Cost-effectiveness of sorafenib for second-line treatment of advanced 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 examined the cost-effectiveness of sorafenib versus the best supportive care for the second-line treatment of advanced renal cell carcinoma. It was part of an independent assessment submitted to the National Institute for Health and Clinical Excellence (NICE). The authors concluded that sorafenib improved the clinical outcomes, but was not cost-effective from the UK National Health Service perspective. The study was well conducted and clearly presented. The authors’ conclusions are robust.

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

Study objective
This study examined the cost-effectiveness of sorafenib versus best supportive care (BSC) for the second-line treatment of advanced renal cell carcinoma. It was part of an independent assessment submitted to the National Institute for Health and Clinical Excellence (NICE) in the UK.

Interventions
BSC was compared with sorafenib 400mg, administered orally, twice daily.

Location/setting
UK/hospital.

Methods
Analytical approach:
The analysis was based on a decision-analytic model, with a 10-year time horizon. The authors stated that the perspective of the UK National Health Service (NHS) was adopted.

Effectiveness data:
The clinical data were derived from a published multinational, multi-centre, phase III, double-blind, randomised controlled trial (RCT) of 903 patients, with 451 in the sorafenib group and 452 in the BSC group. The vast majority of patients (99%) had clear-cell renal carcinoma. It was assumed that compliance with sorafenib was 100%. Overall survival and progression-free survival were the key endpoints. Weibull curves were used to extrapolate the short-term data to the long term.

Monetary benefit and utility valuations:
The utility values were from a published phase II single-arm trial of sunitinib as a second-line treatment for patients with renal cell carcinoma, and were derived using UK European Quality of life (EQ-5D) tariffs.

Measure of benefit:
Quality-adjusted life-years (QALYs) and life-years (LYs) were the summary benefit measures and they were discounted at an annual rate of 3.5%.

Cost data:
The economic analysis included the costs of drugs, consultations (with general practitioners, with nurses, and as outpatients), diagnostic tests (computed tomography and blood tests), pain medications (morphine sulphate), and the treatment of renal cell carcinoma. The unit costs and resource quantities were reported. The costs were derived from NHS Economic Evaluation Database (NHS EED)
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official UK sources and resource use was based on published evidence, guidelines, and information provided by clinical experts. All costs were in UK pounds sterling (£) and referred to 2007 to 2008 prices. A 3.5% annual discount rate was applied.

Analysis of uncertainty:
A probabilistic sensitivity analysis was undertaken, by running 1,000 simulations and applying conventional probability distributions to the model inputs. A deterministic one-way sensitivity analysis was performed by varying the effectiveness, utilities, dose intensity of sorafenib, and cost estimates. The alternative estimates were reported in a table.

Results
Sorafenib produced a gain of 0.27 QALYs or 0.37 LYs, at an additional cost of £20,063, resulting in an incremental cost per QALY gained over BSC of £75,398 and an incremental cost per LY gained of £54,565.

The probabilistic analysis showed that, at a threshold of £30,000 per QALY, the probability of sorafenib being cost-effective was zero.

The deterministic analysis suggested that the most influential inputs were the cost of sorafenib, the fit of the curve for overall survival, the dose intensity of sorafenib, and the utility values. There was no case in which the incremental cost per QALY for sorafenib versus BSC fell below £30,000.

Authors’ conclusions
The authors concluded that sorafenib improved clinical outcomes, but was not cost-effective from the perspective of the UK NHS.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear. Best supportive care, a conservative approach, was compared with a new pharmacological therapy for renal cell carcinoma.

Effectiveness/benefits:
The authors used clinical data from one published study that was the only available phase III RCT of sorafenib. Limited characteristics of the trial were reported, as these details were published elsewhere (Escudier, et al. 2007, see ‘Other Publications of Related Interest’ below for bibliographic details). The design of the large multinational trial should ensure the validity of the clinical inputs. The details of the estimation of the proportion of patients alive over time were presented. Some assumptions were made for compliance, but these were varied in the sensitivity analysis. Both benefit measures were appropriate for capturing the impact of the disease on a patient's health. Some key information on the derivation of utility values was provided. The EQ-5D was an appropriate tool for eliciting the patient preferences for the health conditions.

Costs:
The economic analysis was satisfactorily carried out and was well reported. The unit costs, resource quantities, data sources, price year, use of discounting, and statistical analyses of costs were presented, enhancing the transparency of the analysis. Appropriate economic data appear to have been used and, while the costs were country specific, the patterns of resource consumption might be transferable to similar health care systems.

Analysis and results:
The costs and benefits were appropriately synthesised, using an incremental approach. The results were clearly presented. The issue of uncertainty was satisfactorily investigated, using two approaches, and the results were extensively reported. Conventional discounting was applied to both the costs and benefits. The sample in the RCT was almost exclusively clear-cell renal carcinoma patients (99%) and the authors stated that it was unclear whether their results could be extended to patients with non-clear renal cell carcinoma. The results should be considered to be specific to the UK, as the costs were country specific. The authors stated that sorafenib was an orphan drug and there was a poor prognosis for patients with renal cell carcinoma and no other effective treatments; and these factors should be considered in addition to its cost-effectiveness.
Concluding remarks:
The study was well conducted and clearly presented. The authors' conclusions are robust.

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