Significant Antitumor Activity in a Randomized Phase 2 Study Comparing Two Schedules of Etirinotecan Pegol (NKTR-102)


Background

- Etirinotecan pegol is a unique, long-acting topoisomerase I inhibitor that provides prolonged systemic exposure to SN-38, the active metabolite of irinotecan.
- Etirinotecan pegol has superior efficacy (measured both by tumor growth delay and regression rates) compared to irinotecan against a wide range of human xenograft tumors.1

Study Design & Objectives

Study Design: Randomized Simon Two-Stage

- Phase 1 (11% confirmed PRs)
- Patients may also have received prior anthracycline or capecitabine

Key Eligibility Criteria

- Metastatic disease
- Median cytotoxic regimen
- PD after irinotecan
- Reduced SN-38 T1/2 (~50 Days)
- 10% of patients with reduced SN-38 T1/2 by tumor growth delay and regression rate compared to irinotecan

Study Demographics

- 70 patients (35 per schedule) randomized from February 2009 through May 2010 (median follow-up: 6 months)

Results

Objective Tumor Response Rate by RECIST (Investigator Assessment)

- RECIST version 1.0
- ORR (confirmed)

Response Rate By Prior Therapy

- Prior A/T only
- Prior A/T/C

Response Rate By Tumor Characteristics

- Adequate renal, hepatic, and marrow function
- No known or suspected CHF indications
- No significant pre-existing scarring or GI disorders

Study Drug Administration and Discontinuation Due to AE

- No dose modifications
- No dose reductions
- No dose interruptions

Safety

- No grade 4 or higher laboratory or non-laboratory AEs

Conclusions

- High confirmed objective response rate observed with single-agent etirinotecan pegol in patients with advanced breast cancer previously treated with taxane (14% vs. carbo-paclitaxel 9% with prior anthracycline)2
- 29% confirmed objective response rate
- 32% ORR on 14-day schedule
- 26% on 21-day schedule
- Preliminary estimate for median survival: 10.3 months


2. Source: Data as of May 9, 2011

3. Median (Range)

4. Numbers may add up to more than 100% due to patients included in multiple rows

5. For staging purposes, 3 patients in the Phase 1 study with visceral disease were included in the visceral disease subgroup.

6. Lesions were defined as measurable if > 1.0 cm in the longest diameter. Visceral and other measurable lesions were counted without regard to number of lesions per patient.

7. Most frequent laboratory AEs were neutropenia, anemia, and thrombocytopenia.

8. Only patients with at least one post-baseline scan were included in the analysis. The overall ORR was 29% and the confirmed ORR was 19%.

9. Source: Data as of May 9, 2011

10. Source: Data as of May 9, 2011

11. Source: Data as of May 9, 2011

12. Source: Data as of May 9, 2011

13. Source: Data as of May 9, 2011

14. Source: Data as of May 9, 2011

15. Source: Data as of May 9, 2011