Biweekly administration of 24-h infusion of irinotecan followed by a 1-h infusion of docetaxel: a phase I study.

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Source

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Abstract

We developed a chemotherapy combination regimen based on preclinical data suggesting synchronization of cancer cells in G2/M phase when exposed to irinotecan over a protracted period. This phase I study aimed to determine the toxicity spectrum, and define the dose-limiting toxicity (DLT), maximum tolerated dose (MTD) and recommended optimal dose (ROD) of irinotecan infused over 24 h and followed by a 1-h infusion of 30 mg/m2 docetaxel. Starting dose for irinotecan was 30 mg/m2 and escalation proceeded at 30 mg/m2 increments, in cohorts of three to six patients until the MTD was reached. A dose between the MTD and the previous level was explored to further define the ROD. Thirty-two patients with advanced refractory cancers (median age 64, 19 male) received 190 treatment courses at five dosing levels of irinotecan: 30 mg/m2 (n=6 patients), 60 (n=3), 90 (n=7), 120 (n=8) and 105 (n=8). The MTD and ROD was 120/30 and 105/30 mg/m2. DLTs were diarrhea and neutropenia. Antitumor activity was modest. The ROD of biweekly administration of 24-h irinotecan followed by 1-h docetaxel is 105 and 30 mg/m2, respectively. The low hematological toxicity and modest activity observed leave questions concerning the optimal timing of this combination.