An Industry Supported Symposium at the 2026 Ponte Vedra Beach Women's Health & Robotics Symposium

Advances in LGSOC:

Optimizing Patient Outcomes Through MAPK and FAK Pathway Inhibition

This session is not included in the main event CME/CPD credit

Ponte Vedra Beach, Florida

Saturday, October 10, 2026

7:30 am – 8:30 am



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

Faculty Disclosures

Name	Role	Disclosures
Thomas Herzog, MD	Moderator	• **Scientific Advisory Boards:** Aadi Bioscience, Abbvie, AstraZeneca, Caris, Corcept, DSI, Eisai, Epsilogen, Genmab, GSK, Merck, Mersana, Natera, Pfizer, Pharma&, PMV Pharma, Sutro, Tempus, Zentalis • **Honorarium:** Aadi; Corcept; Merck; Natera
Martin Martino, MD	Speaker	• Intuitive; JNJ Medtech; Medtronic; CMR
Angeles Alvarez Secord	Speaker	• **Research funds to Institution** (AbbVie; Aravive; AstraZeneca; Daiichi Sankyo; Eisai; Ellipses Pharma; Genmab; GSK; Immunogen; Karyopharm; Merck; Mersana; Myriad; Oncoquest/Canaria Bio; Oncoquest; Roche/Genentech; TORL Biotherapeutics; Tubulis; Zentalis) • **Honorarium** (Merck; GSK) • **Advisory Board with Honoraria** (AbbVie; AstraZeneca; BeOne; Corcept; Daiichi Sankyo; Faeth Therapeutics; Foundation Medicine; GSK; Genmab; Gilead; Histosonics; Medtronic; Merck) • **Medical Advisory Board** (Project Nana) • **Steering Committee Uncomp.** (Oncoquest; Genmab) • **Royalties** (Up to Date) • **Board of Directors** (SGO; FWC; GOG Foundation; AAOGF) • **Stock-Divested in June 2024** (Amgen; Johnson & Johnson)

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

Faculty


Thomas Herzog, MD
University of Cincinnati
Martin Martino, MD
Ascension Health
Angeles Alvarez Secord, MD, MHS
Duke University

THANK YOU

Verastem

For Supporting This Activity With
An Independent Medical Education Grant

Learning Objectives

At the conclusion of this activity, participants should be able to:

1. Evaluate emerging clinical evidence supporting targeted therapies for advanced and recurrent LGSOC, including agents targeting MAPK and FAK signaling pathways.

2. Incorporate molecular testing, including *KRAS* mutation assessment and other relevant biomarkers, into treatment selection and sequencing decisions for patients with LGSOC.

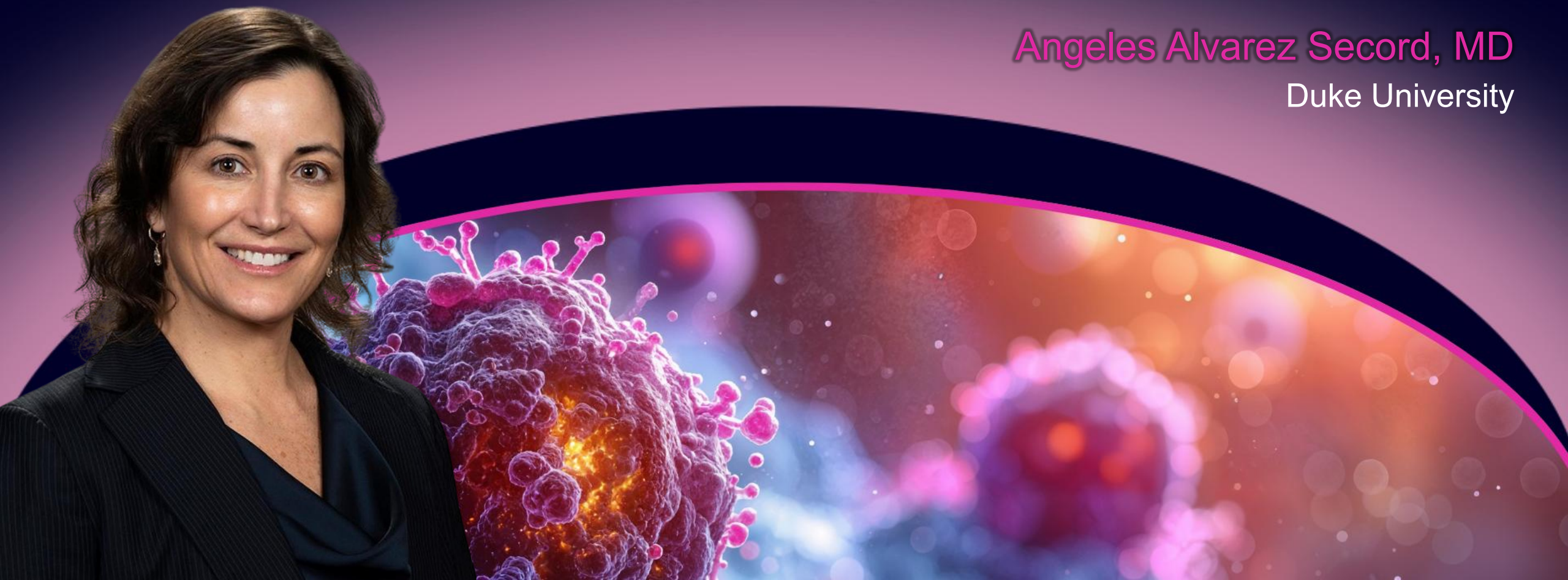
3. Apply evidence-based strategies for the management of targeted therapy-related adverse events to optimize treatment adherence, quality of life, and clinical outcomes.

Agenda

5 minutes	**Welcome, Introduction and Program Overview** Thomas Herzog, MD
15 minutes	**Understanding the Biology of LGSOC and Emerging Therapeutic Targets** Angeles Alvarez Secord, MD
15 minutes	**Translating Evidence into Practice: Targeted Therapy Selection and Sequencing** Martin Martino, MD
20 minutes	**Panel Discussion and Audience Q&A** All Faculty
5 minutes	**Wrap Up and Closing Comments** All Faculty

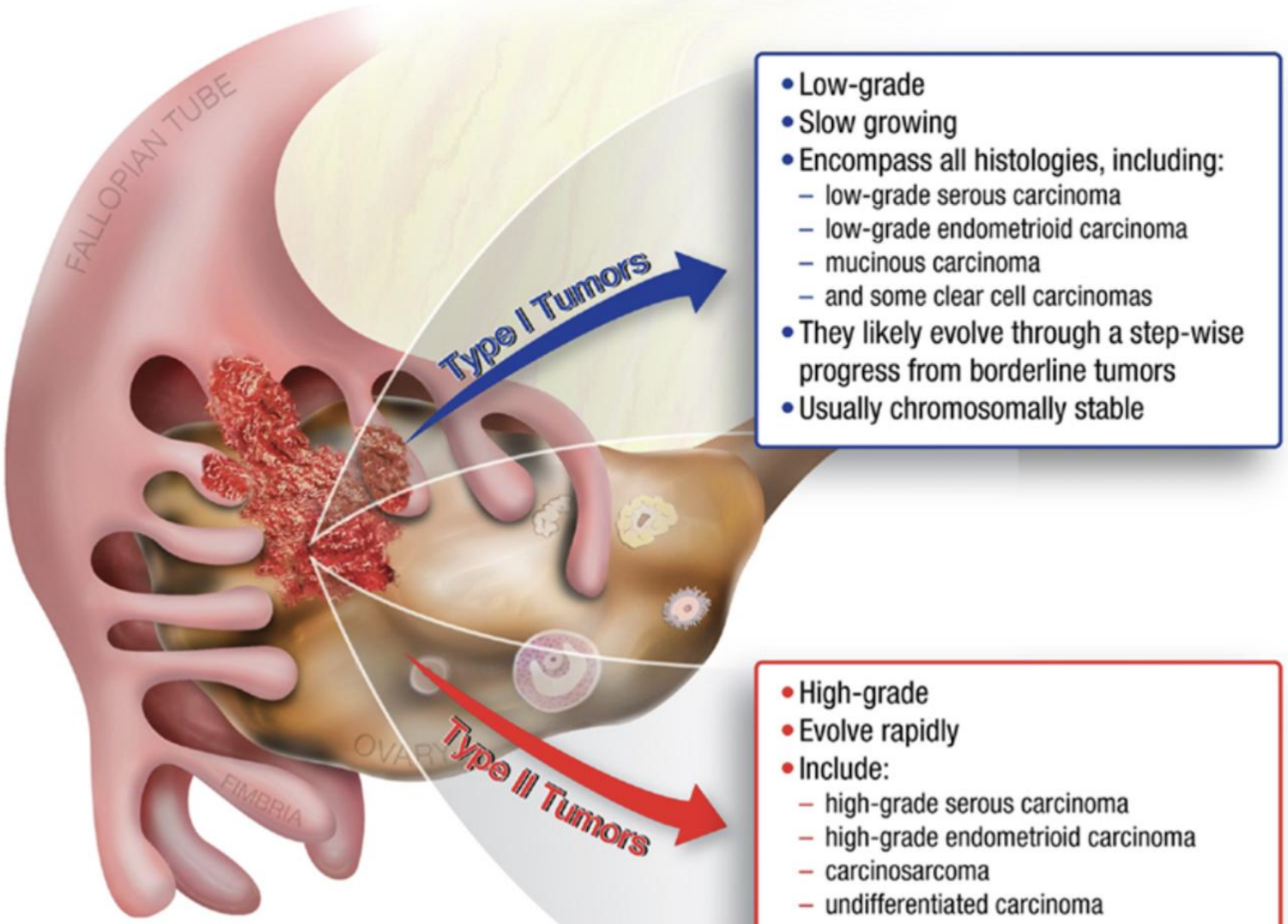
Understanding the Biology of LGSOC and Emerging Therapeutic Targets

Angeles Alvarez Secord, MD
Duke University



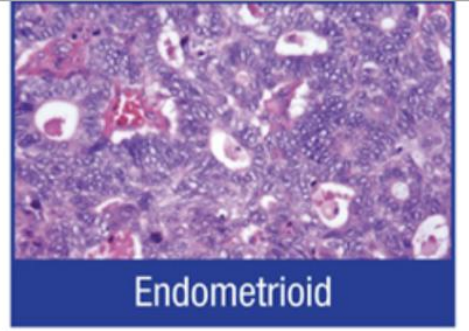
Recurrent low grade serous ovarian cancer

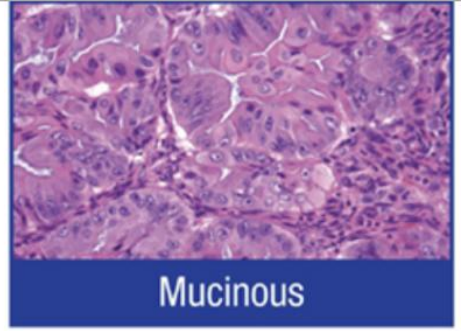
- 56-year-old with recurrent stage IIIA1 low grade serous ovarian cancer.
- She underwent RA-TLH/BSO, omentectomy, PPALND, and peritoneal biopsies followed by carboplatin/liposomal doxorubicin followed by letrozole maintenance.
- Progressed after 2 years letrozole maintenance.
- Trametinib x 3 cycles and progressed.
- **What tumor testing is recommended?**
- **What regimen is recommended?**

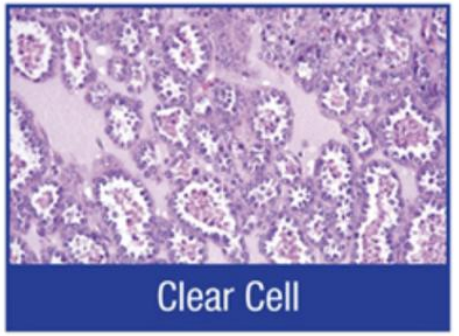


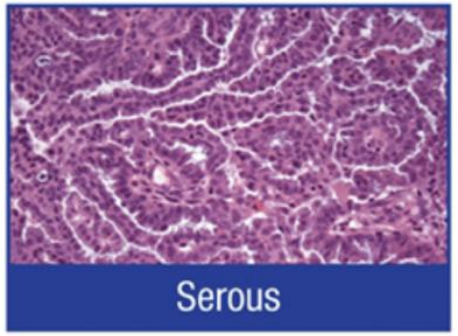
- Low-grade
- Slow growing
- Encompass all histologies, including:
  - low-grade serous carcinoma
  - low-grade endometrioid carcinoma
  - mucinous carcinoma
  - and some clear cell carcinomas
- They likely evolve through a step-wise progress from borderline tumors
- Usually chromosomally stable

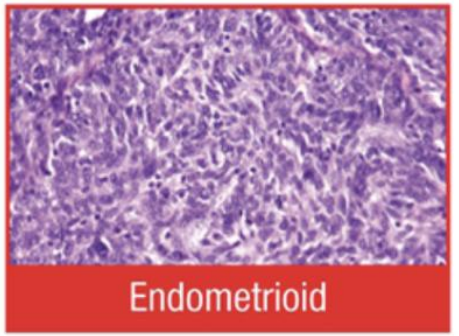
- High-grade
- Evolve rapidly
- Include:
  - high-grade serous carcinoma
  - high-grade endometrioid carcinoma
  - carcinosarcoma
  - undifferentiated carcinoma
  - and some clear cell carcinomas
- No recognizable precursors in the ovary
- Widespread DNA copy number changes

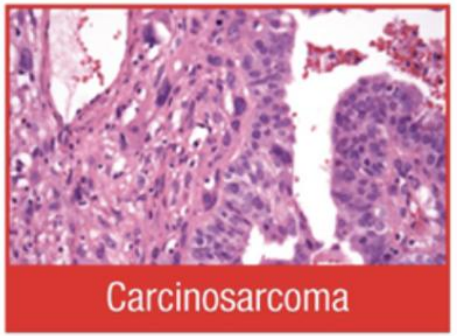

Endometrioid

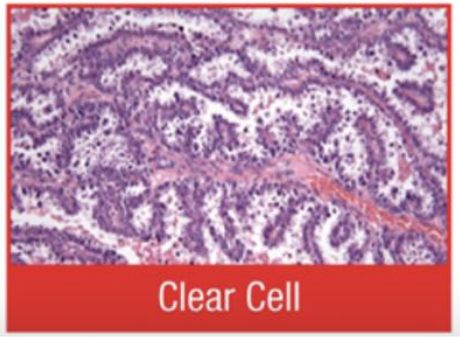

Mucinous

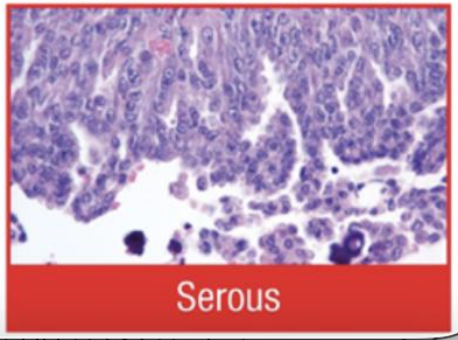

Clear Cell


Serous


Endometrioid


Carcinosarcoma


Clear Cell


Serous

Histology Matters

Jones PM, et al. Front Oncol. 2013;3:217; WHO Classification of Tumours Editorial Board. Female Genital Tumours. 5th ed. IARC; 2020. Figure adapted from Jones and Drapkin, 2013.
DNA, deoxyribonucleic acid.

LGSOC vs HGSOC

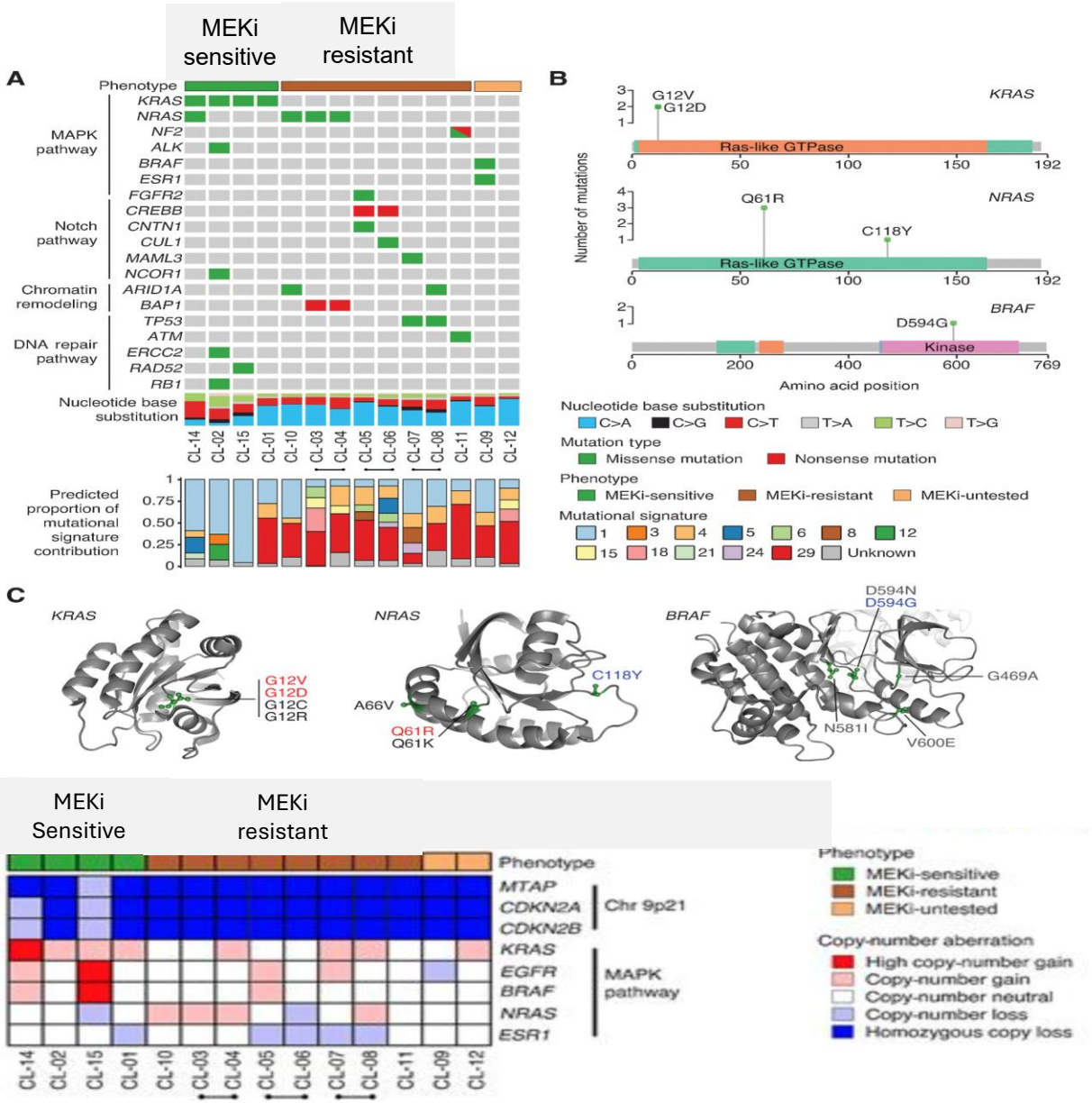
	LGSOC	HGSOC
Frequency	Rare (~10%)	Common (~90%)
Histology	Uniform cells: mild to moderate nuclear atypia; low mitotic index	Pleomorphic cells; marked nuclear atypia; high mitotic index
Pathogenesis	Serous borderline tumors (SBT) common (60%)	STIC precursor; less common associated with SBT (2–12%)
Molecular profile	Frequent MAPK pathway mutations, *TP53* wildtype, low-level CNV	~ ubiquitous *TP53* mutations; common HR genes (i.e., *BRCA1/2),* high CNV
IHC staining	p53 'wildtype' staining, high ER (58-96%)/PR(32-76%) expression	p53 'overexpressed' or completely absent, Ki-67 high
Clinical	Younger (median 43–57 years)	Older (median ~62 years)
	Less responsive to chemo (4%)	Responsive to chemo (50–80%)
	Slow progression	Rapid progression

Moujaber T, et al. *Endocr Relat Cancer*. 2022;29(1):R1–R16. Gershenson DM, et al. *Gynecol Oncol*. 2009;114(1):48–52. WHO Classification of Tumours Editorial Board. *Female Genital Tumours*. 5th ed. IARC; 2020.
BRCA1/2, breast cancer susceptibility genes 1 and 2; CNV, copy-number variation; ER, estrogen receptor; HGSOC, high-grade serous ovarian carcinoma; HRD, homologous recombination deficiency; IHC, immunohistochemistry; LGSOC, low-grade serous ovarian carcinoma; MAPK, mitogen-activated protein kinase; ORR, objective response rate; PR, progesterone receptor; SBT, serous borderline tumor; STIC, serous tubal intraepithelial carcinoma.

Multiomics characterization of LGSOC

14 LGSOC cell lines
122 LGSOC (primary and metastatic)

- Comparison of LGSOC cell line data with LGSOC tumor data enabled predictive biomarker identification of MEK inhibitor (MEKi) efficacy.
- *KRAS* mutations seen exclusively in MEKi-sensitive cell lines.
- *NRAS* mutations found predominantly in MEKi-resistant cell lines.
- *MTAP, CDKN2A*, and *CDKN2B* - common driver genes among all LGSOC cell lines



Shrestha R, et al. *Cancer Res*. 2021;81:1681–1694.
LGSOC, low-grade serous ovarian carcinoma; MAPK, mitogen-activated protein kinase; MEKi, MEK inhibitor.

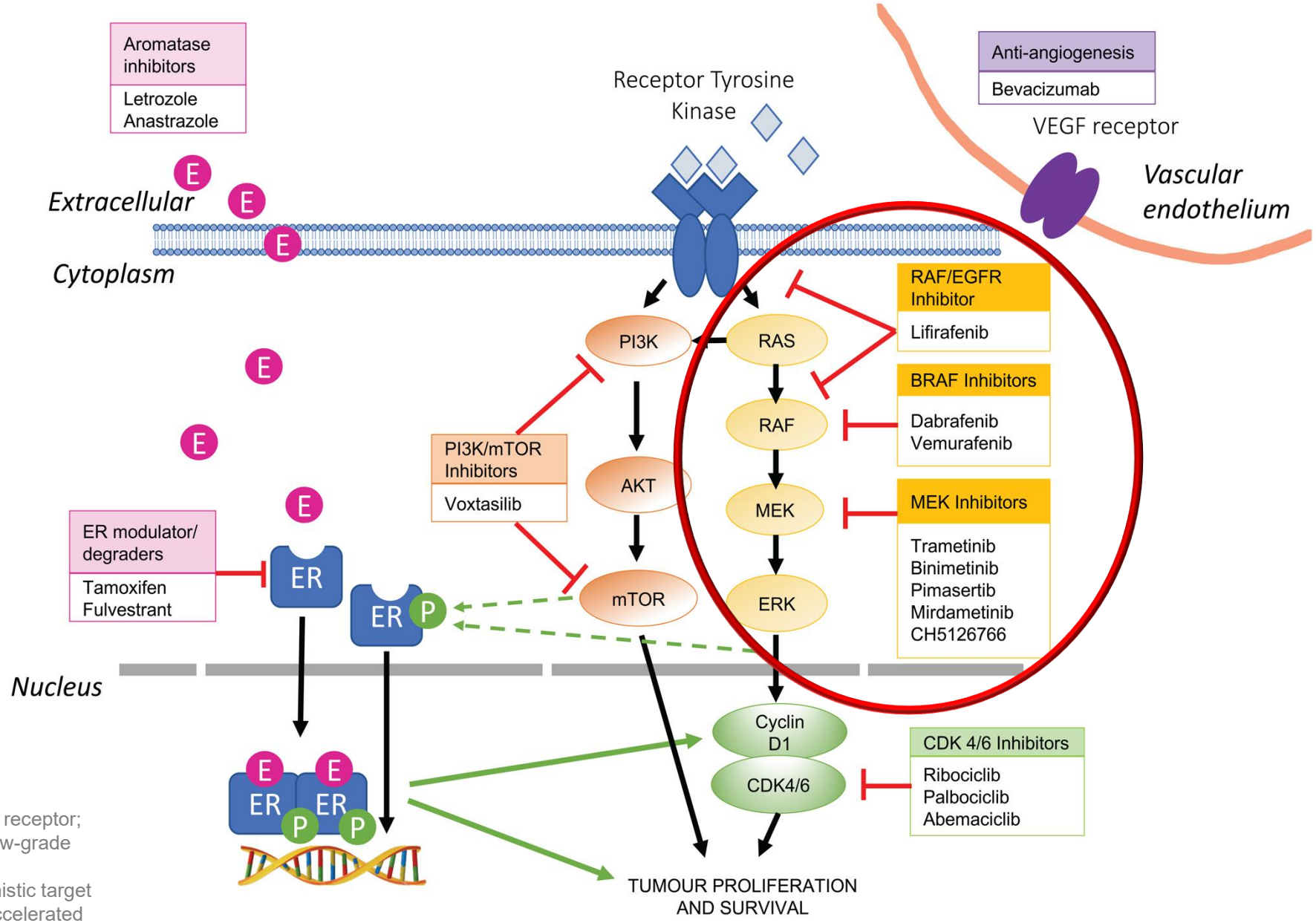
LGSOC: *KRAS*, *BRAF*, and *NRAS* mutations

Mutated gene	Frequency (%)
KRAS	18.6%-54.5%
BRAF	2.3%-33%
NRAS	3.6%-26.3%

	Cases tested	Gene variants, n (%)												
		KRAS								*BRAF*		*NRAS*		
		G12V	G12D	G12R	G12C	G12A	G12S	Q61K	others[e]	V600E	others[f]	Q61R	Q61K	others[g]
GENIE 2020	210[b]	35 (16.7)	22 (10.5)	4 (1.9)	3 (1.4)	2 (1.0)	1 (0.5)	2 (1.0)	1 (0.5)	11 (5.2)	9 (4.3)	16 (7.6)	2 (1.0)	1 (0.5)
Cheasley *et al.* 2021	71[c]	7 (9.9)	8 (11.3)	1 (1.4)	1 (1.4)	1 (1.4)			2 (2.8)	8 (11.3)	1 (1.4)	3 (4.2)	3 (4.2)	
Etemadmoghadam *et al.* 2017	51	6 (11.8)	3 (5.9)		3 (5.9)			1 (2.0)	2 (3.9)	5 (9.8)	1 (2.0)	5 (9.8)	1 (2.0)	
Xing *et al.* 2017	56	4 (7.1)	11 (19.6)			1 (1.8)				9 (16.1)	1 (1.8)	2 (3.6)		
Gershenson *et al.* 2015	79	2 (2.5)	12 (15.2)	1 (1.3)		2 (2.5)	1 (1.3)			3 (3.8)				
Hunter *et al.* 2015	19[d]	1 (5.3)	1 (5.3)	3 (15.8)						3 (15.8)		5 (26.3)		
Jones *et al.* 2012	15	1 (6.7)	3 (20.0)							3 (20.0)				
Wong *et al.* 2010	43	1 (2.3)	5 (11.6)	1 (2.3)		1 (2.3)				1 (2.3)				
COMBINED[a]	540	57 (10.6)	65 (12.0)	10 (1.9)	7 (1.3)	7 (1.3)	2 (0.4)	3 (0.6)	5 (0.9)	43 (8.0)	12 (2.2)	31 (5.7)	6 (1.1)	1 (0.2)
Variant proportion per gene, %		36.5	41.7	6.4	4.5	4.5	1.3	1.9	3.2	78.2	21.8	81.6	15.8	2.6

Moujaber T, et al. *Endocr Relat Cancer*. 2022;29(1):R1–R16.

LGSOC therapeutic targets



Moujaber T, et al. *Endocr Relat Cancer*. 2022;29(1):R1–R16.
CDK, cyclin-dependent kinase; EGFR, epidermal growth factor receptor; ER, estrogen receptor; FAK, focal adhesion kinase; LGSOC, low-grade serous ovarian carcinoma;
MEK, mitogen-activated protein kinase kinase; mTOR, mechanistic target of rapamycin; PI3K, phosphoinositide 3-kinase; RAF, rapidly accelerated fibrosarcoma; VEGF, vascular endothelial growth factor.

LGSC: Case reports and clinical trials

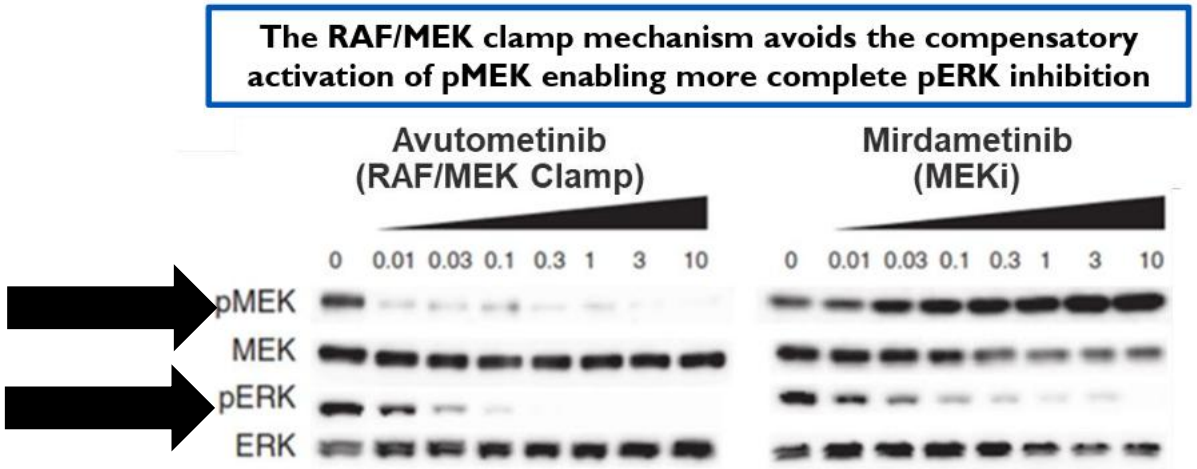
Study Design	Population	Intervention	Response, Tx duration	Reference
Case Studies	*KRAS* p.G12V mut	Selumetinib	PR, 7 years	Takekuma *et al*. 2016
	KRAS p.G12D mut	Trametinib	PR, >10 months	Pejovic *et al*. 2015
	KRASG12V mut	Binimetinib	PR, 31 months	Han *et al*. 2018
	BRAF p.V600E mut	Vemurafenib	PR, 21 months	Combe *et al*. 2015
	BRAF p.V600E mut	Dabrafenib and trametinib	CR, 12 months	Tholander *et al.* 2020
		Encorafenib and binimetinib	SD, 3.5 years	
	BRAF p.V600E mut	Dabrafenib	PR, >11 months	Moujaber *et al*. 2018
		lifirafenib (BGB-283)	PR, > 2 years	Desai *et al*. 2020
Basket trials	RAS/RAF-mut solid tumors. *BRAF* p.V600E (n=1); *KRASG12D (n=1)*	CH5126766/VS-6766	PR, 15 and 31 weeks	Guo *et al*. 2020
	BRAF mut tumors. *BRAF* p.V600E*(n=1)*	Vemurafenib	PR, >12 months	Hyman *et al*. 2015
	Advanced BRAF mutated cancer. *BRAF* p.V600E (n=2)	Dabrafenib and pazaponib	PR, 5 months and 37 months	Haraldsdottir *et al*. 2018

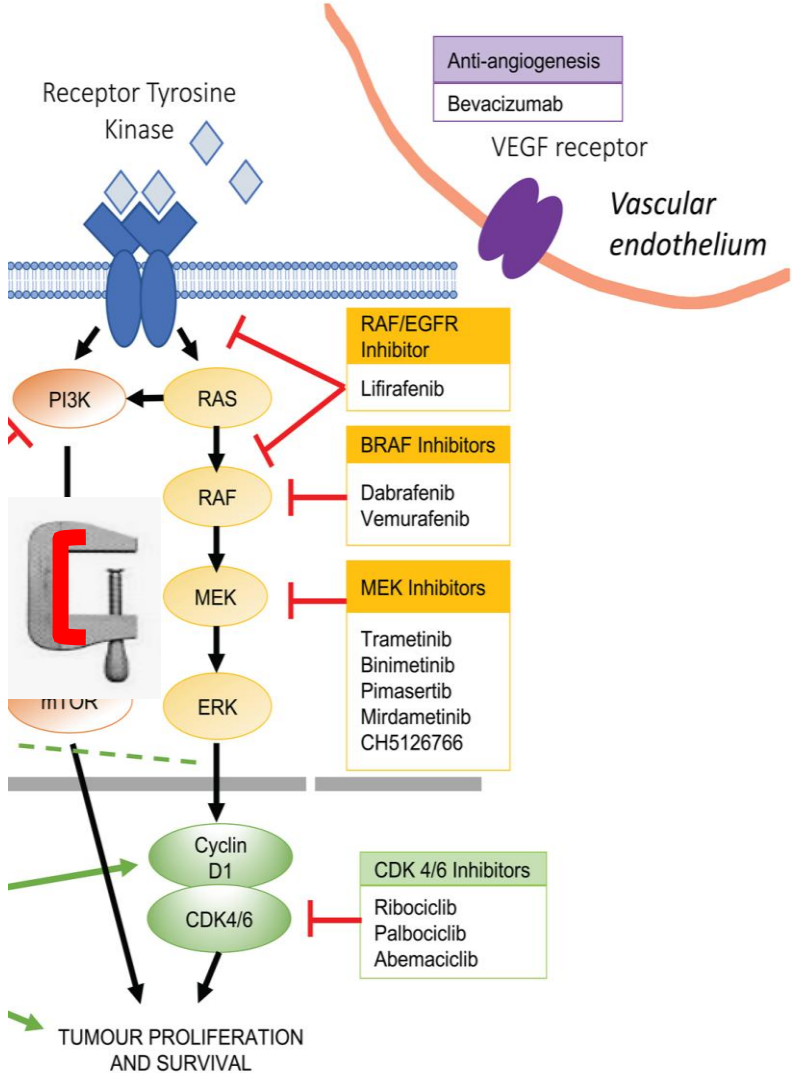
Adapted from Moujaber T, et al. *Endocr Relat Cancer*. 2022;29(1):R1–R16. Individual reports are cited within the table.
CR, complete response; LGSOC, low-grade serous ovarian carcinoma; mut, mutation-positive; PR, partial response; SD, stable disease.

LGSOC therapeutic targets: Adding the "CLAMP"

MEK inhibitors lead upstream protein RAF gets hyperactivated through a cellular feedback loop, direct mechanism of treatment resistance.

Avutometinib acts as a "Clamp" preventing this feedback loop by creating a "**dominant-negative inactive complex"** between RAF and MEK, trapping RAF molecules together with MEK so that RAF cannot phosphorylate other MEK proteins.

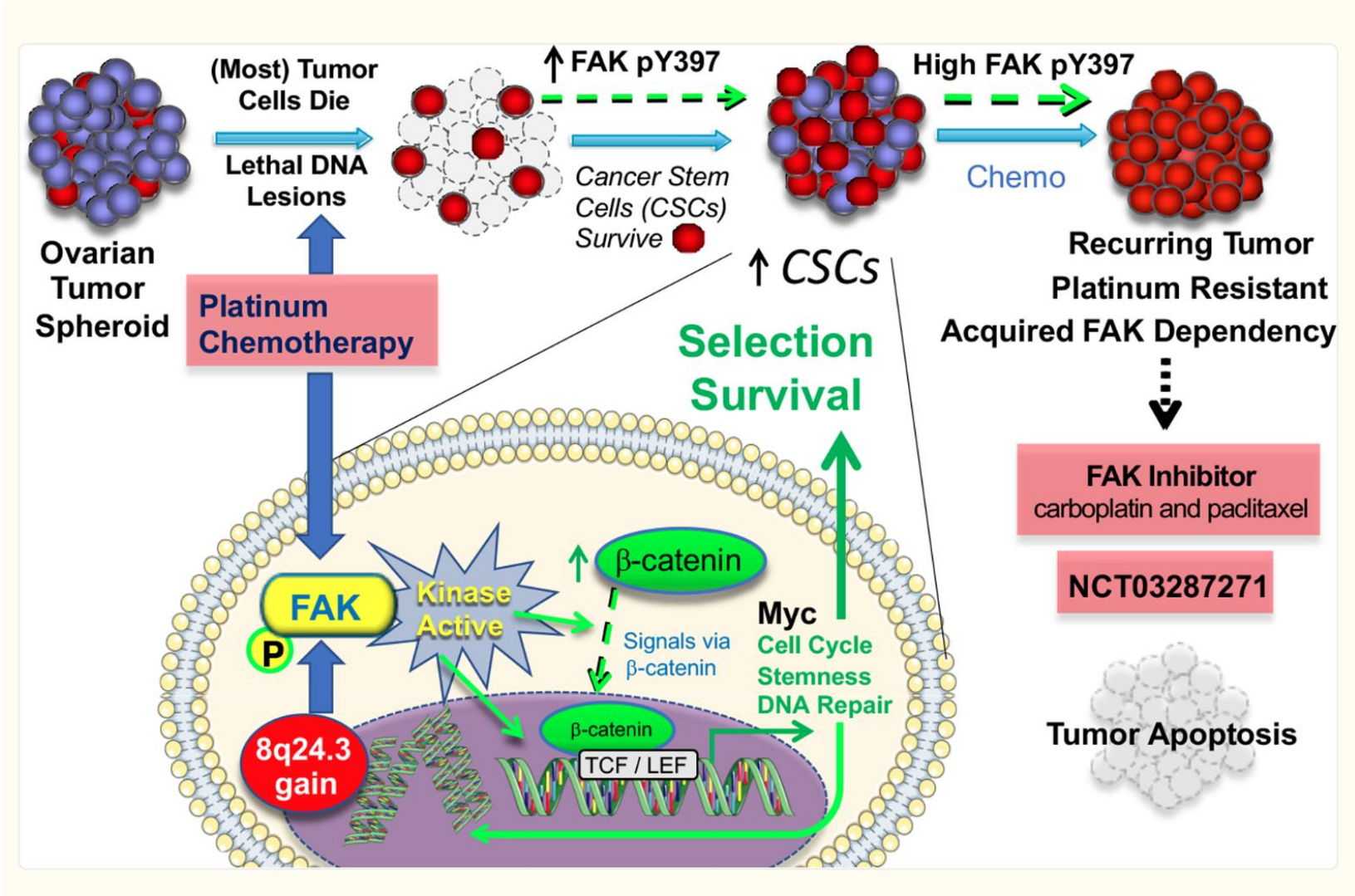




Moujaber T, et al. *Endocr Relat Cancer*. 2022;29(1):R1–R16; Denis L. *Rational Combinations of RAF/MEK Clamp Avutometinib*. 5th Annual RAS-Targeted Drug Development Summit; September 27, 2023. https://www.verastem.com/wp-content/uploads/2025/01/5th-RAS-Summit-Sept-2023-LJD-vF-final.pdf

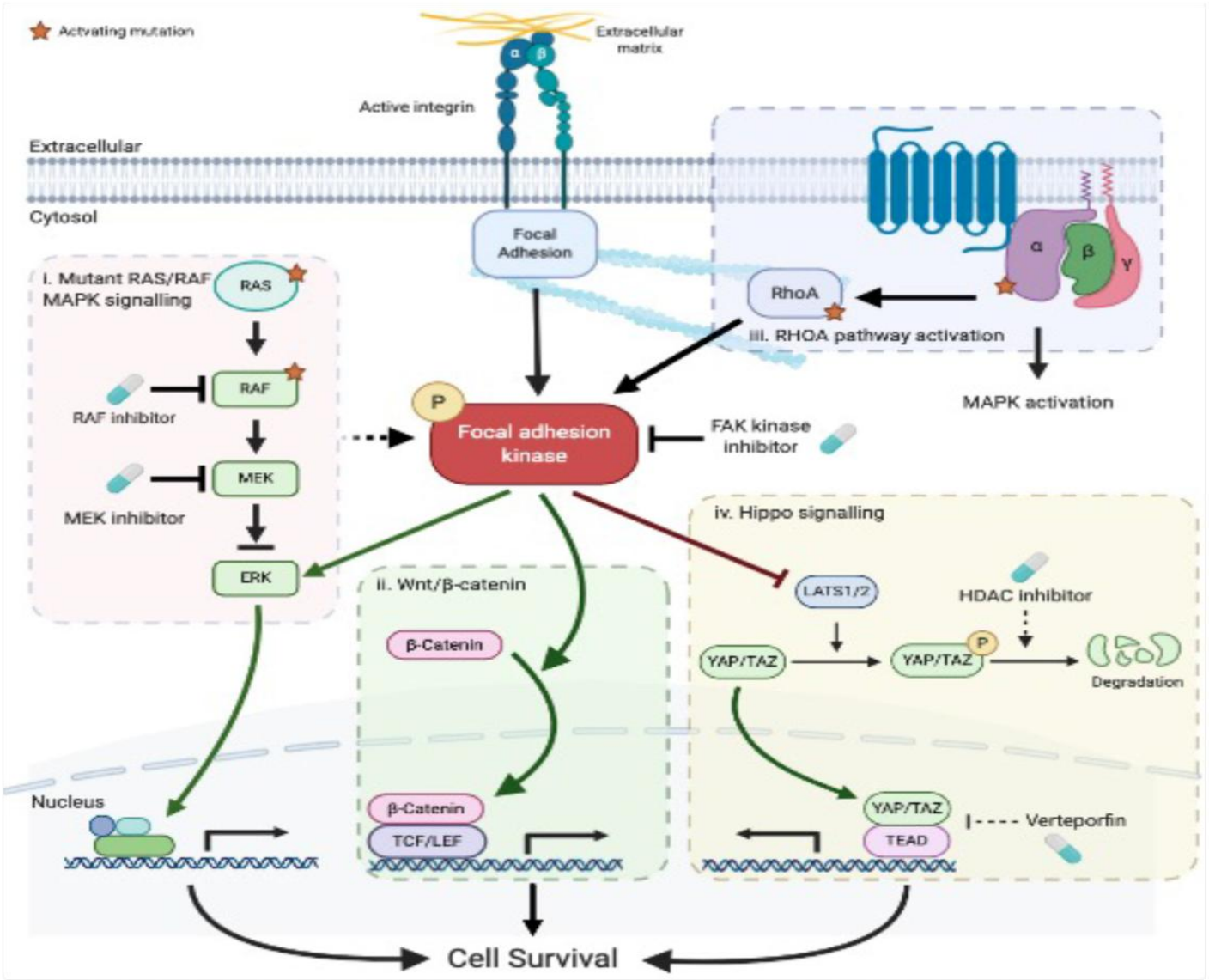
ERK, extracellular signal-regulated kinase; LGSOC, low-grade serous ovarian carcinoma; MAPK, mitogen-activated protein kinase; MEK, MAPK/ERK kinase; pERK, phosphorylated ERK; pMEK, phosphorylated MEK; RAF, rapidly accelerated fibrosarcoma kinase.

FAK mediates resistant to chemotherapy



Dawson JC, et al. *Nat Rev Cancer*. 2021;21:313–324.
Figure adapted from Dawson et al.
CSC, cancer stem cell; FAK, focal adhesion kinase; pY397, phosphorylation at tyrosine 397; TCF/LEF, T-cell factor/lymphoid enhancer factor.

Targeting FAK inhibitor combination therapy



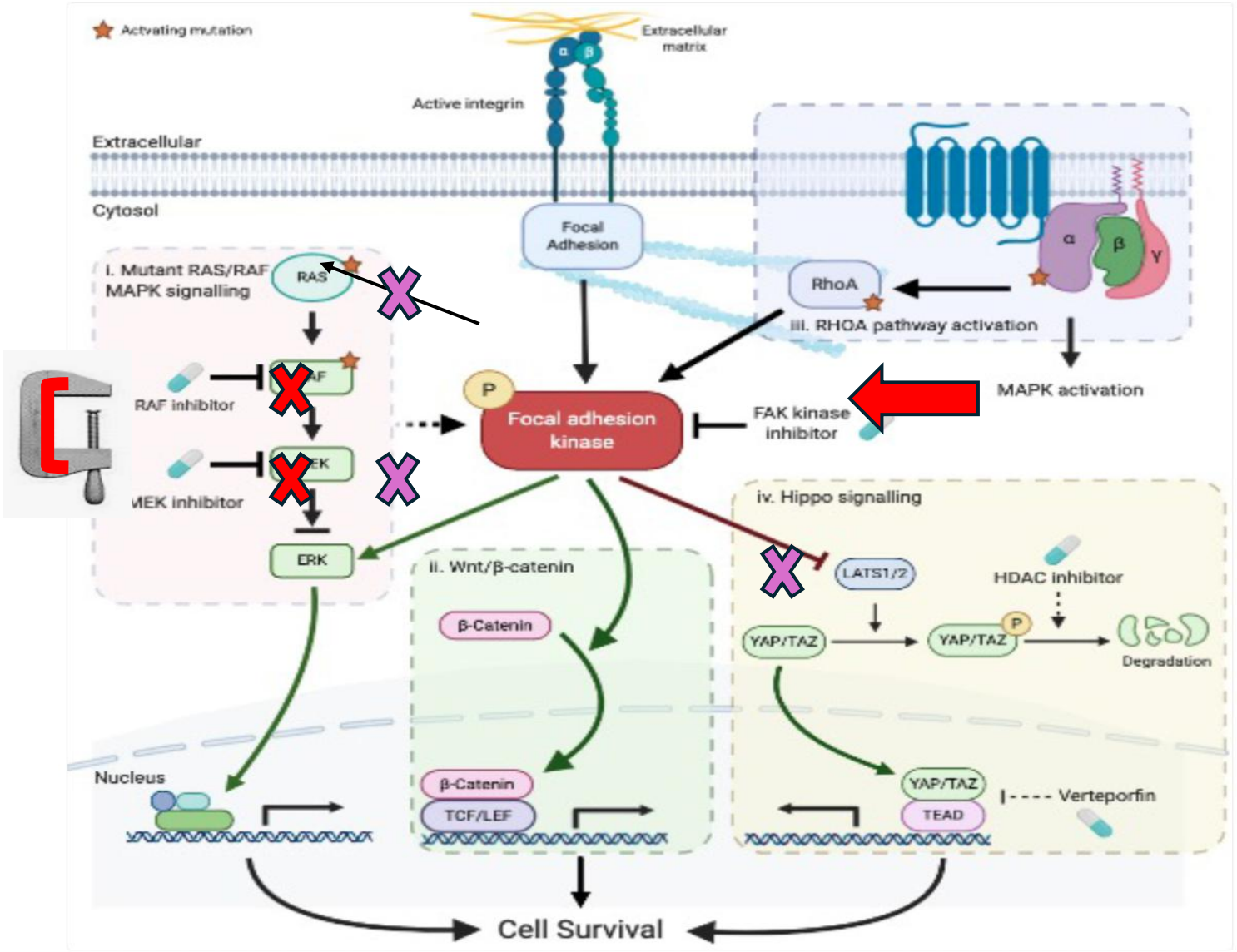
Dawson JC, et al. *Nat Rev Cancer*. 2021;21:313–324. Figure adapted from Dawson et al.

Targeting FAK inhibitor combination therapy

Defactinib is an oral selective FAK inhibitor[1,2]

Avutometinib is an oral dual RAF and MEK inhibitor[3,4]

- Together greater inhibition of MAPK pathway signaling
- Defactinib also inhibits PI3K/AKT, YAP/TEAD, and MYC[5]



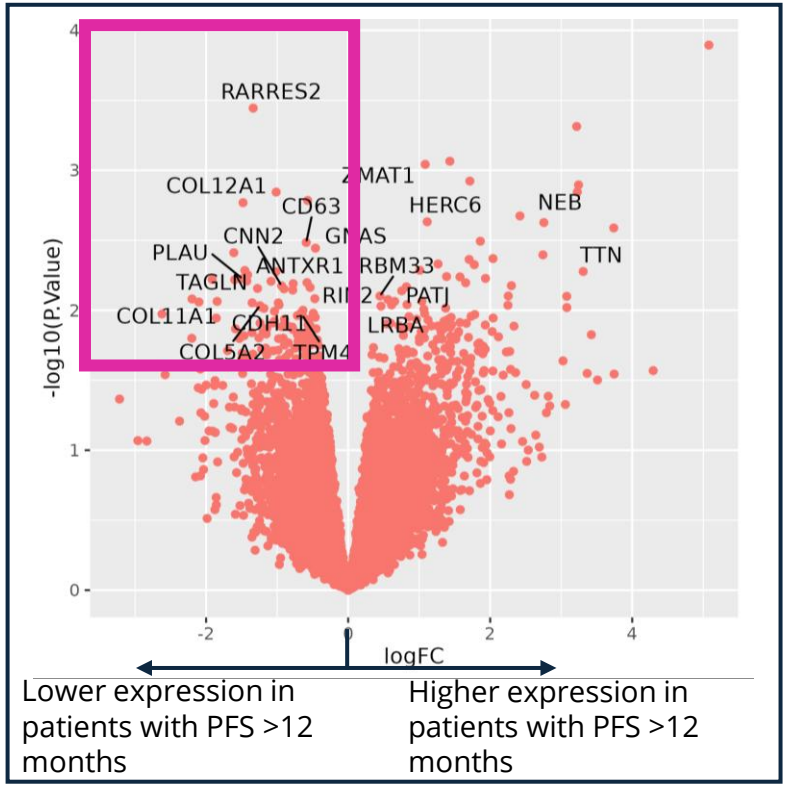
1. Dawson JC, et al. Nat Rev Cancer. 2021;21:313–324. Figure adapted from Dawson et al.[1] 2. Kang Y, et al. J Natl Cancer Inst. 2013;105(19):1485–1495. 3. Ishii N, et al. Cancer Res. 2013;73(13):4050–4060. 4. Lito P, et al. Cancer Cell. 2014;25(5):697–710. 5. Pickard L, et al. Cancer Res. 2025;85(8 suppl 1):Abstract 6368.

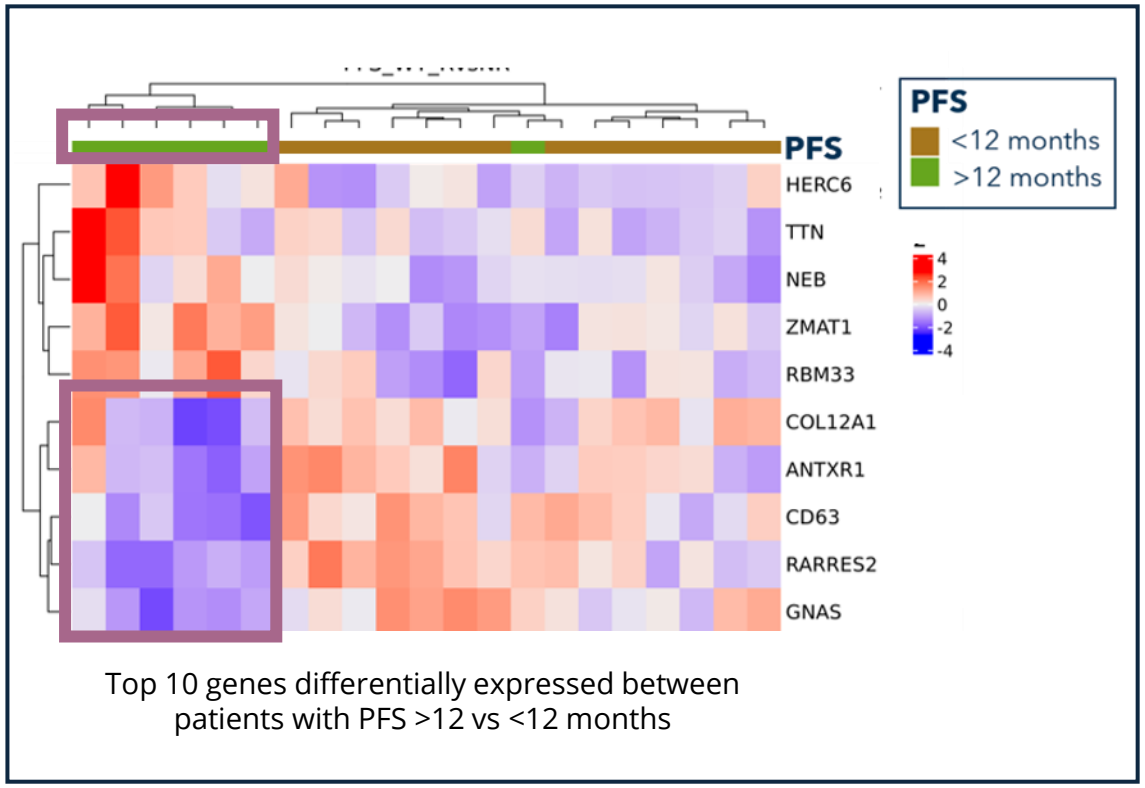
ERK, extracellular signal-regulated kinase; FAK, focal adhesion kinase; HDAC, histone deacetylase; MAPK, mitogen-activated protein kinase; MEK, MAPK/ERK kinase; RHOA, Ras homolog family member A; TCF/LEF, T-cell factor/lymphoid enhancer factor; YAP/TAZ, Yes-associated protein/transcriptional coactivator with PDZ-binding motif.

Exploratory RNA profiling in *KRAS/NRAS/BRAF* wild-type LGSOC

Longer PFS was associated with lower expression of fibroblast-activation remodeling genes.

- Baseline tumor samples were collected from patients in RAMP 201
- RNA profiling was performed with Tempus xR assay
- RNA data were available for 21 patients with *KRAS*/*NRAS*/*BRAF* wild-type tumors
- Showing differentially expressed (P<0.05) genes between patients with PFS >12 months vs <12 months





Patients with PFS >12 months exhibited lower expression of genes associated with fibroblast activation and extracellular matrix remodeling, including *COL12A1*, *ANTXR1* (TEM8), *RARRES2* (chemerin), and *CD63*

Banerjee S. Presented at the International Gynecologic Cancer Society Annual Meeting; 2026.

BRAF, B-Raf proto-oncogene, serine/threonine kinase; KRAS, Kirsten rat sarcoma viral oncogene homolog; LGSOC, low-grade serous ovariancancer; NRAS, neuroblastoma rat sarcoma virus viral oncogene homolog; ORR, overall response rate; PFS, progression-free survival.

LGSOC: Targeting beyond the MAPK pathway

- Other targets to consider?

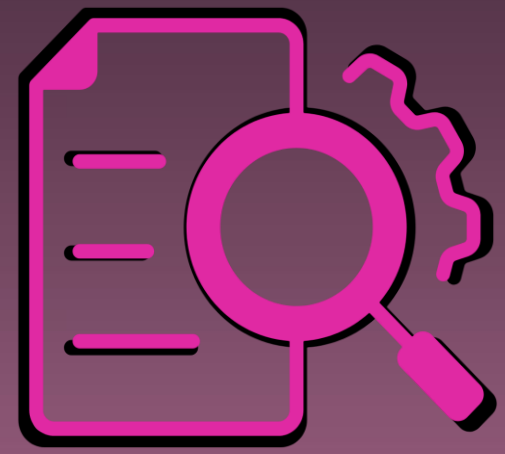
Target	Frequency	Therapy
ER expression	58-96% positive	Endocrine
PR expression	32-76% positive	Endocrine
CDKN2A and *CDKN2B* alteration or loss	Loss in 31.5-53%*	CDK4/6 inhibitors
FRα-high expression	40% using ≥75% of cells with ≥2+ staining	ADC targeting FRα
TROP2 expression	100% positive; 79% moderate-to-strong	ADC targeting TROP2
MUC16 expression	>1.7 log 2-fold expression LGSOC vs HGSOC	ADC targeting MUC16

*in tumors

1. Grisham RN, et al. *Int J Gynecol Cancer*. 2023;33:1331–1344. 2. Gershenson DM, et al. *Gynecol Oncol*. 2022;165:560–567. 3. Manning-Geist BL, et al. *Gynecol Oncol*. 2024;188:52–57. 4. Ottum S, et al. *Gynecol Oncol Rep*. 2026;66:102146. 5. Tarney CM, et al. *Clin Proteomics*. 2025;22:33.
ADC, antibody–drug conjugate; CDK, cyclin-dependent kinase; ER, estrogen receptor; FRα, folate receptor alpha; HGSOC, high-grade serous ovarian carcinoma; LGSOC, low-grade serous ovarian carcinoma; PR, progesterone receptor; TROP2, trophoblast cell-surface antigen 2.

Case Study

Recurrent low grade serous ovarian cancer



- 56-year-old with recurrent stage IIIA1 low grade serous ovarian cancer.
- She underwent RA-TLH/BSO, omentectomy, PPALND, and peritoneal biopsies followed by carboplatin/liposomal doxorubicin followed by letrozole maintenance.
- Progressed after 2 years letrozole maintenance.
- Trametinib x 3 cycles and progressed.
- **What tumor testing is recommended?**
- **What regimen is recommended?**

What tumor testing is recommended?

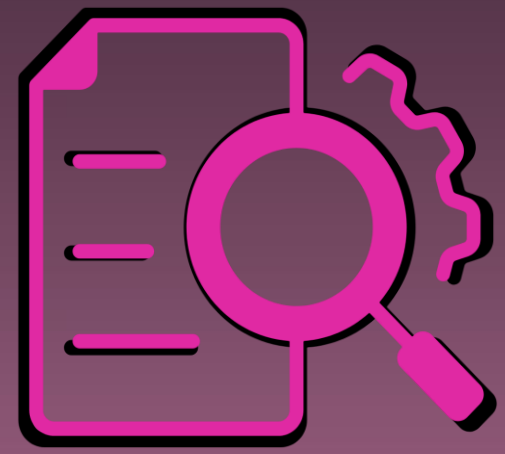
- NGS testing: *ATRX* and *KRAS*
- MSS
- p53 protein expression normal/wildtype
- HER2 protein expression 1+

Any other tumor testing needed?

- FRalpha protein expression PS2+ 50%

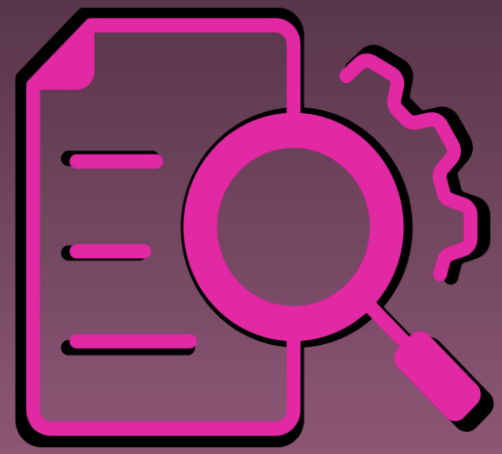
Case Study

Recurrent low grade serous ovarian cancer



Case Study

Recurrent low grade serous ovarian cancer

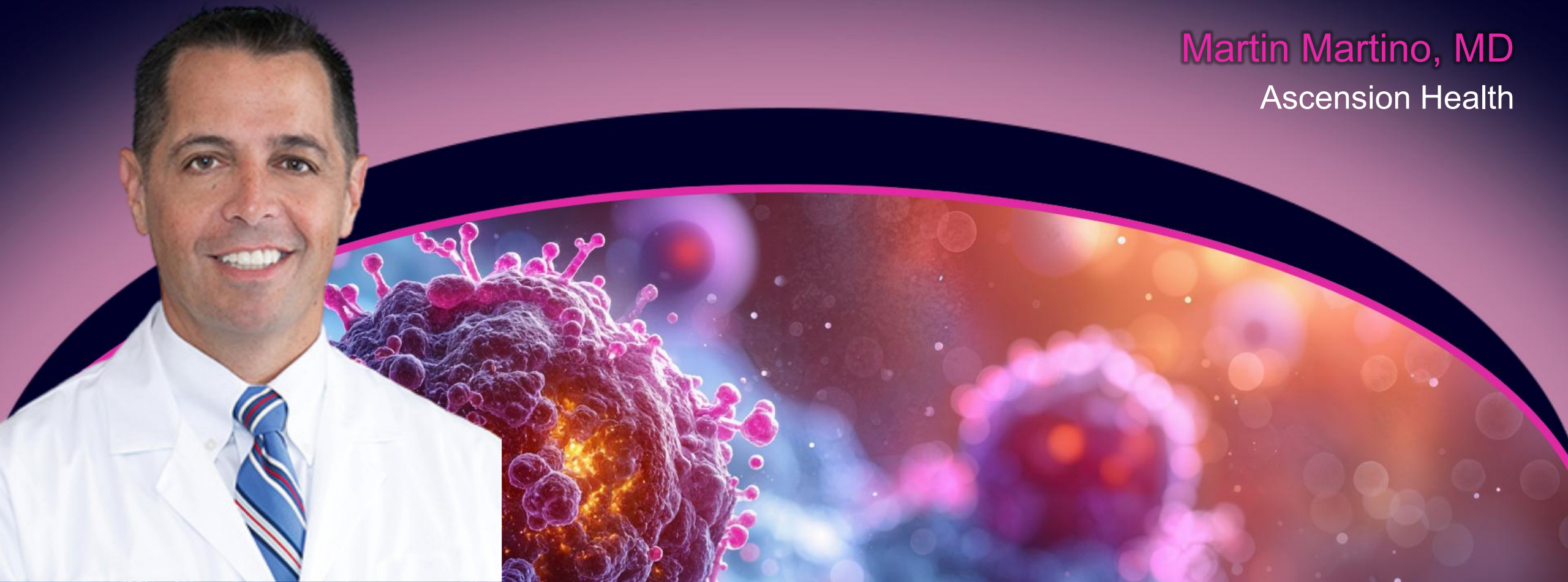


What treatment option would you recommend?

- Aromatase inhibitor and CDK 4/6 inhibitor
- Avutometinib + defactinib
- Bevacizumab
- Fulvestrant
- Weekly paclitaxel

Translating Evidence into Practice: Targeted Therapy Selection and Sequencing

Martin Martino, MD
Ascension Health



Let’s look back at the last case: We now have three decisions to make

56-year-old, recurrent stage IIIA1 LGSOC

Carboplatin/liposomal doxorubicin → letrozole maintenance → trametinib for 3 cycles with progression.

Work-up	Result
NGS	KRAS and ATRX
Other markers	MSS; p53 wild type; HER2 1+; FRα PS2+ 50%

- **Which agent?**
- **In which order?**
- **How do we keep her on it?**



Her treatment journey so far

1

Chemotherapy

- Carboplatin / liposomal doxorubicin

2

Maintenance

- Letrozole; progressed after 2 years

3

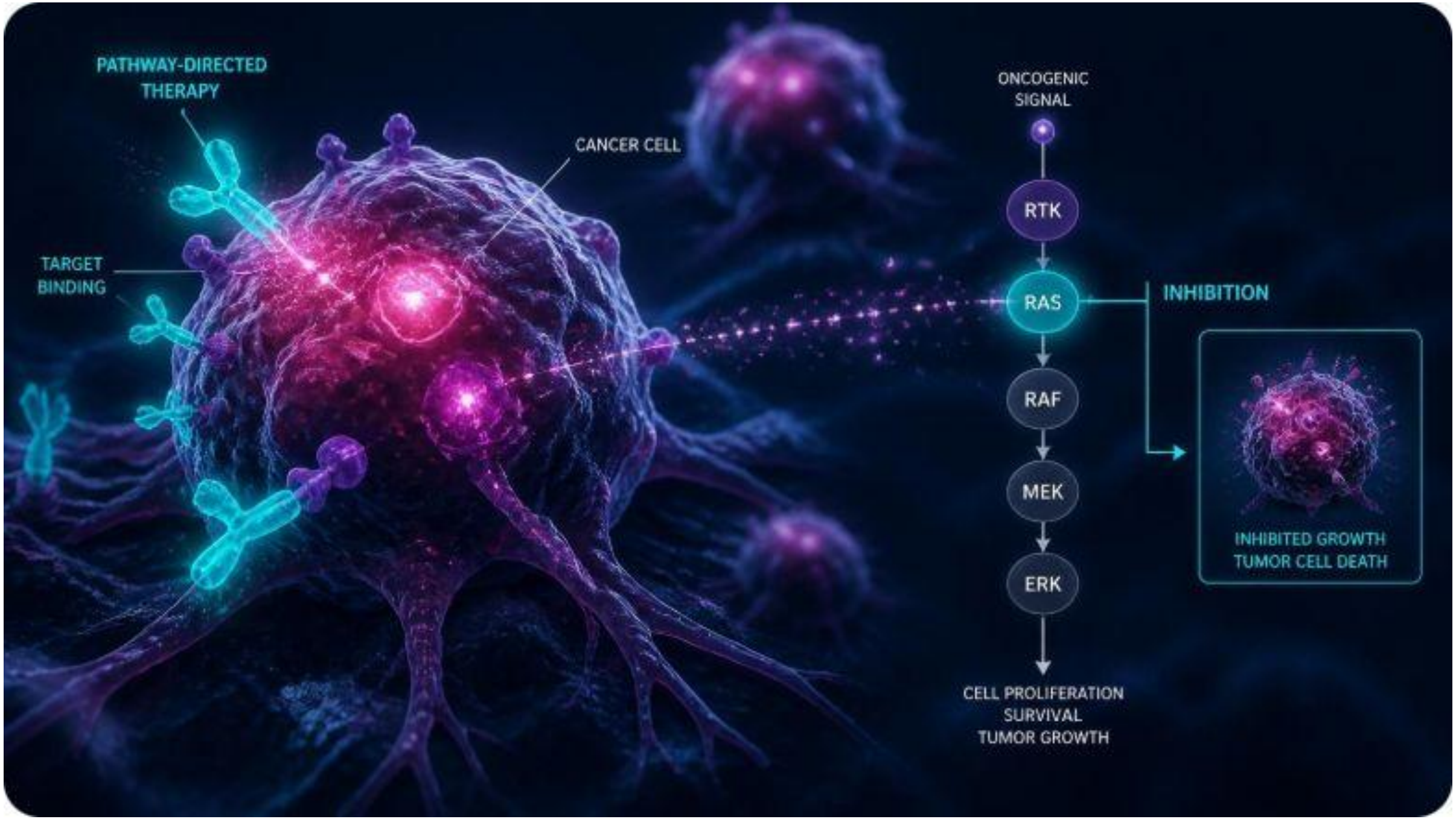
MEK inhibitor

- Trametinib x 3 cycles; progressed

4

Now

- Avutometinib + defactinib


PATHWAY-DIRECTED THERAPY
CANCER CELL
TARGET BINDING
ONCOGENIC SIGNAL
RTK
RAS
INHIBITION
RAF
MEK
ERK
INHIBITED GROWTH
TUMOR CELL DEATH
CELL PROLIFERATION
SURVIVAL
TUMOR GROWTH

Biomarker testing results at recurrence



KRAS (*NRAS/BRAF*) on NGS

Her result: *KRAS* and *ATRX* mutated



P53 IHC

Wild type statining pattern



MSS

Microsatellite stable



HER2 IHC

1+



ER IHC

Relevant to her prior letrozole maintenance



FRα IHC

PS2+ 50%

ER, estrogen receptor; FRα, folate receptor alpha; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; MSS, microsatellite stable; NGS, next-generation sequencing; PS2+, percentage of viable tumor cells with ≥2+ membrane staining.

The single-agent MEK inhibition experience

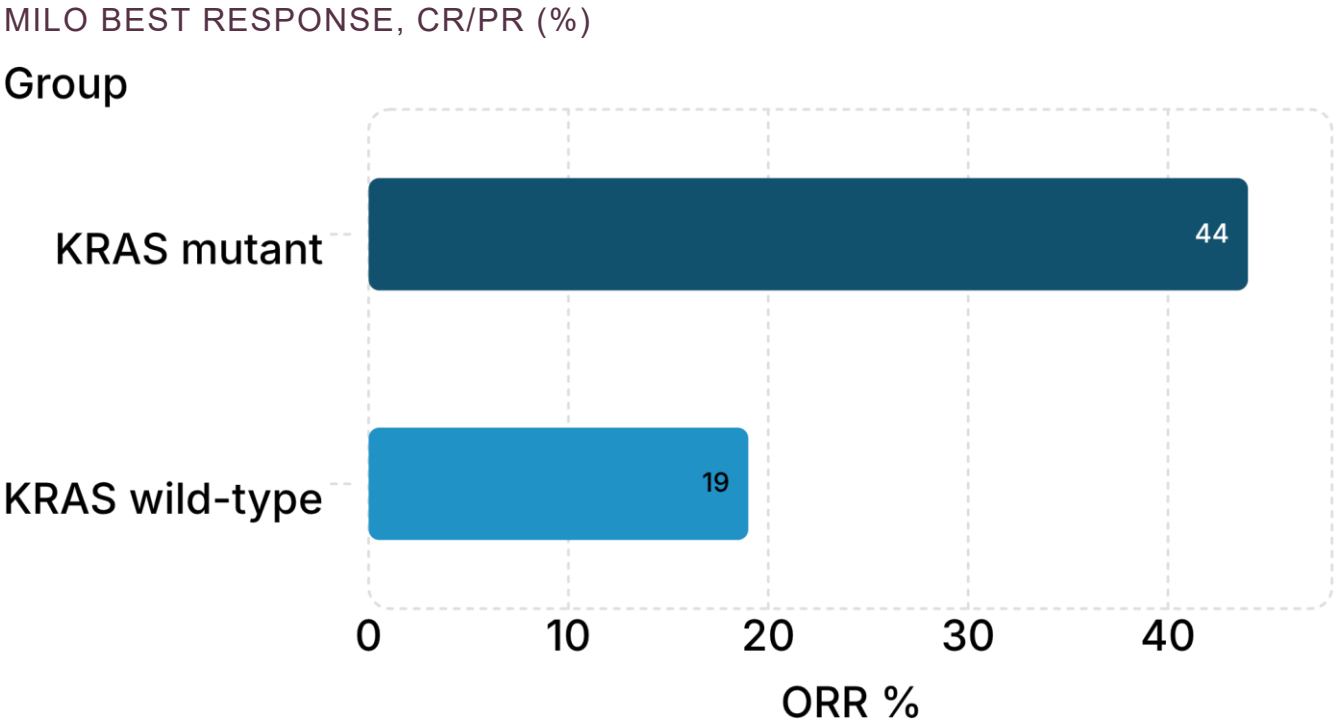
Trial / agent	Efficacy	Tolerability
GOG 281/LOGS — Trametinib	Median PFS: 12.5 vs 7.1 months; HR 0.54 OS 36.4 vs 29.8 months; HR 0.68	92% rash 36% discontinued for toxicity
MILO/ENGOT-ov11— **Binimetinib**	ORR 24% in both arms	76% vs 44% grade ≥3 AEs | 31% vs 17% discontinued because of AEs

Progression still follows, as it did in our patient.

GOG 281; MILO. Data as reported in the IGCS 2026

MEK, mitogen-activated protein kinase kinase; PFS, progression-free survival; OS, overall survival; HR, hazard ratio; ORR, objective response rate; AE, adverse event.

KRAS mutation status predicted benefit in MILO; GOG 281 did not confirm it



MILO

ORR p=0.004

Median PFS 17.7 vs 10.8 months

GOG 281

KRAS/BRAF/NRAS status was not predictive of PFS benefit.

Test to select the combination, not to exclude MEK-pathway therapy.

Grisham RN, et al. *Clin Cancer Res.* 2023;29:4619–4628. Gershenson DM, et al. *Clin Cancer Res.* 2026;32:724–734.

CR/PR, complete/partial response; ORR, objective response rate; PFS, progression-free survival.

ENGOT-ov60/GOG-3052/RAMP 201

Registration-Directed Phase 2 Trial of Avutometinib ± Defactinib in Patients With Recurrent LGSOC

GOG Lead: R Grisham
ENGOT Lead: S Banerjee

Go Forward Regimen

Part A Selection Phase	Part B Expansion Phase	Part C Expansion Phase Combination	Part D Lower Dose in Combination
Avutometinib + Defactinib **3.2 mg BIW 200 mg BID**	**Avutometinib + Defactinib** **3.2 mg BIW 200 mg BID**	**Avutometinib + Defactinib** **3.2 mg BIW 200 mg BID**	**Avutometinib + Defactinib** **1.6 mg BIW 200 mg BID**
KRAS mt (n=16)	*KRAS* mt (n=20)	*KRAS* mt (n=22)	*KRAS* mt (n=11)
KRAS wt (n=15)	*KRAS* wt (n=22)	*KRAS* wt (n=20)	*KRAS* wt (n=16)

Key Inclusion Criteria

- Recurrent LGSOC
- Prior platinum chemotherapy
- Measurable disease (RECIST v1.1)
- Prior MEKi allowed

Avutometinib 4.0 mg BIW	Avutometinib 4.0 mg BIW
KRAS mt (n=16)	*KRAS* mt (total n=15)
KRAS wt (n=17)	*KRAS* wt (total n=22)

Oral dosing for monotherapy and combination therapy: 3 weeks on/1 week off

Go Forward Regimen Selection Criteria (Selection Phase):

1. Observed ORR is comparatively greater than the other regimen.
2. Observed ORR of the leading regimen is ≥15%.

Primary Endpoint: ORR (BICR per RECIST v1.1)

Evaluation of ORR in Combination Arm

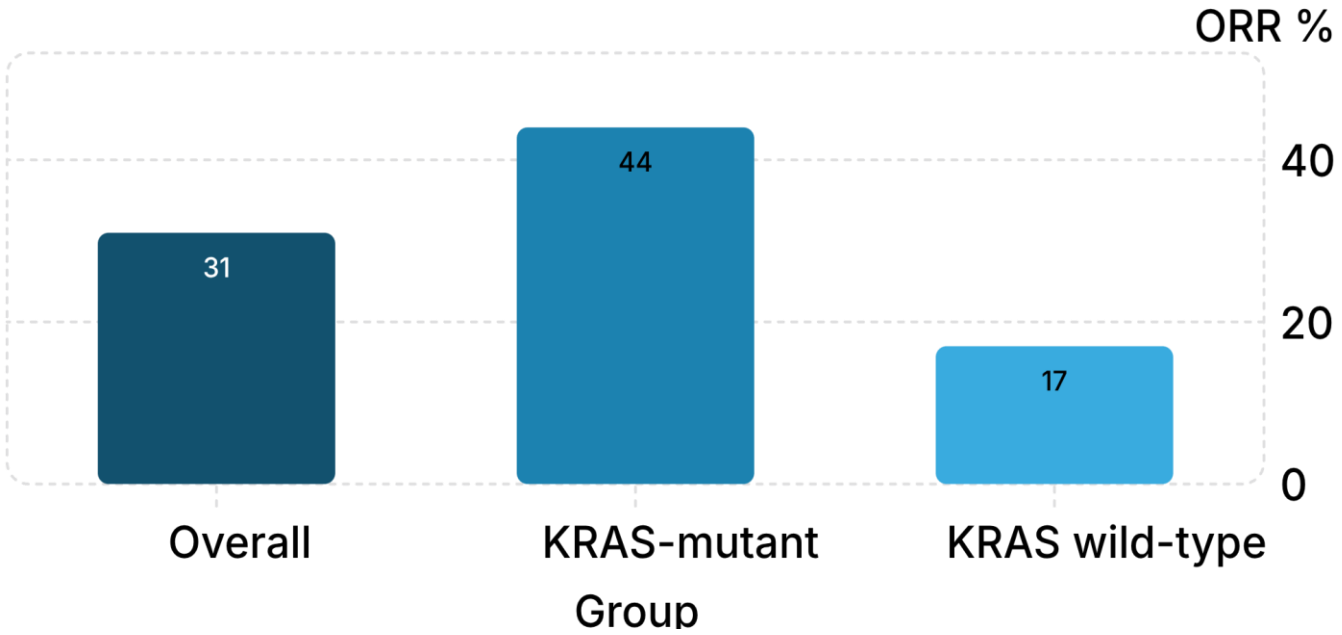
1. In *KRAS* mt pts
2. All patients (*KRAS* mt & wt)

Banerjee SN, et al. J Clin Oncol. 2025;43(25):2782-2792.; ClinicalTrials.gov identifier: NCT04625270

BID, twice daily; BICR, blinded independent central review; BIW, twice weekly; LGSOC, low-grade serous ovarian carcinoma; MEKi, MEK inhibitor; ORR, objective response rate; RECIST, Response Evaluation Criteria in Solid Tumors; wt, wild type.

RAMP 201: MEK + FAK inhibition delivered the deepest responses in *KRAS*-mutant disease

RAMP 201 CONFIRMED ORR (%)



Median PFS

- Overall: **12.9 months**
- *KRAS*-mutant: **31.0 months**
- *KRAS* wild type: **12.8 months**

Prior Treatment (heavily pretreated)

Median 3 prior lines; 86% prior hormonal therapy, 51% bevacizumab, 22% MEK inhibitor.

FRAME phase 1 foundation: ORR 46%; KRAS-mutant 64%; median PFS 23 months.

Banerjee SN, et al. *J Clin Oncol*. 2025;43(25):2782–2792 (NCT04625270; RAMP 201); Banerji U, et al. *Nat Med*. 2025;31(9):3074–3080 (FRAME).
FAK, focal adhesion kinase; LGSOC, low-grade serous ovarian carcinoma; MEK, mitogen-activated protein kinase kinase; ORR, objective response rate; PFS, progression-free survival.
Single-arm evidence; cross-trial comparisons do not establish superiority. FAK, focal adhesion kinase.

201 Adverse Events: Updated Analysis

3.2 mg BIW and Defactinib 200 mg BID

At the time of the current analysis

Dose Interruptions

ts had AEs leading to dose interruption

mon treatment-related AEs managed with ons (≥5% of patients) were:

- blood CPK (25%)
- blood bilirubin/ ubinemia (22%)
- (10%)
- (7%)
- Peripheral edema (6%)
- Blurred vision (6%)
- Nausea (5%)
- Fatigue (5%)

Dose Reductions

- 37% of patients had AEs leading to dose reduction
- The most common treatment-related AEs managed with dose reductions (≥5% of patients) were:
  - Elevated blood CPK (8%)
  - Dermatitis acneiform (5%)

Discontinuations

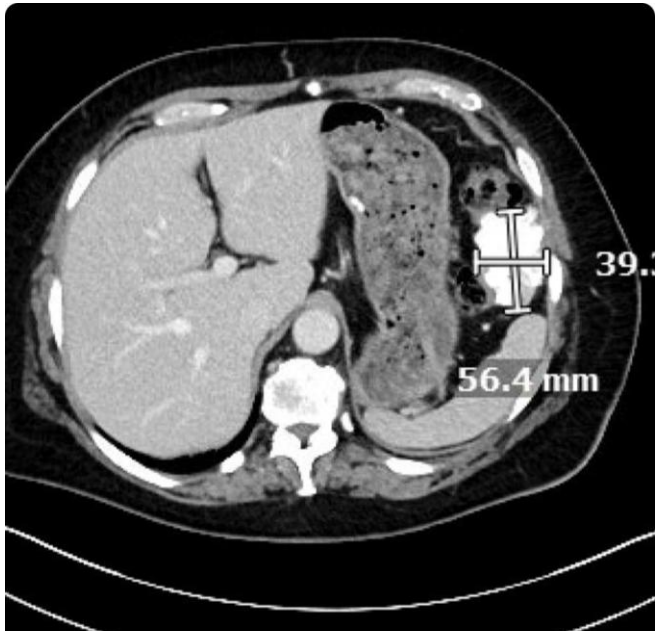
- **12% of patients discontinued for AEs**

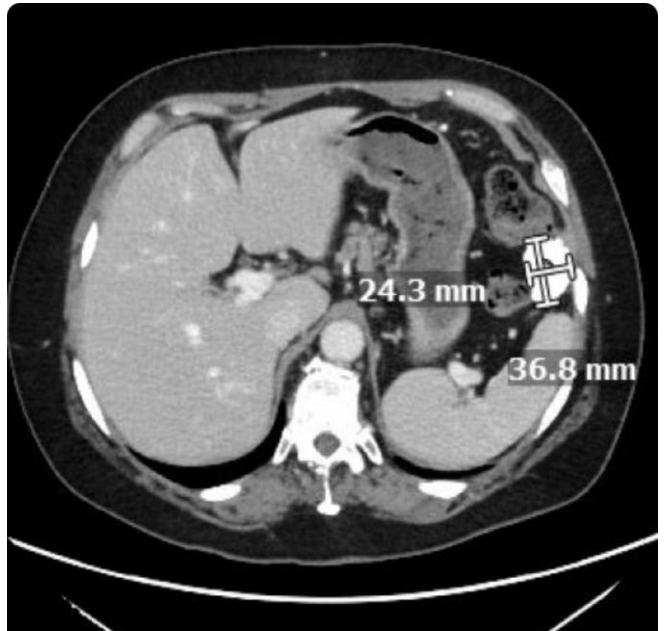
patient: avutometinib plus
nib after trametinib progression

el choice: avutometinib plus defactinib.

exposure did not
in RAMP 201: 22%
K inhibitor.

marked shrinkage
masses after 3





nibitors vs Dual Inhibition

tor alone

s 7.1 mo

Avutometinib + defactinib (RAMP 201)

ORR: 31% overall; 44% *KRAS*-mutant

PFS: 12.9 mo overall; 31.0 mo *KRAS*-mutant

osing, and a monitoring plan that keeps on treatment

pproval May 8, 2025: *KRAS*-mutated recurrent LGSOC after prior systemic therapy.

	Clinic action
	Avutometinib 3.2 mg twice weekly plus defactinib 200 mg twice daily; 3 weeks on, 1 week off
	Comprehensive examination at baseline, before Cycle 2 and every 3 cycles thereafter; promptly evaluate new or worsening symptoms
	Check CPK and liver tests before every cycle, on Day 15 of Cycles 1–4 and as clinically indicated
	Begin topical corticosteroid and an oral antibiotic with treatment; continue for at least the first 2 cycles

ging adverse events to stay on treatment

n

cycle and on
–4; evaluate
lomyolysis

ss regularly



Nausea / GI

Anticipate and manage
early with supportive care



AST / ALT

Check liver tests before each



Rash

Begin topical corticosteroid
and oral antibiotic prophylaxis;
continue for at least 2 cycles



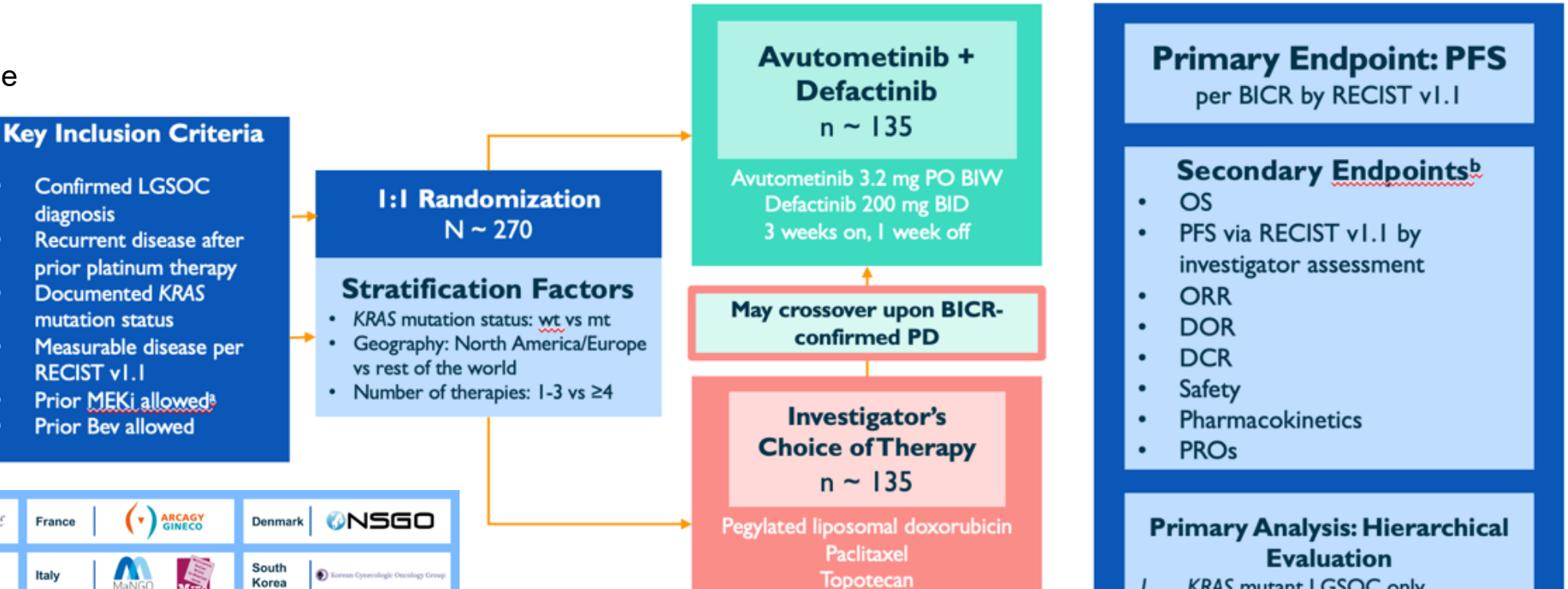
Ocular

Eye examination at baseline, before

97/ENGOT-ov81/GTG-UK/RAMP 301:

Randomized, Open-Label Study of Combination Therapy with Avutometinib + Defactinib vs ce of Treatment in Patients with Recurrent LGSOC

e



home messages

AS at
ence

2

Match the pathway-directed combination

3

Plan monitoring from cycle one

el Discussion and Audience Q&A

All Faculty



rap Up and Closing Comments

All Faculty



THANK YOU

Verastem

For Supporting This Activity With
Independent Medical Education Grant

Thank You

View this symposium
on-demand at www.gog.org

