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Fluorouracil and leucovorin with or without interferon alfa-2a as adjuvant treatment, in patients with high-risk colon cancer: a randomized phase III study conducted by the Hellenic Cooperative Oncology Group.

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Source

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Abstract

BACKGROUND:

It has been shown in randomized studies that adjuvant treatment with the combination of fluorouracil (FU) and levamisole reduced the risk of recurrence and deaths of patients with stage III colon cancer. Pharmacological studies of FU led to its use in combination with a number of modulating agents including interferon-alpha and leucovorin (LV) that appear to enhance its activity in vitro. Furthermore, a meta-analysis suggested that the combination of FU with LV increased the response rate as compared to FU monotherapy in patients with advanced colorectal cancer.

PURPOSE:

To evaluate the impact of adjuvant treatment with the combination of FU and LV with or without interferon alfa-2a (IFN) on disease-free survival (DFS) and overall survival (OS) for patients with stage II or III colon cancer.

PATIENTS AND METHODS:

From August 1989 to July 1997, 280 patients with stage II and III colon cancer entered the study and were randomly assigned to receive either the combination of FU (600 mg/m(2)/week x 6, followed by a 2-week rest) and LV (500 mg/m(2)/week x 6 as a 2-hour infusion, followed by a 2-week rest) for 4 cycles (group A, 139 patients), or the same chemotherapy plus recombinant IFN (3 MU subcutaneously 3 times a week) for 1 year (group B, 141 patients).

RESULTS:

A total of 109 patients (78.9%) of group A and 119 (84.4%) of group B completed four cycles of chemotherapy. Also, 51.4% of patients of group A and 53.9% of group B received > or =80% of the planned dose of FU. One patient (group A) was found to be ineligible and was not included in the analysis. The median relative dose intensity of FU in the two groups was 0.90 and 0.85, respectively. As of August 1998, after a median follow up of 4 years, there was no significant difference in either 3-year DFS (group A, 83.1%; group B, 75.9%, p = 0.14) or OS (group A, 84.5%; group B, 80.0%, p = 0.27). In the Cox model, stage of disease, number of infiltrated nodes, tumor grade and presence of regional implants were identified as significant prognostic factors for OS. Grade 3-4 toxicities, mainly diarrhea, were observed in 26.1% of patients of group A and in 24.8% of group B. There were no treatment-related deaths.

CONCLUSIONS:

The addition of IFN to the combination of FU with LV postoperatively does not improve DFS and OS of patients with stage II or III colon cancer.