Economic evaluation of everolimus versus sorafenib for the treatment of metastatic renal cell carcinoma after failure of first-line sunitinib

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
The study assessed the cost-effectiveness of everolimus versus sorafenib in the treatment of sunitinib-refractory metastatic renal cell carcinoma (mRCC) patients. The authors concluded that everolimus was a potentially cost-effective strategy for mRCC patients post-failure on sunitinib from the perspective of the health care payer. The analysis used conventional and transparent methodology, but the results were based on an indirect comparison of different studies. Future analyses should corroborate the authors’ conclusions.

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

Study objective
The study assessed the cost-effectiveness of everolimus versus sorafenib in the treatment of sunitinib-refractory metastatic renal cell carcinoma (mRCC) patients.

Interventions
Oral everolimus (10mg/day) was compared against oral sorafenib (400mg twice daily). Both treatments were given until disease progression.

Location/setting
USA/hospital.

Methods
Analytical approach:
The analysis was based on a Markov simulation model with a six-year time horizon. The analysis was from the perspective of the USA health care payer.

Effectiveness data:
Most clinical inputs were been derived from a study that reported an indirect comparison between everolimus and sorafenib. In this study, data on everolimus were derived from a pivotal clinical trial (the RECORD-1 study) that compared the study drug with best supportive care. Data on sorafenib came from a single-arm phase II study. Rates of adverse events were taken from full prescribing information for both agents, given the marked differences in adverse events found in the RECORD-1 and phase II studies. Rates of progression-free survival formed a key input of the model and were based on the indirect comparison. Assumptions were made on the long-term progression of the disease.

Monetary benefit and utility valuations:
Health utilities were not available from the two sources of clinical inputs and were derived from a UK analysis on patients who received second-line sorafenib.

Measure of benefit:
Life-years and quality-adjusted life-years (QALYs) were used as the summary benefit measures and discounted at an annual rate of 3%.

Cost data:
The economic analysis included costs of anti-tumour therapies, physician visits, tests, management of adverse events, progression therapy and end-of-life care. Drug costs were based on average wholesale prices. Other costs were derived from official USA sources. Patterns of resource consumption were based on clinical trials, official national guidelines and the published literature. Costs were in USA dollars ($). A 3% annual discount rate was applied.

Analysis of uncertainty:
One-way sensitivity analyses were carried out to identify influential variables. A probabilistic sensitivity analysis was performed using a Monte Carlo simulation and typical probability distributions for groups of inputs. Cost-effectiveness acceptability curves were generated.

Results
Projected life-years and QALYs were 1.805 and 1.298 with everolimus and 0.533 and 0.382 with sorafenib. Total costs were $124,379 with everolimus and $42,736 with sorafenib. The incremental cost per life-year gained with everolimus over sorafenib was $64,155 and the incremental cost per QALY gained was $89,160.

The deterministic sensitivity analysis showed the robustness of the base case results. The most influential input was the assumption about mortality rate after disease progression: when this input was assumed to be the same for both treatment arms, the incremental cost per QALY gained with everolimus rose to $112,807.

The probability of everolimus being cost-effective at a threshold of $70,000 was 15.8%, at $80,000 was 68.3% and at $90,000 was 98%.

Authors’ conclusions
The authors concluded that everolimus was a potentially cost-effective strategy for mRCC patients post-failure on sunitinib from the perspective of the health care payer.

CRD commentary
Interventions:
The selection of the comparators was appropriate. Both strategies appeared to be generalisable to other health care settings.

Effectiveness/benefits:
There was a lack of head-to-head studies and the clinical analysis was based on an indirect comparison. The comparison between results taken from a phase III and a phase II studies meant that there were potential differences between the two studies in methodology and patient populations. The authors stated that the two samples of patients matched for most characteristics, but there were some differences that might have biased the results (some in favour and others against everolimus). Some assumptions were made. Clinical results should be interpreted with caution. Life-years and QALYs were appropriate benefit measures that captured the impact of the disease on patients’ health. Utility weights were taken from a UK population using valid instruments. The authors stated that other studies had shown lower utility estimates than those used in this analysis.

Costs:
The economic analysis appeared consistent with the perspective adopted in the study in terms of cost categories and data sources. Unit costs and resource quantities were presented separately and this enhanced the transparency of the analysis. Reflation exercises in other time periods would not be possible as the price year was not explicitly presented. Resource use for drugs was based on sources used in the clinical analysis. Estimates for other items were taken from typical USA sources. Variations in economic inputs were taken into account in the sensitivity analyses.

Analysis and results:
The study results were presented clearly. Projected costs and benefits of the two treatments were appropriately synthesised using an incremental approach. Various cost-effectiveness thresholds were considered in the sensitivity analyses. The issue of uncertainty was investigated using appropriate approaches and the methods and results were reported clearly. The authors acknowledged some limitations of their analysis (mostly about the need for indirect comparison). They stated that everolimus was cost-effective given the high cost-effectiveness threshold used for oncologic therapies; however, the cost-effectiveness ratios appeared quite high. The study findings were specific to the
USA setting but might be transferable to other countries with similar relative prices and clinical practices.

Concluding remarks:
The analysis used conventional and transparent methodology, but the results were based on an indirect comparison of different studies. Future analyses should corroborate the authors’ conclusions.

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