

A randomized phase III trial of adjuvant chemotherapy with irinotecan, leucovorin and fluorouracil versus leucovorin and fluorouracil for stage II and III colon cancer: a Hellenic Cooperative Oncology Group study.

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Source

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Abstract

BACKGROUND:

Colon cancer is a public health problem worldwide. Adjuvant chemotherapy after surgical resection for stage III colon cancer has been shown to improve both progression-free and overall survival, and is currently recommended as standard therapy. However, its value for patients with stage II disease remains controversial. When this study was designed 5-fluorouracil (5FU) plus leucovorin (LV) was standard adjuvant treatment for colon cancer. Irinotecan (CPT-11) is a topoisomerase I inhibitor with activity in metastatic disease. In this multicenter adjuvant phase III trial, we evaluated the addition of irinotecan to weekly 5FU plus LV in patients with stage II or III colon cancer.

METHODS:

The study included 873 eligible patients. The treatment consisted of weekly administration of irinotecan 80 mg/m² intravenously (i.v.), LV 200 mg/m² and 5FU 450 mg/m² bolus (Arm A) versus LV 200 mg/m² and 5FU 500 mg/m² i.v. bolus (Arm B). In Arm A, treatments were administered weekly for four consecutive weeks, followed by a two-week rest, for a total of six cycles, while in Arm B treatments were administered weekly for six consecutive weeks, followed by a two-week rest, for a total of four cycles. The primary end-point was disease-free survival (DFS) at three years.

RESULTS:

The probability of overall survival (OS) at three years was 0.88 for patients in Arm A and 0.86 for those in Arm B, while the five-year OS probability was 0.78 and 0.76 for patients in Arm A and Arm B, respectively ($P = 0.436$). Furthermore, the probability of DFS at three years was 0.78 and 0.76 for patients in Arm A and Arm B, respectively ($P = 0.334$). With the exception of leucopenia and neutropenia, which were higher in patients in Arm A, there were no significant differences in Grades 3 and 4 toxicities between the two regimens. The most frequently recorded Grade 3/4 toxicity was diarrhea in both treatment arms.

CONCLUSIONS:

Irinotecan added to weekly bolus 5FU plus LV did not result in improvement in disease-free or overall survival in stage II or III colon cancer, but did increase toxicity.