Significant Efficacy in a Phase 2 Study of NKTR-102, a Novel Polymeric Conjugate of Irinotecan, in Patients With Pre-Treated Metastatic Breast Cancer (MBC)


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Background

- NKTR-102 is a smaller-conjugate of Irinotecan with reduced peak concentrations, a continuous exposure profile, and a greater penetration into tumors.
- NKTR-102 has superior efficacy (measured by tumor growth delay and regression rate) compared to irinotecan with reduced peak concentrations, a continuous exposure profile, and a greater penetration into tumors.

Study Design & Objectives

- Study Design: Randomized Simon Two-Stage
- NKTR-102 Breast Cancer Study: Objectives
  - Primary Efficacy Objective: Determion of the objective response rate (ORR) by RECIST v1.0
  - Secondary Objectives: 1. Determination of the optimal schedule of NKTR-102 in breast cancer
  - 2. Evaluation of overall survival (OS) rates
  - 3. Characterization of safety profile

Key Eligibility Criteria

- Male or female patients with advanced breast cancer following taxane therapy (adjuvant or metastatic).
- Patients may also have received prior anthracycline or capecitabine.
- No prior chemotherapy regimen given in the metastatic setting.
- Measurable disease as defined by RECIST version 1.0.

Key Criteria: 1. Unmeasurable disease

Study Demographics

- 35 patients were treated with NKTR-102 at 145 mg/m² q14d.
- 31 patients were treated with NKTR-102 at 145 mg/m² q21d.

Objectives

- Objective Tumor Response Rate by RECIST (Investigator Assessment)
  - Primary Endpoint: ORR (confirmed)
  - Secondary Endpoints: 1. Response rate by tumor characteristics
  - 2. Safety: Summary of drug-related AEs

Maximum Decline in Tumor Measurements (All Patients)

- 6 patients with 100% resolution of target lesions.
- 1 patient with confirmed partial response.
- Number of patients with confirmed partial response: 8/35 (23%)

Response Rate By Prior Therapy

- 5/10 (50%) responders with prior A/T; PD on prior taxane.
- 5/15 (33%) responders with prior taxane.

Safety

- Summary of Drug Related AEs
  - None grade 3 or 4 neuropathy was reported.
  - High confirmed objective response rate (29% overall; 32% q14d; 26% q21d) with anti-tumor activity similar for both schedules.

References


Conclusions

- High confirmed objective response rates (29%, overall; 32%, q14d; 26%, q21d) with a preliminary PFS trend (both q14d and q21d) in patients with advanced breast cancer pre-treated with anthracyclines and taxanes + capecitabine.
- Anti-tumor activity similar for both schedules.
- Confirmed the response confirmed to maintain in heavily treated and poor prognosis subsets.
- FDC: taxane + anthracycline + capecitabine.
- Anti-tumor activity similar for both schedules.
- Safety profile: only grade 3 or 4 adverse events were diarrhoea and neutropenia.}

Table: Clinical benefit (total response rate, progression-free survival (PFS), and overall survival (OS) rates)

<table>
<thead>
<tr>
<th>Group</th>
<th>Response Rate</th>
<th>Progression-Free Survival (PFS)</th>
<th>Overall Survival (OS)</th>
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</thead>
<tbody>
<tr>
<td>NKTR-102 at 145 mg/m² q14d</td>
<td>7/22 (32%)</td>
<td>12/27 (44%)</td>
<td>6/22 (27%)</td>
</tr>
<tr>
<td>NKTR-102 at 145 mg/m² q21d</td>
<td>8/25 (32%)</td>
<td>17/27 (63%)</td>
<td>9/25 (36%)</td>
</tr>
</tbody>
</table>

Figure: Phase 2 Breast Cancer Study: Progression-Free Survival (All Patients)

- Preliminary median PFS > 20 weeks (95% CI: 10 – 24)
- High confirmed objective response rate (29% overall; 32% q14d; 26% q21d) with anti-tumor activity similar for both schedules.
- Confirmed the response confirmed to maintain in heavily treated and poor prognosis subsets.
- FDC: taxane + anthracycline + capecitabine.
- Anti-tumor activity similar for both schedules.
- Safety profile: only grade 3 or 4 adverse events were diarrhoea and neutropenia.