**Introduction**

- Etirinotecan pegol (NKTR-102) is a unique topoisomerase I inhibitor designed for prolonged tumor cell exposure.
- After q21d dosing of etirinotecan pegol to patients with cancer, plasma SN38 exposure is increased and greatly prolonged compared to irinotecan (elimination half-life 5-10 times less).

**Background**

- In a phase 2 trial in heavily pretreated patients with platinum-resistant ovarian cancer, etirinotecan pegol administered q14d or q21d demonstrated confirmed objective RECIST and CA-125 response rates (CR, PR, SD) of 37% and 30%, respectively.

**Model Building Steps**

- Predict the plasma SN38 concentration-time profile for each patient using our previously developed population PK model.
- Investigate the relationship of predicted plasma SN38 concentration with serum CA-125 concentration.

**Model**

- The strong CA-125 response observed in these heavily pretreated patients who responded to the drug (Figure 2) was encouraging and stimulated our focus on this model.

**Results**

- CA-125 concentration-time profiles were well described by the model independent of response pattern.

**Data/Methods**

- In the phase 2 study, patients with platinum-resistant ovarian cancer were randomized to etirinotecan pegol at a dose of 145 mg/m² q14d or q21d.
- Our analysis dataset consisted of the 55 patients whose baseline CA-125 was > 2X upper normal limit and who had at least 1 post-baseline CA-125 measurement.
- The modeled population mean IC50 of SN38 was 1.1 ng/mL.

**Conclusions**

- The strong CA-125 response observed in these heavily pretreated patients who responded to etirinotecan pegol also supported use of the better-tolerated q21d regimen.

**References**