Erlotinib or gefitinib for the treatment of relapsed platinum pretreated non-small cell lung cancer and ovarian cancer: a systematic review

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CRD summary
The review concluded that erlotinib and gefitinib were suitable for treatment of platinum pre-treated non-small cell lung cancer, but may not be useful in ovarian cancer. Potential differences across the trials, uncertain quality of the included trials and the unspecified form of pooling mean that caution is warranted when interpreting the authors’ conclusions.

Authors' objectives
To investigate whether erlotinib or gefitinib have efficacy in patients with relapsed pre-treated non-small cell lung cancer and ovarian cancer.

Searching
MEDLINE and EMBASE were searched to February 2011 for articles published in English. Search terms were reported Reference lists of included articles were searched.

Study selection
Clinical trials of erlotinib or gefitinib (alone or in combination) for the treatment of cancer in patients who had previously received platinum-based chemotherapy were eligible for inclusion. Trials of chemotherapy-naïve patients or first-line therapy were excluded. Maintenance therapy for non-relapsed/non-progressed platinum pre-treated patients were excluded.

The included trials studied: erlotinib (100 to 150mg/day) alone or in combination with bevacizumab or pemetrexed for non-small cell lung cancer and alone or with carboplatin and bevacizumab for ovarian cancer; gefitinib (250 to 500mg/day) alone or in combination with vinorelbine, celecoxib, rofecoxib or cetuximab for non-small cell lung cancer and alone or with tamoxifen, paclitaxel and carboplatin for ovarian cancer. The platinum status for most of the patients recruited to the trials was unknown. Some trials specified some or all patients as platinum refractory or resistant. Some trials also included platinum sensitive patients. The proportion of Asian patients, where reported, comprised 0% to 100%. The reported outcomes included various response and survival measures. Some trials reported the epidermal growth factor receptor (EGFR) status of patients and the resulting proportion of EGFR responders.

The authors did not state how many reviewers performed study selection.

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

Data extraction
Data were extracted on response rates and survival. Trial authors were contacted where data were not reported.

The authors did not state how many reviewers performed data extraction.

Methods of synthesis
A narrative synthesis was presented with data in tables. An unspecified form of pooling was undertaken. Fisher's exact test was reportedly used to test for significant differences in pooled response rates.

Results of the review
Thirty clinical trials were included in the review: 23 trials of non-small cell lung cancer and seven trials of ovarian cancer.

Non-small cell lung cancer: The overall response rate in platinum pre-treated non-small cell lung cancer was significantly higher with 250mg/day gefitinib than with 150mg/day erlotinib (15.25% versus 11.14%). Gefitinib was
superior to erlotinib in patients with overexpression of EGFR as measured by immunohistochemistry. Overall survival was slightly longer with gefitinib (8.64 months) than with erlotinib (8.12 months). Progression-free survival data were slightly longer for gefitinib (2.24 months erlotinib versus 2.82 months gefitinib).

**Ovarian cancer**: In platinum pre-treated ovarian cancer, overall response rates with single agent erlotinib or gefitinib were low (zero to 5.9%), but were higher for combined erlotinib or gefitinib (zero to 61.9%). Survival data varied widely, from eight to 12.16 months for single erlotinib or gefitinib to 8.43 to 25.7 months for combination therapy.

**Authors’ conclusions**
The authors appeared to conclude that erlotinib and gefitinib were suitable for treatment of platinum pre-treated non-small cell lung cancer, particularly in patients with EGFR mutations, but may not be useful in ovarian cancer.

**CRD commentary**
Inclusion criteria for the review were broadly defined. Several relevant data sources were searched. Publication bias was not assessed and could not be ruled out. A separate search for pre-clinical data was beyond the scope of this abstract and was not extracted. The authors did not state how many reviewers were involved in the review process, which made it difficult to assess potential for biases and errors. It appeared that there was no quality assessment of included trials.

Several trials had small sample sizes (fewer than 50 patients in the treatment arm). There were notable differences across the trials for type of drug, platinum status and patient ethnicity. Other patient characteristics such as patient ages and type of cancer cell (such as adenocarcinoma for non-small cell lung cancer) were not reported. Trials were synthesised narratively. A non-specified form of pooling was undertaken.

Potential differences across the trials, uncertain quality of the included trials and the unspecified form of pooling mean that caution is warranted when interpreting the authors’ conclusions.

**Implications of the review for practice and research**
**Practice**: The authors stated that gefitinib should be used in preference to erlotinib in platinum pre-treated non-small cell lung cancer patients.

**Research**: The authors stated that future clinical trials needed to collect tumour biopsies from all patients to ensure the success of personalised chemotherapy.

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