Comparison of docetaxel- and Vinca alkaloid-based chemotherapy in the first-line treatment of advanced non-small cell lung cancer: a meta-analysis of seven randomized clinical trials


CRD summary
This review compared docetaxel-based chemotherapy with Vinca alkaloid-based regimens on overall survival in first-line therapy of advanced non-small cell lung cancer, and concluded that docetaxel-based regimens were significantly more effective in terms of overall survival and safety. Given concerns regarding the review process and quality of included trials, the extent to which the authors' conclusion is reliable is unclear.

Authors' objectives
To compare the impact on overall survival of docetaxel-based chemotherapy versus Vinca alkaloid-based regimens for first-line therapy of advanced non-small cell lung cancer.

Searching
MEDLINE, CANCERLIT, MEDSCAPE, the National Institutes of Health Trials Register, and the Cochrane Library were searched, together with an internet search using Google Scholar. Search dates were not reported, but search terms were presented. No language or publication status restrictions were applied. Conference proceedings and bibliographic records of retrieved articles were searched to identify further relevant studies.

Study selection
Studies were assessed as eligible for inclusion if they were randomised controlled trials (RCTs) that evaluated the effect of docetaxel compared with a Vinca alkaloid as first-line chemotherapy for advanced non-small cell lung cancer. Eligible trials had to include at least one treatment arm with either docetaxel alone or in combination with either a platinum agent or gemcitabine; they also had to include at least one Vinca alkaloid-based treatment arm. Trials that included the administration of granulocyte colony-stimulating factor were also considered. Eligible trials were required to have a Jadad quality assessment score of more than 2 out of 4 points.

Included trials were located in Europe, the USA, and Japan. Included patients were diagnosed as at either stage IIIB, IIIb or IV (advanced metastatic stage) of non-small cell lung cancer [A: author correction: the patient population was exclusively stages IIIB and IV]; their median age ranged from 58-76 years. A variety of drug regimens were reported in the paper. Trial duration ranged from 12 to 41 months. Most trials used overall survival rates or objective response rate as the primary endpoint; one trial used progression free survival as the primary endpoint. Performance status was assessed using Karnofsky performance status, World Health Organisation or Eastern Cooperative Oncology Group criteria.

The authors did not state how many reviewers selected the studies.

Assessment of study quality
Studies were assessed using the Jadad scoring system in terms of: randomisation, sequence generation, concealment and completeness of follow-up. Each criterion was assessed either as being met or not met.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Two authors independently extracted data required to calculate the hazard ratio (HRs) with 95% confidence intervals (CIs) for survival outcomes; and extracted data required to calculate odds ratios (ORs), with 95% confidence intervals, for a range of efficacy and safety outcomes; these included overall survival rate, grade 3/4 neutropenia, febrile neutropenia, grade 3/4 serious adverse events, serious adverse events leading to drug discontinuation, and serious adverse events leading to death.
Authors and trial investigators were contacted for further data where necessary. Disagreements were resolved by consensus.

**Methods of synthesis**

Meta-analyses were conducted. Heterogeneity was assessed using a Q test and judged significant if p was more than 0.10, in which case a random-effects rather than fixed-effect model was used to pool the data using inverse-variance weighting. Funnel plots were drawn to assess publication bias. Sensitivity analysis was performed to assess whether any one trial had a disproportionate influence on the pooled results.

Subgroup analyses were performed to assess different docetaxel-based regimens, and for serious adverse events leading to either drug discontinuation or death.

**Results of the review**

Seven RCTs (n=2,867 patients; range 180 to 1,218 patients) were included in the review. Five trials were assessed as having a Jadad score of 3 out of 4 points; two trials had a rating of 2 out of 4 points.

Pooled overall survival rates showed a statistically significant difference favouring docetaxel-based therapies (HR 0.89, 95% CI 0.82 to 0.96). Docetaxel-based therapies also had a statistically significantly reduced pooled odds of grade 3/4 neutropenia (OR 0.59, 95% CI 0.38 to 0.89) and grade 3/4 serious adverse effects (OR 0.68, 95% CI 0.55 to 0.84) compared with Vinca alkaloid-based treatment; this direction of effect was also present for the pooled odds of serious adverse effects leading to either drug discontinuation or death but, for these outcomes, the results were not statistically significant. Improvements in safety were achieved without increased use of granulocyte-colony stimulating factor, or a decreased dose intensity of docetaxel therapy.

Subgroup and sensitivity analyses did not appear to materially alter the main findings.

No statistically significant heterogeneity was identified for any of the above outcomes, and funnel plots did not indicate that publication bias was present.

**Authors' conclusions**

Docetaxel-based regimens were superior to Vinca alkaloid-based regimens as a first-line therapy for advanced non-small cell lung cancer in terms of overall survival and safety.

**CRD commentary**

This review addressed a clear review question with relevant inclusion and exclusion criteria. Multiple databases were searched and additional measures taken to reduce the potential for language and publication bias. Although the data extraction was carried out with sufficient attempts to minimise error and bias, the processes of study selection and validity assessment were unclear.

An appropriate quality assessment tool was used, but there appeared to be inconsistency in the reported cut-off point for trial inclusion. The chosen method of data synthesis appeared to be appropriate.

Given some concerns regarding the review process, and sub-optimal quality of trials, the extent to which the authors' conclusion is reliable is unclear.

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

**Practice:** The authors stated that docetaxel-based regimens may provide a potential platform on which to add targeted therapies for first-line treatment in the future.

**Research:** The authors stated that further investigations using individual patient data are warranted to provide more detailed analyses of specific subgroups of patients and to examine additional endpoints.
Funding
Sanofi-Aventis.

Bibliographic details

PubMedID
17909357

DOI
10.1097/JTO.0b013e318153fa2b

Original Paper URL
http://journals.lww.com/jto/Abstract/2007/10000/Comparison__of__Docetaxel__and__Vinca__Alkaloid_.aspx

Indexing Status
Subject indexing assigned by NLM

MeSH
Antineoplastic Combined Chemotherapy Protocols /therapeutic use; Carcinoma, Non-Small-Cell Lung /drug therapy; Cisplatin /administration & dosage; Deoxycytidine /administration & dosage /analogs & derivatives; Humans; Lung Neoplasms /drug therapy; Neoplasm Staging; Prognosis; Randomized Controlled Trials as Topic; Survival Rate; Taxoids /administration & dosage; Vinblastine /administration & dosage /analogs & derivatives; Vindesine /administration & dosage

AccessionNumber
12007003496

Date bibliographic record published
01/09/2008

Date abstract record published
30/06/2010

Record Status
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.