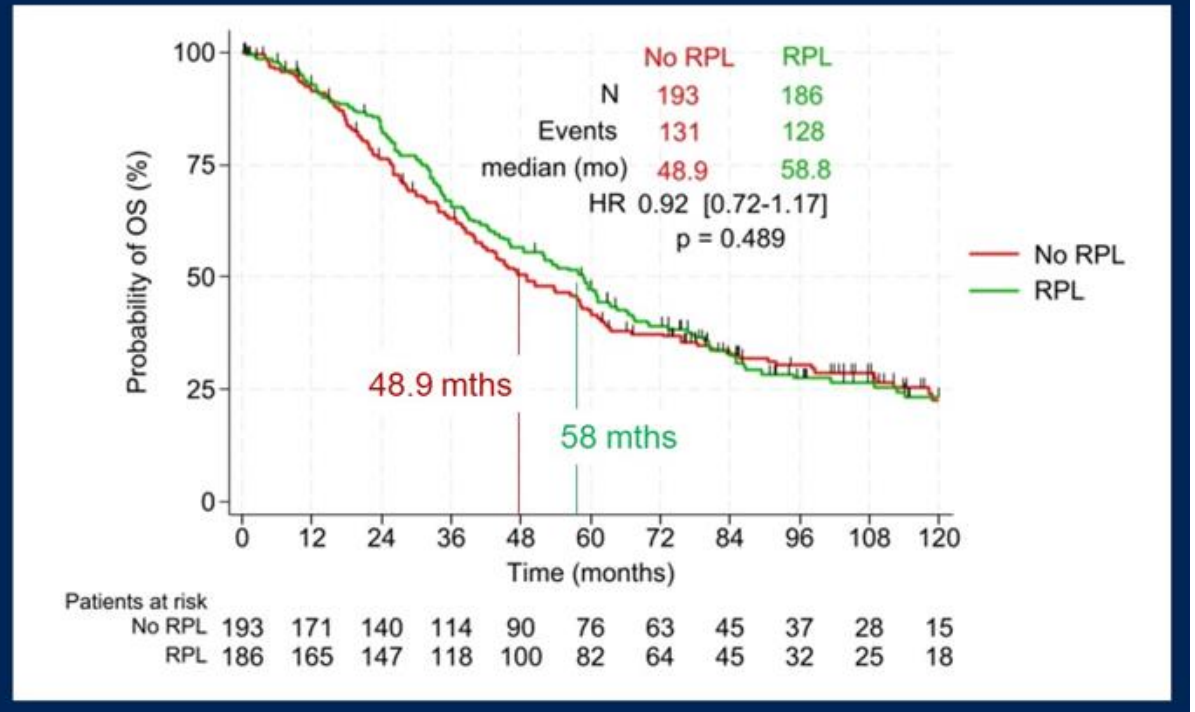
CARACO

Primary endpoint (PFS, ITT Population)



Secondary endpoint (OS, ITT Population)



- Adding retroperitoneal lymphadenectomy to complete cytoreductive surgery, in primary surgery or in interval surgery after neoadjuvant chemotherapy in patients treated for an advanced ovarian cancer, with no suspicious nodes, does not improve progression free survival nor overall survival

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NEO

2024 ASCO ANNUAL MEETING

GCIG GYNECOLOGIC CANCER INTERGROUP

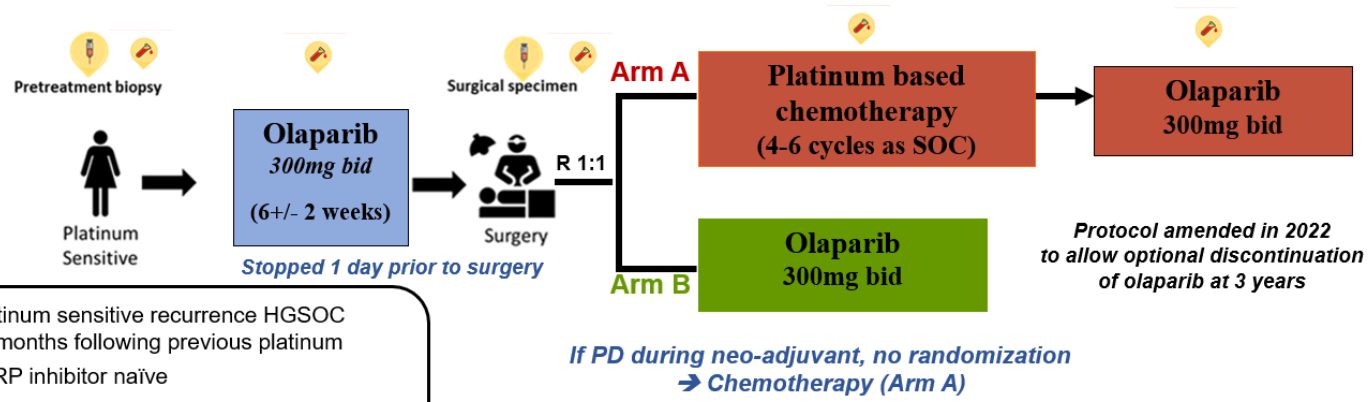
Phase II randomized multi-centre study of neoadjuvant olaparib in patients with platinum sensitive relapsed high grade serous ovarian cancer: The NEO Trial

Stephanie Lheureux, Taymaa May, Michelle K. Wilson, Diane M. Provencher, Susie Lau, Prafull Ghatage, Johanne I Weberpals, Susana N. Banerjee, Iain A. McNeish, Neesha C. Dhani, Sarah Ferguson, Genevieve Bouchard-Fortier, Trevor John Pugh, Xiang Y Ye, Sarah Garisto, Judy Quintos, Janelle Ramsahai, Horace Wong, Valerie Bowering, Amit M. Oza

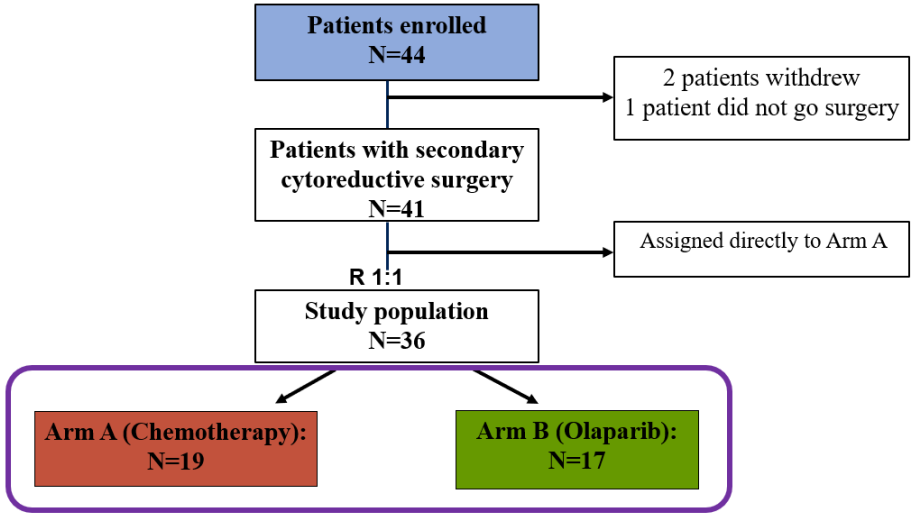
NEO

Study Design

A phase II, Open label, Multi-site, Randomized study



Platinum sensitive recurrence HGSOC
≥6 months following previous platinum
PARP inhibitor naïve
Suitable for secondary cytoreductive surgery
Normal organ and Marrow function
(Hb≥ 100g/L; Plat≥ 100; Cl creat≥ 60mL/min)



Study Objectives

- **Primary**
  - To assess the tumor biological effects of a short pre-operative course of olaparib in patients with platinum sensitive relapsed ovarian cancer –
    Effects measured by the degree of PARP-1 inhibition
  - **To generate initial clinical efficacy data**

- **Secondary**
  - Safety and tolerability of pre-operative olaparib
  - Response rate to olaparib in the neoadjuvant period
  - Survival outcomes with olaparib versus platinum based chemotherapy

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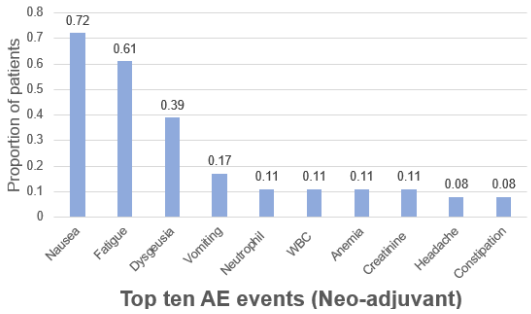
NEO

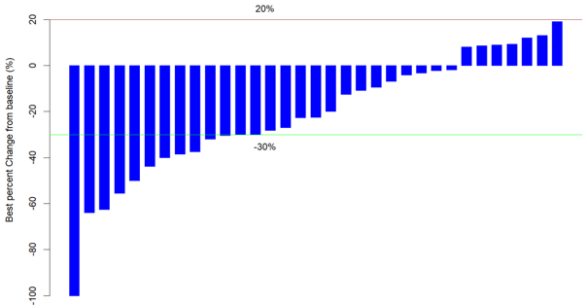
	A. Platinum Based Chemotherapy (N = 19)	*B. Olaparib (N = 17)*	*Total (N = 36)*
Age at enrollment (year)			
Median (Range)	59.0 (39.0 – 80.0)	59.0 (44.0 – 84.0)	59.0 (39.0 – 84.0)
Prior Neoadjuvant Chemotherapy			
No	12 (63.16%)	15 (88.24%)	27 (75.00%)
Yes	7 (36.84%)	2 (11.76%)	9 (25.00%)
Number of Prior Line of Therapy			
Median (Range)	1.0 (1.0 – 3.0)	1.0 (1.0 – 4.0)	1.0 (1.0 – 4.0)
Germline *BRCA* Status			
Mutated	7 (36.84%)	4 (23.53%)	11 (30.56%)
Wild-Type	5 (26.32%)	12 (70.59%)	17 (47.22%)
Unknown	7 (36.84%)	1 (5.88%)	8 (22.22%)
Race			
White	13 (68.42%)	13 (76.47%)	26 (72.22%)
Other	6 (31.58%)	4 (23.53%)	10 (27.78%)

Neo-adjuvant olaparib – Safety & Efficacy (N=36)

- **Olaparib median duration** : 40 (34-48) days
- **Safety:** No grade ≥3 AEs

  2 patients (5%) had at least one dose modification (dose reduction & hold)
- **Objective Response Rate**: 29% (10/35 – 1 missing)





Surgery Period – Safety & Efficacy (N=36 patients)

- **Type of surgery:** 78% Laparotomy
- **Objective Response Rate**: 94% - Complete Response: 74% (26 patients)
- **Median time to start adjuvant therapy:** 1.2 (0.5-3.4) months
- **Surgical complications:** Grade 3 reported surgical related AE – All recovered
  - Abscess: 2 patients
  - Perforation (colonic – bladder – enterotomy): 3 patients
  - Thrombo-embolic events: 2 patients

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NEO

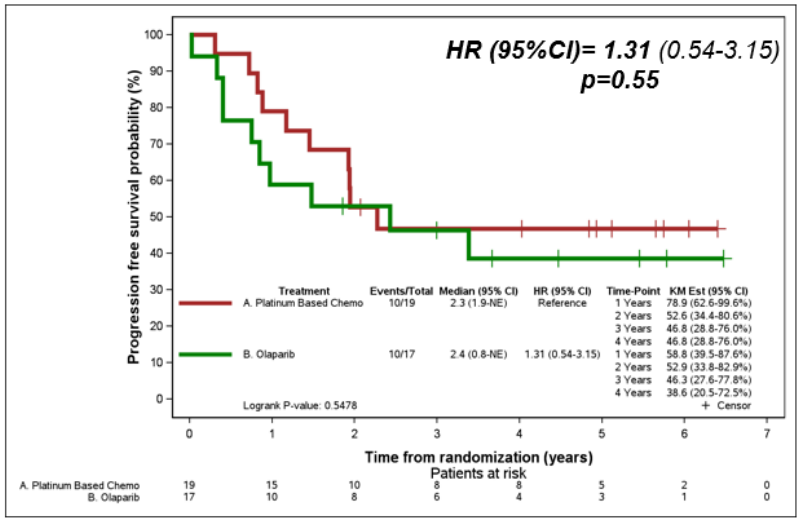
Survival Outcomes

- **ITT Population (N=36)**

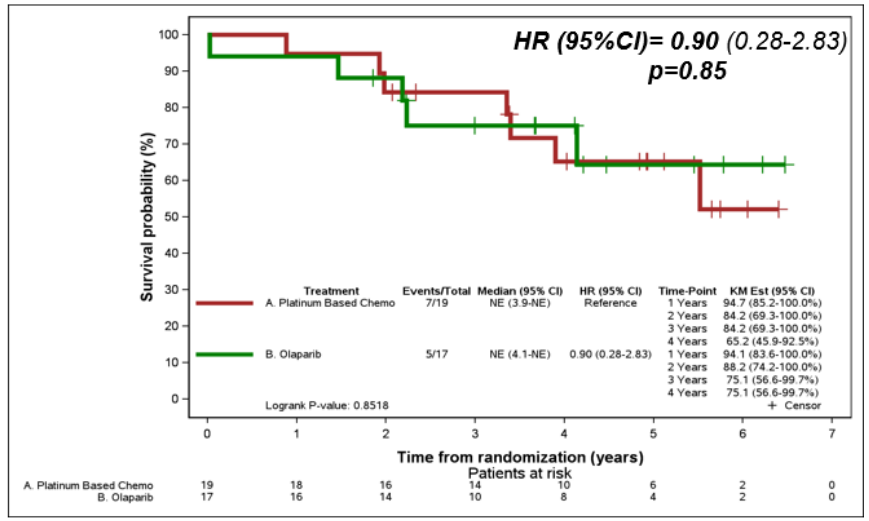
Exploratory Outcomes

- **gBRCA status**

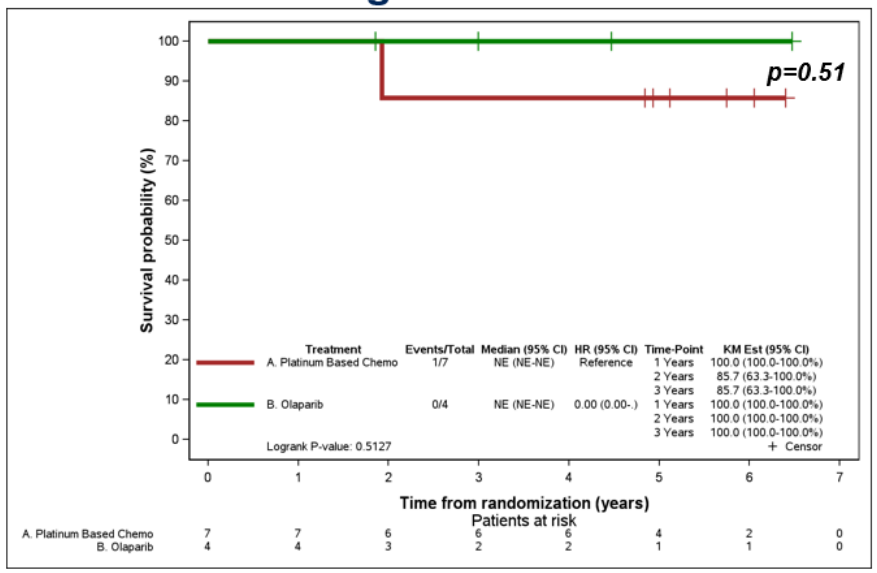
Progression Free Survival (PFS)



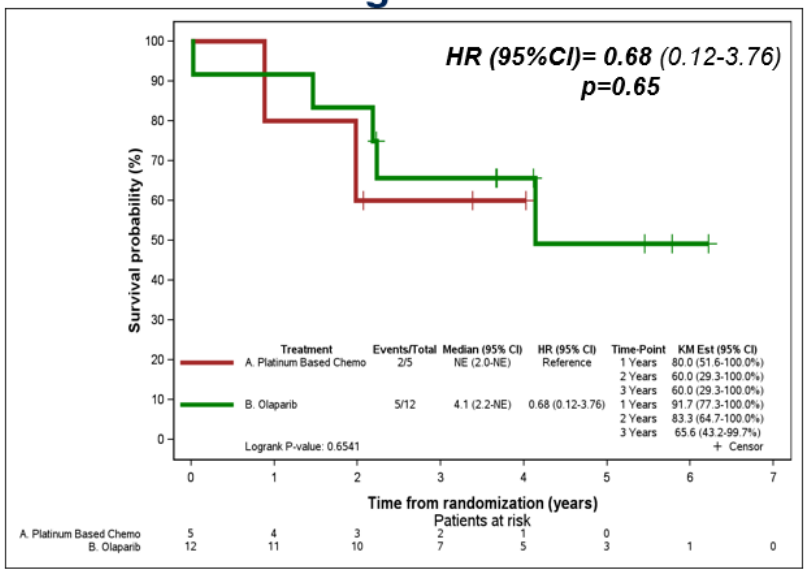
Overall Survival (OS)



OS in g*BRCA* mut



OS in g*BRCA* WT



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Adjuvant Therapy post randomization

Safety: No reported MDS/AML

Treatment Exposure

- *Median cycles*

Arm A= 21.5 – Arm B= 18 cycles (p=0.60)

- *Median time on adjuvant olaparib*

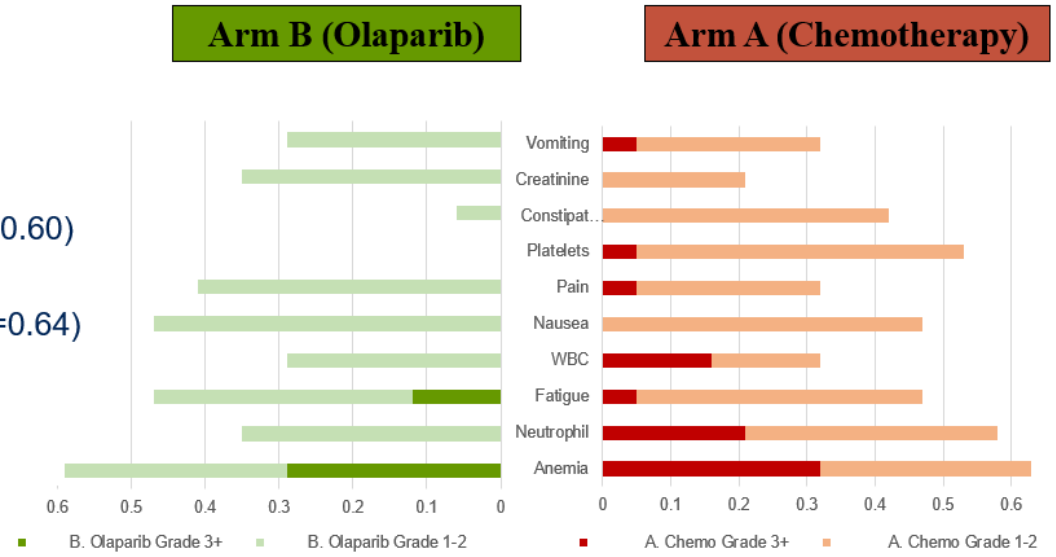
Arm A= 13.8 – Arm B= 14.7 mths (p=0.64)

- *Dose Modification*

Arm A = 15 pts (79%) to chemo
12 pts (63%) to olaparib

Arm B: 14 pts (82%)

- 13 pts off maintenance without progression



Top ten AE events during adjuvant period

- In patients with complete disease resection after secondary cytoreductive surgery, olaparib alone was as effective as chemotherapy followed by olaparib and associated with less toxicity.
- This study suggests the potential for a de-escalation approach with targeted therapy in this selected population.

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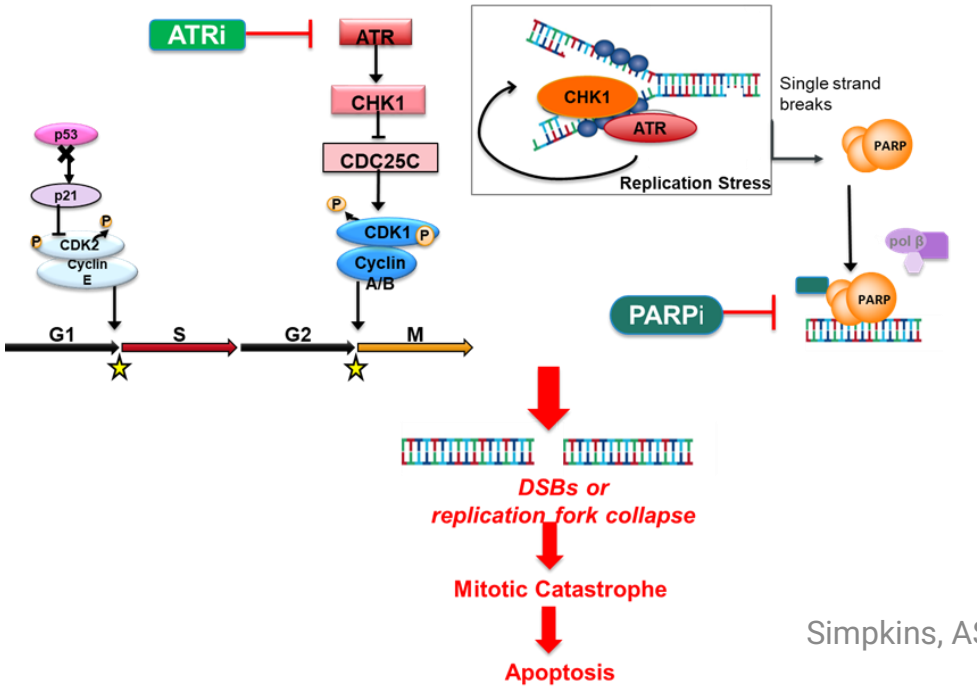
CAPRI

Combination ATR and PARP Inhibitor (CAPRI): A phase 2 study of ceralasertib plus olaparib in patients with recurrent, platinum-sensitive epithelial ovarian cancer (Cohort A).

Fiona Simpkins, Dimitrios Nasioudis, Stephanie L. Wethington, Lainie P. Martin, Janos L. Tanyi, Nawar A. Latif, Drew A. Torigian, Dalia K. Omran, Diego Rodriguez, Simon Smith, Emma Dean, Susan M. Domchek, Ronny Drapkin, Ie-Ming Shih, Eric J. Brown, Wei-Ting Hwang, Deborah K. Armstrong, Geoffrey Shapiro, Stephanie Gaillard, Robert L. Giuntoli II, Joyce F. Liu



Hypothesis: targeting 2 unique DNA repair pathways by combination PARPi and ATRi, will lead to increased DSB and prevent or overcome PARPi resistance

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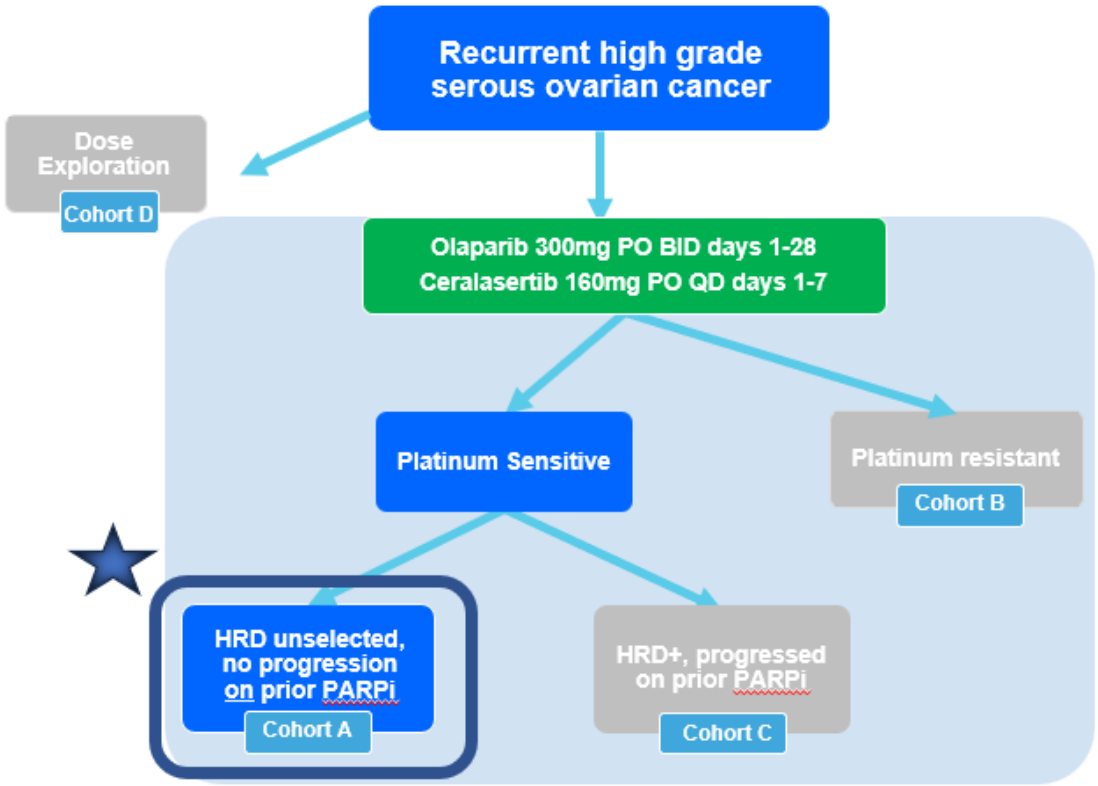
CAPRI

Combination ATR and PARP Inhibition (CAPRI) Phase I/II, Cohort A



Specific Aim (Cohort A)

Safety and objective response rates (ORR) of combination of olaparib (PARPi) and ceralasertib (ATRi) in platinum sensitive recurrent HGSOC, HRD unselected, who had not progressed on prior PARPi

Study Endpoints:

Primary endpoints: ORR, toxicity

Secondary endpoint: PFS

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CAPRI

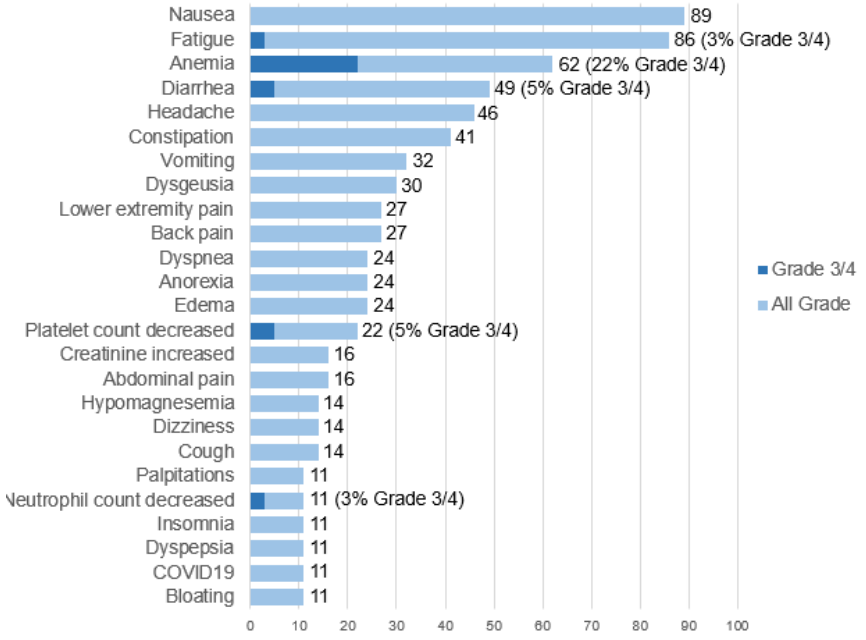
Demographics for Cohort A CAPRI

Characteristic	N=37 N (%) or median (min - max)
Age, years	69 (48-80)
Race	
Non-Hispanic White	34 (91.9%)
Non-Hispanic Black	2 (5.4%)
Asian	1 (2.7%)
ECOG Performance Status	
0	23 (62.2%)
1	14 (37.8%)
Lines of prior systemic treatment	
1	21 (56.8%)
2	11 (29.7%)
≥3	5 (13.5%)
Prior PARPi	2 (5.4%)
Platinum-free interval	
6-12 months	14 (37.8%)
>12 months	23 (62.2%)
Germline testing results (n=37)	
Germline pathogenic/Likely pathogenic gene variant present*	3 (8.1%)
No pathogenic mutation detected	33 (89%)
Not performed	1 (2.7%)
HRD Testing Status (n=34)	
Homologous recombination deficient (HRD) test positive (Myriad MyChoice >42)	8 (23.5%)
Loss of heterozygosity (LOH) high (>16%) (Caris Life Sciences)	2 (5.9%)
Homologous recombination deficient (HRD) test negative (Myriad MyChoice <42)	20 (58.8%)
Not performed	4 (11.8%)

*1 BRCA2, 1 BRIP1, 1 RAD51C

Combination ceralasertib + olaparib was well tolerated

Treatment-related AEs occurring in ≥10% of pts



	Number of pts (%)
Dose reduction due to AE (Total)	**16 (43%)**
Olaparib dose reduction	16 (43%)
Ceralasertib dose reduction	0 (0%)
Dose discontinuation due to AE	**1 (3%)** (G2 nausea/fatigue)

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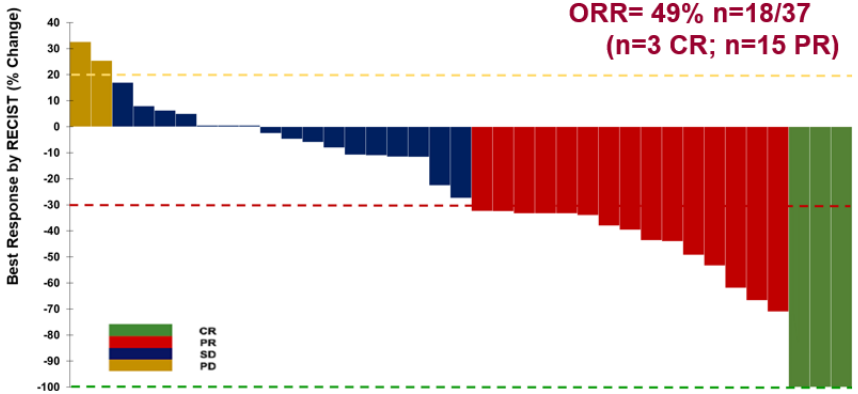
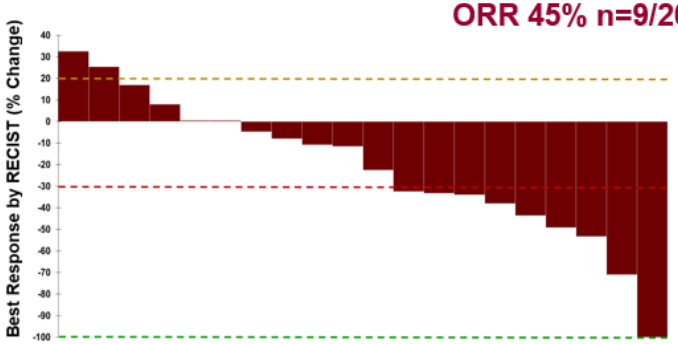
CAPRI

ORR= 49% n=18/37
(n=3 CR; n=15 PR)



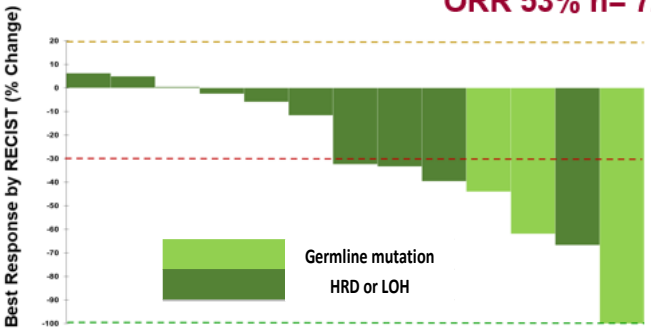
HRD test negative

ORR 45% n=9/20

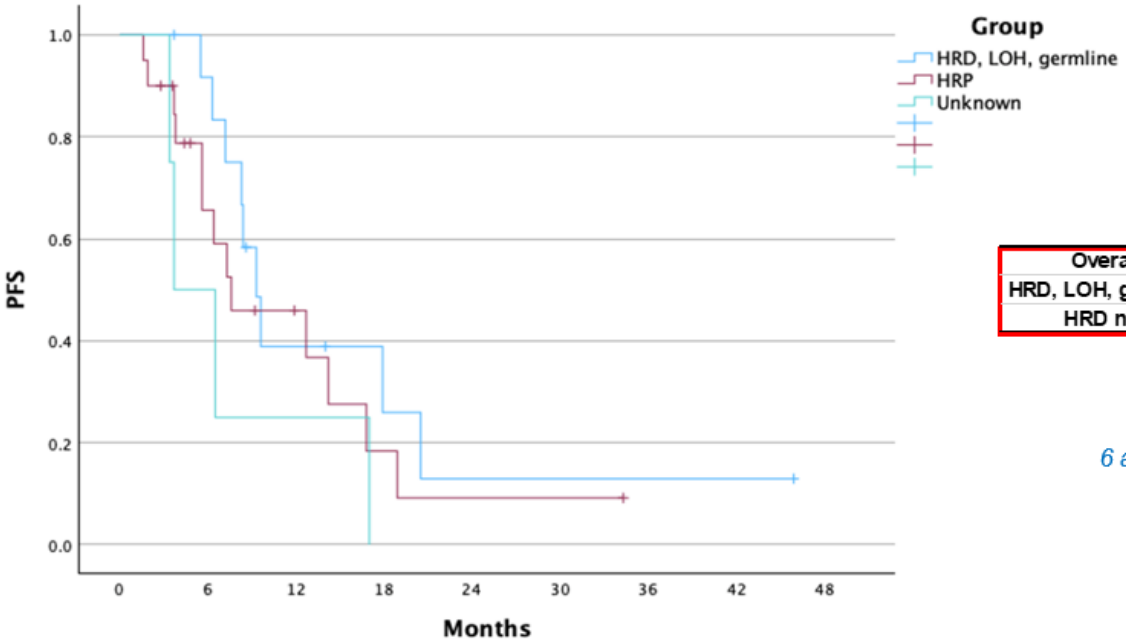


HRD test positive

ORR 53% n= 7/13



Median progression free survival for Cohort A



	mPFS (months)	95% CI
Overall	8.4	5.79-11.01
HRD, LOH, germline	9.3	7.51-11.09
HRD neg	7.6	.684-14.51

6 active patients still on treatment

Combination ceralasertib with olaparib demonstrates clinical activity in platinum sensitive recurrent HGSOC, irrespective of HRD status

HRD status may not predict response to PARPi-ATRi combinations

Combination is tolerable with toxicity similar to that of olaparib monotherapy

Simpkins, ASCO 2024

Review

Cervical Cancer

- Adjuvant Chemotherapy following Concurrent Chemoradiation (CRT) in High-Risk Early-Stage Cervical Carcinoma Patients Following Radical Hysterectomy: Results of *NRG Oncology/RTOG 0724/GOG-0724*

Endometrial Cancer

- Long-term Follow-up of Selinexor Maintenance for Patients with *TP53*wt Advanced or Recurrent Endometrial Cancer: A prespecified Subgroup Analysis From the Phase 3 *ENGOT-EN5/GOG-3055/SIENDO Study*
- A Phase II Study of *Fulvestrant plus Abemaciclib* in Hormone-Receptor Positive Advanced or Recurrent Endometrial Cancer
- Final results of *BrUOG 354*: A randomized phase II trial of nivolumab alone or in combination with ipilimumab for people with ovarian or other extra-renal clear cell carcinomas

Ovarian Cancer

- Omission of lymphadenectomy in advanced epithelial ovarian cancer patients treated with primary or interval cytoreductive surgery after neoadjuvant chemotherapy: the CARACO phase III randomized trial
- Phase II randomized multi-centre study of neoadjuvant olaparib in patients with platinum sensitive relapsed high grade serous ovarian cancer: *The NEO Trial*
- Combination ATR and PARP Inhibitor (*CAPRI*): A phase 2 study of ceralasertib plus olaparib in patients with recurrent, platinum-sensitive epithelial ovarian cancer (Cohort A)

QUESTIONS?