A systematic overview of chemotherapy effects in colorectal cancer.


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A systematic review of chemotherapy trials in several tumour types was performed by The Swedish Council of Technology Assessment in Health Care (SBU). The procedures for the evaluation of the scientific literature are described separately (Acta Oncol 2001; 40: 155-65). This synthesis of the literature on adjuvant and palliative therapy with cytostatics for colorectal cancer is based on 208 scientific articles, including eight meta-analyses and 162 randomised studies. These studies involve approximately 126,800 patients. The conclusions reached can be summarized into the following points: The benefit of postoperative adjuvant chemotherapy with fluorouracil and levamisole in patients with colon cancer stage Dukes' C was demonstrated more than ten years ago in two phase III trials. There was a reduction of recurrence from 56% to 39% and reduction of death from 51% to 40% after more than five years of follow-up. Although this combination has been widely accepted as standard adjuvant treatments for stage Dukes' C colon cancer, there is still debate on whether adjuvant treatment with fluorouracil alone would be equally efficacious. Several phase III trials with postoperative adjuvant chemotherapy with fluorouracil and leucovorin in patients with colon cancer stage Dukes' C have demonstrated a similar statistically significant improvement in disease-free and overall survival in comparison with a control arm. Six months of treatment with fluorouracil and leucovorin is as efficient as twelve months of fluorouracil and levamisole. This treatment is, thus, recommended for routine use. No convincing benefit from adjuvant chemotherapy is proven in colon cancer stage Dukes' B although some randomised trials have shown the same relative survival gain as seen in stage Dukes' C. There is less knowledge on survival benefits from adjuvant chemotherapy for Dukes' stage B and C rectal cancer. In small randomised trials, postoperative radiochemotherapy has, however, improved survival to the same extent as chemotherapy in colon cancer Dukes' stage C. A meta-analysis of nine randomised trials revealed a small but statistically significant benefit in five-year survival and a reduction in the risk of death for the patients receiving immediate postoperative portal vein infusion compared with controls. At present, however, the use of portal vein infusion or intraperitoneal therapy outside of a research trial cannot be recommended in the light of the limited effects. This conclusion is further supported by similarly limited effects in two recently reported very large European multicentre trials. In advanced colorectal cancer, chemotherapy may prolong survival, decrease tumour-related symptoms, improve general well-being or maintain it at a high level for a longer time period compared with best supportive care. These effects have been seen using systemic chemotherapy and using regional chemotherapy in patients with metastases limited to the liver. Subjective responses and quality of life improvements are seen more frequently than objective tumour remissions. Although the impact on overall survival is modest, i.e. an improvement in median survival of five to six months, treatment is recommended also outside clinical trials. High-dose infusional regimens with modulated fluorouracil may turn out to be superior to conventional bolus regimens, since they result in more tumour
regressions, longer times to disease progression and possibly longer survival. A plateau seems, however, to have been reached with fluorouracil, giving objective response rates of up to 30% to 40% with a variety of modulators. Randomised studies of regional therapy, mostly hepatic arterial infusions, of liver metastases in colorectal patients have demonstrated significantly higher response rates than systemic fluorouracil therapy alone without impact on overall survival. The importance of the higher response rates for patient benefit in the predominantly asymptomatic patients with isolated liver metastasis remains to be elucidated. Regional therapy in advanced disease cannot be recommended outside of clinical trials. New cytotoxic agents are emerging with antitumour activity similar to fluorouracil-based chemotherapy. The addition of oxaliplatin or irinotecan to existing fluorouracil regimens improves response rates and duration of response, and possibly overall survival. Based upon the results of two randomised studies, there is a role for irinotecan as second line therapy for selected patients who have failed first-line therapy with fluorouracil plus leucovorin. The role of these agents, alone or in combinations, in clinical routine remains, however, to be determined due to more pronounced toxicity than caused b

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