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

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The James

GOG-P Ovarian Cancer Clinical Trialist

Creating a cancer-free world. One person, one discovery at a time.
Ovarian Cancer: Clinical Impact

Age-adjusted SEER ovarian cancer incidence and prevalence from 2001–2017

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

OVARIO trial design

- Patients with newly diagnosed high-grade serous or endometrioid stage IIIB to IV epithelial ovarian, fallopian tube, or peritoneal cancer who achieved a CR, PR, or NED result after frontline platinum-based chemotherapy + bevacizumab

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

Niraparib (200 or 300 mg QD) + bevacizumab (15 mg/kg Q3W)

Endpoint assessment

- Primary endpoint: PFS rate at 18 months (PFS18)

Parameter | Overall (N=105)
---|---
Biomarker status, n (%) | 
HRd | 49 (47)
BRCAm | 29 (28)
BRCAwt | 16 (15)
HRp | 38 (36)
HRnd* | 18 (17)

Post-surgery macroscopic disease, n (%) | 
Yes | 28 (27)
No | 67 (64)
Unknown | 10 (9)
Missing | 0 (0)

Debulking surgery, n (%) | 
PDS | 39 (37)
NACT/IDS | 66 (63)

Response after surgery/platinum-based CT, n (%) | 
CR/NED | 61 (58)
PR | 44 (42)

Primary endpoint

- PFS rate at 18 months (PFS18)

Secondary endpoints

- PFS
- Overall survival
- RECIST or CA-125 PFS
- Time to first subsequent therapy
- Time to second subsequent therapy
- Safety and tolerability
- Patient-reported outcome

Exploratory endpoints

- PFS rate at 6 months (PFS6) and 12 months (PFS12)

Statistical analysis plan

- Efficacy: PFS18 and PFS24 will be estimated by frequency analysis, with corresponding 95% exact CI will be reported
- The time to event endpoints (PFS, TFST, TSST) will be analyzed using Kaplan-Meier methodology
- Progression will be assessed by RECIST v1.1 per investigator
Median PFS (95% CI) was higher in the HRd subgroup (28.3 months [19.9, NE]) versus HRp(14.2 months [8.6, 16.8]) and HRnd subgroups (12.1 months [8, NE])

OVARIO enrolled a high-risk population

In the overall population, more than half (53%) of patients remained progression free at 24 months

PFS analysis suggests that the combination of niraparib and bevacizumab maintenance is efficacious; clinical benefit was observed in the overall population, and across biomarker subgroups in a continuum
Efficacy and Safety of Niraparib as Maintenance Treatment in Patients with Newly Diagnosed Advanced Ovarian Cancer Using an Individualized Starting Dose (PRIME Study): A Randomized, Double-blind, Placebo controlled, Phase 3 Trial N Li, et al SGO 2022

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

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**Eligible Patients**
- Age ≥18 years
- FIGO stage III/IV ovarian cancer
- High-grade serous or endometroid tumor
- Receipt of primary or interval cytoreductive surgery, irrespective of postoperative residual disease status
- CR/PR to 1L Pt-based chemotherapy

**Stratified randomization**
- Status of gBRCA mutations (gBRCAmut/non-gBRCAmut)
- Tumor HRD status (positive/negative)
- Receipt of neoadjuvant chemotherapy (Y/N)
- Response to 1L Pt-based chemotherapy (CR/PR)

**Primary Endpoint**
- PFS by BICR in the ITT population

**Secondary Endpoints**
- OS and TFST in the ITT population
- PFS and OS in the HRD subgroup
- Safety

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*Individualised starting dose (ISD) was adopted in ALL patients: starting dose of 200 mg administered orally, once daily, but 300 mg for patients with body weight ≥77 kg AND platelet count ≥150,000/μL
- Chinese population
  - ITT population: mPFS, 24.8 vs 8.3 months; HR, 0.45; p<0.001
  - HRD subgroup: mPFS, NR vs 11.0 months; HR, 0.48; p<0.001
  - gBRCAmut patients: mPFS, NR vs 10.8 months; HR, 0.40; p<0.001
  - Non-gBRCAmut patients: mPFS, 19.3 vs 8.3 months; HR, 0.48; p<0.001
ATHENA–MONO (GOG-3020/ENGOT-ov45): A Randomized, Double-blind, Phase 3 Trial Evaluating Rucaparib Monotherapy Vs Placebo As Maintenance Treatment Following Response To First-line Platinum-based Chemotherapy In Ovarian Cancer

Bradley J. Monk, Christine Parkinson, Myong Cheol Lim, David M. O’Malley, Ana Oaknin, Michelle K. Wilson, Robert L. Coleman, Domenica Lorusso, Amit Oza, Sharad Ghamande, Athina Christopoulou, Emily Prendergast, Fuat Demirkiran, Ramey D. Littell, Anita Chudecka-Glaz, Mark A. Morgan, Sandra Goble, Stephanie Hume, Keiichi Fujiiwara, Rebecca S. Kristeleit

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

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

**Randomization 4:4:1:1**

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

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

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

**Study Analyses**

**ATHENA–MONO**
- Arm B (n=400) rucaparib 600 mg BID PO + placebo IV
- Arm D (n=100) placebo PO + placebo IV

**ATHENA–COMBO**
- Arm A (n=400) rucaparib 600 mg BID PO + nivolumab 480 mg IV
- Arm B (n=400) rucaparib 600 mg BID PO + placebo IV

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

Monk ASCO 2022 LBA 5500
Step-down Analysis for Efficacy Endpoints

ATHENA-MONO Hierarchical Step-down
Primary Endpoint: Investigator-Assessed PFS

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

<table>
<thead>
<tr>
<th></th>
<th>HR</th>
<th>Median PFS, mo (Rucaparib vs Placebo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRD</td>
<td>0.45</td>
<td>26.7 vs 12.0</td>
</tr>
<tr>
<td>ITT</td>
<td>0.60</td>
<td>20.0 vs 12.0</td>
</tr>
</tbody>
</table>

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

**Key Secondary Endpoints**
- Final Overall Survival
- HRD
- ITT
- RECIST ORR
- HRD
- ITT

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

Log-rank $P=0.0004$
HR, 0.47; 95% CI, 0.31–0.72

Rucaparib  28.7  23.0–NR
Placebo    11.3  9.1–22.1

Cumulative event rate:
Rucaparib, 43.2%; Placebo, 63.3%

Data cutoff date: March 23, 2022.
HR, hazard ratio; HRD, homologous recombination deficiency; NR, not reached; PFS, progression-free survival.
Primary Endpoint – Investigator-Assessed PFS: ITT Population

![Graph showing progression-free survival (PFS) for Rucaparib and Placebo groups.]

- **Rucaparib**: Median 20.2 months, 95% CI 15.2–24.7
- **Placebo**: Median 9.2 months, 95% CI 8.3–12.2

Log-rank $P<0.0001$
HR, 0.52; 95% CI, 0.40–0.68

**Cumulative event rate:**
- **Rucaparib**: 53.9%
- **Placebo**: 70.3%

**Patients at risk (events)**

<table>
<thead>
<tr>
<th>Group</th>
<th>Months 0</th>
<th>Months 3</th>
<th>Months 6</th>
<th>Months 9</th>
<th>Months 12</th>
<th>Months 15</th>
<th>Months 18</th>
<th>Months 21</th>
<th>Months 24</th>
<th>Months 27</th>
<th>Months 30</th>
<th>Months 33</th>
<th>Months 36</th>
<th>Months 39</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rucaparib</td>
<td>427 (0)</td>
<td>398 (15)</td>
<td>351 (57)</td>
<td>298 (101)</td>
<td>245 (149)</td>
<td>213 (176)</td>
<td>190 (193)</td>
<td>151 (207)</td>
<td>114 (214)</td>
<td>67 (224)</td>
<td>42 (226)</td>
<td>23 (229)</td>
<td>7 (230)</td>
<td>0 (230)</td>
</tr>
<tr>
<td>Placebo</td>
<td>111 (0)</td>
<td>97 (11)</td>
<td>72 (34)</td>
<td>60 (44)</td>
<td>42 (61)</td>
<td>39 (64)</td>
<td>31 (69)</td>
<td>18 (75)</td>
<td>14 (76)</td>
<td>8 (78)</td>
<td>5 (78)</td>
<td>3 (78)</td>
<td>1 (78)</td>
<td>0 (78)</td>
</tr>
</tbody>
</table>

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

HRD positive

**BRCA^{mut}**

<table>
<thead>
<tr>
<th>Median</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rucaparib</td>
<td>NR</td>
</tr>
<tr>
<td>Placebo</td>
<td>14.7</td>
</tr>
</tbody>
</table>

HR, 0.40; 95% CI, 0.21–0.75

**BRCA^{wt}/LOH^{high}**

<table>
<thead>
<tr>
<th>Median</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rucaparib</td>
<td>20.3</td>
</tr>
<tr>
<td>Placebo</td>
<td>9.2</td>
</tr>
</tbody>
</table>

HR, 0.58; 95% CI, 0.33–1.01

HRD negative

**BRCA^{wt}/LOH^{low}**

<table>
<thead>
<tr>
<th>Median</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rucaparib</td>
<td>12.1</td>
</tr>
<tr>
<td>Placebo</td>
<td>9.1</td>
</tr>
</tbody>
</table>

HR, 0.65; 95% CI, 0.45–0.95

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

Data cutoff date: March 23, 2022.
BRCA, BRCA1 or BRCA2; HR, hazard ratio; HRD, homologous recombination deficiency; LOH, loss of heterozygosity; mut, mutant; NR, not reached; PFS, progression-free survival; wt, wild type.

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BICR-Assessed PFS: Exploratory Subgroups

HRD positive

BRCA\textsuperscript{mut}

\begin{tabular}{ccc}
& Median & 95\% CI \\
Rucaparib & NR & NR–NR \\
Placebo & NR & 9.0–NR \\
\end{tabular}

HR, 0.48; 95\% CI, 0.23–1.00

BRCA\textsuperscript{wt}/LOH\textsuperscript{high}

\begin{tabular}{ccc}
& Median & 95\% CI \\
Rucaparib & 27.8 & 16.8–NR \\
Placebo & 9.1 & 3.6–17.5 \\
\end{tabular}

HR, 0.46; 95\% CI, 0.26–0.81

HRD negative

BRCA\textsuperscript{wt}/LOH\textsuperscript{low}

\begin{tabular}{ccc}
& Median & 95\% CI \\
Rucaparib & 12.0 & 9.3–17.3 \\
Placebo & 6.4 & 3.9–9.6 \\
\end{tabular}

HR, 0.60; 95\% CI, 0.40–0.89

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

Data cutoff date: March 23, 2022.

BICR, blinded independent central radiology review; BRCA, BRCA\textsuperscript{1} or BRCA\textsuperscript{2}; HR, hazard ratio; HRD, homologous recombination deficiency; LOH, loss of heterozygosity; mut, mutant; NR, not reached; PFS, progression-free survival; wt, wild type
## PARPi for 1LM: Key Efficacy Data

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

**Median PFS, months; HR<sup>a</sup> (95% CI)**

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

Dear Health Care Provider Letter (Niraparib)

May 2022

IMPORTANT DRUG WARNING

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

Dear Health Care Provider:

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

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

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

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

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

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

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

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


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Q: How does the HCP letter affect your consideration of PARPi use in the Recurrent Setting?
(assume patient is otherwise eligible to receive a PARPi)

A. It doesn’t at all – I question the analysis
B. I believe PARPi maintenance therapy is valuable for patients, but will now limit my treatment duration
C. I believe PARPi maintenance therapy is valuable for patients, but will now limit my patient selection
D. Both B and C
E. I believe PARPi maintenance therapy is potentially dangerous and will significantly limit my administration
F. I don’t believe PARPi maintenance therapy is valuable and this letter confirms my bias
Q: How does the HCP letter affect your consideration of PARPi use in the Primary Setting? (assume patient is otherwise eligible to receive a PARPi)

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

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

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

D. Both B and C

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

F. I don’t believe PARPi maintenance therapy is valuable and this letter confirms my bias
Final overall survival results from SOLO3: Phase III trial assessing olaparib monotherapy versus non-platinum chemotherapy in heavily pre-treated patients with germline BRCA1- and/or BRCA2-mutated platinum-sensitive relapsed ovarian cancer

R Penson et al SGO 2022

- Relapsed, high-grade serous or endometrioid ovarian, primary peritoneal and/or fallopian tube cancer
- gBRCAm
- ECOG performance status 0–2
- ≥2 previous lines of platinum-based chemotherapy
- No prior PARP inhibitor therapy
- Platinum sensitive

Olaparib tablets 300 mg bid (N=178)

- 2:1 randomization, open-label
- Randomization stratified by:
  - Selected chemotherapy
  - Number of prior lines of chemotherapy
  - Time to progression after previous platinum-based chemotherapy

- Study treatment administered until disease progression

Non-platinum chemotherapy† (N=88)

- PLD (n=47)
- Paclitaxel (n=20)
- Gemcitabine (n=13)
- Topotecan (n=8)

Primary endpoint
- ORR by BICR (RECIST v1.1)

Primary ORR analysis DCO: 10 Oct 2018

Secondary endpoints
- OS
- PFS
- PFS2
- TFST
- TSST
- TDT
- HRQoL
- Safety

Final OS analysis DCO: 16 Apr 2021

N=266

- Planned for data maturity of approximately 60% (≈150 deaths)
Final overall survival results from SOLO3: Phase III trial assessing olaparib monotherapy versus non-platinum chemotherapy in heavily pre-treated patients with germline BRCA1- and/or BRCA2-mutated platinum-sensitive relapsed ovarian cancer

R Penson et al SGO 2022

**Overall Survival**

- **Olaparib (N=178)**
  - Median OS, months: 48.9
  - Events, n (%): 116 (65)
  - Median follow-up for OS, months: 34.9

- **Chemotherapy (N=88)**
  - Median OS, months: 25.4
  - Events, n (%): 46 (52)
  - Median follow-up for OS, months: 32.9

**HR 1.07 (95% CI 0.76–1.49); P=0.714**

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

**PFS2**

- **Olaparib (N=178)**
  - Median PFS2, months: 23.6
  - Events, n (%): 114 (64)

- **Chemotherapy (N=88)**
  - Median PFS2, months: 19.6
  - Events, n (%): 48 (55)

**HR 0.80 (95% CI 0.56–1.15); P=0.229**

- **11% of olaparib patients vs 25% of chemotherapy patients left the study prior to death**
What Is the Standard Systemic Treatment for Newly Diagnosed Advanced EOC 2022?

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

IV q 3 week carboplatin + paclitaxel
No bevacizumab
BRCA mut + HRD: Add PARPi (preferred)
HRP: Add PARPi or Observation
BRCA mut HRD: Add PARPi (preferred)
HRP: Continue bevacizumab

Decision #1 NACT vs Primary debulking
No bevacizumab
BRCA mut + HRD: Add PARPi (preferred)
HRP: Add PARPi or Observation
BRCA mut HRD: Add PARPi (preferred)
HRP: Continue bevacizumab

Decision #2 Bevacizumab Y/N
Bevacizumab during chemotherapy and in maintenance
BRCA mut + HRD: Add PARPi (preferred)
HRP: Add PARPi or Observation
BRCA mut HRD: Add PARPi (preferred)
HRP: Continue bevacizumab

Decision #3 Add PARPi?

SOLO-1 PRIMA ATHENA
PRIMA ATHENA
PAOLA-1
GOG 218 GOG 262

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

<table>
<thead>
<tr>
<th>Trial</th>
<th>Size</th>
<th>Anti-angiogenic</th>
<th>PARPi</th>
<th>ICI</th>
<th>Start</th>
<th>Estimated Primary Completion</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIRST[^a] ENGOT OV-44</td>
<td>1405</td>
<td>± Bevacizumab</td>
<td>Niraparib</td>
<td>Dostarlimab</td>
<td>Oct 2018</td>
<td>Jan 2023</td>
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<tr>
<td>DUO-O[^b] ENGOT OV-46</td>
<td>~1254</td>
<td>Bevacizumab</td>
<td>Olaparib</td>
<td>Durvalumab</td>
<td>Jan 2019</td>
<td>June 2023</td>
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<tr>
<td>ATHENA[^c] GOG-3020 ENGOT OV-45</td>
<td>~1000</td>
<td>-</td>
<td>Rucaparib</td>
<td>Nivolumab</td>
<td>May 2018</td>
<td>Dec 2024</td>
</tr>
<tr>
<td>ENGOT OV-43[^d] KEYLYNK-001</td>
<td>~1086</td>
<td>± Bevacizumab</td>
<td>Olaparib</td>
<td>Pembrolizumab</td>
<td>Dec 2018</td>
<td>Aug 2025</td>
</tr>
</tbody>
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Slide courtesy of K Moore
**FLORA-5/GOG-3035: Phase 3 Oregovomab (O) Plus Chemo (PC) in Newly Diagnosed Patients With Advanced Epithelial Ovarian Cancer Following Optimal Debulking Surgery**

Authors: Angeles Alvarez Secord, Sunil Gupta, CW Reddick, John O. Schorge, Sarah Gill on behalf of all FLORA-5 Investigators.

**Phase 2 Study Results (Oregovomab + Chemotherapy)**

**Efficacy**

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

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

**Safety**

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

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

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

**Screening Phase**
- Previously untreated patients with epithelial ovarian, tubal or peritoneal cancer, Stage III or IV s/p optimal primary debulking setting.
- CA125 > 50
- N = 372

**Treatment Phase**
- Carboplatin AUC 6 + paclitaxel 175 mg/m² q 3w + oregovomab C1, 3, 5 + 12 weeks

**Post-Treatment Phase**
- EOT + Safety FU
- PFS follow-up
- OS follow-up

<table>
<thead>
<tr>
<th>Randomization</th>
<th>Carboplatin AUC 6 + paclitaxel 175 mg/m² q 3w + placebo</th>
</tr>
</thead>
</table>

Alvarez-Secord for GOG Foundation
Improving Outcomes for Women with Ovarian Cancer Characterized as HRp is a High Unmet Need

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

![Diagram](https://example.com/diagram.png)

**Screening Phase**
- Previously untreated patients with advanced epithelial ovarian, tubal or peritoneal cancer, s/p neoadjuvant chemotherapy and optimal interval debulking surgery.
- CA125 >50
- N = 230

**Treatment Phase**
- Carboplatin AUC 6 + paclitaxel 175 mg/m2 q 3w + oregovomab C4, 6, +6 weeks and +18 weeks

**Post-Treatment Phase**
- EOT + Safety FU
- PFS follow-up
- OS follow-up

Alvarez-Secord for GOG Foundation
Efficacy and safety of rucaparib maintenance treatment in patients from ARIEL3 with platinum-sensitive, recurrent ovarian carcinoma not associated with homologous recombination deficiency. – Coleman ASCO 2022
Role of cytoreductive surgery for the second ovarian cancer relapse in patients previously treated with chemotherapy alone at first relapse: A subanalysis of the DESKTOP III trial. **Sehouli ASCO 2022**

**Population Flow Chart**

- Randomized: n=407
  - Randomized to surgery, n=205
  - Randomized to chemo alone, n=201
- Died without documented recurrence, n=23
- Documented recurrence, no cytoreductive surgery, n=139
- Documented recurrence, cytoreductive surgery, n=32

**OS after surgery for subsequent relapse**

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

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

*SuBrin A et al. ASCO 2020*

*Coleman RA et al. NEJM 2019*
Rare Tumor
A pilot phase II study of neoadjuvant fulvestrant plus abemaciclib in women with advanced low-grade serous carcinoma. Cobb L et al. ASCO 2022

Abemaciclib: CDK 4/6i

**Interval cytoreductive surgery:**
- Underwent surgical resection to date – 7/15 (47%)
- Achieved complete gross resection – 5/7 (71%)
- Achieved optimal cytoreduction – 7/7 (100%)

*Five patients have transitioned to letrozole maintenance
*Adverse events (grade 3 or 4) possibly related to abemaciclib occurred in 2 patients (13.3%) and included acute kidney injury (6.7%) and neutropenia (6.7%).
Efficacy and safety of Lucitanib + Nivolumab in Patients with Advanced Gynecologic Malignancies

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

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

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

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

Patel et al. ASCO 2022 Abstract 5517
BOUQUET GOG-3051 (WO42178/ENGOT-GYN2)
A Phase II, open-label, multicenter platform study evaluating the
efficacy and safety of biomarker-driven therapies in patients with
persistent or recurrent rare epithelial ovarian tumors
Monk B et al TIP SGO 2022

- Persistent or recurrent rare EOC, FTC, PPC*
- 1–4 priors (incl. at least 1 platinum)
- Representative tumor specimen

*Histologically confirmed non-high-grade serous, non-high-grade endometrioid epithelial ovarian, fallopian tube, or primary peritoneal cancer, e.g., LGSOC, clear cell carcinoma, mucinous carcinoma, carcinosarcoma, undifferentiated carcinoma, malignant Brenner tumors, Gr 1 or 2 endometrioid carcinoma, SCCOHT.

Primary endpoint: cORR (INV)
Secondary efficacy endpoints: DOR, DCR, and PFS by INV; OS; cORR, DOR, DCR, and PFS by IRC

PTEN LOF alterations and/or PIK3CA- or AKT1-activating mutations
- ipatasertib + paclitaxel

BRAF-, KRAS-, and NRAS-activating mutations and/or NF1 LOF alterations
- cobimetinib

ERBB2-amplification and/or mutation
- trastuzumab emtansine

Non-matched
- atezolizumab + bevacizumab

Preliminary Phase
n=20 pts/arm

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

**Part A**
- 64 Pts with Recurrent LGSOC: 32 KRAS mutant & 32 KRAS wild type (wt). Randomized 1:1
  - Arm 1: VS-6766 4mg BIW
  - Arm 2: VS-6766 3.2mg BIW + defactinib 200 mg BID

**Part B**
- Enroll additional 20-28 pts with KRAS mt LGSOC
- Enroll additional 20-28 pts with KRAS wt LGSOC

Evaluate Efficacy and Safety Data: Has a Go-Forward regimen been selected?
- Yes
  - Randomize additional 40 pts with KRAS mt LGSOC 1:1 to Arms 1 & 2
  - Randomize additional 40 pts with KRAS mt LGSOC 1:1 to Arms 1 & 2

Evaluate data at the following milestones:
- 20 additional pts (10 KRAS mt & 10 KRAS wt)
- 40 additional pts (20 KRAS mt & 20 KRAS wt)

Evaluate data after 1st 32 pts (16 KRAS mt & 16 KRAS wt) to determine if Go-Forward regimen can be selected
SGNTUC-019: Phase 2 basket study of tucatinib and trastuzumab in previously treated solid tumors with HER2 alterations: uterine and cervical cancer cohorts (Monk et al. Trial in Progress SGO 2022)
Thank you

The James