Capecitabine plus oxaliplatin compared with 5-fluorouracil plus oxaliplatin in metastatic colorectal cancer: meta-analysis of randomized controlled trials


CRD summary
The review concluded that in patients with metastatic colorectal cancer capecitabine plus oxaliplatin had similar curative effects as 5-fluorouracil plus oxaliplatin and was safer. In light of the limited study quality assessment, statistical analyses and the possibility of missing studies, the authors’ conclusions should not be considered as being reliable.

Authors’ objectives
To evaluate the curative effects and safety of capecitabine plus oxaliplatin compared with 5-fluorouracil plus oxaliplatin in patients with metastatic colorectal cancer.

Searching
Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, Science Direct, EBSCO, EMBASE and unspecified conference proceedings were searched between January 2000 and April 2011 for studies published in English; search terms were reported.

Study selection
Randomised controlled trials (RCTs) in patients with histologically confirmed colorectal cancer were eligible. Studies had to compare a capecitabine plus oxaliplatin regimen (a two-hour intravenous infusion of oxaliplatin 130mg/m² on day one plus oral capecitabine 1,000mg/m² twice daily on days one to 14 every three weeks) with a 5-fluorouracil plus oxaliplatin regimen. The main outcomes of interest were overall response rate, progression-free survival, median overall survival and toxic effects.

It appeared the intervention regimens varied across studies but only acronyms were presented for most (no further details provided). Mean ages ranged from 59 to 66 years. Most patients were male. Primary tumour sites were classified as being colon (the most common), rectum or colorectal. Most participants had Eastern Cooperative Oncology Group performance status scores of between zero and 1.

The authors did not state how many reviewers selected studies.

Assessment of study quality
Study quality was scored using a modified Jadad scale (inappropriate methods scored zero rather than a point deduction and only single-blinding of outcome assessors was considered). Studies received a score between 1 and 5. Studies that scored 3 or more were deemed to be high quality and lower scoring studies were classed as low quality. Details of allocation concealment were extracted.

Two reviewers independently scored the studies. Disagreements were resolved by a third reviewer.

Data extraction
Two reviewers extracted intention-to-treat data in order to calculate odds ratios (OR) with 95% confidence intervals (CI).

Methods of synthesis
Meta-analyses were performed to calculate pooled odds ratios using a fixed-effect model. Where significant heterogeneity was found a random-effects model was used. Heterogeneity was assessed using $I^2$ and the $X^2$ test ($p<0.05$ indicated significant heterogeneity rather than the more commonly used $p<0.10$). Where meta-analysis could not be performed the results were tabulated and summarised briefly in the text.

Results of the review
Seven RCTs were included (3,603 participants). All studies scored 4 points on the modified Jadad scale. None of the trials had any description of concealment of treatment allocation and blinding methods. All studies described the randomisation method and withdrawals appropriately. All analyses were performed according to the intention-to-treat principle.

There was no statistically significant difference between groups for complete response (four RCTs; $I^2=59\%$). For partial response (OR 0.81, 95% CI 0.65 to 1.00; four RCTs; $I^2=0\%$) and overall response rate (OR 0.85, 95% CI 0.71 to 1.02; five RCTs; $I^2=11\%$) results were nearly statistically significant in favour of treatment with capecitabine plus oxaliplatin.

There were no statistically significant differences in individual studies for median overall survival and progression-free survival.

Incidence of hand-foot syndrome in the capecitabine plus oxaliplatin group was significantly higher than in the 5-fluorouracil plus oxaliplatin group (five RCTs; $I^2=58\%$). Stomatitis (three RCTs; $I^2=59\%$) and neutropenia (four RCTs; $I^2=89\%$) occurred significantly more frequently in the 5-fluorouracil plus oxaliplatin group. There were no statistically significant differences between groups for nausea, diarrhoea, fever, thrombocytopenia and peripheral neuropathy.

**Authors' conclusions**

In patients with metastatic colorectal cancer, capecitabine plus oxaliplatin had similar curative effects as 5-fluorouracil plus oxaliplatin and was safer.

**CRD commentary**

The review addressed a clear question and was supported by reproducible eligibility criteria. Use of treatment acronyms, many undefined, made it difficult to see whether the authors had adhered to their eligibility criteria. Attempts to identify studies were undertaken by searching several relevant electronic databases. Language and publication restrictions meant that some relevant studies may have been missed.

Suitable methods were employed to reduce risks of reviewer error and bias during data extraction and assessment of study quality; the authors did not report on whether such methods were used to select studies for inclusion.

Study quality was assessed but the results generated appeared to be of limited value as all studies were rated as being high quality yet none had descriptions of allocation concealment and blinding processes. The value of pooled results obtained from a fixed-effect model in the presence of tangible heterogeneity ($p<0.10$) was questionable. Consequently no investigations into the sources of heterogeneity were made. Sufficient study details were provided.

In light of the limited study quality assessment, synthesis and the possibility of missing studies, the authors' conclusions should not be considered as being reliable.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated a need for high quality studies, particularly in relation to adverse events.

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Not reported.

**Bibliographic details**


**PubMedID**

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.