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ON WOMENS’ CANCER
BUILDING BRIDGES // BREAKING BARRIERS
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LIO-1: Initial Phase 2 Experience of Lucitanib + Nivolumab in Patients With Metastatic or Recurrent Cervical Cancer (NCT04042116; ENGOT-GYN3/AGO/LIO)

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Presenting Author Disclosures

• Advisory boards: Clovis Oncology, Agenus, AstraZeneca, Corcept Therapeutics, Deciphera Pharmaceuticals, Eisai Europe Limited, EMD Serono, F. Hoffmann-La Roche, GlaxoSmithKline, ImmunoGen, KL Logistics, Medison Pharma, Merck Sharp & Dohme de España, Mersana Therapeutics, Novocure GmbH, PharmaMar, prlME Oncology, Roche Farma, Sattucklabs, and Sutro Biopharma

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Unlabeled/Investigational Uses

- I will be discussing unlabeled or investigational uses of lucitanib + nivolumab in patients with cervical cancer
**Introduction**

- Lucitanib is a potent, selective inhibitor of tyrosine kinases including VEGFR1–3, PDGFRα/β, and FGFR1–3\(^1\)
- Tumor-secreted proangiogenic growth factors promote generation of new blood vessels and mediate immunosuppression, which may dampen the effect of immune checkpoint inhibitors. Therefore, inhibiting angiogenesis with a TKI may relieve immunosuppression and enhance PD-(L)1 inhibitor efficacy\(^2,3\)
- LIO-1 is a phase 1/2 study investigating lucitanib + the PD-1 inhibitor nivolumab. Here, we present data from stage 1 of the phase 2 cervical cancer cohort

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**Phase 2: Advanced, recurrent, or metastatic gynecological tumors – Simon 2-stage design**

- Endometrial cancer\(^a\) N up to 22–41
- Cervical cancer N up to 22–40
- Ovarian cancer\(^a\) N up to 22–40
- Clear-cell ovarian/ endometrial cancer N up to 22–40

**Oral lucitanib safety-based dose titration\(^b\)**

- 6 mg QD
- 8 mg QD
- 10 mg QD

C1D1 C2D1 C3D1

+ nivolumab 480 mg IV on day 1 every 28 days\(^c\)

**Primary endpoint**

Investigator-assessed confirmed best ORR by RECIST

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\(^a\)Excluding clear-cell histology. \(^b\)Lucitanib treatment until PD, unacceptable toxicity or other reason for discontinuation. \(^c\)Nivolumab treatment for up to 24 months or until PD, unacceptable toxicity or other reason for discontinuation. C, cycle; D, day; FGFR1–3, fibroblast growth factor receptors 1–3; IV, intravenous; ORR, objective response rate; PD, progressive disease; PD-1, programmed cell death receptor 1; PDGFR, platelet-derived growth factor receptors; PD-L1, programmed cell death ligand 1; QD, once daily; RECIST, Response Evaluation Criteria In Solid Tumors version 1.1; TKI, tyrosine kinase inhibitor; VEGFR1–3, vascular endothelial growth factor receptors 1–3. 1. Bello et al. Cancer Res. 2011;71:1396-405. 2. Fukumura et al. Nat Rev Clin Oncol. 2018;15:325-40. 3. Khan et al. Nat Rev Clin Oncol. 2018;15:310-24.
Key Eligibility Criteria and Baseline Characteristics: LIO-1 Cervical Cancer Cohort

• Key eligibility criteria for cervical cancer cohort:
  – Metastatic or recurrent cervical cancer
  – ≥1 prior regimen of platinum-based chemotherapy, with or without bevacizumab, for metastatic or recurrent disease
  – No prior VEGFR-TKI, or PD-(L)1 inhibitor allowed
  – Measurable disease
  – ECOG PS 0 or 1
  – Fresh biopsy or sufficient archival tumor tissue

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median years (range)</td>
<td>54.0 (36.0–77.0)</td>
</tr>
<tr>
<td>ECOG PS 0, n (%)</td>
<td>10 (45.5)</td>
</tr>
<tr>
<td>Histology, n (%)</td>
<td></td>
</tr>
<tr>
<td>Squamous</td>
<td>10 (45.5)</td>
</tr>
<tr>
<td>Adenocarcinoma (including mucinous)</td>
<td>10 (45.5)</td>
</tr>
<tr>
<td>Adenosquamous</td>
<td>2 (9.1)</td>
</tr>
<tr>
<td>Number of prior anticancer regimens, n (%)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>9 (40.9)</td>
</tr>
<tr>
<td>2</td>
<td>10 (45.5)</td>
</tr>
<tr>
<td>3</td>
<td>3 (13.6)</td>
</tr>
<tr>
<td>Prior bevacizumab, n (%)</td>
<td>10 (45.5)</td>
</tr>
</tbody>
</table>

• Primary endpoint: investigator-assessed confirmed best ORR by RECIST

Data cutoff: January 10, 2022. ECOG PS, Eastern Cooperative Oncology Group performance status; ORR, objective response rate; PD-1, programmed cell death receptor 1; PD-L1, programmed cell death ligand 1; RECIST, Response Evaluation Criteria in Solid Tumors, version 1.1; TKI, tyrosine kinase inhibitor; VEGFR, vascular endothelial growth factor receptor.
Lucitanib + Nivolumab: Investigator-Assessed Tumor Response and Time on Treatment

- Median (range) treatment duration was 4.2 (0.3–13.9) months
- Response duration ranged from 1.9+ to 13.1+ months
  - 6/7 responders had duration of response ≥3 months; 4/7 responders had received prior bevacizumab
- 3/22 responses were required to proceed to stage 2

Data cutoff: January 10, 2022. *Both patients received a maximum dose of lucitanib 6 mg. **2 received a maximum dose of lucitanib 6 mg and 3 received lucitanib 10 mg. 1 additional patient was ongoing but had no post-baseline scans at the time of data cutoff. *Unconfirmed PR. Values shown represent duration of confirmed response; ongoing responses are indicated with a +. A gap between lucitanib dosing and PD occurs when lucitanib was discontinued prior to PD. Patients may have stayed on nivolumab until PD occurred. Two patients who achieved a CR each had 2 target lesions in lymph nodes with measurements <10 mm (ie, nonpathological per RECIST). CR, confirmed complete response; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria In Solid Tumors version 1.1; SD, stable disease.
Best Change in Sum of Target Lesions from Baseline Following Lucitanib + Nivolumab Treatment

Data cutoff: January 10, 2022. CPS, combined positive score; PD-L1, programmed cell death ligand 1; RECIST, Response Evaluation Criteria In Solid Tumors version 1.1.
Summary of TEAEs in Patients Treated With Lucitanib + Nivolumab

- The only grade $\geq 3$ TEAE considered related to study treatment and reported in $\geq 2$ patients was hypertension\(^a\) (n=5 [22.7%])
- 2 (9.1%) patients reported a TEAE leading to lucitanib dose reduction:
  - Hypertension and proteinuria
- 5 (22.7%) patients and 4 (18.2%) patients reported a TEAE leading to discontinuation of lucitanib or nivolumab, respectively:
  - Lucitanib: hypertension\(^a\), myocarditis, proteinuria, and urogenital fistula
  - Nivolumab: hypertension\(^a\), intestinal obstruction, myocarditis, and thyroiditis
- 5 (22.7%) patients reported a serious TEAE considered related to study treatment:
  - Colonic fistula, hyponatremia, pancreatitis, pelvic infection, and thyroiditis

### Most common TEAEs (≥25%), n (%)

<table>
<thead>
<tr>
<th>TEAE</th>
<th>Any-grade</th>
<th>Grade ≥3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any TEAE</td>
<td>21 (95.5)</td>
<td>17 (77.3)</td>
</tr>
<tr>
<td>Hypertension(^a)</td>
<td>16 (72.7)</td>
<td>5 (22.7)</td>
</tr>
<tr>
<td>Fatigue(^b)</td>
<td>13 (59.1)</td>
<td>0</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>11 (50.0)</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>10 (45.5)</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>9 (40.9)</td>
<td>0</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>9 (40.9)</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Hypothyroidism(^c)</td>
<td>8 (36.4)</td>
<td>0</td>
</tr>
<tr>
<td>Vomiting</td>
<td>8 (36.4)</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>6 (27.3)</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Anemia</td>
<td>6 (27.3)</td>
<td>2 (9.1)</td>
</tr>
</tbody>
</table>

Data cutoff: January 10, 2022. \(^a\)Hypertension and hypertensive crisis. \(^b\)Asthenia and fatigue. \(^c\)Increased blood thyroid-stimulating hormone and hypothyroidism.

TEAE, treatment-emergent adverse event.
Conclusions

- Encouraging signs of antitumor activity were observed in patients with metastatic or recurrent cervical cancer treated with lucitanib + nivolumab.
- Adverse events have been manageable and consistent with those previously reported for lucitanib and nivolumab, and other agents of both classes.
- Target lesion reductions were observed in patients without classical biomarkers of response to checkpoint inhibitor therapy (i.e., tumors that are PD-L1 negative).
- Stage 2 has completed enrollment; follow-up and additional biomarker analysis continue.

PD-L1, programmed cell death ligand 1.
Acknowledgements

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