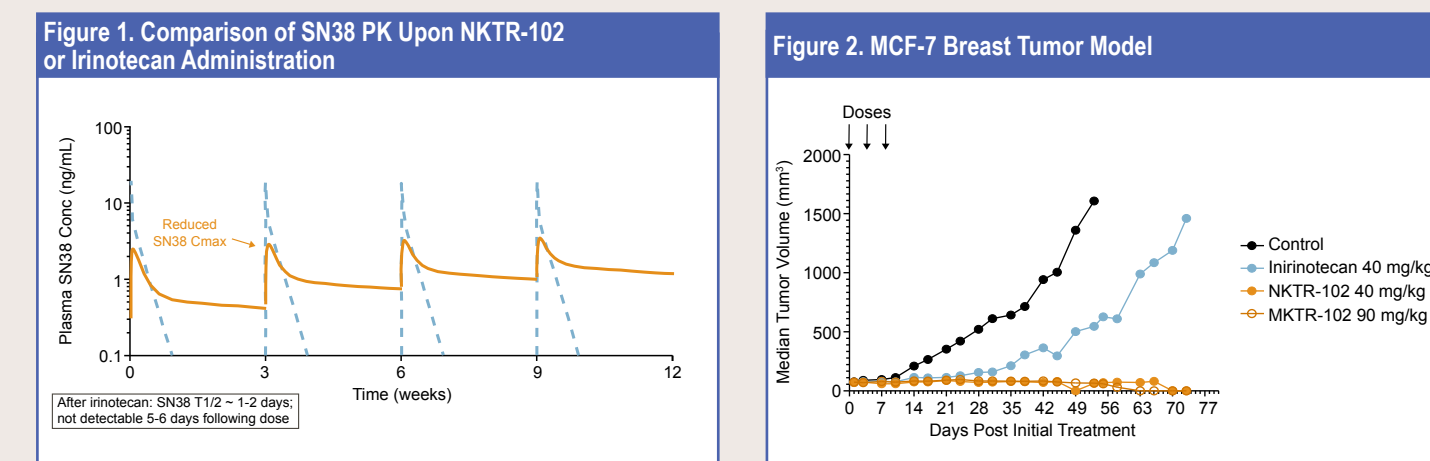
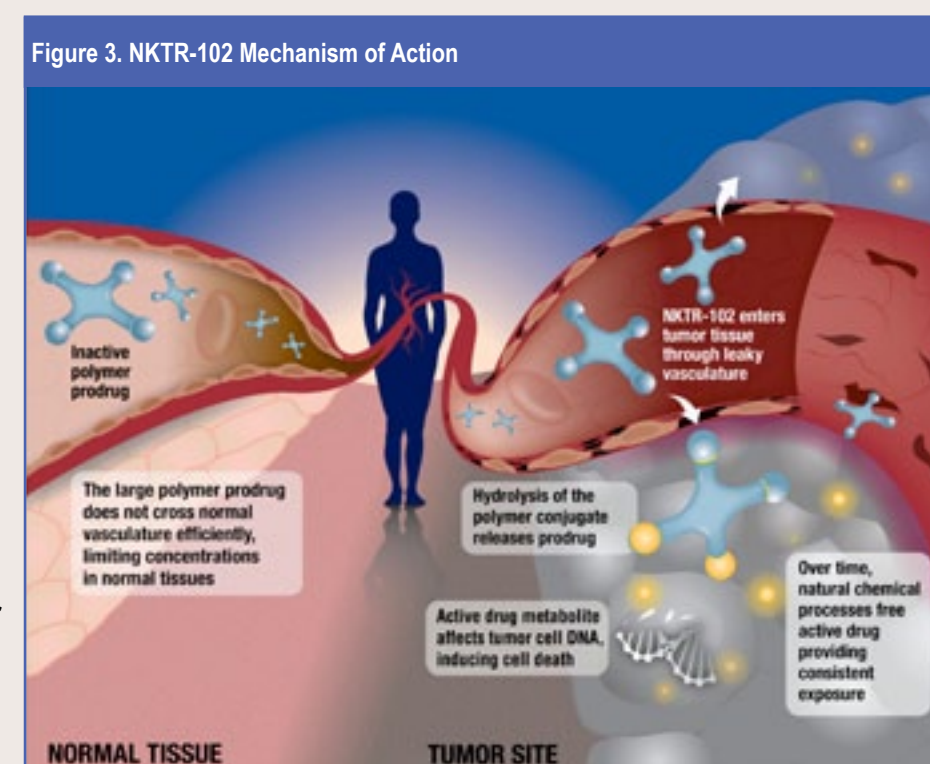


Background

- Nektar Therapeutics is a biopharmaceutical company developing a pipeline of drug candidates that utilizes its advanced polymer conjugate technology to improve the benefits of drugs for patients.
- NKTR-102 is in clinical trials for patients with solid tumors, including breast, ovarian and colorectal cancers.
- NKTR-102 is a next-generation topoisomerase I inhibitor with a unique pharmacokinetic (PK) profile that provides a continuous concentration of active drug with reduced peak concentrations (figure 1).¹
 - Studies have shown NKTR-102 to have a markedly reduced C_{max} (SN-38 peak concentration) that improves tolerability and a continuous exposure to SN-38 compared to irinotecan.
- NKTR-102 has demonstrated better efficacy as measured both by tumor growth delay and regression rate compared to irinotecan against a wide range of human xenograft tumors, including a breast tumor model (figure 2).²



- NKTR-102 is a large molecule, and is believed to penetrate the 'leaky' vasculature within the tumor environment more readily than normal vasculature, increasing exposure of tumor cells to the active anti-tumor agent SN-38 (figure 3).
- Comparison of SN-38 PK upon NKTR-102 or irinotecan administration:
 - Reduced C_{max} (infusional-related toxicities are not seen with NKTR-102).
 - Greatly prolonged elimination half-life (50 days compared to 2 days).
- Topoisomerase I inhibition may result in improved antitumor activity due to lack of 'cross-resistance' to commonly used microtubule inhibitors.



Introduction

- There are currently no topoisomerase I inhibitors approved by the FDA to treat breast cancer. Nektar is currently evaluating the potential of NKTR-102 to address this unmet clinical need.

Topoisomerase I inhibition with irinotecan in MBC

- A previous phase 2 study³ looked at two irinotecan schedules (q3w and weekly) for patients with Metastatic Breast Cancer (MBC) refractory to an anthracycline, a taxane or both:

Endpoint	145 mg/m ² q3w	145 mg/m ² weekly
Overall Response Rate (ORR)	14%	23%
Progression-Free Survival (PFS)	1.9 months	2.8 months
Median Overall Survival (OS)	8.6 months	9.7 months

Topoisomerase I inhibition with NKTR-102 in MBC

- A previous phase 2 study⁴ evaluated NKTR-102 in two treatment regimens (145 mg/m² q2w and q3w; n=70; 35 per treatment regimen), for patients with a median of 2 cytotoxic regimens for MBC (100% prior taxane, 89% anthracycline; 26% with prior ATC):
 - 29% ORR observed with single agent NKTR-102 (both schedules showed similar ORR).
 - ORR was also maintained in other heavily pre-treated and poor prognosis patient subsets:
 - ER+ and/or PR+: 29%.
 - Triple-negative: 39%.
 - Visceral disease: 30%.
 - Side effects were generally manageable; most common severe toxicity was diarrhea (G3 23% in q3w), typically occurring after 3 months of therapy.

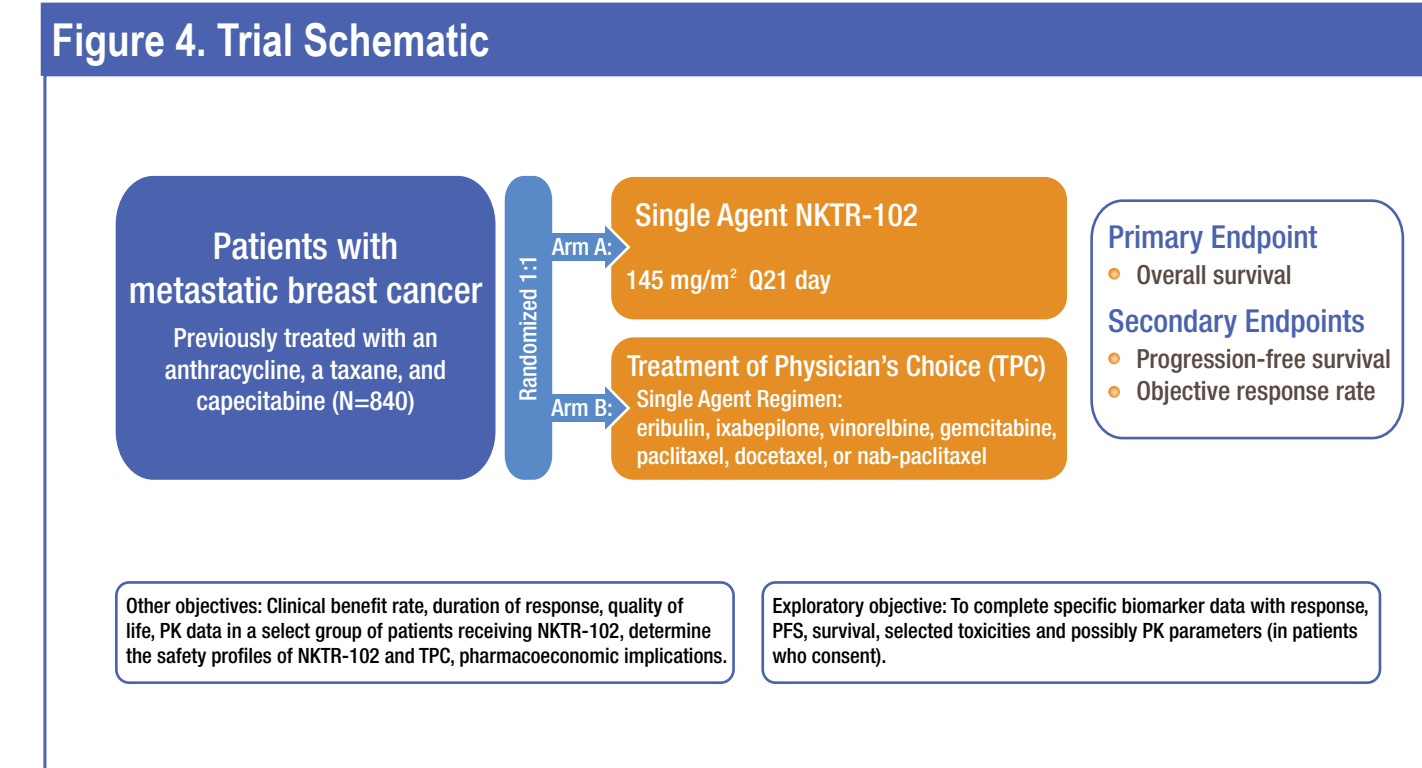
Endpoint	145 mg/m ² q2w	145 mg/m ² q3w
Overall Response Rate (ORR)	31% in ATC (N=16)	
Progression-Free Survival (PFS)	4.6 months	5.3 months
Overall Survival (OS)	10.3 months	13.1 months

The BEACON Study

- The BEACON study (BrEAsT Cancer Outcomes with NKTR-102) is a phase 3 randomized, open-label, international study of NKTR-102 in patients with MBC that will evaluate single agent NKTR-102 in patients who have previously received ATC versus a comparator arm consisting of an active single agent Treatment of Physician's Choice (TPC).
 - Based on better tolerability, OS and PFS, the q3w 145 mg/m² treatment schedule of NKTR-102 has been selected for a planned phase 3 study in MBC.

Study Design

- This study will randomize approximately 840 patients using a 1:1 randomization ratio. Prior to randomization of a patient, the Investigator must determine which TPC will be offered to the patient as part of the informed consent process and must enter the chosen agent into the medical chart and the central randomization system. Randomization will be stratified by geographic region, prior use of eribulin, and receptor status.
- Data will be collected on subsequent anticancer therapies in both treatment arms from the time patients come off the study treatment until the time of primary data analysis for OS.
- An independent data monitoring committee (DMC) will review the safety of NKTR-102 treatment in the study and will assess interim efficacy data.



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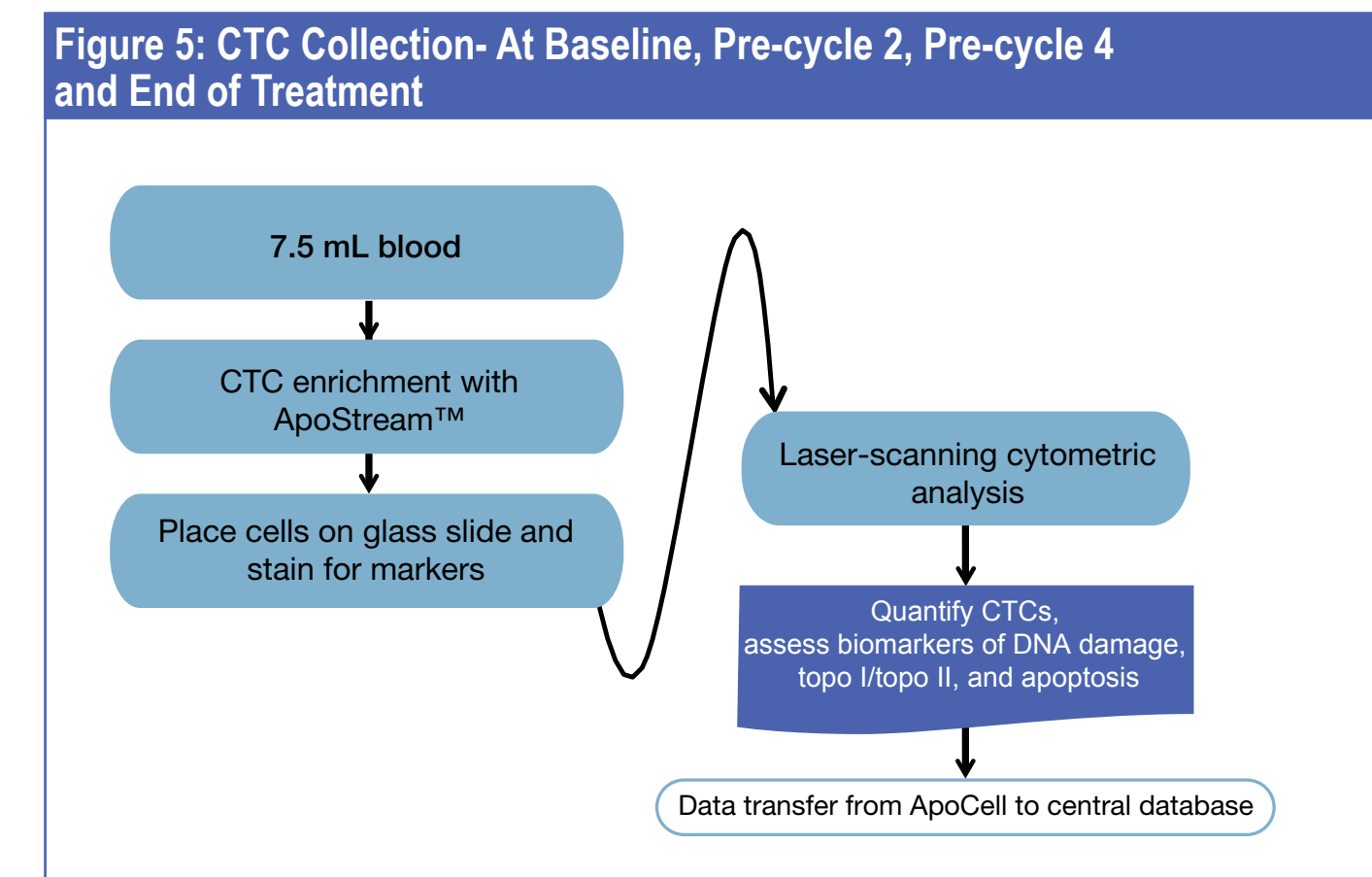


Key Patient Entry Criteria

- Adult females with histologically or cytologically confirmed carcinoma of the breast:
 - Patients: measurable or non-measurable disease by RECIST, locally recurrent or metastatic disease.
 - Prior therapy (administered in the neoadjuvant, adjuvant and/or metastatic setting) must include an anthracycline (unless not medically appropriate or contraindicated for the patient), a taxane, and Xeloda® (capecitabine).
 - Patients must have received a minimum of 2 and a maximum of 5 prior cytotoxic chemotherapy regimens for the treatment of breast cancer, with the last dose administered within 6 months of the date of consent for this trial.
 - Patients must have ECOG performance status of 0-1 with adequate organ function.
 - Patients with brain metastases may be eligible, provided local therapy was completed and use of corticosteroids for this indication discontinued for at least 3 weeks prior to randomization with stable brain metastases (by symptoms and imaging).

Exploratory Biomarkers

- Exploratory biomarkers in BEACON study:
 - Nektar will work with ApoCell, a leader in the field for capturing and analyzing Circulating Tumor Cells (CTCs).
 - An increased harvest of CTCs compared to other technologies, enables Nektar to analyze more biomarkers per sample and to monitor the change in biomarkers over time.
 - Quantify CTCs, assess biomarkers of DNA damage, topo I/topo II, and apoptosis (figure 5).



Statistical Plan and Methods

- Approximately 840 patients (420 patients per treatment group) will be required for sufficient events to occur in the planned follow-up time.
- OS will be compared between treatment groups using a two-sided log-rank test. Stratification factors include: geographic region, prior eribulin use and receptor status.
- A single interim analysis is planned when approximately 50% of the total deaths have occurred. The purpose of this analysis is to determine whether early termination of the study due to overwhelming efficacy, or due to futility can be supported.

Protocol Procedures

- Investigator determination of response and progression by RECIST v1.1.
- Central imaging will not be used in this trial.
- Health-Related Quality of Life: every 8 weeks (prior to imaging).
- Healthcare utilization: every 4 weeks.
- PK in a subset of patients.
- Biomarkers in a subset of patients.
- Central laboratory for safety tests (in addition to local laboratories).

Accrual

- BEACON is open for enrollment and enrollment is expected to be completed by December 2013.
- Regions: Approximately 160 sites in North America, Europe and Asia.
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