Economic evaluation of systemic treatments for cytomegalovirus retinitis in patients with AIDS


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.

Health technology
Systemic treatments for cytomegalovirus (CMV) retinitis in patients with acquired immune deficiency syndrome (AIDS) were examined. Four treatment regimens for induction and maintenance therapy were compared:

- intravenous (IV) cidofovir induction and maintenance (IV/IV cidofovir);
- IV foscarnet induction and maintenance (IV/IV foscarnet);
- IV ganciclovir induction and maintenance (IV/IV ganciclovir); and
- IV ganciclovir induction and oral (PO) ganciclovir maintenance (IV/PO ganciclovir).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with AIDS and newly diagnosed CMV retinitis. No further details of the study population were provided.

Setting
The setting was the Swiss health care system. Further details were not provided, but it appears to have been secondary care. The economic study was carried out in Switzerland and the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1985 and 1998. The cost data reflected 1998 price lists for a Swiss Cantonal hospital.

Source of effectiveness data
The effectiveness data were derived from a systematic review of the literature.

Modelling
A treatment failure model that followed management strategies for treating CMV retinitis in persons with AIDS was developed to assess the economic impact of the different regimens. The model compared four starting regimens and
assessed patients at the end of each treatment cycle for their average life expectancy (13 months).

**Outcomes assessed in the review**
The outcomes assessed were the median time to first and subsequent progression for each treatment regimen, the duration of maintenance treatment and adverse consequences.

**Study designs and other criteria for inclusion in the review**
Clinical reports were included if they met the following inclusion criteria:

- prospective controlled clinical trials published in any language;
- patient population consisting of patients with AIDS and CMV retinitis;
- the reporting of time to progression of CMV retinitis; and
- the use of one of the regimens of interest in at least one arm of the study.

Studies including patients with systemic CMV infection or non-AIDS patients were included if separate data for patients with AIDS and CMV retinitis were provided. Studies with less than 10 patients were excluded.

**Sources searched to identify primary studies**
MEDLINE was searched for relevant studies. The bibliographies of the retrieved articles were checked for additional trials.

**Criteria used to ensure the validity of primary studies**
Not reported.

**Methods used to judge relevance and validity, and for extracting data**
Not reported.

**Number of primary studies included**
Approximately 10 primary studies were included in the review.

**Methods of combining primary studies**
The estimate of time to progression was calculated as the weighted average of the reported results, using study sample size as the weight. The adverse event data were drawn from data compiled and reported in the package inserts of each of the respective products, as well as from the clinical trials identified in the systematic review.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The median time to first regression was 120 days for IV/IV cidofovir, 53 days for IV/IV foscarnet, 48 days for IV/IV ganciclovir and 28 days for IV/PO ganciclovir. The median time to subsequent progression was 88 days for IV/IV cidofovir, 39 days for IV/IV foscarnet, 38 days for IV/IV ganciclovir and 25 days for IV/PO ganciclovir.

The adverse events for each treatment regimen were as follows:
31% of patients on the IV/IV cidofovir regimen had mild neutropenia, compared with 36% of patients on IV/IV foscarnet, 30% of patients on IV/IV ganciclovir and 36% of patients on IV/PO ganciclovir;

20% of patients on the IV/IV cidofovir regimen had severe neutropenia, compared with 17% of patients on IV/IV foscarnet, 25% of patients on IV/IV ganciclovir and 18% of patients on IV/PO ganciclovir;

0% of patients on the IV/IV cidofovir regimen had thrombocytopenia, compared with 16% of patients on IV/IV foscarnet, 6% of patients on IV/IV ganciclovir and 6% of patients on IV/PO ganciclovir;

53% of patients on the IV/IV cidofovir regimen had nephrotoxicity, compared with 33% of patients on IV/IV foscarnet, 2% of patients on IV/IV ganciclovir and 1% of patients on IV/PO ganciclovir;

9% of patients on the IV/IV cidofovir regimen had local catheter-related infection, compared with 9% of patients on IV/IV foscarnet, 9% of patients on IV/IV ganciclovir and 4% of patients on IV/PO ganciclovir;

8% of patients on the IV/IV cidofovir regimen had systemic catheter-related infection, compared with 8% of patients on IV/IV foscarnet, 8% of patients on IV/IV ganciclovir and 1% of patients on IV/PO ganciclovir.

**Measure of benefits used in the economic analysis**
The measures of health benefits were the same as those used in the effectiveness analysis. No summary measure of benefit measure was used in the economic analysis.

**Direct costs**
The direct costs included were the costs of the drug regimens and their delivery, the cost of caring for patients and treating adverse events, and monitoring costs. Discounting was not necessary because of the short duration of the analysis. The price year was 1998.

**Statistical analysis of costs**
No statistical analysis of the costs was reported.

**Indirect Costs**
No indirect costs were included.

**Currency**
Swiss francs (Sfr). The exchange rate was US$1.00 = Sfr 1.45.

**Sensitivity analysis**
Several threshold sensitivity analyses on the base-case parameters were carried out to test the assumptions and data used in the model. The parameters used included the median time to progression, incidence of adverse events and costs.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The mean per-patient 13-month cost used in the model was Sfr 146,742 for IV/IV cidofovir, Sfr 194,809 for IV/IV foscarnet, Sfr 243,964 for IV/IV ganciclovir and Sfr 195,190 for IV/PO ganciclovir.
The average per-cycle cost of treating adverse events was Sfr 1,864 for IV/PO ganciclovir, Sfr 2,477 for IV/IV foscarnet, Sfr 3,512 for IV/IV ganciclovir and Sfr 9,187 for IV/IV cidofovir.

The average incremental costs for the initial cycle were Sfr 48,534 for IV/IV ganciclovir, Sfr 11,932 for IV/PO ganciclovir, Sfr 23,127 for IV/IV foscarnet and Sfr 29,228 for IV/IV cidofovir. The average incremental cost for subsequent cycles of therapy ranged from Sfr 11,575 for IV/PO ganciclovir to Sfr 40,558 for IV/IV ganciclovir.

**Synthesis of costs and benefits**
The estimated benefits and costs were not combined. An incremental cost-effectiveness analysis was not performed.

The 13-month costs for individuals initially randomised to receive IV/IV cidofovir ranged from Sfr 12,601 to Sfr 196,845, depending upon the regimens they were assigned following progression of the disease.

The range for patients initially treated with IV/PO ganciclovir was Sfr 131,973 to Sfr 287,964, and for IV/IV foscarnet Sfr 138,907 to Sfr 276,846. The biggest range of costs was from Sfr 186,936 to Sfr 327,653 for those initially treated with IV/IV ganciclovir.

The lowest estimate of the 13-month costs occurred when patients were initially treated with IV/IV cidofovir following the initial treatment regimen. The highest costs came when individuals initially received IV/IV ganciclovir and then received IV/IV foscarnet following the initial agent.

The sensitivity analysis showed that the costs were most sensitive to changes in efficacy estimates, while treatment regimens were not as sensitive to changes in the incidence of adverse events, and the proportion of patients treated as outpatients versus inpatients.

**Authors' conclusions**
Of the systemic regimens studied for cytomegalovirus (CMV) retinitis, initial treatment with systemic cidofovir appears to have been the least costly over a 13-month period.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of the comparator was clear. The comparators were chosen because they were the four most common systemic treatments for CMV retinitis in patients with AIDS.

**Validity of estimate of measure of effectiveness**
The principal input parameters for the model were derived from a systematic review of the literature. The validity of the estimate of measure of effectiveness might have been affected by limitations of the study. For example, the efficacy rates of cidofovir were based on a single study that analysed only patients who were treatment-nave. Also, the results of the analysis were based upon model patients and on clinical trials, which may lead to results in clinical settings that are not indicative of the results seen in this analysis.

**Validity of estimate of measure of benefit**
The time to first and subsequent progression, and the duration of maintenance treatment were used as the measures of benefit. These were obtained directly from the effectiveness data. As the authors noted, this analysis did not consider important issues relating to quality of life when using each of the treatment regimens. Therefore, it should not be considered a cost-utility analysis of the treatment of CMV retinitis.

**Validity of estimate of costs**
The authors limited their analysis to direct medical costs for the treatments, although they stated that the perspective was that of the Swiss health care system. The costs and the quantities were not reported separately. The price year was
Other issues
The authors made wide comparisons of their findings with those from other studies. They also addressed the issue of the generalisability of their results to other settings. The limitations of the study have already been outlined in the 'Validity of estimate of measure of effectiveness' and 'Validity of estimate of measure of benefit' sections (above).

Implications of the study
All four systemic treatment regimens were effective in delaying disease progression. However, there was substantial variation in treatment and drug costs. The authors pointed out that the results of the analysis must be interpreted in the light of the introduction of highly active antiretroviral therapy, which has significantly changed the clinical progression of infection with human immunodeficiency virus. The authors recommended that the role of treatments for CMV continue to be evaluated and optimised with the new combination antiretroviral therapies.

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Other publications of related interest


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