Phase I clinical trial of the intraperitoneal (IP) administration of a novel nanoparticle formulation of paclitaxel (NTX)

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Abstract

Background: Peritoneal carcinomatosis is a common spread pattern in ovarian cancer and a major cause of morbidity and mortality. Treatment options are limited and standard chemotherapy, particularly IV paclitaxel (PTX), are associated with dose limiting toxicity and poor response. We report Phase I results of an intraperitoneal (IP) Phase I study of a nanoparticle formulation of paclitaxel (NTX) utilizing a new delivery system, Nanotax.

Methods: Patients with extensive peritoneal carcinomatosis from any peritoneal malignancy who were not candidates for surgical cytoreduction were eligible. Nanotax was administered IP as a bolus injection after 500 ml saline followed by IP administration of up to 2 L. Dosing was by 3+3 design using CTCAE V3 toxicities. The objectives of the present Phase I trial were to assess the pharmacokinetics of intraperitoneal (IP) administration of this agent; 2) nanoparticulate paclitaxel will undergo prolonged distribution in the peritoneal cavity and maintain high drug concentrations for 1 week. The updated Phase I results presented here demonstrate the safety, pharmacokinetics and preliminary antitumor activity of Nanotax.

Results: As of the 12th cycle of the study, 21 patients enrolled (range 142 to 740 days). All Cmax in plasma were less than 35 ng/mL, with ascites fluid Cmax ranging from 0.5 to 2.8 ng/mL. The mean half-life was 142 days. NTX was well tolerated. MTD has not yet been reached. CR was seen in 3 patients (15%); SD in 12 patients (66%); PR in 3 patients (15%) and PD in 1 patient (5%).

Conclusions: IP NTX is well tolerated. MTD has not yet been reached. CR was seen in 3 patients (15%); SD in 12 patients (66%); PR in 3 patients (15%) and PD in 1 patient (5%). The updated Phase I results presented here demonstrate the safety, pharmacokinetics and preliminary antitumor activity of Nanotax.

Information on Drug Administration and Response Duration

Baseline Demographic and Clinical Characteristics (Intent-to-Treat)

Cohort 1

Cohort 2

Cohort 3

Maximum Grade Adverse Event Per Category Per Subject by Dosing Cohort (Intent-to-Treat)

Maximum Grade Treatment-Related Adverse Event Per Subject by Dosing Cohort (Intent-to-Treat)

Full Adverse Event Listing by Grade and Category

Grade 3 Events

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