Effect of pexelizumab on mortality in patients with acute myocardial infarction or undergoing coronary artery bypass surgery: a systematic overview


CRD summary
The authors concluded that pexelizumab reduced 30-day mortality. The conclusion is supported by the results presented. However, poor reporting of the review methods make it difficult to confirm the reliability of the authors’ conclusion. The review and all of the included studies were funded by pharmaceutical companies.

Authors’ objectives
To conduct a systematic review, based on individual patient data, to evaluate the effects of pexelizumab on mortality in patients who had an acute myocardial infarction (MI) or were undergoing coronary artery bypass graft (CABG) surgery.

Searching
Published studies were identified by searching MEDLINE, screening reference lists and through personal communication. No details of the search terms or dates were reported. It is unclear whether any language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion in the review.

Specific interventions included in the review
Studies that compared pexelizumab with placebo were eligible for inclusion. The included studies compared pexelizumab 2.0 mg/kg bolus alone or plus infusion (0.05 mg/kg per hour for 20 to 24 hours) with placebo. The main review comparison was bolus pexelizumab plus infusion versus placebo. The review also compared bolus pexelizumab alone versus placebo and any pexelizumab (bolus plus infusion or bolus only) versus placebo.

Participants included in the review
Studies of patients who had an acute ST-elevation MI or who were undergoing CABG surgery were eligible for inclusion. In the included studies, men and women with acute MI were undergoing percutaneous transluminal coronary angioplasty or thrombolytic reperfusion therapy, and men and women were undergoing CABG with and without concomitant valve surgery with cardiopulmonary bypass. The mean age of the patients ranged from 60 to 68 years and the mean weight ranged from 78 to 86 kg. Twenty-three per cent to 33% of the patients were women, most were white (84 to 90%), between 14 and 42% had diabetes, and between 4 and 45% were current smokers.

Outcomes assessed in the review
No inclusion criteria relating to the outcomes were specified. The primary review outcome was all-cause mortality at 30 days. The review also assessed mortality at 180 days.

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. However, they did comment on the level of blinding and baseline comparability of the treatment groups.
**Data extraction**

The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. However, the review authors stated that data for all four studies were housed at the Duke Clinical Research Institute and that all analyses were conducted independently at the Institute. For each study, data were analysed on an intention-to-treat (ITT) basis. Relative risks (RRs) with 95% confidence interval (CIs) were calculated.

**Methods of synthesis**

How were the studies combined?

Pooled RRs with 95% CIs were calculated using a random-effects model for each comparison of interest. Kaplan-Meier survival curves were produced, with corresponding p-values, for mortality up to 180 days.

How were differences between studies investigated?

Statistical heterogeneity was assessed using the chi-squared statistic. Studies in patients with MI were analysed separately from those of patients undergoing CABG.

**Results of the review**

Four RCTs (n=5,916) were included.

All of the studies were double-blind. In all studies the treatment groups appeared comparable at baseline.

Bolus pexelizumab plus infusion was associated with a significant reduction in mortality at 30 days compared with placebo: 2.9% versus 4.2%, representing a 30% reduction. The RR was 0.70 (95% CI: 0.52, 0.95, p=0.02). Reductions in mortality were similar for patients with MI and patients undergoing CABG.

Any pexelizumab (bolus plus infusion or bolus only) was associated with a reduction in mortality at 30 days compared with placebo, but the reduction was not statistically significant: 3.5% versus 4.2%, representing a 15% reduction. The RR was 0.85 (95% CI: 0.66, 1.0975, p=0.215). There was no overall reduction in 30-day mortality between pexelizumab bolus alone and placebo: 5.2% versus 5.4%. The RR was 0.96 (95% CI: 0.66, 1.41, p=0.918).

Pexelizumab bolus plus infusion was associated with a significant reduction in mortality at 180 days compared with placebo (Kaplan-Meier survival curve, p=0.05; based on three studies).

**Authors’ conclusions**

Pexelizumab reduced 30-day mortality.

**CRD commentary**

The review addressed a clear question that was defined in terms of the participants, intervention, outcomes and study design. Although the search was apparently limited, the authors stated that they had been involved in all trials of pexelizumab and so it is likely that all eligible studies were included. Only RCTs were included and some aspects of validity were reported. Since the methods used to select studies and extract the data were not described, it is not known whether any efforts were made to reduce reviewer errors and bias.

The studies were combined using meta-analysis. Results of the assessment of statistical heterogeneity were not reported but a forest plot of the main analysis suggested homogeneity. The conclusion is supported by the results presented; however, incomplete reporting of review methods make it difficult to confirm the reliability of the authors’ conclusion. The review authors conducted the included studies and all of the included studies were funded by pharmaceutical companies.

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

Practice: The authors did not state any implications for practice.
Research: The authors stated the need for large studies to evaluate the effects of pexelizumab on clinical outcomes in acute MI or CABG patients. They stated that ongoing trials are evaluating pexelizumab bolus plus infusion in acute MI patients being treated with a primary percutaneous coronary intervention and during cardiopulmonary bypass.

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