# Review: Palliative chemotherapy reduces death and progression at 12 months in advanced or metastatic colorectal cancer

Colorectal Meta-analysis Collaboration. **Palliative chemotherapy for advanced or metastatic colorectal cancer.** Cochrane Database Syst Rev. 2000;(2):CD001545 (latest version 16 Nov 1999).


## QUESTION

In patients with locally advanced or metastatic colorectal cancer, what are the benefits and harms of palliative chemotherapy?

## DATA SOURCES

Studies were identified by searching MEDLINE, EMBASE/Excerpta Medica, CancerLit, the Cochrane Controlled Trials Register, CINAHL, HealthSTAR, *Science Citation Index*, Edina Biosis, NHS Economic Evaluation Database, Index to Scientific and Technical Proceedings, and PASCAL (to October 1998); hand searching conference abstracts; scanning bibliographies of relevant studies; searching sources of unpublished trials; and contacting authors.

## STUDY SELECTION

Studies in any language were selected if they were randomized controlled trials (RCTs) that compared palliative chemotherapy with supportive care alone in patients with advanced or metastatic colorectal cancer.

## DATA EXTRACTION

The quality of studies was assessed by using the Jadad scale. Authors were contacted for individual patient data (baseline patient characteristics, allocated treatment group, date of randomization, tumor response, survival and progression status, and date of death or last follow-up). 2 reviewers extracted data from published studies, and meta-analysis was done by using both published data and individual patient data.

## MAIN RESULTS

13 RCTs (1365 patients) met the selection criteria. Individual patient data were obtained for 7 RCTs (866 patients). Meta-analysis of published data showed that palliative chemotherapy (5-fluorouracil [5-FU], alone or in combination; fluoridine; irinotecan; or tauromustine) led to a reduction in death and progression at 12 months (Table). Statistically significant heterogeneity existed among these RCTs. Studies with individual patient data were not heterogeneous; they also showed a reduction in death (7 RCTs; number needed to treat [NNT] 6, 95% CI 4 to 11) and progression (3 RCTs, NNT 4) at 12 months. The evidence for toxicity, quality of life, and symptom control was inconclusive because of inconsistent reporting and use of poor-quality methods.

## CONCLUSIONS

In patients with locally advanced or metastatic colorectal cancer, palliative chemotherapy reduces death and progression at 12 months. The evidence on toxicity, symptom control, and quality of life is inconclusive.


*Source of funding: NHS National Cancer Research & Development Programme UK.*

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**Palliative chemotherapy vs supportive care for advanced or metastatic colorectal cancer***

| Outcomes at 12 mo | Number of studies | Weighted event rates | | RRR (95% CI) | NNT (CI) |
|---|---|---|---|---|---|
| | | Chemotherapy | Supportive care | | |
| Death | 10 | 53% | 68% | 22% (7 to 34) | 7 (5 to 20) |
| Progression | 4 | 66% | 76% | 14% (4 to 23) | 10 (6 to 36) |

*Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

## COMMENTARY

This well-conducted meta-analysis by the Colorectal Meta-analysis Collaboration supports the view that palliative chemotherapy is beneficial in treating colorectal cancer. Progression-free survival is prolonged, and deaths are reduced at 12 months. The benefits are substantial and clinically important. When studies with individual patient data are analyzed, relative risk reductions of 35% in deaths and 49% in progression at 12 months are shown. This finding translates into a 16% absolute difference in survival and a 25% increase in progression-free survival (increases of 3.7 mo in median survival and 6 mo in median progression-free survival).

This benefit is probably underestimated. An unknown proportion of patients randomly allocated to supportive care received delayed chemotherapy, and 3 trials allowed chemotherapy at the onset.

The issue is not whether to treat but when and how it is best to treat. Other potential modalities that either improve outcome or decrease toxicity include the use of continuous-infusion 5-FU (1), oral 5-FU (2), and combination chemotherapy (3). Future studies that incorporate measures of quality of life will better define the role of palliative chemotherapy in colorectal cancer.

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***References***

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3. **Saltz LB, Douillard J, Pirotta N, et al.** Combined analysis of two phase III randomized trials comparing irinotecan (C), fluorouracil (F), leucovorin (L) vs F alone as first-line therapy of previously untreated metastatic colorectal cancer (MCRC) [Abstract]. Proc Annu Meet Am Soc Clin Oncol. 2000;18:A938.

  