Platinum-sensitive recurrent ovarian cancer Diversity and Heath Equity in Gynecologic Cancer Clinical Trials

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Disclosures

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Advisory boards: Tesaro/GSK Inc, AstraZeneca, Merck, Eisai, Lily, Mersana, Sutro, Toray, SeaGen, Celsion, Imab, Onconova, Toray, GOG Foundation
Outline

• Ariel 3
• Solo 3
• Atalante
• Diversity in Gynecologic Cancer Trial Enrollment
• Upcoming Phase 3 Trials in PSOC
Overall Survival Results From ARIEL3: A Phase 3 Randomised, Double-blind Study of Rucaparib vs Placebo Following Response to Platinum-Based Chemotherapy for Recurrent Ovarian Carcinoma

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ARIEL3 Study Design

### Patient Eligibility
- High-grade serous or endometrioid epithelial ovarian, fallopian tube, or primary peritoneal cancers
- Sensitive to penultimate platinum
- Responding to most recent platinum (CR or PR)*
- CA-125 within normal range
- No restriction on size of residual tumour
  - ECOG PS ≤1
- No prior PARP inhibitors

### Stratification
- HRR status by NGS mutation analysis
  - BRCA1 or BRCA2
  - Non-BRCA HRR gene
  - None of the above
- Response to recent platinum
  - CR
  - PR
- Progression-free interval after penultimate platinum
  - 6 to ≤12 months
  - >12 months

### Randomisation 2:1
- Rucaparib 600 mg BID
  - n=375
- Placebo BID
  - n=189

### Follow-up
- Until disease progression, death, or withdrawal

- Rucaparib 600 mg BID
  - n=375
- Placebo BID
  - n=189

- Until disease progression, death, or withdrawal
- 28 days after last treatment dose, then long-term follow-up every 12 weeks

### Primary endpoint:
Investigator-assessed PFS
Key secondary endpoint: BICR-assessed PFS

### Final analysis*: completed at 70% data maturity
- Overall survival
- PFS2
- CFI
- TFST
- TSST
- Safety

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A hypothesis of superiority in overall survival was not prespecified in the protocol/study design.

*CR (defined by RECIST) or PR (defined by RECIST and/or a GCIG CA-125 response [CA-125 within normal range]) maintained until entry to ARIEL3 (≤8 weeks from last dose of chemotherapy). Analyses were done for the molecularly defined nested cohorts (BRCA mutant, HRD, and ITT), and exploratory analyses were done in the non-nested subgroups of patients with BRCA wild-type carcinoma.

BICR, blinded independent central review; BID, twice daily; BRCA, BRCA1 and BRCA2; CA-125, cancer antigen 125; CFI, chemotherapy-free interval; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; GCIG, Gynecological Cancer InterGroup; HRD, homologous recombination deficiency; HRR, homologous recombination repair; NGS, next-generation sequencing; PARP, poly(ADP-ribose) polymerase; PD, progressive disease; PFS, progression-free survival; PFS2, PFS on the subsequent line of therapy; PR, partial response; RECIST, Response Evaluation Criteria In Solid Tumours version 1.1; TFST, time to start of first subsequent therapy; TSST, time to start of second subsequent therapy.
No statistical significance was observed in the first secondary endpoint of time to worsening in the FOSI-18 DRS-P subscale in the BRCA mutant cohort\(^1\); therefore, no further statistical significance of subsequent endpoints can be claimed.

*Includes BRCA-mutant and BRCA–wild-type/LOH-high groups.

BRCA, *BRCA1* and *BRCA2*; DRS-P, disease related symptom-physical subscale; FOSI-18, FACT-Ovarian Symptom Index-18; HRD, homologous recombination deficiency; ITT, intent-to-treat; OS, overall survival; PFS, progression-free survival.

**Patient Disposition**

<table>
<thead>
<tr>
<th></th>
<th>Rucaparib</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Randomized, % (n)</strong></td>
<td>100 (375)</td>
<td>100 (189)</td>
</tr>
<tr>
<td><strong>Treated, % (n)</strong></td>
<td>99.2 (372)</td>
<td>100 (189)</td>
</tr>
<tr>
<td><strong>Ongoing, % (n)</strong>*</td>
<td>4.0 (15)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Discontinued, % (n)</strong>†</td>
<td>96.0 (360)</td>
<td>100 (189)</td>
</tr>
<tr>
<td>Disease progression</td>
<td>69.4 (250)</td>
<td>92.1 (174)</td>
</tr>
<tr>
<td>Clinical progression</td>
<td>3.1 (11)</td>
<td>3.2 (6)</td>
</tr>
<tr>
<td>Adverse event</td>
<td>18.1 (65)</td>
<td>0.5 (1)</td>
</tr>
<tr>
<td>Withdraw consent‡</td>
<td>5.0 (18)</td>
<td>3.2 (6)</td>
</tr>
<tr>
<td>Investigator decision</td>
<td>1.1 (4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other§</td>
<td>3.3 (12)</td>
<td>1.1 (2)</td>
</tr>
</tbody>
</table>

- Median duration of follow-up was 6.4 years for rucaparib and 6.4 years for placebo

Data cutoff date: 4 April 2022.

*All patients remaining on treatment after the data cutoff date transitioned to receiving rucaparib via other access mechanisms. †Percentages in subcategories are based on the number of patients who discontinued study drug. ‡Includes categories of patient withdrew consent and withdrew consent for treatment only. §Includes categories of pregnancy, study terminated by sponsor, unknown, noncompliance, and other.
## Summary of Subsequent Therapy

<table>
<thead>
<tr>
<th>BRCA mutant</th>
<th>HRD*</th>
<th>ITT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rucaparib</strong> (n=130)</td>
<td><strong>Rucaparib</strong> (n=236)</td>
<td><strong>Rucaparib</strong> (n=375)</td>
</tr>
<tr>
<td><strong>Placebo</strong> (n=66)</td>
<td><strong>Placebo</strong> (n=118)</td>
<td><strong>Placebo</strong> (n=189)</td>
</tr>
</tbody>
</table>

### Patients without subsequent anticancer therapy, % (n)

<table>
<thead>
<tr>
<th></th>
<th>Rucaparib</th>
<th>Placebo</th>
<th>Rucaparib</th>
<th>Placebo</th>
<th>Rucaparib</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>27.7 (36)</td>
<td>9.1 (6)</td>
<td>23.7 (56)</td>
<td>11.0 (13)</td>
<td>21.9 (82)</td>
<td>11.1 (21)</td>
</tr>
</tbody>
</table>

### Disposition of patients, % (n)†

<table>
<thead>
<tr>
<th></th>
<th>Rucaparib</th>
<th>Placebo</th>
<th>Rucaparib</th>
<th>Placebo</th>
<th>Rucaparib</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ongoing</strong></td>
<td>19.4 (7)</td>
<td>0</td>
<td>25.0 (14)</td>
<td>0</td>
<td>18.3 (15)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Died</strong></td>
<td>30.6 (11)</td>
<td>33.3 (2)</td>
<td>26.8 (15)</td>
<td>38.5 (5)</td>
<td>31.7 (26)</td>
<td>38.1 (8)</td>
</tr>
<tr>
<td><strong>Other</strong>‡</td>
<td>50.0 (18)</td>
<td>66.7 (4)</td>
<td>48.2 (27)</td>
<td>61.5 (8)</td>
<td>50.0 (41)</td>
<td>61.9 (13)</td>
</tr>
</tbody>
</table>

### Patients with ≥1 subsequent anticancer therapy, % (n)

<table>
<thead>
<tr>
<th></th>
<th>Rucaparib</th>
<th>Placebo</th>
<th>Rucaparib</th>
<th>Placebo</th>
<th>Rucaparib</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>72.3 (94)</td>
<td>90.9 (60)</td>
<td>76.3 (180)</td>
<td>89.0 (105)</td>
<td>78.1 (293)</td>
<td>88.9 (168)</td>
</tr>
</tbody>
</table>

### No. subsequent regimens, % (n)§

<table>
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<tr>
<th></th>
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<th>Placebo</th>
<th>Rucaparib</th>
<th>Placebo</th>
<th>Rucaparib</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>22.3 (21)</td>
<td>23.3 (14)</td>
<td>20.0 (36)</td>
<td>19.0 (20)</td>
<td>19.1 (56)</td>
<td>20.2 (34)</td>
</tr>
<tr>
<td>2</td>
<td>30.9 (29)</td>
<td>16.7 (10)</td>
<td>26.1 (47)</td>
<td>19.0 (20)</td>
<td>25.9 (76)</td>
<td>22.0 (37)</td>
</tr>
<tr>
<td>3</td>
<td>18.1 (17)</td>
<td>13.3 (8)</td>
<td>18.9 (34)</td>
<td>17.1 (18)</td>
<td>20.5 (60)</td>
<td>17.3 (29)</td>
</tr>
<tr>
<td>≥4</td>
<td>28.7 (27)</td>
<td>46.7 (28)</td>
<td>35.0 (63)</td>
<td>44.8 (47)</td>
<td>34.5 (101)</td>
<td>40.5 (68)</td>
</tr>
</tbody>
</table>

### Median, No. (range)

<table>
<thead>
<tr>
<th></th>
<th>Rucaparib</th>
<th>Placebo</th>
<th>Rucaparib</th>
<th>Placebo</th>
<th>Rucaparib</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 (1−8)</td>
<td>3 (1−8)</td>
<td>3 (1−8)</td>
<td>3 (1−8)</td>
<td>3 (1−10)</td>
<td>3 (1−8)</td>
</tr>
</tbody>
</table>

### Patients with subsequent PARP inhibitor containing regimen, % (n)§

<table>
<thead>
<tr>
<th></th>
<th>Rucaparib</th>
<th>Placebo</th>
<th>Rucaparib</th>
<th>Placebo</th>
<th>Rucaparib</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>34.0 (32)</td>
<td>71.7 (43)</td>
<td>27.2 (49)</td>
<td>59.0 (62)</td>
<td>20.8 (61)</td>
<td>45.8 (77)</td>
</tr>
</tbody>
</table>

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Data cutoff date: 4 April 2022.

*Includes BRCA-mutant and BRCA wild-type/LOH-high groups. †Percentages are based on the number of patients without subsequent treatment reported. ‡Includes categories of withdrew consent, missing subsequent treatment data, discontinued on study but rolled over to receive treatment through rucaparib access programs or other mechanisms. §Percentages are based on the number of patients with subsequent treatment reported. BRCA, BRCA1 and BRCA2; HRD, homologous recombination deficiency; ITT, intent-to-treat; LOH, loss of heterozygosity; PARP, poly(ADP-ribose) polymerase.
Final OS: Nested Cohorts

- **BRCA-Mutant Cohort**
  - HR, 0.832
  - 95% CI, 0.581–1.192
  - Subsequent PARPi†
    - Placebo: 71.7%
    - Rucaparib: 34.0%

- **HRD Cohort***
  - HR, 1.005
  - 95% CI, 0.766–1.320
  - Subsequent PARPi†
    - Placebo: 59.0%
    - Rucaparib: 27.2%

- **ITT Population**
  - HR, 1.005
  - 95% CI, 0.809–1.223
  - Subsequent PARPi†
    - Placebo: 45.8%
    - Rucaparib: 20.8%

### Data cutoff date: 4 April 2022.

*Includes BRCA-mutant and BRCA–wild-type/LOH-high groups. †Patients receiving a PARP inhibitor during any subsequent treatment.

BRCA, **BRCA1** and **BRCA2**; CI, confidence interval; HR, hazard ratio; HRD, homologous recombination deficiency; ITT, intent-to-treat; LOH, loss of heterozygosity; mo, months; OS, overall survival; PARPi, poly(ADP-ribose) polymerase inhibitor.
Post-progression Outcomes: PFS2 (Nested Cohorts)

**BRCA-Mutant Cohort**

- **Median, mo**
  - Rucaparib (n=130): 26.122.8–32.8
  - Placebo (n=66): 18.415.7–24.4

- **HR, 95% CI**
  - Rucaparib: 0.672 (0.480–0.941)

**HRD Cohort**

- **Median, mo**
  - Rucaparib (n=236): 24.721.9–26.8
  - Placebo (n=118): 18.415.8–22.1

- **HR, 95% CI**
  - Rucaparib: 0.718 (0.558–0.923)

**ITT Population**

- **Median, mo**
  - Rucaparib (n=375): 20.6 18.7–23.5
  - Placebo (n=189): 16.3 14.6–17.9

- **HR, 95% CI**
  - Rucaparib: 0.703 (0.579–0.854)

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*Post-progression outcomes (PFS2, CFI, TFST, TSST) were similar to those previously reported at a data cutoff of December 31, 2017.1*

Data cutoff date: 4 April 2022.

*Includes BRCA-mutant and BRCA–wild-type/LOH-high groups.

BRCA, BRCA1 and BRCA2; CFI, chemotherapy-free interval; CI, confidence interval; HR, hazard ratio; HRD, homologous recombination deficiency; ITT, intent-to-treat; LOH, loss of heterozygosity; mo, months; PFS2, progression-free survival on the subsequent line of therapy; TFST, time to start of first subsequent therapy; TSST, time to start of second subsequent therapy.

Exploratory Analysis of PFS During First Subsequent Platinum-Based Chemotherapy

In the ITT population, 9.2% of patients in the rucaparib group and 25.0% in the placebo group received a PARP inhibitor maintenance therapy following their first subsequent platinum-based chemotherapy.

<table>
<thead>
<tr>
<th>ITT Population</th>
<th>PFI ≤6 months</th>
<th>PFI 6–12 months</th>
<th>PFI &gt;12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Event rate</td>
<td>Median, mo (95% CI)</td>
<td>Log-rank P value</td>
<td>Event rate</td>
</tr>
<tr>
<td>Rucaparib</td>
<td>163/174</td>
<td>7.0 (6.2–7.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Placebo</td>
<td>61/76</td>
<td>11.3 (9.9–14.1)</td>
<td></td>
</tr>
</tbody>
</table>

*Progression free survival from the start of first subsequent therapy to disease progression. †From date of last chemotherapy prior to randomisation to date of PD on ARIEL3 treatment. CI, confidence interval; ITT, intent-to-treat; mo, months; NA, not applicable; PD, disease progression; PFI, progression-free interval; PFS, progression-free survival; R, randomisation.

Data cutoff date: 4 April 2022.
Overall survival by number of prior lines of chemotherapy in patients with BRCA-mutated platinum-sensitive relapsed ovarian cancer receiving olaparib treatment or non-platinum chemotherapy in SOLO3

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For each patient, the investigator declared their choice of non-platinum chemotherapy before randomization; PLD, 50 mg/m² on Day 1 q4w; paclitaxel, 80 mg/m² on Days 1, 8, 15, and 22 q4w; gemcitabine, 1000 mg/m² on Days 1, 8, and 15 q4w; topotecan, 4 mg/m² on Days 1, 8, and 15 q4w.

BICR, blinded independent central review; bid, twice daily; ECOG, Eastern Cooperative Oncology Group; HRQoL, health-related quality of life; PARP, poly(ADP-ribose) polymerase; PFS2, second progression-free survival; PLD, pegylated liposomal doxorubicin; q4w, every 4 weeks; RECIST, Response Evaluation Criteria In Solid Tumors; TDT, time to treatment discontinuation or death; TFST, time to first subsequent therapy or death; TSST, time to second subsequent therapy or death.

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

Olaparib tablets 300 mg bid (N=178)

2:1 randomization, open-label
Stratification factors:
- Selected chemotherapy* (PLD vs paclitaxel vs gemcitabine vs topotecan)
- Number of prior lines of chemotherapy (2 or 3 vs ≥ 4)
- Time to progression after previous PBC (6–12 months vs >12 months)

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)

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

Study treatment until disease progression

Study Design

Primary ORR analysis
DCO: October 10, 2018

Final OS analysis
DCO: April 16, 2021

N=266

First patient enrolled: February 24, 2015
Last patient enrolled and randomized to receive study treatment: April 10, 2018

*For each patient, the investigator declared their choice of non-platinum chemotherapy before randomization;
†PLD, 50 mg/m² on Day 1 q4w; paclitaxel, 80 mg/m² on Days 1, 8, 15, and 22 q4w; gemcitabine, 1000 mg/m² on Days 1, 8, and 15 q4w; topotecan, 4 mg/m² on Days 1, 8, and 15 q4w.

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Post hoc subgroup: 2 prior lines of chemotherapy

PFS and OS favored olaparib over chemotherapy

**PFS**
- Events, n (%): 47 (53) vs 27 (59)
- Median PFS, months: 16.4 vs 9.0
- HR: 0.46 (95% CI 0.29–0.75)

**OS**
- Events, n (%): 53 (60) vs 23 (50)
- Median OS, months: 37.9 vs 28.8
- HR: 0.83 (95% CI 0.51–1.38)

PFS DCO: October 10, 2018; OS DCO: April 16, 2021.
**Post hoc subgroup: ≥3 prior lines of chemotherapy**

PFS numerically favored olaparib over chemotherapy; however, OS favored chemotherapy over olaparib.

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**PFS**

<table>
<thead>
<tr>
<th></th>
<th>Olaparib (N=90)</th>
<th>Chemotherapy (N=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events, n (%)</td>
<td>63 (70)</td>
<td>22 (52)</td>
</tr>
<tr>
<td>Median PFS, months</td>
<td>9.4</td>
<td>9.2</td>
</tr>
</tbody>
</table>

HR 0.87 (95% CI 0.55–1.45)

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**OS**

<table>
<thead>
<tr>
<th></th>
<th>Olaparib (N=90)</th>
<th>Chemotherapy (N=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events, n (%)</td>
<td>63 (70)</td>
<td>23 (55)</td>
</tr>
<tr>
<td>Median OS, months</td>
<td>29.9</td>
<td>39.4</td>
</tr>
</tbody>
</table>

HR 1.33 (95% CI 0.84–2.18)
### Summary of efficacy results

**2 prior lines of chemotherapy**

Favorable OS and PFS with olaparib vs chemotherapy supported by ORR

**≥3 prior lines of chemotherapy**

PFS and ORR numerically favored olaparib vs chemotherapy; however, OS favored chemotherapy vs olaparib

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>OS (Median OS, months)</th>
<th>PFS (Median PFS, months)</th>
<th>ORR (OR %)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All patients</strong></td>
<td>34.9</td>
<td>13.4</td>
<td>0.62</td>
</tr>
<tr>
<td></td>
<td>(28.9–42.8)</td>
<td>(9.2–16.6)</td>
<td>(0.43–0.91)</td>
</tr>
<tr>
<td><strong>2 prior lines of chemotherapy</strong></td>
<td>37.9</td>
<td>16.4</td>
<td>0.46</td>
</tr>
<tr>
<td></td>
<td>(28.9–51.8)</td>
<td>(9.0–22.3)</td>
<td>(0.29–0.75)</td>
</tr>
<tr>
<td><strong>3 prior lines of chemotherapy</strong></td>
<td>25.2</td>
<td>11.1</td>
<td>0.43</td>
</tr>
<tr>
<td></td>
<td>(18.2–35.3)</td>
<td>(7.4–16.3)</td>
<td>(0.24–0.80)</td>
</tr>
<tr>
<td><strong>≥3 prior lines of chemotherapy</strong></td>
<td>29.9</td>
<td>9.4</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>(21.6–39.2)</td>
<td>(7.2–11.8)</td>
<td>(0.55–1.45)</td>
</tr>
<tr>
<td><strong>≥4 prior lines of chemotherapy</strong></td>
<td>30.2</td>
<td>7.4</td>
<td>2.92</td>
</tr>
<tr>
<td></td>
<td>(21.6–38.8)</td>
<td>NC</td>
<td>(1.17–9.78)</td>
</tr>
</tbody>
</table>

**OS DCO:** April 16, 2021. **PFS and ORR DCO:** October 10, 2018.

*The analysis in all patients was performed using a stratified log-rank test with factors as recorded in Interactive Voice Response System for time to disease progression after the end of last PBC (6–12 months vs > 12 months) in the full analysis set. The analysis in the prior line of chemotherapy subgroups was performed using a single Cox proportional hazards model containing the treatment term, the subgroup covariate of interest and the treatment by subgroup interaction for each subgroup. Size of circle is proportional to the number of events. Blue band represents the 95% CI for the overall (all patients) HR;†Unconfirmed ORR is based on BICR in the measurable disease population. NC, not calculable.
A randomized, double-blinded, phase III study of atezolizumab versus placebo in patients with late relapse of epithelial ovarian, fallopian tube, or peritoneal cancer treated by platinum-based chemotherapy and bevacizumab. GINECO-OV236b/ENGOT-ov29

ATALANTE

- Relapsed non-mucinous epithelial OC
  - Platinum-free interval >6 mos
  - 1 or 2 prior chemotherapy lines
    - ECOG PS ≤1

Stratification factors
- PD-L1 ≥ 1% on immune cells vs <1% vs unknown (Ventana clone SP142)
  - Chemotherapy: Cb-PLD or gemcitabine or paclitaxel
  - Platinum-free interval: 6-12 vs >12 months

- Co-primary endpoints are progression-free survival (PFS1) according to investigator in the ITT and PD-L1-positive populations
- Secondary endpoints: TSST, TFST, OS, safety (NCI CTCAE V 4.03) and HrQoL (EORTC QLQ-C30, QOLQ OV-28, EQ5D-5L)

N=614

Biopsy

2 : 1

Carboplatin-based chemotherapy

Bevacizumab + placebo

Up to 24 months

Bevacizumab + atezolizumab

Up to 24 months
Statistical Considerations

- PFS1 was analyzed using a Cox model adjusted by stratification factors with a two-sided $\alpha$ level at 0.025 and 80% power for each PFS co-primary in the ITT and PD-L1-positive populations.

- 491 events in the ITT and 186 in the PD-L1-positive populations were expected to show a reduction in the risk of progression of 27% (difference of median PFS1 of 4.8 months) and of 38% (difference of median PFS1 of 9.0 months), respectively.

- Following a hierarchical approach, if either of the co-primary PFS1 comparisons was significant, overall survival could then be analyzed in both the ITT and PD-L1-positive populations.

* MDD=Minimal Detectable Difference
Progression-free survival (ITT)

The ATALANTE trial did not meet its primary objective: PFS1 in the ITT population.

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>N</th>
<th>Event N (%)</th>
<th>PFS at 6m % (95% CI)</th>
<th>PFS at 12m % (95% CI)</th>
<th>PFS at 18m % (95% CI)</th>
<th>Median PFS (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atezo</td>
<td>410</td>
<td>348 (85)</td>
<td>88 (85-91)</td>
<td>56 (51-61)</td>
<td>32 (28-37)</td>
<td>13.5 mos (12.2-14.2)</td>
</tr>
<tr>
<td>Placebo</td>
<td>204</td>
<td>187 (92)</td>
<td>91 (87-95)</td>
<td>46 (39-53)</td>
<td>23 (18-30)</td>
<td>11.3 mos (11.0-13.5)</td>
</tr>
</tbody>
</table>

Hazard ratio= 0.83 [0.69-0.99]  
P= .041

median follow-up: 36.6 months
The ATALANTE trial did not meet its co-primary objective: PFS1 in the PD-L1 positive population.
Overall Survival (ITT)

- Overall survival data not mature (333 events out of 491 expected): longer follow-up needed
- Trend in favor of the atezolizumab arm in the ITT population

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>N</th>
<th>Events N (%)</th>
<th>Median OS (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atezo</td>
<td>410</td>
<td>207 (51)</td>
<td>35.5 mos (32.4-41.3)</td>
</tr>
<tr>
<td>Placebo</td>
<td>204</td>
<td>126 (62)</td>
<td>30.6 mos (27.9-33.6)</td>
</tr>
</tbody>
</table>

Hazard ratio = 0.81 [0.65-1.01]
Discussion
Visualizing America’s Population By Race

The United States is a unique mosaic of cultural diversity—almost 40% of its people belong to racial or ethnic minorities.

Here, we visualize the breakdown of the U.S. population in 2019, and how this will change over time.

Projected race/ethnicity breakdown (%), 2020-2060

- 60.1% White
- 18.5% Hispanic
- 12.2% Black
- 5.6% Asian
- 0.2% Native Hawaiian/Other Pacific Islander
- 2.8% Multiple Races
- 0.7% American Indian/Alaska Native

Over time, the share of white populations is expected to decline to less than half (44%) of all Americans after 2045.

Source: Visualizing the US Population by Race, visualcapitalist.com
Disparity in Phase 1 gynecologic oncology clinical trials

Race of participants in gynecologic oncology phase 1 clinical trials according to cancer.

<table>
<thead>
<tr>
<th>Cancer site</th>
<th>White</th>
<th>Black</th>
<th>Other</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovary</td>
<td>1559 (88)</td>
<td>73 (4)</td>
<td>147 (8)</td>
<td>1779 (100)</td>
</tr>
<tr>
<td>Cervix</td>
<td>263 (48)</td>
<td>54 (10)</td>
<td>227 (42)</td>
<td>544 (100)</td>
</tr>
<tr>
<td>Endometrium</td>
<td>37 (63)</td>
<td>9 (15)</td>
<td>13 (22)</td>
<td>59 (100)</td>
</tr>
<tr>
<td>Multiple</td>
<td>91 (90)</td>
<td>4 (4)</td>
<td>6 (6)</td>
<td>101 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>1950 (79)</td>
<td>140 (6)</td>
<td>393 (16)</td>
<td>2483 (100)</td>
</tr>
</tbody>
</table>

Relation between race of participants and disease incidence in gynecologic oncology phase 1 clinical trials.

<table>
<thead>
<tr>
<th>Cancer site</th>
<th>CDC white incidence per 1000</th>
<th>CDC black incidence per 1000</th>
<th>Expected W:B ratio</th>
<th>Observed white (n)</th>
<th>Observed black (n)</th>
<th>Observed W:B ratio</th>
<th>Difference in ratios</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovary</td>
<td>13.1</td>
<td>9.7</td>
<td>1 to 0.74</td>
<td>1559</td>
<td>73</td>
<td>1 to 0.04</td>
<td>18.5-fold</td>
</tr>
<tr>
<td>Endometrial</td>
<td>24.5</td>
<td>21.2</td>
<td>1 to 0.87</td>
<td>37</td>
<td>9</td>
<td>1 to 0.24</td>
<td>3.6-fold</td>
</tr>
<tr>
<td>Cervix</td>
<td>7.9</td>
<td>10.7</td>
<td>1 to 1.35</td>
<td>263</td>
<td>54</td>
<td>1 to 0.2</td>
<td>6.8-fold</td>
</tr>
</tbody>
</table>

a Comparison between white vs black participants; other races excluded.

# New FDA Guidance on “Diversity Plans to Improve Enrolment of Participants From Underrepresented Racial and Ethnic Populations in Clinical Trials; Guidance for Industry”

1. Diverse groups need to be a part of the study to evaluate whether a study drug is effective and safe for everyone who will be administered study drug, or what side effects might emerge in one ethnic group or another.

2. Sponsors must present effectiveness and safety data by gender, age, and ethnic group (e.g., race, ethnicity, ancestry) and must identify any modifications of dose or dose interval needed for a specific subgroup, as applicable.

3. Sponsors should discuss their strategy to enrol a diverse study population at any time throughout the medical product’s development.

4. A Diversity Plan is required for clinical studies intended to support a marketing submission for a standalone BLA.

Federal Legislation passed incentives to review barriers and develop new policies for advancing equity in FDA’s Actions in June 2022*

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* Hwang and Brawley. 2022, NEJM, New Federal Incentives for Diversity in Clinical Trials

[https://www.fda.gov/media/157635/download](https://www.fda.gov/media/157635/download)
Barriers to Achieving DEI in Clinical Trials

Clinician Barriers:
- Bias
- Limited time, personnel to search for trials

Patient Barriers:
- Limited info
- Financial barriers
- Distrust
- Language

Trial Barriers:
- Restrictive eligibility criteria
- Numerous visits

Institution Barriers:
- Access to trials
- Diversity of research staff
Trends in Clinical Trial Accrual of Underrepresented Patients with Gynecologic Malignancy

Hannah Charli Karpel, MS¹, Olivia Lara, MD², Michelle Lightfoot, MD, MPH²,³, Bhavana Pothuri, MD, MS²,³

¹NYU Grossman School of Medicine, ²NYU Langone Health, ³Perlmutter Cancer Center
Clinical Trial Characteristics

Disease Sites

- Ovarian: 62.9%
- Endometrial: 25.4%
- Cervical: 11.7%

Race and Ethnicity

- NON-HISPANIC WHITE: 54.6%
- HISPANIC/LATINO/LATINA/LATINX: 16.1%
- BLACK: 15.6%
- ASIAN / ASIAN AMERICAN: 13.7%
Trial Enrollment and Disease Estimate by Race and Ethnicity

### Endometrial Cancer
- **Non-Hispanic white**: SEER Disease Estimate
- **Black**: SEER Disease Estimate
- **Asian/Asian American**: SEER Disease Estimate
- **Hispanic/Latino**: SEER Disease Estimate

### Ovarian Cancer
- **Non-Hispanic white**: SEER Disease Estimate, Trial Enrollment
- **Black**: SEER Disease Estimate, Trial Enrollment
- **Asian / Asian American**: SEER Disease Estimate, Trial Enrollment
- **Hispanic/Latino**: SEER Disease Estimate, Trial Enrollment
Clinical Trial Accrual by Race/Ethnicity Pre and Post NCI Call-to-Action in 2020

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Pre NCI (N=108), N (%)</th>
<th>Post NCI (N=97), N (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic white</td>
<td>63 (58.3)</td>
<td>49 (50.5)</td>
<td>0.3</td>
</tr>
<tr>
<td>Black</td>
<td>8 (7.4)</td>
<td>24 (24.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hispanic / Latino / Latina/Latinx</td>
<td>16 (14.8)</td>
<td>17 (17.5)</td>
<td>0.6</td>
</tr>
<tr>
<td>Asian / Asian American</td>
<td>21 (19.4)</td>
<td>7 (7.2)</td>
<td>0.01</td>
</tr>
</tbody>
</table>
Discussion
Platinum Sensitive Ovarian Cancer Recurrence: Upcoming Phase 3 Studies with ADC’s

• GOG-3049/UP-NEXT – UpRi versus placebo

• GOG-3078/GLORIOSA – Mirvetuximab/Bevacizumab versus Bevacizumab

• ADC, antibody-drug conjugate.
Upifitimab Rilsodotin (UpRi)

XMT-1536 (upifitamab rilsodotin; UpRi): A potent NaPi2b Dolaflexin ADC with a high drug-to-antibody ratio and a controlled bystander effect

Dolaflexin
Improved therapeutic index vs other platforms
- Polymer scaffold
- High Drug to Antibody Ratio (DAR) ~10-12
- Excellent drug like properties

DolaLock Payload
Efficacy without severe neutropenia, neuropathy, or ocular toxicity
- Novel auristatin
- Controlled bystander effect
- Selectively toxic to rapidly dividing cells
- Not a PgP substrate
- Induces immunogenic cell death
GOG-3049 / ENGOT-ov71-NSGO-CTU

UP-NEXT
Phase 3 Study of UpRi Monotherapy Maintenance vs Placebo in Platinum-Sensitive Recurrent Ovarian Cancer

Key Enrollment Criteria

- Patients with platinum-sensitive recurrent HGSOC
- Best response to last line of treatment: NED, CR, PR, or SD
- 2–4 prior platinum-containing chemotherapy regimens
- NaPi2b-positive (TPS ≥ 75%) tumor (archival or fresh biopsy)
- Prior PARPi required for patients with known deleterious BRCA mutations
- HGSOC, including fallopian tube and primary peritoneal cancer.
- Carboplatin or cisplatin ± paclitaxel, doxorubicin, pegylated liposomal doxorubicin, or gemcitabine.
- For SD, no increase in disease confirmed by central review of imaging and absence of CA-125 rise >15% in 7 days prior to first dose.

Primary Endpoint
- PFS by BICR

Secondary Endpoints
- PFS by Investigator
- ORR by Investigator
- OS
- Safety

NCT05329545: Trial Currently Enrolling Patients

UpRi 30mg/m² (capped at BSA 2.2 m²) IV q4w

Placebo q4w

All patients continue until PD or unacceptable AE, or up to 18 months

N=350 Randomized 2:1

AE, adverse event; BICR, blinded independent central review; BRCA mut, breast cancer susceptibility gene mutated; CR, complete response; HGSOC, high-grade serous ovarian cancer; IV, intravenous; NaPi2b, sodium-dependent phosphate transport protein 2B; NED, no evidence of disease; ORR, overall response rate; OS, overall survival; PARPi, poly(ADP-ribose) polymerase inhibitor; PD, progressive disease; PFS, progression-free survival; PR, partial response; q4w, every 4 weeks; SD, stable disease; TPS, tumor proportion score; UpRi, upifitamab rilsodotin.
Mechanism of Action of Mirvetuximab Soravtansine

Name\(^1,2\): IMGN853
Antibody target: High FR\(\alpha\)^3
Payload: DM4\(^3\)
Conjugation: Via lysine (random)^4
DAR\(^5\): ~ 3.4
MOA: Microtubule disruption^3
Bystander targeting: Yes\(^3\)

DAR, drug-to-antibody ratio; FR\(\alpha\), folate receptor alpha; MOA, mechanism of action.

RANDOMIZED PHASE 3 TRIAL FOR MIRVETUXIMAB + BEVACIZUMAB MAINTENANCE IN FRα-HIGH PLATINUM-SENSITIVE OVARIAN CANCER

INITIATING IN Q4 2022

STRATIFIED BY:
- Prior PARPi
- Prior Bevacizumab
- Response to prior therapy

PRIMARY ENDPOINT
PFS

SECONDARY ENDPOINTS
OS, DOR

ENROLLMENT AND KEY ELIGIBILITY
438 patients
Platinum-sensitive HGS ovarian cancer
1 prior platinum treatment
Prior PARPi required if BRCA+
CR, PR, or SD after treatment with platinum-based doublet + bevacizumab required

1:1 Randomization
Mirvetuximab 6 mg/kg + Bevacizumab vs Bevacizumab

FRα: folate receptor alpha; PFS: progression free survival; OS: overall survival; DOR: duration of response; PARPi: poly ADP-ribose polymerase inhibitor; BRCA: BReast CAncer gene; CR: complete response; PR: partial response; SD: stable disease