Cost-effectiveness analysis of LHRH agonists in the treatment of metastatic prostate cancer in Italy

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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 assess the cost-effectiveness of five three-month formulations of luteinising hormone-releasing hormone agonists. The authors concluded that leuprorelin 22.5mg was the most cost-effective treatment. The methods were good, and they and the results were reported sufficiently. Within the scope of the analysis, the authors’ conclusions were appropriate.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to assess the cost-effectiveness of five three-month formulations of luteinising hormone-releasing hormone (LHRH) agonists, in the treatment of metastatic prostate cancer.

Interventions
The five formulations of LHRH agonists were leuprorelin (leuprolide acetate) 11.25mg, leuprorelin 22.5mg, triptorelin 11.25mg, buserelin 9.9mg, and goserelin 10.8mg.

Location/setting
Italy/secondary care.

Methods
Analytical approach:
A decision analytic Markov model, using TreeAge Pro software, was developed using a patient-level, micro-simulation. The time horizon was the lifetime of the patient. The authors reported that the perspective was that of the Italian National Health Service.

Effectiveness data:
The clinical and effectiveness parameters were from several sources. The clinical data for total and progression-free survival were from the records of 129 patients with metastatic prostate cancer, in a hospital database. The effectiveness of LHRH agonists in lowering testosterone levels was from a literature search of the MEDLINE database. The search date, the key terms, and the number of reviewers who selected articles were reported. The references of identified studies were searched. Results from all the relevant studies were meta-analysed, using a Bayesian random-effects model, and each drug was assumed to have a common effect distribution. Progression-free survival and total survival functions were derived using data from the cohort of patients on the hospital database. Cox regression models were used.

Monetary benefit and utility valuations:
None.

Measure of benefit:
The summary measure of benefit was months lived. Future outcomes, over the lifetime of the patient, were discounted at an annual rate of 3.5%.
Cost data:
The direct costs included those of the acquisition of LHRH agonists, monitoring tests and examinations, chemotherapy, and follow-up procedures. The resource use for procedures, tests, and examinations was based on guideline recommendations and the cost information was from Italian national price lists. The resources for chemotherapy were from published trials. The costs of drugs were their ex-factory prices. All costs were reported in Euros (EUR). Future costs were discounted at an annual rate of 3.5%.

Analysis of uncertainty:
The base-case results were calculated for 20,000 simulated patients, with the characteristics of each patient extracted from distributions based on the cohort of 129 patients. A probabilistic sensitivity analysis was performed to assess the uncertainty surrounding the survival models used. This was achieved by repeating 1,000 cycles of 5,000 patients, who were randomly selected from distributions representing the uncertainty of each estimate.

Results
The average months lived per patient was 60.31 (SD 34.09) for leuprorelin 22.5mg, 59.49 (SD 33.75) for leuprorelin 11.25 mg, 57.93 (SD 32.93) for goserelin, 59.87 (SD 33.99) for triptorelin, and 60.35 (SD 34.15) for buserelin.

The average lifetime cost per patient was EUR 13,981 (SD 5,150) for leuprorelin 22.5mg, EUR 15,114 (SD 5,502) for leuprorelin 11.25mg, EUR 16,579 (SD 6,133) for goserelin, EUR 15,935 (SD 5,909) for triptorelin, and EUR 14,546 (SD 5,277) for buserelin.

Compared with leuprorelin 22.5mg, leuprorelin 11.25mg, goserelin, and triptorelin were all dominated, as they were more costly and less effective. Compared with leuprorelin 22.5mg, the incremental cost-utility ratio of buserelin was EUR 11,700 per month of life gained.

The probabilistic sensitivity analysis showed that buserelin was only cost-effective in more than 50% of cases, if the willingness to pay was greater than EUR 280,000 per life-year gained.

Authors' conclusions
The authors concluded that leuprorelin 22.5mg was the most cost-effective of the available depot formulation LHRH agonists.

CRD commentary
Interventions:
The interventions were reported clearly and in detail. They appear to have been valid comparators in the authors’ setting.

Effectiveness/benefits:
The sources for the clinical and effectiveness data were clearly reported, with their references. The effectiveness data were from a review of the literature in the MEDLINE database. This review was not systematic, but the methods were adequately reported. The authors highlighted this limitation, but stated that it was likely that all the major relevant articles were identified. Both progression-free and total survival were derived using Cox regression models, based on the assumption of a constant hazard ratio over time. These data were incorporated into the simulation model and tested in the probabilistic sensitivity analysis.

Costs:
The perspective was explicitly reported and all the major costs relevant to this health care system perspective were analysed. The sources for the unit costs and resource use were reported. The time horizon and discount rate were reported, but the price year was not, which will hamper any future inflationary exercises. Overall the cost section appears to have been adequately performed.

Analysis and results:
All the information on costs and outcomes was synthesised using a decision analytic Markov model. Full details of the model were provided, including a diagram. The uncertainty was assessed in a probabilistic sensitivity analysis, but this
only assessed the uncertainty in survival, and not in other model parameters. As a result, the overall model uncertainty was not assessed. The authors reported that the main limitation of their study was that some of the estimates were based on data from one Italian clinical centre.

Concluding remarks:
The methods were good, and they and the results were reported adequately. Within the scope of the analysis, the authors’ conclusions were appropriate.

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