NEPHROLOGY

Nephrology **18** (2013) 235–236 doi:10.1111/nep.12019

COCHRANE COMMENTARIES

Edited by Angela Webster (angela.webster@sydney.edu.au)
Written by Maleeka Ladhani (mladhani@med.usyd.edu.au)

Pre-emptive treatment for cytomegalovirus viraemia to prevent cytomegalovirus disease in solid organ transplant recipients

What is this review about?

This review evaluated the benefits and harms of antiviral agents as pre-emptive treatment to prevent symptomatic cytomegalovirus (CMV) disease in all solid organ transplant recipients. Pre-emptive treatment is commenced when evidence of active CMV replication is found on routine surveillance. This review includes pre-emptive treatment versus placebo or treatment when symptomatic, pre-emptive treatment versus prophylaxis and different regimens of pre-emptive treatment.

What are the findings?

Pre-emptive treatment with any antiviral medication (ganciclovir or valganciclovir) significantly reduced the risk of CMV disease compared with placebo or no treatment in kidney and liver transplants. There were no trials in recipients of other solid organs. CMV organ involvement or CMV associated symptoms were also significantly reduced. However the confidence intervals were wide indicating imprecision. There was no significant difference in the risk of acute rejection, all-cause mortality, graft loss, leucopaenia or renal dysfunction.

Comparing pre-emptive with prophylactic antiviral treatment there was no significant difference in CMV disease, all-cause mortality, graft loss, acute rejection or other viral, bacterial or fungal infections. CMV infection was obviously higher in the pre-emptive group as this was a prerequisite for treatment. Leucopaenia was significantly less common with pre-emptive therapy. Results were not significantly different for low or high risk CMV status organ recipients though there were limited data addressing these patient groups. The antiviral agents compared were pre-emptive ganciclovir versus prophylactic ganciclovir, pre-emptive valganciclovir versus prophylactic valganciclovir or valaciclovir, and pre-emptive ganciclovir versus prophylactic acyclovir.

Pre-emptive oral versus intravenous ganciclovir showed no significant difference in risk of CMV disease, all-cause mortality or other infections. There was no difference between efficacy of oral or IV preparations of antiviral agent ganciclovir.

What are the findings based on?

A total of 15 trials (N = 1098 with 1063 included in the analyses) were included in the data synthesis. Six trials (N = 291 with 288 in the analysis) compared pre-emptive antiviral therapy with placebo or no specific therapy, eight trials (N = 785 with 753 included in the analysis) compared pre-emptive therapy with prophylaxis and the last trial compared pre-emptive oral with intravenous ganciclovir in liver transplant recipients (N = 22 all of whom were included in the analysis). The range of follow up of these studies was 3 to 18 months.

Assessment of domains of methodological quality in the design and reporting of included trials identified only five (33%) trials with appropriate sequence generation and four trials (27%) with adequate allocation concealment. The majority of trials were judged as having low risk of attrition bias (93%) and seven trials (47%) had selective reporting of outcomes leading to a high risk of bias. Blinding of participants was done in only two trials (13%) and no trials reported blinding of outcome assessment. Of the 15 trials, 5 (33%) were funded by pharmaceutical companies.

Implications for practice

- Pre-emptive treatment is more effective than no treatment (Figure 1)
- No conclusions can be made about the relative efficacy of pre-emptive therapy and prophylaxis because of inconsistency between the results of individual trials (Figure 2).
- Leucopaenia is less common with pre-emptive compared with prophylaxis treatment

Clinical perspective

Pre-emptive treatment for CMV disease aims to reduce the number of transplant recipients being exposed to long term prophylaxis by focusing treatment on recipients with laboratory evidence of CMV infection. Theoretically this could reduce the risk of resistant strains of CMV and late onset CMV disease, however, these outcomes were not reported in these trials. The downside of pre-emptive treatment is an increased burden of monitoring, and potential effects of

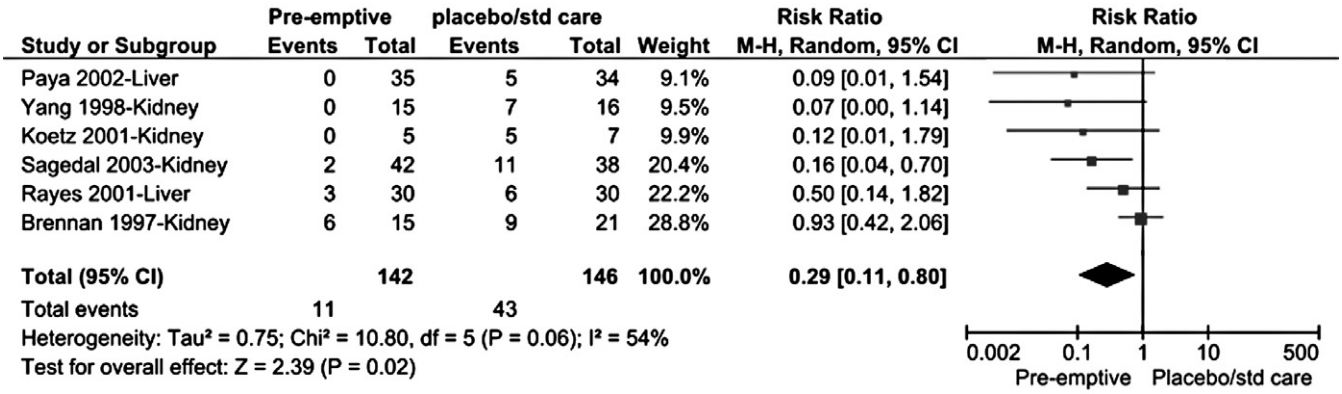

Fig. 1 Pre-emptive treatment versus placebo or no treatment: outcome CMV disease.

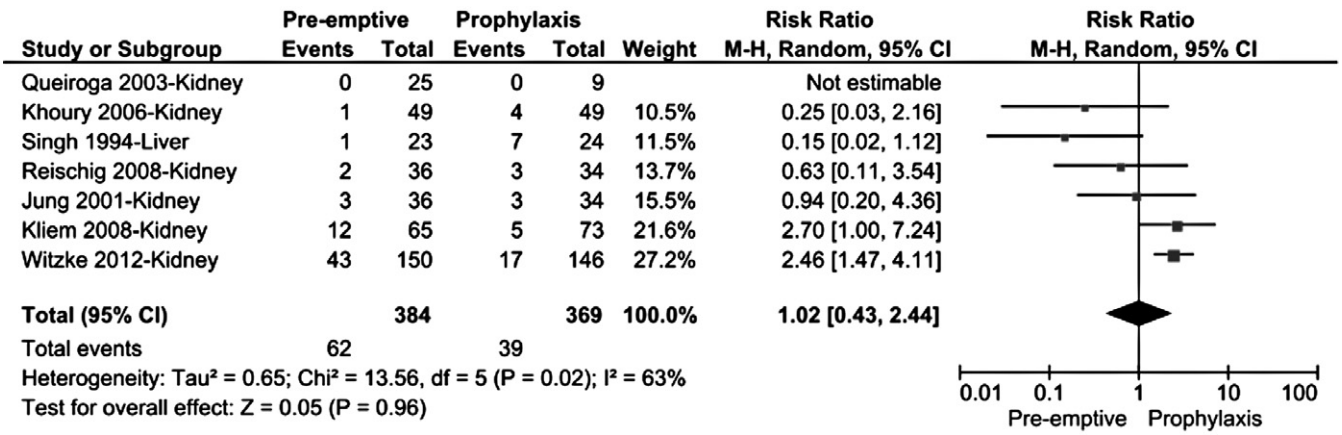

Fig. 2 Pre-emptive treatment versus prophylaxis: outcome CMV disease.

some recipients being exposed to periods of CMV infection before commencing treatment. This review of small trials of pre-emptive treatment demonstrated that pre-emptive therapy was significantly more effective than placebo or no treatment in preventing CMV disease. However because of small patient numbers and heterogeneity between studies, no firm conclusions can be drawn as to the relative benefits and harms of these different regimens for preventing CMV disease in solid organ transplant recipients.

Owers DS, Webster AC, Strippoli GFM, Kable K, Hodson EM. Pre-emptive treatment for cytomegalovirus viraemia to prevent cytomegalovirus disease in solid organ transplant recipients. *Cochrane Database of Systematic Reviews* 2013, Issue 2. Art. No.: CD005133. DOI: 10.1002/14651858.CD005133.pub3