Emerging Opportunities in Newly Diagnosed Advanced Ovarian Cancer

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GOG Highlight Reel

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Financial Disclosures

I have the following financial relationships to report over the past 24 months:

• Duke receives Clinical trial grant funding from AbbVie, Aravive, AstraZeneca, Clovis, Eisai, Ellipses Pharma, GSK, I-MAB Biopharma, Immunogen, Merck, Oncoquest, Roche/Genentech, Seagen, Inc, Theradex, VBL, and the National Cancer Trial Network.

• Participation on Steering Committees (uncompensated): Aravive (AxXelerate); Roche/Genentech (AtTEND trial); VBL (OVAL trial); and Oncoquest (GOG-3035/FLORA-5).

• SGO Board of Directors, GOG Foundation Board of Directors, AAOGF Board of Trustees
Objectives

• **Review updated survival data from front-line ovarian cancer PARPi maintenance therapy trials**
  - SOLO-1/GOG 3004, PAOLA-1, and PRIMA/GOG 3012

• **Review HIPEC trials**

• **Discuss context of these findings and identify gaps in care.**

• **Highlight ongoing GOG-F front-line trials**
  - FLORA-5/GOG 3035
  - HOTT
Ovarian Cancer: Clinical Impact

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

Incidence

Prevalence

Mortality


10-year survival is ~ 17%
SOLO1/GOG 3004: Updated overall survival at 7-year follow up for newly diagnosed advanced ovarian cancer patients with a \textit{BRCA} mutation

- Newly diagnosed stage III-IV, high-grade serous or endometrioid ovarian, tubal, or peritoneal cancer
- \textit{BRCA} mutation
- ECOG PS 0-1
- Cytoreductive surgery*
- In clinical CR^ or PR after platinum-based therapy

\*Upfront or interval attempt at optimal cytoreductive surgery for stage III disease and either biopsy and/or upfront or interval cytoreductive surgery for stage IV disease
^Including patients with no evidence of disease

- Primary endpoint: PFS – IA
- Secondary endpoints: OS TFST TSST Safety

For up to 2 years until disease progression

Olaparib 300 mg bid (N=260)
Placebo (N=131)

2:1 randomization
Stratified by response to platinum-based chemotherapy

Primary PFS analysis$^1$ (DCO 17 May 2018)

<table>
<thead>
<tr>
<th>Olaparib (N=260)</th>
<th>Placebo (N=131)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events, n (%)</td>
<td>102 (39.2)</td>
</tr>
<tr>
<td>Median PFS, months</td>
<td>NR</td>
</tr>
<tr>
<td>3-year PFS rate, %</td>
<td>60.4</td>
</tr>
<tr>
<td>HR 0.30 (95% CI 0.23--0.41)</td>
<td></td>
</tr>
</tbody>
</table>

Updated PFS analysis$^2$ (DCO 5 March 2020)

<table>
<thead>
<tr>
<th>Olaparib (N=260)</th>
<th>Placebo (N=131)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events, n (%)</td>
<td>118 (45.4)</td>
</tr>
<tr>
<td>Median PFS, months</td>
<td>56.0</td>
</tr>
<tr>
<td>5-year PFS rate, %</td>
<td>48.3</td>
</tr>
<tr>
<td>HR 0.33 (95% CI 0.25--0.43)</td>
<td></td>
</tr>
</tbody>
</table>

Moore, K \textit{et al} \textit{N Engl J Med} 2018; Banerjee S \textit{et al} \textit{Lancet Oncol} 2021

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SOLO1/GOG 3004: Updated Overall Survival Analysis

Statistical Analysis

- Prespecified descriptive OS analysis conducted at 7 years after last patient randomized
  - OS unadjusted for subsequent PARPi therapy
  - Two-sided P value of <0.0001 required to declare statistical significance
- Prespecified final OS analysis currently planned to be conducted at approximately 60% data maturity
SOLO1/GOG 3004: Updated Overall Survival Analysis Patients Disposition

<table>
<thead>
<tr>
<th>Completed treatment at 2 years per protocol, n (%)</th>
<th>Olaparib: 123 (47.3)</th>
<th>Placebo: 35 (26.9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continued treatment beyond 2 years, n (%)</td>
<td>Olaparib: 26 (10.0)</td>
<td>Placebo: 3 (2.3)</td>
</tr>
<tr>
<td>Still receiving treatment at DCO, n (%)</td>
<td>Olaparib: 7 (2.7)</td>
<td>Placebo: 0</td>
</tr>
<tr>
<td>Discontinued treatment for reasons other than completing the prescribed regimen, n (%)</td>
<td>Olaparib: 130 (50.0)</td>
<td>Placebo: 95 (73.1)</td>
</tr>
<tr>
<td>Objective disease progression</td>
<td>Olaparib: 53 (20.4)</td>
<td>Placebo: 78 (60.0)</td>
</tr>
<tr>
<td>Adverse event</td>
<td>Olaparib: 31 (11.9)</td>
<td>Placebo: 3 (2.3)</td>
</tr>
<tr>
<td>Patient decision</td>
<td>Olaparib: 23 (8.8)</td>
<td>Placebo: 2 (1.5)</td>
</tr>
<tr>
<td>Other†/unknown reason</td>
<td>Olaparib: 23 (8.8)</td>
<td>Placebo: 12 (9.2)</td>
</tr>
<tr>
<td>Median (range) duration of treatment, months</td>
<td>Olaparib: 24.6 (0.0–97.5)</td>
<td>Placebo: 13.9 (0.2–60.9)</td>
</tr>
<tr>
<td>Median (IQR) duration of follow-up for OS, months</td>
<td>Olaparib: 88.9 (85.7–93.6)</td>
<td>Placebo: 87.4 (84.3–91.7)</td>
</tr>
</tbody>
</table>
SOLO1/GOG 3004: Updated Overall Survival Analysis Overall Survival

N=260 N=131

44.3% patients in placebo arm received subsequent PARPi, compared to 14.6% of patients in the olaparib group

Events, n (%)

Median OS, months

Olaparib Placebo

84 (32.3) 65 (49.6)

NR 75.2

HR 0.55 (95% CI 0.40–0.76); P=0.0004*

P < 0.0001 required to declare statistical significance

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SOLO1/GOG 3004: Updated Overall Survival Analysis TFST and TSST

DiSilvestro P. ESMO 2022
### SOLO1/GOG 3004: Updated Overall Survival Analysis Safety

<table>
<thead>
<tr>
<th>Event</th>
<th>Primary PFS analysis (DCO 17 May 2018)</th>
<th>7-year descriptive OS analysis (DCO 7 March 2022)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Olaparib (N=260)</td>
<td>Placebo (N=130)</td>
</tr>
<tr>
<td>Median (range) duration of treatment, months</td>
<td>24.6 (0.0–52.0)</td>
<td>13.9 (0.2–45.5)</td>
</tr>
<tr>
<td>Any TEAE, n (%)</td>
<td>256 (98.5)</td>
<td>120 (92.3)</td>
</tr>
<tr>
<td>Grade ≥3 TEAEs, n (%)</td>
<td>102 (39.2)</td>
<td>24 (18.5)</td>
</tr>
<tr>
<td>Serious TEAEs, n (%)</td>
<td>54 (20.8)</td>
<td>16 (12.3)</td>
</tr>
<tr>
<td>TEAE leading to dose interruption, n (%)</td>
<td>135 (51.9)</td>
<td>22 (16.9)</td>
</tr>
<tr>
<td>TEAE leading to dose reduction, n (%)</td>
<td>74 (28.5)</td>
<td>4 (3.1)</td>
</tr>
<tr>
<td>TEAE leading to treatment discontinuation, n (%)</td>
<td>30 (11.5)</td>
<td>3 (2.3)</td>
</tr>
<tr>
<td>AEs of special interest, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDS/AML*</td>
<td>3 (1.2)</td>
<td>0</td>
</tr>
<tr>
<td>New primary malignancies*</td>
<td>5 (1.9)</td>
<td>3 (2.3)</td>
</tr>
<tr>
<td>Pneumonitis/ILD</td>
<td>5 (1.9)</td>
<td>0</td>
</tr>
</tbody>
</table>

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PAOLA-1/ENGOT-ov25: Final overall survival results for newly diagnosed advanced ovarian cancer patients

- Newly diagnosed stage III-IV, high-grade serous or endometrioid ovarian, tubal, or peritoneal cancer*
- Upfront or interval Cytoreductive surgery
- Platinum-taxane based therapy plus ≥ 2 cycles of bevacizumab
- NED/CR/PR

*Patients with other epithelial non-mucinous ovarian cancer eligible if BRCAm present.

Primary endpoint: PFS – IA
Secondary endpoints: PFS2 OS
*OS planned for 3 years after the primary PFS analysis or 60% of data maturity

OS will be tested at full 5% alpha at OS data cutoff
Predefined OS subgroup analysis by tumor BRCAm and HRD score

Maintenance therapy
Olaparib tablets 300 mg bid x 2 years
+ bevacizumab

2:1 randomization stratified by:
- Tumour BRCAm status
- First-line treatment outcome†

Placebo x 2 years
+ bevacizumab

Ray-Coquard I. ESMO 2022
PAOLA-1/ENGOT-ov25: Final overall survival results for newly diagnosed advanced ovarian cancer patients

### Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Olaparib + bevacizumab (N=537)</th>
<th>Placebo + bevacizumab (N=269)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, median, years (range)</strong></td>
<td>61 (32–87)</td>
<td>60 (26–85)</td>
</tr>
<tr>
<td><strong>FIGO stage, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>378 (70)</td>
<td>186 (69)</td>
</tr>
<tr>
<td>IV</td>
<td>159 (30)</td>
<td>83 (31)</td>
</tr>
<tr>
<td><em><em>HRD status,</em> n (%)</em>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HRD positive</td>
<td>255 (47)</td>
<td>132 (49)</td>
</tr>
<tr>
<td>tBRCAm</td>
<td>157 (29)</td>
<td>80 (30)</td>
</tr>
<tr>
<td>HRD positive excluding tBRCAm</td>
<td>97 (18)</td>
<td>55 (20)</td>
</tr>
<tr>
<td>HRD negative/HRD unknown</td>
<td>282 (53)</td>
<td>137 (51)</td>
</tr>
<tr>
<td>HRD negative</td>
<td>192 (36)</td>
<td>85 (32)</td>
</tr>
<tr>
<td><strong>Upfront surgery</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• No residual macroscopic disease</td>
<td>160 (59)</td>
<td>85 (62)</td>
</tr>
<tr>
<td>• Residual macroscopic disease</td>
<td>111 (41)</td>
<td>53 (38)</td>
</tr>
<tr>
<td><strong>History of cytoreductive surgery, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interval cytoreductive surgery</td>
<td>228 (42)</td>
<td>110 (41)</td>
</tr>
<tr>
<td>• No residual macroscopic disease</td>
<td>163 (71)</td>
<td>75 (68)</td>
</tr>
<tr>
<td>• Residual macroscopic disease</td>
<td>65 (29)</td>
<td>35 (32)</td>
</tr>
<tr>
<td>No surgery</td>
<td>38 (7)</td>
<td>21 (8)</td>
</tr>
<tr>
<td><strong>Response after surgery/PBC, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NED</td>
<td>290 (54)</td>
<td>141 (52)</td>
</tr>
<tr>
<td>CR</td>
<td>106 (20)</td>
<td>53 (20)</td>
</tr>
<tr>
<td>PR</td>
<td>141 (26)</td>
<td>75 (28)</td>
</tr>
</tbody>
</table>

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PAOLA-1/ENGOT-ov25: Final overall survival results for newly diagnosed advanced ovarian cancer patients

Overall Survival ITT Population

- **Olaparib + bevacizumab (N=537)**
  - Events: 288 (53.6)
  - Median OS, months: 56.5
  - 5-year OS rate, %: 47.3
  - HR: 0.92 (95% CI 0.76–1.12); P=0.4118

- **Placebo + bevacizumab (N=269)**
  - Events: 158 (58.7)
  - Median OS, months: 51.6
  - 5-year OS rate, %: 41.5

Patients receiving a PARP inhibitor during any subsequent treatment
- Olaparib + bevacizumab: 19.6% (105/537)
- Placebo + bevacizumab: 45.7% (113/269)

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PAOLA-1/ENGOT-ov25: Final overall survival results for newly diagnosed advanced ovarian cancer patients

Overall Survival HRD Population

- **5-year OS rate**: 65.5%
- **5-year OS rate**: 48.4%
- **5-year OS rate for Olaparib + bevacizumab**
  - Events, n (%): 93 (36.5)
  - Median OS, months: 75.2 (unstable*)
  - 5-year OS rate, %: 65.5
  - HR 0.62 (95% CI 0.45–0.85)

- **5-year OS rate for Placebo + bevacizumab**
  - Events, n (%): 69 (52.3)
  - Median OS, months: 57.3
  - 5-year OS rate, %: 48.4

- **38% reduction in risk of death for olaparib + bevacizumab vs bevacizumab alone**

- **Patients receiving a PARP inhibitor during any subsequent treatment**
  - Olaparib + bevacizumab: 17.3% (44/255)
  - Placebo + bevacizumab: 50.8% (67/132)
PAOLA-1/ENGOT-ov25: Final overall survival results for newly diagnosed advanced ovarian cancer patients

Overall Survival Subgroup Analysis \textit{BRCAm} and HRD Status

\textbf{BRCAm}:

- 5-year OS rate: 73.2%
- 5-year OS rate: 53.8%

\textbf{HRD positive} excluding \textit{BRCAm}:

- 5-year OS rate: 54.7%
- 44.2%

\textbf{HRD negative}:

- 5-year OS rate: 32.3%
- 25.7%

\textbf{No. at risk:}

\begin{itemize}
  \item \textit{Olaparib + bevacizumab} (N=157)
  \item \textit{Placebo + bevacizumab} (N=80)
\end{itemize}

\textbf{Events, n (%)}:

\begin{itemize}
  \item \textit{Olaparib + bevacizumab}: 48 (30.6)
  \item \textit{Placebo + bevacizumab}: 37 (46.3)
\end{itemize}

\textbf{Median OS, months}:

\begin{itemize}
  \item \textit{Olaparib + bevacizumab}: 75.2 (unstable)
  \item \textit{Placebo + bevacizumab}: 66.9
\end{itemize}

\textbf{5-year OS rate, \%}:

\begin{itemize}
  \item \textit{Olaparib + bevacizumab}: 73.2
  \item \textit{Placebo + bevacizumab}: 53.8
\end{itemize}

\textbf{PARPi as subsequent treatment, n (\%)}:

\begin{itemize}
  \item \textit{Olaparib + bevacizumab}: 38 (24.2)
  \item \textit{Placebo + bevacizumab}: 44 (55.0)
\end{itemize}

\textbf{HR 0.60 (95\% CI 0.39--0.93)}

\textbf{HR 0.71 (95\% CI 0.45--1.13)}

\textbf{HR 1.19 (95\% CI 0.88--1.63)}

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PAOLA-1/ENGOT-ov25: Final overall survival results for newly diagnosed advanced ovarian cancer patients

Adverse Events of Special Interest

<table>
<thead>
<tr>
<th></th>
<th>Primary PFS analysis (DCO: 22 March 2019)</th>
<th>Final PFS2 analysis (DCO: 22 March 2020)</th>
<th>Final OS analysis (DCO: 22 March 2022)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Olaparib + bevacizumab (N=535)</td>
<td>Olaparib + bevacizumab (N=535)</td>
<td>Olaparib + bevacizumab (N=535)</td>
</tr>
<tr>
<td>MDS/AML/AA, n (%)</td>
<td>6 (1.1)</td>
<td>7 (1.3)</td>
<td>9 (1.7)</td>
</tr>
<tr>
<td></td>
<td>Placebo + bevacizumab (N=267)</td>
<td>Placebo + bevacizumab (N=267)</td>
<td>Placebo + bevacizumab (N=267)</td>
</tr>
<tr>
<td></td>
<td>1 (0.4)</td>
<td>4 (1.5)</td>
<td>6 (2.2)</td>
</tr>
<tr>
<td>New primary malignancies, n (%)⁺</td>
<td>7 (1.3)</td>
<td>13 (2.4)</td>
<td>22 (4.1)</td>
</tr>
<tr>
<td></td>
<td>Placebo + bevacizumab (N=267)</td>
<td>Placebo + bevacizumab (N=267)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 (1.1)</td>
<td>5 (1.9)</td>
<td>8 (3.0)</td>
</tr>
<tr>
<td>Pneumonitis/ILD/bronchiolitis, n (%)†</td>
<td>6 (1.1)</td>
<td>6 (1.1)</td>
<td>7 (1.3)</td>
</tr>
<tr>
<td></td>
<td>Placebo + bevacizumab (N=267)</td>
<td>Placebo + bevacizumab (N=267)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>2 (0.7)</td>
</tr>
</tbody>
</table>

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PRIMA/GOG 3012/ENGOT-ov26: Updated long-term PFS and safety

**Stratification Factors**
- Neoadjuvant chemotherapy administered: Yes or no
- Best response to first platinum therapy: CR or PR
- Tissue homologous recombination test status: deficient or proficient/not-determined

**Hierarchical PFS Testing**
- Patients with homologous recombination deficient tumors, followed by the overall population.
  - Statistical assumption: a hazard ratio benefit in PFS of 0.5 in homologous recombination deficient patients
  - 0.65 in the overall population
  - >90% statistical power and one-sided type I error of 0.025

**Randomization**
- 2:1 Randomization

**Endpoint assessment**
- **Primary Endpoint:** Progression-free survival by BICR
- **Key Secondary Endpoint:** Overall Survival
- **Secondary Endpoints:** PFS2, TFST, PRO, Safety

**Endpoint assessment**
- Patients were treated with niraparib or placebo once daily for 36 months or until disease progression

- Patients with newly-diagnosed OC at high risk for recurrence after response to 1L platinum-based chemotherapy

- Body weight ≥77 kg and platelets ≥150,000/μL started with 300 mg QD
- Body weight <77 kg and/or platelets <150,000/μL started with 200 mg QD

**Excluded stage III no visible residual after CRS and BEV maintenance.**
- Residual tumour after CT ≤ 2 cm
- Normal CA125 or CA125 decrease by >90% during front-line therapy

- Normal CA125 or CA125 decrease by >90% during front-line therapy

OS remains immature – 41.2% of overall population
Subsequent PARPi therapy: 9.2% niraparib group vs 33.3% placebo-group
PRIMA/GOG-3012/ENGOT-ov26: Updated long-term PFS

HRD and Overall Population

HRD

<table>
<thead>
<tr>
<th>Population</th>
<th>Niraparib mPFS</th>
<th>Placebo mPFS</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRD population (N=373)</td>
<td>24.5 months</td>
<td>11.2 months</td>
<td>0.52 (0.40–0.68) P&lt;0.001</td>
</tr>
</tbody>
</table>

Overall

<table>
<thead>
<tr>
<th>Population</th>
<th>Niraparib mPFS</th>
<th>Placebo mPFS</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall population (N=733)</td>
<td>13.8 months</td>
<td>8.2 months</td>
<td>0.66 (0.56–0.79) P&lt;0.001</td>
</tr>
</tbody>
</table>

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PRIMA/GOG-3012/ENGOT-ov26: Updated long-term PFS

HRD BRCAm, HRD BRCAwt, and HRP Subgroup Analysis

- **HRd BRCAm**
  - Hazard ratio: 0.45
  - (95% CI 0.32–0.64)

- **HRd BRCAwt**
  - Hazard ratio: 0.66
  - (95% CI 0.44–1.00)

- **HRp**
  - Hazard ratio: 0.65
  - (95% CI 0.49–0.87)

Gonzalez-Martin A. ESMO 2022
PRIMA/GOG-3012/ENGOT-ov26: Updated long-term PFS
Dose Interruptions and Reductions

Gonzalez-Martin A. ESMO 2022
<table>
<thead>
<tr>
<th>Treatment</th>
<th>PRIMA&lt;sup&gt;1, 6&lt;/sup&gt; (N=733)</th>
<th>PRIME&lt;sup&gt;2&lt;/sup&gt; (N=384) (study in China)</th>
<th>SOLO-1&lt;sup&gt;3, 8&lt;/sup&gt; (N=391)</th>
<th>ATHENA-MONO&lt;sup&gt;4&lt;/sup&gt; (N=538)</th>
<th>PAOLA-1&lt;sup&gt;5, 7&lt;/sup&gt; (N=806)</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>Olaparib/Bev vs Bev</td>
</tr>
<tr>
<td><strong>PFS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ITT</td>
<td></td>
<td>13.8 vs 8.2</td>
<td>24.8 vs 8.3</td>
<td>20.2 vs 9.2</td>
<td>22.1 vs 16.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.66 (0.56-0.79)</td>
<td>0.45 (0.34-0.60)</td>
<td>0.52 (0.40-0.68)</td>
<td>0.59 (0.49-0.72)</td>
</tr>
<tr>
<td><strong>BRCAwt/HRp</strong></td>
<td></td>
<td>8.1 vs 5.4*</td>
<td>14.0 vs 5.5</td>
<td>12.1 vs 9.1</td>
<td>16.9 vs 16.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.49 (0.49-0.87)</td>
<td>0.41 (0.25-0.65)</td>
<td>0.65 (0.45-0.95)</td>
<td>1.00 (0.75-1.35)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>BRCAwt/HRd</strong></td>
<td></td>
<td>19.6 vs 8.2*</td>
<td>24.8 vs 11.1</td>
<td>20.3 vs 9.2</td>
<td>28.1 vs 16.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.66 (0.44-1.00)</td>
<td>0.58 (0.36-0.93)</td>
<td>0.58 (0.33-1.01)</td>
<td>0.43 (0.28-0.66)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>BRCAm</strong></td>
<td></td>
<td>22.1 vs 10.9</td>
<td>NR vs 10.8</td>
<td>56.0 vs 13.8</td>
<td>37.2 vs 21.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.45 (0.32-0.64)</td>
<td>0.40 (0.23-0.68)</td>
<td>0.33 (0.25-0.43)</td>
<td>0.31 (0.20-0.47)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>OS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ITT</td>
<td></td>
<td></td>
<td></td>
<td>56.5 vs 51.6</td>
<td>0.92 (0.76-1.12)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>36.8 vs 40.4</td>
<td>1.19 (0.88-1.63)</td>
</tr>
<tr>
<td>HRD negative</td>
<td></td>
<td></td>
<td></td>
<td>NR vs 52</td>
<td>0.71 (0.45-1.13)</td>
</tr>
<tr>
<td>HRd/Excluding BRCAm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRCAm</td>
<td>NR vs 75.2</td>
<td>0.55 (0.40-0.76)</td>
<td></td>
<td>75.2 vs 66.9</td>
<td>0.60 (0.39-0.93)</td>
</tr>
</tbody>
</table>

### Key Phase III Studies of Front-Line Intraperitoneal Therapy

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Eligibility</th>
<th>Median OS</th>
<th>Hazard ratio</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWOG 8501/GOG 104¹</td>
<td>546</td>
<td>Stage III, ≤2 cm residual</td>
<td>IP: 49 mo</td>
<td>0.76</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IV: 41 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GOG 114/SWOG 9227²</td>
<td>462</td>
<td>Stage III, ≤1 cm residual</td>
<td>IP: 63.2 mo</td>
<td>0.81</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IV: 52.2 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GOG 172³</td>
<td>415</td>
<td>Stage III, ≤1 cm residual</td>
<td>IP: 65.6 mo</td>
<td>0.75</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IV: 49.7 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GOG 252⁴</td>
<td>1560</td>
<td>Stage II-IV, Maximal CRS</td>
<td>IV: 75.5 mo. IPcarbo: 78.2 mo. IP cis: 72.9 mo.</td>
<td>0.95 1.05</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Retrospective analysis of GOG 114 and 172⁵**
- N = 876, median follow-up 10.7 years: Median OS for IP vs IV: **61.8 vs 51.4 mo**, HR = 0.77, p = 0.002

**Subgroup analysis of GOG 252⁴**
- Stage III R0/R1: Median OS for IPcarbo, IPcis vs IV: **78.2, 74.1 vs 74.6 mo**
- Stage II/III R0/R1: Median OS for IPcarbo, IPcis vs IV: **84.7, 76.3 vs 80.0 mo**
- Stage II/III R0: Median OS for IPcarbo, IPcis vs IV: **104.8, NR vs 98.8 mo**

Dutch Gynaecological Oncology Audit Observational Study: N=668

HIPEC: Longer LOS >7 days OR 3.9 (p<0.001) and increased complications OR 1.5 (p=0.03). No association with incidence severe complications (Clavien-Dindo ≥G3) (OR 0.7, p=0.38) and 30-day-mortality.

**Median RFS (mos)**

<table>
<thead>
<tr>
<th></th>
<th>HIPEC</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>14.2</td>
<td>10.7</td>
</tr>
</tbody>
</table>

**Median OS (mos)**

<table>
<thead>
<tr>
<th></th>
<th>HIPEC</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>45.7</td>
<td>33.9</td>
</tr>
</tbody>
</table>

**Safety outcomes**

similar – Grade 3/4 toxicity 0-6% in HIPEC arm

**Elective colostomy:**

72% HIPEC vs 43% no HIPEC p=0.04

Dutch Gynaecological Oncology Audit Observational Study: N=668

HIPEC: Longer LOS >7 days OR 3.9 (p<0.001) and increased complications OR 1.5 (p=0.03). No association with incidence severe complications (Clavien-Dindo ≥G3) (OR 0.7, p=0.38) and 30-day-mortality.
Adverse Events | HIPEC N (%) | Control N (%) | P
--- | --- | --- | ---
Increased PT INR | 75 (81.5%) | 60 (65.2%) | 0.01
Acute kidney injury | 19 (20.7%) | 6 (6.5%) | 0.005
Electrolyte disturbance | 74 (80.4%) | 41 (44.6%) | 0.001
Grade 3 or 4 | 86 (93.5%) | 80 (87%) |
Subgroup Analysis: PDS and NACT/IDS

N=107

N=77

Lim et al. JAMA Surg 2022

NCT01091636
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MADE TO MEASURE
Phase 2 Randomized Clinical Trial Results (Oregovomab + Chemotherapy)

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

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

**FLORA-5/QPT-ORE-005/GOG 3035**

Randomized Trial of Oregovomab and Chemotherapy in Newly Diagnosed Stage III & IV Ovarian, Primary Peritoneal, and Fallopian Tube Cancer

- Newly diagnosed stage III or IV epithelial ovarian, tubal, or peritoneal cancer
- BRCA wild-type
- ECOG PS 0-1
- Primary or interval cytoreductive surgery to R1 or R0

**N=602**

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Total Screened</th>
<th>In Screening</th>
<th>Screening Failure</th>
<th>Total Randomized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort 1</td>
<td>394</td>
<td>9</td>
<td>141</td>
<td>244</td>
</tr>
<tr>
<td>Cohort 2</td>
<td>231</td>
<td>7</td>
<td>53</td>
<td>171</td>
</tr>
</tbody>
</table>

Primary endpoint: PFS – IA; Secondary endpoints: OS, Safety, QoL
Exploratory: iRECIST, TFST, TSST, PFS2, Biomarkers

**PI: Alvarez Secord A, Barroilhet L**

NCT04498117
HOTT/GOG 3068: HIPEC in Ovarian Treatment Trial

Randomized Trial of Hyperthermic Intraperitoneal Chemotherapy (HIPEC) with Cisplatin vs. no HIPEC at Time of Optimal Interval Cytoreductive Surgery followed by Niraparib Maintenance in Newly Diagnosed Stage III & IV Ovarian, Primary Peritoneal, and Fallopian Tube Cancer

**Stratification:**
- HRD status
- R0 vs R1
- Stage (III vs IV)

**Primary endpoint:** PFS
**Secondary endpoints:** OS, Toxicity, Prognostic effects of HRD, R0/1, Stage III/IV

**PI:** Zivanovic O, Randall L
THANK YOU

We WIN when we do it together . . .