**Etitinotec Pegol (NKTR-102) in Patients With Metastatic Breast Cancer (MBC): Modeling CA27.29 Response and its Correlation with Tumor Response**

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**INTRODUCTION**

- Detection of the circulating MUC-1 antigen in peripheral blood.
- Cancer cells, with well-characterized assays that allow monitoring therapy in patients with advanced disease.

**BACKGROUND**

- **CA15-3 and CA27.29** are glycoproteins secreted by breast cancer cells, with well-characterized assays that allow monitoring therapy in patients with advanced disease.
- The most widely used serum tumor markers in breast cancer.
- The role for monitoring therapy in patients with advanced disease.

**OBJECTIVES**

- To evaluate the correlation of CA27.29 decline from baseline within patients who discontinued due to disease progression with tumor response to etinotecan pegol.
- To evaluate the correlation of CA27.29 with RECIST response.

**MATERIALS AND METHODS**

- **Phase 2 Study** of etinotecan pegol in patients with MBC.
- **Phase 3 Study** of etinotecan pegol compared to an active single agent Treatment Regimen (TPC).
- **BEACON Study** (BrEAst Cancer Outcomes with NKTR-102).
- **Etinotecan Pegol** is in clinical trials for patients with solid tumors.
- **Population PK Model** was developed using etinotecan pegol data from the phase 2 study and PK model of etinotecan pegol from the phase 3 study.

**RESULTS**

- Larger declines in CA27.29 from baseline were associated with better RECIST response.
- For PD and SD, the median of the maximum CA27.29 decline was larger for PD.
- For SD ≥ 6 months, the median of the maximum CA27.29 decline was larger for SD ≥ 6 months.

**CONCLUSIONS**

- The PK/PD model described CA27.29 profiles accurately, providing a tool to predict drug response from SNP38.
- Change in CA27.29 from baseline may be an early marker for treatment response to etinotecan pegol.

**REFERENCES**

- For SD ≥ 6 months, the median of the maximum CA27.29 decline was larger for SD ≥ 6 months.
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**DATA**

- **Tumor Response**
  - **RECIST** response was defined as either complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD).
  - **Correlation of CA27.29 with RECIST Response**
  - The modeled population mean IC50 for CA27.29 was 145 ng/mL and the median half-life of CA27.29 decline was estimated to be 15 days.

**Table 1. Phase 2 Efficacy Results in Patients with MBC**

<table>
<thead>
<tr>
<th>Schedule</th>
<th>n</th>
<th>ORR</th>
<th>CR</th>
<th>PR</th>
<th>SD</th>
<th>PD</th>
<th>PFS (months)</th>
<th>OS (months)</th>
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<tbody>
<tr>
<td>q21d</td>
<td>22</td>
<td>14</td>
<td>2</td>
<td>5</td>
<td>6</td>
<td>0</td>
<td>5.3</td>
<td>13.1</td>
</tr>
<tr>
<td>q21d</td>
<td>22</td>
<td>17</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>0</td>
<td>5.3</td>
<td>13.1</td>
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</table>

**Table 2. Baseline CA27.29 Measurements (Units) at Screening**

<table>
<thead>
<tr>
<th>Schedule</th>
<th>n</th>
<th>CA27.29 (U/mL)</th>
<th>Median</th>
<th>25%</th>
<th>75%</th>
<th>Mean</th>
<th>SD</th>
<th>CV%</th>
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<tr>
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<td>22</td>
<td>38.0</td>
<td>14.0</td>
<td>12.5</td>
<td>71.5</td>
<td>33.4</td>
<td>38</td>
<td>99</td>
</tr>
<tr>
<td>q21d</td>
<td>22</td>
<td>38.0</td>
<td>14.0</td>
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**Figure 1. Observed Changes in Serum CA27.29 Profiles Following a 145 mg/m² Dose of Etinotecan Pegol**

- We observed large declines in CA27.29 from baseline at both schedules.
- The half-life of CA27.29 decline was estimated to be 15 days.

**Figure 2. Correlation of CA27.29 with RECIST Response**

- Of the 45 patients, 43 patients had pre- and post-treatment tumor measurements for correlation of CA27.29 response with tumor size.

**Figure 3. Change (%) in Serum CA27.29 Profiles Following a 145 mg/m² Dose of Etinotecan Pegol**

- There were no significant changes from baseline (p > 0.05) for either schedule.

**Figure 4. Observed Changes in Serum CA27.29 Profiles Following a 145 mg/m² Dose of Etinotecan Pegol**

- We observed large declines in CA27.29 from baseline at both schedules.

**Figure 5. Observed Percent Change of Serum CA27.29 Time Course Stratified by Response (Each Line Represents One Patient)**

- 93% (14/15) of the patients with RECIST CR or PR exhibited at least 10% declines in CA27.29 from baseline during the study.

**Table 3. Correlation of CA27.29 with RECIST Response**

<table>
<thead>
<tr>
<th>Schedule</th>
<th>n</th>
<th>SD &lt; 6 months</th>
<th>SD ≥ 6 months</th>
<th>CR</th>
<th>PD</th>
<th>CA27.29 Decline from Baseline (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>q21d</td>
<td>22</td>
<td>8</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>58.0</td>
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<td>q21d</td>
<td>22</td>
<td>10</td>
<td>2</td>
<td>3</td>
<td>0</td>
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</tr>
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**Figure 6. Projections of SNP38 Concentrations following q14d and q21d**

- For q14d and q21d, the median of the maximum SNP38 concentration was larger for q14d.
- For q14d and q21d, the median of the maximum SNP38 concentration was larger for q14d.

**Figure 7. Larger Declines in CA27.29 from Baseline were Associated with Better RECIST Response**

- For PD and SD, the median of the maximum CA27.29 decline was larger for PD.
- For SD > 6 months, the median of the maximum CA27.29 decline was larger for SD > 6 months.
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**Table 4. Correlation of CA27.29 with RECIST Response**

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**Figure 8. Correlation of CA27.29 with RECIST Response**

- Of the 45 patients, 43 patients had pre- and post-treatment tumor measurements for correlation of CA27.29 response with tumor size.

**Table 5. Correlation of CA27.29 with RECIST Response**

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**Figure 9. Correlation of CA27.29 with RECIST Response**

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**Table 6. Correlation of CA27.29 with RECIST Response**

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