Review of second-line chemotherapy for advanced gastric adenocarcinoma

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CRD summary
This review assessed the effects of second-line chemotherapy for unresectable or recurrent gastric and gastroesophageal junction adenocarcinoma. The authors concluded that second-line chemotherapy can provide benefit in patients with gastric adenocarcinoma. Given the paucity of the evidence base reviewed and limitations in the conduct of the review, the authors’ conclusions may not be reliable or robust.

Authors’ objectives
To assess the effects of second-line chemotherapy in unresectable or recurrent gastric and gastroesophageal junction adenocarcinoma.

Searching
MEDLINE and PubMed were searched for trials published between 1996 and 2003; the search terms were reported and no language restrictions were used. The bibliographies of the identified studies were handsearched.

Study selection
Study designs of evaluations included in the review
Phase II or III trials were eligible for inclusion. All of the included trials were Phase II trials.

Specific interventions included in the review
Studies of any second-line chemotherapy, excluding immunotherapy or non-cytotoxic agents, were eligible for inclusion. The specific interventions assessed were cisplatin, paclitaxel (with or without carboplatin), docetaxel, mitomycin C, folinic acid, 5-fluorouracil, (with or without folinic acid), raltirexed, oxaliplatin, etoposide and irinotecan. The dosages and regimens for drugs used in each study were listed.

Participants included in the review
Studies of patients with histologically proven recurrent or primarily unresectable gastric or gastroesophageal adenocarcinoma who had previously been treated with a single regimen of palliative chemotherapy, with response assessed by WHO or RECIST criteria, were eligible for inclusion. In the included trials, 71% of the patients were male and 29% female, and the median age was 57 years (range: 26 to 78). All patients had recurrent or primarily unresectable gastric cancer.

Outcomes assessed in the review
The outcomes of interest were symptom improvement, survival and the selection of patients for second-line treatment. In the review, data for the following outcomes were given: response rate (complete and partial), symptomatic benefit and median survival (both among all patients and split by responders versus nonresponders).

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. The extracted data included the response rate, duration of response and median survival.
Methods of synthesis
How were the studies combined?
Most of the results were reported as a narrative summary of the individual studies. The mean response rates across studies were calculated.

How were differences between studies investigated?
Differences between the studies which could account for differing results were reported in the narrative summary.

Results of the review
Twelve phase II trials, involving 285 participants, were included.

The mean response rate across the trials was 20.8% (range: 0 to 52), most of which were partial responses. Four trials reported at least one complete response (range: 5 to 9.5%). The mean stable disease rate was 26% (range: 0 to 41). The mean tumour control rate was 51%. The response rate was 29% (range: 19 to 45) in cisplatin-based regimens (3 trials) and 25% (range: 22 to 27) in paclitaxel-based regimes (2 trials). One trial reported symptomatic benefit in 44% of the patients. Median survival (9 trials) was 5.6 months (range: 2.5 to 11). In 7 trials, survival of responders was longer than that of nonresponders.

Authors' conclusions
Second-line therapy can provide benefit in patients with gastric adenocarcinoma.

CRD commentary
The review question was defined in terms of the interventions, participants, outcomes and study designs. The literature search involved only one database and made no attempt to find unpublished or grey literature; it is therefore possible that additional relevant studies might have been missed. There were no tests for publication bias. The quality of the included studies was not formally assessed. Since the authors did not report how the articles were selected, or who performed the selection and data extraction, is it not known whether any efforts were made to minimise reviewer bias and errors in the review process.

Although details of studies were tabulated and briefly discussed in the text of the review, further demographic data on the participants included in the review would have been useful. The authors presented the results across all included trials, which might not have been appropriate as the studies differed in terms of the interventions, dosages, regimens and participant characteristics. Overall, given the paucity of the evidence base reviewed and limitations in the conduct of the review, the authors' conclusions may not be reliable or robust.

Implications of the review for practice and research
Practice: The authors stated that the choice of second-line agent depends on first-line treatment. Cisplatin-based therapy may be effective as a salvage treatment if not used first-line, and paclitaxel used alone or in combination with platinum can provide symptomatic benefit in patients who have failed platinum-based first-line therapy, as well as tolerable toxicity.

Research: The authors stated that randomised controlled trials are required to compare second-line single-agent paclitaxel with best supportive care in patients who have failed first-line cisplatin-based therapy.

Bibliographic details

PubMedID
Indexing Status
Subject indexing assigned by NLM

MeSH
Adenocarcinoma /drug therapy; Antineoplastic Agents /therapeutic use; Clinical Trials, Phase II as Topic; Esophageal Neoplasms /drug therapy; Esophagogastric Junction; Humans; Palliative Care; Salvage Therapy; Stomach Neoplasms /drug therapy; Survival Analysis

AccessionNumber
12005009516

Date bibliographic record published
31/05/2006

Date abstract record published
31/05/2006

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.