Meta-analysis of chemotherapy with irinotecan or oxaliplatin-involved regimen for untreated metastatic advanced colorectal cancer
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CRD summary
This review concluded that oxaliplatin (OXA+5-FU/LV) chemotherapy was superior or at least equal to irinotecan (IRI+5-FU/LV) chemotherapy for prolonging overall survival and time to progression. Differences in toxicity profiles were observed. The conclusions of this review reflect the evidence presented, but a lack of detail makes it difficult to verify the results.

Authors' objectives
To compare the chemotherapy regimens 5-fluorouracil and leucovorin in combination with either irinotecan (IRI+5-FU/LV) or oxaliplatin (OXA+5-FU/LV) in untreated advanced metastatic colorectal cancer.

Searching
MEDLINE and EMBASE (from inception), Cochrane Central Register of Controlled Trials (CENTRAL) (issue 2, 2008) and CBM (from 1978) and CNKI (from 1994) were searched up to May 2008. Internet searches were performed. Ongoing trials were sought. Search terms were reported.

Study selection
Randomised or quasi-randomised controlled trials that compared IRI+5-FU/LV with OXA+5-FU/LV in the treatment of advanced colorectal cancer were eligible. Trial inclusion criteria had to involve physical examinations and blood tests that included complete blood count with serum-based testing of liver functioning, prothrombin time (for those on warfarin), creatinine clearance and electrocardiography performed within 14 days of enrolment. Patients had to have performance status of zero to two (World Health Organisation) or two or less (Eastern Cooperative Oncology). Overall survival was the primary outcome. Secondary outcomes were median survival, time to progression and toxic effects. Doses and treatment schedules varied across the studies.

Two independent reviewers performed the study selection. Disagreements were resolved by discussion.

Assessment of study quality
Quality was assessed using the methods of the Cochrane Collaboration that covered method of randomisation, allocation concealment, blinding and loss to follow-up.

Two independent reviewers performed the quality assessment. Disagreements were resolved by discussion or referral to a third person.

Data extraction
Hazard ratios (HR) were extracted or calculated for time to event outcomes and relative risks (RR) were calculated for binary outcomes, all with corresponding 95% confidence intervals (CI). Data collection and analysis were performed by two reviewers.

Methods of synthesis
Statistical heterogeneity was measured using the Q statistic (taken to be statistically significant if p<0.10) and the I² statistic. A fixed-effect model was used to pool data in the absence of significant heterogeneity, otherwise a random effects model was used. In the absence of pooling, results were presented narratively. Publication bias was assessed using Begg's and Egger's tests and funnel plots.

Results of the review
Seven trials (2,107 participants) were included. Three trials had adequate methods of randomisation. None of the trials
reported use of allocation concealment or blinding. All seven trials reported losses to follow-up. Six trials used intention-to-treat analyses.

**Survival**: OXA-based chemotherapy improved overall survival compared to the IRI-based regimen (HR 1.28 for IRI versus OXA, 95% CI 1.13 to 1.45; five trials with \( p = 0.064 \) for heterogeneity). There was no evidence of publication bias. Six trials reported median survival, which ranged from 14 to 17.6 months for IRI-based chemotherapy compared to 13.7 to 19.5 months for OXA-based chemotherapy. Survival tended to be longer for OXA-based chemotherapy and this was statistically significant in three trials.

**Progression-free survival**: Six trials reported time to progression and this was longer for OXA-based chemotherapy in four trials. Time to progression ranged from 5.5 to 8.9 months for IRI-based and 7.0 to 9.7 months to OXA-based chemotherapy. The difference was statistically significant in two trials.

**Toxicity**: Combined results of seven trials showed that nausea/vomiting/emesis and diarrhoea were significantly more likely with IRI-based chemotherapy and paraesthesia, sensory neuropathy and thrombocytopenia were significantly more likely with the OXA-based regimen. Full numerical results for 14 types of toxicity were reported in the paper.

**Authors’ conclusions**
The OXA+5-FU/LV regimen was superior or at least equal to the IRI+5-FU/LV regimen in prolonging overall survival and time to progression. The difference between these two combination therapies was mainly in the toxicity profile. There were more gastrointestinal events observed with IRI-regimen and more thrombocytopenia and neurotoxicity with the OXA-regimen.

**CRD commentary**
This review had a clearly stated research question and specified inclusion criteria for study design, interventions, participants and outcomes. The literature search covered several electronic databases. It was unclear whether there were any language restrictions, so language bias was a possibility. Publication bias was assessed and no evidence for it was found. Review methods were performed by two reviewers independently to reduce error or bias. Study quality was assessed using an appropriate tool for randomised trials and the results were reported.

Methods of meta-analysis appeared appropriate. There was a lack of detail about the included trials; only details of the treatments were reported and some only reported limited results without statistical testing.

The conclusions of this review reflect the evidence presented, but a lack of detail makes it difficult to verify the results.

**Implications of the review for practice and research**
**Practice**: The authors stated that OXA+5-FU/LV chemotherapy might be considered a first-line standard of care for patients with advanced colorectal cancer and one that is more active and better tolerated than IRI+5-FU/LV

**Research**: The authors stated that further statistical analysis was needed to support the conclusions that OXA+5-FU/LV was superior or at least equal to IRI+5-FU/LV in prolonging median survival and time to progression.

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Record Status
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.