Off-label use of bevacizumab: advanced adenocarcinoma of the pancreas

Mauger Rothenberg B, Aronson N, Ziegler KM, Bonnell CJ, Gere MA

CRD summary
This review concluded that the addition of bevacizumab to a treatment regimen did not increase overall survival among patients with locally advanced or metastatic pancreatic cancer. Some caution should be exercised in interpreting conclusions, as evidence was very limited and there was a lack of reporting of all details of the review process.

Authors' objectives
To determine the incremental benefit of using bevacizumab in patients with advanced adenocarcinoma of the pancreas.

Searching
The authors searched MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) for English language studies up to July 2009. Search terms were reported. Reference lists of relevant articles and abstracts from the American Society of Clinical Oncology were also checked.

Study selection
Phase III trials of bevacizumab for patients with adenocarcinoma of the pancreas were eligible for the review. Relevant study outcomes were overall survival, progression-free survival, greater tumour response and adverse events.

Included trials compared gemcitabine and bevacizumab with gemcitabine alone or gemcitabine and erlotinib with or without bevacizumab. Median patient age ranged from 61 to 63.8 years. Patients had metastatic or locally advanced pancreatic cancer. Individual trial exclusion criteria varied (full details in the paper).

The authors did not state how studies were selected for the review.

Assessment of study quality
The authors did not appear to conduct a formal assessment of study quality, but key quality issues were discussed in the paper.

Data extraction
The authors did not state how data were extracted for the review.

Methods of synthesis
The authors conducted a narrative synthesis.

Results of the review
Two phase III trials were included in the review (n=1,209 patients).

One trial, comparing gemcitabine and bevacizumab with gemcitabine alone, was stopped early after interim analysis with 64% of the information on overall survival and 436 deaths (93% of the deaths expected at final analysis). It was considered unlikely that significant differences in overall survival would be detected with further follow-up. No statistically significant difference in progression-free survival was found.

The other trial, comparing gemcitabine and erlotinib with or without bevacizumab, did not demonstrate a statistically significant increase in overall survival. A statistically significant increase of one month progression-free survival with bevacizumab was observed (hazard ratio 0.73, 95% CI 0.61 to 0.86). Adverse events were detailed in this trial, but no statistical tests of significance between treatment groups were reported.

Authors' conclusions
The authors concluded that the addition of bevacizumab to a treatment regimen did not increase overall survival among
patients with locally advanced or metastatic pancreatic cancer.

**CRD commentary**

Inclusion criteria for this review were defined in terms of study design, participants, interventions and outcomes. Searching encompassed a range of databases and other sources. However, the restriction to trials in English language may have led to papers being missed. No details were provided on methods to reduce bias and error in the review process.

There was no formal assessment of study quality, but key issues were discussed. Meta-analysis would not have been possible given the limited study results.

Given the lack of reporting of all details of the review process and the limited evidence available, the authors’ conclusions should be treated with some caution.

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

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

**Research:** The authors highlighted that a number of clinical trials of bevacizumab for pancreatic cancer are in progress. They commented that data on quality of life would be useful.

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