Cost-effectiveness of novel relapsed-refractory multiple myeloma therapies in Norway:
lenalidomide plus dexamethasone vs bortezomib

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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
This study examined the cost-effectiveness of lenalidomide plus dexamethasone, compared with bortezomib, for patients with relapsed-refractory multiple myeloma. The authors concluded that lenalidomide in addition to dexamethasone provided good value compared with bortezomib, from the perspective of the third-party payer in Norway. Clear methods were used to assess the available evidence and key areas of uncertainty were considered. The authors' conclusions appear to be robust.

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

Study objective
This study examined the cost-effectiveness of lenalidomide plus dexamethasone, compared with bortezomib, for patients with relapsed-refractory multiple myeloma.

Interventions
Lenalidomide was given at 25mg for 21 days, in cycles of 28 days, alongside dexamethasone. This was compared with bortezomib, which was administered as a 1.3mg per m², three-to-five-second bolus, intravenous, injection on days one, four, eight, and 11, followed by 10 days of rest, for eight three-week cycles.

Location/setting
Norway/secondary care.

Methods
Analytical approach:
The analysis was based on a discrete-event simulation, with a two-year time horizon. The authors stated that the perspective of the third-party payer was adopted.

Effectiveness data:
The clinical inputs were from three published trials: two for lenalidomide plus dexamethasone, and one for bortezomib. The data from the two lenalidomide trials were pooled, and an indirect method was used to compare the efficacy and safety of the two treatments. Parametric survival analysis, using patient-level data, was used to obtain the model inputs. The rate of complete or partial response was the key input for the model. Overall survival data were from the three trials.

Monetary benefit and utility valuations:
The utility values were from a published cost-utility study of patients with multiple myeloma, conducted by the Dutch-Belgian Hemato-Oncology Cooperative Study Group.

Measure of benefit:
Life-years and quality-adjusted life-years (QALYs) were the summary benefit measures. A 4% annual discount rate was applied.

Cost data:
The economic analysis included the costs of drugs, administration, monitoring, and management of adverse events. The quantities of resources were those recorded in the clinical trials or they were collected from clinical experts via a structured questionnaire. Their values were based on Norwegian price lists, physician fees, and the Norwegian DRG database. All costs were in Norwegian kroner (NOK) and were discounted at an annual rate of 4%.

Analysis of uncertainty:
One-way sensitivity analyses were carried out by varying the time horizon, costs, discount rate, survival following progression, and time to progression. Both published and assumed ranges of values were considered.

Results
The expected costs were NOK 689,207 with lenalidomide plus dexamethasone and NOK 500,962 with bortezomib. The projected QALYs were 2.95 with lenalidomide and 2.19 with bortezomib, and the life-years were 4.06 with lenalidomide and 3.11 with bortezomib.

For lenalidomide, compared with bortezomib, the incremental cost per QALY gained was NOK 247,078, and the incremental cost per life-year gained was NOK 198,714. Accepted cost-effectiveness thresholds in Norway range from NOK 350,000 to NOK 425,000.

The most influential inputs were the cost of lenalidomide plus dexamethasone, the time horizon, and the survival following progression. In particular, the confidence intervals surrounding the survival following progression decreased and increased the incremental cost per QALY from NOK 118,392 to NOK 412,993. A longer time horizon of four years raised the cost per QALY to NOK 441,457.

Variations in other inputs did not alter the base-case findings.

Authors’ conclusions
The authors concluded that lenalidomide in addition to dexamethasone provided good value compared with bortezomib, from the perspective of the third-party payer in Norway.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear as they were the available treatments for these patients.

Effectiveness/benefits:
The source trials were selected without a systematic search. There were no head-to-head clinical trials, so an indirect method was used to compare the clinical efficacy and safety of the two treatments; this method was clearly presented. The authors reported that the patient characteristics in the three trials were similar, allowing a valid comparison between the two treatments. There were differences between the trials that could not be controlled for, including cross-over from dexamethasone to lenalidomide or bortezomib, and attempts were made to adjust the clinical results for potential differences. These trials were well described should have had good internal validity. Several clinical outcomes were reported. Both life-years and QALYs were appropriate as they capture the impact of the disease on the patients’ health. The sources for the utility values were reported, but the instruments used to elicit the preferences were not.

Costs:
The categories of costs reflected the perspective of the third-party payer as only the direct costs were considered. The authors stated that productivity losses were minimal as most patients were over 65 years old. The resource use for drugs and adverse events was mainly from the clinical trials, which should have ensured detailed data, but might not have fully reflected clinical practice. Other data were assumed by experts who were relevant to the authors’ settings, and Norwegian sources were used for the unit costs. Few details were given and the unit costs and resource use were not presented separately. The price year was not reported, hindering reflation exercises.

Analysis and results:
The results were clearly presented and an incremental approach was appropriately used to synthesise the costs and benefits. The uncertainty was investigated in a deterministic analysis that focused on varying individual inputs. The discrete-event simulation used patient-level data, which took into account variations in patient characteristics. The
authors acknowledged some limitations to their analysis mainly due to the indirect comparison. They stated that the clinical data for bortezomib were based on 11 cycles, but the costs were for eight cycles (based on European recommended treatment), meaning that the costs of bortezomib might have been underestimated. They reported that the costs and effects were incurred over two years, so it is unclear why both QALY and life-year results were greater than two and a longer time horizon might have been used. The study results were specific to Norway as stated by the authors.

Concluding remarks:
Clear methods were used to assess the available evidence and key areas of uncertainty were considered. The authors’ conclusions appear to be robust.

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