Reviewer's report

Title: Effect of Ganciclovir for the Treatment of Severe Cytomegalovirus-Associated Pneumonia in Children without Specific Immunocompromised Status

Version: 1 Date: 18 February 2013

Reviewer: Klaus Hamprecht

Reviewer's report:

To the Authors

The submitted manuscript of Doan et al. to BMC Infectious Diseases entitled

“Effect of Ganciclovir for the treatment of severe CMV-associated pneumonia…”

describes the effect of ganciclovir (GCV) for treatment of severe CMV-associated pneumonia in not-immunosuppressed infants ranging in age from 45-85 days post partum.

There is only one phase III randomised trial (CASG 102 study) to study the outcome of congenitally CMV infected newborns (cCMV) (Kimberlin et al., J Pediatrics 2003). Actual algorithms for treatment of cCMV include either symptomatic focal organ disease or focal CNS disease (Kadambari et al., Early Human Development, 2011).

The study presented here includes immunocompetent infants with diagnosis of severe CMV-associated pneumonia.

In principal the results shown are interesting, however some important clinical and virological information is still lacking for better understanding of the interested reader.

Major compulsory revisions

A The following questions related to the study design and demographics arise therefore:

1. ) Are the infants ranging in age from 45-85 days p.p., term infants or are there also preterm infants? It would be helpful to know the individual gestational ages and birth weights.

2. ) Are the infants congenitally or postnatally infected with CMV? In both cases severe CMV-associated pneumonia can be found, but during postnatal CMV infections pneumonia will arise most frequently late (4-8 weeks after birth)

B Questions relating to nutrition of the infants
3. Are all infants fed with breast milk? It's important to know how the infants were exposed to CMV prior GCV treatment.

C Questions to the virological monitoring
4. Did the infants shed CMV into urine at the treatment start and did the authors analyse also urine following GCV treatment?
5. It would be very interesting to see the individual viral loads in blood and in tracheal secretions before and during antiviral treatment.
6. The Figures 1 and 2 can be replaced by tables. Instead of these a new figure including the individual VL courses under therapy should be given.

D Question to the role of CMV in pneumonia of the infants
10. The diagnosis of CMV pneumonia in stem cell transplant recipients has been defined exactly (Ljungman et al., 2008) with respect to clinical symptoms, X-ray, quantitative CMV PCR or viral culture from tracheal secretions. How the diagnosis of CMV pneumonia was defined in this study?

E Question to the outcome of the GCV treatment
1. In table 1 is shown, that one infant died. In which way CMV was involved?
2. Was there any evidence of treatment failure in this fatal case or any other case?

Minor essential revisions

A
1) Did the infants have primary CMV infections? See page 6: 70% of all infants had CMV IgM. Did they also show low avidity?
2) To the role of coinfections: rapid test systems based on immunochromatography for FLU are normally not sensitive enough to exclude H1N12009 and seasonal FLU.
3) the data on ADV and EV subfamilies should be shown
4) What's about hMPV?

B
1) Did some infants receive donor breast milk? Was the serology of the donor mothers known?
2) Or received the infants formula nutrition? In these cases cCMV has to be excluded.

C
1 With which rationale the authors changed the treatment regimen with respect to GCV concentrations given by Kimberlin et al?

Klaus Hamprecht
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests