

An Educational Symposium at the 2026 WAGO Annual Meeting

Evolving Evidence and Treatment Strategies **Low-Grade Serous**

O V A R I A N C A N C E R

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In Person

Friday, June 19, 2026

12:20 pm - 1:50 pm PST

This educational activity is supported by an independent medical education grant from Verastem

Welcome & Introductions



GOG Faculty Disclosure Information

Evolving Evidence and Treatment Strategies in Low Grade Serous Ovarian Cancer (LGSOC)

Industry Supported Symposium

Friday, June 19, 2026 | Napa Valley, California

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GOG Faculty Disclosure Information

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Speaker Disclosures Chase, MD	Dana	Speaker	AstraZeneca; Immunogen; GSK; Clovis	Consultant
Tewari, MD	Krish	Speaker	Merck; AstraZeneca; Eisai; AbbVie; GenMab/SeaGen; Regeneron; GSK	Advisory Board (Merck; AstraZeneca; Eisai; AbbVie; GenMab/SeaGen; Regeneron; GSK) Consultant (Merck; AstraZeneca; Eisai; GenMab/SeaGen; Regeneron; GSK) Speakers' Bureau (Merck; AstraZeneca; Eisai; GenMab/Seagen; Regeneron; GSK)
Engbert	Holley	Staff	Nothing to disclose	
Rush	Heather	Staff	Nothing to disclose	
Shumaker	Kara	Reviewer/Staff	Nothing to disclose	
Small, MPH	Michelle N	Reviewer/Staff	Nothing to disclose	
Alvarez Secord, MD	Angeles	Reviewer/Edu-Chair	AbbVie; Aravive; AstraZeneca; Daiichi Sankyo; Ellipses Pharma; Genmab; GSK; Immunogen; Karyopharm; Merck; Mersana; Myriad; Oncoquest/Canaria Bio; Oncoquest; Roche/Genentech; TORL Biotherapeutics; Zentalis; Foundation Medicine; Gilead; Histosonics; Medtronic; Porject Nana; Up to Date; SGO; FWC; GOG Foundation; Amgen; Johnson & Johnson	Research funds to Institution (AbbVie; Aravive; AstraZeneca; Daiichi Sankyo; Ellipses Pharma; Genmab; GSK; Immunogen; Karyopharm; Merck; Mersana; Myriad; Oncoquest/Canaria Bio; Oncoquest; Roche/Genentech; TORL Biotherapeutics; Zentalis) Honorarium (Merck; GSK) Advisory Board with Honoraria (AbbVie; AstraZeneca; Daiichi Sankyo; Foundation Medicine; GSK; Genmab; Gilead; Histosonics; Medtronic; Merck) Medical Advisory Board (Porject Nana) Steering Committee Uncomp. (Oncoquest; Genmab) Royalties (Up to Date) Board of Directors (SGO; FWC; GOG Foundation) Stock-Divested in June 2024 (Amgen; Johnson & Johnson)
Duska, MD	Linda	Edu-Co-Chair/ Reviewer	Merck; Corcept	Honoraria (Merck) Speakers Bureau (Corcept) Research Funding (Merck)
Blank, MD	Stephanie	Reviewer	American Board of Obstetrics and Gynecology; Merck; AstraZeneca; GlaxoSmithKline; Pfizer; Seattle Genetics/Astellas; Acrivon; Zentalis; NX Development Corp.	Leadership (American Board of Obstetrics and Gynecology) Research Funding (Merck; AstraZeneca; GlaxoSmithKline; Pfizer; Seattle Genetics/Astellas; Acrivon; Zentalis; NX Development Corp.)
Gien, MD	Lilian	Reviewer	Glaxo Smith Kline; Merck; Abbvie; AstraZeneca	Speaker Honoraria (Glaxo Smith Kline; Merck) Advisory Board (Abbvie; AstraZeneca)
Mutch, MD	David	Reviewer	Nothing to disclose	
Zweizig, MD	Susan	Reviewer	Nothing to disclose	

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All presentations will discuss details that are in the public domain.



Moderator



Thomas Herzog, MD

University of Cincinnati

Faculty



Dana Chase, MD

UCLA School of Medicine



Krish Tewari, MD

University of California, Irvine
Chao Family Comprehensive Cancer Center



Learning Objectives

After participating in this activity, learners will have a better understanding of:

- Current competitive landscape, new indication, Folate Receptor Alpha Data
- What's next including the future of ADCs in Low Grade Serous Ovarian Cancer, MEK Inhibitors and understanding the KRAS mutated gene
- Adverse Events and helping patients with adverse reactions and dose modifications.
- Biomarkers and Understanding first line management of recurrent disease



Agenda

5
minutes

Welcome & Introduction

Thomas Herzog, MD

20
minutes

Current Competitive Landscape & New Indications

Dana Chase, MD

25
minutes

What's Next in LGSOC Cancer Treatment

Krish Tewari, MD

20
minutes

Adverse Events & Patient Support, A Panel Discussion

All Faculty

20
minutes

Q&A and Closing Remarks

All Faculty



THANK YOU

Verastem

For Supporting This Activity With
An Independent Medical Education Grant



Current Competitive Landscape & New Indications



Dana Chase, MD

UCLA School of Medicine



Epidemiology

Type	US cases/year	Incidence rate
HGSOC	~13,000-14,000	~6-7/100,000
Borderline (BOT)	~3,000	1.5-2.5/100,000
LGSOC	~1,500-2,000	0.11-0.86/100,000

Incidence decreasing?
Maybe better pathology criteria?

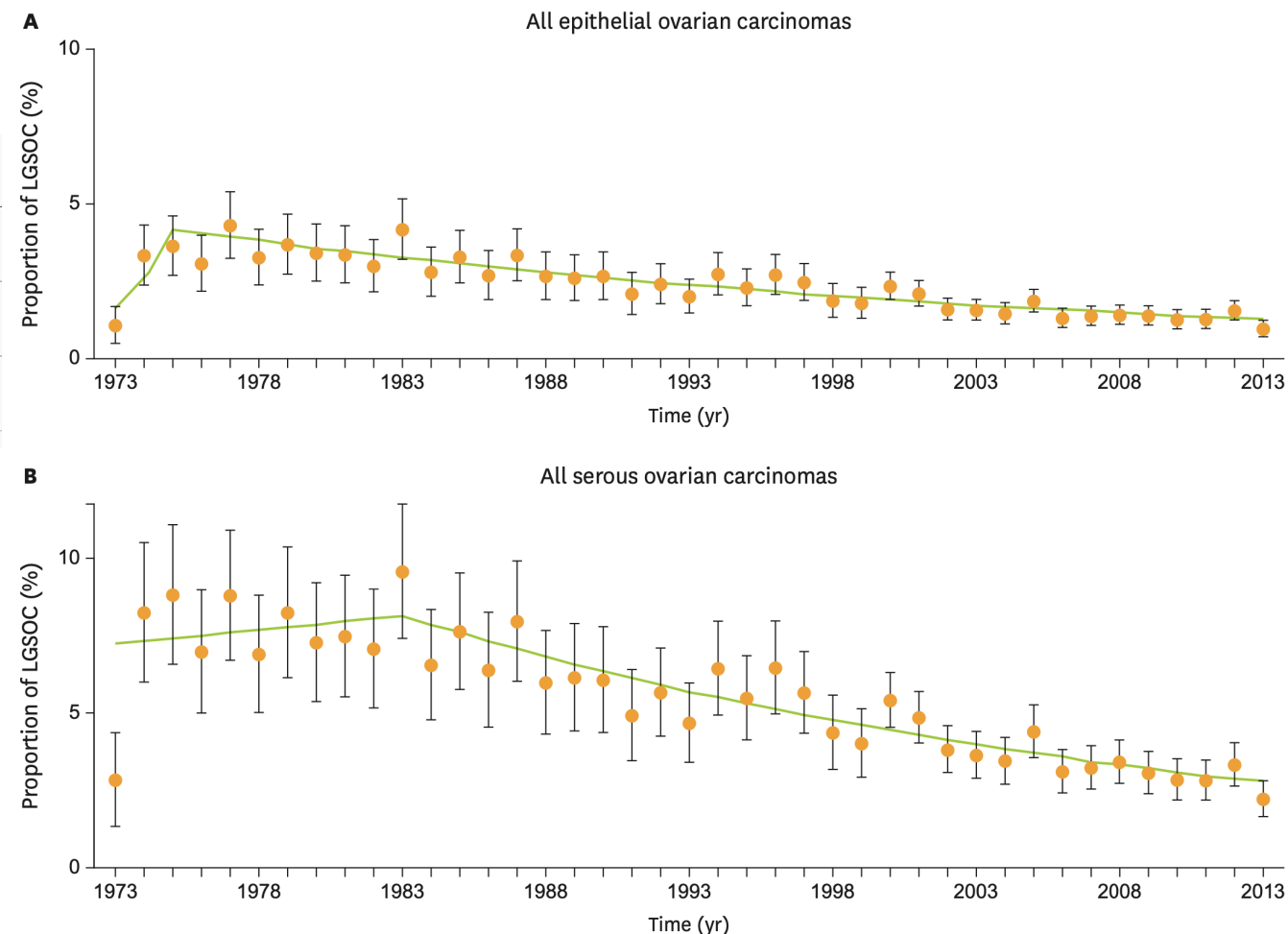


Fig. 1. Trends of LGSOCs (all stages). Dots represent proportion of LGSOC at given year, and bars represent 95% CI. (A) All epithelial ovarian carcinomas. (B) All serous ovarian carcinomas.
CI, confidence interval; LGSOC, low-grade serous ovarian carcinoma.

Serous Borderline Tumor versus Low-Grade Serous Ovarian Carcinoma

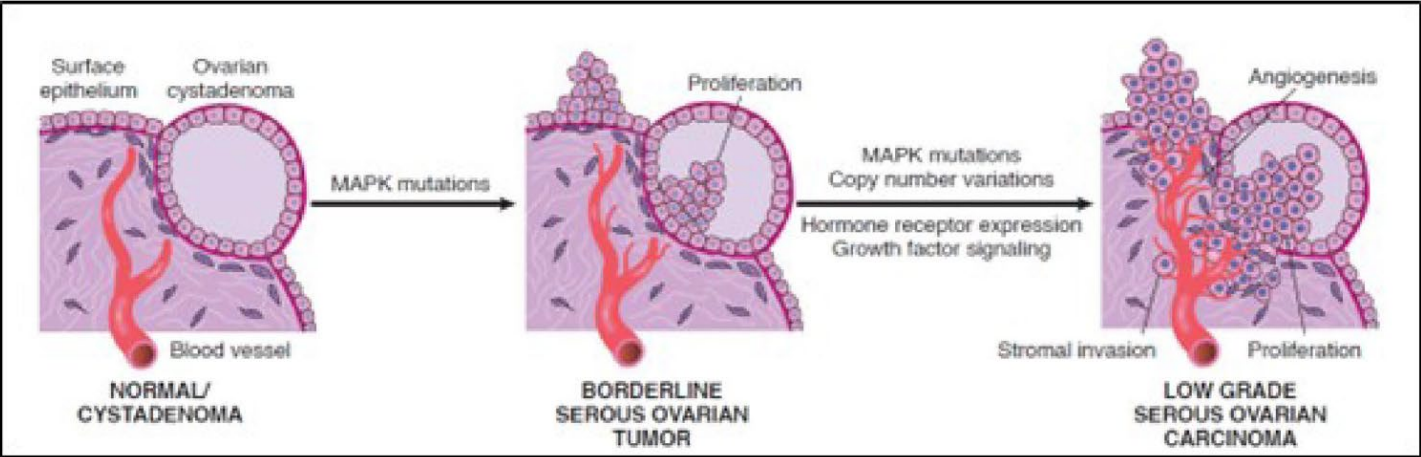


Fig. 8 Figure shows stepwise progression of cystadenoma to low-grade serous ovarian cancer (LGSOC). MAPK=mitogen-activated protein kinase

Abbreviations: SBOT, serous borderline ovarian tumor; LGSOC, low-grade serous ovarian carcinoma; CA-125, cancer antigen 125; EOC, Epithelial Ovarian Carcinoma; CT, computed tomography; MR, magnetic resonance.
Sandra Segaran K, et al. *Abdom Radiol (NY)*. 2026;51(3):1541-1553.

Table 1 Differentiating features of SBOT and LGSOC [21, 27]

	SBOT	LGSOC
Median age at presentation	36	54
BRAF mutation present	40% (this mutation may protect against progression to LGSOC)	5%
Implants	Noninvasive implants are small volume, measuring less than 1 cm, and do not cause omental caking.	Invasive. The majority of metastases showed partial or complete calcification. Muscle metastases are seen frequently.
Bilaterality	30%	70–80%
CA 125	Not elevated in 75%	Elevated: not as high as HGSOE
Progression	15–20% to LGSOC	Virtually none to HGSOE
CT imaging	Cystic with ill-defined soft tissue. The tumors have thinner walls and less solid tissue than EOC	Calcification is common
MR imaging	Mixed cystic and solid lesion with papillary branching projections. Small mural nodules may be seen	Papillary projections are commonly seen in LGSOC. Diffusion restriction is more obvious in LGSOC compared to SBOT
Treatment	Conservative Surgery, even if peritoneal implants	Cytoreductive Surgery
5 Year Survival	90%–98%	90% for stage I/II; 40% for stage III/IV

Low-Grade vs High-Grade Serous Ovarian Carcinoma

Table 2 Differences between high-grade and low-grade serous ovarian cancer [37–40]

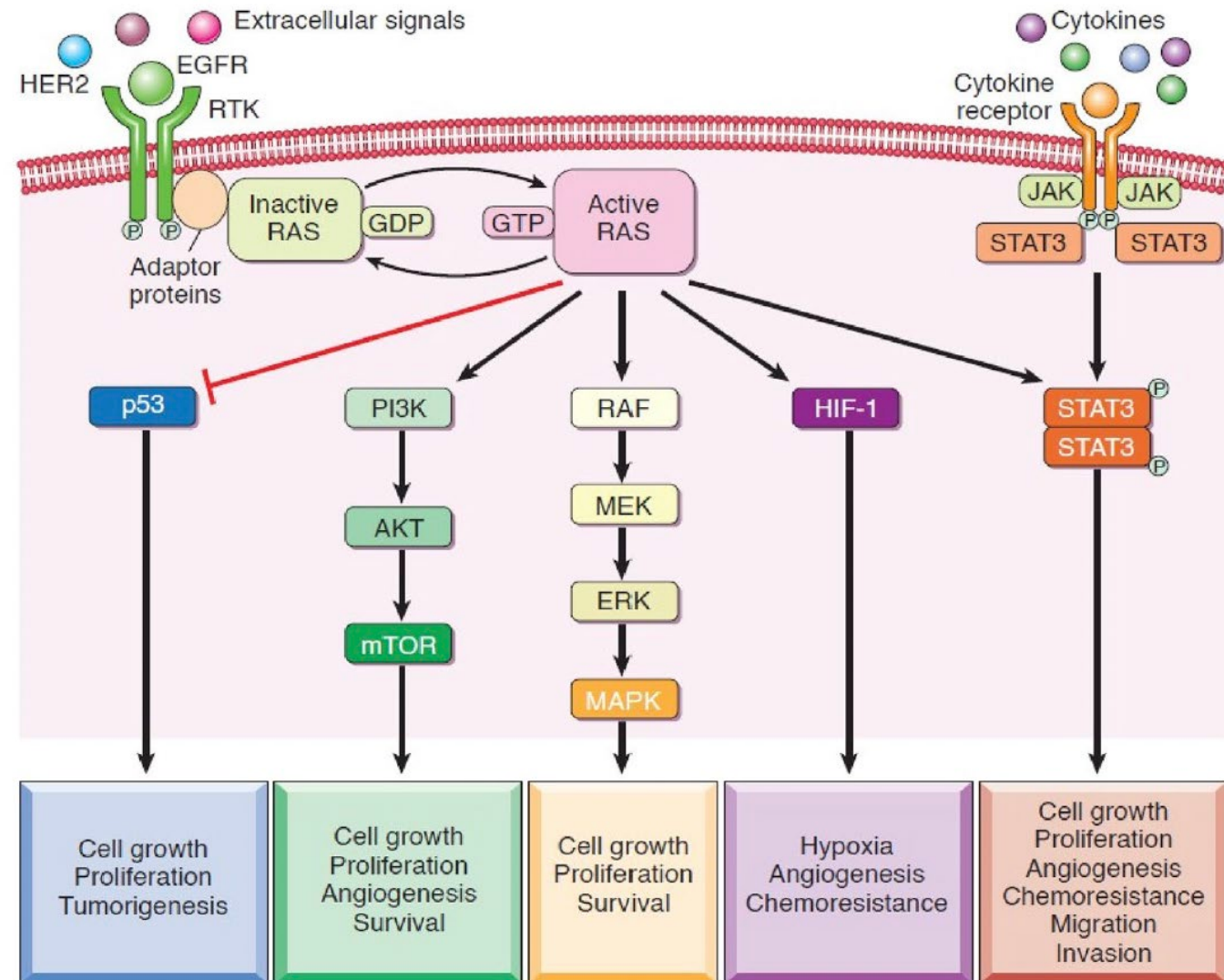
Clinical Features	LGSOC	HGSOC
Age at Dx (median)	50 years	65 years
Mutations	RAS (30–60%), BRAF, MAPK pathway (70%)	TP53 (>95%), BRCA (15%)
FIGO Stage at Dx	I/II –33%; III – 64%; IV – 3%	I/II – 15%; III – 70%; IV – 15%
Cytoreductive Surgery	Vital and always done first	Important
Platinum sensitivity	4–20%	75–85%
PFS/OS (months)	90/100	35/57

Dx: Diagnosis

PFS: Progression-free survival

OS: Overall survival

Abbreviations: LGSOC, low-grade serous ovarian carcinoma; HGSOC, high-grade serous ovarian carcinoma; Dx, diagnosis; FIGO, International Federation of Gynecology and Obstetrics; MAPK, mitogen-activated protein kinase; TP53, tumor protein p53; BRCA, breast cancer susceptibility gene; GDP, guanosine diphosphate; GTP, guanosine triphosphate
 Sandrasegaran K, et al. *Abdom Radiol (NY)*. 2026;51(3):1541-1553.



Histopathologic Comparison of LGSOC, HGSOC, and SBOT

LGSOC (A)

1. Uniform population of cuboidal or columnar cells
2. Stromal invasion
3. Mild to moderate nuclear atypia
4. Invasive branches with various architectural patterns.
5. Psammoma bodies are prevalent
6. Nuclei are small and consistent

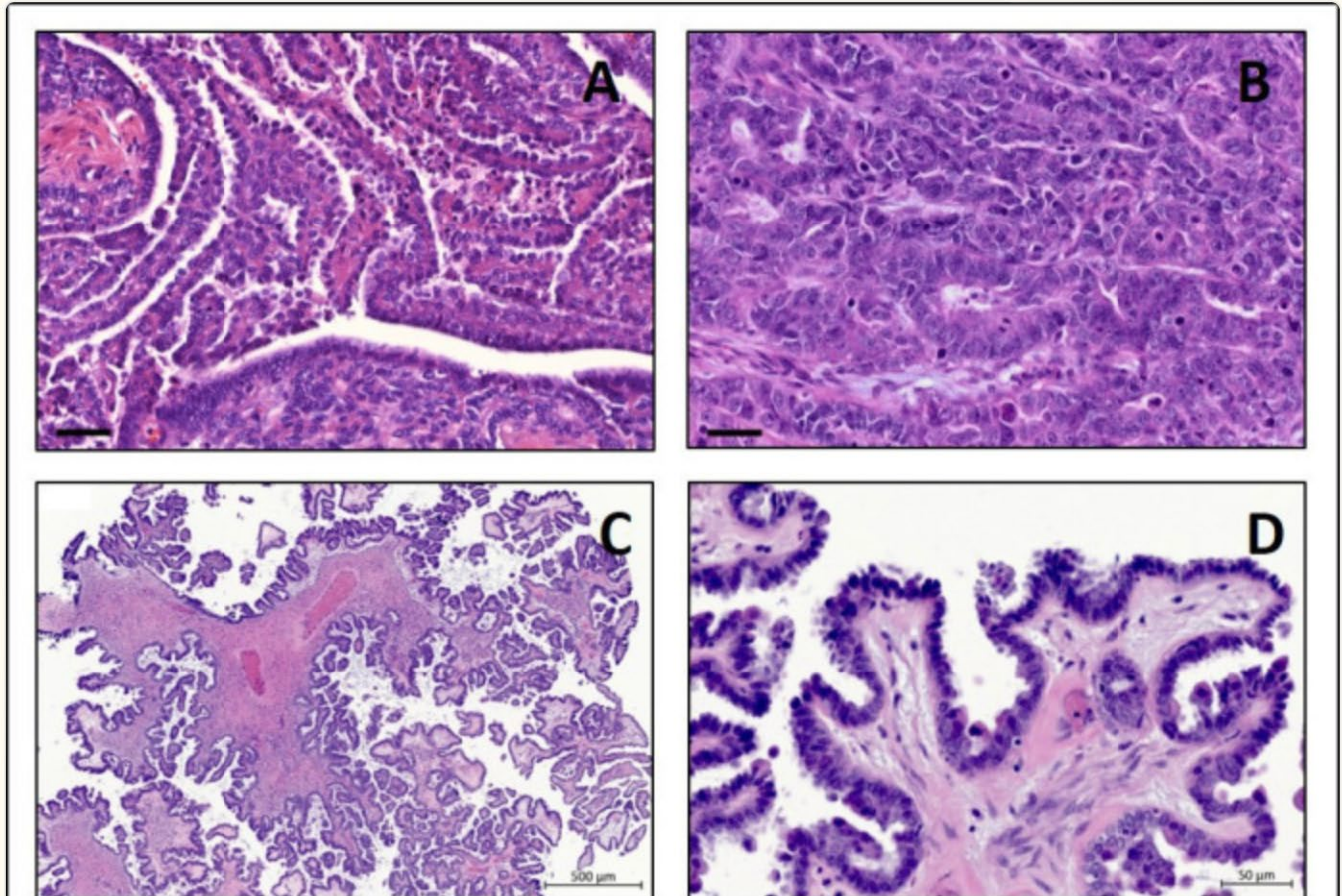
HGSOC (B)

1. High-grade nuclei are large and atypical,
2. Necrosis is common within the tumors

SBOT (C-D)

1. Hierarchical branching papillae with stromal cores and stratified epithelium
2. Micropapillary subtype, elongated micropapillae without stromal cores, arising directly from large papillae and surrounded by clear space., 'medusa head' appearance

Figure 2. Hematoxylin and eosin: (A) low-grade serous ovarian cancer; (B) high-grade serous ovarian cancer; (C-D) serous borderline ovarian tumor.



NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer

Principles of Systemic Therapy: Primary Systemic Therapy Regimens^d – Epithelial Ovarian/Fallopian Tube/Primary Peritoneal

Primary Therapy for Stage I Disease			
	Preferred	Other Recommended	Useful in Certain Circumstances
- High-grade serous - Endometrioid (grade 2/3) - Clear cell carcinomae - Carcinosarcomae	Carboplatin/Paclitaxel every 3 weeks^{h,i}	- Carboplatin/Liposomal Doxorubicin - Carboplatin/Docetaxel	- Cisplatin/Paclitaxel <u>For carcinosarcoma:</u> - Carboplatin/Ifosfamide - Cisplatin/Ifosfamide/Mesna - Ifosfamide/Mesna/Paclitaxel (category 2B)^h
Mucinous carcinoma (stage IA, IB, and IC, grades 1–3) ^e	- Capecitabine/Oxaliplatin - Carboplatin/Paclitaxel every 3 weeks^{h,i} - Fluorouracil/Leucovorin/Oxaliplatin	- Carboplatin/Docetaxel - Carboplatin/Liposomal Doxorubicin	Cisplatin/Paclitaxel
Low-grade serous (stage IC)/Grade 1 endometrioid (stage IC) ^{e,f,g}	- Carboplatin/Paclitaxel every 3 weeks^{h,i} ± maintenance Letrozole (category 2B^g) or other hormonal therapy (category 2B)^j - Hormone therapy (aromatase inhibitors: Anastrozole, Exemestane, Letrozole) (category 2B)	- Carboplatin/Docetaxel ± maintenance Letrozole (category 2B^g) or other hormonal therapy (category 2B)^j - Carboplatin/Liposomal Doxorubicin ± maintenance Letrozole (category 2B^g) or other hormonal therapy (category 2B)^j - Hormone therapy (Leuprolide acetate, Goserelin acetate, Tamoxifen,^k Fulvestrant) (category 2B)	Cisplatin/Paclitaxel

^dSee **Discussion** for references.
 ^eThere are limited data on the primary systemic therapy regimens for these LCOG.
 ^fBorderline disease with invasive implants may be treated as low-grade serous disease. See **LCOC-7** and **LCOC-9**.
 ^gFor low-grade serous, maintenance letrozole is a category 2A recommendation. For grade 1 endometrioid, maintenance letrozole is a category 2B recommendation.
 ^hAlbumin-bound paclitaxel may be substituted for those experiencing a hypersensitivity reaction to paclitaxel. However, albumin-bound paclitaxel will not overcome infusion reactions in all patients.
 ⁱIndividuals >70 years of age and those with comorbidities may be intolerant to the combination chemotherapy regimens recommended in these NCCN Guidelines. Based on clinical judgment and expected tolerance to therapies, alternate dosing (**OV-D, 7 of 12**) may be appropriate for these individuals with epithelial ovarian cancer (including carcinosarcoma, clear cell, mucinous, and low-grade serous). Algorithms have been developed for predicting chemotherapy toxicity.
 ^jOther hormonal therapy options include: aromatase inhibitors (eg, anastrozole, exemestane), leuprolide acetate, goserelin acetate, or tamoxifen.
 ^kTamoxifen is not recommended for low-grade serous carcinoma.

Note: All recommendations are NCCN Category 2A unless otherwise indicated.

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NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer

Principles of Systemic Therapy:

Acceptable Recurrence Therapies for Epithelial Ovarian (including LCOC)/Fallopian Tube/Peritoneal Cancer

Recurrence Therapy for Platinum-Resistant Disease (alphabetical order)		
Preferred	Other Recommended	Useful in Certain Circumstances
<u>Cytotoxic Therapy</u> - Albumin-bound Paclitaxel/Relacorilant - Docetaxel - Gemcitabine - Liposomal Doxorubicin - Liposomal Doxorubicin + Bevacizumab - Paclitaxel (Weekly) - Paclitaxel (Weekly) + Bevacizumab - Oral Cyclophosphamide + Bevacizumab - Topotecan - Topotecan + Bevacizumab <u>Targeted Therapy (single agents)</u> - Mirvetuximab soravtansine-gynx (for FRα-expressing tumors [≥75% positive tumor cells] (category 1))	<u>Cytotoxic Therapy</u> - Albumin-bound Paclitaxel - Capecitabine - Carboplatin - Carboplatin/Docetaxel - Carboplatin/Paclitaxel (Weekly) - Carboplatin/Gemcitabine ± Bevacizumab - Carboplatin/Liposomal Doxorubicin ± Bevacizumab - Carboplatin/Paclitaxel ± Bevacizumab - Cisplatin/Gemcitabine - Cyclophosphamide - Doxorubicin - Gemcitabine ± Bevacizumab - Ifosfamide/Mesna - Irinotecan - Ixabepilone ± Bevacizumab (category 2B) - Oral Cyclophosphamide + Pembrolizumab + Bevacizumab - Oral Etoposide - Oxaliplatin - Paclitaxel - Pemetrexed - Sorafenib/Topotecan - Vinorelbine <u>Targeted Therapy (single agents)</u> - Bevacizumab - Pazopanib (category 2B) <u>Hormone Therapy</u> - Aromatase inhibitors (Anastrozole, Exemestane, Letrozole) - Goserelin acetate - Leuprolide acetate - Megestrol acetate - Tamoxifen	- Albumin-bound Paclitaxel/Carboplatin (for confirmed taxane hypersensitivity) - Carboplatin/Paclitaxel (for age >70) <u>Immunotherapy</u> - Dostarlimab-gxly (for dMMR/MSI-H recurrent or advanced tumors) - Paclitaxel + Pembrolizumab ± Bevacizumab (for PD-L1- positive tumors [CPS≥1]) - Pembrolizumab (for patients with MSI-H or dMMR solid tumors, or TMB-H tumors ≥10 mutations/megabase) - For clear cell carcinoma: - Ipilimumab + Nivolumab <u>Hormone Therapy</u> - Fulvestrant (for low-grade serous carcinoma) <u>Targeted Therapy</u> - Dabrafenib/Trametinib (for BRAF V600E positive tumors) - Entrectinib or Larotrectinib or Repotrectinib (for <i>NTRK1/2/3</i> gene fusion-positive tumors) - Fam-trastuzumab deruxtecan-nxki (for HER2-positive tumors [IHC 3+ or 2+]) - Mirvetuximab soravtansine-gynx + Bevacizumab (for FRα- expressing tumors [≥25% positive tumor cells]) - Selpercatinib (for RET gene fusion-positive tumors) <u>For low-grade serous carcinoma:</u> - Avutometinib/Defactinib (for KRAS-mutated tumors) - Trametinib - Binimetinib (category 2B) <u>For mucinous carcinoma:</u> - FOLFIRI ± Bevacizumab (category 2B)

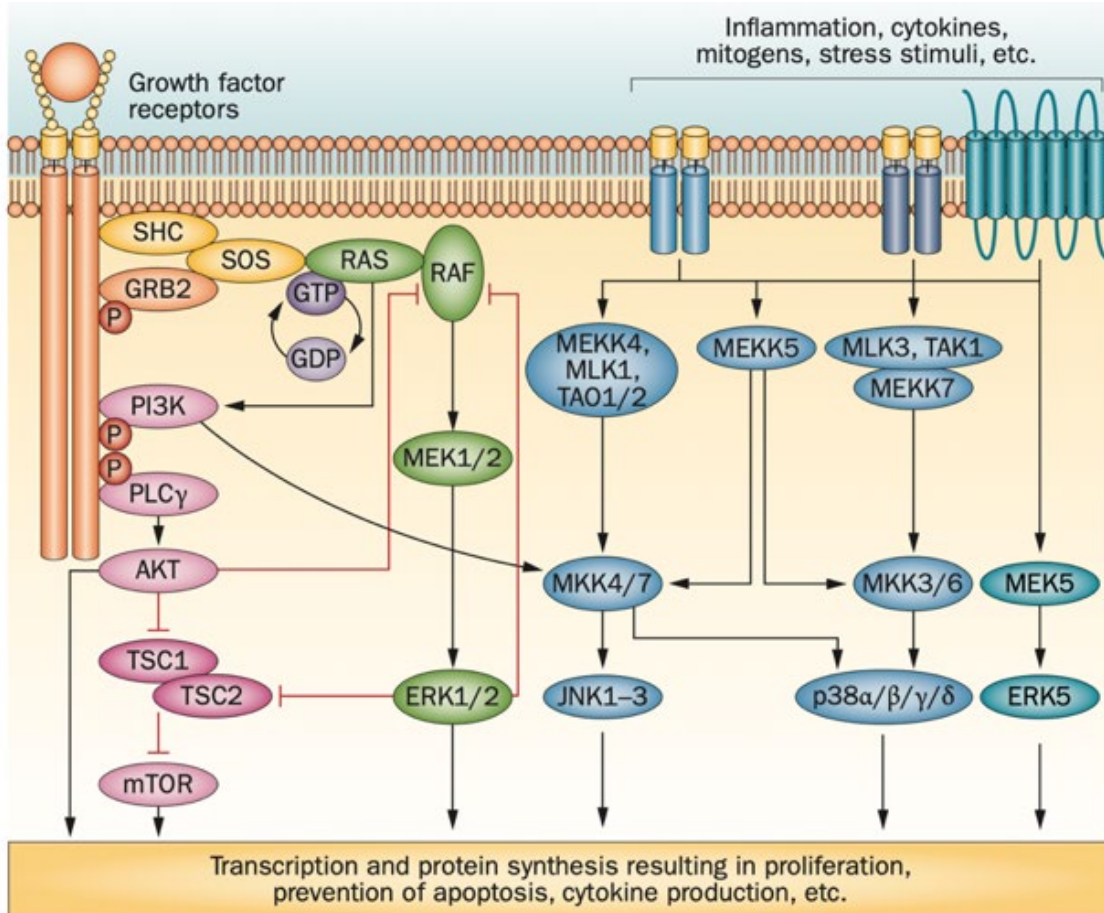
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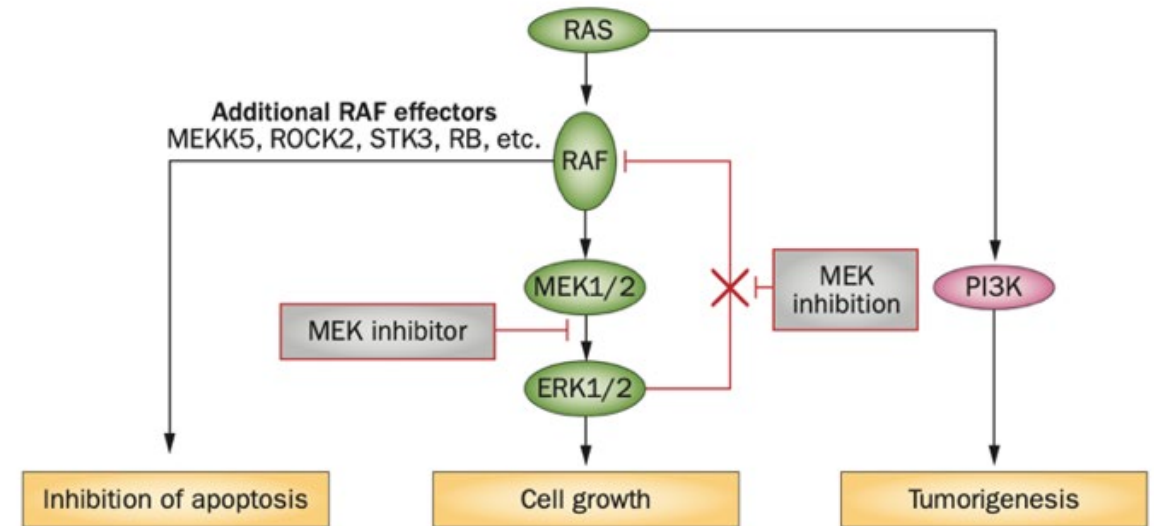
**MILO, GOG 281,
RAMP 201**



MAPK Pathway: MEK1/2 Mediates Cellular Signals Transduced from RAS-RAF



- ***LGSOC MAPK pathway mutations***
- *KRAS 20-40%, NRAS 7-26%, BRAF 5-33%*



MILO/ENGOT-ov1 1: Binimetinib Versus Physician's Choice Chemotherapy in Recurrent or Persistent Low-Grade Serous Carcinomas of the Ovary, Fallopian Tube, or Primary Peritoneum

Bradley J. Monk, MD¹; Rachel N. Grisham, MD²; Susana Banerjee, PhD³; Elsa Kalbacher, MD⁴; Mansoor Raza Mirza, MD⁵; Ignacio Romero, MD⁶; Peter Vuytsteke, MD^{7,8}; Robert L. Coleman, MD⁹; Felix Hilpert, MD¹⁰; Amit M. Oza, MD¹¹; Anneke Westermann, MD, PhD¹²; Martin K. Oehler, MD, PhD¹³; Sandro Pignata, MD, PhD¹⁴; Carol Aghajanian, MD¹; Nicoletta Colombo, MD¹⁵; Esther Drill, DrPH²; David Cibula, MD, PhD¹⁶; Kathleen N. Moore, MD¹⁷; Janna Christy-Bittel, MSN¹⁸; Josep M. del Campo, MD¹⁹; Regina Berger, PhD²⁰; Christian Marth, MD, PhD²¹; Jalid Sehouli, MD²²; David M. O'Malley, MD²³; Cristina Churrua, MD²⁴; Adam P. Boyd, PhD¹⁸; Gunnar Kristensen, MD, PhD²⁵; Andrew Clamp, MD, PhD²⁶; Isabelle Ray-Coquard, MD, PhD²⁷; and Ignace Vergote, MD, PhD²⁸

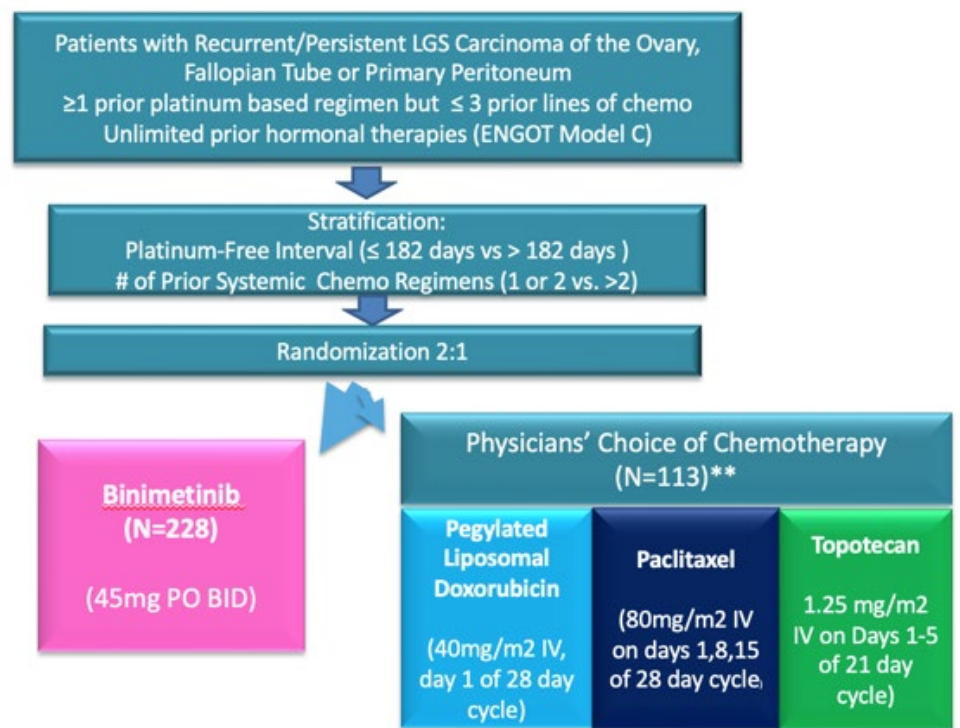


TABLE 3. Best Response by Local RECIST 1.1 Radiology Read in those patients treated with binimetinib

Local Best Response	KRAS Mutant (n = 43), No. (%)	KRAS Wild-Type (n = 90), No. (%)	P
			.004
CR/PR	19 (44)	17 (19)	
SD/PD	24 (56)	73 (81)	

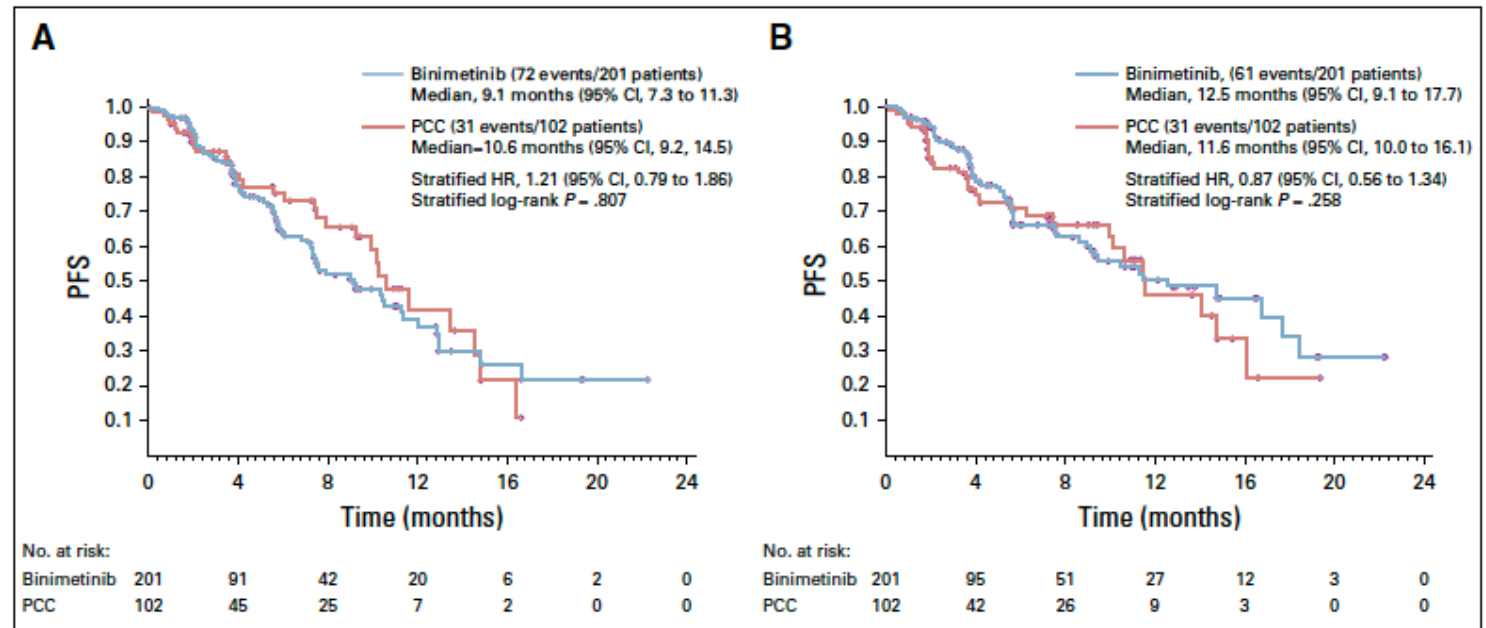
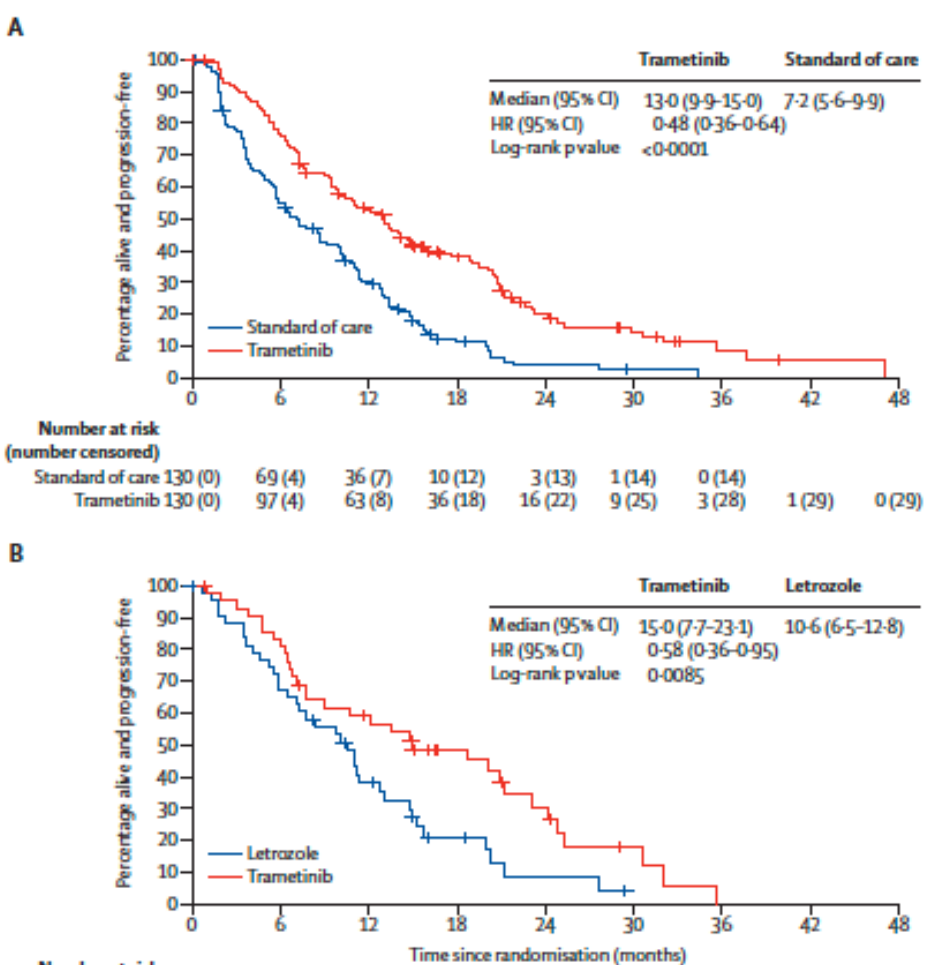
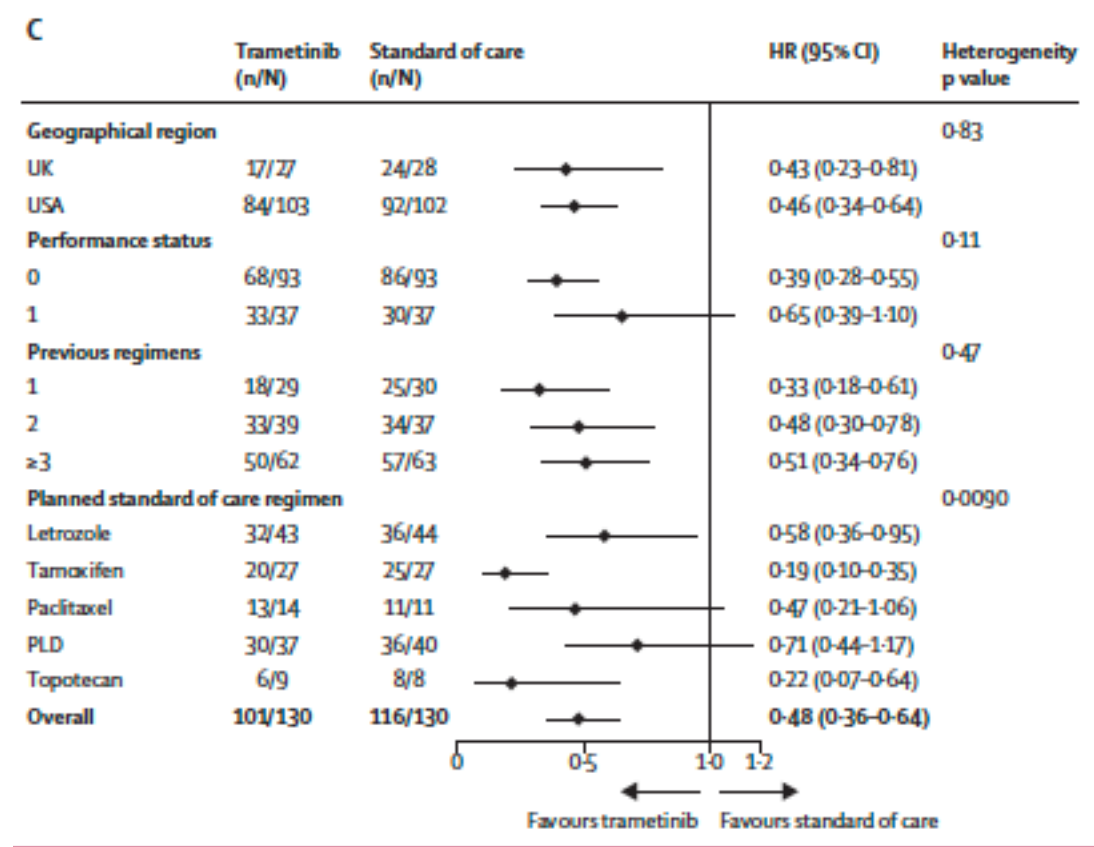


FIG 2. Kaplan-Meier plot of progression-free survival per (A) blinded independent central review and (B) local assessment. HR, hazard ratio; PCC, physician's choice chemotherapy; PFS, progression free survival.

Abbreviations: CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; HR, hazard ratio; PCC, physician's choice chemotherapy; PFS, progression-free survival; BID, twice daily; IV, intravenous.
Monk BJ, et al. J Clin Oncol. 2020;38(32):3753-3762; ClinicalTrials.gov Identifier: NCT01849874

Trametinib versus standard of care in patients with recurrent low-grade serous ovarian cancer (GOG 281/LOGS): an international, randomised, open-label, multicentre, phase 2/3 trial

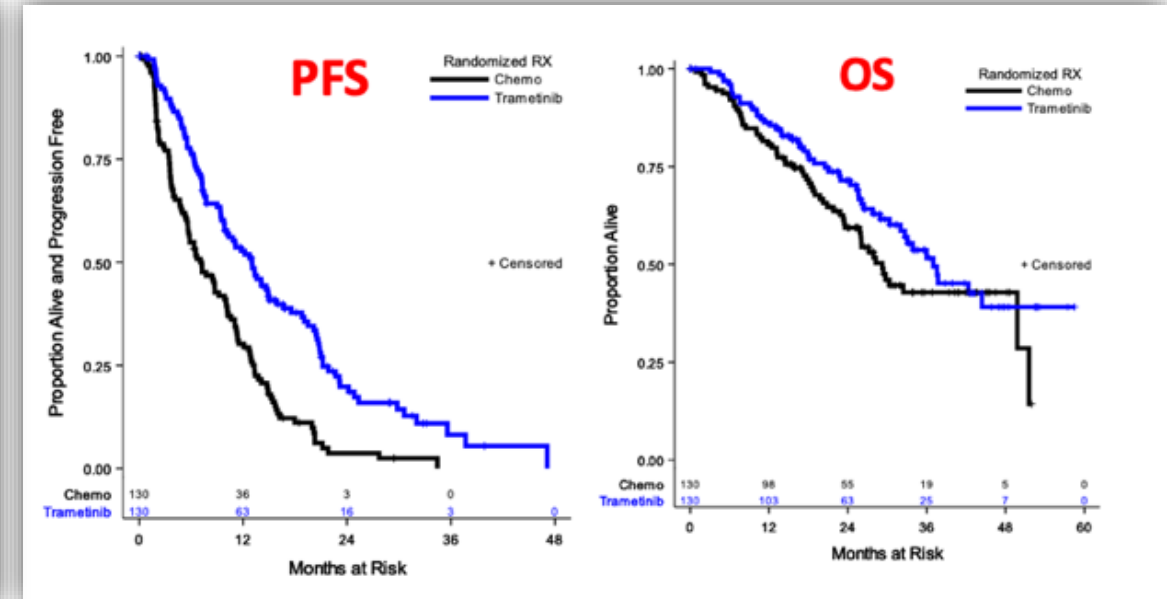
David M Gershenson, Austin Miller, William E Brady, James Paul, Karen Carty, William Rodgers, David Millan, Robert L Coleman, Kathleen N Moore, Susana Banerjee, Kate Connolly, Angeles Alvarez Secord, David M O'Malley, Oliver Dorigo, Stephanie Gaillard, Hani Gabra, Brian Slamonvitz, Parviz Hanjani, John Farley, Michael Churchman, Ailish Ewing, Robert L Hollis, C Simon Harrington, Helen Q Huang, Lari Wenzel, Charlie Gouley



Overall, ORRs were markedly more favourable for trametinib than standard-of-care therapy in mutation-positive patients (11 [50%] of 22 vs two [9%] of 22) than in mutation-negative patients (four [8%] of 48 vs three [7%] of 42), although this did not reach statistical significance (multiple comparison adjusted $p=0.11$, test for interaction).

GOG281/LOGS: Trametinib vs Standard of Care

Arm	No. Pts CR + PR /Treated	Objective Response Rate (95% CI)	Stable Disease Rate	Response Duration Months (95% CI)	Odds Ratio For ORR (95% CI)	P-Value
Trametinib	34/130	26.2% (19.0-34.0)	59.2%	13.6 (8.1-18.8)	5.4 (2.4-12.2)	< 0.0001
Control (SOC)	8/130	6.2% (2.0-10.0)	70.8%	5.9 (2.8-12.2)		
Letrozole	6/44	13.6%	70.5%			
Tamoxifen	0/27	0%	66.7%			
Paclitaxel	1/11	9.1%	63.6%			
PLD	1/40	2.5%	80.0%			
Topotecan	0/8	0%	50.0%			



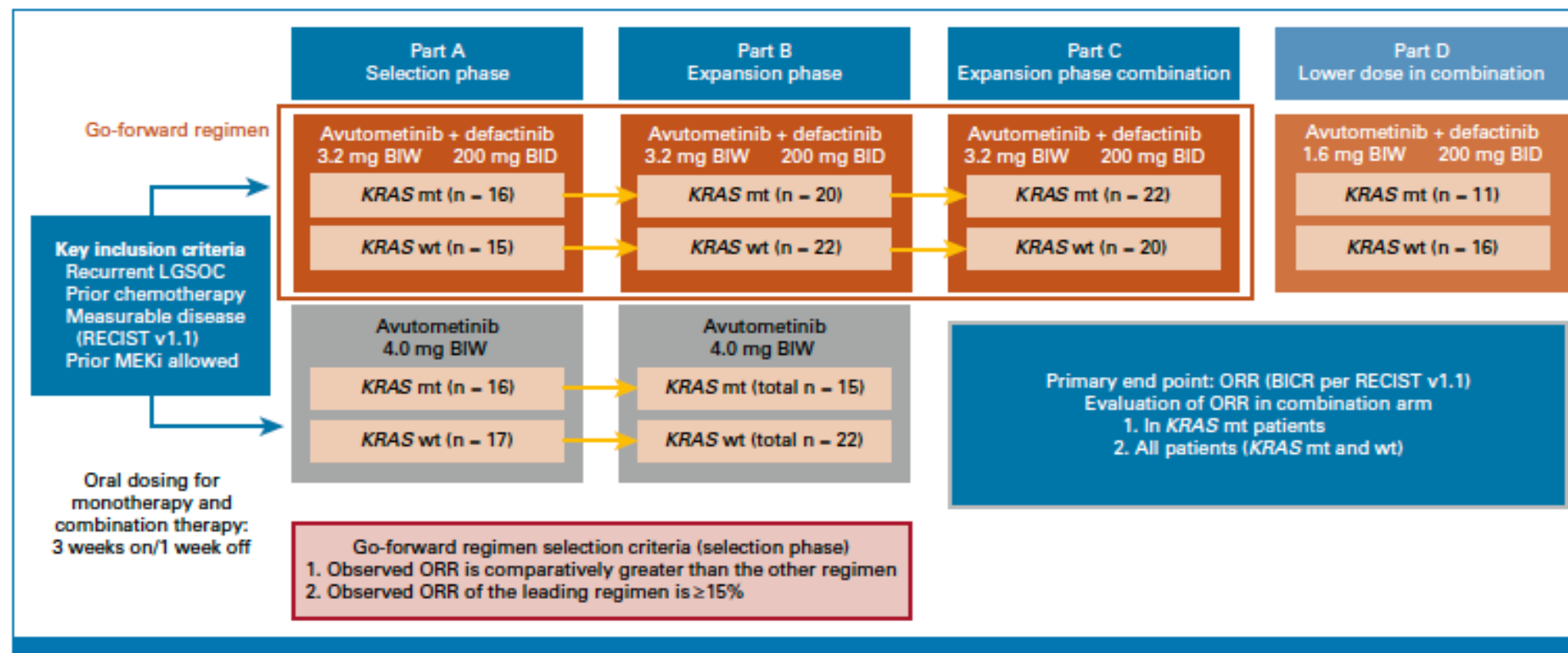
- **Median PFS:** 13.0 vs 7.2 months (HR = 0.48; p < 0.0001)
- **Median OS:** 37.0 vs 29.2 months (HR = 0.75; p = 0.054)

Final Overall Survival (IGCS 2025)

Abbreviations: HR, hazard ratio; LGSOC, low-grade serous ovarian carcinoma; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PLD, pegylated liposomal doxorubicin; SOC, standard-of-care therapy.

Gershenson DM, et al. *Lancet*. 2022;399(10324):541-553. *ClinicalTrials.gov* Identifier: NCT02101788

Efficacy and Safety of Avutometinib + Defactinib in Recurrent Low-Grade Serous Ovarian Cancer: Primary Analysis of ENGOT-OV60/GOG-3052/RAMP 201



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Mechanism of Action

- **Avutometinib** inhibits MEK and RAF by stabilising the MEK-RAF complex, blocking both MEK activity and the feedback reactivation of MEK by RAF
- **Defactinib** inhibits FAK kinase, a mechanism of adaptive resistance to MEK inhibition, and an activator of a variety of oncogenic signaling pathways

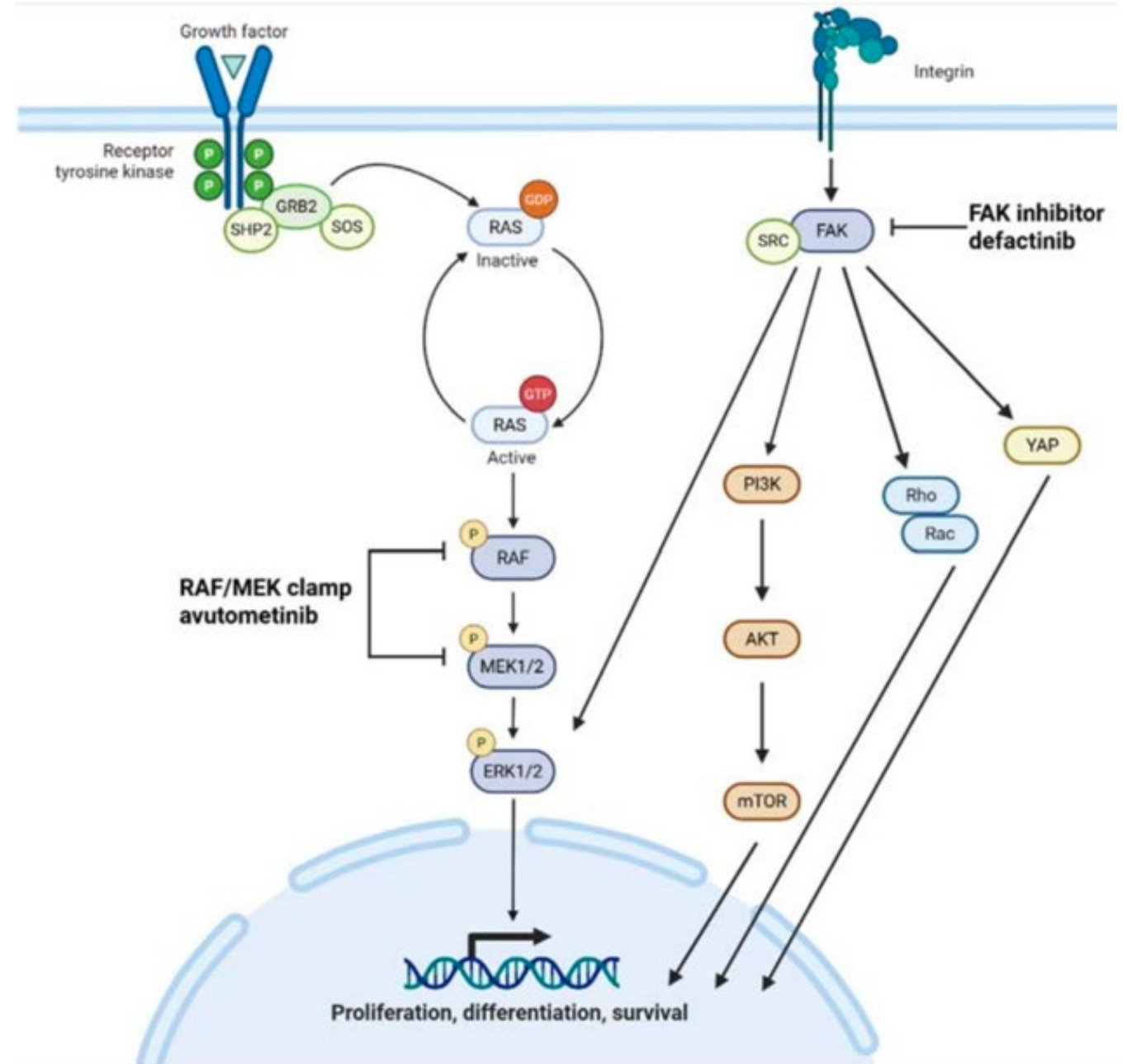


TABLE 1. Baseline Characteristics in the Avutometinib (3.2 mg two times per week) + Defactinib (200 mg two times per day) Group and the Avutometinib (4.0 mg two times per week) Group

Characteristic	Avutometinib (3.2 mg two times per week) + Defactinib (200 mg two times per day)			Avutometinib (4.0 mg two times per week)		
	All Patients, n = 115	KRAS mt, n = 58	KRAS wt, n = 57	All Patients, n = 70	KRAS mt, n = 31	KRAS wt, n = 39
Age (years), median (min, max)	54 (21, 87)	60 (29, 87)	45 (21, 80)	54 (21, 77)	57 (27, 74)	48 (21, 77)
Race, ^a No. (%)						
White	88 (77)	43 (74)	45 (80)	59 (84)	24 (77)	35 (90)
Asian	4 (3)	2 (3)	2 (4)	1 (3)	1 (3)	0
Black or African American	5 (4)	3 (5)	2 (4)	1 (3)	1 (3)	0
Other	5 (4)	0	5 (9)	2 (3)	2 (6)	0
Not reported	13 (11)	10 (17)	3 (5)	6 (9)	3 (10)	3 (8)
Unknown	0	0	0	1 (1)	0	1 (3)
ECOG PS, No. (%)						
0	78 (68)	42 (72)	36 (63)	50 (71)	19 (61)	31 (80)
1	37 (32)	16 (28)	21 (37)	20 (29)	12 (39)	9 (20)
Prior systemic regimens, No., median (min, max)	3 (1, 9)	3 (1, 9)	3 (1, 9)	3 (1, 10)	3 (1, 10)	3 (1, 9)
Prior platinum-based chemotherapy, No. (%)	114 (99)	58 (100)	56 (98)	69 (99)	30 (97)	39 (100)
Prior hormonal therapy, No. (%)	99 (86)	49 (85)	50 (88)	58 (83)	25 (81)	33 (85)
Prior bevacizumab, No. (%)	59 (51)	23 (40)	36 (63)	34 (49)	17 (55)	17 (44)
Prior MEK inhibitor therapy, No. (%)	25 (22)	12 (21)	13 (23)	18 (26)	8 (26)	10 (26)

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group Performance Status; KRAS, Kirsten rat sarcoma virus homolog; MEK, mitogen-activated extracellular signal-regulated kinase; mt, mutant; wt, wild type.

^aSelf-reported.

TABLE 2. ORR (RECIST v1.1) by BICR in the Avutometinib (3.2 mg two times per week) + Defactinib (200 mg two times per day) Group and the Avutometinib (4.0 mg two times per week) Monotherapy Group

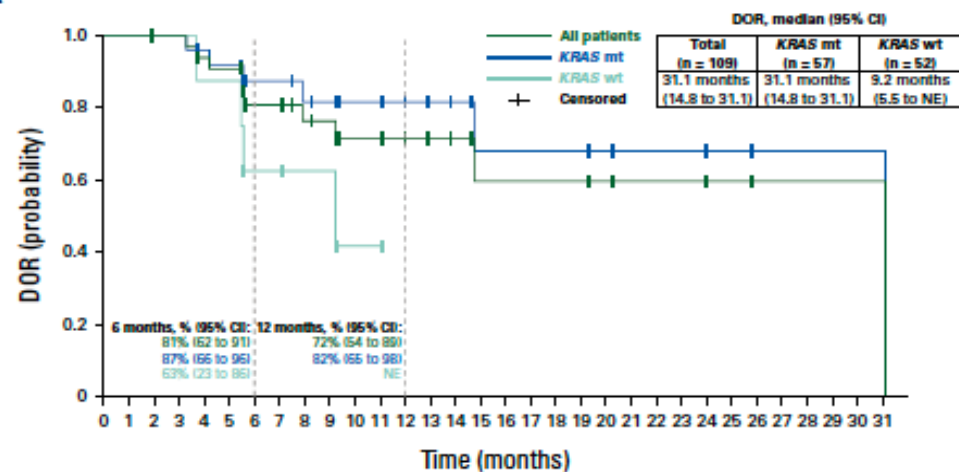
Clinical Outcome	Avutometinib (3.2 mg two times per week) + Defactinib (200 mg two times per day)			Avutometinib (4.0 mg two times per week)		
	All Patients, n = 109	KRAS mt, n = 57	KRAS wt, n = 52	All Patients, n = 69	KRAS mt, n = 30	KRAS wt, n = 39
Confirmed ^a ORR, No. (%)	34 (31)	25 (44)	9 (17)	12 (17)	7 (23)	5 (13)
Complete response	2 (2)	2 (4)	0	1 (1)	1 (3)	0
Partial response	32 (29)	23 (40)	9 (17)	11 (16)	6 (20)	5 (13)
Stable disease, ^b No. (%)	62 (57)	28 (49)	34 (65)	43 (62)	17 (57)	26 (67)
Progressive disease, No. (%)	9 (8)	2 (4)	7 (14)	7 (10)	3 (10)	4 (10)
Not evaluable, No. (%)	4 (4)	2 (4)	2 (4)	7 (10)	3 (10)	4 (10)

Abbreviations: BICR, blinded independent central review; KRAS, Kirsten rat sarcoma virus homolog; mt, mutant; ORR, objective response rate; wt, wild type.

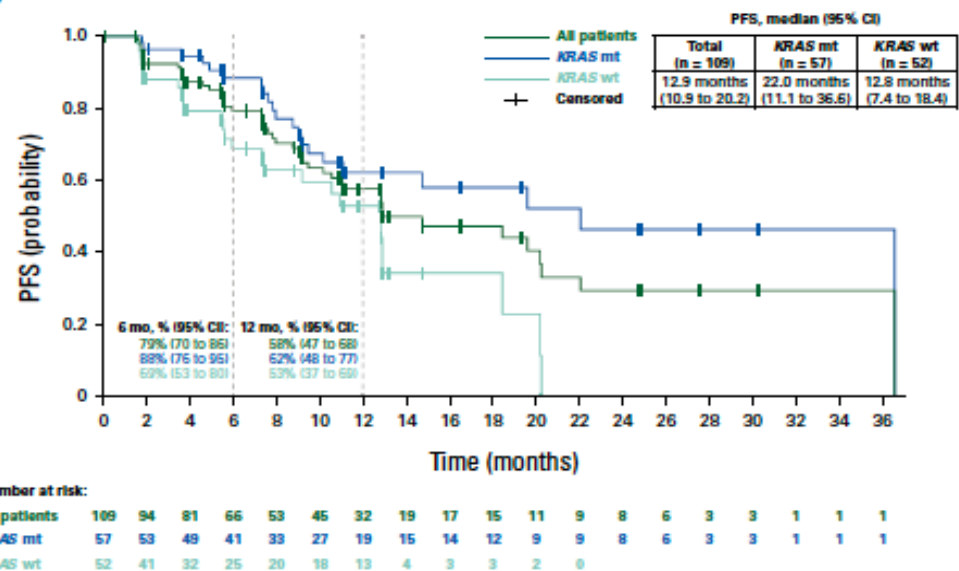
^aBy BICR.

^bIncludes unconfirmed partial response; stable disease (or unconfirmed partial response) must occur ≥53 days after first dose date.

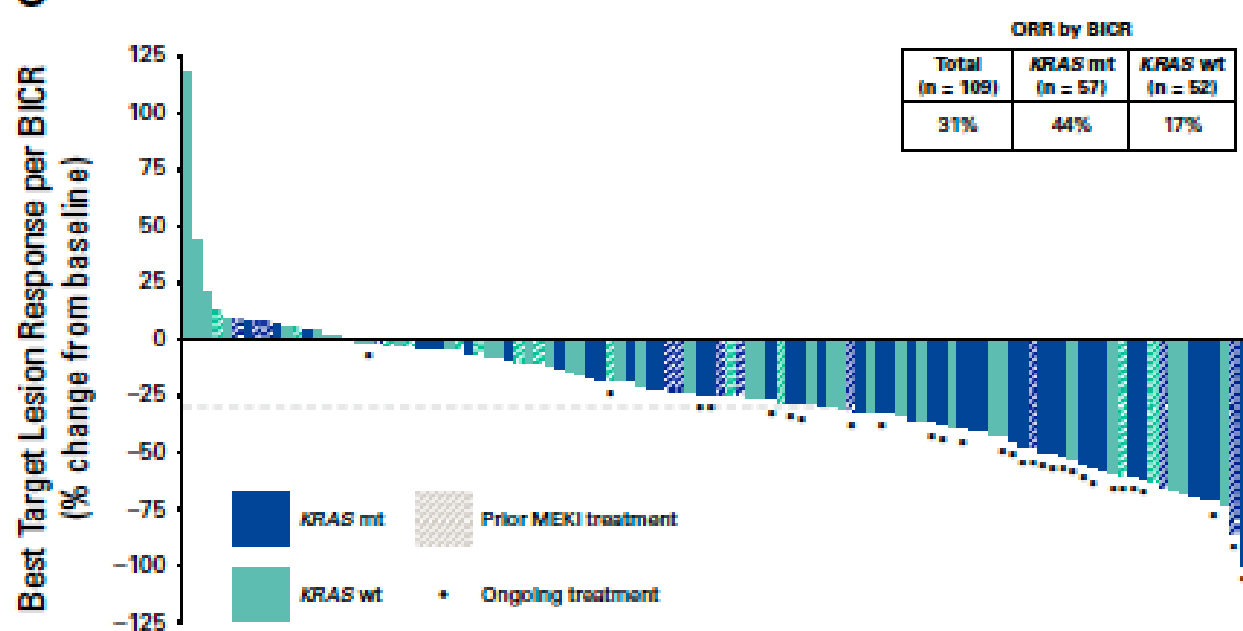
A



B



C



Responses Observed in both KRAS
Mutant and KRAS
Wild-Type Recurrent LGSOC

FDA Accelerated Approval

May 8, 2025

Avutometinib 3.2 mg BIW + Defactinib
200 mg BID

KRAS mutated recurrent LGSOC

Abbreviations: BICR, blinded independent central review; BID, twice daily; CR, complete response; LGSOC, low-grade serous ovarian carcinoma; mt, mutant; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; wt, wild type.

Banerjee SN, et al. Presented at IGCS 2024. J Clin Oncol. 2025;43(25):2782-2792. ClinicalTrials.gov identifier: NCT06072781

Adverse Events Profile for Avutometinib + Defactinib (parts A-C)

- 80% (92/115) of patients had AEs leading to **dose interruption**
 - 38% (44/115) for elevations in CPK
- 36.5% (42/115) of patients had AEs leading to **dose reduction**
- 10% (12/115) of patients **discontinued for AEs**; most common increased CPK (n=4)
- 7% (8/115) of patients had **serious AEs** considered by the investigator to be related to study treatment: the only event occurring in more than 1 patient was abdominal pain
- 4 **deaths** (within 30 days of discontinuation): GI hemorrhage, large intestine perforation, clinical progression, clinical deterioration (none considered related to study treatment)

**Most common adverse events (preferred term) considered by the investigator to be related to study drug (either avutometinib or defactinib).*

Abbreviations: E, adverse event; AST, aspartate aminotransferase; BID, twice daily; CPK, creatine phosphokinase; GI, gastrointestinal; GOG, Gynecologic Oncology;
Banerjee SN, et al. Presented at IGCS 2024. J Clin Oncol. 2025;43(25):2782-2792. ClinicalTrials.gov identifier: NCT06072781

Treatment-Related Adverse Events (>20% of patients)* n (%)	Avutometinib + Defactinib 3.2 mg BIW + 200 mg BID 3 weeks on/1 week off N= 115	
Preferred term	All Grades	Grade ≥3
Non-laboratory AEs		
Nausea	77 (67.0)	3 (2.6)
Diarrhea	67 (58.3)	9 (7.8)
Oedema peripheral	61 (53.0)	1 (0.9)
Fatigue	50 (43.5)	3 (2.6)
Vomiting	49 (42.6)	3 (2.6)
Vision blurred	47 (40.9)	0
Rash	41 (35.7)	2 (1.7)
Dermatitis acneiform	39 (33.9)	5 (4.3)
Dry skin	30 (26.1)	0
Anemia	26 (22.6)	6 (5.2)
Laboratory-related AEs		
Increased blood CPK	69 (60.0)	28 (24.3)
Increased blood bilirubin increased/ hyperbilirubinemia	38 (33.0)	5 (4.3)
AST increased	36 (31.3)	2 (1.7)

RAMP201: Adverse Events of Interest Associated with MEK Inhibitors

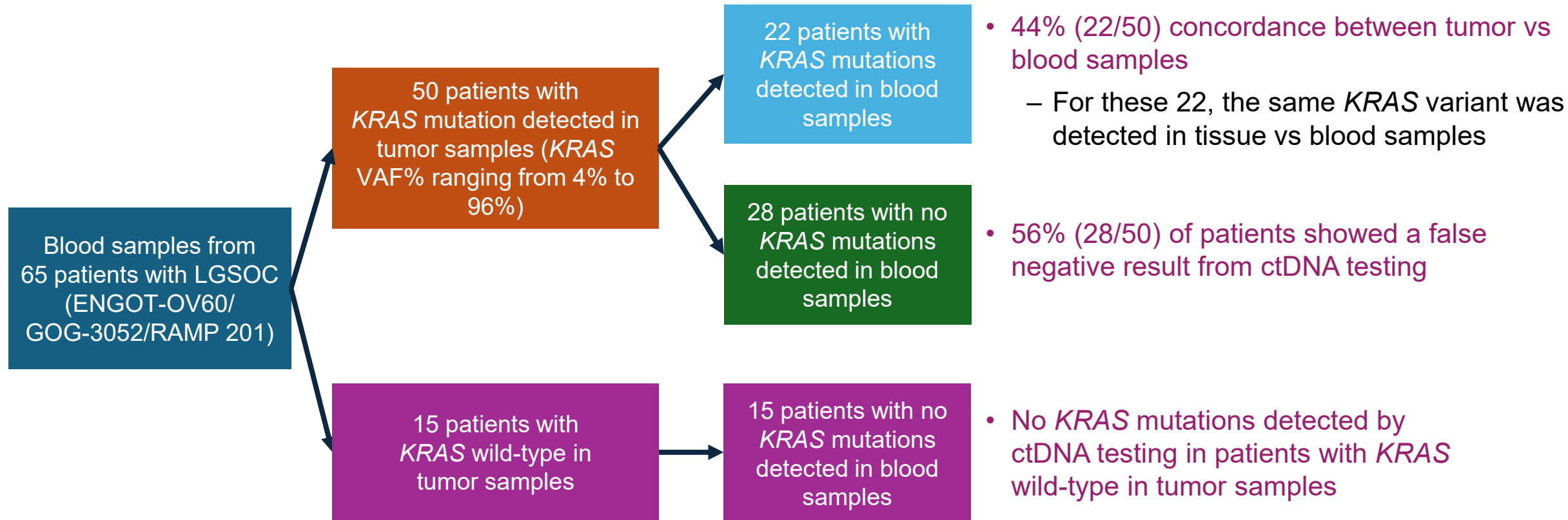
Treatment-Related Adverse Events, n (%)*		Avutometinib + Defactinib 3.2 mg BIW + 200 mg BID 3 weeks on/1 week off N=115
Preferred term	All Grades	Grade ≥3
Ocular events		
Blurred vision	47 (40.9)	0
Visual impairment	7 (6.1)	0
Retinal pigment epithelial detachment	6 (5.2)	0
Retinal detachment	4 (3.5)	0
Serous retinal detachment	2 (1.7)	0
Serous retinopathy	2 (1.7)	0
Retinopathy	2 (1.7)	0
Retinal vein occlusion	1 (0.9)	0
Pneumonitis	1 (0.9)	0
Hypertension	4 (3.5)	1 (0.9)
Ejection fraction decreased	1 (0.9)	0
Congestive heart failure	0	0

*Adverse events (preferred term) considered by the investigator to be related to study drug (either avutometinib or defactinib).

BID, twice daily; BIW, twice weekly

ctDNA in LGSOC: Results from RAMP201 Samples

In Patients With *KRAS* Mutations Detectable in Tumor Samples, 44% (22/50) Concordance Between *KRAS* Detection in Tumor vs Blood Samples



ctDNA, circulating tumor DNA; *KRAS*, Kirsten rat sarcoma virus; LGSOC, low-grade serous ovarian cancer; VAF, variant allele frequency.

Conclusions

- Clinical Trials changing the treatment landscape for advanced LGSOC
- Systemic treatment options improving for LGSOC
- Avutometinib and Defactinib combination in *KRAS* mutated recurrent disease is the first approved (FDA accelerated approval) therapy in LGSOC

What's Next in LGSOC Cancer Treatment



Krish Tewari, MD

University of California, Irvine



Next up...

Emerging Therapies for Low Grade Serous Ovarian Cancer

Therapies for Recurrent LGSOC Disease

- Scientific Rationale to Explain RAMP-201 Results
- RAMP-301 - Phase 3 Randomized Avutometinib plus Defactinib vs Physician's Choice ChemoRx
- 2nd & 3rd Generation Antibody-Drug Conjugates Targeting Folate Receptor 2 α
 - Mirvetuximab — SORAYA, FORWARD-1, MIRASOL & U.S. FDA Approval
 - Rinatabart sesutecan - RAINFOL-01 - US FDA Fast Track Designation
 - DB-1305/BNT325 - Phase 1/2 Anti-Trop2 ADC - US FDA Fast Track Designation
- NCI-Match EAY-131 Subprotocol H - Dabrafenib + Trametinib for BRAFV600E Mutations
- GOG-3026 - Phase 2 Ribociclib plus Letrozole

Trials in the Upfront Setting for LGSOC

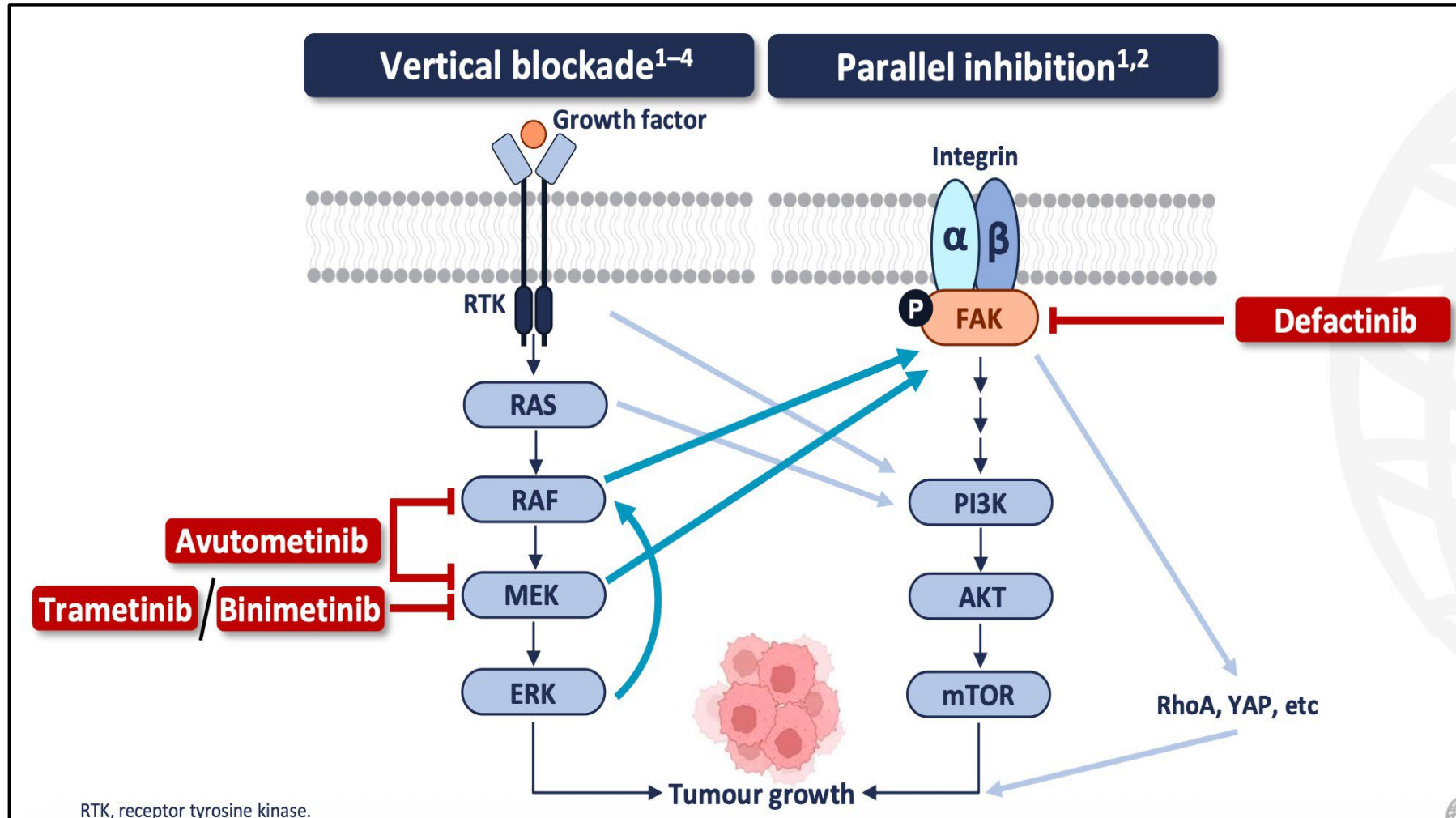
- NRG-GY019 - Phase 3 Letrozole alone vs Carbo-Taxol - both arms followed by Letrozole
- CHAMELEON - Combined Targeted & Hormonal Treatment
- BOUQUET (GOG-3051) — Phase 2 Biomarker-Driven Targeted Therapy



Treatment of Recurrent LGSOC

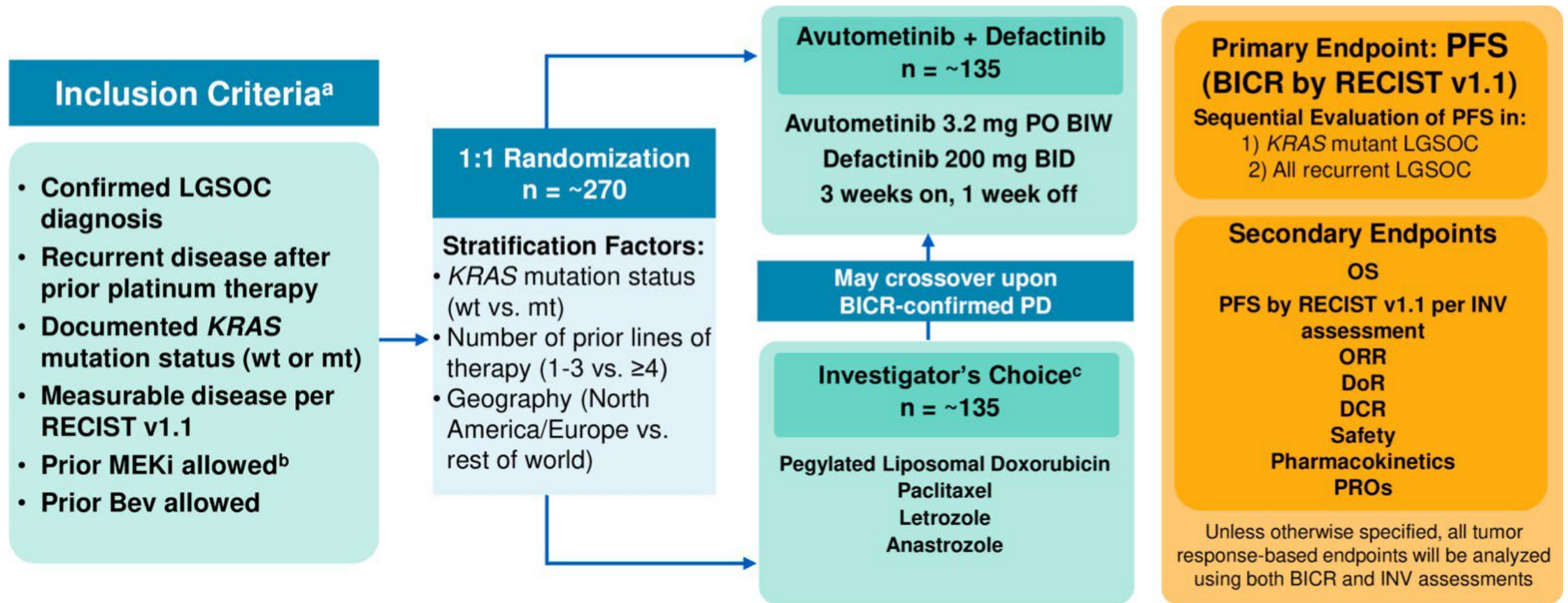


Scientific Rationale RAF/MEK and FAK Blockade



RAMP-301

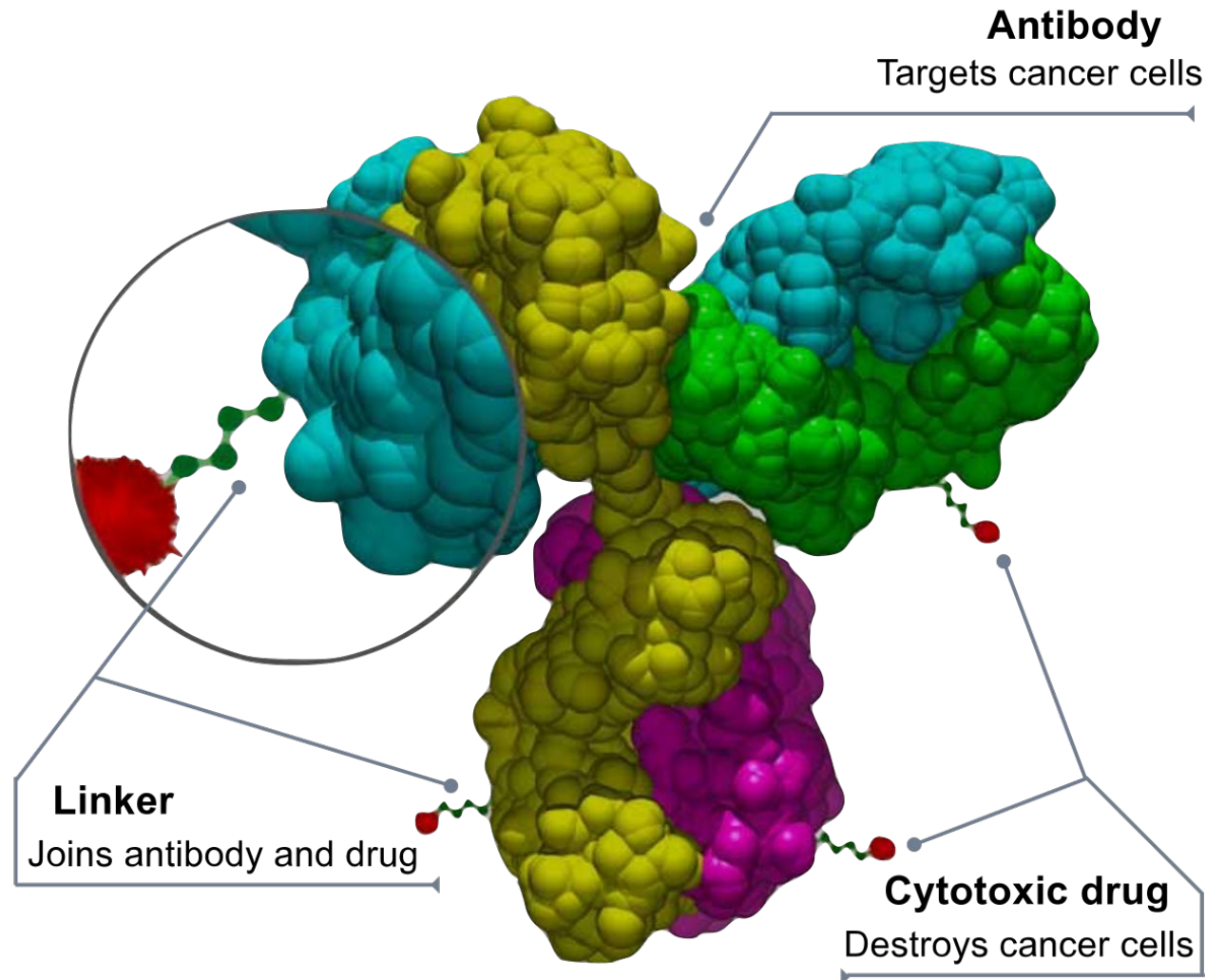
Phase 3 Confirmatory, Registration Trial - Enrollment Complete



Abbreviations: BICR, blinded independent central review; BID, twice daily; DCR, disease control rate; DOR, duration of response; INV, investigator; *KRAS*, Kirsten rat sarcoma viral oncogene homolog; LGSOC, low-grade serous ovarian cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PROs, patient-reported outcomes; RECIST, Response Evaluation Criteria in Solid Tumors.
Grisham R, et al. *Int J Gynecol Cancer*. 2025;35(11):101832; *ClinicalTrials.gov* NCT06072781.

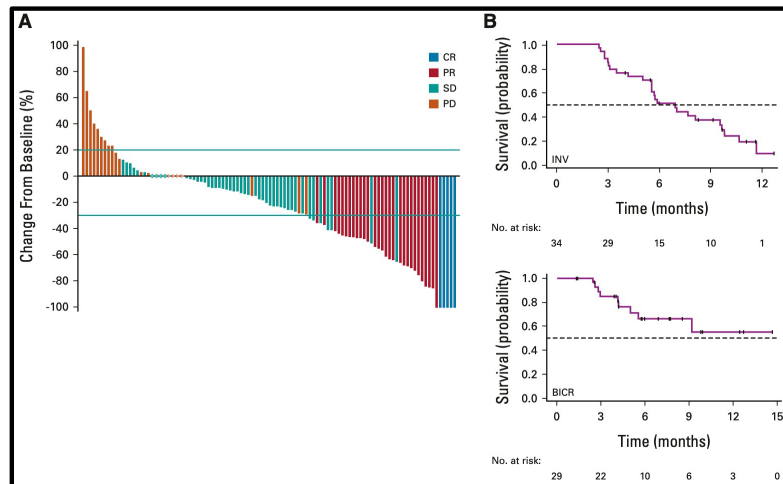
Antibody-Drug Conjugates

Trojan Horses & Multiple Warheads

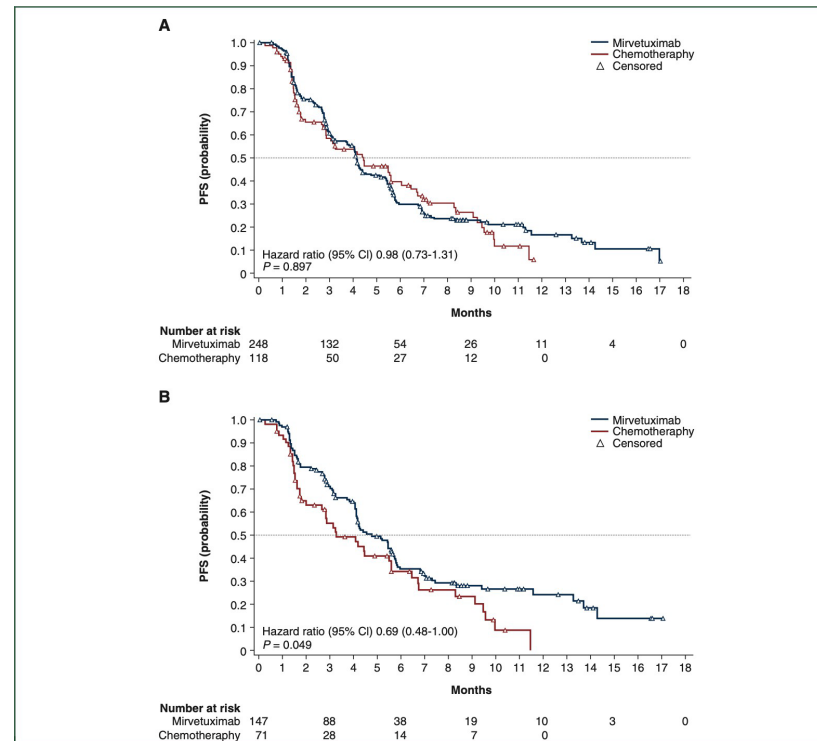
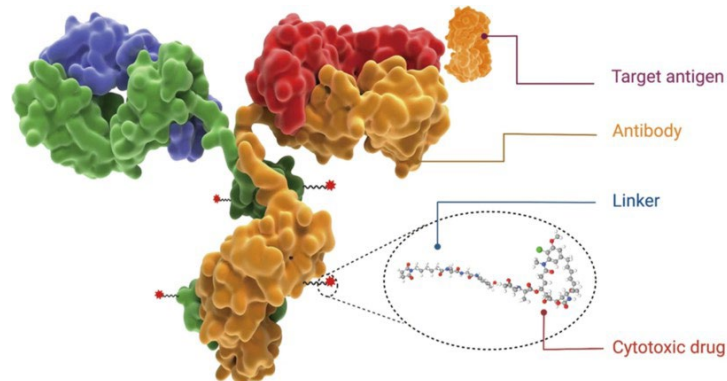


SORAYA, FORWARD-1 & MIRASOL

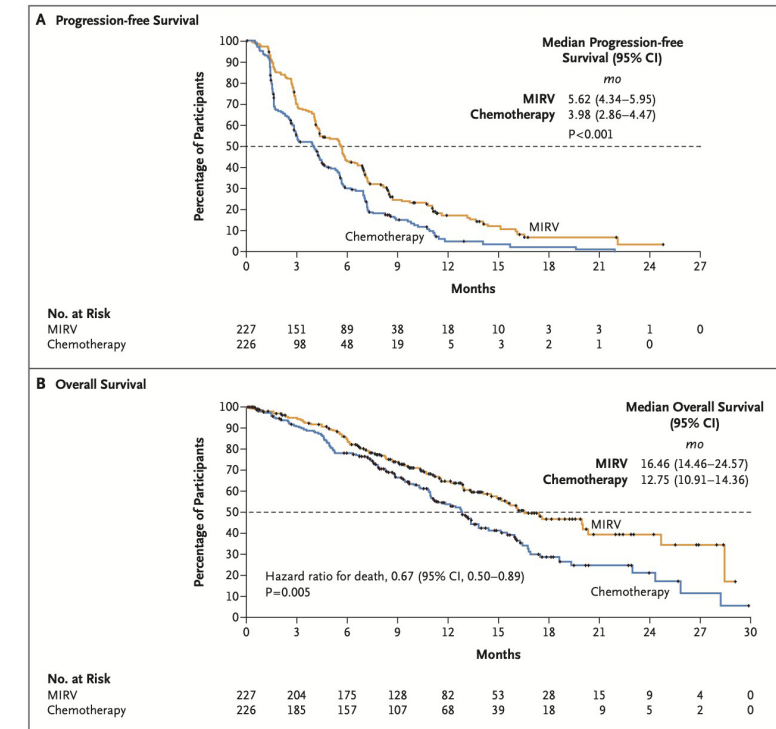
Mirvetuximab - 2nd Generation ADC



Matulonis UA, et al. *J Clin Oncol* 2023;41:2436-45. [ClinicalTrials.gov NCT04296890](https://clinicaltrials.gov/ct2/show/study/NCT04296890).



Moore KN, et al *Annals Oncol* 2021;32:757-65. [ClinicalTrials.gov NCT02631876](https://clinicaltrials.gov/ct2/show/study/NCT02631876).



Moore KN, et al. *N Engl J Med* 2023;389:2162-74. [ClinicalTrials.gov number, NCT04209855](https://clinicaltrials.gov/ct2/show/study/NCT04209855)



**U.S. FOOD & DRUG
ADMINISTRATION**

FDA approves mirvetuximab soravtansine-gynx for FRα positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer

On March 22, 2024, the Food and Drug Administration approved mirvetuximab soravtansine-gynx (Elahere, ImmunoGen, Inc. [now a part of AbbVie]) for adult patients with FRα positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have [received](#) one to three prior systemic treatment regimens. Patients are selected based on an FDA-approved test. Mirvetuximab soravtansine-gynx previously received accelerated approval for this indication.



RAINFOL-01

Rinatabart Sesutecan - 3rd Generation ADC

US FDA Breakthrough Therapy Designation - Endometrial Cancer

US FDA Fast Track Designation - HGS & Endometrioid FR2α+ Ovarian cancer

Study Design and Patient Demographics

Objective: Report safety and efficacy of single-agent Rina-S Q3W from dose escalation (OC and EC) and dose expansion (OC) of an open-label, multicenter phase 1/2 study (NCT05579366)¹

Study Design

Part A – Dose Escalation

- Solid tumors^a dose escalation (n = 53) included patients regardless of FRα expression with previously treated OC (n = 32; 23 received Rina-S 100-120 mg/m² Q3W) and EC (n = 11; 5 received Rina-S 100-120 mg/m² Q3W)

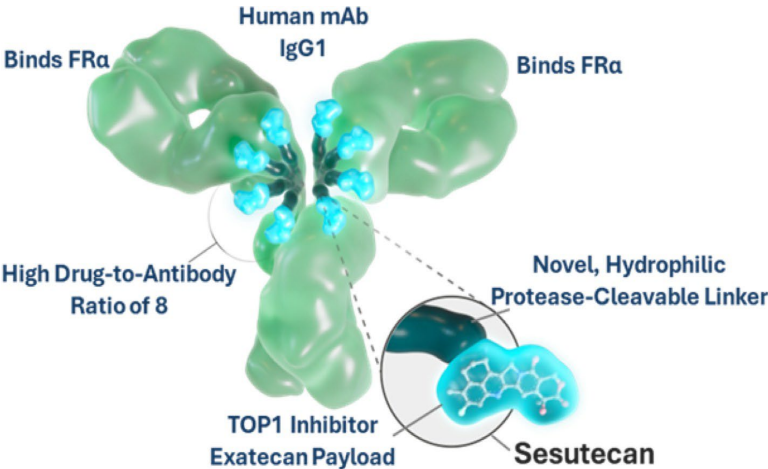
Part B – Dose Expansion

- Planned tumor-specific dose expansion includes OC, EC, and EGFR-mutant NSCLC regardless of FRα expression^b
- **Cohort B1 - OC Dose Expansion**
 - Inclusion criteria
 - Histologically or cytologically confirmed OC (must have epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer)
 - Prior treatment (1-3 prior lines for PROC or 4 prior lines regardless of platinum-sensitivity status)
 - ECOG PS 0-1
 - Measurable disease per RECIST v1.1
 - Adequate hematologic, hepatic, renal, and cardiac function
 - Randomized 1:1 to receive Rina-S 100 mg/m² or Rina-S 120 mg/m² Q3W

Patient Demographics and Disease Characteristics in OC Dose Expansion

	Rina-S 100 mg/m ² n = 22	Rina-S 120 mg/m ² n = 20
OC Dose Expansion		
Age, median (range), years	62.5 (42-82)	64.5 (37-83)
Prior lines of therapy, median (range)	3 (1-5)	3 (1-4)
Bevacizumab, n (%)	20 (90.9)	18 (90.0)
PARPi, n (%)	15 (68.2)	13 (65.0)
Mirvetuximab soravtansine, n (%)	4 (18.2)	4 (20.0)
Platinum sensitivity status, n (%)		
Resistant	20 (90.9)	19 (95.0)
Sensitive	2 (9.1)	1 (5.0)

DCO: July 28, 2024



^aPatient populations included patients with epithelial OC, EC, HER2- BC, NSCLC, and mesothelioma. ^bFRα levels retrospectively assessed.
BC, breast cancer; DCO, data cutoff; EC, endometrial cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; FRα, folate receptor α; HER2, human epidermal growth factor receptor 2; NSCLC, non-small cell lung cancer; OC, ovarian cancer; PARPi, poly-ADP ribose polymerase inhibitor; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumours; Rina-S, rinatabart sesutecan.
1. National Library of Medicine. <https://www.clinicaltrials.gov/study/NCT05579366>. Accessed: August 7, 2024.

RAINFOL-01

Antitumor Activity | OC – Dose Expansion

Rina-S showed encouraging antitumor activity at 120 mg/m² Q3W, including a complete response, in patients with heavily pretreated OC

OC Dose Expansion	Rina-S	
	100 mg/m ² n = 22 ^b	120 mg/m ² n = 18 ^b
Confirmed ORR, ^{a,b} % (95% CI)	18.2 (5.2-40.3)	50.0 (26.0-74.0)
Best overall response, ^b n (%)		
CR	0	1 (5.6)
PR	4 (18.2)	8 (44.4)
SD	15 (68.2)	7 (38.9)
PD	3 (13.6)	1 (5.6)
Not evaluable	0	1 (5.6)
DCR, % (95% CI)	86.4 (65.1-97.1)	88.9 (65.3-98.6)
Median DOR (95% CI)	NR (NR-NR)	

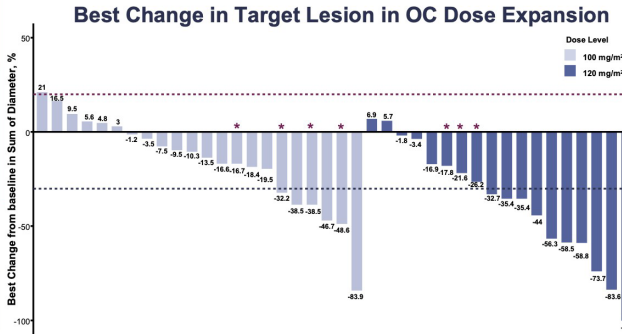
Treatment duration, range: 3.0-42.0+ weeks
Median on-study follow-up: 24 weeks

^aBased on investigator assessment. ^bResponse-evaluable population. ^cOne patient in the 120 mg/m² cohort with prior mirvetuximab soravtansine was not response-evaluable.

CI, confidence interval; CR, complete response; DCR, disease control rate; DOR, duration of response; NR, not reached; OC, ovarian cancer; ORR, objective response rate; PD, progressive disease; PR, partial response; Q3W, every 3 weeks; Rina-S, rinatartab sesutecan; SD, stable disease.



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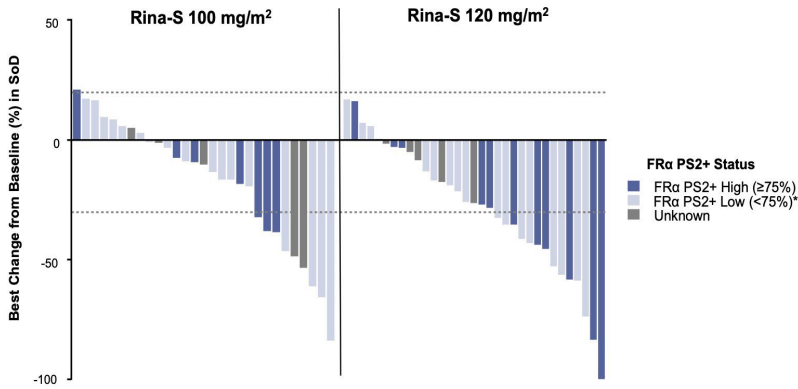


Median no. of cycles: 6.5 (100 mg/m²) and 7.0+ (120 mg/m²)

Response by FRα Expression | OC – Dose Escalation & Expansion

Responses in patients with OC were observed regardless of FRα expression levels

Best Change in Target Lesion SoD by FRα PS2+ Status in OC Dose Escalation and Expansion



*Clinical activity was observed at lower cutoffs (FRα PS1+ <25%).

FRα, folate receptor α; OC, ovarian cancer; PS, positive staining; SoD, sum of diameter; Rina-S, rinatartab sesutecan.



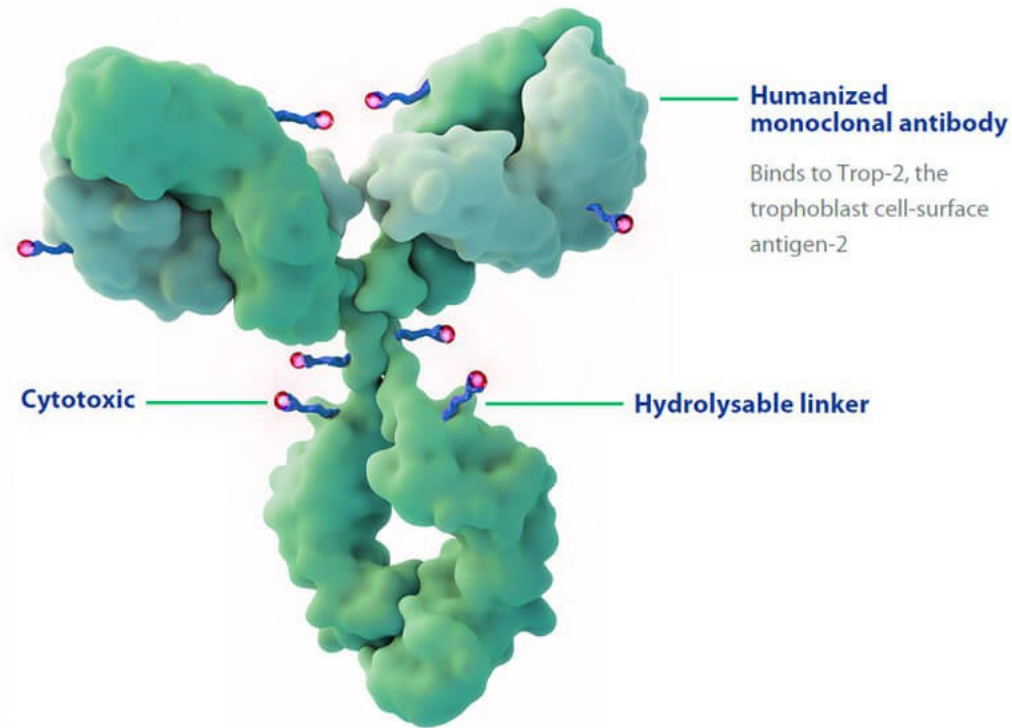
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Abbreviations: RINA-S, Rinatartab Sesutecan; ADC, antibody-drug conjugate; BOR, best overall response; CI, confidence interval; DOR, duration of response; FRα, folate receptor alpha; OC, ovarian cancer; ORR, objective response rate; PR, partial response; SD, stable disease.

Lee EK, et al. Presented at ESMO 2024. ClinicalTrials.gov Identifier: NCT05579366; Figure adapted from Lee EK, et al.

DB-1305/BNT325 Phase 1/II

Anti-Trop2 ADC - US FDA Fast Track Designation PROC

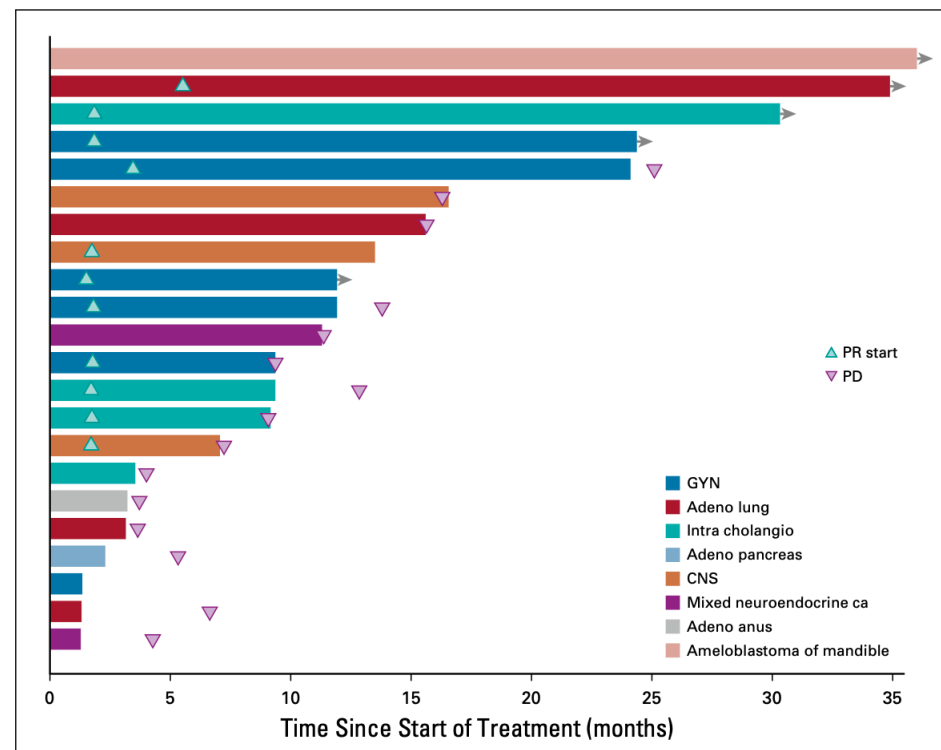


	3 mg/kg Q3W N = 19	Overall (2–5 mg/kg Q3W) N = 38
Unconfirmed BOR, n (%)		
CR	1 (5.3)	2 (5.3)
PR	7 (36.8)	12 (31.6)
SD	7 (36.8)	17 (44.7)
PD	3 (15.8)	5 (13.2)
NE	0	1 (2.6)
Missing	1 (5.3)	1 (2.6)
Unconfirmed ORR, n (%) [95% CI]	8 (42.1) [20.3, 66.5]	14 (36.8) [21.8, 54.0]
Confirmed ORR, n (%) [95% CI]	7 (36.8) [16.3, 61.6]	10 (26.3) [13.4, 43.1]
DCR, n (%) [95% CI]	15 (78.9) [54.4, 94.0]	31 (81.6) [65.7, 92.3]
Median DOR (95% CI), months	NE (NE, NE)	6.4 (2.8, NE)
Median PFS (95% CI), months	NE (2.7, NE)	7.6 (4.4, NE)
BOR, best overall response; CR, complete response; DCR, disease control rate; DOR, duration of response; NE, not estimable; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease.		

Abbreviations: ADC, antibody-drug conjugate; BOR, best overall response; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; DCR, disease control rate; PFS, progression-free survival; PROC, platinum-resistant ovarian cancer.

Rubinstein M, et al. Presented at: SGO Annual Meeting on Women's Cancer; 2025. [ClinicalTrials.gov Identifier: NCT05438329](https://clinicaltrials.gov/ct2/show/study/NCT05438329)

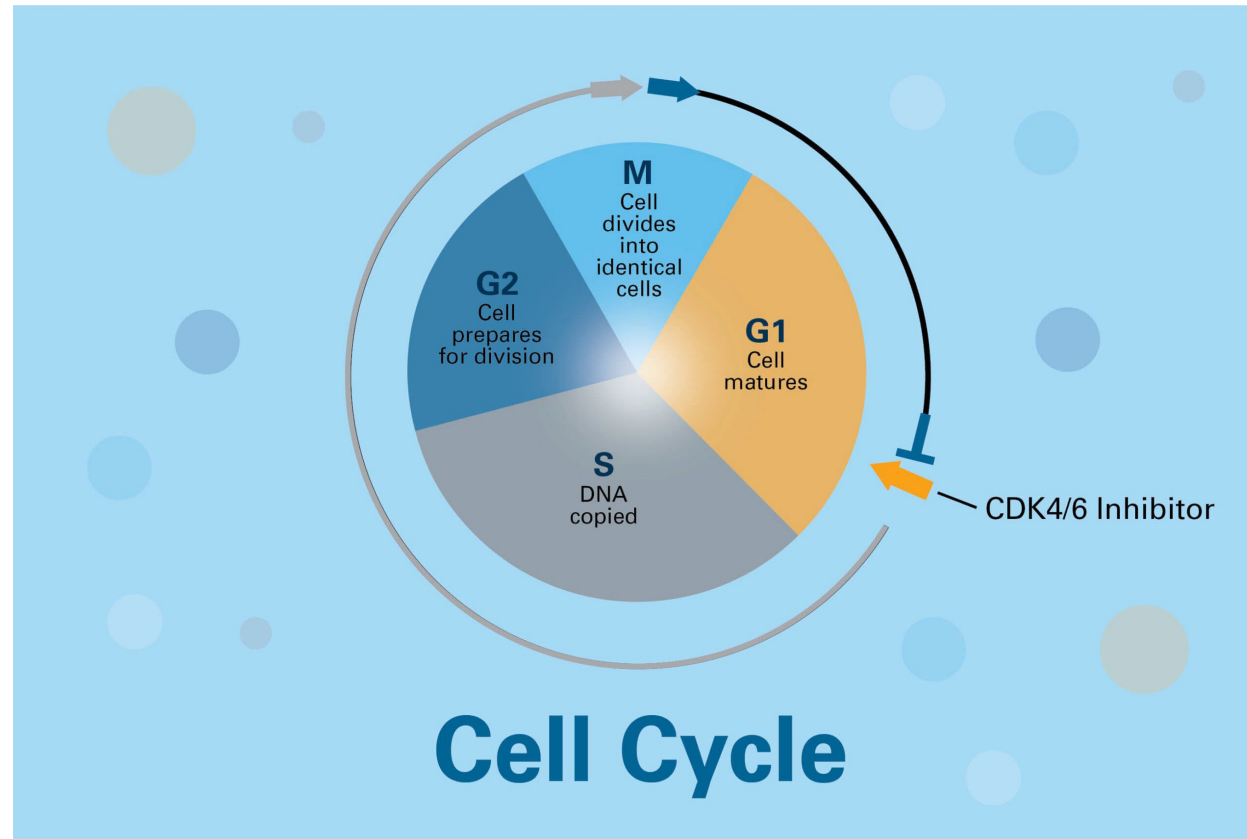
Dabrafenib + Trametinib for BRAF^{V600E} Mutations



Salama AKS, et al. *J Clin Oncol* 2020;38(33):3895-3904.: [ClinicalTrials.gov Identifier: NCT02465060](https://ClinicalTrials.gov/ct2/show/study/NCT02465060)

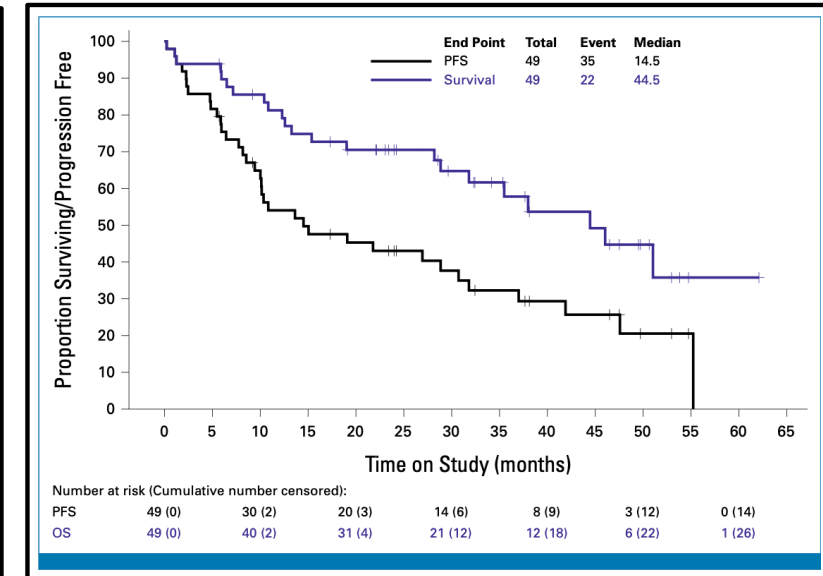
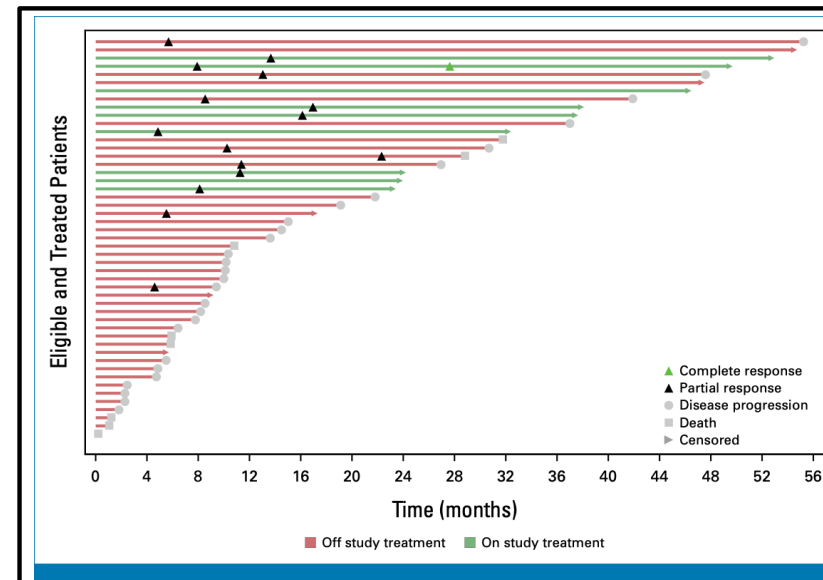
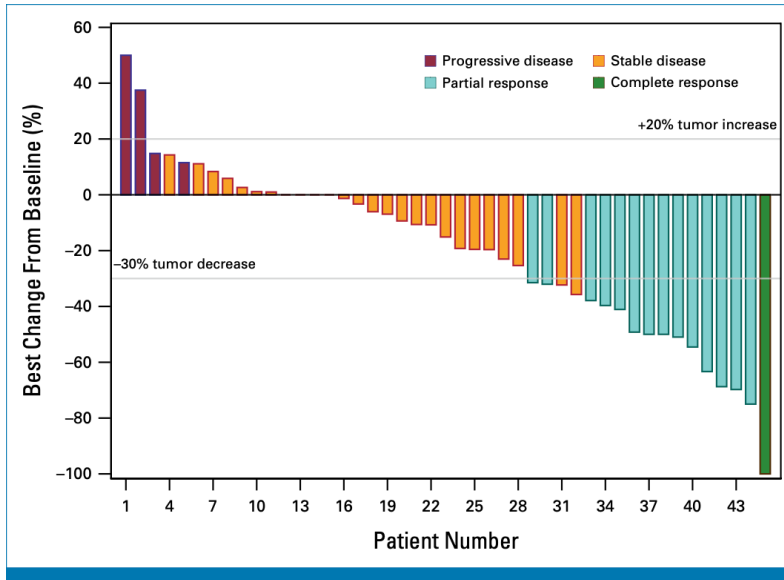
CDK 4/6 Inhibitors

Established in Hormone Receptor+ HER2-negative Breast Cancer



GOG-3026

Phase 2 Ribociclib plus Letrozole in recurrent LGSOC



1st Line Therapy for LGSOC



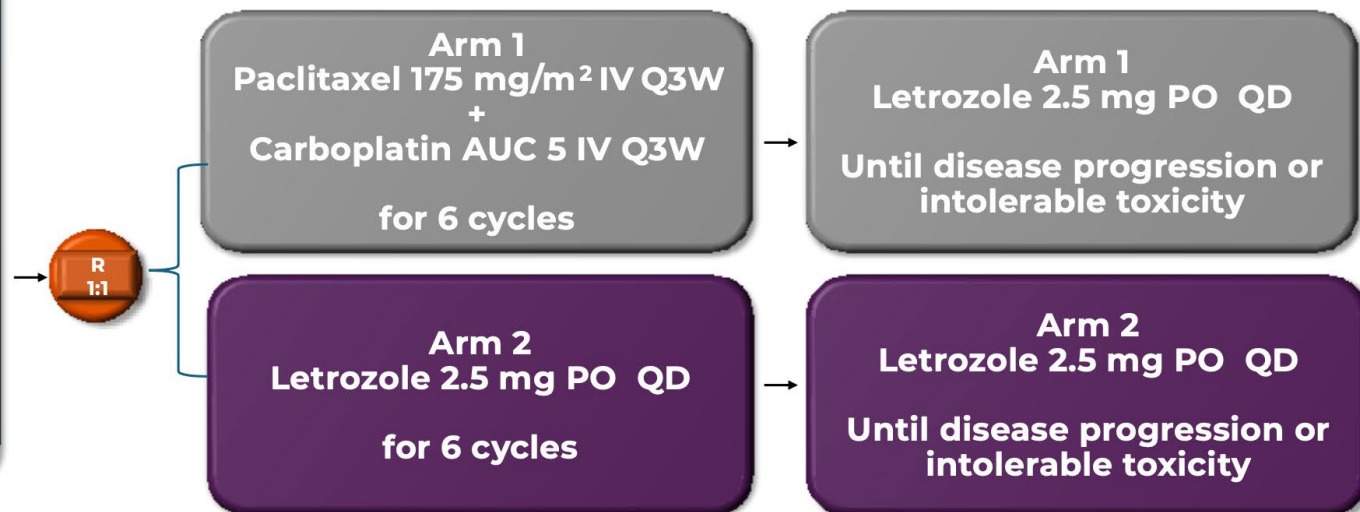
NRG-GY019

Key Eligibility Criteria

- Stage II-IV LGSOC
- Pathology report showing results of institutional p53 wildtype IHC testing
- ECOG PS 0, 1, or 2
- Attempt at maximal cytoreductive surgery
- No prior chemo

Stratification Factors

- Residual disease status
- Country



Endpoints

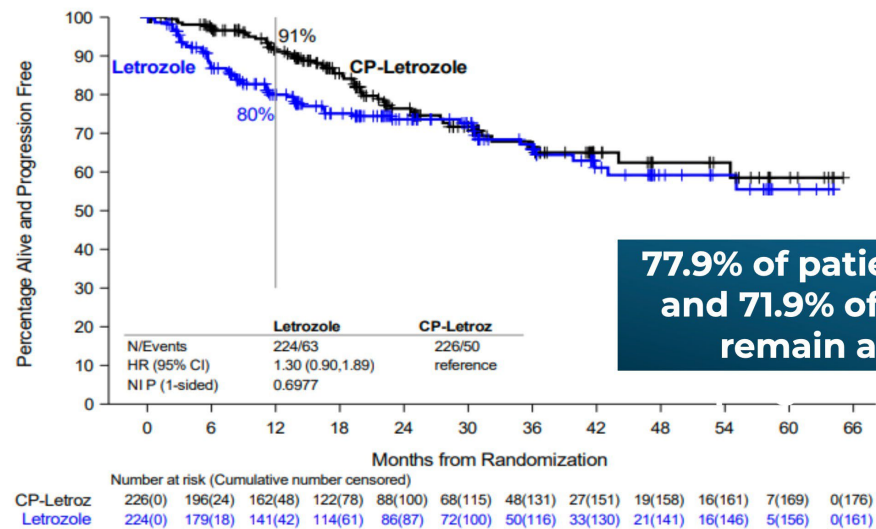
- **Primary:** PFS by investigator
- **Secondary:** Safety, OS, ORR/DOR per RECIST v1.1

Abbreviations: ECOG, Eastern Cooperative Oncology Group; IHC, immunohistochemistry; IV, intravenous; LGSOC, low-grade serous ovarian carcinoma; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, oral; PS, performance status; Q3W, every 3 weeks; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors.

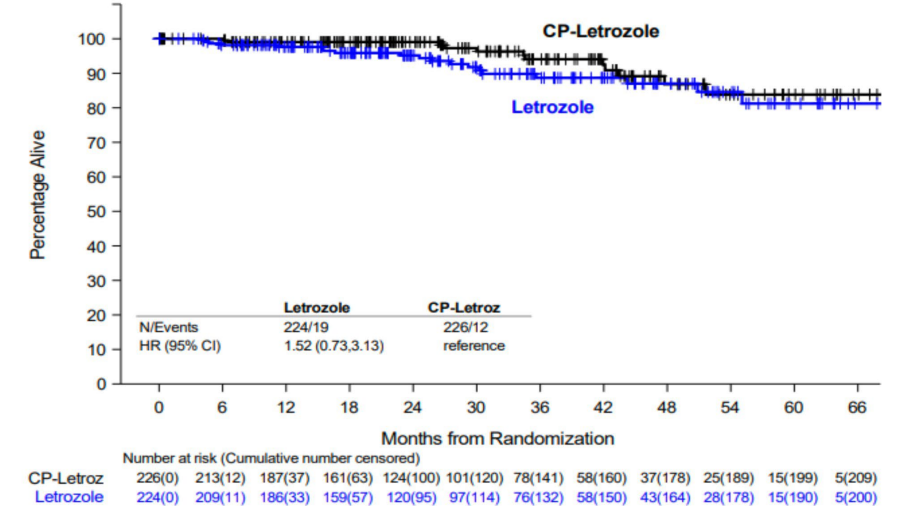
Fader AN, et al. Presented at SGO Annual Meeting 2026 (LBA02); Fader AN, et al. Gynecol Oncol. 2023;176(Suppl 1):S195; ClinicalTrials.gov Identifier: NCT04095364.

NRG-GY019

Progression-Free Survival (PFS)



Overall Survival (OS)

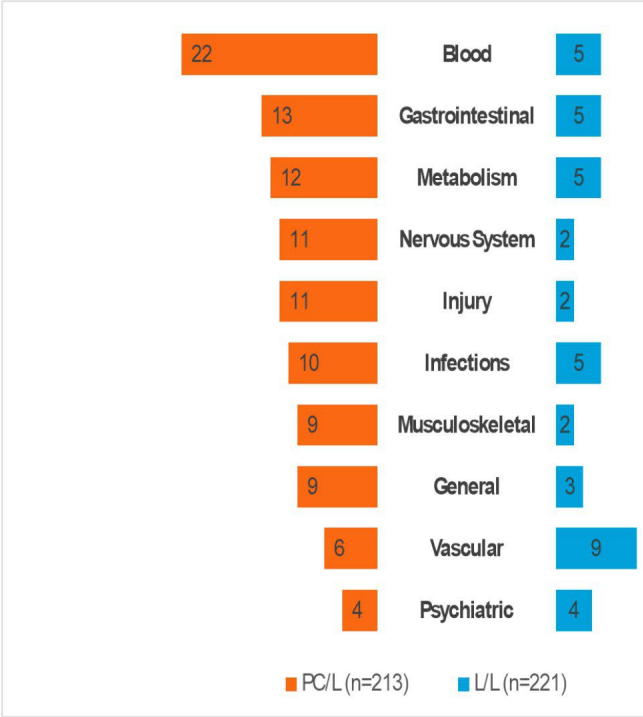


NRG-GY019

Adverse Event Summary

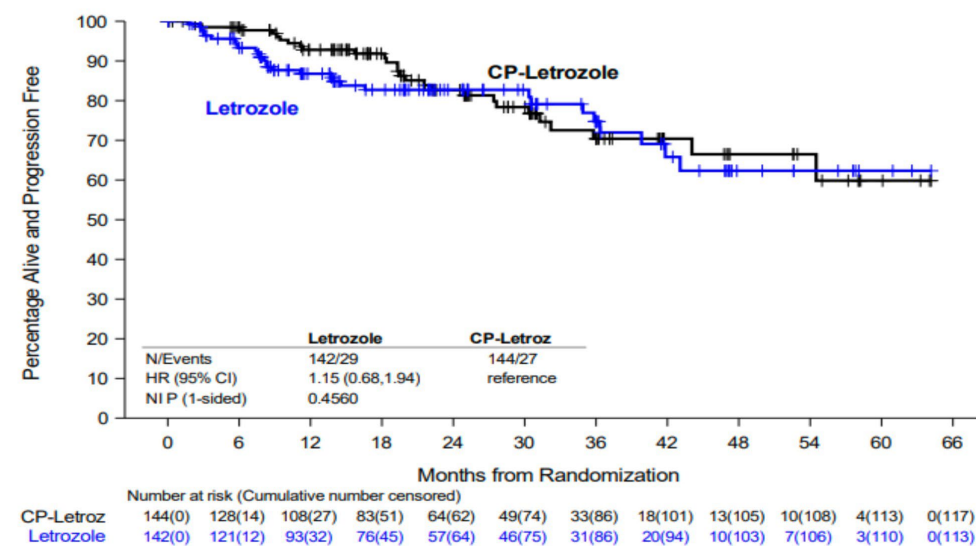
Adverse Event	Cycle 1-6		Cycle 7+	
	PC/L (n=213)	L/L (n=221)	PC/L (n=191)	L/L (n=189)
Any Adverse Event	213 (100)	214 (96.8)	191 (100)	189 (100)
Grade 3-5	100 (46.9)	39 (17.6)	79 (41.4)	66 (34.9)
Leading to death	0 (0)	1 (0.5)	0 (0)	1 (0.5)

During cycles 1-6, the odds of observing at least 1 grade 3/4 adverse event was **3.99 (95%CI: 2.57, 6.18 p<0.001)** higher in the patients on the CP/L than the patients on the L arm.

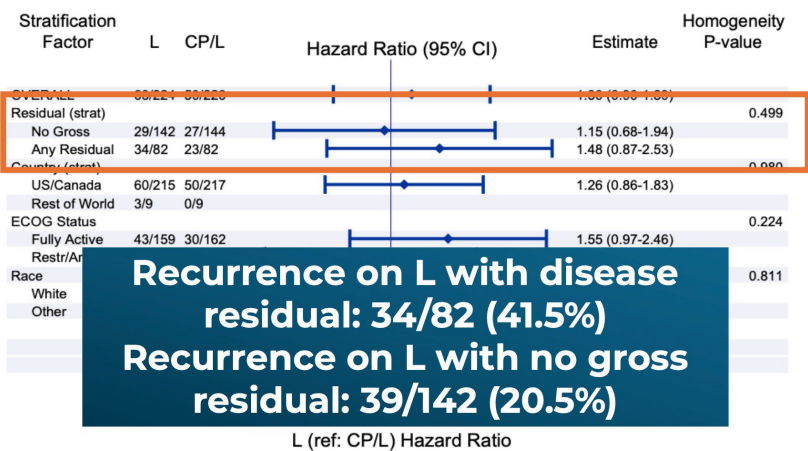


NRG-GY019

PFS in Patients with No Gross Residual Disease After Cytoreductive Surgery



PFS: Subgroup Analysis

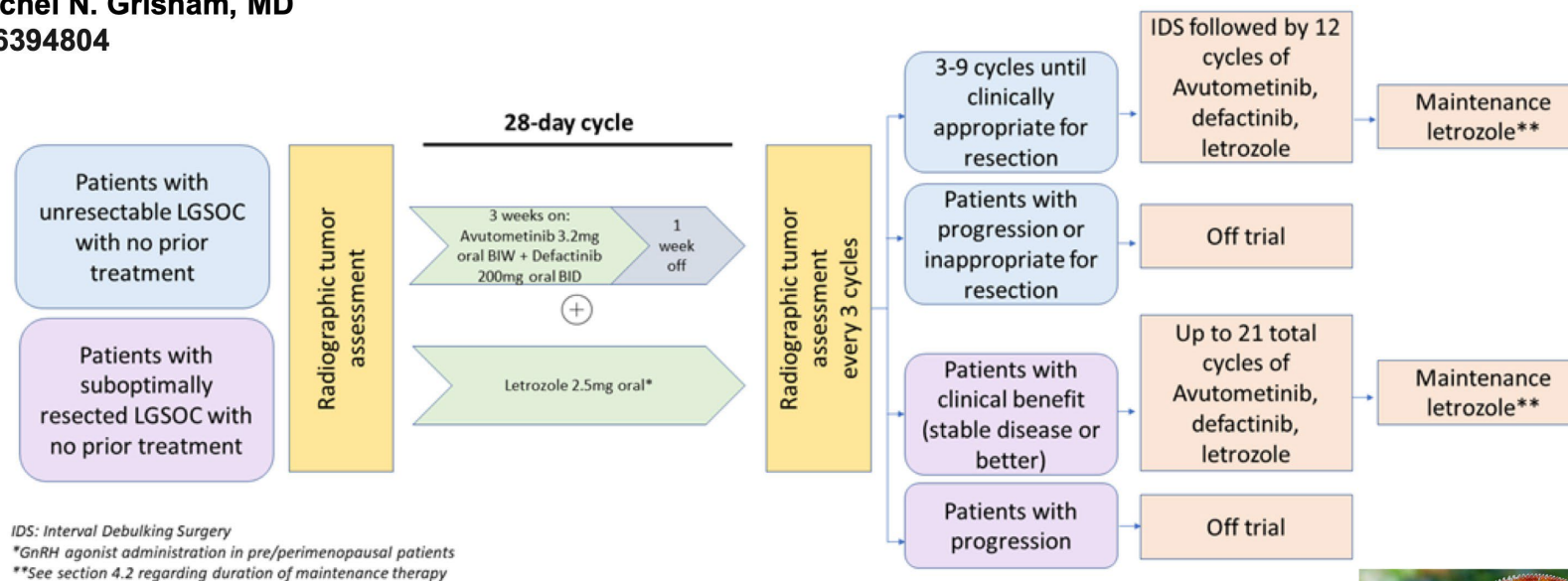


Abbreviations: CI, confidence interval; CP/L, carboplatin/paclitaxel followed by letrozole maintenance; L, letrozole; HR, hazard ratio.
Fader AN, et al. Presented at SGO Annual Meeting 2026 (LBA02); Fader AN, et al. Gynecol Oncol. 2023;176(Suppl 1):S195; ClinicalTrials.gov Identifier: NCT04095364.

CHAMELEON

Combination targeted and Hormonal treatment of Low-grade serous Ovarian cancer in the upfront setting (CHAMELEON) Study Schema

PI: Rachel N. Grisham, MD
NCT06394804

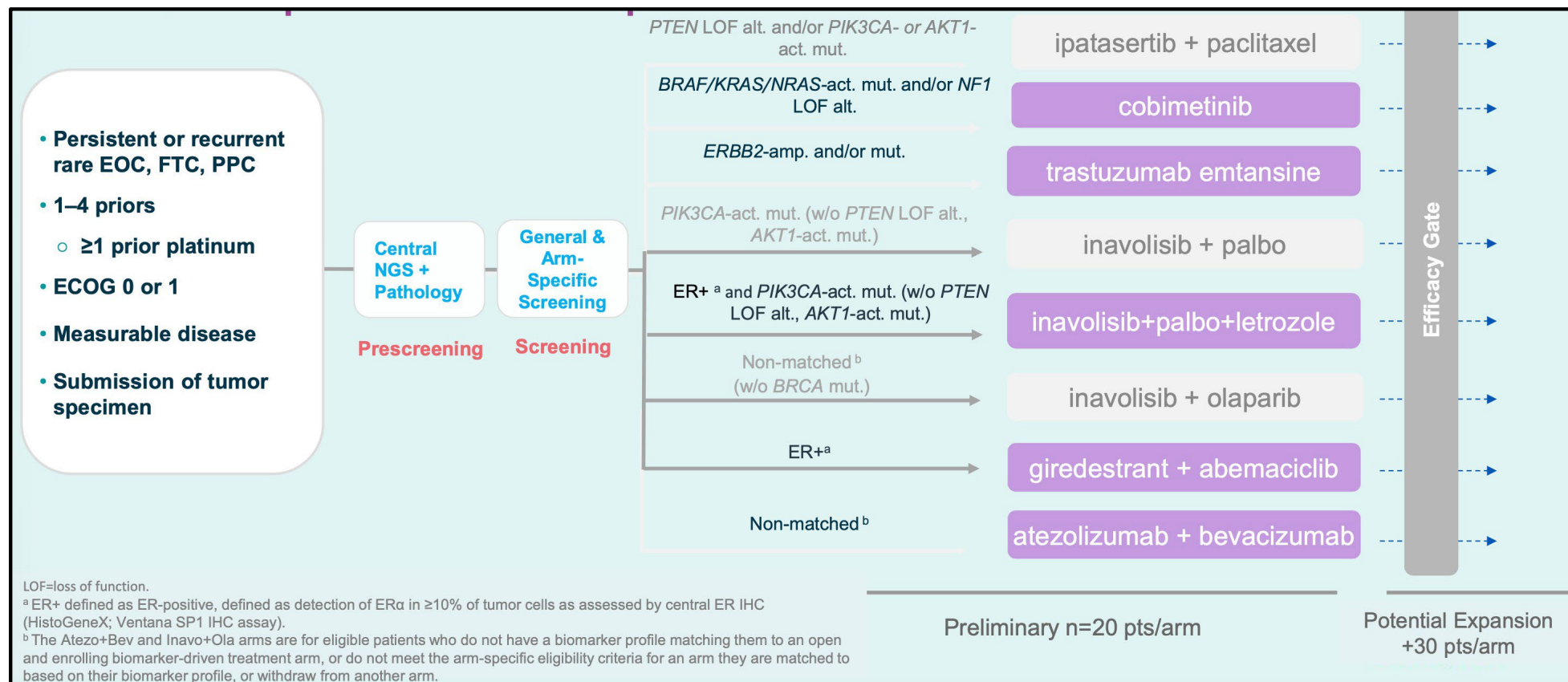


<https://clinicaltrials.gov/study/NCT06394804#study-overview>



BOUQUET

GOG-3051



Adverse Events & Patient Support, A Panel Discussion

All Faculty



Adverse Events Profile for Avutometinib + Defactinib (parts A-C)

- 80% (92/115) of patients had AEs leading to **dose interruption**
 - 38% (44/115) for elevations in CPK
- 36.5% (42/115) of patients had AEs leading to **dose reduction**
- 10% (12/115) of patients **discontinued for AEs**; most common increased CPK (n=4)
- 7% (8/115) of patients had **serious AEs** considered by the investigator to be related to study treatment: the only event occurring in more than 1 patient was abdominal pain
- 4 **deaths** (within 30 days of discontinuation): GI hemorrhage, large intestine perforation, clinical progression, clinical deterioration (none considered related to study treatment)

**Most common adverse events (preferred term) considered by the investigator to be related to study drug (either avutometinib or defactinib).*

Abbreviations: E, adverse event; AST, aspartate aminotransferase; BID, twice daily; CPK, creatine phosphokinase; GI, gastrointestinal; GOG, Gynecologic Oncology; Banerjee SN, et al. Presented at IGCS 2024. J Clin Oncol. 2025;43(25):2782-2792. ClinicalTrials.gov identifier: NCT06072781

Treatment-Related Adverse Events (>20% of patients)* n (%)	Avutometinib + Defactinib 3.2 mg BIW + 200 mg BID 3 weeks on/1 week off N= 115	
Preferred term	All Grades	Grade ≥3
Non-laboratory AEs		
Nausea	77 (67.0)	3 (2.6)
Diarrhea	67 (58.3)	9 (7.8)
Oedema peripheral	61 (53.0)	1 (0.9)
Fatigue	50 (43.5)	3 (2.6)
Vomiting	49 (42.6)	3 (2.6)
Vision blurred	47 (40.9)	0
Rash	41 (35.7)	2 (1.7)
Dermatitis acneiform	39 (33.9)	5 (4.3)
Dry skin	30 (26.1)	0
Anemia	26 (22.6)	6 (5.2)
Laboratory-related AEs		
Increased blood CPK	69 (60.0)	28 (24.3)
Increased blood bilirubin increased/ hyperbilirubinemia	38 (33.0)	5 (4.3)
AST increased	36 (31.3)	2 (1.7)

RAMP201: Adverse Events of Interest Associated with MEK Inhibitors

Treatment-Related Adverse Events, n (%)*		Avutometinib + Defactinib 3.2 mg BIW + 200 mg BID 3 weeks on/1 week off N=115
Preferred term	All Grades	Grade ≥3
Ocular events		
Blurred vision	47 (40.9)	0
Visual impairment	7 (6.1)	0
Retinal pigment epithelial detachment	6 (5.2)	0
Retinal detachment	4 (3.5)	0
Serous retinal detachment	2 (1.7)	0
Serous retinopathy	2 (1.7)	0
Retinopathy	2 (1.7)	0
Retinal vein occlusion	1 (0.9)	0
Pneumonitis	1 (0.9)	0
Hypertension	4 (3.5)	1 (0.9)
Ejection fraction decreased	1 (0.9)	0
Congestive heart failure	0	0

*Adverse events (preferred term) considered by the investigator to be related to study drug (either avutometinib or defactinib).

BID, twice daily; BIW, twice weekly

Q&A and Closing Remarks

All Faculty



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In support of improving patient care, this activity has been planned and implemented by The GOG Foundation, Inc. (GOG).

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