Cost-effectiveness of temsirolimus for first 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 temsirolimus versus interferon-alpha for the first-line treatment of patients with advanced renal cell carcinoma and a poor prognosis. It was part of an independent assessment submitted to the National Institute for Health and Clinical Excellence (NICE) in the UK. The authors concluded that temsirolimus was not likely to be a cost-effective alternative to interferon-alpha. The study appears to have been well conducted and was clearly presented. The authors’ conclusions are robust.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of temsirolimus versus interferon-alpha for the first-line treatment of patients with advanced renal cell carcinoma and a poor prognosis. This was part of an independent assessment submitted to the National Institute for Health and Clinical Excellence (NICE) in the UK.

Interventions
Temsirolimus 25mg, administered intravenously once a week, was compared with interferon-alpha, which started at a dose of three million units three times per week for the first week, and increased to nine million units three times per week for the second week, and to 18 million units three times per week in the third week, if this dose was tolerated. Both drugs were administered until the disease progressed, symptoms deteriorated, or there were intolerable adverse events. No second-line treatments were considered.

Location/setting
UK/hospital and the community.

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

Effectiveness data:
A systematic review identified one published phase III clinical trial. This was a multinational, multi-centre, randomised controlled trial (RCT) of 626 eligible patients, with 209 receiving temsirolimus, 207 receiving interferon-alpha, and 210 receiving both drugs (Hudes, et al. 2007, see ‘Other Publications of Related Interest’ below for bibliographic details). The mean age of patients was 59 years, 69% were male, and 81% had clear-cell renal carcinoma. All the clinical data and the data on drug compliance were from this trial. Progression-free survival was the key endpoint and Weibull curves were used to extrapolate the short-term data to the long term.

Monetary benefit and utility valuations:
The utility values were derived from the RCT using the European Quality of life (EQ-5D) questionnaire.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and they were discounted at an annual rate of 3.5%.
Cost data:
The economic analysis included the costs of drugs (acquisition and administration), computed tomography, monitoring (consultant visits), blood tests, best supportive care (general practitioner visits, community nurse visits, and morphine sulphate), and death. The estimates of resource use were based on guidelines for clinical practice and expert opinion. The drug costs were from the British National Formulary. Other costs were from NHS reference costs and the Costs of Health and Social Care. All costs were in UK pounds sterling (£) for the reference year 2007 to 2008. They were discounted at an annual rate of 3.5%.

Analysis of uncertainty:
A series of one-way and probabilistic sensitivity analyses were carried out by varying the estimates of effectiveness, the utility, and the costs. Conventional probability distributions were used and 1,000 simulations were run. Subgroup analyses were also performed, considering only those patients with clear-cell renal carcinoma and those with or without nephrectomy.

Results
Compared with interferon-alpha, temsirolimus produced a mean gain of 0.24 QALYs per patient at a mean additional cost of £22,331, resulting in an incremental cost per QALY of £94,632. This figure ranged from £74,369 to £154,752 depending on the patient subgroup.

At a willingness-to-pay of £30,000 per QALY, the probability of temsirolimus being cost-effective was close to zero for all patient groups.

The most influential model inputs were the clinical efficacy, the health state utilities, the drug costs, and the cost of temsirolimus administration. For example, when a greater overall survival associated with temsirolimus, the incremental cost per QALY decreased. There was no case in which the cost per QALY was lower than £56,000.

Authors' conclusions
Despite its superior clinical efficacy over interferon-alpha, temsirolimus might not be considered to be a cost-effective use of health care resources, due to its high acquisition cost.

CRD commentary
Interventions:
The comparators were appropriately selected as the new treatment, temsirolimus, was compared with the standard immunotherapy, interferon-alpha. The authors stated that recently there had been a re-evaluation of the benefits of interferon-alpha for these patients and some centres in the UK no longer offered the treatment. Best supportive care could have been a comparator.

Effectiveness/benefits:
The source for the clinical estimates and the utilities was identified by a literature review, but its methods and conduct were not reported. All the data were derived from a RCT, which was funded by the manufacturer of temsirolimus (Wyeth). Little information on this source was provided, but the design of a RCT should ensure the validity of the clinical evidence. The authors acknowledged that the results of the subgroup analyses were not clear, due to the uncertainty in the efficacy of treatment for smaller groups of patients. The details of the methods used to assess the expected survival in the long term were reported. QALYs were an appropriate benefit measure as they captured the impact of the disease on both quality of life and survival.

Costs:
The economic analysis was satisfactorily carried out and was well presented. The cost categories and their sources were consistent with the perspective. The unit costs and resource quantities were clearly reported, as were the price year and the use of discounting. The cost estimates were treated deterministically, in the base case, but stochastic distributions were used in the probabilistic analysis.

Analysis and results:
The costs and benefits were clearly reported and were appropriately synthesised in an incremental analysis. The issue of
uncertainty was satisfactorily investigated, using various approaches, and the findings were extensively presented and discussed. Little information on the decision model was reported. The authors acknowledged some limitations to their study and these mainly related to the fact that only one source of effectiveness was available and the lack of published cost data for renal cell carcinoma. It was unclear whether the results of this study could be extended to patients with non-clear renal cell carcinoma. The authors stated that temsirolimus was an orphan drug and it was the only effective treatment for patients with renal cell carcinoma and a poor prognosis; therefore other issues besides cost-effectiveness might need to be considered.

Concluding remarks:
This study appears to have been well conducted and was clearly presented. The authors’ conclusions are robust.

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