A systematic review and economic model of the clinical effectiveness and cost-effectiveness of docetaxel in combination with prednisone or prednisolone for the treatment of hormone-refractory metastatic prostate cancer


CRD summary
This well-conducted review concluded that docetaxel plus prednisone appears to be the most effective treatment for men with metastatic hormone-refractory prostate cancer. The review was based partially on an indirect comparison of treatments and the authors advised a cautious approach to the conclusions.

Authors' objectives
To evaluate the clinical and cost-effectiveness of docetaxel (Taxotere) for the treatment of metastatic hormone-refractory prostate cancer (mHRPC). Cost-effectiveness analyses are only briefly mentioned in this abstract, which focused on the clinical effectiveness.

Searching
Twenty-one resources (including a range of electronic databases) were searched from inception to April 2005; full details of the search strategy were given. No language or other restrictions were applied. The bibliographies of all included studies, the industry submission, and papers retrieved for background information were checked for any further relevant studies. Foreign language papers were then excluded from the review.

Study selection
Study designs of evaluations included in the review
To be eligible, studies needed to be randomised controlled trials (RCTs). Studies reported only in abstract form were excluded.

Specific interventions included in the review
To be eligible, trials needed to evaluate docetaxel in combination with prednisone/prednisolone or mitoxantrone in combination with a corticosteroid. The comparators included any chemotherapy regimen, best supportive care including radiotherapy, or placebo.

Participants included in the review
To be eligible, studies needed to be of men with mHRPC.

Outcomes assessed in the review
Studies that assessed the following outcomes were eligible for inclusion: overall survival, progression-free survival, response rate (including complete and partial response), prostate-specific antigen (PSA) decline, adverse effects of treatments, pain, health-related quality of life and costs.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed studies for inclusion in the review, with any discrepancies resolved by consensus or recourse to a third reviewer.

Assessment of study quality
One reviewer assessed the quality of the included studies, which was independently checked by a second reviewer. Any disagreements were resolved by consensus or by recourse to a third reviewer. Quality was assessed according to criteria based on established guidelines, which included randomisation, allocation concealment, blinding and loss to follow-up.

Data extraction
One reviewer extracted the data, which were independently checked for accuracy by a second reviewer. Any disagreements were resolved by consensus or by recourse to a third reviewer. Where multiple publications of the same
study were found, data were extracted and reported as a single study. Where sufficient data were available, treatment effects were presented as the relative risk or hazard ratio together with associated 95% confidence intervals (CIs). Time-to-event data were estimated for each study.

**Methods of synthesis**

How were the studies combined?
The studies were combined in a narrative, with meta-analysis used only when the data permitted. There was only one trial that compared docetaxel plus prednisone alone with another chemotherapy regimen; no trials had compared docetaxel plus prednisone versus best supportive care. Hence an adjusted indirect comparison was made to quantify the relative efficacy of docetaxel plus prednisone versus corticosteroids.

How were differences between studies investigated?
Differences between the studies were outlined in the report.

**Results of the review**

Seven RCTs (n=2,656) were included in the review.

A direct comparison trial (1,006 patients) of docetaxel plus prednisone versus mitoxantrone plus prednisone showed statistically significantly higher overall survival for docetaxel plus prednisone: the hazard ratio for death was 0.76 (95% CI: 0.62, 0.94). Other outcomes such as response rate, quality of life, pain response and PSA decline were also in favour of docetaxel plus prednisone, with statistically significant benefits for all outcomes except response rate. These outcomes were associated with more grade 3 to 4 adverse events. It was also found that docetaxel plus estramustine and docetaxel plus estramustine plus prednisone were superior to mitoxantrone plus prednisone in terms of overall survival, response rate and progression-free survival, although only response rate showed a statistically significant benefit. Three trials that compared mitoxantrone plus a corticosteroid with a corticosteroid alone showed, overall, very little difference between the groups. Indirect comparisons between trials revealed that docetaxel plus prednisone was superior to corticosteroids alone: the hazard ratio for death was 0.75 (95% CI: 0.57, 0.99).

**Cost information**

An economic model was developed to establish the cost-effectiveness of docetaxel compared with a range of other treatments. The findings of the model were that mitoxantrone plus a corticosteroid was probably cheaper and more effective than corticosteroid alone. Compared with mitoxantrone plus prednisone/prednisolone, the use of docetaxel plus prednisone/prednisolone (3 weekly) appeared to be cost-effective at a willingness-to-pay of £33,000 per quality-adjusted life-year.

**Authors’ conclusions**

Docetaxel plus prednisone appears to be the most effective treatment for men with mHRPC.

**CRD commentary**

This review had clear inclusion criteria for the study design, participants, interventions and outcomes. It was based on an extensive search of the relevant literature. Validity was assessed and methodological problems with the studies were highlighted. Review methods were described in full and methodological decisions explained and justified. The reviewers were careful to consider when meta-analyses were appropriate to conduct. The reviewers made plain the limitations of the indirect comparison used. The conclusions of this well-conducted review are likely to be reliable.

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

Practice: The authors concluded that docetaxel plus prednisolone appears to be the most effective treatment for men with mHRPC.

Research: The authors stated that future research should include an assessment of quality of life and utility gain associated with different treatments, including adverse effects of treatments, using generic instruments suitable for the purpose of cost-effectiveness analyses.
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