Cost-utility analysis of palonosetron-based therapy in preventing emesis among breast cancer patients
Avritscher EB, Shih YC, Sun CC, Gralla RJ, Grunberg SM, Xu Y, Elting LS

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 palonosetron-based compared with generic ondansetron-based therapy to prevent emesis in breast cancer patients who were receiving multiple cycles of anthracycline and cyclophosphamide chemotherapy. The authors concluded that the palonosetron-based two-drug strategy exceeded the recommended cost-effectiveness threshold, but was comparable with other supportive care interventions for patients with breast cancer. The study was well presented and was based on conventional and appropriate cost-effectiveness methodology, which should ensure the validity of the authors’ conclusions.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of palonosetron-based therapy to prevent emesis in breast cancer patients who were receiving multiple cycles of anthracycline and cyclophosphamide as chemotherapy, compared with generic ondansetron-based therapy.

Interventions
Six strategies were considered, three based on ondansetron and three based on palonosetron. All six strategies included dexamethasone, two included aprepitant after emesis, and two included aprepitant from the first cycle.

The ondansetron two-drug regimen was ondansetron 32mg intravenously plus dexamethasone 8mg intravenously on day one, followed by dexamethasone 4mg orally twice a day on days two to five.

The ondansetron two-drug plus aprepitant regimen was ondansetron 32mg intravenously plus dexamethasone 8mg intravenously on day one, followed by dexamethasone 4mg orally twice a day on days two to five. If emesis occurred, the following cycles were ondansetron 16mg orally plus aprepitant 125mg orally plus dexamethasone 12mg orally on day one, followed by aprepitant 80mg orally on days two to three.

The palonosetron two-drug regimen was palonosetron 0.25mg intravenously plus dexamethasone 8mg intravenously on day one, followed by dexamethasone 4mg orally twice a day on days two to five.

The palonosetron two-drug plus aprepitant regimen was palonosetron 0.25mg intravenously plus dexamethasone 8mg intravenously on day one, followed by dexamethasone 4mg orally twice a day on days two to five. If emesis occurred, the following cycles were palonosetron 0.25mg intravenously plus aprepitant 125mg orally plus dexamethasone 12mg orally on day one, followed by aprepitant 80mg orally on days two to three.

The ondansetron three-drug regimen was ondansetron 16mg orally plus aprepitant 125mg orally plus dexamethasone 12mg orally on day one, followed by aprepitant 80mg orally on days two to three.

The palonosetron three-drug regimen was palonosetron 0.25mg intravenously plus aprepitant 125mg orally plus dexamethasone 12mg orally on day one, followed by aprepitant 80mg orally on days two to three.

Location/setting
Methods

Analytical approach:
The analysis was based on a Markov model with a time horizon of four cycles of chemotherapy, each lasting 21 days (12 weeks). The authors stated that the study was carried out from the perspective of the third-party payer.

Effectiveness data:
The clinical data were from selected relevant studies. The evidence on the efficacy of ondansetron and palonosetron in controlling emesis was from head-to-head randomised controlled trials. The efficacy of the other regimens was from non-randomised studies. Some estimates were from several studies and some assumptions were made. The key input was the efficacy of prophylaxis, which was defined as the probability of acute emesis control.

Monetary benefit and utility valuations:
The utility values were from a published study of preferences elicited using a visual analogue scale from a sample of ovarian cancer patients who were undergoing chemotherapy.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure.

Cost data:
The economic analysis included the costs of anti-emetics, office visits, and rescue medicines. The cost of hospitalisation for emesis, which was rare, was considered using data from the Healthcare Cost and Utilization Project, which included 2,342 patients with breast cancer. The costs were based on Medicare reimbursement data using cost-to-charge ratios where relevant. The resource use data were based on patterns of consumption in clinical trials and other studies. All costs were in US dollars ($) and the price year was 2008.

Analysis of uncertainty:
One-way sensitivity analyses were carried out on the model inputs, using plausible ranges of values, confidence intervals, or minimum and maximum values in the published trials. A probabilistic analysis was performed using a Monte Carlo simulation.

Results

The projected costs were $269 with ondansetron two-drug, $635 with ondansetron two-drug plus aprepitant, $858 with palonosetron two-drug, $1,177 with palonosetron two-drug plus aprepitant, $1,336 with ondansetron three-drug, $1,939 with palonosetron three-drug therapy. The benefits were 0.1989 with ondansetron two-drug, 0.2010 with ondansetron two-drug plus aprepitant, 0.2040 with palonosetron two-drug, 0.2056 with palonosetron two-drug plus aprepitant, 0.205 with ondansetron three-drug, 0.2094 with palonosetron three-drug therapy.

Compared with the next less-costly alternative after excluding dominated (more expensive and less effective or less cost-effective) strategies, the incremental cost per QALY gained was $115,490 with palonosetron two-drug compared with ondansetron two-drug therapy, $199,375 with palonosetron two-drug plus apreiptant compared with palonosetron two-drug therapy, and $200,526 with palonosetron three-drug compared with palonosetron two-drug plus apreiptant therapy.

The most interesting result of the sensitivity analysis was the impact of changes in the probability of emesis control with the ondansetron two-drug therapy, for which the incremental cost per QALY dropped to $53,892 if the probability of control was lowered to 46%. Variations in other inputs did not substantially alter the base-case conclusions.

The palonosetron two-drug therapy was cost-effective at a benchmark of $100,000 per QALY in 39% of simulations and the palonosetron two-drug plus apreiptant therapy was cost-effective in 26%. The cost of palonosetron had to decrease by 11% to make the palonosetron two-drug therapy cost-effective compared with ondansetron two-drug therapy at the $100,000 per QALY threshold.

Authors' conclusions
The authors concluded that the palonosetron-based two-drug strategy exceeded the cost-effectiveness threshold of $100,000 per QALY, but was comparable with other supportive care interventions for patients with breast cancer.

**CRD commentary**

**Interventions:**
The selection of the comparators was appropriate as several available treatments and combinations of treatments were considered. The dosages were reported in detail.

**Effectiveness/benefits:**
The clinical evidence for the two main treatments was from head-to-head clinical trials, which are generally considered to be valid sources of evidence due to their methodological strengths. Other data came from non-randomised studies, which were not described; more details would have allowed a better judgement of the quality of these clinical inputs. The authors did not state the criteria used to select the base-case values for the analysis. Some assumptions were required where trial-based evidence was not available. The utility values were elicited using a visual analogue scale, which has been shown to provide valid utility scores for nausea and vomiting. QALYs were appropriate for capturing the impact of the interventions, given their effects on women’s health.

**Costs:**
The cost categories reflected the perspective adopted. The unit costs were not presented separately from the resource quantities and the costs were generally reported as category totals. This is a typical approach when Medicare is used. A cost-to-charge ratio was appropriately applied. The sources for the resource use were reported and reflected the US context. Some cost categories were varied in the sensitivity analysis, which focused mainly on the drug cost.

**Analysis and results:**
The results were extensively presented. The projected costs and benefits were appropriately synthesised, using an incremental approach, which allowed the exclusion of inferior (dominated) strategies. The uncertainty was investigated using two approaches, which appear to have been appropriate and considered the impact of model inputs varied individually and simultaneously. The authors justified their selection of a short time horizon, which corresponded to the standard duration of four cycles of anthracycline and cyclophosphamide chemotherapy. They stated that a limitation of their analysis was the fact that the model did not consider the adverse effects of anti-emetics. They also stated that the results could not be transferred to other settings with different cost structures and the uncertainty around the cost-effectiveness estimates meant that further studies were needed.

**Concluding remarks:**
The study was well presented and was based on conventional and appropriate cost-effectiveness methodology, which should ensure the validity of the authors’ conclusions.

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