Reviewer's report

Title: Variable viral clearance despite adequate ganciclovir plasma levels during valganciclovir treatment for cytomegalovirus disease in D+/R- transplant recipients

Version: 1 Date: 6 May 2009

Reviewer: Anders Åsberg

Reviewer's report:

General comments:
The presentation of the effect of ganciclovir exposure on the outcome of seven cases of SOT patients treated with valganciclovir for CMV disease is well written and of clinical interest, even though it is few patients. With the introduction of oral treatment of CMV disease it has become more important to evaluate individual variability in drug exposure on the outcome and these results indicate that there is no direct effect between ganciclovir exposure and clinical effect on DNAemia eradication. The present finding needs to be confirmed in a larger material.

Major compulsory revisions:
1. The pharmacokinetic population model was developed majorly based on patients under prophylaxis treatment. Please discuss possible differences in ganciclovir pharmacokinetics in this population as compared with the population of SOT patients treated for CMV disease.

Minor essential revisions:
1. Conclusions: In both conclusions it is stated that the patients showed variable DNAemia clearance despite adequate ganciclovir plasma concentrations. However, there is no reference to any therapeutic window for ganciclovir in the paper. This should be discussed, maybe the anticipated adequate level really is not adequate?

Discretionary revisions:
2. Is it not more common to refer to Myfortic as Mycophenolate sodium, not Mycophenolate acid?
3. It would be interesting for the reader to get some more information about the structural model and covariates included in the population model. Please insert this information.
4. The assay for analysis of CMV DNAemia seems to have a higher LOQ than the most commonly commercially available. Is it an in house assay? In conjunction to this, what was the definition of DNAemia clearance? Below 1000 copies?
5. Please state the definition of recurrence in the paper. One or two negative DNAemia samples?
6. Page 6, line 7: “Systemic exposure”, not “exposition”!?!?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

The reviewer has received grants from F. Hoffmann-La Roche in the field of CMV within the last years and have published himself in the same research area.