Cost-effectiveness of pulmonary resection and systemic chemotherapy in the management of metastatic soft tissue sarcoma: a combined analysis from the University of Texas M D Anderson and Memorial Sloan-Kettering Cancer Centers


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
Three strategies for the treatment of patients with pulmonary metastases from soft tissue sarcoma (STS) were examined. The strategies were pulmonary resection (PR), anthracycline-based 6-cycle systemic chemotherapy, and PR plus systemic chemotherapy (PR+C).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with STS pulmonary metastases.

Setting
The setting was hospital care. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness data were gathered from 1982 to 1997. There was no information on when the resource use data were collected. The price year was 2001.

Source of effectiveness data
The effectiveness evidence was derived from a single study and authors' assumptions.

Link between effectiveness and cost data
The costing was not conducted on the same sample of patients as that used in the effectiveness study.

Study sample
The use of power calculations was not reported. A sample of 1,124 consecutive patients with STS pulmonary metastases, who were treated and followed up, was considered in the analysis. A sub-group of 235 patients who underwent complete resection formed the PR group. The remaining 889 patients provided the data for the no treatment group. It was not stated whether some patients were excluded from the initial study sample for any reason.
Study design
Limited information on the design of the study and the methods of assessing the outcome was reported. This appears to have been a retrospective cohort study that was conducted in a single centre, the Memorial Sloan-Kettering Cancer Center.

Analysis of effectiveness
The primary health outcome measure was the median survival obtained with no treatment and PR. The baseline comparability of the two groups of patients was not discussed.

Effectiveness results
The estimated mean survival was 32 months (median 13) with no treatment and 75 months (median 31) with PR.

Clinical conclusions
The effectiveness study showed that the PR led to a substantial improvement in survival in comparison with no treatment.

Modelling
A simple decision tree model was constructed to assess the survival and costs associated with the four alternative strategies for treating patients with STS pulmonary metastases. The structure of the tree was reported, but no further details.

Methods used to derive estimates of effectiveness
The authors made some assumptions, which were used to estimate the disease-specific survival of chemotherapy and PR+C.

Estimates of effectiveness and key assumptions
The mean disease-specific survival was 44 months (median 25) with chemotherapy and 87 months (median 43) with PR+C. This was based on the unproven assumption that chemotherapy provides survival benefits of 12 months with respect to the base-case (no treatment and PR, respectively) in STS metastatic patients.

Measure of benefits used in the economic analysis
The summary benefit measure used in the economic analysis was median survival. This was estimated from the cohort of patients and authors' assumptions. An annual discount rate of 3% was applied.

Direct costs
Discounting was not relevant since all the costs were incurred within the first year of treatment. The unit costs and the quantities of resources used were not reported separately. The health services included in the economic evaluation were chemotherapy and PR, including professional services incurred by the hospital, other in-hospital costs and outpatient visits. The cost/resource boundary of the study was unclear. The costs were estimated using information from the cost accounting system of the University of Texas M D Anderson Cancer Center. Resource use was derived from a different series of patients who were treated at the University of Texas M D Anderson Cancer Center following standard protocols. Some assumptions were made in the cost calculations. All the costs were presented in 2001 values using the medical component of the consumer price index.

Statistical analysis of costs
No statistical tests of the costs were conducted.
**Indirect Costs**
The indirect costs were not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way sensitivity analyses were conducted to address variability in the data, arising from the numerous assumptions made in the analysis. The study parameters examined were estimated survival after chemotherapy, survival after PR, and the use of four cycles of chemotherapy. Finally, the minimum chemotherapy benefit (survival) necessary to obtain an incremental cost-effectiveness ratio (ICER) below the threshold of $50,000 was calculated. The analysis was also conducted on a specific sub-group of patients defined by age, tumour grade and site, and disease-free interval. Some ranges of variations were based on alternative data derived from the literature.

**Estimated benefits used in the economic analysis**
The estimated, undiscounted mean survival was 32 months (median 13) with no treatment 75 months (median 31) with PR, 44 months (median 25) with chemotherapy and 87 months (median 43) with PR+C.

**Cost results**
The estimated undiscounted costs per patient were $0 with no treatment, $20,339 with PR, $99,033 with chemotherapy and $119,732 with PR+C.

**Synthesis of costs and benefits**
The costs and benefits of the treatment strategies were combined by calculating ICERs.

Compared with no treatment, the undiscounted incremental cost per life-year gained was $14,357 with PR, $104,210 with chemotherapy and $51,159 with PR+C. The ICER of PR+C relative to PR was $108,036 per life-year gained. Chemotherapy alone was dominated.

The sensitivity analysis showed that the ICERs of PR and PR+C were sensitive to tumour site (more extreme tumours led to a higher ICER). They were also sensitive to disease-free interval (higher ICERs were associated with less than 12 months of disease-free interval).

Compared with no treatment, the ICER of PR was always smaller than that of PR+C, even for extremes of chemotherapy benefits.

The use of four cycles of chemotherapy led to lower ICERs ($69,497 for chemotherapy and $37,012 for PR+C).

The minimum chemotherapy benefit necessary to obtain an ICER below the threshold of $50,000 was at least 32 months’ survival with 6-cycle systemic chemotherapy and at least 14 months with 6-cycle PR+C. The corresponding benefits of 4-cycle therapy must be at least 17 months for systemic chemotherapy and at least 4 months for PR+C.

**Authors’ conclusions**
For patients with soft tissue sarcoma (STS) pulmonary metastases, pulmonary resection (PR) represented the most cost-effective strategy in comparison with systemic chemotherapy or PR plus chemotherapy (PR+C). Chemotherapy alone was dominated and the incremental value of adding chemotherapy was unclear. Better cost-effectiveness results (lower incremental cost-effectiveness ratios, ICERs) could be achieved in patients with low tumour grade, non-extremity tumour, or a disease-free interval of at least 12 months.
CRD COMMENTARY - Selection of comparators

The authors justified the choice of the comparators. Basically, all possible available treatment strategies for STS were covered. PR was selected as trials had shown that it could cure patients with pulmonary metastases. Systemic chemotherapy is a commonly used approach for STS patients, although no study has demonstrated its efficacy. The combination of PR+C was included since this represents a further commonly used treatment strategy. Finally, the no treatment option was considered for comparative purposes. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness

The analysis of effectiveness was based on a retrospective cohort study. This was used so that clinical data derived from a large series of STS metastatic patients could be included in the analysis. However, as the authors acknowledged, the design is open to the impact of bias and confounding factors, which could not be excluded. The use of a randomised trial would have been more appropriate. Few details of the patients' characteristics were given and the methods used to estimate the clinical outcomes were not reported. Further information can, however, be found elsewhere (Billingsley et al., see Other Publications of Related Interest). Some assumptions, derived from common opinion, were also made. Extensive sensitivity analyses were conducted to investigate variability in the data.

Validity of estimate of measure of benefit

The selection of the benefit measure appears to have been appropriate for assessing the impact of the intervention on the patients' health. Quality of life outcomes were not considered because the retrospective analysis did not permit the assessment of temporal differences in quality of life among strategies. The use of survival permits comparisons with the benefits of other health care technologies. The authors stated that the benefits were discounted, but only undiscounted results were reported.

Validity of estimate of costs

The perspective adopted in the study was not explicitly reported but the authors stressed that true costs, rather than charges or reimbursement rates, were used. The information on the unit costs and the quantities of resources used was unclear. The sources of the cost and resource data were provided. The price year was reported, which facilitates reflation exercises in other settings. The cost estimates were specific to the study setting and no sensitivity analyses of the economic inputs were conducted. The authors noted that the costs might vary in other regions, but the relative differences should be similar. Moreover, the costs were treated deterministically.

Other issues

The authors did not compare their findings with those from other studies. They also did not extensively address the issue of the generalisability of the study results. However, sensitivity analyses were conducted, which enhanced the external validity of the analysis. The authors stressed that their conclusions should be limited to patients with STS pulmonary metastases who could be treated by any of the four strategies considered in the study. The authors highlighted some limitations of their analysis, such as the use of different patient cohorts for clinical outcomes and costs.

Implications of the study

The results of the study supported the therapeutic principle that metastases should be resected whenever possible. The authors suggested that future studies should consider gains in quality of life as well as improvements in survival.

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Other publications of related interest

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