
# 2023 Ovarian Cancer Medical Update

Ross Harrison, MD MPH

# THEMES

Surgical Innovations

Antibody-drug Conjugates in Ovarian Cancer

Advances in Targeted Therapy

# THEMES

**Surgical Innovations**

Antibody-drug Conjugates in Ovarian Cancer

Advances in Targeted Therapy

# OVHIPEC-1

Upfront ovarian cancer treatment consists of surgery + chemotherapy

Could outcomes be improved by performing **HIPEC** during ovarian cancer surgery?

Rationale:

- Hyperthermia is cytotoxic
- Synergism with chemotherapy
- Increased tumor exposure to treatment
- Induction of apoptosis in tumor cells

1 trial previously found improved survival with HIPEC for patients treated with neoadjuvant chemotherapy

**HIPEC:**

**H**yperthermic
**I**ntra**PE**ritoneal
**C**hemotherapy

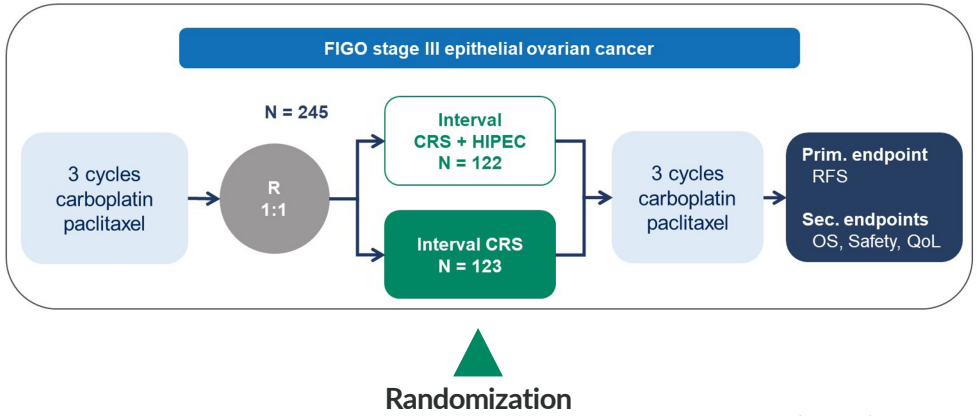
# OVHIPEC-1

Long-term survival outcomes unknown

Randomized to surgery with or without HIPEC after 3 cycles of neoadjuvant chemotherapy

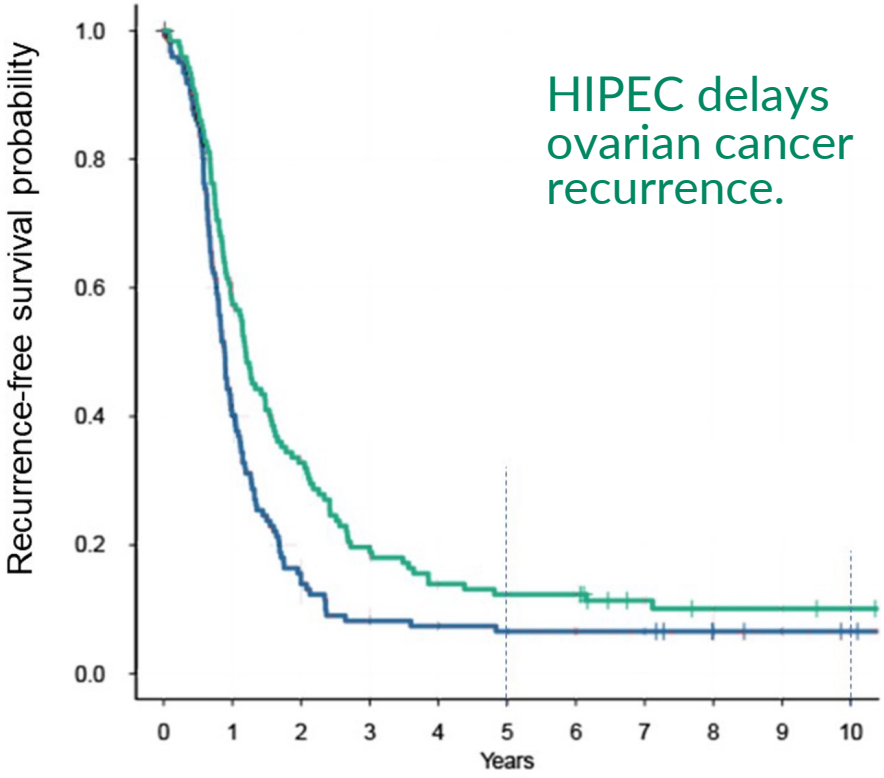
## Eligibility Criteria:

- Newly diagnosed stage III epithelial ovarian, fallopian tube, or peritoneal cancer
- At least stable disease after 3 cycles of neo-adjuvant chemotherapy
- WHO performance score 0-2, adequate renal and bone marrow function
- Treated with interval cytoreductive surgery with residual disease <1 cm
- No history of previous malignancy within 5 years prior to inclusion



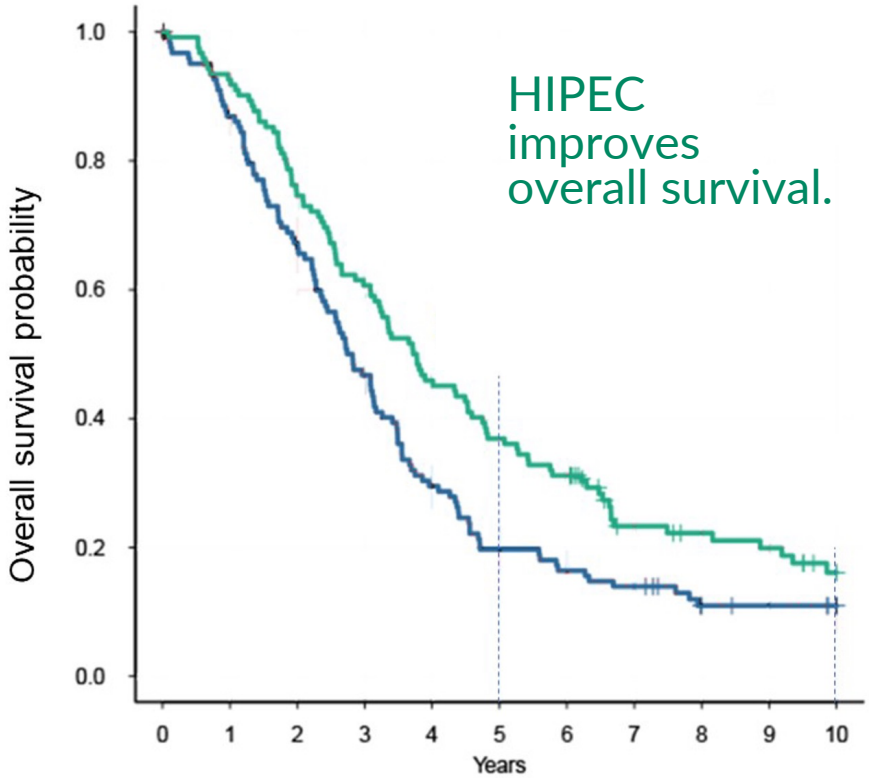

Sonke et al. ASCO 2023.

# OVHIPEC-1




HIPEC delays ovarian cancer recurrence.

| | CRS-HIPEC | CRS |
|---|---|---|
| Median RFS, mo | 14.3 | 10.7 |



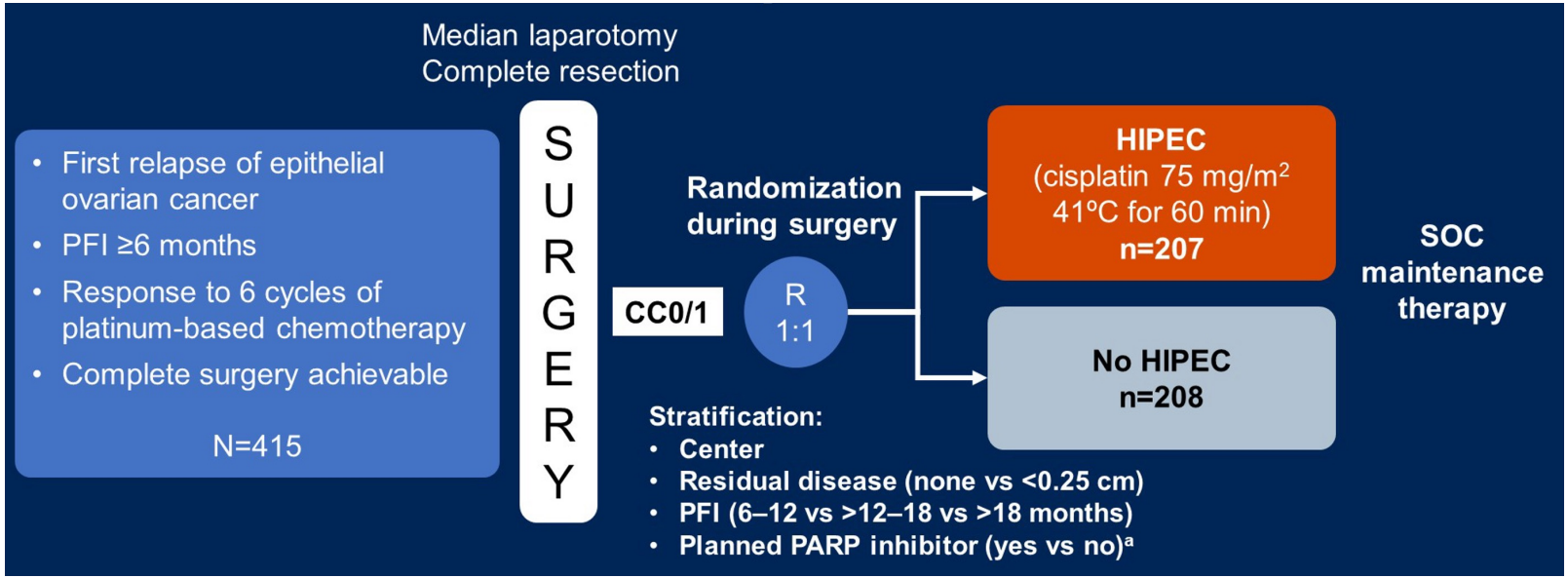

HIPEC improves overall survival.

| | CRS-HIPEC | CRS |
|---|---|---|
| Median OS, mo | 44.9 | 33.3 |

Sonke et al. ASCO 2023.

# CHIPOR

## Should HIPEC be done for patients who have recurrent ovarian cancer?




Classe et al. ASCO 2023.

# CHIPOR

Patients with platinum-sensitive recurrent ovarian cancer

Patients were treated with chemotherapy *before* surgery

Randomization during surgery

## Patients

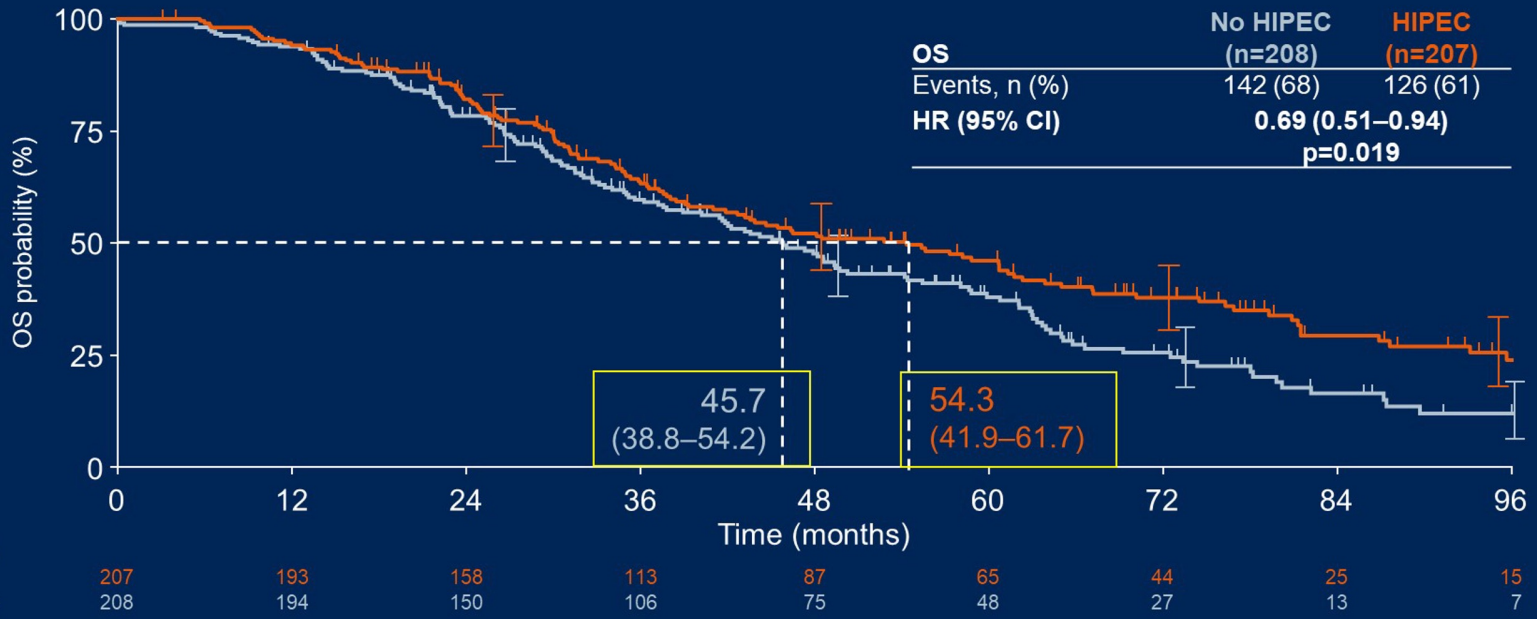
| | HIPEC | No HIPEC |
|---|---|---|
| Age* | 59 | 62 |
| Platinum-free Interval* | 18 months | 17 months |
| Complete Resection | 87% | 87% |

* median

Classe et al. ASCO 2023.

# CHIPOR

## Overall Survival




Classe et al. ASCO 2023.

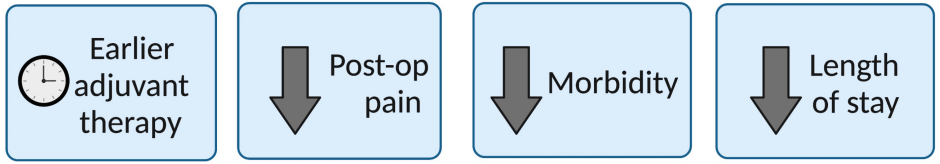
# Minimally Invasive Surgery

Upfront ovarian cancer treatment consists of surgery + chemotherapy

The use of neoadjuvant chemotherapy has increased substantially

Preoperative chemotherapy significant decreases the amount of cancer found during surgery

*Could we make ovarian cancer surgery safer by avoiding open surgery?*



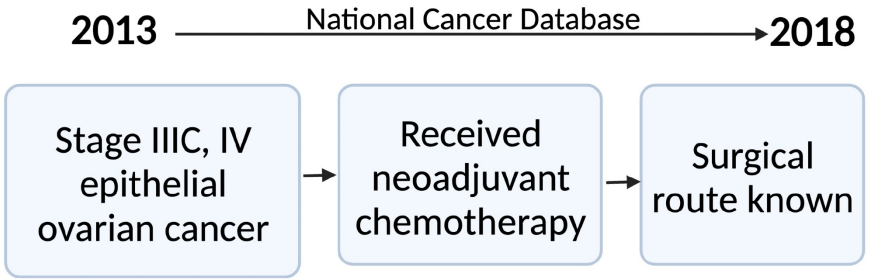

Jorgensen et al. SGO 2023.

# Minimally Invasive Surgery

Is this already happening?

Analysis of the National Cancer Database

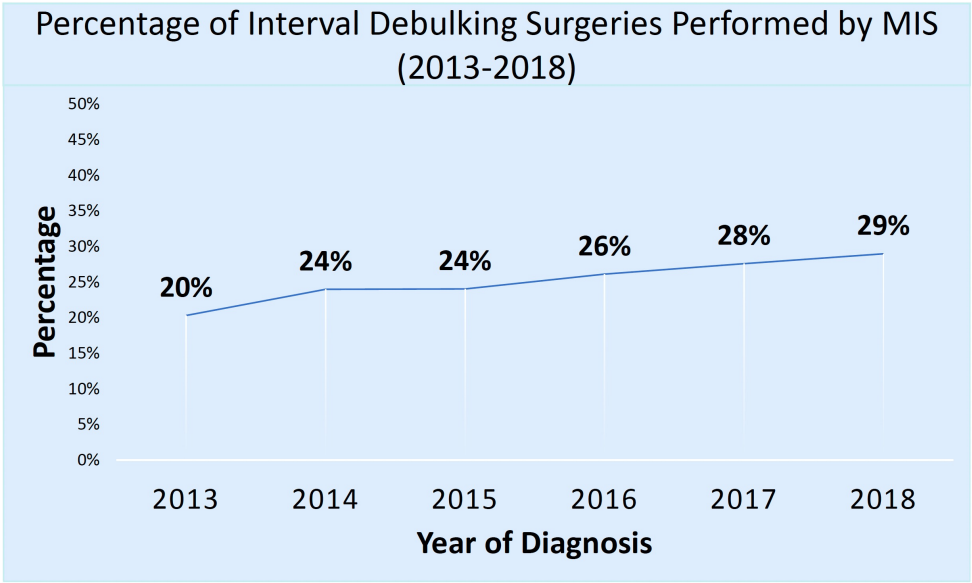
Patients who received preoperative chemotherapy

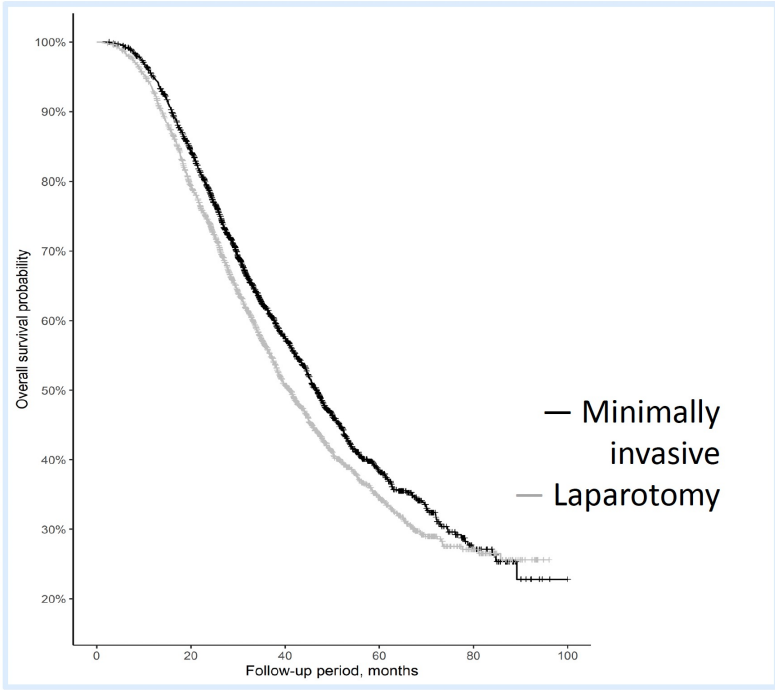



**Primary**
Overall Survival

**Secondary**
- 5-year survival
- 30-, 90-day mortality
- Unplanned readmission
- Extent of surgery
- Residual disease
- Length of stay

# Minimally Invasive Surgery




Jorgensen et al. SGO 2023.

# THEMES

Surgical Innovations

**Antibody-drug Conjugates in Ovarian Cancer**

Advances in Targeted Therapy

# MIRASOL

Mirvetuximab is an antibody-drug conjugate (ADC) targeting folate receptor alpha (FRα)

30-40% of ovarian cancers have high FRα expression

# MIRASOL

## An open-label, phase 3 randomized trial of MIRV vs investigator's choice chemotherapy in patients with FRα-high platinum-resistant ovarian cancer

**Patient Population**
(N=453)

**Enrollment and Key Eligibility**
Platinum-resistant disease
(PFI ≤6 mo)

FRα detected by IHC with PS2+ intensity among ≥75% of viable tumor cells

High-grade serous histology

1º platinum-refractory disease excluded (primary PFI <3 mo)

1-3 prior lines of therapy

Prior BEV and PARPi allowed

Patients with BRCA mutations allowed

1:1 Randomization

**Treatment Regimen-Experimental**

**MIRV**
(6 mg/kg AIBW Q3W)

**Treatment Regimen-Control**

**Investigator's Choice Chemotherapy**
(Paclitaxel, PLD, or Topotecan)

**Stratification Factors**
IC chemo: paclitaxel, PLD, or topotecan
Prior lines of therapy: 1 vs 2 vs 3

**Primary Endpoint**
**PFS by INV**
**(BICR sensitivity analysis)**

**Key Secondary Endpoints**
**1) ORR by INV**
**2) OS**
**3) PROs[a]**

**Secondary Endpoints**
**Safety and tolerability**
**DOR**
**CA-125 response[b]**
**PFS2**

# MIRASOL

33% improvement in overall survival

35% improvement in progression-free survival

2 in 5 patients treated with mirvetuximab saw response to treatment

## Results

| | Mirvetuximab | Chemotherapy |
|---|---|---|
| Overall Survival* | 16.5 months | 12.8 months |
| Progression-free Survival* | 5.6 months | 4.0 months |
| Overall Response Rate | 42% | 16% |
| Complete Response | 5% | -- |
| Partial Response | 37% | 16% |

* median

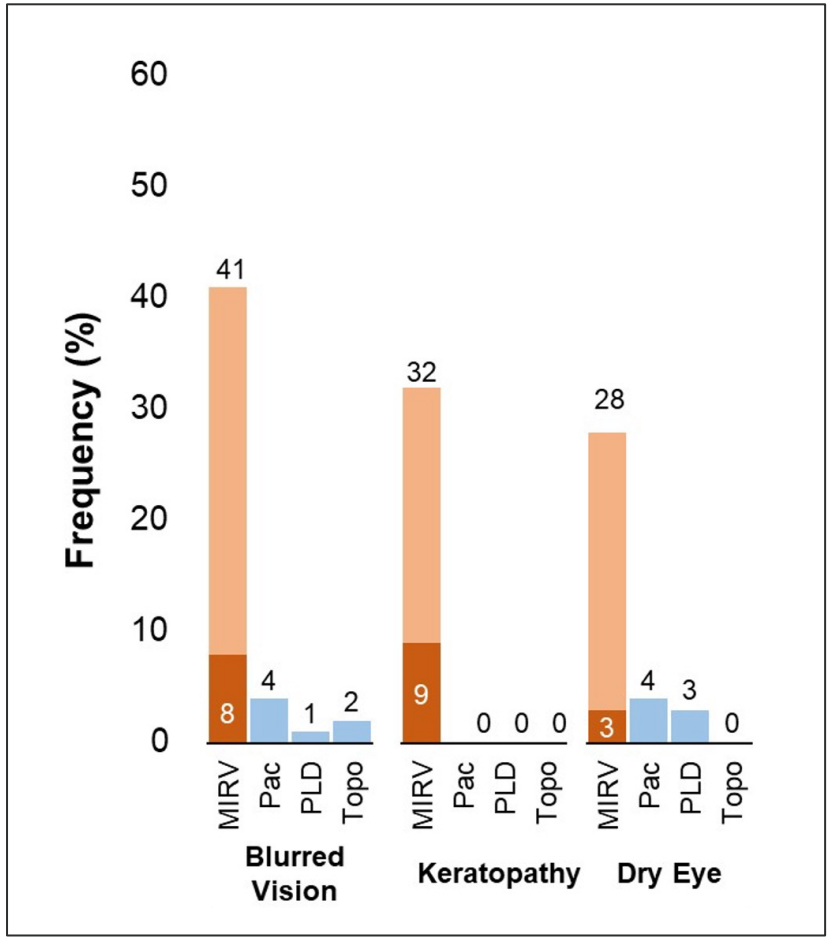
Moore et al. ASCO 2023.

# MIRASOL

Different types of side effects compared with chemotherapy

Low blood counts rarely become an issue with mirvetuximab

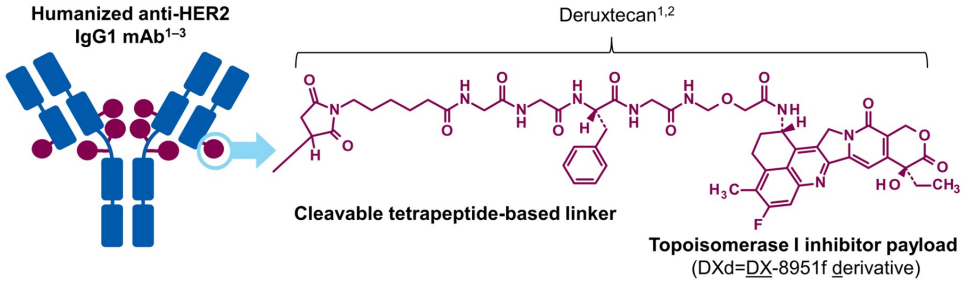
Eye problems much more common




Moore et al. ASCO 2023.

# DESTINY

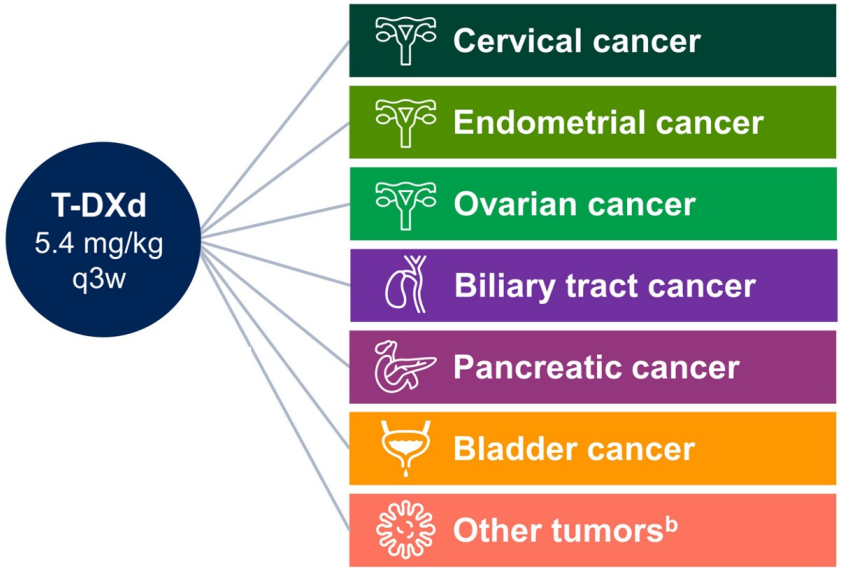
PanTumor02




HER2-targeted treatments are an important part of breast cancer treatment

Many other types of solid tumors also express HER2

Trastuzumab Deruxtecan is an ADC that targets HER2




Meric-Bernstam et al. ASCO 2023.

# DESTINY

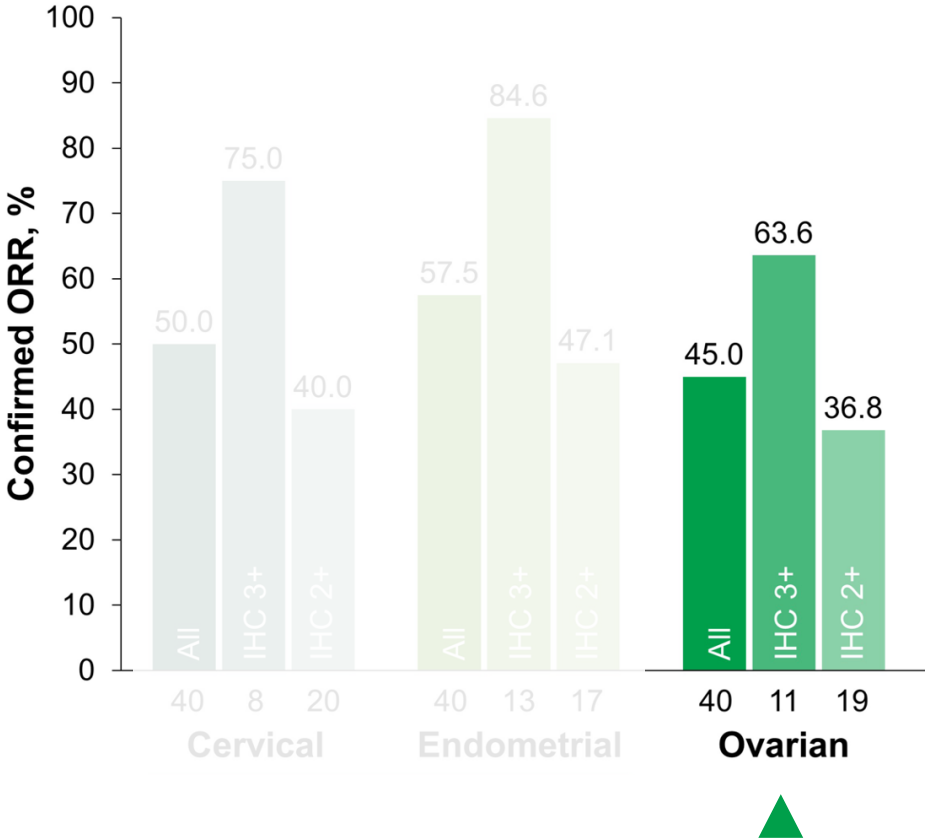
PanTumor02

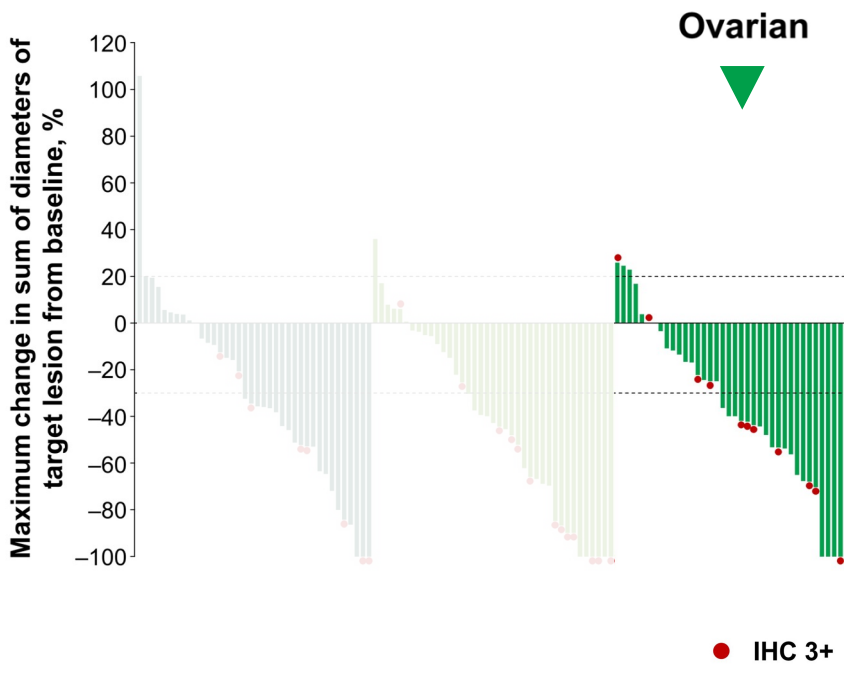
| | | Cervical (n=40) | Endometrial (n=40) | Ovarian (n=40) |
|---|---|---|---|---|
| Investigator assessment | | | | |
| **ORR, n (%)** | | 20 (50.0) | 23 (57.5) | **18 (45.0)** |
| Best overall response, n (%) | Complete response | 2 (5.0) | 7 (17.5) | 4 (10.0) |
| | Partial response | 18 (45.0) | 16 (40.0) | 14 (35.0) |
| | Stable disease | 12 (30.0) | 13 (32.5) | 14 (35.0) |
| | PD | 7 (17.5) | 4 (10.0) | 7 (17.5) |
| | Not evaluable | 1 (2.5) | 0 | 1 (2.5) |
| DCR[a] at 12 weeks, n (%) | | 27 (67.5) | 32 (80.0) | 28 (70.0) |
| Median DOR, months (95% CI) | | 9.8 (4.2–NE) | NR (9.9–NE) | 11.3 (4.1–NE) |
| Independent central review: ORR, n (%) | | 16 (40.0) | 21 (52.5) | 17 (42.5) |

Meric-Bernstam et al. ASCO 2023.

# DESTINY

**PanTumor02**



# THEMES

Surgical Innovations

Antibody-drug Conjugates in Ovarian Cancer

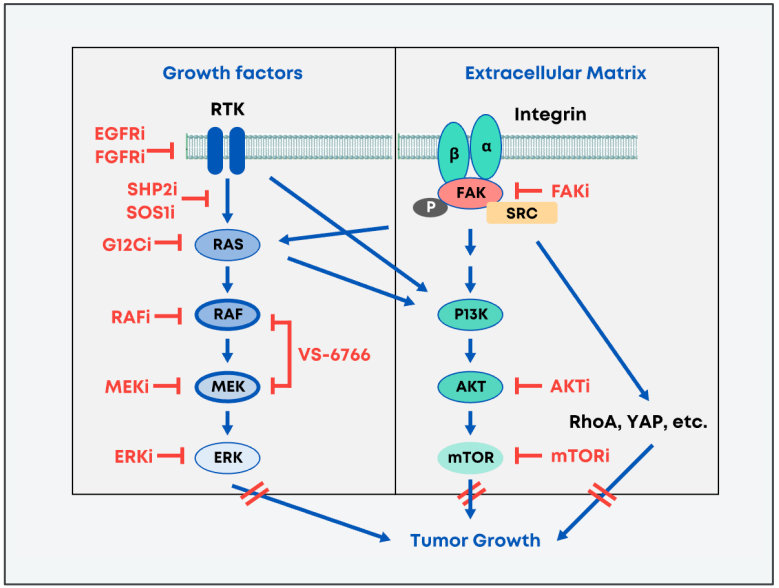
**Advances in Targeted Therapy**

# GOG-3052/ RAMP 201

Phase 2 trial evaluating avutometinib & defactinib

Patients with recurrent low-grade serous carcinoma

Randomized to avutometinib or combination treatment

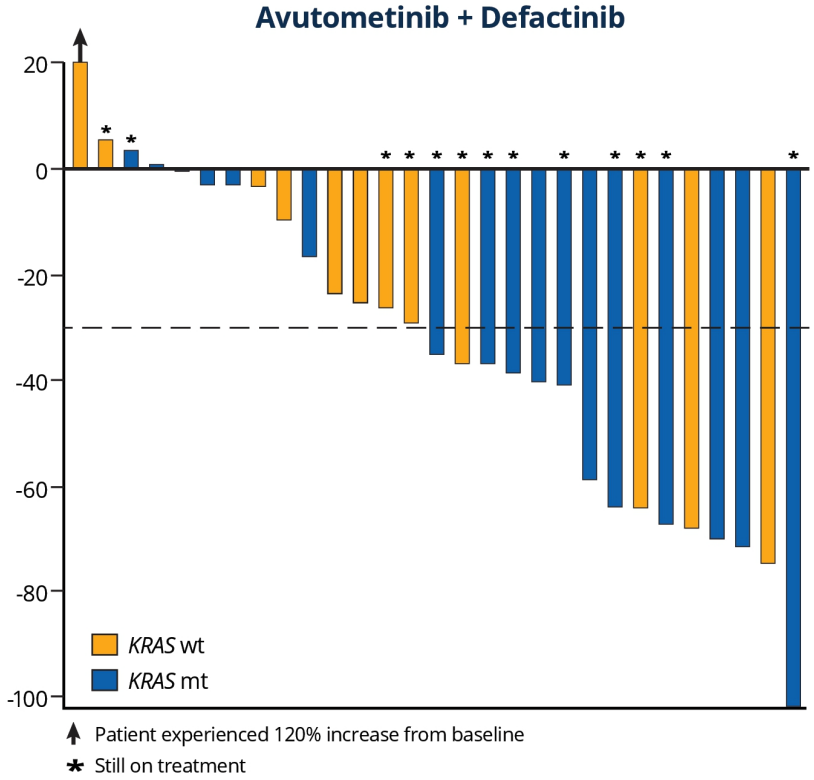


# GOG-3052/ RAMP 201

10% overall response rate with avutometinib alone

45% overall response rate with combination treatment

Patients with ***KRAS*** mutation seemed more likely to response



# GOG-3052/ RAMP 201

↓↓↓ dose in 20-30% patients from side effects

12% of patients stopped treatment due to toxicity

↑↑↑ CPK common reason for stopping treatment

## Side Effects*

| | |
|---|---|
| Nausea | 50-60% |
| Diarrhea | 50-70% |
| Swelling | 40-50% |
| Acne | 35-40% |
| Rash | 30-40% |
| Dry Skin | 20-30% |
| Fatigue | 30-40% |

* most side effects were grade 1-2

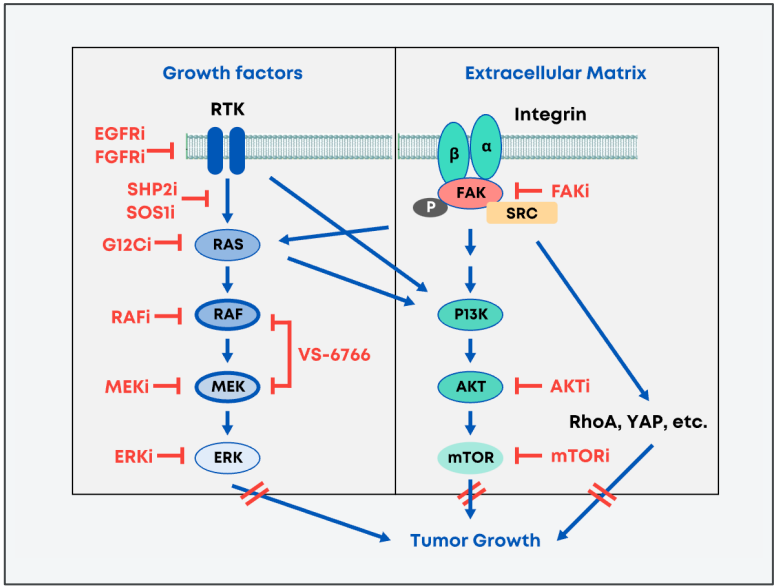
Banerjee et al. ASCO 2023.

# GOG-3052/ RAMP 201

Phase 2 trial evaluating avutometinib & defactinib

Patients with recurrent low-grade serous carcinoma

Randomized to avutometinib or combination treatment



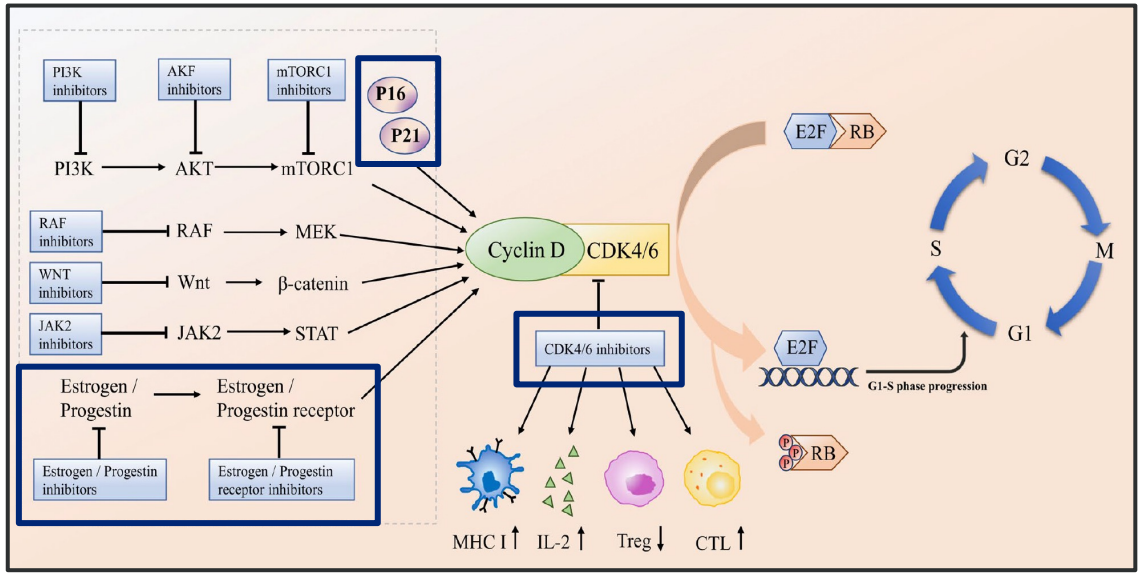
# GOG-3026

Letrozole established part of treatment for low grade serous carcinoma

Abnormal expression of p16 in ovarian cancer

Ribociclib is an CDK4/6 inhibitor

GOG-3026 evaluated the combination of letrozole + ribociclib for treatment of low-grade serous carcinoma



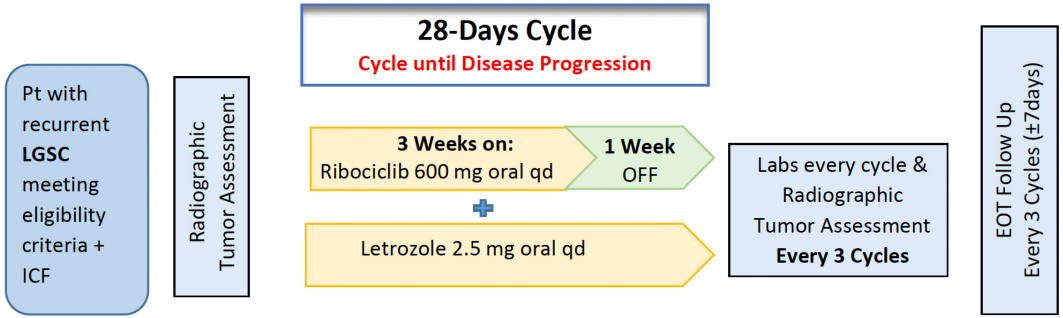

G1-to-S Checkpoint Regulation of the Cell Cycle

Slomovitz et al. SGO 2023.

# GOG-3026

Patients with recurrent low grade serous carcinoma

Except for those who had already been treated with letrozole or a CDK4/6 inhibitor




Slomovitz et al. SGO 2023.

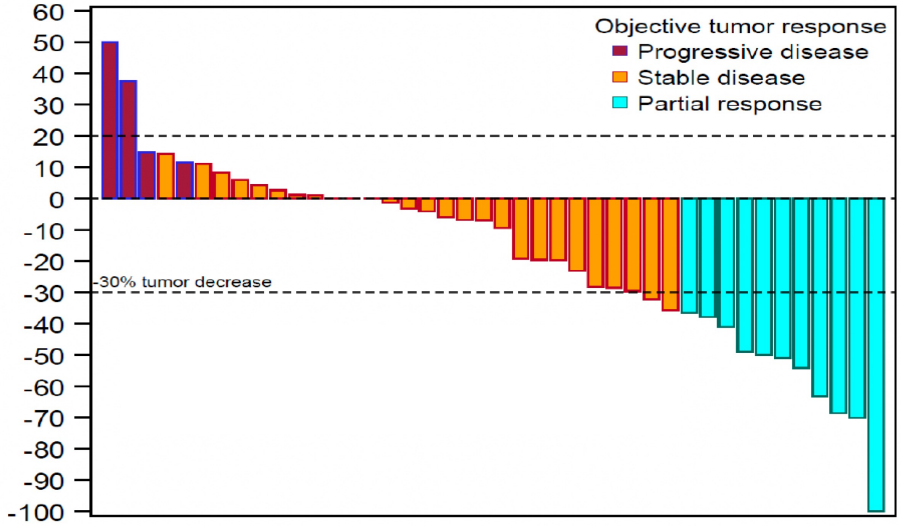
# GOG-3026

23% had partial response to treatment

Most patients either had stable disease with treatment

… or saw some treatment response

*Very similar to most other trials for low-grade serous carcinoma*




Slomovitz et al. SGO 2023.

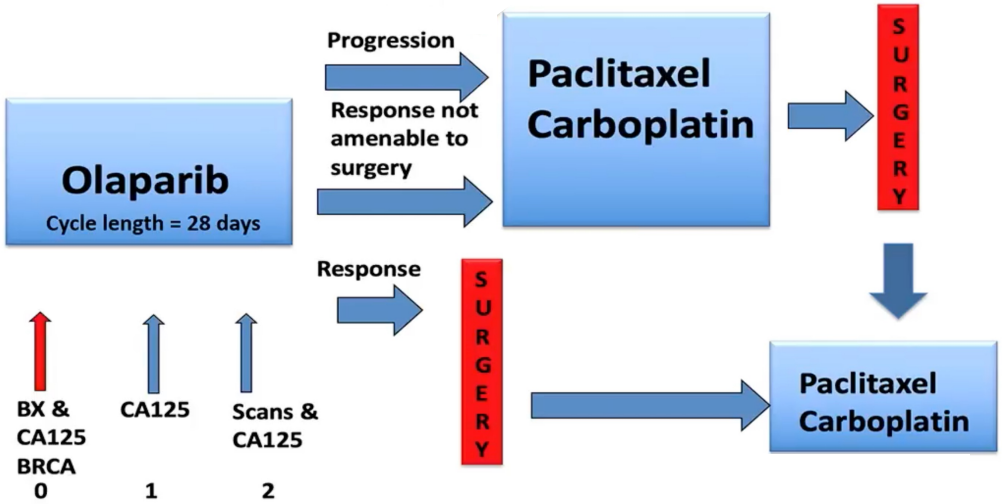
# NOW

Can we use a PARP inhibitor as neoadjuvant treatment before debulking surgery?

Single-arm feasibility study

Patients:

- High grade serous carcinoma
- Plan for neoadjuvant treatment before surgery
- No prior treatment
- *BRCA1*, *BRCA2*, *RAD51C/D*, *PALB2* mutation



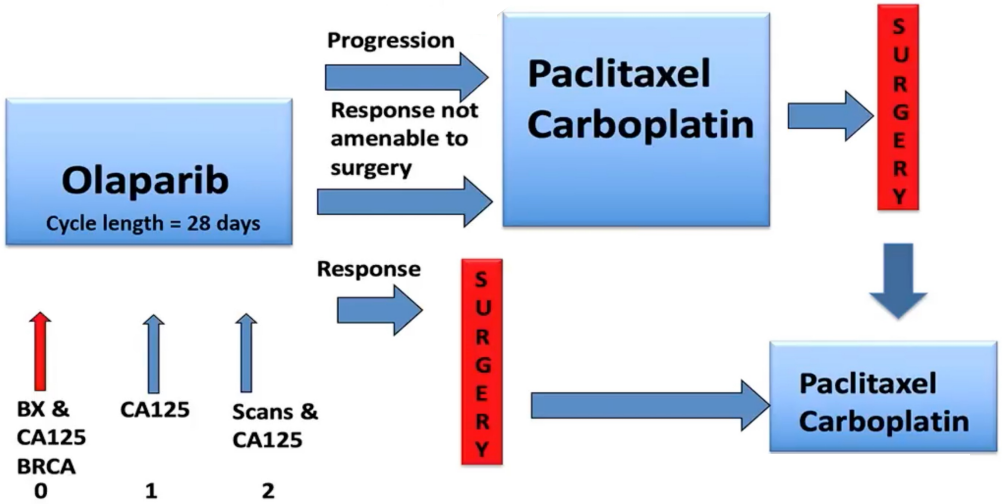
# NOW

Can we use a PARP inhibitor as neoadjuvant treatment before debulking surgery?

Single-arm feasibility study

Patients:

- High grade serous carcinoma
- Plan for neoadjuvant treatment before surgery
- No prior treatment
- *BRCA1*, *BRCA2*, *RAD51C/D*, *PALB2* mutation



# NOW

Relatively small group of carefully selected patients

Most patients underwent surgery immediately after neoadjuvant olaparib

*No preoperative chemotherapy*

1 patient had pathologic complete response

## Outcomes

| Surgery* | |
|---|---|
| After Olaparib | 87% |
| After Olaparib + Chemotherapy | 7% |
| **Surgery Outcome** | |
| Microscopic | 86% |
| <1 cm | 14% |

* One patient did not undergo surgery

# Questions?

OHSU