GOG Partners
Cervical Trials in Progress: The Checkpoint Era

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GOG Partners
GOG Partners Cervical Cancer Trials in Progress

- **ENGOT Cx-11/GOG-3047/KEYNOTE-A18**: A Randomized, Phase 3, Double-Blind Study of Chemoradiotherapy With or Without Pembrolizumab for the Treatment of High-risk, Locally Advanced Cervical Cancer (US PI: Linda Duska, Co-PI: Ritu Salani)

- **GEICO 68-C/ENGOT Cx10/JGOG1084/GOG-3030**: Bevacizumab and Atezolizumab in Cervical Cancer (BEATcc): A Phase 3, Randomized Study of Chemotherapy and Bevacizumab with or without Atezolizumab for Metastatic, Recurrent, or Persistent Cervical Cancer (US PI: Leslie Randall, Co-PI: Katherine Moxley)

- **RaPiDS (GOG-3028)**: A Randomized Phase II Study of Balstilimab (AGEN2034) as Monotherapy or in Combination with Zalifrelimab (AGEN1884) in Second-Line Cervical Cancer (US PI: Dave O’Malley, Co-PI: Camille Gunderson)
Cervical Cancer: Summary of High-Risk Disease Treatment

Locally Advanced Disease (36%)
- FIGO IB3/IIb/IIIb
  - Chemoradiotherapy (preferred)
  - Surgery if Feasible

Metastatic Disease (15%)
- FIGO IVa
  - Platinum-based Chemotherapy +/- Bevacizumab
- FIGO IVb
  - Pembrolizumab (PD-L1+/MSIh/dMMR/TMBh) or Single-agent Chemotherapy

Est. 1999

1 NCCN Cervical Cancer Guidelines v2.2019
2 SEER Cancer Stat Facts: Cervical Cancer, National Cancer Institute, Bethesda, MD
Autologous TILs (LN-145) 2L+
FDA Breakthrough Designation

- 78% of patients had a reduction in tumor burden
- Median follow up is 7.4 months
- Mean number of TIL cells infused: $28 \times 10^9$
- Median number of IL-2 doses administered was 6.0

ORR = 44.4%
CR = 11.1%

KEYNOTE-158: Study Design

- Ongoing, international, multicohort, open-label, phase 2 study of pembrolizumab in select advanced solid tumors that have progressed on standard-of-care therapy (NCT02628067)

- End points
  - Primary: ORR (RECIST v1.1, independent central review)
  - Secondary: DOR, PFS, OS

Patients
- Age ≥18 years
- Histologically or cytologically confirmed advanced cervical cancer
- Progression on/intolerance to ≥1 line of standard therapy
- ECOG PS 0 or 1
- Tumor sample for biomarker analysis

Pembrolizumab 200 mg Q3W
- Treat for 2 years\(^a\) or until progression\(^b\), intolerable toxicity, or study withdrawal
- Survival follow-up

\(^a\)Patients with stable disease or better when pembrolizumab was discontinued and subsequent progressive disease were eligible to resume pembrolizumab for up to 1 year. \(^b\)Clinically stable patients remained on pembrolizumab until progressive disease was confirmed in a second assessment performed ≥4 weeks later. DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; OS, overall survival; ORR, objective response rate; PFS, progression-free survival; Q3W, once every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.
### Summary of Response (RECIST v1.1, Central Review)

<table>
<thead>
<tr>
<th></th>
<th>Overall&lt;sup&gt;a&lt;/sup&gt; N = 98</th>
<th>PD-L1 Positive&lt;sup&gt;b&lt;/sup&gt; n = 82</th>
<th>PD-L1 Negative&lt;sup&gt;c&lt;/sup&gt; n = 15</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ORR,&lt;sup&gt;d&lt;/sup&gt; % (95% CI)</strong></td>
<td>14.3 (8.0-22.8)</td>
<td>17.1 (9.7-27.0)</td>
<td>0 (0-21.8)</td>
</tr>
<tr>
<td><strong>Best overall response, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete response</td>
<td>5 (5.1)</td>
<td>5 (6.1)</td>
<td>0</td>
</tr>
<tr>
<td>Partial response</td>
<td>9 (9.2)</td>
<td>9 (11.0)</td>
<td>0</td>
</tr>
<tr>
<td>Stable disease</td>
<td>16 (16.3)</td>
<td>13 (15.9)</td>
<td>3 (20.0)</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>55 (56.1)</td>
<td>44 (53.7)</td>
<td>10 (66.7)</td>
</tr>
<tr>
<td>Non-evaluable&lt;sup&gt;e&lt;/sup&gt;</td>
<td>4 (4.1)</td>
<td>3 (3.7)</td>
<td>1 (6.7)</td>
</tr>
<tr>
<td>No assessment&lt;sup&gt;f&lt;/sup&gt;</td>
<td>9 (9.2)</td>
<td>8 (9.8)</td>
<td>1 (6.7)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Includes 1 patient with unknown PD-L1 expression level. <sup>b</sup>CPS ≥1. <sup>c</sup>CPS <1. <sup>d</sup>At the time of analysis, all responses were confirmed. <sup>e</sup>Target lesions not captured on ≥1 post-baseline imaging assessment. <sup>f</sup>Post-baseline tumor assessment not performed. Data cutoff date: June 27, 2019.
GOG 3016/ENGOT-cx9: Randomized Phase III Trial of Cemiplimab Versus Investigator’s Choice Chemotherapy in Cervical Cancer: “EMPOWER- CERVICAL 1”

Metastatic cervical cancer resistant to platinum-based chemotherapy, ≥ Second-Line (N = 436)
ECOG PS 0 or 1

Primary Endpoint is OS

Statistical Considerations for Study Design

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Power</td>
<td>90%</td>
</tr>
<tr>
<td>Median Survival</td>
<td>7 months</td>
</tr>
<tr>
<td>Hazard Ratio</td>
<td>0.7</td>
</tr>
<tr>
<td>Timing of Final Analysis (Ha)</td>
<td>30.5 months</td>
</tr>
</tbody>
</table>

Cemiplimab 350 mg IV every 3 weeks

Accrual completed 5/29/2020
## EMPOWER/GOG 3016/ENGOT cx-9
### Interim analysis press release 3.15.2021

<table>
<thead>
<tr>
<th></th>
<th>Median OS (mos.) Cemiplimab</th>
<th>Median OS (mos.) MD choice chemotherapy</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intent to treat (ITT)</td>
<td>12</td>
<td>8.5</td>
<td>0.69 (0.56-0.84) p&lt;0.001</td>
</tr>
<tr>
<td>Squamous cell histology</td>
<td>11</td>
<td>8.8</td>
<td>0.73 (0.58-0.91) p=0.003</td>
</tr>
<tr>
<td>Adenocarcinoma histology</td>
<td>13.3</td>
<td>7</td>
<td>0.56 (0.36-0.85) p&lt;0.005</td>
</tr>
</tbody>
</table>

Toxicity-related treatment discontinuations in 8% cemiplimab vs 5% chemotherapy patients.

ENGOT cx-11/GOG-3047/KEYNOTE-A18
A Randomized, Phase 3, Double-Blind Study of Chemoradiotherapy With or Without Pembrolizumab for the Treatment of High-risk, Locally Advanced Cervical Cancer

D. Lorusso¹; Y. Xiang²; N. Colombo³; R.L. Coleman⁴; L.M. Randall⁵; L. Duska⁶; K. Hasegawa⁷; A. Nogueira Rodrigues⁸; D. Cibula⁹; M. R. Mirza¹⁰; B. You¹¹; A. Oaknin¹²; M. Christiaens¹³; C. Taskiran¹⁴; J. Sehouli¹⁵; J. Korach¹⁶; C. Marth¹⁷; S. Keefe¹⁸; M. Puglisi¹⁸; S. Pignata¹⁹

ClinicalTrials.gov Identifier: NCT004221945

Sponsor: Merck Sharp & Dohme Corp.
PACIFIC: Phase III Trial of Durvalumab Post-CRT Maintenance for Locally-advanced, Unresectable NSCLC

Study Population
- NSCLC Stage 3 Unresectable
- Prior ≥2 cycles of platinum-based Tx with concurrent radiation
- N= 713

Efficacy Endpoints

<table>
<thead>
<tr>
<th>Primary:</th>
<th>PFS, OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary:</td>
<td>12 mo PFS, 18 mo PFS, 24 mo OS, ORR, DOR, Time to death, Time to distant metastasis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Durvalumab</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of Events/No of Patients</td>
<td>214/476</td>
</tr>
<tr>
<td>PFS (95% CI)</td>
<td>16.8 (13-18.1)</td>
</tr>
<tr>
<td>OS (95% CI)</td>
<td>NR (34.7-NR)</td>
</tr>
<tr>
<td>12 mo PFS (95% CI)</td>
<td>55.9 (51-60.4)</td>
</tr>
<tr>
<td>18 mo PFS (95% CI)</td>
<td>44.2 (37.7-50.5)</td>
</tr>
<tr>
<td>24 mo OS (95% CI)</td>
<td>66.3 (61.7-70.4)</td>
</tr>
</tbody>
</table>

Antonia et al, NEJM 2017, Antonia et al, NEJM 2018
Duska, et al, SGO 2020: 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

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

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

CRT was SOC per institution, complete in 8 weeks

Duska L, et al. SGO 2020
GOG-3047/KEYNOTE-A18: Schema

Figure 2. ENGOT-cx11/GOG 3047/KEYNOTE-A18 Study Design

Participants
High-risk locally advanced cervical cancer
- FIGO 2014 stage IB2-IIA (node-positive disease)
- FIGO 2014 stage IIIVA (either node-positive or node-negative disease)

Randomization 1:1 N=380

Cisplatin (40 mg/m² × 3 infusions [Q1W]) and radiotherapy (EBRT followed by brachytherapy) in combination with Pembrolizumab 200 mg Q3W (5 cycles)

Pembrolizumab 400 mg QGW (15 cycles)

Placebo QSW (15 cycles)

Randomization is stratified by
- Planned type of EBRT (IMRT or VMAT vs non-IMRT or non-VMAT)
- Stage at screening (FIGO 2014 stage IB2-IIA vs stage IIIA/IV)
- Planned total radiotherapy dose (<70 Gy vs ≥70 Gy)

Co-Primary Endpoints:
- PFS and OS

Secondary Endpoints:
- ORR
- DOR
- Safety
- HR-QOL

EBRT, external beam radiotherapy; FIGO, International Federation of Gynecology and Obstetrics; IMRT, intensity-modulated radiotherapy; OS, overall survival; QnW, every n weeks; VMAT, volumetric-modulated arc therapy. An optional fifth dose may be administered according to local practice.
GEICO 68-C/ENGOT Cx10/JGOG1084/GOG-3030:

Bevacizumab and Atezolizumab in Cervical Cancer (BEATcc):
A Phase 3, Randomized Study of Chemotherapy and Bevacizumab with or without Atezolizumab for Metastatic, Recurrent, or Persistent Cervical Cancer

Leslie M. Randall¹, Laurance Gladieff², Munetaka Takekuma³, Hanna Dahlstrand⁴, Kristina Lindelmann⁵, Ugo De Giorgi⁶, Nicoletta Colombo⁷, Linn Woelber⁸, Ana Oaknin⁹

ClinicalTrials.gov Identifier: NCT03556839
Sponsor: GEICO/Roche
GOG 240: Mature OS

ITT

16.8 months vs 13.3 months

Not Previously Irradiated

HR 0.77 (95% CI 0.62-0.95); P = .007

HR 0.64; 95% CI 0.37-1.10; P = .11

ITT, intent to treat
• Primary Stage IVB, persistent or recurrent carcinoma of the cervix
• Measurable disease by RECIST v1.1
• ECOG-PS: 0-1
• No previous systemic chemotherapy for advanced or recurrent disease
• Available tissue (archival or fresh)
• N=404 pts

Control Arm

Cis- or carboplatin + paclitaxel + bevacizumab (GOG 240) until disease progression, unacceptable toxicity, death or withdrawal of consent

Experimental Arm

Cis- or carboplatin + paclitaxel + bevacizumab + atezolizumab until disease progression, unacceptable toxicity, death or withdrawal of consent

Stratification Factors:
- Prior ChemoRT
- Histology: SCC vs Adeno (including AdenoSquamous)
- Chemotherapy Backbone: Cisplatin vs Carboplatin

Primary Endpoint:
Overall survival (OS)

Secondary Endpoints:
- PFS
- ORR
- DOR
- Safety
- HR-QOL

ClinicalTrials.gov Identifier: NCT03556839
# US BEAT cc/GOG-3030 Participating Sites

<table>
<thead>
<tr>
<th>Institution Name</th>
<th>PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>LSU Shreveport</td>
<td>Destin Black</td>
</tr>
<tr>
<td>University of Virginia</td>
<td>Linda Duska</td>
</tr>
<tr>
<td>Lyndon Baines Johnson Hospital</td>
<td>Michaela Onstad</td>
</tr>
<tr>
<td>Women &amp; Infants Hospital of Rhode Island</td>
<td>Cara Mathews</td>
</tr>
<tr>
<td>University of Oklahoma Health Sciences Center</td>
<td>Katherine Moxley</td>
</tr>
<tr>
<td>Virginia Commonwealth University</td>
<td>Leslie Randall</td>
</tr>
<tr>
<td>University of California, Irvine</td>
<td>Krish Tewari</td>
</tr>
</tbody>
</table>
RaPiDS (GOG-3028): A Randomized Phase II Study of Balstilimab as Monotherapy or in Combination with Zalifrelimab in Second-Line Cervical Cancer

David M O’Malley, Leslie M. Randall, Brent A. Blumenstein, Marek Ancukiewicz, Remigiusz Kaleta, and Bradley J. Monk

ClinicalTrials.gov Identifier: NCT03894215
Sponsor: Agenus
**Preliminary Data, ESMO 2020**

Two Parallel, Single-arm Trials Testing Balstilimab Alone and with Zalifrelimab in Recurrent/Metastatic Cervical Cancer

<table>
<thead>
<tr>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Histologically confirmed SCC, ASC, AC of the cervix relapsed after platinum-based treatment</td>
</tr>
<tr>
<td>• Measurable baseline dx</td>
</tr>
<tr>
<td>• ECOG PS 0–1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment (for up to 24 mon)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bal</strong> <em>(n = 161)</em></td>
</tr>
<tr>
<td>3 mg/kg q2w</td>
</tr>
<tr>
<td>(NCT03104699)</td>
</tr>
<tr>
<td><strong>Bal + Zal</strong> <em>(n = 155)</em></td>
</tr>
<tr>
<td>Bal 3 mg/kg q2w+ Zal 1 mg/kg q6w</td>
</tr>
<tr>
<td>(NCT03495882)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imaging every 6 wks through 2 yrs</td>
</tr>
</tbody>
</table>

**Primary endpoint:** Independent Review Committee (IRC) ORR by RECIST 1.1

**Secondary endpoints:** OS, PFS, DOR

O’Malley et al, ESMO 2020
Tumor Response with Balstilimab Monotherapy

• Patients with ≥1 prior chemotherapy

**ORR [95% CI]**

<table>
<thead>
<tr>
<th>Status</th>
<th>18/138 (13%) [8, 20]</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>3/138 (2%)</td>
</tr>
<tr>
<td>PR</td>
<td>15/138 (11%)</td>
</tr>
<tr>
<td>DOR (mon)</td>
<td>15.4 [1.3+, 15.4]</td>
</tr>
<tr>
<td>PD-L1 (+) (%) [95% CI]</td>
<td>15/84 (18%) [11, 27]</td>
</tr>
<tr>
<td>PD-L1 (-) (%) [95% CI]</td>
<td>3/37 (8%) [3, 21]</td>
</tr>
</tbody>
</table>
• Tumor Response with Balstilimab plus Zalifrelimab
  • Patients with ≥1 prior chemotherapy

<table>
<thead>
<tr>
<th>ORR [95% CI]</th>
<th>24/119 (20%) [14, 28]</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>6/119 (5%)</td>
</tr>
<tr>
<td>PR</td>
<td>18/119 (15%)</td>
</tr>
<tr>
<td>DOR (mon)</td>
<td>NR [1.3+, 15.4+]</td>
</tr>
<tr>
<td>PD-L1 (+) [%] [95% CI]</td>
<td>16/61 (26%) [17, 38]</td>
</tr>
<tr>
<td>PD-L1 (-) [%] [95% CI]</td>
<td>3/33 (9%) [3, 24]</td>
</tr>
</tbody>
</table>

O’Malley et al, ESMO 2020
FDA Grants Balstilimab/Zalifrelimab Dual Immunotherapy Fast Track Designation in Cervical Cancer

March 12, 2020
Jason M. Broderick

The FDA has granted a Fast Track designation to the combination of the PD-1 inhibitor balstilimab and the CTLA-inhibitor zalifrelimab for the treatment of patients with relapsed or refractory metastatic cervical cancer.
GOG-3028 - A Two Arm, Randomized, Non Comparative Blinded Phase 2 Trial of AGEN2034 (anti PD-1) as a Monotherapy or in Combination Therapy with AGEN1884 (anti-CTLA4) or with Placebo in Women with Recurrent Cervical Cancer (Second Line) – 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)

**Randomization 1:1**
- Balstilimab (300 mg) every 3 weeks
- Placebo every 6 weeks
- Treatment up to 24 months

**Primary Endpoint**
- ORR according to RECIST 1.1

**Treatment up to 24 months**
- Balstilimab (300 mg) every 3 weeks
- Placebo every 6 weeks
- Zalifrelimab (1 mg/kg) every 6 weeks
Thank You!!
lrandall@gog.org