Economic evaluation of sunitinib malate for the first-line treatment of metastatic renal cell carcinoma

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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 objective was to examine the cost-effectiveness of sunitinib malate as a first-line treatment in metastatic renal cell carcinoma in comparison with either interferon-alpha or interleukin-2. The authors concluded that sunitinib was a cost-effective alternative to interferon-alpha or interleukin-2. The study was well conducted and was satisfactorily described. The sensitivity analysis reduced the impact of the methodological limitations and the authors’ conclusions appear to be valid.

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

Study objective
The objective was to examine the cost-effectiveness of sunitinib malate as a first-line treatment in metastatic renal cell carcinoma in comparison with either interferon-alpha or interleukin-2.

Interventions
All treatments were administered for six weeks. Oral sunitinib (50mg per day) was given for four weeks followed by two weeks without treatment. Interferon-alpha was administered subcutaneously on three non-consecutive days each week, in increasing doses from 3 million units (MU) to 9MU per injection. Interleukin-2 was given as infusions of 18MU per m$^2$ of body surface area per day for five days, once every three weeks.

Location/setting
USA/out-patient.

Methods
Analytical approach:
This economic evaluation was based on a Markov model with a 10-year time horizon. The authors stated that a societal perspective was taken.

Effectiveness data:
The clinical evidence came from selected sources. The data on sunitinib versus interferon-alpha came from a pivotal phase III randomised controlled trial (RCT). The data for interleukin-2 treatment were derived from another multicentre RCT, in which interferon-alpha was the comparator. The overall survival was the key clinical outcome and the methodology used to calculate this endpoint was explicitly reported. The opinions of experts were used for some assumptions.

Monetary benefit and utility valuations:
The utility values for sunitinib and interferon-alpha were derived from trial data using the European Quality of life (EQ-5D) questionnaire. The utility values for interleukin-2 were assumed to be similar to those for interferon-alpha.

Measure of benefit:
The summary benefit measures were progression-free years, life-years (LYs), and quality-adjusted life-years (QALYs).
Cost data:
The economic analysis included the costs of drugs, routine follow-up, adverse events, management of disease progression, and best supportive care. The resource use data were based on expert opinion, for most items, supplemented with some published estimates and data from US databases. The unit costs were estimated using Current Procedural Terminology codes. All costs were in US dollars ($) and the price year was 2006.

Analysis of uncertainty:
The global issue of uncertainty was investigated in a probabilistic analysis using second-order Monte Carlo simulations and the input distributions were based on recommendations in accordance with the nature of each variable. Cost-effectiveness acceptability curves were generated. A one-way sensitivity analysis was undertaken to identify the most influential model inputs. Alternative sources of costs and the use of a discount rate of 5% were investigated. A managed care perspective was also considered.

Results
The mean cost per patient over 10 years was $224,970 with sunitinib, $217,436 with interferon-alpha, and $228,411 with interleukin-2. The progression-free years were 0.92 with sunitinib, 0.51 with interferon-alpha, and 0.57 with interleukin-2. The LYs were 2.09 with sunitinib, 1.98 with interferon-alpha, and 1.85 with interleukin-2. The QALYs were 1.33 with sunitinib, 1.19 with interferon-alpha, and 1.13 with interleukin-2.

The incremental analysis showed that interleukin-2 was dominated by the other treatments, which were both less expensive and more effective. The mean incremental cost per progression-free year gained with sunitinib over interferon-alpha was $18,611, the incremental cost per LY gained was $67,215, and the incremental cost per QALY gained was $52,593.

The probabilistic sensitivity analysis showed that, at a threshold of $50,000 per QALY, sunitinib had 45.9% probability of being cost-effective compared with interferon-alpha and at a threshold of $100,000, the probability was 64.9%. The deterministic sensitivity analysis indicated that the most influential model inputs were the utility values, cost of sunitinib, and cost of best supportive care. Reducing the time horizon to one or two years increased the incremental cost per QALY for sunitinib. The use of discounting did not substantially alter the findings.

Authors' conclusions
The authors concluded that sunitinib was a cost-effective alternative to treatment with interferon-alpha or interleukin-2.

CRD commentary
Interventions:
The authors provided a justification for their selection of the comparators. Interferon-alpha and interleukin-2 were commonly used treatments for metastatic renal cell carcinoma, while sunitinib was a valid alternative. The dosages were clearly presented.

Effectiveness/benefits:
The clinical data came from a selection of known, relevant RCTs. The methodological characteristics of these were not reported, but their design should have ensured the internal validity of the inputs. Extensive information on the approach used to derive the adjusted survival was reported. In general, the clinical analysis was carried out credibly. The derivation of the utility values was described. The EQ-5D is a valid instrument with which to elicit patient preferences. Generalisable benefit measures were used, which will permit cross-disease comparisons to be made.

Costs:
The economic analysis appears to have been restricted to health care costs even though the authors reported that a societal perspective was taken. The sources of data and some key details on the resource quantities were reported. The use of Current Procedural Terminology codes does not allow a breakdown of cost items and most of the costs were reported as macro-categories. The price year was given, which will facilitate reflation exercises in other time periods.

Analysis and results:
The approach used to analyse the costs and benefits was appropriate and the incremental analysis allowed the identification of the most cost-effective strategy. The issue of uncertainty was satisfactorily addressed using a variety of methods. Discounting was not performed in the base case, but the sensitivity analysis showed that it did not have a strong impact on the results. The authors acknowledged that the clinical trial for sunitinib did not have sufficient power to detect statistically significant differences in the EQ-5D scores, which introduced uncertainty around these inputs. The need for assumptions on health care consumption increased the model uncertainty.

Concluding remarks:
The study was well conducted and was satisfactorily described. The sensitivity analysis reduced the impact of the methodological limitations. The authors’ conclusions appear to be valid.

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