An estimated 40,000 women in the United States (U.S.) are diagnosed with endometrial cancer (EC) annually and it is the most common gynecologic malignancy. Treatment options for patients with recurrent or persistent EC are limited. The PI3K/mTOR pathway has been implicated in the pathogenesis of EC. Mutations in the catalytic p110 isoforms, respectively. GDC-0980 also potently inhibits mammalian target of rapamycin (mTOR) kinase with an apparent dissociation constant of 17 nM.

**Table 3. Study Drug Exposure and Discontinuation Reasons.**

<table>
<thead>
<tr>
<th>Treatment cycle</th>
<th>Diabetic (n=13)</th>
<th>Non-Diabetic (n=56)</th>
<th>All (n=69)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days on study</td>
<td>62 (9–122)</td>
<td>69 (6–226)</td>
<td>77 (6–226)</td>
</tr>
<tr>
<td>Drug exposure, median (range)</td>
<td>5 (2–99)</td>
<td>7 (4–104)</td>
<td>8 (4–104)</td>
</tr>
<tr>
<td>Discontinuation, n (%)</td>
<td>5 (38%)</td>
<td>7 (12%)</td>
<td>10 (14%)</td>
</tr>
<tr>
<td>Disease progression</td>
<td>1 (8%)</td>
<td>2 (3%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Physician decision</td>
<td>1 (8%)</td>
<td>2 (3%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Discontinued by patient</td>
<td>1 (8%)</td>
<td>2 (3%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (8%)</td>
<td>2 (3%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Median time on study was 69 (12–226) days for non-diabetic and 27 (4–122) days for diabetic.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discontinuation prior to first tumor assessment occurred in 19 patients, with 8/13 diabetics discontinued prior to Cycle 2 due to hyperglycemia (14/3 non-diabetic).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22/56 (39%) of all enrolled patients required a dose reduction</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 3. Study Drug Exposure and Discontinuation Reasons.**

- **Treatment cycle:** The treatment cycle duration is defined as the interval from the first dose of study drug to the last dose of study drug.
- **Days on study:** The days on study are defined as the duration from the first dose of study drug to the last dose of study drug.
- **Drug exposure, median (range):** The median and range of drug exposure are calculated as the total number of days on study (days on study / number of patients).
- **Discontinuation, n (%):** The number and percentage of patients who discontinued treatment due to adverse events.
- **Disease progression:** The proportion of patients who experienced disease progression.
- **Physician decision:** The proportion of patients who discontinued treatment due to physician decision.
- **Discontinued by patient:** The proportion of patients who discontinued treatment due to patient decision.
- **Other:** Other reasons for discontinuation.

**Figures:**

- **Figure 1:** Comprehensive Biomarker Analysis of Tumor Samples.
- **Figure 2:** Progression-Free Survival, Efficacy Evaluateable Population.
- **Figure 3:** Overall Survival.
- **Figure 4:** Best Percent Change from Baseline (Tumor SLD).

**References:**


**Acknowledgments:**

- Thanks to the many patients for their participation in this trial.
- Genentech, Inc. provided support for the preparation of this report.

**CONCLUSIONS:**

- Evaluation of the anti-tumor activity of 45 mg GDC-0980 daily was limited by tolerability, especially in diabetic patients.
- The trial provided data for anti-tumor activity assessed by ORR and suggests that patients with a PI3K pathway mutation may have derived enhanced benefit from GDC-0980.
- Incidence of PTVCA1/3 mutations in the endometrioid tumor samples collected in this study were lower than observed in prior published data.

**EFFICACY:**

- Efficacy was not observed in the evaluable population.
- No patients with a confirmed response had at least one lesion in a PI3K pathway gene.
- PI3K pathway alterations were highly prevalent and concurrent 21% overall and 76% in endometrioid.
- PTEN protein loss and K-RAS mutation almost exclusively in endometrioid histology.
- Copy number alterations almost exclusively in serous, clear cell, and endometrioid histology.
- Mutation location for PTVCA1/3 mutations are not restricted to hotspots.

**REFERENCES:**