OVARIAN CANCER – FIRST LINE AND PLATINUM SENSITIVE- THE CURRENT LANDSCAPE

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THE OHIO STATE UNIVERSITY
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GOG-P Ovarian Cancer Clinical Trialist

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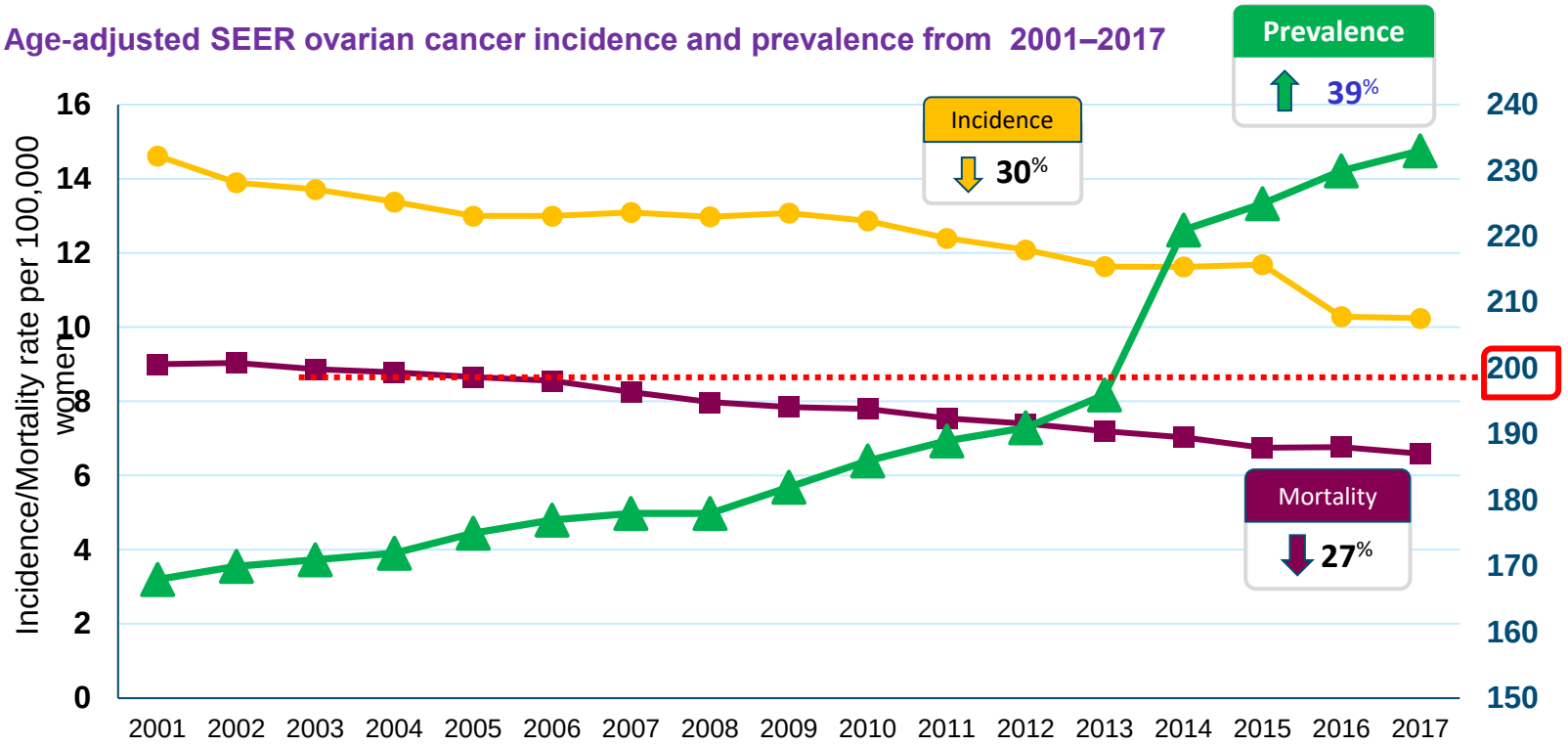
Ovarian Cancer: Clinical Impact



SEER=Surveillance, Epidemiology and End Results.

National Cancer Institute Surveillance, Epidemiology and End Results Program (SEER). SEER Cancer Statistics Review (CSR) 1975-2016 - Ovary. 2016; https://seer.cancer.gov/csr/1975_2016/sections.html. Accessed Apr 14, 2020.

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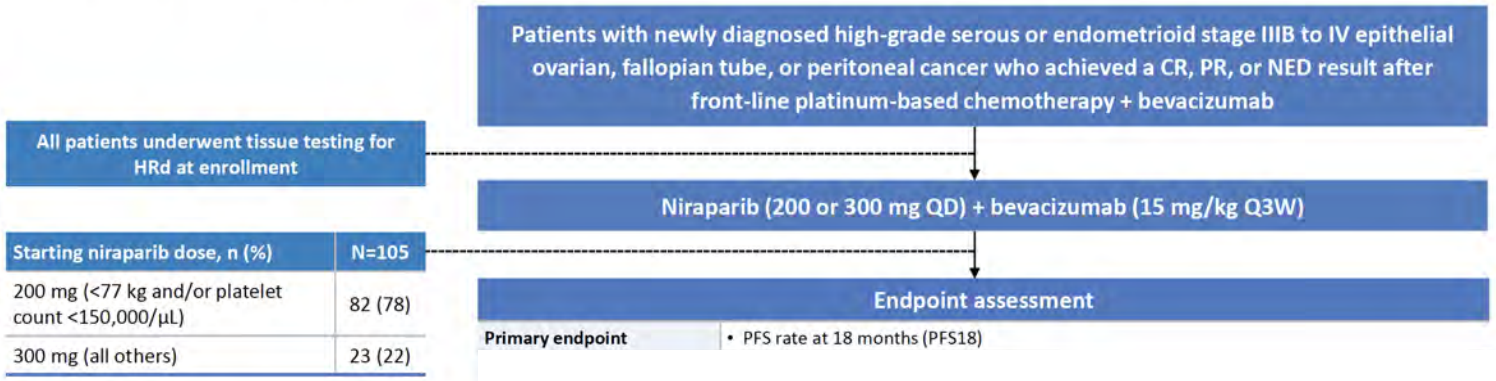
Phase 2 OVARIO Study of Niraparib + Bevacizumab Therapy in Advanced Ovarian Cancer Following Frontline Platinum-Based Chemotherapy with Bevacizumab – M. Hardesty, et al SGO 2022

OVARIO trial design



Starting niraparib dose, n (%)	N=105
200 mg (<77 kg and/or platelet count <150,000/µL)	82 (78)
300 mg (all others)	23 (22)

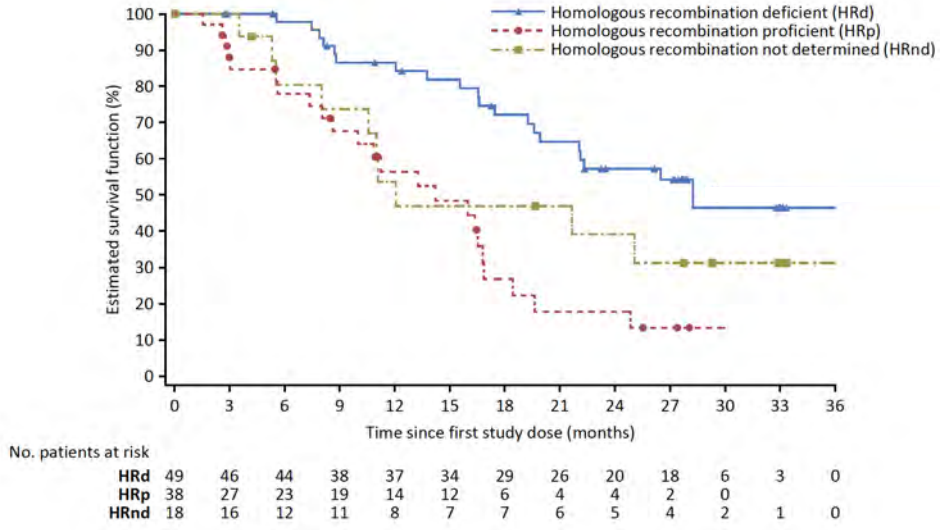
Parameter	Overall (N=105)
Biomarker status, n (%)	
HRd	49 (47)
*BRCA*m	29 (28)
*BRCA*wt	16 (15)
HRp	38 (36)
HRnd*	18 (17)
Post-surgery macroscopic disease, n (%)	
Yes	28 (27)
No	67 (64)
Unknown	10 (9)
Missing	0 (0)
Debulking surgery, n (%)	
PDS	39 (37)
NACT/IDS	66 (63)
Response after surgery/platinum-based CT, n (%)	
CR/NED	61 (58)
PR	44 (42)

Primary endpoint	• PFS rate at 18 months (PFS18)
Secondary endpoints	• PFS • Overall survival • RECIST or CA-125 PFS • Time to first subsequent therapy • Time to second subsequent therapy • Safety and tolerability • Patient-reported outcome
Exploratory endpoints	• PFS rate at 6 months (PFS6) and 12 months (PFS12)
Statistical analysis plan	• Efficacy: PFS18 and PFS24 will be estimated by frequency analysis, with corresponding 95% exact CI will be reported • The time to event endpoints (PFS, TFST, TSST) will be analyzed using Kaplan-Meier methodology • Progression will be assessed by RECIST v1.1 per investigator

Phase 2 OVARIO Study of Niraparib + Bevacizumab Therapy in Advanced Ovarian Cancer Following Frontline Platinum-Based Chemotherapy with Bevacizumab – M. Hardesty, et al SGO 2022

Parameter	Overall N=105	HRd n=49	HRp n=38	HRnd n=18
18-month PFS rate, % (95% CI)	62 (52, 71)	76 (61, 87)	47 (31, 64)	56 (31, 78)
24-month PFS rate, % (95% CI)	53 (43, 63)	63 (48, 77)	42 (26, 59)	50 (26 ,74)

- **Overall population median (95% CI) values:**
  - PFS 19.6 months (16.5–25.1)
  - TFST 17.5 months (14.5–20.7)
  - TSST NE (32.1–NE)
- OS was immature with an event rate of 23.8%



- Median PFS (95% CI) was higher in the HRd subgroup (28.3 months [19.9, NE]) versus HRp(14.2 months [8.6, 16.8]) and HRnd subgroups (12.1 months [8, NE])
- OVARIO enrolled a high-risk population
- In the overall population, more than half (53%) of patients remained progression free at 24 months
- PFS analysis suggests that the combination of niraparib and bevacizumab maintenance is efficacious; clinical benefit was observed in the overall population, and across biomarker subgroups in a continuum

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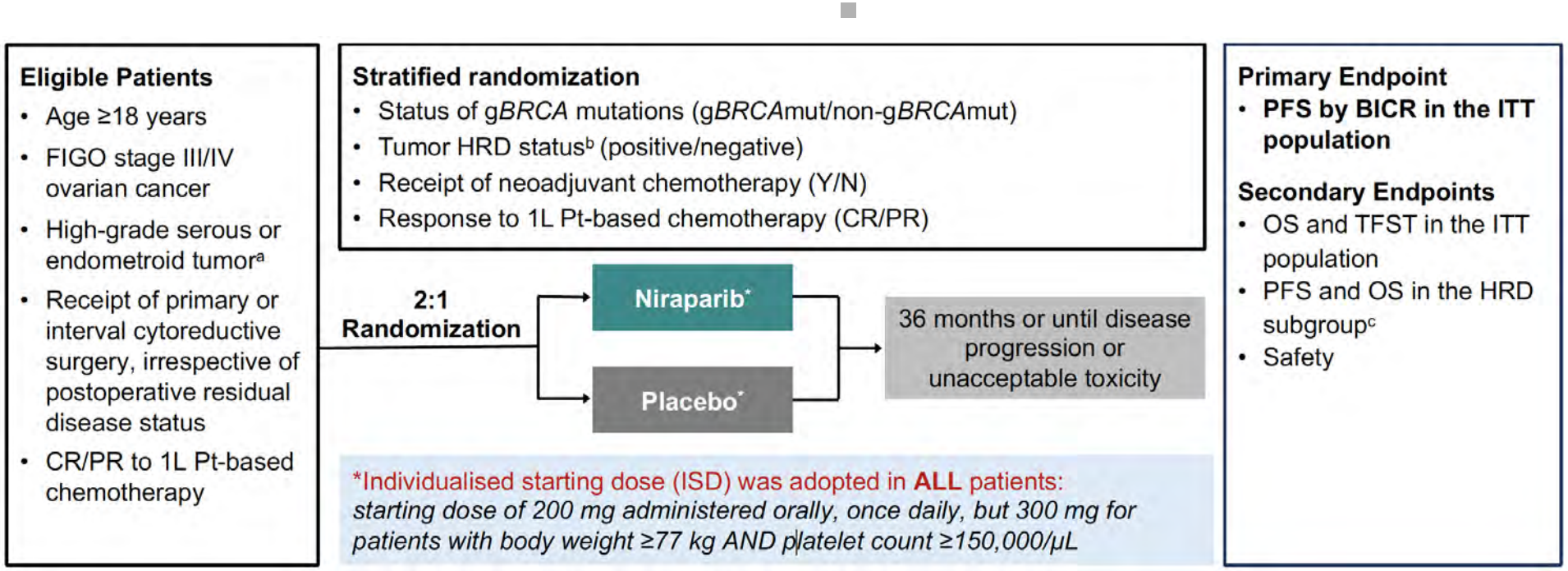
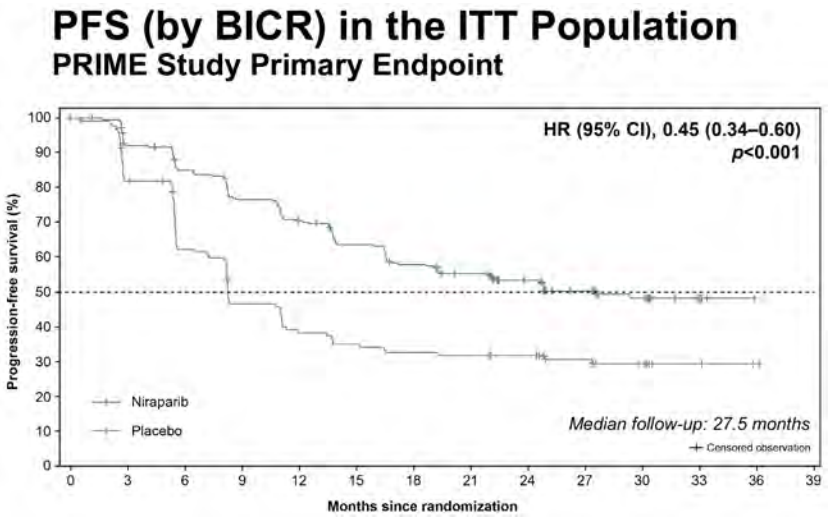
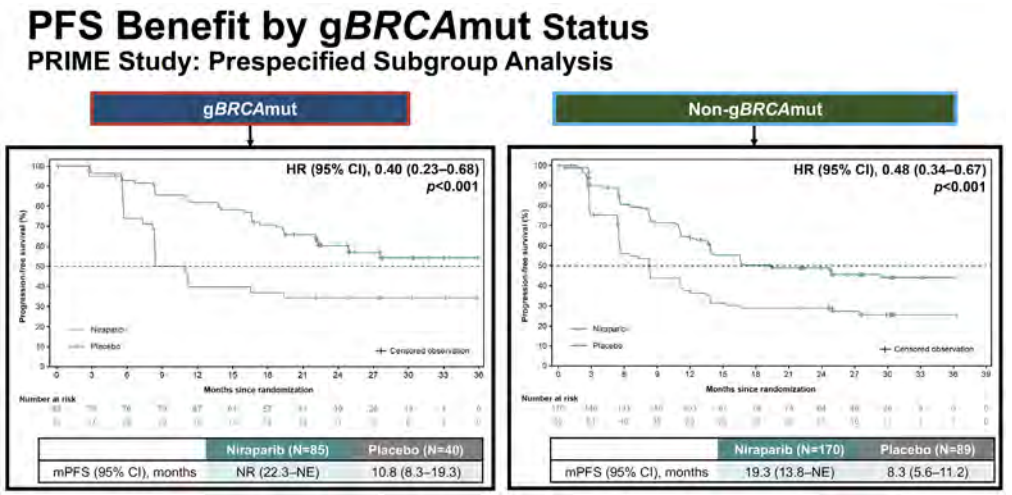
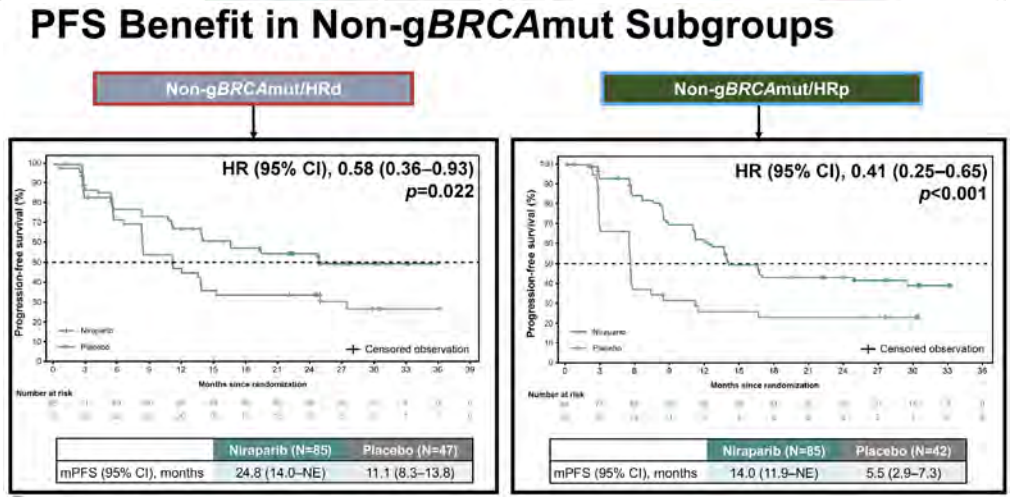
Efficacy and Safety of Niraparib as Maintenance Treatment in Patients with Newly Diagnosed Advanced Ovarian Cancer Using an Individualized Starting Dose (PRIME Study): A Randomized, Double-blind, Placebo controlled, Phase 3 Trial N Li, et al SGO 2022

PRIME study was designed to prospectively assess the efficacy and safety of niraparib with ISD as maintenance therapy in patients with newly diagnosed advanced ovarian cancer after a response to 1L Pt-based chemotherapy, regardless of biomarker status and postoperative residual disease status.









- Chinese population
- ITT population: mPFS, 24.8 vs 8.3 months; HR, 0.45; p<0.001
- HRD subgroup: mPFS, NR vs 11.0 months; HR, 0.48; p<0.001
- gBRCAmut patients: mPFS, NR vs 10.8 months; HR, 0.40; p<0.001
- Non-gBRCAmut patients: mPFS, 19.3 vs 8.3 months; HR, 0.48; p<0.001

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N Li, et al SGO 2022

2022 ASCO® ANNUAL MEETING

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ENGOT European Network of Gynaecological Oncological Trial groups

NRG Oncology-Japan

ATHENA–MONO (GOG-3020/ENGOT-ov45): A Randomized, Double-blind, Phase 3 Trial Evaluating Rucaparib Monotherapy Vs Placebo As Maintenance Treatment Following Response To First-line Platinum-based Chemotherapy In Ovarian Cancer

Bradley J. Monk,[1] Christine Parkinson,[2] Myong Cheol Lim,[3] David M. O'Malley,[4] Ana Oaknin,[5] Michelle K. Wilson,[6] Robert L. Coleman,[7] Domenica Lorusso,[8] Amit Oza,[9] Sharad Ghamande,[10] Athina Christopoulou,[11] Emily Prendergast,[12] Fuat Demirkiran,[13] Ramey D. Littell,[14] Anita Chudecka-Głaz,[15] Mark A. Morgan,[16] Sandra Goble,[17] Stephanie Hume,[17] Keiichi Fujiwara,[18] Rebecca S. Kristeleit[19]

[1]GOG Foundation, HonorHealth Research Institute, University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, AZ, USA; [2]Addenbrooke's Hospital, Cambridge, UK; [3]National Cancer Center Korea, Goyang-si, Gyeonggi-do, Republic of Korea; [4]The Ohio State University, James Cancer Center, Columbus, OH, USA; [5]Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [6]Auckland City Hospital, Auckland, New Zealand; [7]US Oncology Research, The Woodlands, TX, USA; [8]MITO and Fondazione Universitario A. Policlinico Gemelli IRCCS and Catholic University of Sacred Heart, Rome, Italy; [9]Princess Margaret Hospital Cancer Centre, Toronto, Ontario, Canada; [10]Augusta University, Augusta, GA, USA; [11]St. Andrews General Hospital, Patras, Greece; [12]Minnesota Oncology and Metro-Minnesota Community Oncology Research Consortium, Minneapolis, MN, USA; [13]Istanbul University, Cerrahpaşa, Istanbul, Turkey; [14]Kaiser Permanente Northern California Gynecologic Cancer Program, San Francisco, CA, USA; [15]Pomeranian Medical University, Szczecin, Poland; [16]University of Pennsylvania Health System, Philadelphia, PA, USA; [17]Clovis Oncology, Inc., Boulder, CO, USA; [18]Saitama Medical University International Medical Center, Hidaka, Saitama, Japan; [19]Guy's and St Thomas' NHS Foundation Trust, London, UK

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ATHENA–MONO Study Schema

Athena
RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 3 STUDY OF NIVOLUMAB AND RUCAPARIB

Key Patient Eligibility

- Newly diagnosed, stage III–IV, high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer
- Completed frontline platinum-doublet chemotherapy and surgery
  - Achieved investigator-assessed CR or PR
  - Received cytoreductive surgery (primary or interval; R0/complete resection permitted)
- ECOG PS 0 or 1
- No prior treatment for ovarian cancer, including any maintenance treatment, other than frontline platinum regimen

Randomization 4:4:1:1

- **Arm A (n≈400)** rucaparib 600 mg BID PO + nivolumab 480 mg IV
- **Arm B (n≈400)** rucaparib 600 mg BID PO + placebo IV
- **Arm C (n≈100)** placebo PO + nivolumab 480 mg IV
- **Arm D (n≈100)** placebo PO + placebo IV

Treatment for 24 months*, or until radiographic progression, unacceptable toxicity, or other reason for discontinuation

Randomization Stratification Factors

- Tumor HRD test status†
- Disease status post-chemotherapy
- Timing of surgery

Study Analyses

ATHENA–MONO

- **Arm B (n≈400)** rucaparib 600 mg BID PO + placebo IV
- **Arm D (n≈100)** placebo PO + placebo IV

ATHENA–COMBO

- **Arm A (n≈400)** rucaparib 600 mg BID PO + nivolumab 480 mg IV
- **Arm B (n≈400)** rucaparib 600 mg BID PO + placebo IV

*After initiation of oral/IV combination study treatment (IV drug was initiated cycle 2 day 1; 28-day cycles). †Centrally assessed, determined by FoundationOne CDx ($BRCA^{mut}$, $BRCA^{wt}/LOH^{high}$ [LOH ≥16%], $BRCA^{wt}/LOH^{low}$ [LOH <16%], $BRCA^{wt}/LOH^{indeterminate}$). BID, twice daily; BRCA, *BRCA1* or *BRCA2*; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; HRD, homologous recombination deficiency; IV, intravenous; LOH, loss of heterozygosity; mut, mutant; PO, by mouth; PR, partial response; wt, wild type.

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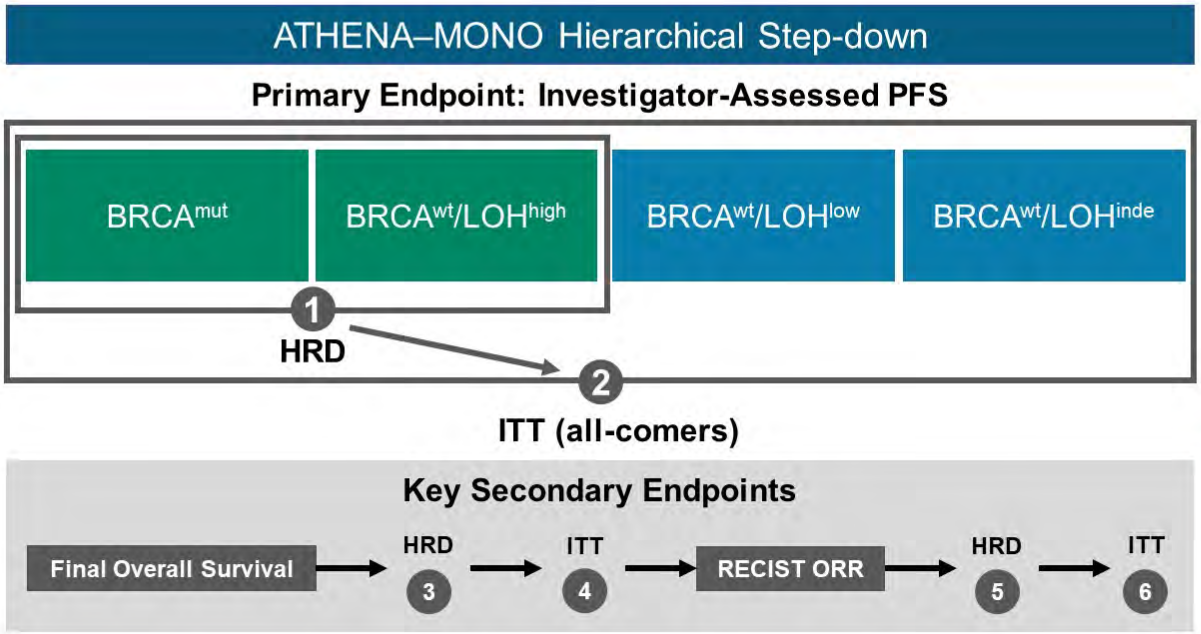
Step-down Analysis for Efficacy Endpoints



- 90% power at a two-sided significance level of 0.025
- Sample size assumptions for primary endpoint:

	HR	Median PFS, mo (Rucaparib vs Placebo)
HRD	0.45	26.7 vs 12.0
ITT	0.60	20.0 vs 12.0

- BICR-assessed PFS is a stand-alone secondary efficacy endpoint outside of the step-down analysis

BICR, blinded independent central radiology review; BRCA, *BRCA1* or *BRCA2*; HR, hazard ratio; HRD, homologous recombination deficiency; inde, indeterminate; ITT, intent-to-treat; LOH, loss of heterozygosity; mut; mutant; ORR, objective response rate; PFS, progression-free survival; RECIST, Response Evaluation Criteria In Solid Tumors, version 1.1; wt, wild type

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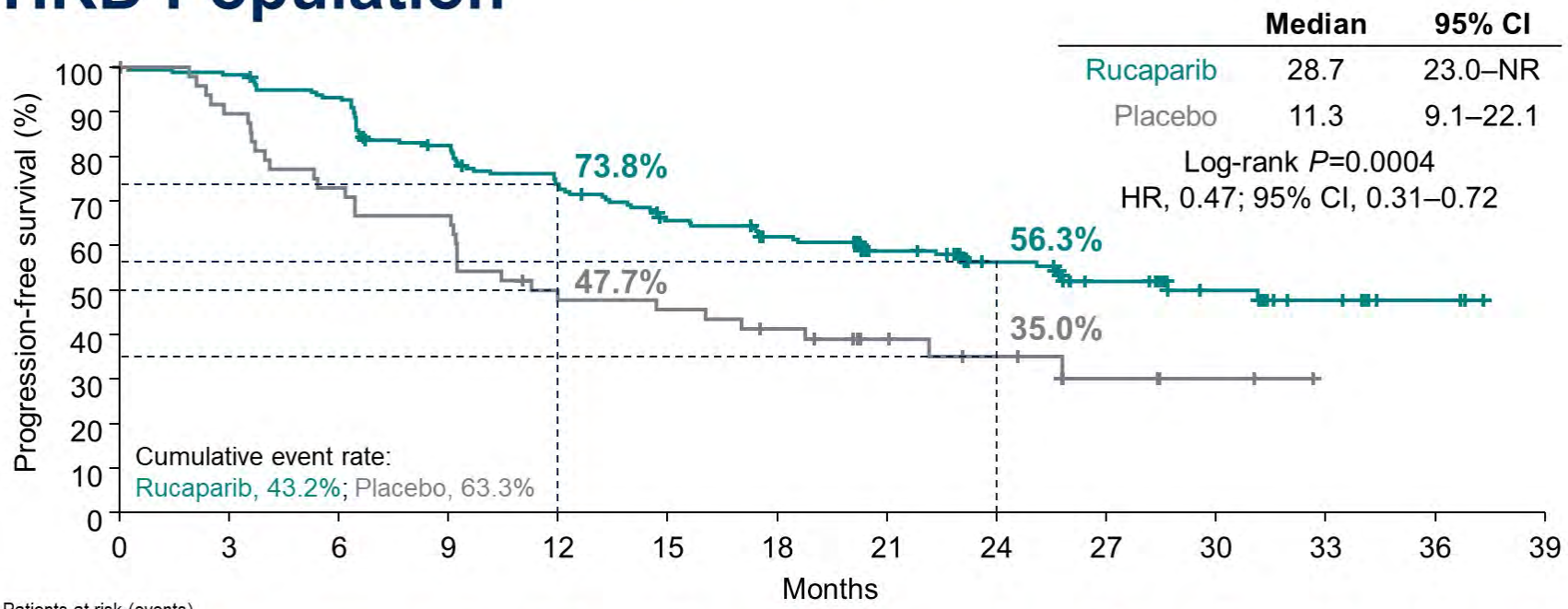
Primary Endpoint – Investigator-Assessed PFS: HRD Population



Patients at risk (events)

Rucaparib	185(0)	175(3)	165(12)	143(31)	127(46)	110(60)	100(66)	82(71)	59(74)	36(78)	22(79)	12(80)	3(80)	0(80)
Placebo	49(0)	43(5)	35(13)	32(16)	22(25)	21(26)	18(28)	11(29)	8(30)	4(31)	2(31)	0(31)		

Data cutoff date: March 23, 2022.
HR, hazard ratio; HRD, homologous recombination deficiency; NR, not reached; PFS, progression-free survival.

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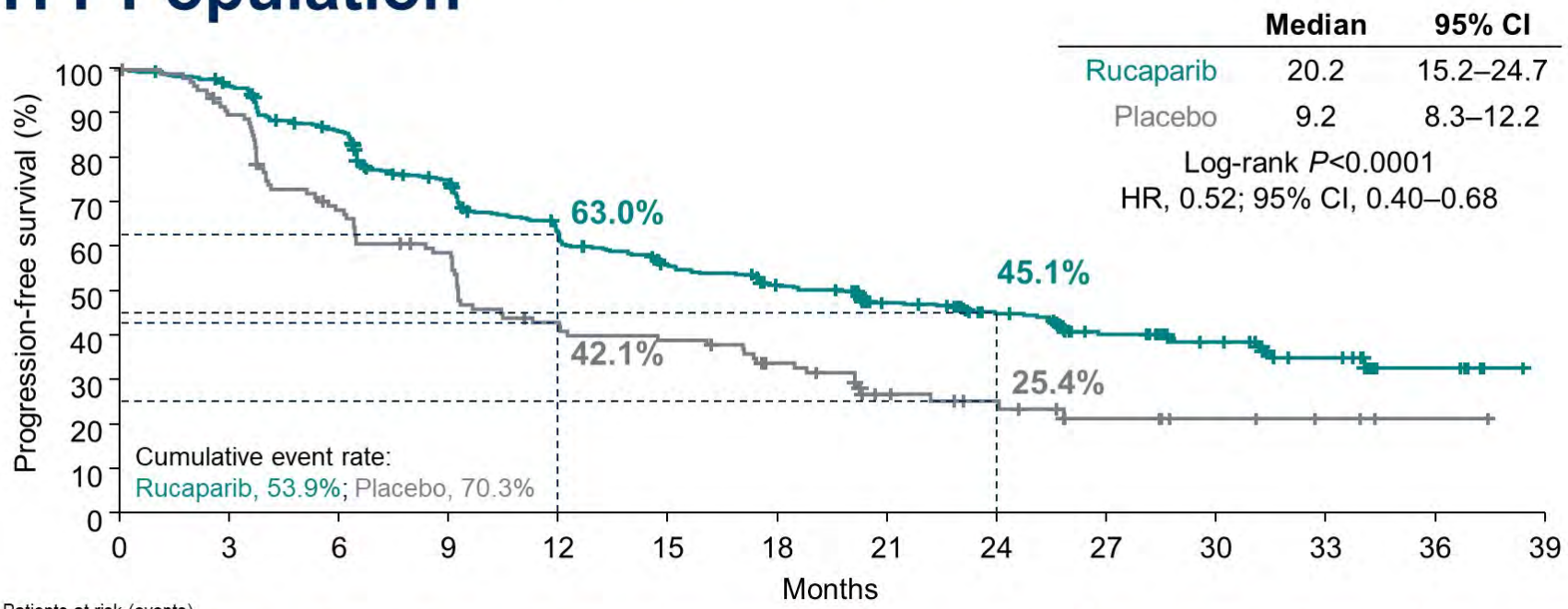
Primary Endpoint – Investigator-Assessed PFS: ITT Population



Patients at risk (events)

Rucaparib	427 (0)	398 (15)	351 (57)	298 (101)	245 (149)	213 (176)	190 (193)	151 (207)	114 (214)	67 (224)	42 (226)	23 (229)	7 (230)	0 (230)
Placebo	111 (0)	97 (11)	72 (34)	60 (44)	42 (61)	39 (64)	31 (69)	18 (75)	14 (76)	8 (78)	5 (78)	3 (78)	1 (78)	0 (78)

Data cutoff date: March 23, 2022.
HR, hazard ratio; ITT, intent-to-treat; PFS, progression-free survival.

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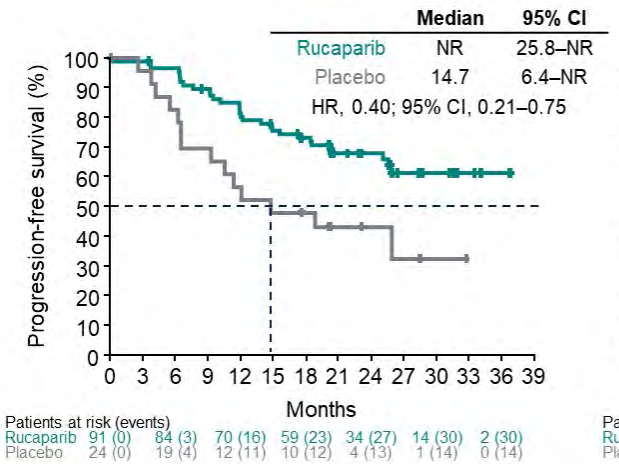
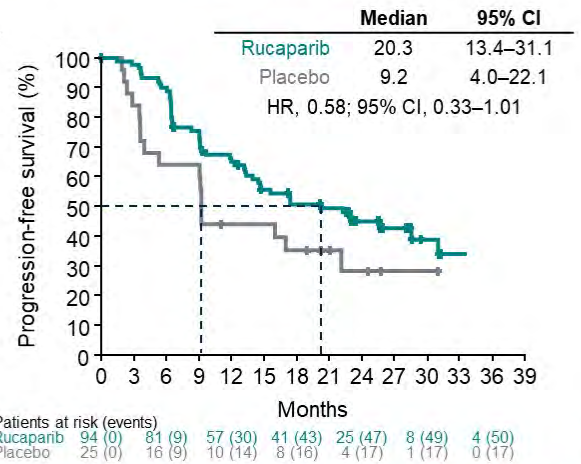
Investigator-Assessed PFS: Exploratory Subgroups

HRD positive

BRCA^{mut}

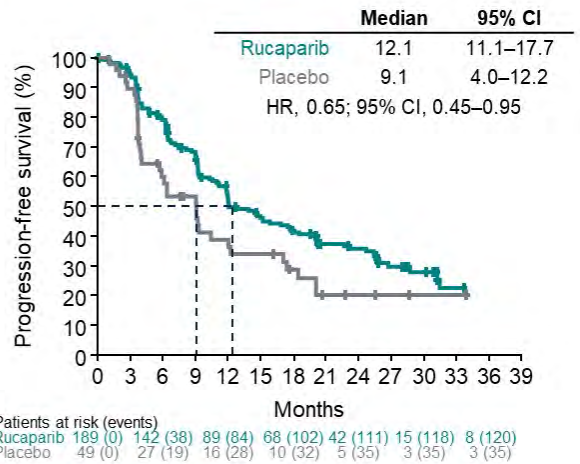


BRCA^{wt}/LOH^{high}



HRD negative

BRCA^{wt}/LOH^{low}



- Rucaparib demonstrated treatment benefit vs placebo regardless of BRCA mutation and HRD status

Data cutoff date: March 23, 2022.

BRCA, *BRCA1* or *BRCA2*; HR, hazard ratio; HRD, homologous recombination deficiency; LOH, loss of heterozygosity; mut, mutant; NR, not reached; PFS, progression-free survival; wt, wild type.

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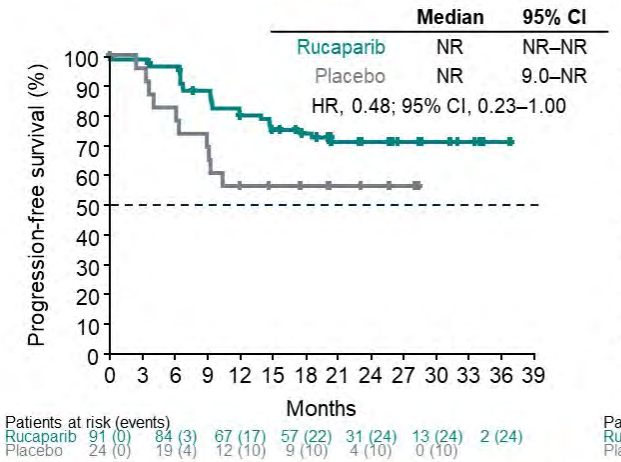
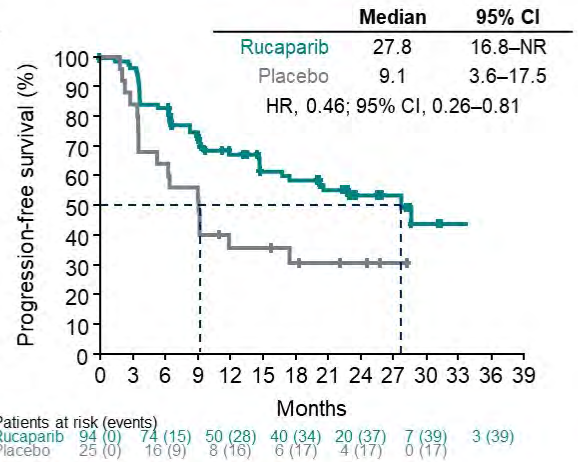
BICR-Assessed PFS: Exploratory Subgroups

HRD positive

BRCA^{mut}

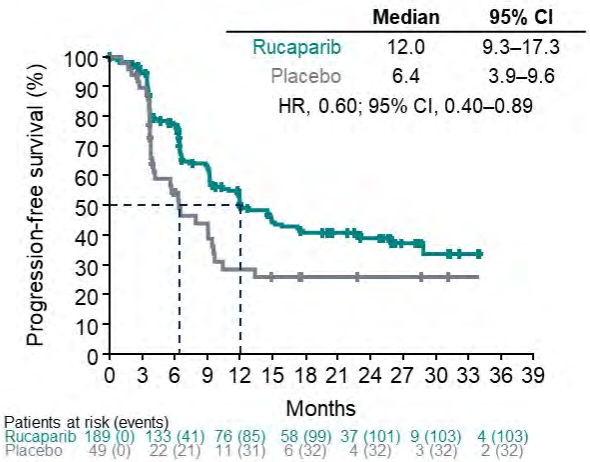


BRCA^{wt}/LOH^{high}



HRD negative

BRCA^{wt}/LOH^{low}



- Data were similar with BICR-assessed PFS for HRD subgroups

Data cutoff date: March 23, 2022.

BICR, blinded independent central radiology review; BRCA, *BRCA1* or *BRCA2*; HR, hazard ratio; HRD, homologous recombination deficiency; LOH, loss of heterozygosity; mut, mutant; NR, not reached; PFS, progression-free survival; wt, wild type

Monk ASCO 2022 LBA 5500

PARPi for 1LM: Key Efficacy Data

Efficacy	PRIMA[1] (N=733)	PRIME[2] (N=384) (study performed only in China)	SOLO-1[3] (N=391) (5-year follow-up)	ATHENA-MONO[4] (N=538)	ATHENA-MONO[4] (N=538)	PAOLA-1[5] (N=806)	OVARIO[6] (N=105) (updated analysis)
Treatment	Niraparib vs placebo	Niraparib vs placebo	Olaparib vs placebo	Rucaparib vs placebo	Rucaparib vs placebo	Olaparib/Bev vs Bev	Niraparib/Bev
BICR or Investigator	BICR	BICR	Investigator	Investigator (Primary)	BICR	Investigator	Investigator?
ITT	N=733 13.8 vs 8.2 0.62 (0.50-0.76)	N=384 24.8 vs 8.3 0.45 (0.34-0.60)	-	N=538 20.2 vs 9.2 0.52 (0.40-0.68)	N=538 25.9 vs 9.1 0.47 (0.36-0.63)	N=806 22.1 vs 16.6 0.59 (0.49-0.72)	N=105 19.6
*BRCA*wt/HRp	n=249 8.1 vs 5.4 0.68 (0.49-0.94)	n=127[b] 14.0 vs 5.5 0.41 (0.25-0.65)	-	n=238 12.1 vs 9.1 0.65 (0.45-0.95)	n=238 12.0 vs 6.4 0.60 (0.40-0.89)	n=211 16.9 vs 16.0 1.00 (0.75-1.35)[b]	n=38 14.2
*BRCA*wt/HRd	n=150 19.6 vs 8.2 0.50 (0.31-0.83)	n=132[c] 24.8 vs 11.1 0.58 (0.36-0.93)	-	n=119 20.3 vs 9.2 0.58 (0.33-1.01)	n=119 27.8 vs 9.1 0.46 (0.26-0.81)	n=152 28.1 vs 16.6 0.43 (0.28-0.66)[b]	n=16 28.3
*BRCA*m	n=223 22.1 vs 10.9 0.40 (0.27-0.62)	n=125[d] NR vs 10.8 0.40 (0.23-0.68)	n=391 56.0 vs 13.8 0.33 (0.25-0.43)	n=115 NR vs 14.7 0.40 (0.21-0.75)	n=115 NR vs NR 0.48 (0.23-1.0)	n=90 37.2 vs 21.7 0.31 (0.20-0.47)[b]	n=29 NR
Median duration of follow-up, months	13.8	27.5	59	26.1	26.1	22.9	28.7

Median PFS, months; HR[a] (95% CI)

[a] HR for disease progression or death. [b] Non-*gBRCA*m/HRp. [c] Non-*gBRCA*m/HRd. [d] g*BRCA*m population. 1LM, first-line maintenance; *BRCA*wt, *BRCA* wild type; g*BRCA*m, germline *BRCA* mutant; HR, hazard ratio; HRd, homologous recombination deficient; HRp, homologous recombination proficient; ITT, intention-to-treat; NA, not available; NR, not reached; PARPi, poly(ADP-ribose) polymerase inhibitor; PFS, progression-free survival.

1. Gonzalez-Martin A, et al. *N Engl J Med.* 2019;381(25):2391-2402. 2. Li N, et al. Presented at SGO 2022. Abstract 244. 3. Banerjee S, et al. *Lancet Oncol*. 2021;22(12):1721-1731. 4. Monk B, et al. JCO on line June 6, 2022.
5. Ray-Coquard I, et al. *N Engl J Med*. 2019;381(25):2416-2428. 6. Hardesty M, et al. Presented at SGO 2022. Abstract 170B.

Dear Health Care Provider Letter (Niraparib)

May 2022

IMPORTANT DRUG WARNING

Subject: Zejula (Niraparib) Important Drug Warning For The Maintenance Treatment In Recurrent Ovarian Cancer (2L+)

Dear Health Care Provider:

The purpose of this letter is to inform you of important information for Zejula® (niraparib) a poly (ADP-ribose) polymerase (PARP) inhibitor indicated for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy received in the 2nd line or higher settings. GlaxoSmithKline (GSK) would like to inform you of updated overall survival (OS) data from the ENGOT- OV16/NOVA study.

Updated OS Data from the ENGOT-OV16/NOVA study, a Phase III trial which evaluated the efficacy and safety of niraparib as maintenance treatment for patients with platinum-sensitive recurrent ovarian cancer

https://www.zejulahcp.com/content/dam/cf-pharma/hcp-zejulahcp-v2/en_US/pdf/ZEJULA%20(niraparib)%20Dear%20HCP%20Letter.pdf

ENGOT-OV16/NOVA Long-term Follow-up: OS

BRCAmut: mOS 43.6 vs. 41.6 for niraparib vs placebo (HR=0.93 (95% 0.63-1.36)

BRCAwt: mOS 31.1 vs. 36.5 months for niraparib vs placebo (HR =1.10 (95% CI 0.83-1.46)

BRCAwt/HRD mOS 37.3 vs. 41.4 months for niraparib vs placebo (HR 1.32 (95% CI 0.84-2.06)

The current OS result indicate a possible OS detriment to patients in the overall BRCAwt cohort who received niraparib

For a PARPi naïve patient with PSOC – does this impact your practice?

Figure 2: OS Kaplan Meier curve for the non-g*BRCA*mut HRD positive subgroup

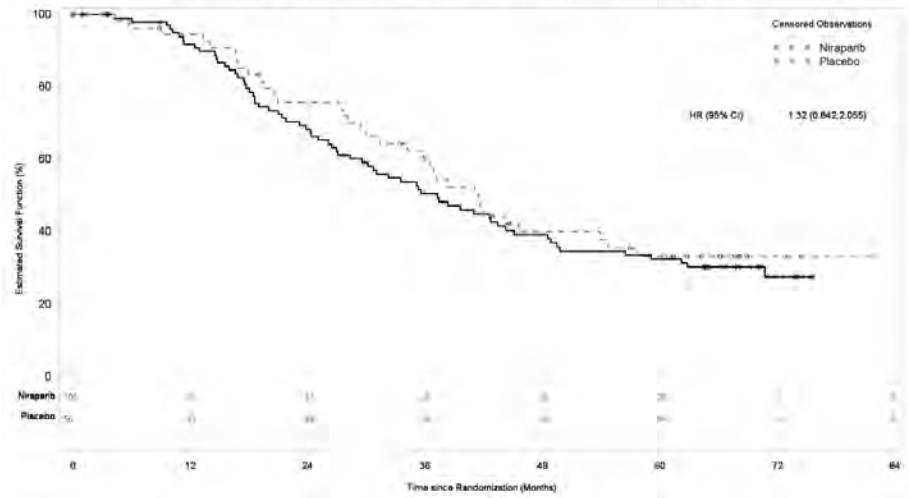


Figure 1: OS Kaplan Meier curve for the non-g*BRCA*mut cohort

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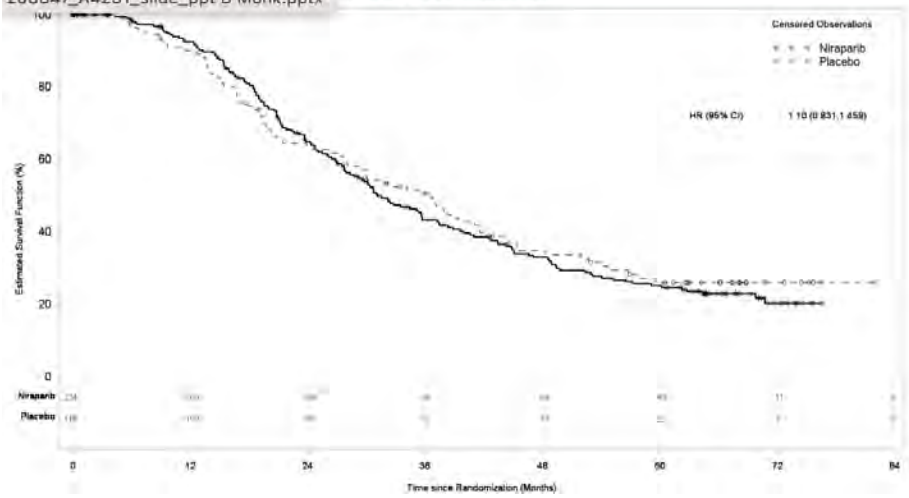

https://www.zejulahcp.com/content/dam/cf-pharma/hcp-zejulahcp-v2/en_US/pdf/ZEJULA%20(niraparib)%20Dear%20HCP%20Letter.pdf

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Q: How does the HCP letter affect your consideration of PARPi use in the Recurrent Setting?

(assume patient is otherwise eligible to receive a PARPi)

A. It doesn't at all – I question the analysis

B. I believe PARPi maintenance therapy is valuable for patients, but will now limit my treatment duration

C. I believe PARPi maintenance therapy is valuable for patients, but will now limit my patient selection

D. Both B and C

E. I believe PARPi maintenance therapy is potentially dangerous and will significantly limit my administration

F. I don't believe PARPi maintenance therapy is valuable and this letter confirms my bias

Q: How does the HCP letter affect your consideration of PARPi use in the Primary Setting?

(assume patient is otherwise eligible to receive a PARPi)

A. It doesn't at all – it questions the analysis

B. I believe PARPi maintenance therapy is valuable for patients, but will now limit my treatment duration

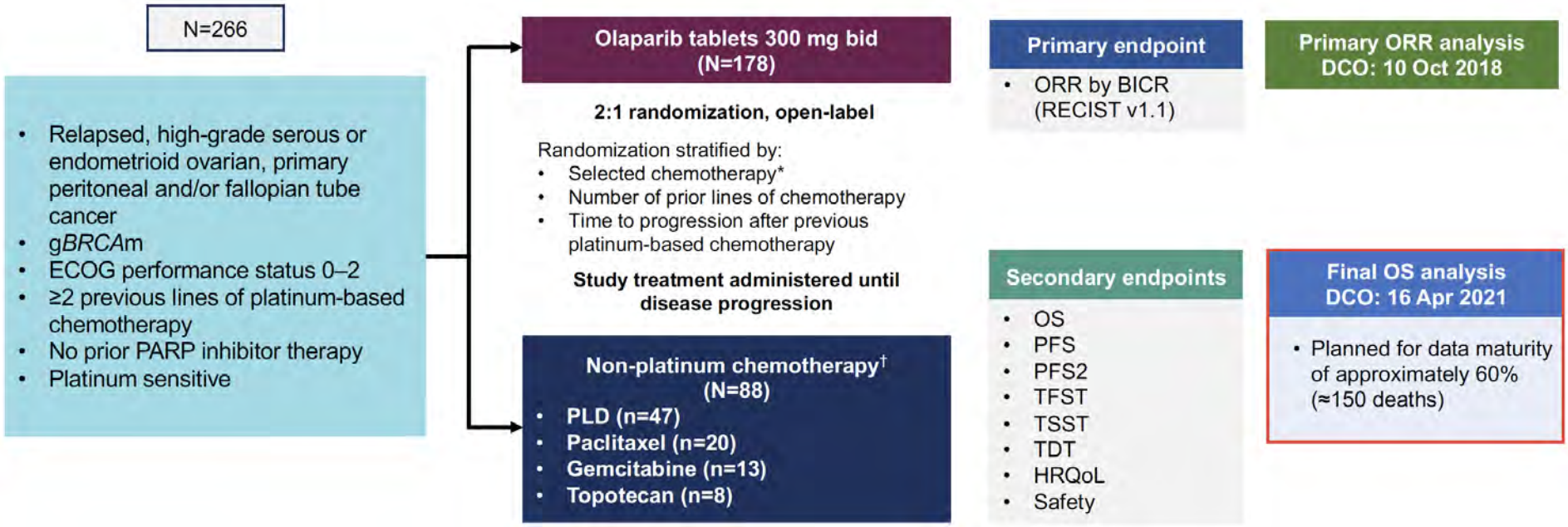
C. I believe PARPi maintenance therapy is valuable for patients, but will now limit my patient selection

D. Both B and C

E. I believe PARPi maintenance therapy is potentially dangerous and will significantly limit my administration

F. I don't believe PARPi maintenance therapy is valuable and this letter confirms my bias

Final overall survival results from SOLO3: Phase III trial assessing olaparib monotherapy versus non-platinum chemotherapy in heavily pre-treated patients with germline BRCA1- and/or BRCA2-mutated platinum-sensitive relapsed ovarian cancer R Penson et al SGO 2022



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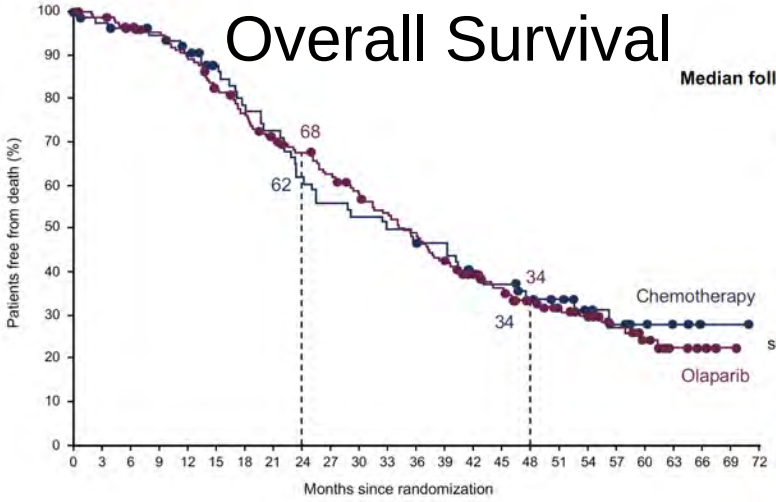
Final overall survival results from SOLO3: Phase III trial assessing olaparib monotherapy versus non-platinum chemotherapy in heavily pre-treated patients with germline BRCA1- and/or BRCA2-mutated platinum-sensitive relapsed ovarian cancer R Penson et al SGO 2022

Overall Survival

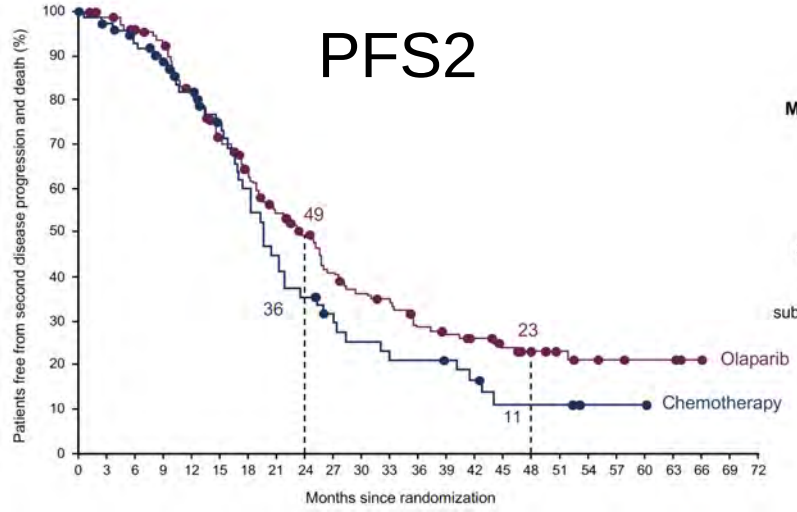


	Olaparib (N=178)	Chemotherapy (N=88)
Median follow-up for OS, months	48.9	25.4
Events, n (%)	116 (65)	46 (52)
Median OS, months	**34.9**	**32.9**
HR 1.07 (95% CI 0.76–1.49); *P*=0.714		

	Olaparib	Chemotherapy
Subsequent anticancer therapy, n	119	54
PARP inhibitor as first subsequent therapy, n (%)	3 (3)	23 (43)
Any subsequent PARP inhibitor therapy, n (%)	9 (8)	33 (61)

11% of olaparib patients vs 25% of chemotherapy patients left the study prior to death

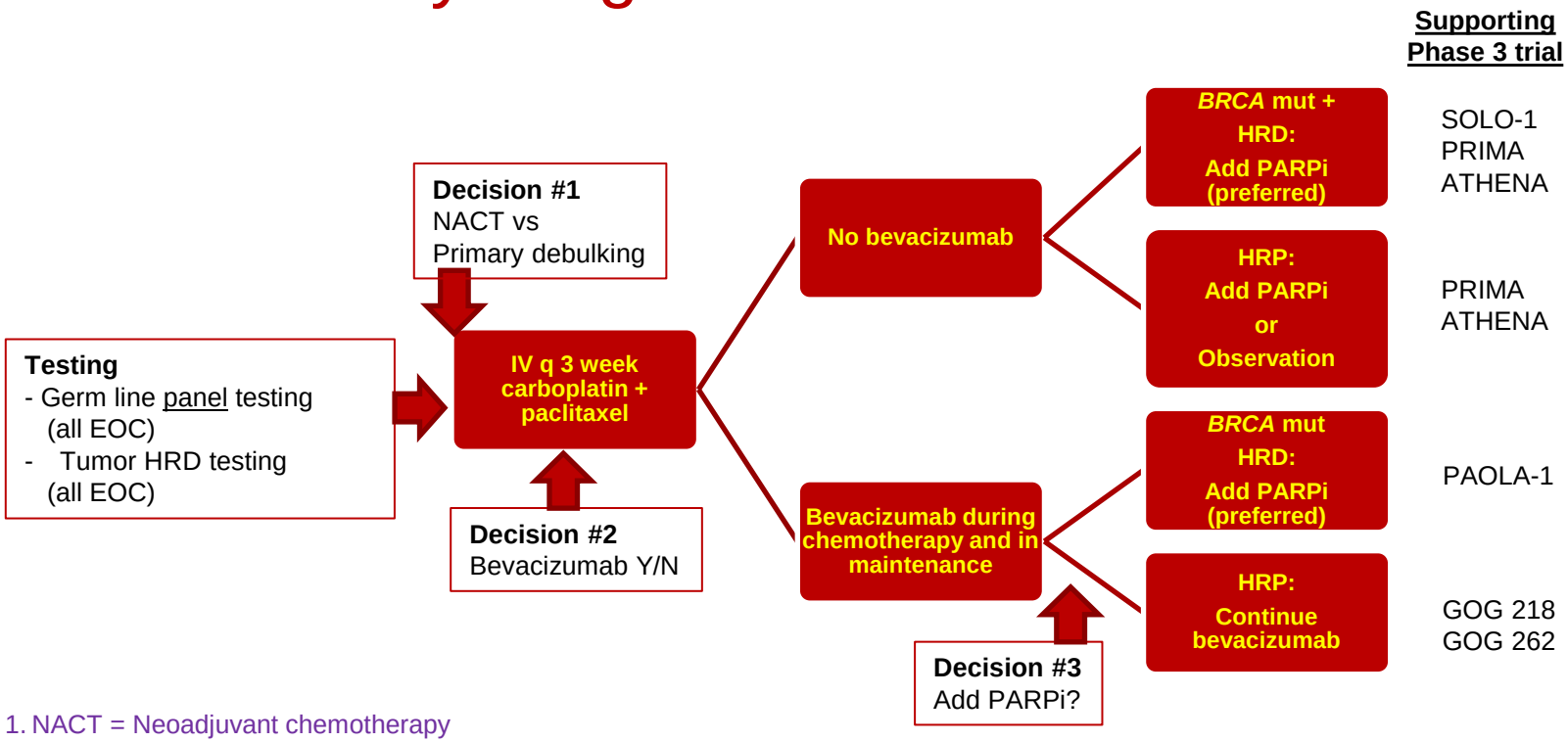
PFS2



	Olaparib (N=178)	Chemotherapy (N=88)
Events, n (%)	114 (64)	48 (55)
Median PFS2, months	**23.6**	**19.6**
HR 0.80 (95% CI 0.56–1.15); *P*=0.229		

	Olaparib	Chemotherapy
Subsequent anticancer therapy, n	119	54
PARP inhibitor as first subsequent therapy, n (%)	3 (3)	23 (43)

What Is the Standard Systemic Treatment for Newly Diagnosed Advanced EOC 2022?



1. NACT = Neoadjuvant chemotherapy
2. EOC=Epithelial ovarian cancer
3. HRD = Homologous recombination deficient
4. HRP = Homologous recombination proficient
5. PARPi = Poly ADP Ribose inhibitor

Selecting new upfront regimens for advanced ovarian cancer with biomarker guidance. Chan JK, Liang SY, Kapp DS, Chan JE, Herzog TJ, Coleman RL, Monk BJ, Richardson MT. Gynecol Oncol. 2020 Dec;159(3):604-606.

Future Directions in the Front Line: What is Potentially Exciting?

Trial	Size	Anti-angiogenic	PARPi	ICI	Start	Estimated Primary Completion
FIRST[a] ENGOT OV-44	1405	± Bevacizumab	Niraparib	Dostarlimab	Oct 2018	Jan 2023
DUO-O[b] ENGOT OV-46	~1254	Bevacizumab	Olaparib	Durvalumab	Jan 2019	June 2023
ATHENA[c] GOG-3020 ENGOT OV-45	~1000	-	Rucaparib	Nivolumab	May 2018	Dec 2024
ENGOT OV-43[d] KEYLYNK-001	~1086	± Bevacizumab	Olaparib	Pembrolizumab	Dec 2018	Aug 2025

- a. ClinicalTrials.gov. NCT03602859; b. ClinicalTrials.gov. NCT03737643; c. ClinicalTrials.gov. NCT03522246; d. NCT03740165.

Slide courtesy of K Moore

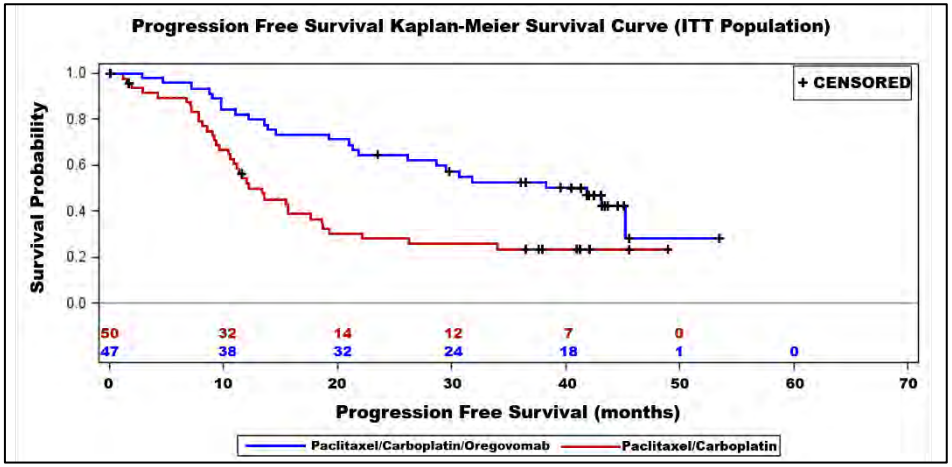
FLORA-5/GOG-3035: Phase 3 Oregovomab (O) Plus Chemo (PC) in Newly Diagnosed Patients With Advanced Epithelial Ovarian Cancer Following Optimal Debulking Surgery

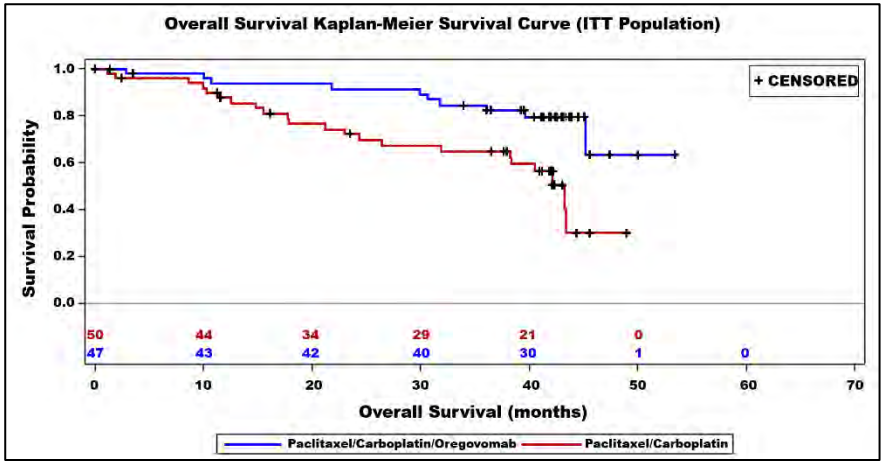
Authors: Angeles Alvarez Secord [1], Sunil Gupta [2], CW Reddick [2], John O. Schorge [3], Sarah Gill[4] on behalf of all FLORA-5 Investigators.
1 Duke University Medical Center, 2 OncoQuest Pharmaceuticals Inc., 3 Tufts Medical Center, 4 Lewis Cancer & Research Pavilion at St. Joseph's/Candler

Abstract Number: TPS5606

Phase 2 Study Results (Oregovomab + Chemotherapy)

Efficacy





Median PFS 41.8 months (95% CI: 21.8 -NE) CPO arm and 12.2 months (95% CI: 10.4–18.6) CP arm; hazard ratio (HR) 0.46 (95% CI: 0.28–0.77), p=0.0027, log rank test

Median OS not yet estimable CPO arm, 43.2 months (95% CI: 31.8 - NE) CP arm; HR 0.35, (95% CI: 0.16–0.74) p=0.0043, log rank test

Safety

There were no differences in the overall safety pattern between the CPO and the CP patients.

Brewer, M., et al (2020). Gynecol Oncol. 2020 Mar;156(3):523-529.

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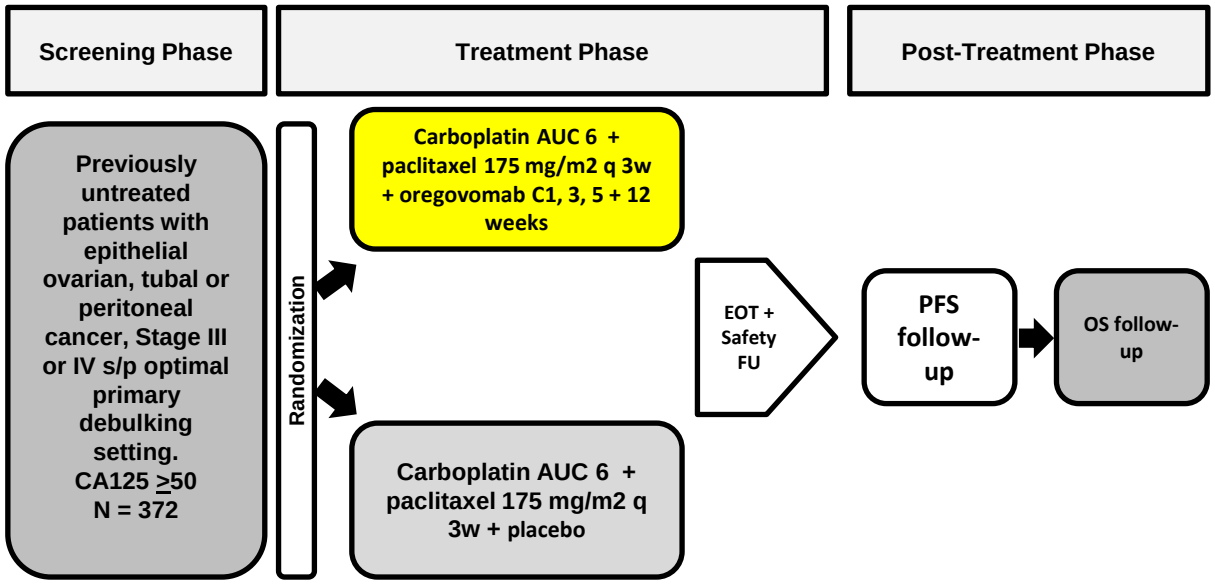
The Ohio State University Wexner Medical Center

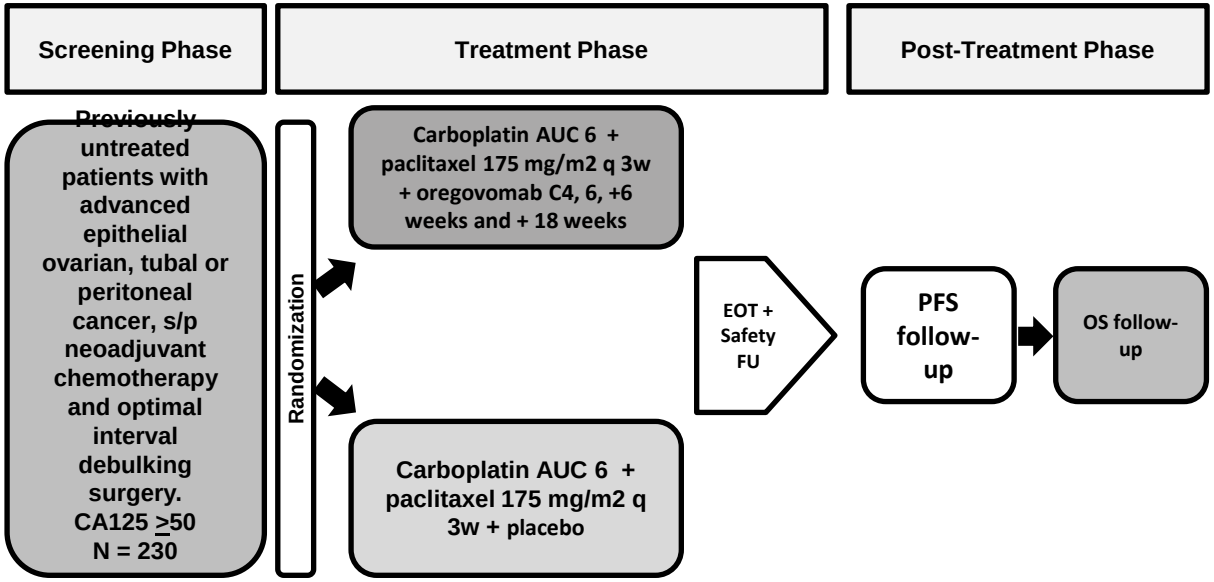
Improving Outcomes for Women with Ovarian Cancer Characterized as HRp is a High Unmet Need

One ongoing trial: GOG 3035: **RPh3 Study of CP +/- oregovomab (primary surgery cohort)**



Improving Outcomes for Women with Ovarian Cancer Characterized as HRp is a High Unmet Need

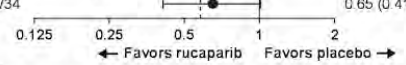
One ongoing trial: GOG 3035: **RPh3 Study of CP +/- oregovomab (NACT cohort)**



Efficacy and safety of rucaparib maintenance treatment in patients from ARIEL3 with platinum-sensitive, recurrent ovarian carcinoma not associated with homologous recombination deficiency. – Coleman ASCO 2022

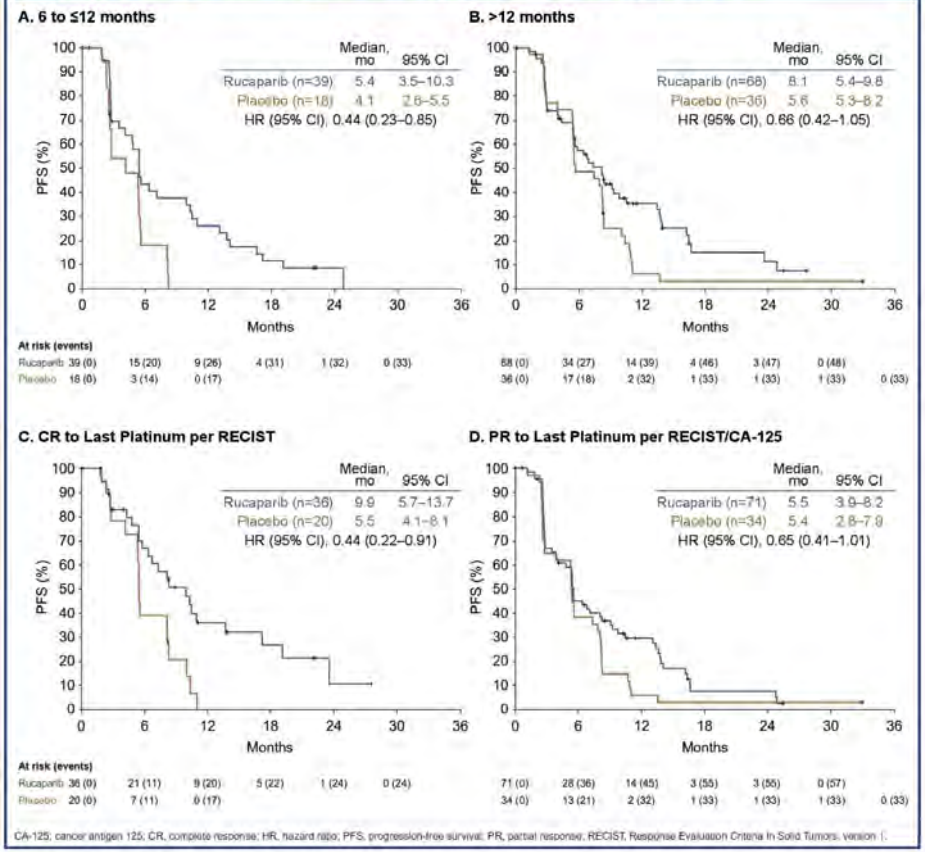
Figure 1. Investigator-Assessed PFS of Patients With HRD-Negative Carcinomas

	Rucaparib (events/patients in subgroup)	Placebo (events/patients in subgroup)	HR (95% CI)	Treatment by subgroup interaction *P* value
HRD negative	81/107	50/54	0.58 (0.40–0.85)	
Age (years)				
<65	40/57	26/29	0.48 (0.25–0.90)	0.49
≥65	41/50	24/25	0.56 (0.31–1.03)	
Race				
White	67/86	38/42	0.64 (0.42–0.98)	0.14
Other/Unknown	14/21	12/12	0.52 (0.22–1.23)	
Measurable disease at baseline				
Yes	38/45	21/21	0.60 (0.32–1.12)	0.31
No	43/62	29/33	0.53 (0.31–0.89)	
Bulky disease at baseline				
Yes	23/27	9/9	0.62 (0.25–1.54)	0.74
No	58/80	41/45	0.59 (0.39–0.91)	
Prior chemotherapy regimens				
2	52/73	36/39	0.65 (0.42–1.03)	0.57
≥3	29/34	14/15	0.48 (0.22–1.06)	
Previous bevacizumab use				
Yes	22/28	11/12	0.60 (0.25–1.45)	0.62
No	59/79	39/42	0.57 (0.37–0.88)	
Prior platinum regimens				
2	52/73	37/40	0.64 (0.41–1.00)	0.69
≥3	29/34	13/14	0.51 (0.23–1.15)	
Time to PD with penultimate platinum				
6 to ≤12 months	33/39	17/18	0.44 (0.23–0.85)	0.51
>12 months	48/68	33/36	0.66 (0.42–1.05)	
Response to last platinum				
RECIST CR	24/36	17/20	0.44 (0.22–0.91)	0.32
RECIST/CA-125 PR	57/71	33/34	0.65 (0.41–1.01)	



No multiplicity adjustment for subgroup analyses was specified in the study protocol. This analysis is exploratory in nature and does not control for the Type I error rate. *P* values were nonsignificant for the treatment by subgroup interaction tests.
CA-125, cancer antigen 125; CR, complete response; HR, hazard ratio; HRD, homologous recombination deficiency; PD, progressive disease; PFS, progression-free survival; PR, partial response; RECIST, Response Evaluation Criteria In Solid Tumors, version 1.1.

Figure 2. Kaplan-Meier Estimates of PFS in Subgroups Based on (A, B) Time to Disease Progression with Penultimate Platinum and (C, D) Response to Last Platinum



CA-125, cancer antigen 125; CR, complete response; HR, hazard ratio; PFS, progression-free survival; PR, partial response; RECIST, Response Evaluation Criteria In Solid Tumors, version 1.

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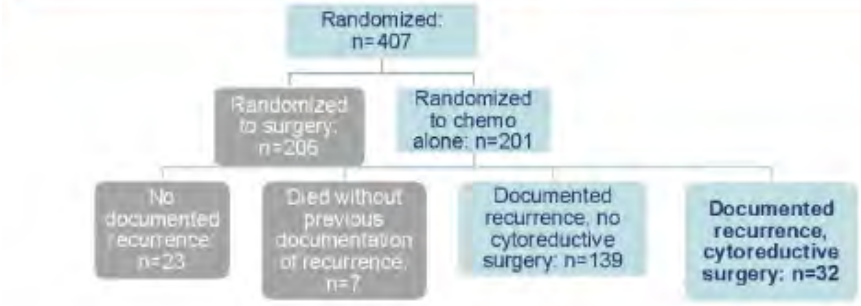
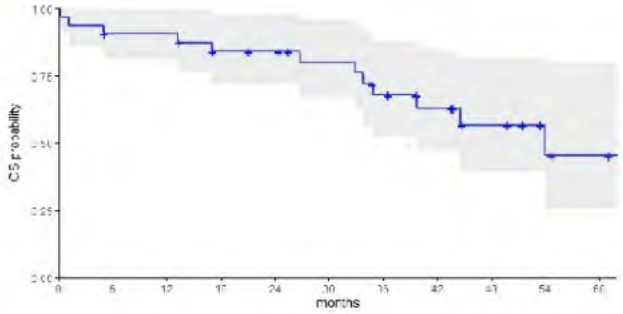
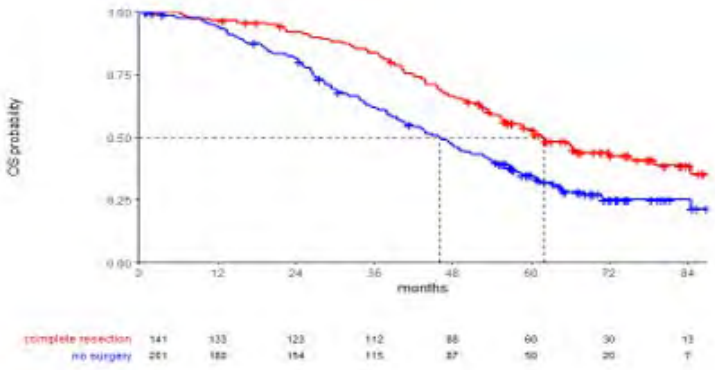
Role of cytoreductive surgery for the second ovarian cancer relapse in patients previously treated with chemotherapy alone at first relapse: A subanalysis of the DESKTOP III trial. **Sehouli ASCO 2022**

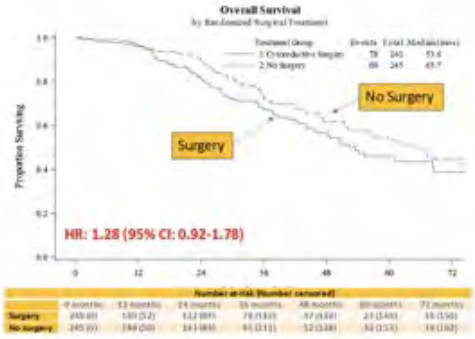
Population Flow Chart

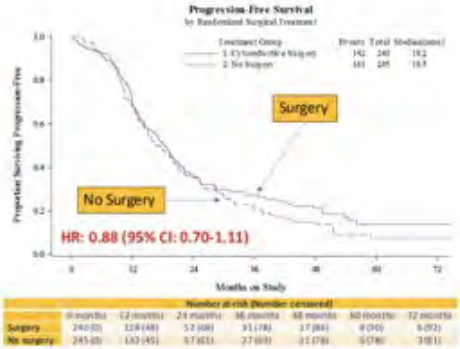


OS after surgery for subsequent relapse









DESKTOP-3:
OS: HR 0.57; 95% CI 0.43-0.76

DuBois A et al. ASCO 2020

GOG 213:
OS: HR 1.28; 95%CI 0.92-1.78

Coleman RA et al. NEJM 2019

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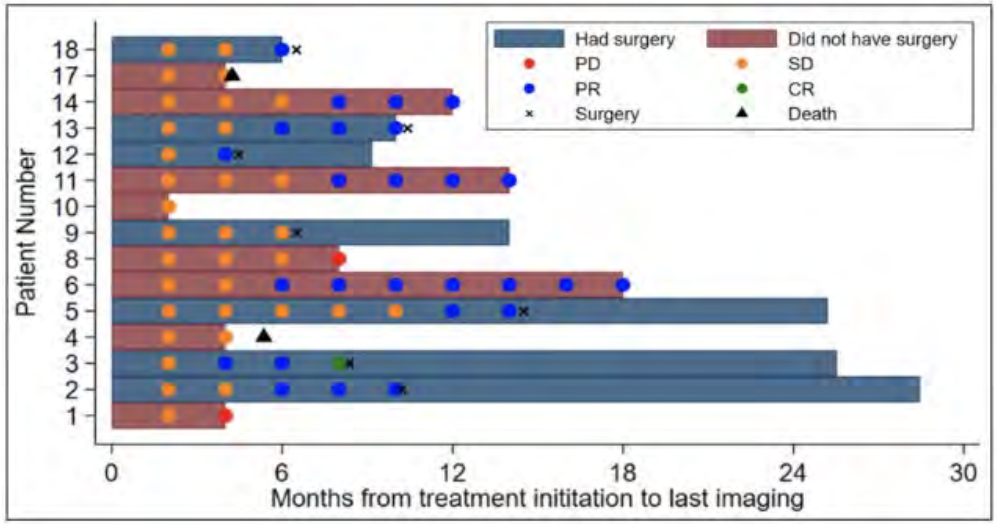
Wexner Medical Center

Rare Tumor

A pilot phase II study of neoadjuvant fulvestrant plus abemaciclib in women with advanced low-grade serous carcinoma. Cobb L et al. ASCO 2022

Abemaciclib: CDK 4/6i



Interval cytoreductive surgery:

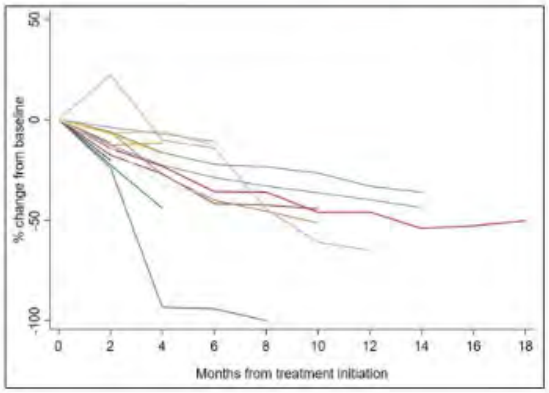
Underwent surgical resection to date – 7/15 (47%)

Achieved complete gross resection – 5/7 (71%)

Achieved optimal cytoreduction – 7/7 (100%)

*Five patients have transitioned to letrozole maintenance

*Adverse events (grade 3 or 4) possibly related to abemaciclib occurred in 2 patients (13.3%) and included acute kidney injury (6.7%) and neutropenia (6.7%).



BORR	# of Subjects	%
Complete Response	1	6.7%
Partial Response	8	53.3%
SD	6	40%
BORR	9	60%
PD	0	20%
Total with at least one scan	15	100%

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Wexner Medical Center

Efficacy and safety of Lucitanib + Nivolumab in Patients with Advanced Gynecologic Malignancies

Endometrial Cancer[b]
- Recurrent disease
- ≥1 prior platinum-based chemotherapy regimen
- Up to 10 patients who have progressed on treatment with 1 prior PD-(L)1 inhibitor administered as monotherapy

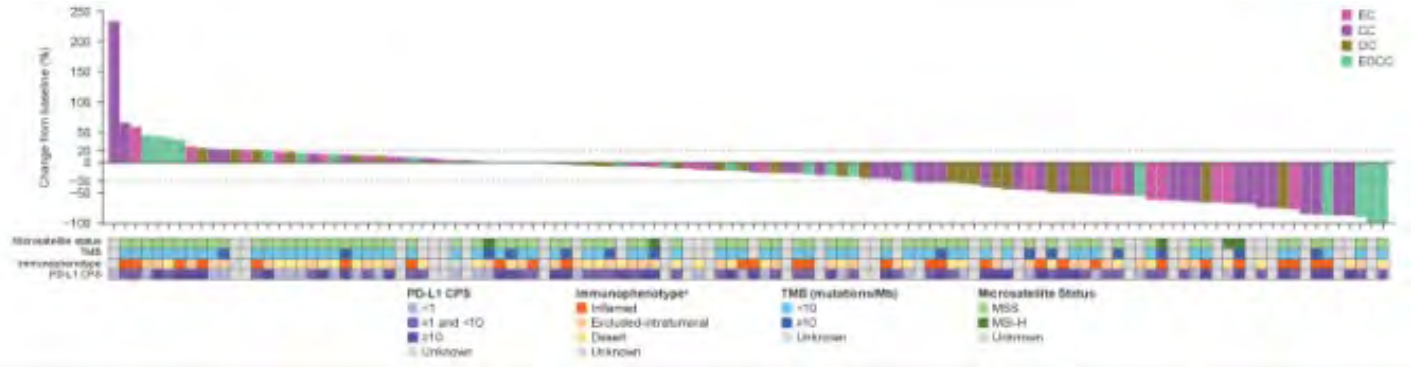
Cervical Cancer
- Persistent or recurrent disease
- ≥1 prior regimen of platinum-based chemotherapy, with or without bevacizumab

Ovarian Cancer[b]
- Recurrent high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer
- ≥2 prior chemotherapy regimens (including ≥1 platinum doublet) OR disease progression ≤6 months after completing 1L platinum-based chemotherapy ie, primary platinum resistance (up to 10 patients)

Endometrial or Ovarian Cancer With Clear-Cell Histology
- Recurrent, metastatic clear-cell carcinoma of ovarian, fallopian tube, primary peritoneal, or endometrial origin
- ≥1 prior platinum- and taxane-based chemotherapy regimen

	EC (n=22)	CC (n=46)	OC (n=33)	EOCC (n=23)
Confirmed ORR, n (%)	**5 (22.7%)**	**12 (26.1%)**	**4 (12.1%)**	**6 (26.1%)**
[95% CI]	[7.8–45.4]	[14.3–41.1]	[3.4–28.2]	[10.2–48.4]
CR	0	2 (4.3)	0	1 (4.3)
PR	5 (22.7)	10 (21.7)	4 (12.1)	5 (21.7)
SD	8 (36.4)	19 (41.3)	18 (54.5)	7 (30.4)
PD	9 (40.9)	12 (26.1)	7 (21.2)	9 (39.1)
NE	0	3 (6.5)	4 (12.1)	1 (4.3)
DCR, n (%)	**11 (50.0%)**	**22 (47.8%)**	**11 (33.3%)**	**11 (47.8%)**
[95% CI]	[28.2–71.8]	[32.9–63.1]	[18.0–51.8]	[26.8–69.4]

CC, cervical cancer; CR, complete response; DCR, disease control rate (CR/PR/SD ≥16 weeks); EC, endometrial cancer; EOCC, endometrial/ovarian clear-cell cancer; NE, not evaluable; OC, ovarian cancer; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease

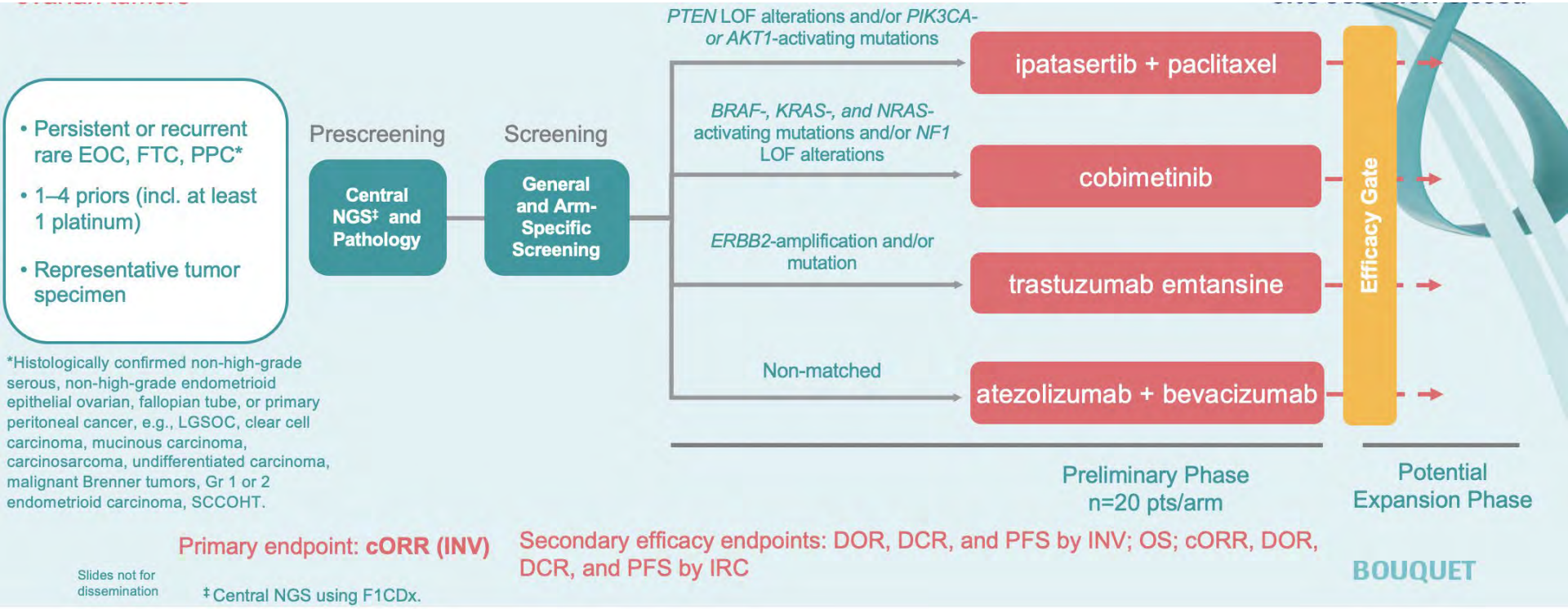


Patel et al. ASCO 2022 Abstract 5517

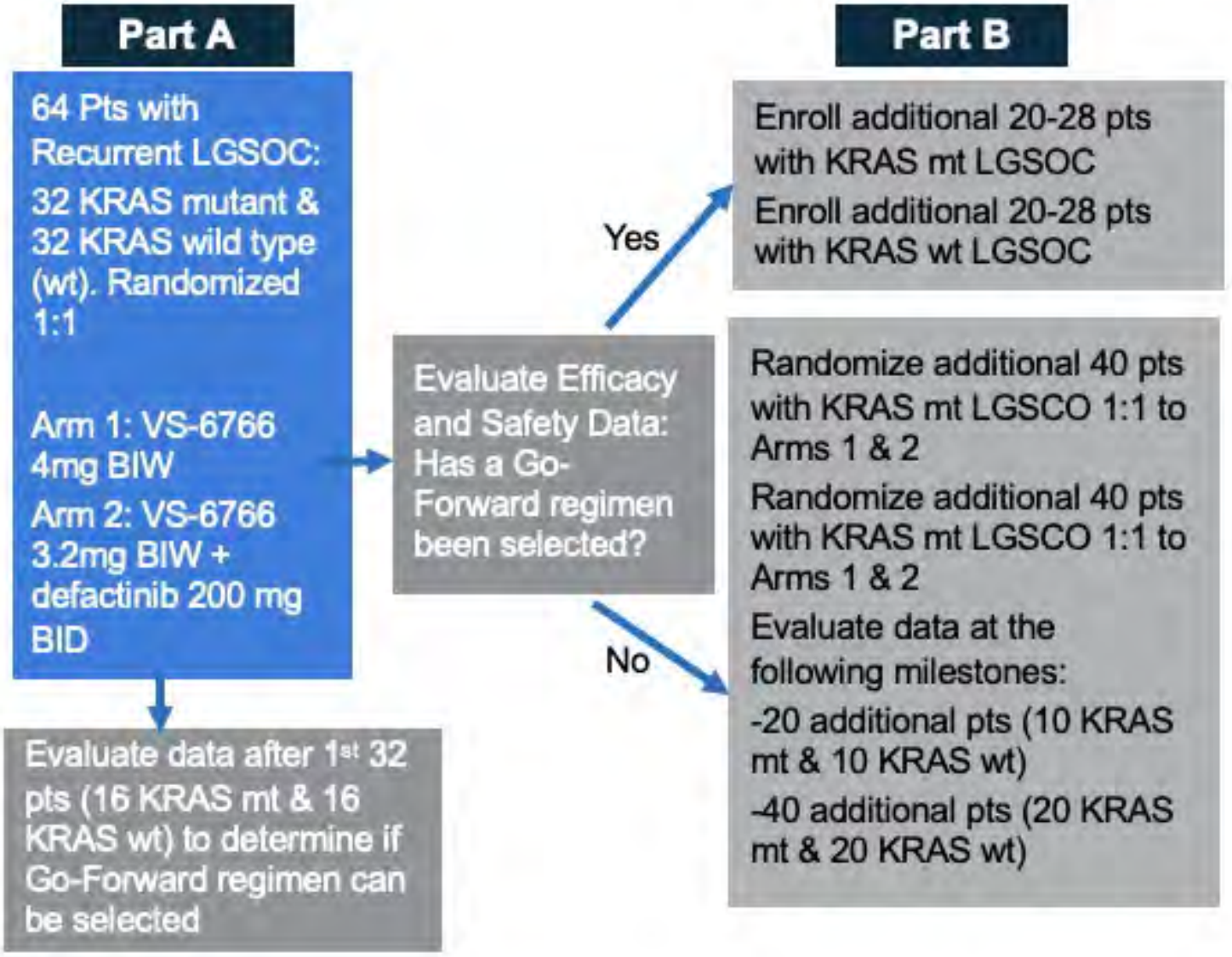
BOUQUET GOG-3051 (WO42178/ENGOT-GYN2)

A Phase II, open-label, multicenter platform study evaluating the efficacy and safety of biomarker-driven therapies in patients with persistent or recurrent rare epithelial ovarian tumors

Monk B et al TIP SGO 2022

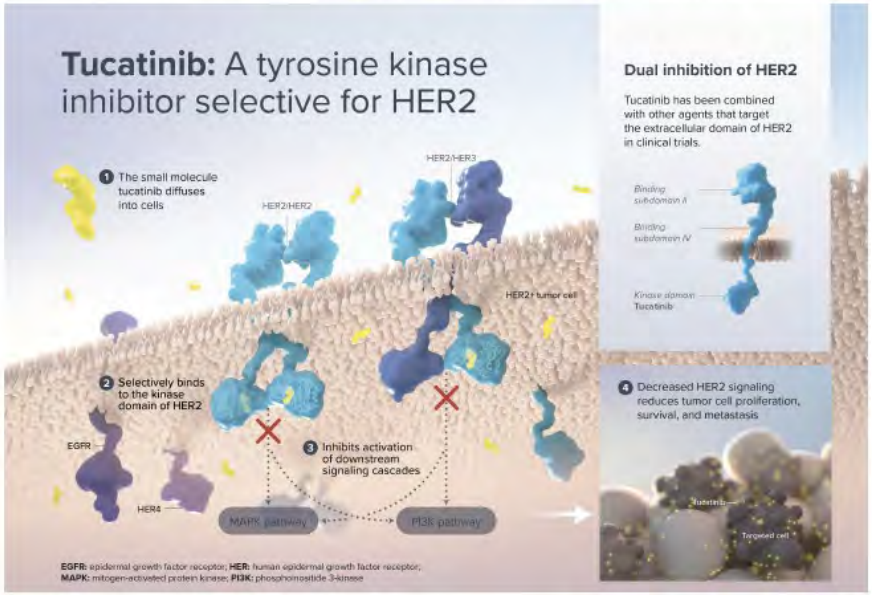


GOG-3052/VS-6766-201:RAMP 201: A phase 2 study of VS-6766 (dual RAF/MEK inhibitor) alone and in combination with Defactinib (FAK inhibitor) in recurrent low-grade serous ovarian cancer

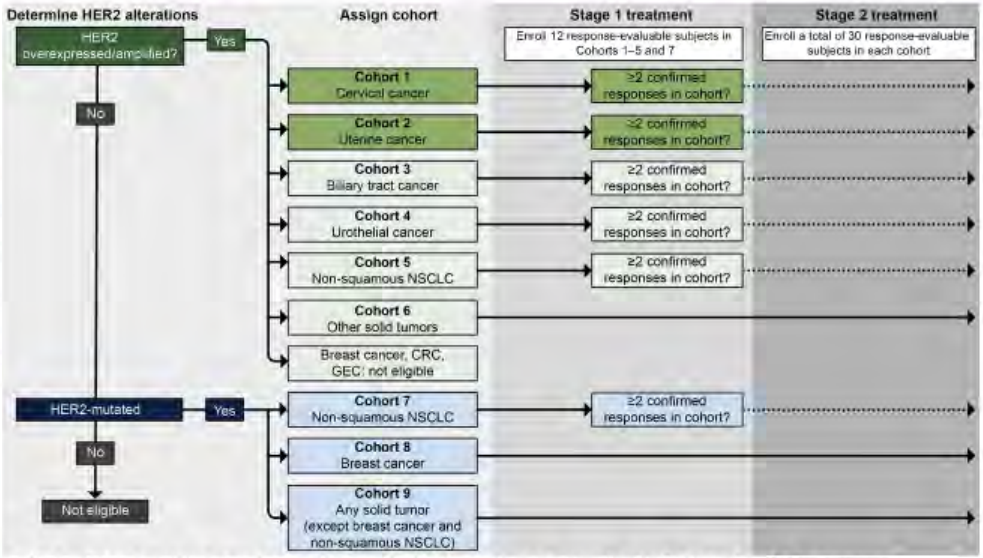


SGNTUC-019: Phase 2 basket study of tucatinib and trastuzumab in previously treated solid tumors with HER2 alterations: uterine and cervical cancer cohorts (Monk et al. Trial in Progress SGO 2022)

TUCATINIB PROPOSED MECHANISM OF ACTION



STUDY SCHEMA



a. If a sufficient number of patients with a particular tumor type are enrolled in Cohorts 6 or 9, the sponsor may evaluate that tumor type in a separate cohort, drawn from optional Cohorts 10 to 15.

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Thank you

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Creating a cancer-free world. One person, one discovery at a time.