Cost-effectiveness analysis of trastuzumab (Herceptin) in HER2-overexpressed metastatic breast cancer


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 trastuzumab for the management of women with human epidermal growth factor receptor two (HER2)-positive metastatic breast cancer. The authors concluded that trastuzumab was a cost-effective treatment from the perspective of the French health care system. The analysis had some methodological limitations, especially relating to the clinical data. Further studies are needed to corroborate these findings.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of trastuzumab for the management of women with human epidermal growth factor receptor two (HER2)-positive metastatic breast cancer.

Interventions
Trastuzumab was given at a loading dose of 4mg per kg followed by weekly doses of 2mg per kg until progression or for a maximum of one year. This was after or in combination with standard chemotherapy, using taxanes, and was compared against standard chemotherapy alone, using taxanes, anthracycline-based chemotherapy, or both.

Location/setting
France/out-patient.

Methods
Analytical approach:
The analysis was based on a single study that followed-up patients until their death. The authors stated that the perspective of the health care system was adopted.

Effectiveness data:
The evidence came from a retrospective comparative study with a historical control. All 47 eligible patients, who were treated for first metastatic progression, at the authors' institution, were included in the analysis. There were 19 patients (mean age 55 years, range 26 to 75) in the control group and they were treated before the introduction of trastuzumab. There were 28 patients (mean age 51 years, range 27 to 73) in the trastuzumab group. Patients' charts up to their deaths were analysed and overall survival (from the first metastatic progression until death) was the key outcome.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
Life-years (LYs) saved were the summary benefit measure and LYs without metastatic progression were also estimated.

Cost data:
The following cost categories were considered: in-patient hospitalisation, chemotherapy, imaging tests, and granulocyte-colony stimulating factor. The resource use data were derived from the sample of patients included in the clinical trial. The unit costs were from the accounting system at the authors' institution, which used drug prices negotiated by the
Federation of French Cancer Hospitals and procedure costs established by the French Social Security system, both at a national level. All costs were in Euros (EUR) and the price year was 2002.

Analysis of uncertainty:
A bivariate sensitivity analysis was undertaken on the unit cost of trastuzumab and the unit cost of hospitalisation, using arbitrary alternative values. A bootstrapping method was used to determine confidence intervals around the mean costs and benefits.

Results
The expected survival was 37.02 months and the costs were EUR 39,607 in the trastuzumab group, while the survival was 18.98 months and the costs were EUR 12,795 in the control group. The greatest cost component was that of trastuzumab (40%) in the trastuzumab group and hospitalisation (60%) in the control group. The incremental cost per LY gained with trastuzumab was EUR 17,800, while the incremental cost per extra LY without metastatic progression was EUR 69,111.

In the bootstrapped analysis, the incremental cost per LY gained with trastuzumab over no treatment was EUR 27,492 (95% CI 20,964 to 34,020).

The bivariate analysis showed that with variations in the costs of trastuzumab and of hospital stay, the incremental cost-effectiveness ratio ranged from EUR 8,000 to EUR 20,000.

Authors' conclusions
The authors concluded that trastuzumab was a cost-effective treatment for patients with metastatic breast cancer, from the perspective of the French health care system.

CRD commentary
Interventions:
The selection of the comparators was appropriately justified. Trastuzumab had become the standard care for these cancer patients, but its cost-effectiveness had not been unequivocally demonstrated. Conventional chemotherapy regimens were considered as the comparator. The dosages of the strategies were clearly reported.

Effectiveness/benefits:
The clinical data were from a study, in which the two groups of patients were enrolled over different periods and, as the clinical outcomes were not studied concurrently, time-related bias cannot be ruled out. The patients' characteristics were similar at baseline, but a justification for the size of the sample was not given. The difference between the two groups in overall survival (the main clinical endpoint) was statistically significant, but in progression-free survival it was not. Lys were a valid benefit measure, because expected survival is the key output of a cancer therapy. Lys can also be compared with the benefits of other health care programmes. The authors' stated that it was not possible to collect utility weights because the analysis was retrospective, but the inclusion of quality of life would have favoured trastuzumab.

Costs:
The economic analysis included the cost categories that were relevant from the perspective of the health care payer. No information on the unit costs and resource quantities was provided. The authors stated that some categories of costs (e.g. some pharmacy costs and those of immunohistochemical assays) were excluded from the analysis, as they were likely to be negligible. The price year was clearly stated, facilitating deflation exercises in other time periods. The total costs were broken down into key categories and the impact of each cost category on the total costs was analysed.

Analysis and results:
The study results were clearly reported. The costs and benefits were synthesised in an incremental analysis. Bootstrapping was a valid way to comprehensively assess the uncertainty. A two-way sensitivity analysis was also appropriately performed on the two most influential economic inputs. Discounting of the costs and benefits was not mentioned, but could have been relevant. The authors acknowledged that the main limitation of their analysis was the small sample size, which was due to difficulty in identifying patients who were eligible for trastuzumab, but did not
receive it (the control group). Some previous economic evaluations had shown less favourable results for trastuzumab.

**Concluding remarks:**
The analysis had some methodological limitations, especially relating to the clinical data. Further studies are needed to corroborate these findings.

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