Emerging opportunities in cervical cancer

Leslie M. Randall, MD, MAS
The Diane Harris Wright Professor and Director
Division of Gynecologic Oncology
Virginia Commonwealth University
Cervical Cancer Trials Advisor, GOG Partners

Friday, November 11, 2022
Cervical Cancer: Treatment Landscape

Early Stage
FIGO IA1-IB2, IIA

- Open Radical Surgery
- Risk-based Adjuvant Treatment

Locally Advanced
FIGO IB3-IVA

- Chemoradiotherapy

Metastatic (FIGO IVB), Recurrent, Persistent

- CPS <1
  - GOG 240

- CPS ≥1
  - KEYNOTE 826

SHAPE (extrafascial hysterectomy for IA2-IB1)
SENTICOL (sentinel nodes)
RACC
GOG 3043/ROCC (robotic vs open RH)
GOG 263 (adj CRT intermed risk)
GOG 724 (outback adj chemo high risk)

NRG GY006 (CRT +/- triapine)
CALLA (CRT +/- durva)
GOG 3047/KN A18 (CRT +/-pembro)
ATOMICC
ATEZOLACC
Interlace (chemo induction CRT)

GOG 3047/KN A18 (CRT +/- pembrolizumab)
ATOMICC
ATEZOLACC
Interlace (chemo induction CRT)

CPS <1: Pembrolizumab
CPS<1: Tisotumab vedotin (+/- pembrolizumab)

POST IO or CPS <1

1 NCCN Cervical Cancer Guidelines v2.2019
Outline of major IGCS/ESMO updates

• IO for locally advanced disease
  o CALLA

• IO combinations for metastatic disease
  o Checkmate 358

• Alternative targets for recurrent disease
  o SUMMIT
CALLA Study Design

15 countries, 120 sites

Eligible population
- Women aged ≥18 years
- Histologically confirmed cervical adenocarcinoma, squamous carcinoma, or adenosquamous carcinoma
- High-risk LACC (FIGO 2009)
  - Stages IB2 to IIB, node positive (N≥1)
  - Stages IIIA to IVA with any node (N≥0)
- WHO ECOG performance status of 0 or 1

Stratification factors
- Disease stage
  - FIGO Stage IB2–IIB and LN+
  - FIGO Stage ≥III and LN−
  - FIGO Stage ≥III and LN+
- Region of world

Primary Endpoint:
Progression-Free Survival\(^a\) (Investigator-assessed)

Key Secondary Endpoints:
- Overall survival
- Objective response rate
- Duration of response
- Incidence of local or distant progression / 2° malignancy
- Safety and tolerability

Chemoradiotherapy Regimen

Platinum agent
Cisplatin 40 mg/m² or carboplatin AUC2 q1w × 5 weeks

EBRT
45 Gy in 25 fractions at 1.8 Gy/fraction, 5 fractions per week

Brachytherapy
High-dose rate: 27.5–30 Gy; Low/pulsed-dose rate: 35–40 Gy

N=770
1:1

Placebo
q4w × 24 doses

Platinum + EBRT + brachytherapy

Durvalumab 1500 mg q4w × 24 doses

Key Milestones
First patient in February 2019
Last patient in December 2020
Data cutoff January 20, 2022

\(a\)According to RECIST 1.1 or histopathologic confirmation of local tumor progression.
PACIFIC: Anti-PD-L1 therapy post-CRT for locally-advanced lung cancer

Primary Endpoint: Progression-Free Survival

Hazard Ratio (95% CI)
0.84 (0.65–1.08)

P-value = 0.174

Maturity: 31%

Median follow-up: 18.5 m vs 18.4 m
Overall Survival

Probability of overall survival

Time from randomization (months)

No. at risk

Hazard Ratio (95% CI)
0.78 (0.55–1.10)
Nominal P-value = 0.156

Maturity: 17%
Median follow-up: 20.4 m vs 20.3 m

Not formally tested per multiple testing procedure
<table>
<thead>
<tr>
<th>Reference</th>
<th>N</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Javelin 100 HNSCC Lancet Oncol 2021</td>
<td>697</td>
<td>Concurrent CRT+/- avelumab</td>
</tr>
<tr>
<td>GORTEC-REACH ESMO 2021</td>
<td>430</td>
<td>Concurrent cetuximab/avelumabRT vs cisRT</td>
</tr>
<tr>
<td>PembroRad</td>
<td>131</td>
<td>Concurrent cetuximabRT vs. pembroRT</td>
</tr>
<tr>
<td>KEYNOTE 412 ESMO 2022</td>
<td>804</td>
<td>Concurrent CRT+/- pembro</td>
</tr>
</tbody>
</table>
Why a trial with so strong biological rationale failed?

Is it a matter of **strategy**?

Or a matter of **trial**?

Dr. Ketta Lorusso, discussant, IGCS
## Trial: Demographics

<table>
<thead>
<tr>
<th></th>
<th>Durvalumab + CRT (N=385)</th>
<th>Placebo + CRT (N=385)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median follow-up, months (range)</strong></td>
<td>18.5 (0–32.6)</td>
<td>18.4 (0–32.3)</td>
</tr>
<tr>
<td><strong>Median age, years</strong></td>
<td>50</td>
<td>48</td>
</tr>
<tr>
<td><strong>Race, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>130 (33.8)</td>
<td>125 (32.5)</td>
</tr>
<tr>
<td>Black/African American</td>
<td>10 (2.6)</td>
<td>12 (3.1)</td>
</tr>
<tr>
<td>Asian</td>
<td>152 (39.5)</td>
<td>148 (38.4)</td>
</tr>
<tr>
<td>American Indian/Alaska Native</td>
<td>47 (12.2)</td>
<td>56 (14.5)</td>
</tr>
<tr>
<td>Other</td>
<td>46 (11.9)</td>
<td>44 (11.4)</td>
</tr>
<tr>
<td><strong>Ethnicity, Hispanic/Latino, n (%)</strong></td>
<td>175 (45.5)</td>
<td>164 (42.6)</td>
</tr>
<tr>
<td><strong>Country/Region, a n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latin America</td>
<td>176 (45.7)</td>
<td>165 (42.9)</td>
</tr>
<tr>
<td>Asia</td>
<td>151 (39.2)</td>
<td>144 (37.4)</td>
</tr>
<tr>
<td>United States/Europe</td>
<td>40 (10.4)</td>
<td>55 (14.3)</td>
</tr>
<tr>
<td>Russian Federation</td>
<td>17 (4.4)</td>
<td>20 (5.2)</td>
</tr>
</tbody>
</table>

*aEurope comprises Hungary and Poland only; 1 patient in each arm participated from South Africa.*
# Trial: Exposure to Study Treatments

<table>
<thead>
<tr>
<th></th>
<th>Durvalumab + CRT (N=385)</th>
<th>Placebo + CRT (N=385)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Durvalumab/placebo relative dose intensity,a,d median (range), %</strong></td>
<td>95.8 (34–104)</td>
<td>95.0 (31–100)</td>
</tr>
<tr>
<td><strong>Number of patients who received CRT, n (%)</strong></td>
<td>385 (100)</td>
<td>383 (99.5)</td>
</tr>
<tr>
<td><strong>Number of cycles of cisplatin/carboplatin, n (%)b,d</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 cycles</td>
<td>199 (51.7)</td>
<td>220 (57.3)</td>
</tr>
<tr>
<td>6 cycles</td>
<td>136 (35.3)</td>
<td>126 (32.8)</td>
</tr>
<tr>
<td><strong>EBRT delivered, n (%)</strong></td>
<td>385 (100)</td>
<td>383 (99.5)</td>
</tr>
<tr>
<td>EBRT completed per protocol, n (%)</td>
<td>371 (96.4)</td>
<td>379 (98.4)</td>
</tr>
<tr>
<td><strong>EBRT total dose, median, cGy</strong></td>
<td>5400</td>
<td>5400</td>
</tr>
<tr>
<td><strong>Brachytherapy delivered, n (%)</strong></td>
<td>366 (95.1)</td>
<td>367 (95.3)</td>
</tr>
<tr>
<td>Brachytherapy completed per protocol, n (%)</td>
<td>363 (94.3)</td>
<td>360 (93.5)</td>
</tr>
<tr>
<td><strong>Equivalent EQD2 dose, median, cGy</strong></td>
<td>8387</td>
<td>8387</td>
</tr>
<tr>
<td><strong>Radiotherapy delivered in ≤59 days, n (%)</strong></td>
<td>278 (72.2)</td>
<td>279 (72.5)</td>
</tr>
</tbody>
</table>

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*aPercentage of the actual dose intensity delivered relative to the intended dose intensity through treatment discontinuation.
*b1 patient on the durvalumab + CRT arm received >6 cycles of platinum chemotherapy, all other patients not shown in table received <5 cycles.
*cReported for ex-Japan population only. Median total EBRT dose reported, Japan patients: w/ midline block (n=50/52), 5400 cGy; w/o midline block (n=2/52), 5960 cGy. Median equivalent EQD2 dose reported, Japan patients: 7027 cGy (durvalumab + CRT); 6926.5 cGy (placebo + CRT). EQD2, equi-effective dose in 2 Gy per fraction.
*dSafety analysis set; durvalumab + CRT (N=385); placebo + CRT (N=384).
Trial: Statistical Assumptions

• PFS Analysis
  — Intent-to-treat population (ITT)
  — Planned at 32% maturity
  — 90% power with 5% 2-sided alpha to detect a HR of 0.65
  — Known at the time: GOG 120 PFS at 30 months 67%, PA node- population

• OS Analysis
  — Interim analysis planned at time of PFS analysis: expected maturity 25%

Data Cutoff: January 20, 2022
Trial: PACIFIC: Anti-PD-L1 therapy post-CRT for locally-advanced lung cancer

Mileskin L et al. ASCO 2021
Trial: Primary Endpoint: Progression-Free Survival

Hazard Ratio (95% CI)
0.84 (0.65–1.08)

P-value = 0.174

Maturity: 31%
Median follow-up: 18.5 m vs 18.4 m

Probability of progression-free survival

Time from randomization (months)

Durvalumab + CRT
Placebo + CRT

No. at risk

12 m PFS rate
76.0%
73.3%

24 m PFS rate
65.9%
62.1%
# Trial: PFS Subgroup Analysis

<table>
<thead>
<tr>
<th>Lymph nodes</th>
<th>Durvalumab + CRT (Events/Total)</th>
<th>Placebo + CRT (Events/Total)</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>112/385</td>
<td>128/385</td>
<td>0.84 (0.65–1.08)</td>
</tr>
<tr>
<td>Disease stage (FIGO 2009)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IB2–IIB, node positive</td>
<td>35/134</td>
<td>39/133</td>
<td>0.87 (0.55–1.38)</td>
</tr>
<tr>
<td>Stage ≥III, LN−</td>
<td>28/108</td>
<td>26/107</td>
<td>1.11 (0.65–1.91)</td>
</tr>
<tr>
<td>Stage ≥III, LN+</td>
<td>49/143</td>
<td>63/145</td>
<td>0.71 (0.49–1.03)</td>
</tr>
<tr>
<td>Chemotherapy received</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carboplatin</td>
<td>14/26</td>
<td>9/20</td>
<td>0.94 (0.41–2.27)</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>98/359</td>
<td>118/363</td>
<td>0.82 (0.62–1.07)</td>
</tr>
<tr>
<td>PD-L1 expression status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1%</td>
<td>102/356</td>
<td>117/352</td>
<td>0.83 (0.64–1.09)</td>
</tr>
<tr>
<td>&lt;5%</td>
<td>19/60</td>
<td>25/64</td>
<td>0.73 (0.40–1.32)</td>
</tr>
<tr>
<td>≥5%</td>
<td>85/311</td>
<td>95/300</td>
<td>0.84 (0.63–1.13)</td>
</tr>
<tr>
<td>Lymph nodes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Para-aortic lymph node</td>
<td>15/47</td>
<td>20/38</td>
<td>0.60 (0.30–1.17)</td>
</tr>
<tr>
<td>No para-aortic lymph node</td>
<td>97/338</td>
<td>108/347</td>
<td>0.89 (0.68–1.17)</td>
</tr>
<tr>
<td>Pelvic lymph node</td>
<td>75/246</td>
<td>97/268</td>
<td>0.79 (0.58–1.06)</td>
</tr>
<tr>
<td>No pelvic lymph node</td>
<td>37/139</td>
<td>31/117</td>
<td>1.04 (0.64–1.68)</td>
</tr>
</tbody>
</table>

The diagram shows the favorability of Durvalumab + CRT and Placebo + CRT for different subgroups with hazard ratios and 95% confidence intervals.
## Strategy: Induction IO for locally-advanced tumors, preoperative

<table>
<thead>
<tr>
<th>Reference</th>
<th>Tumor type</th>
<th>Stage</th>
<th>N</th>
<th>Therapy</th>
<th>pCR</th>
<th>pPR</th>
</tr>
</thead>
<tbody>
<tr>
<td>PURE-01 JCO 2018</td>
<td>Urothelial</td>
<td>III</td>
<td>50</td>
<td>Pembro x 3</td>
<td>42%</td>
<td>54%</td>
</tr>
<tr>
<td>NABUCCO Nature Med 2020</td>
<td>Urothelial</td>
<td>III</td>
<td>24</td>
<td>Ipi/nivo x 3</td>
<td>46%</td>
<td>58%</td>
</tr>
<tr>
<td>RACE IT ESMO 2022</td>
<td>Urothelial</td>
<td>III</td>
<td>31</td>
<td>Nivo x 1 then RT Concurrent nivo</td>
<td>39%</td>
<td>58%</td>
</tr>
<tr>
<td>Lin et al J Imm Cancer 2022</td>
<td>Rectal</td>
<td>T3/T4</td>
<td>30</td>
<td>Short RT CAPOX + camrelizumab x 2</td>
<td>48%</td>
<td></td>
</tr>
<tr>
<td>Cercek NEJM 2022</td>
<td>Rectal</td>
<td>T2/T3</td>
<td>14</td>
<td>Dostarlimab x 8</td>
<td>100%</td>
<td></td>
</tr>
</tbody>
</table>
?Strategy: PA node + focus-highest risk

- N=36
- Increase T cell diversity, no diff between arms
- 28% pCR at 1\textsuperscript{st} brachytx
- Higher pre-tx TCR diversity assoc w/pCR
- DFS 12 mo 72%
Strategy: Randomized phase 2 translational study of pembrolizumab during and after CRT

Primary Carcinoma of the Cervix:
Squamous, adenosquamous, adenocarcinoma
Stages IB2-IVA or IB1 wpositive nodes (FIGO 2009)
PET/CT and MRI pelvis
Tissue biopsy and peripheral blood collection

PET/CT required
MRI pelvis (optional)
Tissue biopsy and peripheral blood collection

Randomized 1:1

ARM1 (sequential):
CDDP 40 mg/m² weekly for 5-6 weeks
Concurrent XRT: EBRT plus brachytherapy
3 cycles of consolidative pembrolizumab: 200 mg every 21 days beginning week 9 for 3 cycles

ARM2 (concurrent):
CDDP 40 mg/m² weekly for 5-6 weeks
3 cycles of concurrent pembrolizumab: 200 mg every 21 days beginning day 1 for 3 cycles
Concurrent XRT: EBRT plus brachytherapy

CRT was SOC per institution, complete in 8 weeks

Duska L, et al. SGO 2020
IO Combos Metastatic Disease
CheckMate 358

Key eligibility criteria:
- Histologically confirmed squamous cell carcinoma of the cervix
  - Recurrent/metastatic disease
- ≤ 2 prior therapies for recurrent/metastatic disease
- ≥ 1 target lesion
- ECOG performance status 0-1
- HPV: positive or unknown

- Database lock: December 13, 2021
- Minimum follow-up: 24 months

Treatment until disease progression, unacceptable toxicity, withdrawal of consent, or maximum of 24 months:

- Nivolumab (n = 19)
  - NIVO 240 mg Q2W

- N3+I1 (n = 45)
  - NIVO 3 mg/kg Q2W + IPI 1 mg/kg Q6W

- N1+I3 (n = 45)
  - NIVO 1 mg/kg Q2W + IPI 3 mg/kg Q2W x 4 cycles followed by NIVO 240 mg Q2W

First line: n = 44
Second line: n = 23

Assessments:
- Imaging every 8 weeks for year 1 of treatment
- Imaging every 12 weeks beyond year 1

Primary endpoint:
- Investigator-assessed ORR

Secondary endpoints:
- DOR
- Investigator assessed PFS
- OS

For all treatment arms, an ORR of ≥ 10% will be considered of clinical interest, and an ORR of ≥ 25% will be considered of strong clinical interest.

Oaknin A et al ESMO 2022
Investigator-assessed objective response rate

<table>
<thead>
<tr>
<th></th>
<th>NIVO</th>
<th>N3+I1 (randomized)</th>
<th>N1+I3 Pooled (randomized + expansion)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (n = 19)</td>
<td>All (n = 45)</td>
<td>1L (n = 18)</td>
</tr>
<tr>
<td>ORR, % (95% CI)</td>
<td>26 (9-51)</td>
<td>31 (18-47)</td>
<td>39 (17-64)</td>
</tr>
<tr>
<td>PD-L1 ≥ 1%, responders/evaluable (%)</td>
<td>3/11 (27)</td>
<td>9/25 (36)</td>
<td>4/12 (33)</td>
</tr>
<tr>
<td>PD-L1 &lt; 1%, responders/evaluable (%)</td>
<td>1/7 (14)</td>
<td>3/15 (20)</td>
<td>2/3 (67)</td>
</tr>
<tr>
<td>Median DOR, months (95% CI)</td>
<td>NR (35.3-NR)</td>
<td>24.4 (8.7-NR)</td>
<td>34.6 (6.6-NR)</td>
</tr>
</tbody>
</table>

- As expected, more responses were noted in the first- vs second-or-later-line setting
- N1+I3 showed a higher response rate than N3+I1 in both first- and second-or-later-line setting
- Durable responses were observed regardless of tumor PD-L1 status across all treatment arms
  - There are fewer responses seen in patients with PD-L1 < 1% treated with nivolumab monotherapy compared with patients with PD-L1 < 1% treated with nivolumab and ipilimumab

*PD-L1 expression by tumor proportion score.
Other IO combos reported

<table>
<thead>
<tr>
<th>Drug Combination</th>
<th>n</th>
<th>ORR (95% CI)</th>
<th>ORR PDL1+ (95% CI)</th>
<th>ORR PDL1- (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balstilimab + Zalifrelimab¹</td>
<td>155</td>
<td>25.6% (18.8-33.9)</td>
<td>32.8%</td>
<td>9.1%</td>
</tr>
<tr>
<td>Cadonilimab²</td>
<td>100</td>
<td>33.0% (23.9-43.1)</td>
<td>43.8% (31.4-56.7)</td>
<td></td>
</tr>
<tr>
<td>Tisotumab vedotin + pembrolizumab³</td>
<td>34</td>
<td>38.2% (22.2-56.4)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. O'Malley DM et al. JCO 2022
2. Wu XH et al. SGO 2022
3. Vergote I et al. ASCO 2022
Discussion
Ongoing Trials
Key eligibility criteria

- FIGO 2014 stage IB2–IIIB (node-positive disease) or FIGO 2014 stage III–IVA (either node-positive or node-negative disease)
- RECIST v1.1 measurable or non-measurable disease
- Treatment naive
- ECOG PS 0 or 1

Stratification factors

- IMRT or VMAT versus non-IMRT and non-VMAT
- Stage at initial diagnosis of cervical cancer (FIGO 2014 Stage IB2–IIIB [node-positive disease] vs FIGO 2014 Stage III–IVA [either node-positive or node-negative disease])
- Planned total radiotherapy dose (EBRT + brachytherapy dose) of <70 Gy vs ≥70 Gy

Endpoints

- Dual primary: PFS, OS
Key similarities in CALLA and KEYNOTE A-18

<table>
<thead>
<tr>
<th>Design</th>
<th>1:1 Randomized phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approach</td>
<td>IO during and following CRT as maintenance</td>
</tr>
<tr>
<td>Enrollment</td>
<td>Global</td>
</tr>
</tbody>
</table>
## Key differences in CALLA and KEYNOTE A-18

<table>
<thead>
<tr>
<th>Eligibility</th>
<th>CALLA</th>
<th>A-18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allows 1 pelvic node+</td>
<td></td>
<td>Must have 2 pelvic or aortic node + but allows PET SUV 2.5+</td>
</tr>
<tr>
<td>Target</td>
<td>PD-L1</td>
<td>PD1</td>
</tr>
<tr>
<td>Agent</td>
<td>Durvalumab</td>
<td>Pembrolizumab</td>
</tr>
<tr>
<td>Primary endpoint(s)</td>
<td>PFS</td>
<td>PFS/OS</td>
</tr>
<tr>
<td>Stratification factors</td>
<td>Stage Region of world</td>
<td>IMRT/VMAT vs non Total RT dose &lt;70 vs ≥70 Gy Stage (1B2-IIB node + vs III/IVA node +/-)</td>
</tr>
<tr>
<td>Enrollment</td>
<td>45% Latin America 40% Asia 10% US/Europe</td>
<td>TBD but different</td>
</tr>
</tbody>
</table>
GOG-3024/ ENGOT-cx8/innovaTV 205

A Phase 1b/2 Open-Label Trial of Tisotumab Vedotin (HuMax®-TF-ADC) Monotherapy and in Combination with Other Agents in Subjects with Recurrent or Stage IVB Cervical Cancer (Amendment 7)

Arm H

- Subjects with cervical cancer who have not received prior systemic therapy for recurrent or Stage IVB disease.
  - First line
  - ECOG 0-1
  - ≥1 measurable lesion disease per RECIST 1:1

- DLT evaluation period. Enroll and treat 6 subjects (TV + carbo + pembro + BEV only) through Cycle 1

- Safety committee review

- Expand enrollment to ~30 subjects (TV + carbo + pembro + BEV)

- First six enrolled patients must be eligible for bevacizumab.

- First six patients will be evaluated by an internal safety committee for dose limiting toxicities (DLT) after their first cycle (approximately 21 days).
  - DLTs <2 patients then enrollment is expanded for a total of approximately 30 patients.
  - DLTs ≥2 patients, enrollment will be paused, and a comprehensive review is conducted.

- At full enrollment, there will be approximately 30 patients (mix of BEV eligible and BEV ineligible).
GOG-3028 - A Two Arm, Randomized, Non Comparative Blinded Phase 2 Trial of Balstilimab +/- Zalifrelimab in Second Line Cervical Cancer

RaPiDS

Patient Eligibility

- Cervical cancer that has relapsed after a platinum-based treatment (first line) regimen for advanced (recurrent, unresectable, or metastatic) disease
- Measurable disease on imaging based on RECIST version 1.1
- ECOG PS ≤1
- Sufficient and adequate formalin-fixed paraffin embedded (FFPE)

Treatment up to 24 months

- Randomization 1:1
  - Balstilimab (300 mg) every 3 weeks
  - Placebo every 6 weeks
  - Zalifrelimab (1 mg/kg) every 6 weeks

Primary Endpoint
- ORR according to RECIST 1.1

PI: Dave O’Malley
Alternative targets for Metastatic Disease

TCGA Cervix. Nature 2017
Neratinib in HER2-mutant, recurrent/metastatic cervical cancer: updated findings from the phase 2 SUMMIT basket trial

Claire F. Friedman,1 Anishka Desouza,1 Anna Tinkler,1 Elena Corneli,1 Valentina Gambardella,1 Jonathan Goldman,1 Sherene Loi,1 Michelle L. Maliska,9 Ana Olovin1,12 Ivan Spanggaard,62 An VanderWalde,11 Arne E. Frazier,10 Be Zhang,1 Lisa D. Ellis,9 David B. Solit1

1Memorial Sloan Kettering Cancer Center, New York, NY, USA; 2UC Irvine Comprehensive Cancer Center, Los Angeles, CA, USA; 3UC San Francisco, San Francisco, California, USA; 4McGill University Health Centre, Montreal, Quebec, Canada; 5Kemetic and Columbia University Medical Center, New York, NY, USA; 6Hospital Clinico Universitario de Valencia, Valencia, Spain; 7The Northwestern University Feinberg School of Medicine, Chicago, IL, USA; 8Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; 9National Clinical Investigator, Toronto, University of California San Francisco, San Francisco, CA, USA; 10Department of Medicine, University of British Columbia, Vancouver, BC, Canada; 11UT Southwestern Medical Center, Dallas, TX, USA; 12Nanotronics Medical Imaging, LLC, Carlsbad, CA, USA

Figure 3. Individual response by duration of treatment

Figure 4. Individual best change in target lesion from baseline (RECIST-evaluable)

Adverse event, n (%) | All adverse events (N=22) | Treatment-related adverse events (N=22) |
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<tbody>
<tr>
<td></td>
<td>All grades</td>
<td>Grade ≤3</td>
</tr>
<tr>
<td>Constipation</td>
<td>12 (54.5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>20 (90.9)</td>
<td>5 (22.7)</td>
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<tr>
<td>Nausea</td>
<td>12 (54.5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>9 (40.9)</td>
<td>0 (0)</td>
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Cut-off date: July 15, 2022. *Note: Extreme responder had surgical resection at week 56 and was not evaluable.

Cut-off date: July 15, 2022. RECISt-1 evaluable patients at baseline (n=20); 2 other patients not shown were RECIST evaluable only. Co-mutation data based on local enrolment analyses.