

COCHRANE COMMENTARIES

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Antiviral medications for preventing cytomegalovirus disease (CMV) in solid organ transplant recipients

What is this review about?

This review evaluates the benefits and harms of antiviral medications as prophylaxis after solid organ transplant (kidney, heart, liver, lung, pancreas) to prevent CMV disease. This includes prophylaxis with antiviral medications compared with placebo or no treatment, the comparative efficacy and safety of different antiviral medications and of different durations of the same antiviral agent. It does not include a comparison of prophylaxis versus pre-emptive treatment, as this is discussed in a separate systematic review (see the accompanying commentary).

What are the findings?

The use of antiviral prophylaxis versus no prophylaxis reduced CMV disease (see the forest plot in Fig. 1), CMV infection and all cause mortality (see forest plot in Fig. 2), primarily by reducing CMV related mortality, in transplant recipients of all ages who have at risk CMV status (CMV +ve or CMV -ve recipients of CMV +ve organs) pre-transplantation. There was also a reduction in herpes

simplex and zoster, bacterial and protozoal infections. No significant benefit was found for fungal infections, acute rejection or graft loss. There was an increase in the risk of neurological dysfunction (hallucinations, headaches etc) with ganciclovir and valaciclovir compared with placebo or no treatment. The decrease in CMV disease was consistent regardless of organ transplanted, treatment with an anti-lymphocyte agent and CMV serostatus. Comparing antiviral medications, ganciclovir was more effective than aciclovir for CMV disease prevention and also resulted in less leucopaenia. Valganciclovir did not differ significantly from ganciclovir. Considering duration of treatment, extended duration prophylaxis in kidney or lung transplant recipients significantly reduced the risk of CMV disease compared with the standard 3 months of therapy with the only trade off being more leucopaenia, with no other severe treatment associated side effects noted.

What are the findings based on?

Thirty seven randomised control trials (4342 patients) were included in the data synthesis. Nineteen trials compared

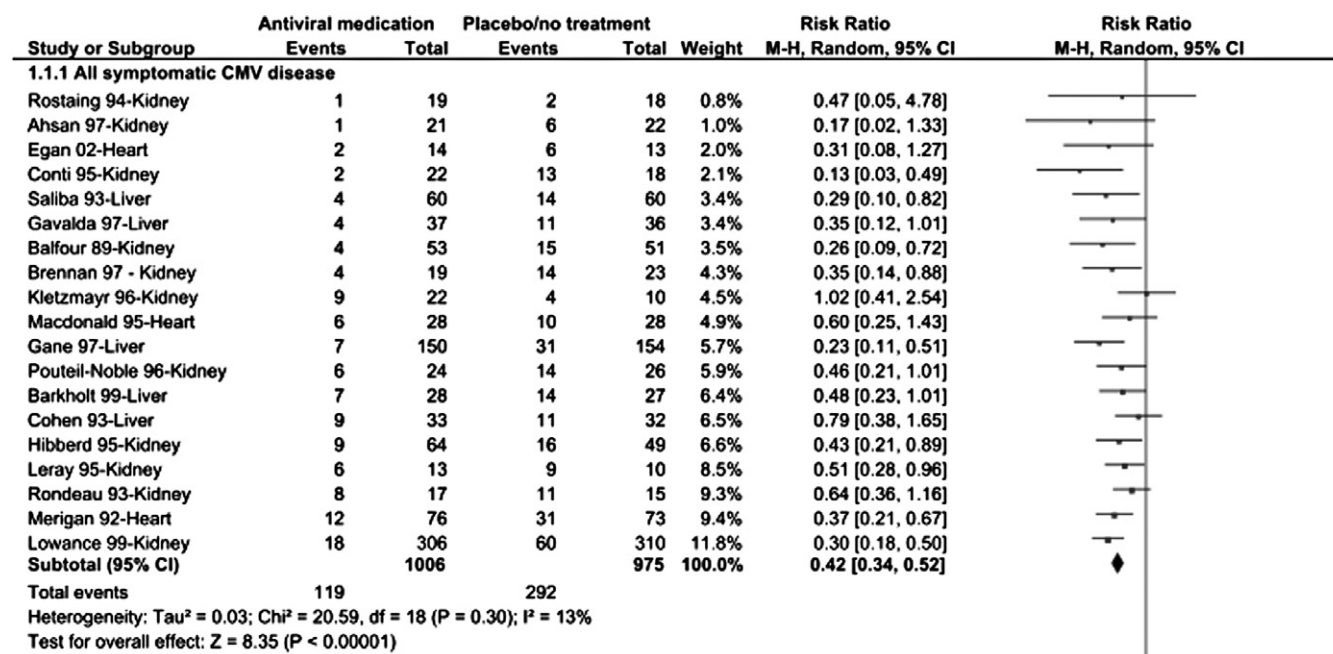


Fig. 1 Prophylaxis versus placebo or no treatment: outcome CMV disease.

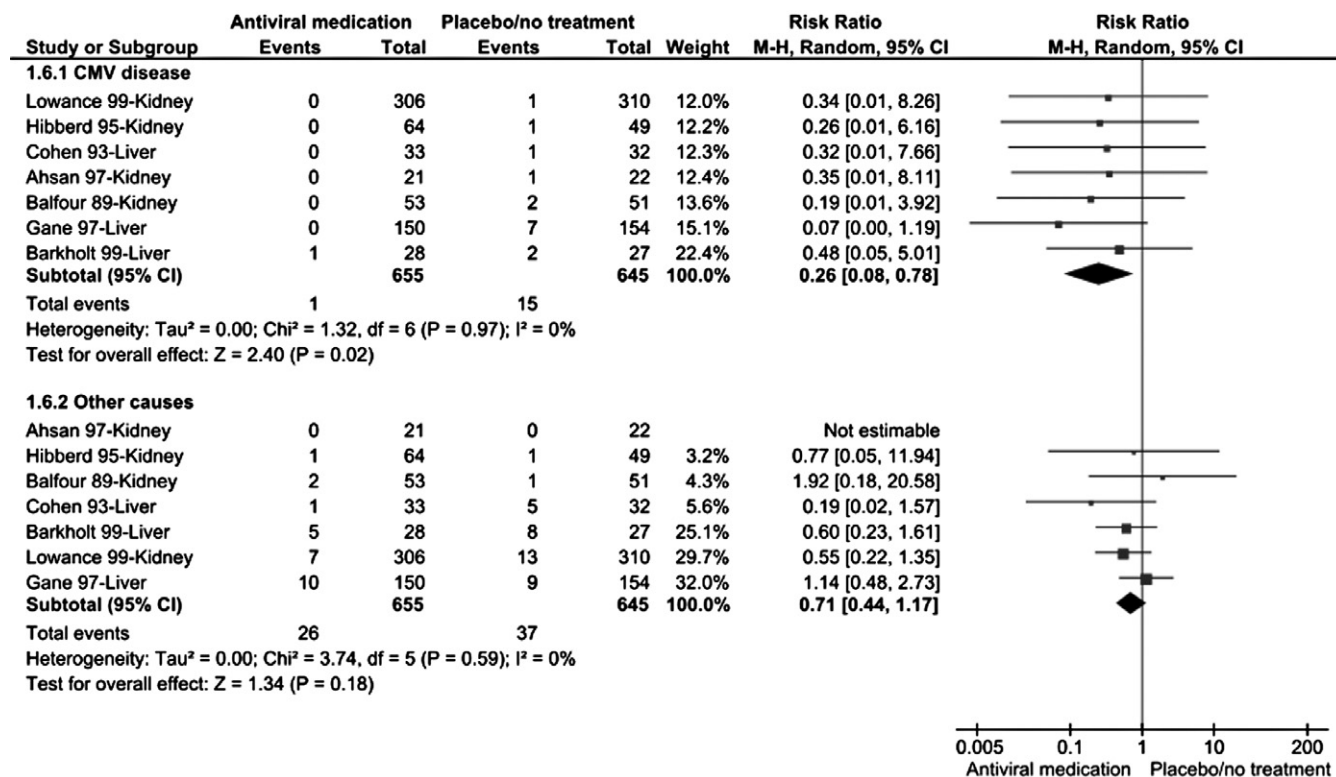


Fig. 2 Prophylaxis versus placebo or no treatment: outcome all-cause mortality.

aciclovir (6 trials), ganciclovir (11 trials) or valaciclovir (2 trials) with placebo or no treatment for recipients of different solid organ transplants (17 trials kidney, 12 trials liver, 3 trials heart, 2 trials lung, 2 trials all, 1 trial combined heart/lung). Fifteen of these trials excluded negative CMV status in both donor and recipient. A further 13 trials compared different antiviral agents and 5 trials compared different regimens of the same antiviral agent.

Domains of methodological quality in the design and reporting of included trials were generally not well reported. Sequence generation and allocation concealment were at low risk of bias in 12/37 trials (32%). Ten out of 37 (27%) trials and 9/37 (24%) trials had appropriate blinding of participants/investigators and outcome assessors respectively. Attrition bias was low in the majority of trials (92%). Thirteen of the 37 (35%) trials were sponsored by the pharmaceutical industry.

Implications for practice

- CMV prophylaxis in CMV positive recipients or in CMV negative recipients of CMV donor positive organs for at least three months reduces the risk of CMV disease and all-cause mortality in solid organ transplant recipients

- CMV prophylaxis also reduces the risk of other opportunistic infections
- Valganciclovir is as effective as ganciclovir which is more effective than aciclovir
- Extended duration CMV prophylaxis may be considered for higher risk kidney and lung transplant candidates

Clinical perspective

This systematic review supports the use of prophylaxis to prevent CMV disease with antiviral medications in all solid organ transplant recipients with either positive CMV donor and/or recipient serostatus. There is insufficient information to comment on its use in CMV seronegative recipients of organs from seronegative donors. Extended duration of antiviral prophylaxis in kidney and lung transplants has been shown to be more effective than standard 3 month prophylaxis.

Hodson EM, Ladhani M, Webster AC, Strippoli GFM, Craig JC. Antiviral medications for preventing cytomegalovirus disease in solid organ transplant recipients. *Cochrane Database of Systematic Reviews* 2013, Issue 2. Art. No.: CD003774. DOI: 10.1002/14651858.CD003774.pub4.