Empower Cervical 1: R2810-ONC-1676/GOG-3016/ENGOT CX9/GEICO 72-C
GCIG Meeting

Ana Oaknin, MD PhD
Head of Gynecologic Cancer Program. Vall d’Hebron Institute of Oncology (VHIO).
Vall d’Hebron University Hospital.
GEICO Vice-Chairman
Barcelona, Spain
R2810-ONC-1676/GOG-3016/ENGOT CX9/GEICO 72-C:
Study Design
An Open Label, Randomized, Phase 3 Clinical Trial of REGN2810 Versus Therapy of Investigator’s Choice Chemotherapy in Recurrent or Metastatic Platinum-Refractory Cervical Carcinoma
Sponsored by Regeneron Pharmaceuticals

Study Population: Cervical Cancer, with progression or recurrence within 6 months of last dose of platinum therapy that was used to treat metastatic, persistent or recurrent disease

Screening, Randomization, and Stratification (N = 436): Randomization – 1:1
Stratification –
  • Histology: Squamous vs adenocarcinoma vs adenosquamous
  • Geographic Region
  • Prior Bevacizumab (Y/N)
  • ECOG PS 0 vs 1

Experimental Therapy
REGN2810
350 mg IV Q3W

Control Therapy, Investigator’s Choice
Any of the following, given IV:
  • Paclitaxel 500 mg/m² on day 1 (Q3W)
  • Topotecan 1.0 mg/m² on days 1-5 (Q3W)
  • Irinotecan 100 mg/m² weekly x 4, followed by 10-14 days rest (Q4ID)
  • Nucleoside analogs:
    • Gemcitabine 1000 mg/m² on days 1 and 8 (Q3W)
    • Vines alaflor:
    • Vinorelbine 30 mg/m² on days 1 and 8 (Q3W)

Duration of Treatment:
Treatment until progression, unacceptable toxicity, or until 96 weeks (16 cycles, each 6 weeks)
• Option for treatment beyond progression with REGN2810
• Option for retreatment for patients who complete 16 cycles and then experience PD in post-treatment follow-up

Post-Treatment Follow-up:
For safety, progression events, and OS

Study Endpoints:
Primary: OS
Key Secondary: PFS, ORR

ClinicalTrials.gov NCT03257267
R2810-ONC-1676/GOG-3016/ENGOT CX9/GEICO 72-C

ENGOT Participant Groups / Countries

<table>
<thead>
<tr>
<th>ENGOT Lead Group:</th>
<th>GEICO (Spain), PI Dr. Ana Oaknin</th>
</tr>
</thead>
<tbody>
<tr>
<td>BGOG (Belgium)</td>
<td>PGOG (Poland)</td>
</tr>
<tr>
<td>MaNGO (Italy)</td>
<td>HeCOG (Greece)</td>
</tr>
<tr>
<td>MITO (Italy)</td>
<td>NCRI (UK)</td>
</tr>
</tbody>
</table>
## R2810-ONC-1676/GOG-3016/ENGOT CX9/GEICO 72-C

### ENGOT Participant Groups / PIs

<table>
<thead>
<tr>
<th>Group</th>
<th>Sites</th>
<th>Patients</th>
<th>PI</th>
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<tbody>
<tr>
<td>GEICO</td>
<td>10</td>
<td>32</td>
<td>Dr. Ana Oaknin</td>
</tr>
<tr>
<td>PGOG</td>
<td>03</td>
<td>29</td>
<td>Dr. Beata Mackowiak</td>
</tr>
<tr>
<td>BGOG</td>
<td>07</td>
<td>35</td>
<td>Dr. Ignace Vergote</td>
</tr>
<tr>
<td>MaNGO</td>
<td>05</td>
<td>20</td>
<td>Dr. Domenica Lorusso*</td>
</tr>
<tr>
<td>MITO</td>
<td>05</td>
<td>25</td>
<td>Dr. Domenica Lorusso</td>
</tr>
<tr>
<td>HeCOG</td>
<td>06</td>
<td>28</td>
<td>Dr. Flora Zagouri</td>
</tr>
<tr>
<td>NCRI</td>
<td>05</td>
<td>20</td>
<td>Dr. Azmat Sadozye</td>
</tr>
</tbody>
</table>

41 sites, 189 patients

*Italy (MITO&MANGO) will have a common PI.*
R2810-ONC-1676/GOG-3016/ENGOT CX9/GEICO 72-C : Recruitment update

Trial Sample Size: 436 patients

<table>
<thead>
<tr>
<th></th>
<th>Global numbers</th>
<th>Total Screened subjects</th>
<th>Total Randomized</th>
<th>Total Dosed subjects</th>
<th>Total SF</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL</td>
<td>327</td>
<td>250</td>
<td>241</td>
<td>59</td>
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ClinicalTrials.gov NCT03257267
### ENGOT Groups Study Timelines

<table>
<thead>
<tr>
<th>GROUP</th>
<th>Submission Planned</th>
<th>SIV-FPI Planned</th>
</tr>
</thead>
</table>
| **GEICO**  
Dr. Ana Oaknin | Amendment for news sites addition approved in Nov 2018 | SIV(s) for 2 of the 5 the new sites performed in April 2019. The rest planned in May / June 2019 |
| **BGOG**  
Dr. Ignace Vergote | Submission already done: Mar 2019 | 1st SIV-FPI planned in July 2019 |
| **MaNGO**  
Dr. Domenica Lorusso | Submission already done: Feb 2019 | 1st SIV-FPI planned in June 2019 |
| **MITO**  
Dr. Domenica Lorusso | Submission already done: Feb 2019 | 1st SIV-FPI planned in June 2019 |
| **HeCOG**  
Dr. Flora Zagouri | Submission planned for May 2019 | 1st SIV planned in July 2019 (To be readjusted once submission is completed) |
| **NCRI**  
Dr. Azmat Sadozye | Submission approved in January 2019. HRA approval pending. | 1st SIV-FPI planned in June 2019 |
R2810-ONC-1676/GOG-3016/ENGOT CX9/GEICO 72-C:
Recruitment update
ENGOT Groups breakdown

<table>
<thead>
<tr>
<th>ENGOT Group</th>
<th>Total Sites Planned to Participate</th>
<th>ENGOT Sites Selected</th>
<th>ENGOT Sites Initiated (Activated)</th>
<th>ENGOT Screened Subjects</th>
<th>ENGOT Total Randomized</th>
<th>ENGOT Total Dosed</th>
<th>ENGOT Total Screen Fail</th>
<th>ENGOT In Screening</th>
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<tr>
<td>GEICO</td>
<td>10</td>
<td>10</td>
<td>7</td>
<td>26</td>
<td>25</td>
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<td>POGG</td>
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<tr>
<td>NCRI</td>
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<tr>
<td>MaNGO</td>
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<td>0</td>
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<td>0</td>
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</tr>
<tr>
<td>MITO</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>BGOG</td>
<td>7</td>
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<td>0</td>
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<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>HeCOG</td>
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<td>4</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>ENGOT Totals</td>
<td>41</td>
<td>39</td>
<td>10</td>
<td>57</td>
<td>49</td>
<td>46</td>
<td>6</td>
<td>5</td>
</tr>
</tbody>
</table>

ClinicalTrials.gov NCT03257267
BEATcc Trial: ENGOT-Cx10 / GEICO 68-C / JGOG1084 / GOG-3030
GCIG Meeting

Ana Oaknin, MD PhD
Head of Gynecologic Cancer Program. Vall d’Hebron Institute of Oncology(VHIO).
Vall d’Hebron University Hospital.
GEICO Vice-Chairman
Barcelona, Spain
This is a phase III, randomized, open-label, multi-center study to assess the efficacy of Atezolizumab administered concurrent to the combination of Cisplatin and Paclitaxel plus Bevacizumab in previously untreated patients with metastatic (stage IVB), persistent, or recurrent carcinoma of the cervix.

**Study Population:** 404 patients

ClinicalTrials.gov Identifier: NCT03556839
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
• N=404 pts

Control Arm

Cisplatin + paclitaxel + bevacizumab (GOG#240) until disease progression, unacceptable toxicity, death or withdrawal of consent

Experimental Arm

Cisplatin + paclitaxel + bevacizumab + atezolizumab until disease progression, unacceptable toxicity, death or withdrawal of consent

Primary Endpoints:
Overall survival (OS)

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

Stratification Factors:
• Prior concurrent Cisplatin-RDT
• Histology: SCC vs ADK (including AdenoSquamous)
• Chemotherapy Backbone: Cisplatin vs Carboplatin

A tumor specimen is mandatory at study entry. This may be an archival biopsy or, in its absence, a tumor biopsy obtained within 3 months of randomization from a non-irradiated lesion.

ClinicalTrials.gov Identifier: NCT03556839
First line standard treatment in most cervical cancer patients is based on Platinum/Paclitaxel/Bevacizumab with a median overall survival of 16.8 months.

Human papillomavirus (HPV) infection is the cause of more than 90% of cervical cancers
- PD-L1 has been shown to be a biomarker of HPV infection of the cervix and is significantly up-regulated in cervical cancer
- This suggests that anti-PD-L1 therapy may have a role in the treatment of cervical cancer

Currently, Nivolumab and Pembrolizumab have shown interesting activity in metastatic and/or recurrent cervical cancer previously pretreated with ORR of 26.33% and 12% respectively.
- Remarkably, Nivolumab, in chemo-naïve patients, achieves an ORR of 28.6% (95% CI, 3.7, 71.0). These responses were observed regardless of PD-L1 or HPV status.

Given that both VEGF and PD-L1 are important in cervical cancer pathogenesis, this study is designed to test the hypothesis that breaking of immune tolerance by PD-1/PD-L1 blockade will enhance the efficacy of anti-VEGF therapy in the treatment of patients with metastatic, persistent or recurrent cervical cancer.

**Inclusion Criteria**

- **ECOG**- Performance Status of 0-1
- **Stage IVB, persistent or recurrent cervical cancer** not amenable for curative treatment with surgery and/or radiation therapy
- **Histologies**: squamous cell, adenocarcinoma, or adenosquamous
- **No prior systemic anti-cancer therapy** for metastatic, persistent or recurrent disease.
  - Concurrent chemo-radiotherapy treatment with curative intent or adjuvant chemo-radiotherapy must have been completed ≥3 months (90 days) prior to enrollment.
  - Palliative radiation therapy (e.g., for pain or bleeding) 6 weeks prior enrollment is allowed as long as this does not affect measurable disease and patients are recovered from its symptoms.
- **Measureable disease** by RECIST v1.1 criteria
- A **tumour specimen is mandatory** at study entry
- Adequate organ function

ClinicalTrials.gov Identifier: NCT03556839
BEATcc Trial: Study Population:

Main Exclusion Criteria:

- Prior radiotherapy delivered using **cobalt** (rather than a linear accelerator)
- Patients with **Stage IVA not amenable to concurrent chemo-radiation** as primary treatment.
- Ongoing disease **involving the bladder or rectum** at screening/baseline:
  - In patients with pelvic disease, absence of tumor in the bladder or rectal mucosa must be demonstrated by MRI (preferred method, or endoscopy/cystoscopy if MRI is not easily accessible) within 28 days before enrolment
- Patients **previously treated with chemotherapy** except when used concurrently with radiation therapy. Patients who have received either **concurrent paclitaxel with radiation** therapy or **carboplatin/paclitaxel as adjuvant** therapy are **ineligible** for the study
- Evidence of **abdominal free air**
- **Bilateral hydronephrosis**, unless it can be alleviated by ureteral stent(s) or percutaneous drainage
- General Exclusion Criteria for Bevacizumab use
- General Exclusion Criteria for Atezolizumab use

ClinicalTrials.gov Identifier: NCT03556839

Version 2.0, 5 Feb 2019
1. Participant Groups / Countries

2. Sample Size

3. Recruitment Status

4. Groups Study Timelines
BEATcc Review: 
Participant Groups / Countries

- **GEICO**: 19 sites, 76 patients  
  PI: Dr. Ana Oaknin
- **AGO**: 15 sites, 60 patients  
  PI: Dr. Linn Woelber
- **GINECO**: 16 sites, 72 patients  
  PI: Dr. Laurence Gladieff
- **GOF-F**: 15 sites, 40 patients  
  PI: Dr. Leslie Randall
- **JGOG**: 8 sites, 30 patients  
  PI: Dr. Munetaka Takekuma
- **MaNGO**: 7 sites, 50 patients  
  PI: Dr. Nicoletta Colombo
- **MITO**: 10 sites, 40 patients  
  PI: Dr. Ugo De Giorgi
- **NSGO**: 7 sites, 39 patients  
  PI: Dr. Mansoor Raza Mirza
BEATcc: Sample Size: 404 patients

- GEICO: 76 patients
- AGO: 60 patients
- GINECO: 72 patients
- GOG-F: 40 patients
- MaNGO: 50 patients
- JGOG: 30 patients
- MITO: 40 patients
- NSGO: 39 patients
**BEATcc: Recruitment Status**

**Recruitment Planned vs Actual**

- **Patients Randomized**: 24 patients
- **Patients in Screening**: 2 patients
- **Screening Failures**: 4 patients
# BEATcc: Groups Study Timelines

<table>
<thead>
<tr>
<th>GROUP</th>
<th>Submission Planned</th>
<th>SIV-FPI Planned</th>
</tr>
</thead>
<tbody>
<tr>
<td>GEICO</td>
<td><strong>Submission: performed on 11Jun2018</strong></td>
<td>1st SIV: performed on 25Sep2018</td>
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<tr>
<td></td>
<td><strong>Approval: received on 3Aug2018</strong></td>
<td>FPI: occurred in October 2018</td>
</tr>
<tr>
<td>AGO</td>
<td><strong>Submission: planned end May 2019</strong></td>
<td>1st SIV: planned in August 2019</td>
</tr>
<tr>
<td></td>
<td><strong>Approval: Expected August 2019</strong></td>
<td>FPI: planned in August 2019</td>
</tr>
<tr>
<td>GINECO</td>
<td><strong>Submission: performed on 26Feb2019</strong></td>
<td>1st SIV: planned in May 2019</td>
</tr>
<tr>
<td></td>
<td>CA Approval received</td>
<td>FPI: planned in May 2019</td>
</tr>
<tr>
<td></td>
<td>EC Approval expected in May 2019</td>
<td></td>
</tr>
<tr>
<td>GOG-F</td>
<td>To be confirmed</td>
<td>To be confirmed</td>
</tr>
<tr>
<td>JGOG</td>
<td><strong>Submission: performed on 8Feb2019</strong></td>
<td>1st SIV: performed on 26Feb2019</td>
</tr>
<tr>
<td></td>
<td>Approval received</td>
<td>FPI: planned in May 2019</td>
</tr>
<tr>
<td>MaNGO</td>
<td><strong>Submission: performed on 30Mar2019</strong></td>
<td>1st SIV: planned in June 2019</td>
</tr>
<tr>
<td></td>
<td>Approval: expected by 7th June</td>
<td>FPI: planned in June 2019</td>
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<tr>
<td>MITO</td>
<td><strong>Submission: performed on 30Mar2019</strong></td>
<td>1st SIV: planned in June 2019</td>
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<tr>
<td></td>
<td>Approval: expected by 7th June</td>
<td>FPI: planned in June 2019</td>
</tr>
<tr>
<td>NSGO</td>
<td><strong>Submission: planned in May 2019</strong></td>
<td>1st SIV: planned in July/August 2019</td>
</tr>
<tr>
<td></td>
<td>Approval: expected in July/August 2019</td>
<td>FPI: planned in July / August 2019</td>
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Thank you for your attention