Economic analysis of the TAX 317 trial: docetaxel versus best supportive care as second-line therapy of advanced non-small-cell lung cancer
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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The health intervention examined in the study was second-line chemotherapy for advanced non-small-cell lung cancer (NSCLC). The therapy was based on docetaxel (100 mg/m² or 75 mg/m²) administered intravenously over one hour every 21 days.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised good performance (Eastern Cooperative Oncology Group performance status <= 2) status patients with a diagnosis of stage IIB or IV NSCLC, who had been previously treated with cisplatin-based chemotherapy.

Setting
The setting was a hospital (tertiary care cancer centre). The economic study was carried out in Canada.

Dates to which data relate
No dates for resource use or effectiveness data were reported (although the effectiveness data were published in 2000). The price year was 1999.

Source of effectiveness data
The effectiveness evidence was derived from a single study, whose main results were already published (see "Other Publications of Related Interest" below).

Link between effectiveness and cost data
The costing was carried out retrospectively on a subsample of patient used in the effectiveness analysis.

Study sample
Power calculations and the method of sample selection were not reported. An overall sample of 204 patients was recruited: 104 patients were included in the docetaxel arm (49 docetaxel receiving docetaxel 100 mg/m² and 55 receiving docetaxel 75 mg/m²). Patients' demographics were not reported. Patients received the higher dose of docetaxel during the first half of the study and were then switched to the lower dose due to high toxicity rates. The
group of 55 patients receiving docetaxel 75 mg/m² was compared with a sample of 49 patients receiving BSC.

**Study design**
This was a multi-centred, randomised controlled trial, carried out in 36 centres in Europe and North America and in several Canadian centres. The method and unit of randomisation were not reported. Patients were followed up until death. Assessment was carried out at baseline, every 3 weeks during the first 18 weeks, and every 6 weeks after 18 weeks. Loss to follow-up was not reported.

**Analysis of effectiveness**
The basis for the analysis of the clinical study (intention to treat or treatment completers only) was not reported. The primary health outcome assessed in the analysis was the mean survival. Episodes of toxicities, such as anaemia, neutropenia, thrombocytopenia, febrile neutropenia, infection, asthenia (grade 3, 4), and treatment-related deaths, were also assessed. The comparability of the study groups was not reported.

**Effectiveness results**
Median survival was statistically significantly longer both in the docetaxel 100 mg/m² group (7 months) versus the BSC group (4.6 months) and in the docetaxel 75 mg/m² group (7.5 months) versus the BSC group (4.6 months).

The mean survival was 9.10 months in the docetaxel 100 mg/m² group compared to 7.11 in the BSC group, (p=0.07), and 9.48 months in the docetaxel 75 mg/m² group compared to 5.40 in the BSC group, (p<0.001).

The occurrence of toxicities is shown below.

**Anaemia:** docetaxel 100 mg/m² group (104 patients) 11 (10.6%), docetaxel 75 mg/m² group (55 patients) 3 (5.5%), and BSC group (all patients) 10 (10%).

**Neutropenia:** docetaxel 100 mg/m² group (104 patients) 79 (76%), docetaxel 75 mg/m² group (55 patients) 37 (67.3%), and BSC group (all patients) 0.

**Thrombocytopenia:** docetaxel 100 mg/m² group (104 patients) 1 (1%), docetaxel 75 mg/m² group (55 patients) 0, and BSC group (all patients) 0.

**Febrile neutropenia:** docetaxel 100 mg/m² group (104 patients) 12 (11.5%), docetaxel 75 mg/m² group (55 patients) 1 (1.8%), and BSC group (all patients) 0.

**Infection:** docetaxel 100 mg/m² group (104 patients) 35 (33.7%), docetaxel 75 mg/m² group (55 patients) 17 (39.9%), and BSC group (all patients) 21 (21%).

**Asthenia (grade 3, 4):** docetaxel 100 mg/m² group (104 patients) 21 (20.2%), docetaxel 75 mg/m² group (55 patients) 10 (18.2%); and BSC group (all patients) 28 (28%).

**Treatment-related deaths:** docetaxel 100 mg/m² group (104 patients) 6 (5.8%), docetaxel 75 mg/m² group (55 patients) 1 (1.8%), and BSC group (all patients) 0.

**Clinical conclusions**
The authors concluded that the docetaxel therapy was effective in increasing patient survival, although it was associated with several toxicity episodes.

**Measure of benefits used in the economic analysis**
The benefit measure used in the economic analysis was patient survival which was derived from the effectiveness analysis. Benefits were not discounted, but this was appropriate as survival lasted less than one year.
Direct costs
Costs were not discounted because mean patient survival was less than one year. Unit costs and quantities of resources were reported separately. The economic analysis included the costs related to the treatment of NSCLC, such as outpatient assessment, chemotherapy administration, hospitalisation, radiation therapy, community-based nursing and supportive care, and minor miscellaneous items. The costs of hospitalisation comprised hotel costs and personnel costs. The cost/resource boundary adopted was that of the Canadian public health care system. The estimation of costs was based on a subsample of 68 patients treated in Canada and unit costs were mainly derived from the Ontario Health Insurance Plan fee schedule and some Canadian hospitals. This subsample was shown to be representative of the overall study population used in the effectiveness analysis. Resource use was based on actual data derived from the clinical trial. The period during which quantities of resources used were collected, was not reported. The price year was 1999.

Statistical analysis of costs
No statistical analysis of costs was carried out.

Indirect Costs
Indirect costs were not included in the analysis.

Currency
Canadian dollars (Can$).

Sensitivity analysis
One-way sensitivity analyses were carried out to account for variability in the data and potential measurement errors by varying the following variables: days in hospital; cost and survival of docetaxel; costs of medications, clinic visits, and investigations; and number of chemotherapy cycles.

Estimated benefits used in the economic analysis
As reported above, the mean survival was 9.10 months in the docetaxel 100 mg/m^2 group and 7.11 in the BSC group, with a incremental survival of 1.99 months, which did not achieve statistical significance, (p=0.07). The mean survival was 9.48 months in the docetaxel 75 mg/m^2 group and 5.40 months in the BSC group, and the incremental survival of 4.08 months was statistically significant, (p<0.001).

Cost results
Total costs per patient were Can$18,398.27 in the in the docetaxel 100 mg/m^2 group and Can$8,821.52 in the BSC group.

Total costs per patient were Can$17,738.96 in the docetaxel 75 mg/m^2 group and Can$6,935.04 in the BSC group.

The incremental per patient cost was Can$9,576.75 for docetaxel 100 mg/m^2 versus BSC and Can$10,630.18 for docetaxel 75 mg/m^2 versus BSC.

Synthesis of costs and benefits
An incremental cost-effectiveness analysis was carried out to combine the costs and survival of the intervention. The incremental cost per life-year gained was Can$57,749.26 for docetaxel 100 mg/m^2 versus BSC and Can$31,776.23 for docetaxel 75 mg/m^2 versus BSC. Survival was the factor that mostly affected the study results: variations by +/- 20% resulted in an estimated incremental cost per life-year gained that ranged from Can$18,374 to Can$117,434.
Authors' conclusions
The authors concluded that the second-line therapy based on docetaxel was effective in extending patient survival, but no cost-savings were observed. The estimated cost per life-year gained appeared to be within an acceptable range for health care interventions.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. Best supportive care was selected as it represented the routine intervention for patients with advanced NSCLC. You, as a user of this database, should assess whether it represents a currently implemented intervention in your own setting.

Validity of estimate of measure of effectiveness
The analysis of the effectiveness was based on a multicentre randomised controlled trial published separately from the current study. The quality of that study has not been assessed as part of this commentary. The study sample appears to have been representative of the study population. Quality of life assessments were carried out but the results were not reported. The method of randomisation and the comparability of study groups at baseline were not given. However, the main findings of the clinical study were reported in a separate paper (see “Other Publications of Related Interest” below).

Validity of estimate of measure of benefit
The benefit measure used in the economic analysis was patient survival, which was derived from the effectiveness analysis. It represents a widely used benefit measure in the case of treatments for patients undergoing chemotherapy.

Validity of estimate of costs
All direct medical costs relevant to the perspective adopted in the study were included in the analysis. Unit costs and the quantities of resources were reported and the price year was given, thus facilitating reflation exercises to other settings. Although costs were quite specific to the study setting, several sensitivity analyses were carried out on key costs, due to variability in data and potential errors in measurement. The authors noted that their estimates of costs may have overestimated the true costs of the intervention. A potential limitation was the fact that a subsample of patients was used for the cost analysis, rather than the whole sample of patients used in the effectiveness analysis.

Other issues
The authors made several comparisons of their findings with those from other studies. The issue of the generalisability of the study results to other settings was not explicitly addressed but several sensitivity analyses were carried out and unit costs were reported, thus enhancing the external validity of the analysis. The study enrolled patients with advanced NSCLC and this was reflected in the conclusions of the analysis. The authors reported some limitations of their analysis, mainly related to the retrospective nature of the costing. It was also noted that extrapolating between different health care systems could be misleading, thus caution is required when generalising the conclusions of the analysis.

Implications of the study
The authors suggest that the survival and economic benefits of second-line docetaxel appear to be appropriate for a specific sample of good performance status patients with advanced NSCLC previously treated with cisplatin-based therapy.

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Other publications of related interest

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