Economic evaluation of sunitinib malate in second-line treatment of metastatic renal cell carcinoma in Finland


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 examined the cost-effectiveness of sunitinib as second-line therapy, compared with usual care, in cytokine-refractory patients with metastatic renal cell carcinoma. The authors concluded that sunitinib was a potentially cost-effective second-line therapy for metastatic renal cell carcinoma in comparison with usual care from the perspective of the health care payer in Finland. The quality of the study methodology was good, especially with respect to the probabilistic approach of the decision model. However, the authors’ conclusions should be treated with some caution given the lack of clinical studies with direct comparisons between the treatment analysed.

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

Study objective
The aim of the study was to examine the cost-effectiveness of sunitinib malate as second-line therapy, compared with usual care, in cytokine-refractory patients with metastatic renal cell carcinoma.

Interventions
The study examined the use of sunitinib malate (50 mg orally on 28 consecutive days followed by a 2-week rest period) administered in 6-week cycles until disease progression or intolerable adverse effects. Sunitinib was compared with usual care, such as best supportive care (BSC) including palliative biochemotherapy.

Location/setting
Finland/hospital.

Methods
Analytical approach:
The economic evaluation was based on a probabilistic Markov state-transition model with three disease states. The time horizon was 5 years. The authors stated that the perspective of the health care payer was adopted in the analysis.

Effectiveness data:
The clinical data were derived from a selection of known, relevant studies. Treatment effectiveness was based on two recently published single-arm clinical trials that involved a total of 168 patients. Data from these two studies were pooled to obtain median progression-free survival, while median overall survival was taken only from one of the trials. The characteristics of the patient population and survival rates for the BSC arm were obtained from a sample of 39 patients identified in Finnish university hospitals over the period June to August 2006. These data were supported by expert opinion. Survival rates were then transformed into monthly transition probabilities in order to populate the decision model.

Monetary benefit and utility valuations:
The utility estimates were obtained from sunitinib trials using the EQ-5D quality-of-life instrument that was administered on days 1 and 28 of every 6-week cycle.

Measure of benefit:
The three benefit measures used were overall survival, progression-free survival and quality-adjusted life-years
(QALYs). All measures were estimated using the probabilistic model and were discounted at an annual rate of 5%.

Cost data:
The health service costs included in the analysis were drugs (cancer medications, additional interferon-alpha products, analgesics and bisphosphonates), imaging examinations (radiography, computed tomography, sonography, and magnetic resonance) and health care services (ward care days, outpatient visits and radiotherapy). Costs common to both strategies were assumed to be similar between treatment arms and were not included in the analysis. The costs for health care services were derived from case-mixed rates adjusted for Finnish regional price differences. The drug costs were calculated using the most economic generic product prices in the official price list. The resource use data for the BSC arm of the model were derived from the local sample of patients. Treatment patterns for sunitinib were based on the expert panel and published studies. The price year was 2005. The costs were in euros (EUR). An annual discount rate of 5% was applied.

Analysis of uncertainty:
The issue of uncertainty was extensively addressed by means of a probabilistic sensitivity, which assigned stochastic distributions to model inputs. Cost-effectiveness acceptability curves were also generated and were presented graphically. Moreover, the analysis investigated the impact of variations in the discount rate, time horizon and the use of alternative statistical approaches to estimate survival times. An alternative analysis was also performed in which it was assumed that sunitinib would be continued for an additional month after the progression had occurred.

Results
In comparison with usual care, sunitinib prolonged overall survival by approximately 1 year and progression-free survival by 6.7 months, and led to a gain of 0.74 QALYs. The additional cost of sunitinib was EUR 32,630 per patient.

The incremental analysis resulted in a cost per progression-free month gained of EUR 4,802, a cost per life-year gained of EUR 30,831 and a cost per QALY gained of EUR 43,698.

The probabilistic sensitivity analysis indicated that, at a threshold for willingness-to-pay of EUR 45,000 per QALY, the probability of sunitinib being cost-effective was approximately 70%.

Other variations used in the sensitivity analysis did not substantially alter the base-case findings, and sunitinib therapy always produced an incremental cost per QALY gained lower than EUR 50,000 in comparison with BSC.

Authors’ conclusions
The authors concluded that, from the perspective of the health care payer in Finland, sunitinib was a potentially cost-effective second-line therapy for metastatic renal cell carcinoma in comparison with usual care.

CRD commentary
Interventions:
The selection of the comparator was appropriate in that it reflected the current standard of care in the authors’ setting.

Effectiveness/benefits:
The authors selected the sources used to derive the clinical estimates. No details of a systematic review of the literature were reported. The use of pivotal sunitinib trials to derive treatment effectiveness was appropriate given their relevance. However, they were single-arm studies and, as a consequence, data for the comparator (i.e. BSC) were derived from other sources. Thus, as the authors noted, mixing different sources might cause bias due to heterogeneity in the patient populations and types of interventions delivered. Furthermore, the sample of local patients used to derive BSC-related data was relatively small, although the authors justified the selection of these data on the grounds of the representativeness of the two institutions where patients were treated. Details of the statistical approach used to estimate progression-free and overall survival were reported. This represents a key aspect of the analysis given the important role played by survival times. The use of QALYs with utility weights derived, using the EQ-5D, from patients receiving sunitinib represents a strength of the analysis.

Costs:
The categories of costs included in the analysis were consistent with the viewpoint of the study. The authors justified the exclusion of some categories of costs. The quantities of resources used were reported but the unit costs were not. Much of the information on resource consumption was based on the expert panel, owing to the paucity of published information. This was particularly true for the derivation of data on sunitinib treatment patterns in the Finnish setting. Other details such as the price year and discounting were reported. Extensive statistical tests were performed on the economic estimates.

**Analysis and results:**
The costs and benefits were combined, but only incremental results for them were presented. The issue of uncertainty was satisfactorily addressed. Details of the probabilistic approach underlying the whole analysis were given. Overall, the authors discussed and addressed most of the potential limitations of their analysis, thus reinforcing the robustness of the whole study. The authors did not explicitly address the problem of the generalisability of their findings to other settings.

**Concluding remarks:**
The quality of the study methodology was good, with satisfactory reporting and extensive details of the statistical approach. However, the authors’ conclusions should be treated with some caution given the lack of clinical studies with direct comparisons of the treatments analysed.

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