Phase I trial of weekly irinotecan and paclitaxel combined with carboplatin in patients with advanced cancer: a Hellenic Cooperative Oncology Group Study.

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Source

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Abstract

This trial aimed to define a recommended safe dose (RSD) of weekly paclitaxel and irinotecan combined with carboplatin in patients with advanced cancer. Patients with advanced cancer were eligible for this trial. Dose-limiting toxicity (DLT) was considered to be any grade greater than or equal to 3 (G> or =3) nonhematological toxicity except nausea/vomiting, G4 hematological toxicity of more than 4 days without recombinant human granulocyte colony-stimulating factor support, concurrent diarrhea G> or =2 and neutropenia G> or =3, and a treatment delay for more than 14 days because of toxicity. Patients were given carboplatin area under the curve (AUC) 5 mg*min/ml on day 1 combined with irinotecan and paclitaxel on days 1 and 8, every 3 weeks. The starting dose of both irinotecan and paclitaxel was 50 mg/m and a toxicity-guided escalation/de-escalation was planned by 10 mg/m steps. Sixteen patients were enrolled. DLTs occurred in three of the four patients treated at the starting dose level, which defined that dose as the maximum tolerated dose. Accrual continued with irinotecan and paclitaxel doses, which were de-escalated by one step. At this dose level, two of the 12 patients developed DLT, which defined that dose as the RSD. We concluded that the maximum tolerated dose of weekly irinotecan and paclitaxel when given in combination with carboplatin AUC 5 mg*min/ml was 50 mg/m and the RSD 40 mg/m. DLTs were febrile neutropenia, concurrent neutropenia (G3) and diarrhea (G3), and prolonged treatment delay because of toxicity. The most common non-DLT G3/G4 toxicity was leukopenia and neutropenia (18%), and thrombocytopenia and diarrhea (6%). A patient with metastatic endometrial carcinoma treated at the RSD had a compete response of retroperitoneal lymph node metastases, lasting for more than 3 years. Two other patients had their minimal tumor shrinkage documented. Paclitaxel (40 mg/m) and irinotecan (40 mg/m) can safely be administered on days 1 and 8 in combination with carboplatin AUC 5 mg*min/ml given on day 1. At the recommended doses this is a well-tolerated regimen with noticeable antitumor activity and warrants further investigation in phase II studies.