Latest Molecular-Driven Clinical Trial Data in Front-Line Advanced Endometrial Cancer

Domenica Lorusso, MD, PhD
Catholic University of Rome and Fondazione Policlinico Gemelli IRCCS

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Seoul, South Korea
Declaration of Interest

- Honoraria: AstraZeneca, Clovis, Genmab, Immunogen, Merck, Roche, Tesaro/GSK, PharmaMar
- Consulting or Advisory Role: AstraZeneca, Clovis Oncology, GSK, MSD, Immunogen, Genmab, Amgen, Seagen, PharmaMar, AstraZeneca, Merck Serono, Seagen, Genmab, Oncoinvest, Corcept, Sutro
- Speakers' Bureau: AstraZeneca, Clovis Oncology, GSK, MSD, PharmaMar
- Research Funding: Clovis (Inst), Merck (Inst), PharmaMar (Inst), Tesaro/GSK (Inst)
- Expert Testimony: Clovis
- Travel, Accommodations, Expenses: AstraZeneca, Clovis, PharmaMar, Roche, Tesaro

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## Recurrent Endometrial Cancer: Data for approved single-agent immunotherapies

<table>
<thead>
<tr>
<th>Parameter</th>
<th>KEYNOTE-158(^1): Pembrolizumab in MSI-H EC Cohorts D + K (n = 99)</th>
<th>GARNET(^2): Dostarlimab Cohort A1(^\dagger): MMRd EC (n = 106(^*))</th>
<th>GARNET(^2): Dostarlimab Cohort A2(^\dagger): pMMR EC (n = 142(^2))</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR, % (95% CI)</td>
<td>48 (37-60)</td>
<td>43.4 (33.8-53.4)</td>
<td>13.4 (8.3-20.1)</td>
</tr>
<tr>
<td>Best overall response n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>11 (14)</td>
<td>11 (10.4)</td>
<td>3 (2.1)</td>
</tr>
<tr>
<td>PR</td>
<td>27 (34)</td>
<td>35 (33.0)</td>
<td>16 (11.3)</td>
</tr>
<tr>
<td>SD</td>
<td>14 (18)</td>
<td>13 (12.3)</td>
<td>31 (21.8)</td>
</tr>
<tr>
<td>PD</td>
<td>23 (29)</td>
<td>39 (36.8)</td>
<td>77 (54.2)</td>
</tr>
<tr>
<td>Median DoR, mo (range)</td>
<td>NR (2.9-49.7+)</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

*3 patients were not evaluable for a response. \(^\dagger\)Median follow-up time for cohort A1 was 13.8 mo (9.5-22.1) and cohort A2 was 11.5 mo (11.0-25.1).
Immune-Checkpoint Inhibitor in Biomarker-Selected EC Following Platinum: Phase I GARNET Study

dMMR/MSI-H EC Cohort

mDoR: not reached
Probability of remaining in response at 2 yr: **84%**
## Historical Response to Anti–PD-1 Therapy pMMR/MSS Disease

<table>
<thead>
<tr>
<th>Parameter</th>
<th>KEYNOTE-028(^1)</th>
<th>NCT01375842(^2)</th>
<th>GARNET(^3)</th>
<th>NCT02912572(^4)</th>
<th>PHAEDRA(^5)</th>
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</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>Pembrolizumab</td>
<td>Atezolizumab</td>
<td>Dostarlimab</td>
<td>Avelumab</td>
<td>Durvalumab</td>
</tr>
<tr>
<td>Phase</td>
<td>Ib</td>
<td>Ia</td>
<td>I/II</td>
<td>II</td>
<td>II</td>
</tr>
<tr>
<td>Cohort</td>
<td>Previously treated or metastatic PD-L1+ EC</td>
<td>Incurable or metastatic EC</td>
<td>Previously treated recurrent/advanced pMMR EC</td>
<td>pMMR recurrent EC</td>
<td>Recurrent pMMR EC</td>
</tr>
<tr>
<td>Patients, n</td>
<td>23</td>
<td>15</td>
<td>142</td>
<td>16</td>
<td>35</td>
</tr>
<tr>
<td>ORR, %</td>
<td>13(^*)</td>
<td>13(†)</td>
<td>13.4</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>mPFS</td>
<td>1.8 mo</td>
<td>1.4 mo</td>
<td>--</td>
<td>1.9 mo</td>
<td>--</td>
</tr>
<tr>
<td>mOS</td>
<td>NR</td>
<td>9.6 mo</td>
<td>--</td>
<td>6.6 mo</td>
<td>--</td>
</tr>
</tbody>
</table>

Immunotherapy Combination
Leveraging ICI’s Activity

Radiotherapy
Release of neo-antigens “abscopal effect”

Chemotherapy
inducing immunogenic cell death
Release of neo-antigens
disrupting strategies that tumors use to evade immune recognition.
Study 309/KEYNOTE-775: Lenvatinib + Pembrolizumab After Platinum in Advanced EC

- Confirmatory, randomized, open-label phase III study

Patients with advanced, metastatic, or recurrent EC with measurable disease after 1 previous platinum-based CT*; ECOG PS 0/1; tissue available for MMR testing (N = 827)

Stratified by MMR status (pMMR vs dMMR), within pMMR by region, ECOG PS 0 vs 1, prior history of pelvic radiation

Lenvatinib 20 mg PO QD + Pembrolizumab 200 mg IV Q3W (n = 411)

Doxorubicin 60 mg/m² IV Q3W or Paclitaxel 80 mg/m² IV QW 3 wk on/1 wk off (n = 416)

Until PD or unacceptable toxicity

Primary endpoints: PFS by BICR, OS

- Secondary endpoints: ORR, health-related quality of life, pharmacokinetics, safety
- Key exploratory endpoint: DoR

FDA Accelerated Approval September 2019
FDA Priority Review May 2021
For patients with endometrial cancer who are not MSI-H or dMMR
Study 309/KEYNOTE-775: PFS and OS Benefit

**pMMR**

**Median PFS, Mo (95% CI)**
- LEN + pembrolizumab: 6.7 (5.6-7.4)
- Chemotherapy: 3.8 (3.6-5.0)

**HR for progression or death,**
0.60 (0.50-0.72)

**No. at risk:**
- LEN + pembrolizumab: 346, 265, 166, 116, 80, 61, 61, 55, 43, 24, 18, 14, 9, 6, 4, 1, 0, 0
- Chemotherapy: 351, 177, 83, 38, 23, 16, 12, 9, 6, 4, 3, 1, 0, 0

**Median OS, Mo (95% CI)**
- LEN + pembrolizumab: 18.0 (14.9-20.5)
- Chemotherapy: 12.2 (11.0-14.1)

**HR for progression or death,**
0.70 (0.58-0.83)

**No. at risk:**
- Chemotherapy: 351, 324, 267, 217, 171, 138, 111, 86, 71, 53, 40, 21, 6, 3, 1

**All Comers**

**Median PFS, Mo (95% CI)**
- LEN + pembrolizumab: 7.3 (5.7-7.6)
- Chemotherapy: 3.8 (3.6-4.2)

**HR for progression or death,**
0.56 (0.48-0.66)

**No. at risk:**
- Chemotherapy: 416, 214, 95, 43, 27, 19, 15, 11, 8, 6, 5, 1, 0

**Median OS, Mo (95% CI)**
- LEN + pembrolizumab: 18.7 (15.6-21.3)
- Chemotherapy: 11.9 (10.7-13.3)

**HR for progression or death,**
0.65 (0.55-0.77)

**No. at risk:**
- LEN + pembrolizumab: 411, 383, 337, 292, 258, 229, 211, 186, 160, 125, 91, 58, 30, 10, 2
- Chemotherapy: 416, 378, 305, 246, 196, 158, 129, 104, 84, 64, 49, 28, 6, 3, 1

Makker. NEJM. 2022;386:437. Makker. JCO. 2023;[Epub].
## Treatment Exposure, Safety, and Discontinuation in All Comers

<table>
<thead>
<tr>
<th></th>
<th>LEN + PEMBRO (n = 406)</th>
<th>TPC (n = 388)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median duration of treatment, days (range)</strong></td>
<td>231 (1-817)</td>
<td>104.5 (1-785)</td>
</tr>
<tr>
<td>Patients with any TEAEs (%)</td>
<td>99.8</td>
<td>99.5</td>
</tr>
<tr>
<td>Grade ≥ 3</td>
<td>88.9</td>
<td>72.7</td>
</tr>
<tr>
<td>Patients with any TEAEs leading to dose reductions (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>66.5</td>
<td>12.9</td>
</tr>
<tr>
<td>Patients with any grade TEAEs leading to discontinuation (%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>33.0</td>
<td>8.0</td>
</tr>
<tr>
<td>LEN&lt;sup&gt;c&lt;/sup&gt;</td>
<td>30.8</td>
<td>--</td>
</tr>
<tr>
<td>Pembro&lt;sup&gt;c&lt;/sup&gt;</td>
<td>18.7</td>
<td>--</td>
</tr>
<tr>
<td>LEN + pembro</td>
<td>14.0</td>
<td>--</td>
</tr>
<tr>
<td>Patients with any grade TEAEs leading to interruption (%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>69.2</td>
<td>27.1</td>
</tr>
<tr>
<td>LEN&lt;sup&gt;c&lt;/sup&gt;</td>
<td>58.6</td>
<td>--</td>
</tr>
<tr>
<td>Pembro&lt;sup&gt;c&lt;/sup&gt;</td>
<td>50.0</td>
<td>--</td>
</tr>
<tr>
<td>LEN + pembro</td>
<td>30.8</td>
<td>--</td>
</tr>
</tbody>
</table>

<sup>a</sup>Includes LEN only or Treatment of Physician’s Choice (TPC).

<sup>b</sup>Includes LEN or pembro or LEN + pembro or TPC.

<sup>c</sup>Regardless of action taken with the other drug in the combination arm.
## Study 309/KEYNOTE-775: TEAEs

<table>
<thead>
<tr>
<th>TEAE, %</th>
<th>Lenvatinib + Pembrolizumab (n = 406)</th>
<th>Doxorubicin or Paclitaxel (n = 388)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any Grade</td>
<td>Grade ≥3*</td>
</tr>
<tr>
<td>Hypertension</td>
<td>65.0</td>
<td>39.2</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>58.9</td>
<td>1.5</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>55.7</td>
<td>8.1</td>
</tr>
<tr>
<td>Nausea</td>
<td>51.7</td>
<td>3.4</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>46.6</td>
<td>7.6</td>
</tr>
<tr>
<td>Vomiting</td>
<td>37.7</td>
<td>3.0</td>
</tr>
<tr>
<td>Weight decrease</td>
<td>35.5</td>
<td>10.8</td>
</tr>
<tr>
<td>Fatigue</td>
<td>34.0</td>
<td>5.4</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>32.3</td>
<td>1.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TEAE, %</th>
<th>Lenvatinib + Pembrolizumab (n = 406)</th>
<th>Doxorubicin or Paclitaxel (n = 388)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any Grade</td>
<td>Grade ≥3*</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>30.5</td>
<td>5.2</td>
</tr>
<tr>
<td>Constipation</td>
<td>28.3</td>
<td>0.7</td>
</tr>
<tr>
<td>Anemia</td>
<td>28.1</td>
<td>6.9</td>
</tr>
<tr>
<td>UTI</td>
<td>27.6</td>
<td>4.2</td>
</tr>
<tr>
<td>Headache</td>
<td>26.4</td>
<td>0.5</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>9.1</td>
<td>2.0</td>
</tr>
<tr>
<td>Alopecia</td>
<td>5.9</td>
<td>0</td>
</tr>
</tbody>
</table>

*In the lenvatinib and pembrolizumab arm, 6.4% of patients suffered grade 5 AEs, and 5.2% of patients in the TPC arm suffered grade 5 AEs.

Makker. NEJM. 2022;386:437. Makker. JCO. 2023;[Epub].
ICls in unselected EC population
Combination approaches to enhance ICls efficacy

Radiotherapy
- Release of neo-antigens "abscopal effect"

Chemotherapy
- Inducing immunogenic cell death
- Release of neo-antigens
- Disrupting strategies that tumors use to evade immune recognition.

PARPi and ICls
- Neoantigens repertoire expansion
- Upregulation of costimulatory cell-surface receptors
- MCH II expression
- T cells infiltration

Anti-VEGF and ICls
- Vasculature normalization
- Maturation of DC
- Antigen presentation
- T cells infiltration and trafficking
- Downregulation of PD-L1 expression
Clinically Significant Data

**Dr. Mirza presents RUBY Part 1 data**

**July 31, 2023: Dostarlimab + chemotherapy approved as 1L treatment for dMMR/MSI-H EC (US)**

**Dr. Eskander presents GY018 data**

Eskander RN, Pembrolizumab plus Chemotherapy in Advanced Endometrial Cancer; N Engl J Med 2023; 388:2159-2170;

Mirza MR, Dostarlimab for Primary Advanced or Recurrent Endometrial Cancer; N Engl J Med 2023; 388:2145-2158
RUBY Part 1 | ENGOT-en6 | GOG-3031

Eligible patients
- Histologically or cytologically proven EC with recurrent or advanced disease
- Stage III or IV disease or first recurrence of EC with low potential for cure by use of radiation therapy or surgery alone or in combination
  - Carcinosarcoma, clear cell, serous, or mixed histology
- Naive to systemic therapy or systemic anticancer therapy and recurrence or PD ≥6 months after completing treatment
- ECOG PS 0 or 1
- Adequate organ function

Stratification
- MMR/MSI status
- Prior radiotherapy
- Disease status

Part 1 R 1:1 N=494
dMMR, n=118

Dostarlimab 500 mg IV
Carboplatin AUC
5 mg/mL/min
Paclitaxel 175 mg/m²
Q3W for 6 cycles

Dostarlimab 1000 mg IV
Q6W up to 3 years^a

Placebo
Carboplatin AUC
5 mg/mL/min
Paclitaxel 175 mg/m²
Q3W for 6 cycles

Placebo IV
Q6W up to 3 years^a

Follow-up

Primary end points: PFS (IA), OS
Secondary end points: PFS (BICR), PFS2, ORR/DOR/DCR, QOL, PK and immunogenicity, safety
Overall population
(dMMR/MSI-H and pMMR/MSS)
PFS maturity: 63.2%

HR, 0.64 (95% CI, 0.51-0.80)
P<0.001
Median duration of follow-up:
25.4 mo (19.2-37.8)
**RUBY Part 1 | ENGOT-en6 | GOG-3031**

**Overall population**
(dMMR/MSI-H and pMMR/MSS)
OS maturity: 33.4%

HR, 0.64 (95% CI, 0.46-0.87)
P=0.0021
Median duration of follow-up: 25.4 mo (19.2–37.8)

**Censored**

Received subsequent immunotherapy:
- 34.5% of patients in placebo arm
- 15.5% of patients in dostarlimab arm

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RUBY Molecular Classification Algorithm

In RUBY Part 1, molecular classification was performed for all participants with WES results – 400 of 494 patients.

<table>
<thead>
<tr>
<th>Integrated diagnosis</th>
<th>POLεmut (EDM)</th>
<th>dMMR (or MSI-H)</th>
<th>TP53 aberrant</th>
<th>NSMP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence in RUBY (n/N)</td>
<td>1.25% (5/400)</td>
<td>22.75% (91/400)</td>
<td>22% (88/400)</td>
<td>54% (216/400)</td>
</tr>
<tr>
<td>Diagnostic test</td>
<td>WES</td>
<td>Results of local (IHC, NGS, PCR) or central test (IHC) provided for RUBY at randomization</td>
<td>WES</td>
<td></td>
</tr>
</tbody>
</table>

EC (histological subtype independent)

POLE status
- POLε pathogenic
- POLE non-pathogenic

MMR status
- dMMR
- MMRp

p53 status
- P53-mut
- P53 WT

Efficacy per molecular classification was an exploratory analysis.
dMMR, mismatch repair deficient; IHC, immunohistochemistry; MMRp, mismatch repair proficient; MSI-H, microsatellite instability-high; mut, mutated; NGS, next generation sequencing; NSMP, no specific molecular profile; PCR, polymerase chain reaction; POLε, polymerase epsilon; SCNA, somatic copy number alterations; TIL, tumor-infiltrating lymphocytes; TLS, tertiary lymphoid structures; TP53, tumor protein 53; WES, whole exome DNA sequencing; WT, wild type.
PFS According to Molecular Subgroup

Data based on exploratory analysis based on 400 patients from the RUBY trial with known molecular classification with whole exome sequencing.

CP, carboplatin-paclitaxel; D, dostarlimab; dMMR, mismatch repair deficient; HR, hazard ratio; MSI-H, microsatellite instability–high; mut, mutated; NR, not reached; NSMP, no specific molecular profile; OS, overall survival; PBO, placebo; POLε, polymerase epsilon; TP53, tumor protein 53.
OS According to Molecular Subgroup

Data based on exploratory analysis based on 400 patients from the RUBY trial with known molecular classification with whole exome sequencing.

- **POLε mut**: TP53 mut, carboplatin-paclitaxel; D: dostarlimab; dMMR, mismatch repair deficient; HR, hazard ratio; MSI-H, microsatellite instability–high; mut, mutated; NR, not reached; NSMP, no specific molecular profile; OS, overall survival; PBO, placebo; POLε, polymerase epsilon; TP53, tumor protein 53.
Eligible patients
• Histologically confirmed recurrent or advanced (stage III, IVA, or IVB) EC
• ECOG PS of 0-2
• Results of institutional MMR IHC testing
• Submission of tumor specimens for centralized MMR IHC testing
• No prior chemotherapy treatment for EC
• Prior adjuvant chemotherapy allowed if completed ≥12 months before enrollment

Stratification
• MMR status
• ECOG PS (0, 1 or 2)
• Prior chemotherapy (yes/no)

Primary end point: PFS (IA)
Secondary end points: AEs, ORR, DOR, OS, QOL, concordance between institutional MMR IHC and centralized MMR IHC

GY018 | KEYNOTE-868

dMMR population\textsuperscript{1-3}  
PFS Maturity: 37.7%

![Graph showing probability of PFS over time with endpoints and comparison between Pembrolizumab + C/P and Placebo + C/P.]

<table>
<thead>
<tr>
<th>No. of risk (no. of events)</th>
<th>Pembrolizumab + C/P</th>
<th>Placebo + C/P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. with event, %</td>
<td>23.2 (30.6-NR)</td>
<td>52.2 (6.4-9.9)</td>
</tr>
</tbody>
</table>

HR, 0.30 (95% CI, 0.19-0.48)  
P<0.001  
Median duration of follow-up: 12 mo

GY018 | KEYNOTE-868

pMMR population\(^1-3\)

PFS Maturity: 38.1%

HR, 0.54 (95% CI, 0.41-0.71)
P<0.001

Median duration of follow-up: 7.9 mo

ICIs in unselected EC population
Combination approaches to enhance ICIs efficacy

ICIs and PARP inhibitors
- Neoantigens repertoire expansion
- Upregulation of costimulatory cell-surface receptors
- MCH II expression
- T cells infiltration

Anti-VEGF and ICIs
- Vasculature normalization
- Maturation of DC
- Antigen presentation
- T cells infiltration and trafficking
- Downregulation of PD-L1 expression

Radiotherapy
- Release of neo-antigens
- "abscopal effect"

Chemotherapy
- Inducing immunogenic cell death
- Release of neo-antigens
- Disrupting strategies that tumors use to evade immune recognition.
ICI’s Activity and PARP inhibitors: Combination Approaches

- **Phase 2: Talazoparib** 1mg PO daily and Avelumab 10 mg/kg IV every 2 weeks in N= 35 previously pretreated recurrent MSS EC patients.

- **Phase 2 DOMEC trial:** Durvalumab 1500 mg i.v. every 4 weeks and Olaparib 300mg/12h in N=50 previously pretreated recurrent (20%dMMR) EC patients.
PARPis plus ICIs in advanced Endometrial Cancer
Ongoing phase III randomized trials

**RUBY trial: Study design**
Multicenter Phase 3 study that will evaluate the efficacy and safety of DOSTARLIMAB + carboplatin-paclitaxel followed by DOSTARLIMAB + NIRAPARIB

**DUO-E trial: Study design**
Multicenter Phase 3 study that will evaluate the efficacy and safety of DURVALUMAB + carboplatin-paclitaxel followed by DURVALUMAB + OLAPARIB or DURVALUMAB or OLAPARIB

clinicaltrials.gov:01244789; clinicaltrials.gov:05173987
DuO-E study design

Patients
- Newly diagnosed FIGO 2009 Stage III/IV or recurrent endometrial cancer
- Known MMR status
- Naive to first-line systemic anticancer treatment for advanced disease
- Naive to PARP inhibitors and immune-mediated therapy
- Adjuvant chemotherapy allowed if ≥12 months from last treatment to relapse
- All histologies except sarcomas

Endpoints
- Primary
  - PFS (RECIST per investigator) in:
    - Durva vs Control
    - Durva+Ola vs Control
- Key secondary
  - OS (analytical)
  - Safety
- Exploratory
  - PFS in Durva+Ola vs Durva
  - Subgroup analyses of PFS
    - Including MMR, PD-L1, HRRm

Chemotherapy phase
- Control
  - CP* (q3w)
  - Durvalumab pbo (IV q3w)

- Durva
  - CP* (q3w)
  - Durvalumab (1120 mg IV q3w)

- Durva+Ola
  - CP* (q3w)
  - Durvalumab (1120 mg IV q3w)

Maintenance phase
- Patients without disease progression
  - Durvalumab pbo (IV q4w)
  - Olaparib pbo (tablets bid)

- Patients with disease progression, unacceptable toxicity or other discontinuation criteria were met
  - Durvalumab (1500 mg IV q4w)
  - Olaparib (300 mg tablets bid)

*N=718

Stratified by:
- MMR status (proficient vs deficient)
- Disease status (recurrent vs newly diagnosed)
- Geographic region (Asia vs non-Asia)

"Six cycles of carboplatin at an area under the concentration–time curve of 5 or 6 mg per mL/min and paclitaxel 175 mg/m². bid, twice daily; CP, carboplatin/paclitaxel; durva, durvalumab; FIGO, International Federation of Gynaecology and Obstetrics; IV, HRRm, homologous recombination repair mutation; intravenously; ola, olaparib; pbo, placebo; q3(4)w, every 3(4) weeks; R, randomisation; RECIST, Response Evaluation Criteria for Solid Tumours."
The median (range) duration of follow-up for PFS was 12.6 (0.0–31.6), 15.4 (0.0–29.1), and 15.4 (0.0–31.7) months in censored patients for the Control, Durva, and Durva+Ola arms, respectively. PFS rates were estimated by the KM method. *CI for median PFS is derived based on the Brookmeyer–Crowley method; †The primary PFS analysis for each comparison was performed separately. The HR and CI were estimated from a Cox proportional hazards model stratified by MMR and disease status. The CI was calculated using a profile likelihood approach. The P value was calculated using a log-rank test stratified by MMR and disease status. HR, hazard; ITT, intent-to-treat; KM, Kaplan–Meier.
OS: ITT population
Secondary endpoint; interim analysis

The median (range) duration of follow-up for OS was 18.6 (0.5–32.9), 18.4 (2.1–33.0), and 18.7 (1.1–33.4) months in censored patients for the Control, Durva, and Durva+Ola arms, respectively. OS rates were estimated by the KM method. *CI for median OS is derived based on the Brookmeyer–Crowley method; †The HRs were estimated from an unstratified Cox proportional hazards model. The CI was calculated using a profile likelihood approach. P values were calculated using an unstratified log-rank test. P values failed to reach statistical significance. NR, not reached.

**Events, n (%)**
- Control (N=241): 82 (34.0)
- Durva (N=238): 65 (27.3)
- Durva+Ola (N=239): 52 (21.8)

**Median OS (95% CI), months**
- Control: 25.9 (23.9–NR)
- Durva: NR (NR–NR)
- Durva+Ola: NR (NR–NR)

**HR (95% CI) vs Control†**
- Durva+Ola: 0.77 (0.56–1.07); P=0.120
- Durva: 0.59 (0.42–0.83); P=0.003

**HR (95% CI) vs Durva†**
- Durva+Ola: 0.77 (0.53–1.10)

Overall data maturity 27.7%
Subgroup analysis of PFS by MMR status

Prespecified exploratory analysis

Exploratory subgroup analysis. MMR status evaluated using the Ventana immunohistochemistry MMR panel. Rates were estimated by the KM method.

*CI for median PFS was derived based on the Brookmeyer–Crowley method; †The HR and CI were estimated from an unstratified Cox proportional hazards model.
Subgroup analysis of PFS by PD-L1 status
Prespecified exploratory analysis

PD-L1 positive (TAP≥1%; 69% of population)

PD-L1 negative (TAP<1%; 31% of population)

*CI for median PFS was derived based on the Brookmeyer–Crowley method; †The HR and CI were estimated from an unstratified Cox proportional hazards model.