

ASGO Webinar #62

# Review Course: First-Half 2025 Breakthroughs

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## Endometrial cancer

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# Updated Phase 3 Trials Reinforce the Role of Molecular Subtyping in Adjuvant and Maintenance Therapies for Endometrial Cancer

In the first half of 2025, no new phase 3 trials with positive results were published for endometrial cancer. However, updated data from important phase 3 trials were presented. These findings highlight the importance of tailoring adjuvant and maintenance treatment strategies based on molecular subtypes.

# Outlines – updates of 4 trials

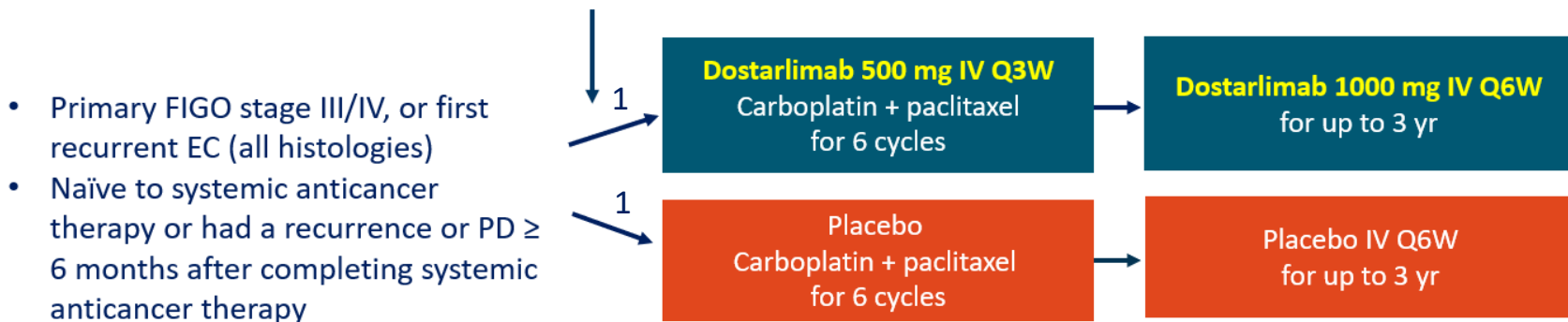
- GOG3031/RUBY
- DUO-E trial
- GOG-3055/SIENDO
- GOG-258

Trial name	Setting	Aim	Patient population
<b>GOG-3031</b> <b>RUBY</b>	<ul style="list-style-type: none"> <li>1<sup>st</sup> line adjuvant &amp; maintenance</li> <li>2<sup>nd</sup> line adjuvant &amp; maintenance (first recurrence)</li> </ul>	To investigate <b>dostarlimab (anti PD-1 Ab)</b> in combination with carboplatin-paclitaxel followed by dostarlimab maintenance compared to chemotherapy alone	<ul style="list-style-type: none"> <li>Primary <b>FIGO stage III/IV, or first recurrent EC</b></li> <li>For first recurrence, prior adjuvant systemic Tx permitted (TFI ≥ 6m)</li> </ul>
<b>GOG-3041</b> <b>DUO-E</b>	<ul style="list-style-type: none"> <li>1<sup>st</sup> line adjuvant &amp; maintenance</li> <li>2<sup>nd</sup> line adjuvant &amp; maintenance (first recurrence)</li> </ul>	To assess the efficacy of <b>durvalumab (anti PD-L1 Ab)</b> in combination with carboplatin-paclitaxel followed by durvalumab maintenance <u>with or without olaparib</u>	<ul style="list-style-type: none"> <li>Primary <b>FIGO stage III/IV, or first recurrent EC</b></li> <li>For first recurrence, prior adjuvant systemic Tx permitted (TFI ≥ 12m)</li> </ul>
<b>GOG-3055</b> <b>SIENDO</b>	<ul style="list-style-type: none"> <li>1<sup>st</sup> line maintenance</li> <li>2<sup>nd</sup> line maintenance (first recurrence)</li> </ul>	To evaluate <b>selinexor (exportin 1 inhibitor)</b> as a maintenance treatment versus placebo in patients with stage IV or first relapse of EC	<ul style="list-style-type: none"> <li>Primary <b>FIGO stage IV, or first recurrent EC</b></li> <li>Had received ≥12 weeks of taxane-platinum-based chemotherapy for advanced or first-line recurrent EC and achieved PR or CR</li> </ul>
<b>GOG-258</b>	<ul style="list-style-type: none"> <li>1<sup>st</sup> line adjuvant</li> </ul>	To determine whether treatment with chemoradiation increased RFS and OS when compared with chemotherapy in locally advanced endometrial cancer	<ul style="list-style-type: none"> <li>Primary <b>FIGO stage III-IVA EC</b></li> <li>Primary FIGO stage I/II serous or clear cell EC and positive cytology</li> </ul>

# Carboplatin + Paclitaxel ± Dostarlimab as Frontline Treatment for Advanced or Recurrent EC (GOG-3031/RUBY): Part 1

- Randomized, placebo-controlled phase III study of chemotherapy + dostarlimab in patients with histologically/cytologically advanced or recurrent endometrial cancer

*Stratified by MMR status (deficient vs proficient) and previous external pelvic radiotherapy (yes vs no)*



- **Primary endpoints:** PFS, OS

- **Secondary endpoints:** PFS by BICR, PFS2, ORR, DoR, DCR, HRQoL/PRO, and safety

# Dostarlimab/Chemo Improves Long-Term duration of response (DOR) in Advanced Endometrial Cancer

## Results

### Overall population

mOS: 44.6 m (Dostarlimab) vs. 28.2 m (Placebo)  
(HR 0.69, P=0.002)

mDOR: 10.6 m (Dostarlimab) vs. 6.2 m (Placebo)  
24-month DOR rates: 37.0% (Dostarlimab) vs. 14.3% (Placebo)

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### dMMR/MSI-H population

mOS: not reached (Dostarlimab) vs. 31.4 m (Placebo)  
(HR 0.32, 95% CI 0.166-0.629)

mDOR: NR (Dostarlimab) vs. 5.4 m (Placebo)  
24-month DOR rates: 62.2% (Dostarlimab) vs. 13.2% (Placebo)

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### pMMR/MSS population

mOS: 34.0 m (Dostarlimab) vs. 27.0 m (Placebo)  
(HR 0.79, 95% CI 0.602-1.044)

mDOR: 8.6 m (Dostarlimab) vs. 6.3 m (Placebo)  
24-month DOR rates: 27.6% (Dostarlimab) vs. 14.7% (Placebo)

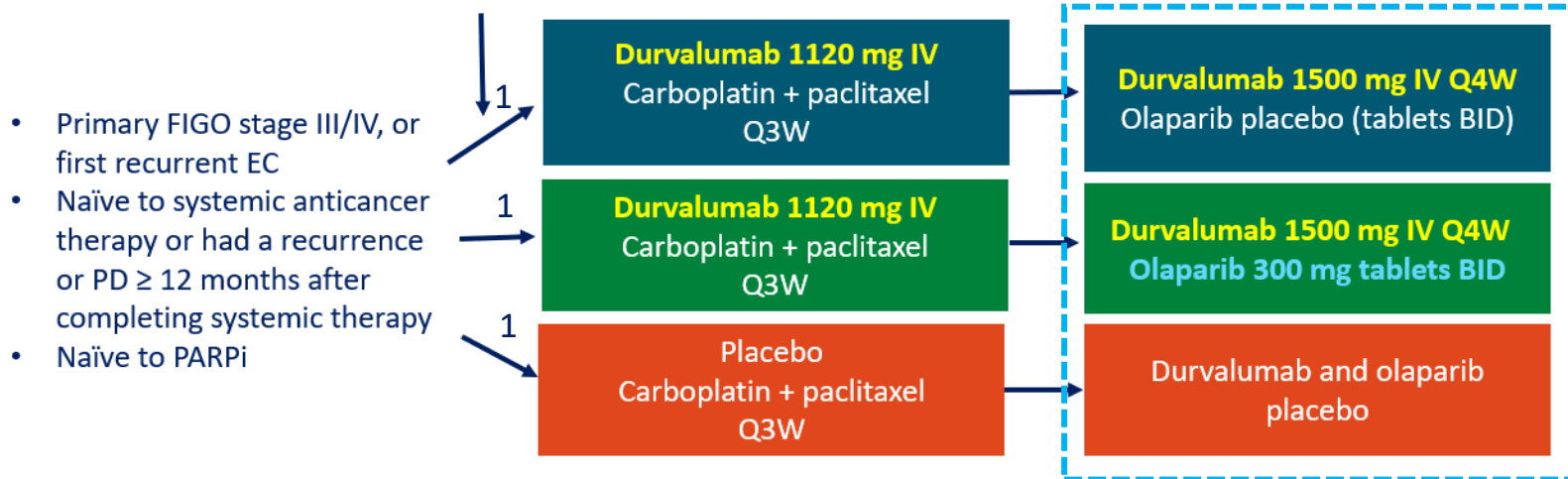
## Clinical significance

- Dostarlimab plus chemotherapy followed by dostarlimab maintenance showed statistically **significant OS benefit** in the overall population.
- 2.6 times more likely to maintain a response lasting at least 24 months.
- Longer-term (> 3-year) follow-up data demonstrated significant benefits in both dMMR and pMMR populations, with increased chances of achieving a DOR lasting at least 24 months.

# Carboplatin + Paclitaxel ± Durvalumab ± Olaparib as Frontline Treatment for Advanced or Recurrent EC (DUO-E)

- Randomized, multicenter, double-blind, placebo-controlled phase III study

*Stratified by MMR status (deficient vs proficient)*



- **Primary endpoints:** PFS
- **Secondary endpoints:** OS

# Olaparib Combo Enhances PFS Across pMMR Endometrial Cancer Subgroups

## Results

### pMMR population

mPFS: 15.0.m (CP + D + O) vs. 9.9 m (CP + D) vs. 9.7 m (CP)

(HR 0.71, 95% CI 0.57-0.89 [CP + D vs. CP])

(HR 0.65, 95% CI 0.43-0.69 [CP + D + O vs. CP])

### pMMR population with detectable ctDNA

(HR 0.61, 95% CI 0.41-0.88 [CP + D vs. CP])

(HR 0.36, 95% CI 0.23-0.56 [CP + D + O vs. CP])

### pMMR population with positive PD-L1 expression

(HR 0.44, 95% CI 0.31-0.61 [CP + D + O vs. CP])

### pMMR population with serous histology

(HR 0.46, 95% CI 0.27-0.76 [CP + D + O vs. CP])

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### dMMR population

mPFS: 31.8.m (CP + D + O) vs. not reached (CP + D) vs. 7.0 m (CP)

(HR 0.42, 95% CI 0.22-0.80 [CP + D vs. CP])

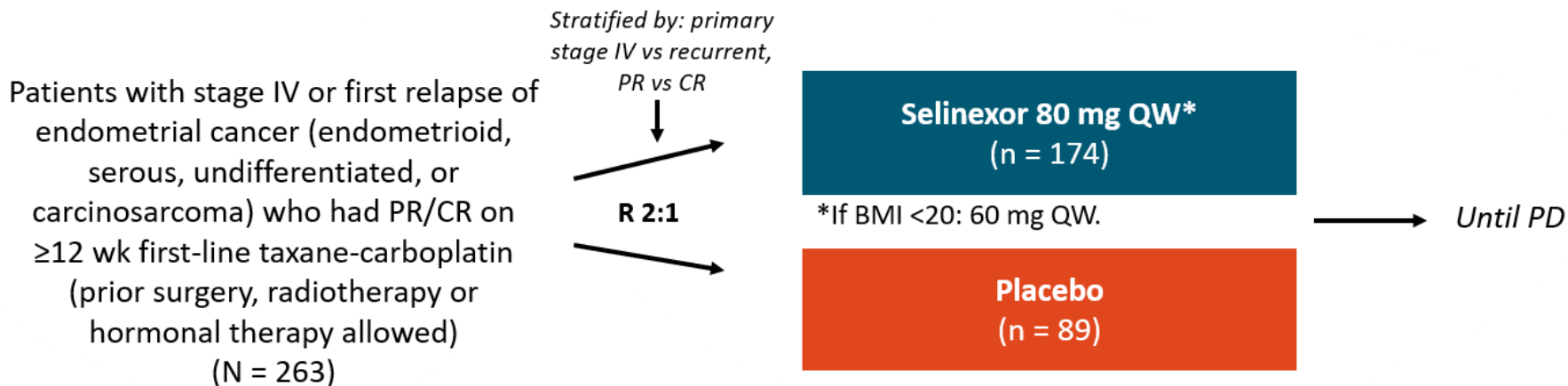
(HR 0.41, 95% CI 0.21-0.75 [CP + D + O vs. CP])

(HR 0.97, 95% CI 0.49-1.98 [CP + D + O vs. CP + D])

## Clinical significance

- Addition of durvalumab to chemotherapy followed by maintenance durvalumab with or without olaparib improves PFS compared to chemotherapy alone in patients with advanced or recurrent EC, regardless of MMR status.
- Olaparib maintenance after durvalumab/chemotherapy improved PFS in pMMR endometrial cancer across various biomarker subgroups, especially in patients with detectable ctDNA, positive PD-L1 expression, and serous histology.

# Oral Selinexor as Maintenance Therapy After First-Line Chemotherapy for Advanced or Recurrent Endometrial Cancer (GOG-3055/SIENDO)



**Pre-defined exploratory endpoints:**  
histologic subtype, molecular subclassification (including *P53*, MMR, and *POLE* EDM)

# Consistent Improvements in PFS2, TFST, and TSST Provide Supportive evidence For the Substantial Signal of PFS Improvement with Selinexor in TP53wt

## Results

### TP53wt population

mPFS: 28.4 m (Selinexor) vs. 5.2 m (Placebo) (HR 0.44, P=0.0005)

mTFST: 31.7 m (Selinexor) vs. 10.6 m (Placebo) (HR 0.41, P=0.0002)

mTSST: NR (Selinexor) vs. 22.1 m (Placebo) (HR 0.47, P=0.0041)

mPFS2: NR (Selinexor) vs. 35.2 m (Placebo) (HR 0.62, P=0.0581)

### TP53wt/pMMR population

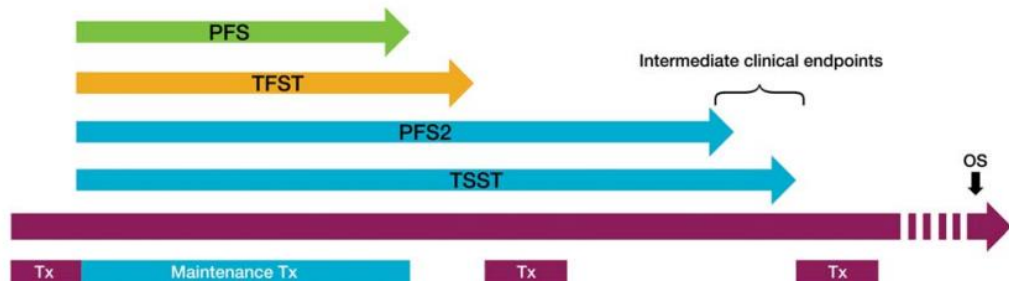
mPFS: 39.5 m (Selinexor) vs. 4.9 m (Placebo) (HR 0.36, P=0.001)

### TP53wt/dMMR population

mPFS: 13.1 m (Selinexor) vs. 3.7 m (Placebo) (HR 0.49, P=0.0825)

## Clinical significance

- Selinexor maintenance improves PFS for patients with stage IV or recurrent **TP53wt** EC who achieved PR or CR on prior chemotherapy.
- Selinexor maintenance showed sustained clinical benefit in patients with TP53wt advanced or recurrent EC, improving PFS, TFST, TSST and PFS2 compared with placebo, regardless of mismatch repair status.



TFST, time to first subsequent therapy or death  
TSST, time to second subsequent therapy or death

# Molecular classification of endometrial cancers and association with RFS and OS outcomes: Ancillary analysis of GOG-0258

## GOG-258 final results: no improvement in survival by adding radiotherapy to chemotherapy in advanced EC

Can molecular testing identify which patients with high-risk or advanced EC benefit from the addition of radiation therapy to chemotherapy?

**Table 2**  
Relapse-free survival rates and overall survival rates with adjusted hazard ratios for molecular status by ProMiSe algorithm.

	5-year RFS rate (%)	p-value*	HR (95 % CI)*	5-year OS rate (%)	10-year OS rate (%)	p-value*	HR (95 % CI)*
p53wt	69	<0.001	Reference	85	74	<0.001	Reference
p53abn	29		3.39 (2.34–4.91)	39	24		4.64 (3.16–6.79)
dMMR	58		1.30 (0.85–1.97)	77	61		1.53 (0.99–2.36)
p53wt CRT vs CT	77 vs 60	0.11	0.54 (0.32–0.94)**	89 vs 80	76 vs 71		0.67 (0.38–1.20)
p53abn CRT vs CT	29 vs 29		0.76 (0.46–1.24)	41 vs 37	23 vs 25		0.95 (0.59–1.52)
dMMR CRT vs CT	53 vs 64		1.34 (0.70–2.56)	73 vs 81	56 vs 67		1.40 (0.73–2.69)

\* Adjusted for age > 65, gross residual disease status, and treatment.

\*\* Adjusted p-value for CRT vs CT is 0.02.

-> RFS seemed to be improved in patients with p53wt cancers who received chemoradiation in addition to chemotherapy

***Thank you for listening***



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