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.

NKT-102 is in clinical trials for patients with solid tumors, including breast, ovarian and colorectal cancers.

NKT-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). – Studies have shown NKT-102 to have a markedly reduced Cmax (SN-38 peak concentration) that improves tolerability and a continuous exposure to SN-38 compared to irinotecan.

NKT-102 has demonstrated better efficacy as measured by tumor growth delay and regression rate compared to irinotecan. NKT-102 is in clinical trials for patients with metastatic breast cancer (MBC). Topoisomerase I inhibition with NKT-102 in MBC

Intervention

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

Topoisomerase I Inhibition with NKT-102 in MBC

A previous phase 2 study showed two different schedules (250 mg/m² q3w and 500 mg/m² q7w) were well-tolerated and had clinical activity. (100% prior taxane, 89% anthracycline; 26% with prior ATC): 20% ORR observed with single agent NKT-102 (both schedules showed similar ORR).

ORR was also maintained in other heavily pre-treated and poor prognosis patient subtypes: ER+ and/or PR+ 39%; Triple-negative: 30%; Visceral metastases: 30%; Side effects were generally manageable; most common severe toxicity was diarrhea (≥3 ≥3 in 9%, typically occurring after 3 months of therapy.

The BEACON Study

The BEACON study (BEaast Cancer Outcomes With NKTR-102) is a phase 3 randomized, open-label, international study of NKT-102 in patients with MBC who have previously received ATC as a comparator arm consisting of an active single agent Treatment of Physician's Choice (TPC).

This study will randomize approximately 840 patients using a 1:1 randomization ratio. Prior to randomization, 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.

The BEACON Study

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 (administration of 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 maximum of two prior cytotoxic chemotherapy regimens for the treatment of breast cancer, metastatic breast cancer (by symptoms and imaging).

Neoadjuvant Clinical Trials

- Table 2 presents overall results from patients with MBC who received NKT-102 as a single agent or in combination with an anthracycline in 2 studies. (100% prior taxane, 89% anthracycline; 26% with prior ATC): 20% ORR observed with single agent NKT-102 (both schedules showed similar ORR).

Incident drug monitoring committees (DMC) will review the safety of NKT-102 treatment in the study and will assess interim and final data. The purpose of this analysis is to determine whether early termination of the study due to overall efficacy, or due to efficacy can be supported.

Study Design

- The study will be stratified by geographic region, prior use of an anthracycline, and Xeloda® (capecitabine).
- Randomization will be stratified by geographic region, prior use of an anthracycline, and Xeloda® (capecitabine).
- Patients who have previously received ATC versus a comparator arm 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 35% of the total deaths have occurred. The purpose of this analysis is to determine whether early termination of the study due to overall efficacy, or due to efficacy can be supported.

Inclusion Criteria

- 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.

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Protocol Procedures

- Investigator determination of response and progression by RECIST 1.1.
- Disease-Related Quality of Life: every 8 weeks (prior to imaging).
- Healthcare utilization: every 4 weeks.
- PR in a 4+8 patient (per local TTP criteria).
- Biomarkers in a subset of patients.
- Central accrual: safety for clinical trials (in addition to local laboratories).

Conclusion

BEACON is open for enrollment and enrollment is expected to be completed by December 2013.

References

Ahmad Awada,1 Carol Zhao,2 Alison L. Hannah,3 Edith A. Perez3

Versus Treatment of Physician’s Choice (TPC) in Patients With Locally Recurrent or Metastatic Breast Cancer Previously Treated With An Anthracyne, a Taxane, and XeCITa® (capecitabine).

The BEACON Study (BEaast Cancer Outcomes With NKTR-102): A Phase 3 Open-Label, Randomized, Multicenter Study of NKTR-102 Versus Treatment of Physician’s Choice (TPC) in Patients With Locally Recurrent or Metastatic Breast Cancer Previously Treated With An Anthracyne, a Taxane, and XeCITa® (capecitabine).

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