Economic evaluation of new targeted therapies for the first-line treatment of patients with metastatic renal cell carcinoma


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.

CRD summary
This study assessed the cost-effectiveness of three targeted molecular therapies (bevacizumab plus interferon-alpha, sorafenib, and sunitinib), as first-line treatment for metastatic renal cell carcinoma. The authors concluded that sunitinib was a cost-effective alternative to sorafenib or bevacizumab plus interferon-alpha, in the USA, and to bevacizumab plus interferon-alpha, in Sweden. The methods were valid and various areas of uncertainty were considered. The authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study assessed the cost-effectiveness of three targeted molecular therapies, as first-line treatment for metastatic renal cell carcinoma.

Interventions
The three first-line treatments were sunitinib malate, sorafenib tosylate, and bevacizumab plus interferon-alpha. The assumed dosages were 50mg per day for sunitinib (full dose) for four weeks followed by two weeks without treatment, 400mg twice daily for sorafenib, and 10mg per kg every two weeks for bevacizumab, with injections of nine million units of interferon-alpha three times a week. Second-line treatment varied depending on the first-line treatment, and included either of the other two options or temsirolimus.

Location/setting
USA and Sweden/hospital.

Methods
Analytical approach:
The analysis was based on a Markov model, with a 10-year time horizon. The authors stated that it was carried out from the perspective of the third-party payer.

Effectiveness data:
The clinical data were from published pivotal clinical trials of the three treatments. The sunitinib data were from a phase III, first-line trial with 375 patients. The sorafenib data were from a randomised, phase II, first-line cross-over trial of 97 patients and from a randomised, double-blind, placebo-controlled, phase III, second-line trial. The bevacizumab plus interferon data were from a randomised, double-blind, phase III, first-line trial of 327 patients. An indirect comparison was required due to the lack of head-to-head clinical trials. Hazard ratios were assumed to be constant over time and after the end of the trials. Survival was the key input for the model.

Monetary benefit and utility valuations:
The utility values were from published clinical trials. As data were not available for sorafenib and bevacizumab plus interferon-alpha, the utility values for patients on sunitinib were used for sorafenib and those for patients on interferon-alpha from the sunitinib trial were used for bevacizumab plus interferon (for toxicity).

Measure of benefit:
Life-years, progression-free life-years (PFLYs), and quality-adjusted life-years (QALYs) were the summary benefit measures. A 3% annual discount rate was applied.

Cost data:
The economic analysis included the costs of the drugs, specialist visits, hospitalisations, general practitioner and nurse visits, laboratory tests (blood counts, metabolic panels and thyroid function), chest or pelvis computed tomography scans, X-rays and magnetic resonance imaging, and treatment for serious adverse events. The patterns of resource consumption were mainly estimated by expert opinion and using data from the clinical trials. The unit costs were from published literature and databases. All costs were in US dollars ($) and were discounted at an annual rate of 3%. Swedish costs in kronor were converted to $. The price year was 2008.

Analysis of uncertainty:
A probabilistic sensitivity analysis was carried out, using Monte Carlo simulation with 5,000 iterations. Probability distributions were assigned to the model inputs on the basis of recommendations and to fit the nature of each variable. A one-way sensitivity analysis was performed, using a range of values for each model input. Cost-effectiveness acceptability curves were generated for various societal willingness-to-pay (WTP) thresholds.

Results
In the USA, the total costs were $369,347 with sunitinib, $382,923 with sorafenib, and $437,144 with bevacizumab plus interferon-alpha. The QALYs were 1.876 with sunitinib, 1.706 with sorafenib, and 1.714 with bevacizumab plus interferon-alpha. Sunitinib was dominant as it was more effective and less expensive than the alternative treatments.

In Sweden sorafenib was not considered, as it was recommended only as a second-line option. The total costs were $167,951 with sunitinib, and $215,215 with bevacizumab plus interferon-alpha. The QALYs were 1.862 with sunitinib, and 1.703 with bevacizumab plus interferon-alpha. Sunitinib was dominant.

The most influential inputs were the hazard risks for survival, the best supportive care costs, the drug prices, and the utilities for each treatment. The base-case findings were not altered and sunitinib remained dominant or cost-effective in all cases.

At a threshold of $100,000 per QALY gained, sunitinib was cost-effective, over the comparators, in 74% of simulations for the USA and, at a threshold of $76,760 per QALY gained, 99% of simulations for Sweden.

Authors' conclusions
The authors concluded that first-line metastatic renal cell carcinoma treatment with sunitinib was a cost-effective alternative to sorafenib or bevacizumab plus interferon-alpha, in the USA, and to bevacizumab plus interferon-alpha, in Sweden.

CRD commentary
Interventions:
The comparators were selected as the new first-line treatments for metastatic renal cell carcinoma. In the USA, all three drugs were considered, while in Sweden, sorafenib was not included as it was recommended for second-line treatment only.

Effectiveness/benefits:
No systematic review was reported to identify the relevant sources of evidence, but all data were from published clinical trials, which should have ensured the validity of these inputs. These sources were clearly described in terms of interventions, design, patient sample, and endpoints, but the data for sorafenib as first-line treatment were from a phase II trial. The authors acknowledged that the lack of head-to-head comparisons was a problem. Some assumptions were needed for the long-term treatment effects. Extensive sensitivity analysis was conducted on the most uncertain parameters. The benefit measures were appropriately selected to capture the impact of cancer on the patients' health and to allow comparisons with the benefits of other interventions. The utility weights for the QALYs were from the patients included in the clinical trials.

Costs:
The cost categories were appropriate for the perspective of the third-party payer. The costs were presented as category totals and were not broken down into individual items. Few data sources and resource quantities were provided, reducing the transparency of the analysis. Expert opinion was used for most of the resources used, and this should be representative of the countries analysed. The price year, discount rate, and currency conversions were clearly stated. The impact of variations in the cost estimates was considered in the sensitivity analysis.

Analysis and results:
The results were clearly presented. An incremental analysis was conducted, and sunitinib was found to be dominant. Valid approaches were used to assess the uncertainty; these methods were clearly described and the results were extensively reported. The authors compared their results with those of other published studies that generally had similar findings. The cost-effectiveness results were similar for the USA and Sweden, and might be relevant to other developed countries.

Concluding remarks:
The methods were valid and various areas of uncertainty were considered. The authors’ conclusions appear to be robust.

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