BEGONIA: Phase 1b/2 Study of Durvalumab (D) Combinations in Locally Advanced/Metastatic Triple-Negative Breast Cancer (TNBC): Results from Arm D + P + Capivasertib (C), and Arm 5 D + P + Oleclumab (O)

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Keyvo\textsuperscript{TM} (capivasertib) is a small molecule inhibitor of dual AKT1/2/3 and IRAK1 kinases currently in clinical development. The BEGONIA trial was a phase 1b/2 study that examined the combination of durvalumab (D) with olaparib (P), capivasertib (C), or oleclumab (O) in women with locally advanced or metastatic triple-negative breast cancer (mTNBC).

**Results**

- Of the 9 patients evaluable for PI3K pathway alterations in the D + P + C arm, 3 (33.3%) had a confirmed objective response (ORR) and 6 (66.7%) had stable disease (SD). The confirmed ORR was 20% (95% CI 10-42) and the disease control rate (DCR) was 90% (95% CI 77-98).
- Of the 23 patients evaluable for CD73 in the D + P + O arm, 13 (56.5%) had high expression.
- The first 6 patients treated in the D + P + C and D + P + O arms were evaluated for dose-limiting toxicities (DLTs). No DLTs were observed with D + P + C or D + P + O during the safety run in.

**Conclusion**

The study demonstrated that the combination of durvalumab with capivasertib or oleclumab had promising activity in women with locally advanced or mTNBC, warranting further investigation.

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**References**


**Contact Email**

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**Table 1: Patient demographics and disease characteristics**

<table>
<thead>
<tr>
<th>Arm</th>
<th>Age (years), median</th>
<th>Prior treatments for early-stage mTNBC</th>
<th>PI3K pathway alterations</th>
<th>CD73 expression</th>
<th>Neutropenia</th>
<th>Lipase increased</th>
</tr>
</thead>
<tbody>
<tr>
<td>D + P</td>
<td>53</td>
<td>3.0 (1–9)</td>
<td>6 (25.0)</td>
<td>3 (12.5)</td>
<td>6 (25.0)</td>
<td>1 (4.2)</td>
</tr>
<tr>
<td>D + P + C</td>
<td>65</td>
<td>3.0 (1–9)</td>
<td>5 (20.0)</td>
<td>2 (8.3)</td>
<td>7 (28.6)</td>
<td>2 (8.3)</td>
</tr>
<tr>
<td>D + P + O</td>
<td>58</td>
<td>3.0 (1–10)</td>
<td>7 (29.2)</td>
<td>6 (20.0)</td>
<td>6 (25.0)</td>
<td>1 (4.2)</td>
</tr>
</tbody>
</table>

**Table 2: Response and survival outcomes**

<table>
<thead>
<tr>
<th>Arm</th>
<th>Confirmed ORR (%)</th>
<th>Disease control rate (%)</th>
<th>Median OS (mos)</th>
<th>Median PFS (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>D + P</td>
<td>20 (95% CI 10-42)</td>
<td>90 (95% CI 77-98)</td>
<td>9.4 NC</td>
<td>4.9 NC</td>
</tr>
<tr>
<td>D + P + C</td>
<td>33 (10-80)</td>
<td>70 (10-80)</td>
<td>9.4 NC</td>
<td>4.9 NC</td>
</tr>
<tr>
<td>D + P + O</td>
<td>20 (10-80)</td>
<td>70 (10-80)</td>
<td>9.4 NC</td>
<td>4.9 NC</td>
</tr>
</tbody>
</table>

**Figure 1: BEGONIA Study Design**

- Patients with PI3K pathway-altered tumors were defined as having Tier 1 functionally altered AKT, NR4A3, or NR4A1.
- PD-L1 expression was assessed by immunohistochemistry using an SP263-based assay.
- Retrospective biomarker analyses were conducted on all 3 AKT isoforms, and oleclumab (O) is a monoclonal antibody targeting CD73.

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**Figure 2a: Treatment exposure and duration of response**

- The first 6 patients treated in the D + P + C and D + P + O arms were evaluated for dose-limiting toxicities (DLTs). No DLTs were observed with D + P + C or D + P + O during the safety run in.

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**Figure 2b: % change from baseline of target tumor size**

- The first 6 patients treated in the D + P + C and D + P + O arms were evaluated for dose-limiting toxicities (DLTs). No DLTs were observed with D + P + C or D + P + O during the safety run in.

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**Figure 3: Patient disposition and characteristics**

- Of the 9 patients evaluable for PI3K pathway alterations in the D + P + C arm, 3 (33.3%) had a confirmed objective response (ORR) and 6 (66.7%) had stable disease (SD). The confirmed ORR was 20% (95% CI 10-42) and the disease control rate (DCR) was 90% (95% CI 77-98).
- Of the 23 patients evaluable for CD73 in the D + P + O arm, 13 (56.5%) had high expression.
- The first 6 patients treated in the D + P + C and D + P + O arms were evaluated for dose-limiting toxicities (DLTs). No DLTs were observed with D + P + C or D + P + O during the safety run in.