Cost-effectiveness of cytomegalovirus (CMV) disease prevention in patients with AIDS: oral ganciclovir and CMV polymerase chain reaction testing

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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.

Health technology
Strategies to prevent cytomegalovirus (CMV) disease in patients with AIDS: oral ganciclovir (GCV) (1g three times daily) and CMV polymerase chain reaction testing (every three months).

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
A hypothetical cohort of HIV-infected patients with CD4 cell counts <50 x 10^6

Setting
Hospital. The economic study was carried out in New York, USA.

Dates to which data relate
The main effectiveness data were derived from studies conducted between 1992 and 1996. Resource and cost data were obtained from 1993-1996 sources. The price year was not clearly stated.

Source of effectiveness data
CMV disease incidence, survival of patients with CMV disease, survival of patients without CMV disease, effectiveness of oral GCV in preventing CMV disease, adverse reaction rate, proportion of CMV disease cases with preceding positive CMV PCR tests and the specificity of the CMV PCR test were derived from previously published studies.

Modelling
A Markov model was used.

Outcomes assessed in the review
The outcomes assessed were CMV disease incidence, survival of patients with CMV disease, survival of patients without CMV disease, effectiveness of oral GCV in preventing CMV disease, adverse reaction rate, proportion of CMV disease cases with preceding positive CMV PCR tests and specificity of CMV PCR test.

Study designs and other criteria for inclusion in the review
No specific study design was included in the analysis.

**Sources searched to identify primary studies**
Not stated.

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

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

**Number of primary studies included**
9 studies were included in the review.

**Methods of combining primary studies**
Narrative method.

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

**Results of the review**
The CMV disease incidence was 0.0150 per month. The survival of patients with CMV disease was 267 days. The survival of patients without CMV disease was 366 days. The effectiveness of oral GCV in preventing CMV disease was 0-49%. The adverse reaction rate was 2% per month. The proportion of CMV disease cases with preceding positive CMV PCR tests was 70%. The specificity of the CMV PCR test was 100%. These data were used as the principal inputs to the Markov model.

**Measure of benefits used in the economic analysis**
The measures of benefit were the number of CMV disease cases prevented by the interventions, life expectancy and disease-free life expectancy.

**Direct costs**
Oral GCV, severe oral GCV adverse reaction, CMV disease case and CMV PCR test costs were included in the analysis. Quantities were reported separately from costs. The quantity/cost boundary adopted was the hospital. Discounting was not undertaken. The price year was not clearly stated.

**Statistical analysis of costs**
Not undertaken.

**Indirect Costs**
Not considered.

**Currency**

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Sensitivity analysis
A one-way sensitivity analysis was performed on oral GCV effectiveness, oral GCV adverse reaction rate, oral GCV preventive therapy costs, PCR testing sensitivity, PCR testing specificity and PCR test costs.

Estimated benefits used in the economic analysis
Oral ganciclovir preventive therapy reduces the lifetime number of CMV disease cases by 50 per 1,000 strong cohort, extends life expectancy by 5 days and disease-free life expectancy by 18 days. Periodic PCR testing reduces the lifetime number of CMV disease cases by eight per cohort of 1,000 patients, extends life expectancy by 1 day and disease-free life expectancy by 3 days.

Cost results
The incremental cost per patient (lifetime) was found to be $7,733 for oral GCV and $467 for PCR testing.

Synthesis of costs and benefits
Oral ganciclovir preventive therapy costs $1,762,517 per year of life extended. Periodic PCR testing costs $495,158 per year of life extended. The sensitivity analyses indicated that oral GCV becomes cost-effective under a combination of conditions: when the effectiveness is 49% or greater, the adverse reaction rate is 2% or less per month, oral GCV preventive therapy costs $6 or less per day. PCR testing becomes cost effective under a combination of conditions: when PCR testing is sensitive enough to detect 80% of the pre-symptomatic CMV cases through testing every 3 months, the PCR test has a specificity of 100%, the PCR test costs $117 or less, oral GCV is 49% effective in preventing asymptomatic CMV cases from progressing to symptomatic CMV disease, the adverse reaction rate is 2% or less per month and oral GCV preventive therapy costs $6 or less per day.

Authors' conclusions
Oral ganciclovir preventive therapy and periodic plasma testing for CMV PCR with oral ganciclovir for those with positive tests results in small benefits at great cost. They are not cost-effective prevention strategies for persons with advanced HIV infection and positive CMV serologies.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator is clear. Two different clinical trials provide controversial conclusions about oral ganciclovir (GCV) and CMV polymerase chain reaction testing (every three months) in preventing CMV disease in patients with AIDS. However, the authors noted that other potentially more effective interventions exist (for example pre-emptive treatment and valaciclovir) which were not included in the study. You, as a user of this database, should consider whether these are widely used health technologies in your own setting.

Validity of estimate of measure of benefit
The estimate of measure of benefit used in the economic analysis is likely to be internally valid. The data have not been used selectively although it should be noted that the search strategy for the literature review was not outlined by the authors. However, the solutions determined by the model were tested using sensitivity analysis in order to validate the robustness of the findings.

Validity of estimate of costs
Resource quantities were reported separately from the prices. Adequate details of the methods of quantity and cost estimation were given. Important cost items do not appear to have been omitted.
Other issues
The authors' conclusions are likely to be justified given the uncertainties in the data. However, as the authors acknowledged, the decision analysis has the disadvantage of exposing the uncertainty of pertinent variables. The issue of generalisability to other settings or countries was not addressed. However, appropriate comparisons were made with other studies in terms of alternative strategies to prevent CMV disease. Results do not appear to have been presented selectively. However, in employing a model the study suffers from the well-accepted limitations of using hypothetical patients.

Implications of the study
The safety, efficacy, cost and cost-effectiveness of all potential interventions for CMV prevention need to be assessed, preferably in the context of a prospective randomized-controlled trial in order to validate the results presented here.

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