INTRODUCTION

- Tumor cells require glutamine for growth and survival.
- Glutaminase 2 (GLS) controls the first rate-limiting step in glutamine metabolism and is highly expressed in triple negative breast cancer (TNBC).

CB-839 is an orally active, highly selective inhibitor of GLS with preclinical and clinical activity in TNBC.

CB-839 enhances the anti-tumor activity of paclitaxel in vitro and in vivo.

CB-839 in combination with full dose weekly paclitaxel is active and tolerable.

CB-839 did not increase the severity or frequency of expected paclitaxel toxicities.

One DLT during dose escalation:
- Grade 3 neutropenia on day 400 mg BID.
- Patient tolerated a reduced dose of paclitaxel.

Low rate of Grade 3 peripheral neuropathy (4.2%).

CB-839 500 mg BID selected as dose for expansion (RP2D).

Based on PK, pharmacodynamics, and clinical activity.

CB-839 is in combination with full-dose weekly paclitaxel, active, and tolerated.

CB-839 did not increase the severity or frequency of expected paclitaxel toxicities.

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RESULTS

• 136 OBRs in African American patients (6 of 11) that had previously progressed on prior taxane in the advanced metastatic setting

Change in Tumor Burden Over Time

- Rapid responses and durable clinical benefit in patients previously progressed on prior taxane in the advanced metastatic setting

Time on Study

- Durable responses and long term stable disease in heavily pre-treated TNBC patients

Demographics

<table>
<thead>
<tr>
<th>Age</th>
<th>n (%), Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>26 (17)</td>
<td>50 (6-74)</td>
</tr>
<tr>
<td>22 (14)</td>
<td>31 (21-40)</td>
</tr>
</tbody>
</table>

EQUO Score

<table>
<thead>
<tr>
<th>n (%), Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
</tbody>
</table>

Treatment failure (n, %)

<table>
<thead>
<tr>
<th>Advanced/Metastatic setting (n)</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior Therapy (n)</td>
<td>60</td>
<td>32</td>
<td>28</td>
</tr>
</tbody>
</table>

CB-839 Dose, BID (n, %)

<table>
<thead>
<tr>
<th>Dose (mg)</th>
<th>600</th>
<th>500</th>
<th>400</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%), Median (range)</td>
<td>12 (20)</td>
<td>12 (20)</td>
<td>4 (6.7)</td>
</tr>
</tbody>
</table>

Grade 3-4 Adverse Events

- Neutropenia: Grade 3 (52%), Grade 4 (2%).
- Neutrophil Count: Grade 3 (37%), Grade 4 (2%).
- Neutrophil Count decrease: Grade 3 (13%).
- Pain: Grade 3 (12%).
- Nausea: Grade 3 (9%).
- Altered Glutamine Metabolism of Cancer Cells

CB-839 is an orally active, highly selective inhibitor of GLS with preclinical and clinical activity in TNBC.

Dose Escalation

- CB-839 500 mg BID, 400 mg BID, 300 mg BID, 200 mg BID, 100 mg BID, 50 mg BID, 25 mg BID.
- Weekly dose escalation.
- Dose cohort expansion: 200 mg, 250 mg, 300 mg, 350 mg (RP2D).

CB-839 + Paclitaxel Combination Study Design

- CB-839 + paclitaxel combination (NCT03057600)
- CB-839 400 mg BID (27 patients), 500 mg BID (22 patients), 600 mg BID (22 patients).

CB-839 + Paclitaxel in combination with full dose weekly paclitaxel is active and tolerable.

CB-839 did not increase the severity or frequency of expected paclitaxel toxicities.

Grade 1-4 Adverse Events

- Neutropenia: Grade 1-2 (97%), Grade 3-4 (3%).
- Neutrophil Count: Grade 1-2 (97%), Grade 3-4 (3%).
- Pain: Grade 1-2 (97%), Grade 3 (3%).
- Nausea: Grade 1-2 (97%), Grade 3 (3%).

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CB-839 in combination with full dose weekly paclitaxel is active and tolerable.

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