Effective treatment and prophylaxis of hyperuricemia and impaired renal function in tumor lysis syndrome with low doses of rasburicase

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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 study objective was to examine the clinical and economic impact of using rasburicase, at a lower dosage than that recommended by the manufacturer, to reduce uric acid levels in patients with tumour lysis syndrome (TLS). The authors concluded that low doses of rasburicase were effective and cost-saving for prophylaxis and treatment of TLS in a German hospital. The study was carried out and presented in a simple and transparent fashion, thus supporting the validity of the authors’ conclusions. However, a direct comparison of the two options under analysis would have been more appropriate.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to examine the clinical and economic impact of rasburicase for the reduction of uric acid (UA) levels in patients with tumour lysis syndrome (TLS), using a lower dosage than that recommended by the manufacturer. Rasburicase could be used for both prophylaxis and treatment of TLS.

Interventions
The study examined an initial dose of 3 to 4.5 mg and subsequent dosages as needed for prophylaxis and treatment of TLS. A median dose of 0.049 mg/kg was used. This strategy was compared with no intervention (baseline values). The manufacturer's recommended dose is 0.15 to 0.2 mg/kg over 5 to 7 days, a total of about 92.4 mg on average per patient.

Location/setting
Germany/hospital.

Methods
Analytical approach:
This economic evaluation was based on data derived from a single study. The time horizon of the analysis was restricted to the duration of treatment (6 days). The authors did not report the perspective of the analysis.

Effectiveness data:
The clinical estimates were derived from a single clinical study, the design of which was a within-comparison study with clinical end points valued at baseline and at the end of treatment (follow-up of 6 days corresponding to the duration of therapy). A sample of 50 consecutive patients was enrolled from January 2002 to July 2006 in the authors’ institution, of which 8 patients were given prophylaxis and 42 were treated for TLS. The median age was 67 years (range: 16 to 88) and 21 were female. The key clinical end point was the treatment effect in terms of reductions in UA and creatinine levels after the first dose and within 7 days.

Monetary benefit and utility valuations:
None.

Measure of benefit:
The health outcomes were left disaggregated and no summary benefit measure was used. In effect, a cost-consequences
analysis was performed. The key clinical end points were the reductions in UA and creatinine levels.

Cost data:
The economic analysis was restricted to drug costs. The unit costs per vial were reported, but not the source of this cost. It looks as though a "European" price and a "US" price were used. Resource use (quantity of drug used) was based on data from the clinical study. The costs were in euros (EUR) and US dollars ($). The price year was not reported.

Analysis of uncertainty:
Not performed.

Results
UA and creatinine levels at baseline were 856.5 μmol/L (range: 339 to 1,659) and 192.7 μmol/L (range: 65.4 to 761.1), respectively.

After treatment, UA and creatinine levels were 160.6 μmol/L (range: 5.9 to 779.2) and 111.4 μmol/L (range: 46.9 to 610), respectively.

Median UA levels were lowered by 70% in the prophylaxis group and by 79% in the treatment group.

The cost analysis indicated that, for a typical patient with a body weight of 77 kg, the cost for a 6-day course of rasburicase would be EUR 4,378 when using the manufacturer’s recommended dose and EUR 167 when using a low-dose strategy.

In the US, the corresponding costs would be $24,381 and $774. Thus, the low-dose strategy led to a reduction of 96.8% in drug costs in comparison with the recommended dosage.

Authors’ conclusions
The authors concluded that low doses of rasburicase were effective and cost-saving compared with recommended higher doses of rasburicase for prophylaxis and treatment of TLS in a German hospital.

CRD commentary
Interventions:
The rationale for the comparators selected for the clinical analysis was not clear. In effect, the low-dose rasburicase therapy was compared with a no-intervention strategy, although it would have been helpful to have compared it against the recommended-dose rasburicase strategy, as in the analysis of the costs.

Effectiveness/benefits:
The clinical data were based on a within-group comparison study, which was appropriate for the study objective, despite the fact that a clinical trial with two comparison groups would have been more appropriate. The authors described the methods and clinical findings in full. Statistical tests were appropriately performed to compare the end points achieved before and after treatment. The clinical and demographic characteristics of the patient sample were reported. A potential limitation of the analysis was the relatively small sample size and the fact that patients were identified at a single medical institution, which might reduce the representativeness of the patient population.

Costs:
The analysis of the costs was restricted to drug costs. Although it might appear that the use of a wider perspective would have been more appropriate, the inclusion of medication costs reflects the scope of the analysis. Clearly, the provision of more details on the sources of costs and the price year would have been helpful. Nevertheless, the analysis demonstrated the authors’ objective. Furthermore, the unit costs of vials and quantities of medications used were reported. This enhances the possibility of replicating the analysis in other settings.

Analysis and results:
The costs and benefits were not combined since a cost-consequences analysis was performed. The issue of uncertainty was not addressed and sensitivity analyses were not carried out. However, the analysis relied on a sample of patients
which was likely to reflect real-world data. The issue of the generalisability of the study results to other settings was not explicitly addressed. Nevertheless, the analysis presented economic data for both the European and the US markets. Thus, the external validity of the analysis was good.

Concluding remarks:
Overall, the study was carried out in a simple and transparent fashion. The reporting of the methods and results was satisfactory. The authors’ conclusions appear valid, but a direct comparison of the two options would have been more appropriate.

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