Frontline gefitinib in advanced non-small cell lung cancer: meta-analysis of published randomized trials

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CRD summary
This review concluded that gefitinib could not be recommended for frontline management of unselected patients with advanced non-small cell lung cancer. Evidence appeared to support the author's conclusion, but the lack of reporting of trial quality and review methods made it difficult to assess its reliability.

Authors' objectives
To evaluate the efficacy of gefitinib for patients with locally advanced or metastatic non-small cell lung cancer.

Searching
PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews, and DARE were searched for peer-reviewed studies published in English. Search terms were reported, but search dates were not. Proceedings of the main oncology conferences and reference lists of primary studies and reviews were screened.

Study selection
Randomised controlled trials (RCTs) were eligible for inclusion if they evaluated the efficacy of gefitinib-based therapy in chemotherapy-naive patients with locally advanced or metastatic non-small cell lung cancer. Trials were also eligible if they compared gefitinib with placebo or no treatment in patients who had all been offered initial induction with chemoradiation or chemotherapy. The review assessed objective response rate, progression-free survival, overall survival and quality of life.

The included trials compared: gefitinib plus chemotherapy versus chemotherapy alone; gefitinib alone versus chemotherapy; and gefitinib plus best supportive care versus best supportive care alone. Chemotherapeutic agents were reported. Most included patients were male, smokers and non-Asian; many had non-adenocarcinoma non-small cell lung cancer. The median age per treatment group ranged from 57 to 76 years. The percentage of patients with stage IIIB cancer ranged from 15 to 55% and 67 to 84% had stage IV cancer. Trials included patients with known and unknown epidermal growth factor receptor status.

The author did not state how papers were selected for the review.

Assessment of study quality
The author did not state that validity was assessed.

Data extraction
Log hazard ratios (HR) and variances were extracted or calculated for each trial.

The author stated that data were checked and compared with the original publications, but did not state how many reviewers were involved in this process.

Methods of synthesis
Pooled hazard ratios and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using fixed-effect and random-effects models. Heterogeneity was assessed using the X2 and I2 statistics. Where significant heterogeneity was found (p≤0.1), potential sources were investigated and a random-effects model used. Patients whose epidermal growth factor receptor status was known were also analysed separately.

The possibility of publication bias was explored using a funnel plot.
Results of the review
Seven RCTs were included in the review (n=4,585 patients).

Overall, there was no statistically significant difference between gefitinib and control for objective response rate, progression-free survival or overall survival. No significant heterogeneity was found for overall survival, but significant heterogeneity was found for response rate (p=0.02) and progression-free survival (p<0.00001).

Epidermal growth factor receptor mutation status (two RCTs, 587 patients): Among patients with known mutant epidermal growth factor receptor status, gefitinib was associated with a statistically significant increase in objective response rate compared with control (OR 2.81, 95% CI 1.71 to 4.62; no significant heterogeneity), but there was no significant difference between gefitinib and control for the other outcomes (progression-free survival and overall survival).

Quality of life (three RCTs): Gefitinib was associated with a statistically significant improvement in quality of life compared with control assessed using the Functional Assessment of Cancer Therapy-Lung questionnaire (OR 1.38, 95% CI 1.06 to 1.79) and the Trial Outcome Index (OR 1.87, 95 CI 1.13 to 3.09), but there was no significant difference on the Lung-Cancer Subscale of the functional assessment questionnaire. No significant heterogeneity was found for quality of life analyses.

Authors’ conclusions
Gefitinib could not be recommended for front-line management of unselected patients with advanced non-small cell lung cancer based on available evidence.

CRD commentary
The review question was clearly stated and inclusion criteria were appropriately defined. Several relevant sources were searched. No attempts were made to minimise language bias, but some attempts were made to minimise publication bias by searching conference abstracts. Methods used to select studies and extract data were not described, so it was not known whether efforts were made to reduce reviewer errors and bias.

Trial validity was not assessed, which made it difficult to judge the quality of the included trials. Appropriate methods were used to pool data. Forest plots were presented. Heterogeneity was assessed; where heterogeneity was found, potential sources were explored.

Evidence appeared to support the author’s conclusion, but the lack of reporting of trial quality and review methods made it difficult to assess its reliability.

Implications of the review for practice and research
Practice: The author stated that gefitinib cannot be recommended for front-line management of unselected patients with advanced non-small cell lung cancer.

Research: The author did not state any implications for research.

Funding
None.

Bibliographic details

PubMedID
20835310
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.