Reviewer's report

Title: A Prospective Study Comparing Quantitative Cytomegalovirus (CMV) Polymerase Chain Reaction in Plasma and pp65 Antigenemia Assay in Monitoring Patients after Allogeneic Stem Cell Transplantation.

Version: 1 Date: 7 July 2006

Reviewer: Angela Caliendo

Reviewer’s report:

General
In this study the authors compared pp65 and a plasma based PCR for use in monitoring patients after allogeneic stem cell transplantation. Thirty-eight consecutive patients were followed in this study and monitored weekly for the first one hundred days after stem cell transplant. Specimens were tested in both the COBAS AMPLICOR CMV MONITOR test and the pp65Ag test. The clinical decision making regarding preemptive therapy was based on the antigenemia test not on the PCR test. A total of 534 blood samples were tested in both antigenemia and PCR. Of the thirty-eight patients, 28 of them had detectable CMV by either antigen or PCR. Overall there were more positive samples with the antigenemia test than with the PCR assay. There were only three patients that developed active disease and in one of these patients, the PCR and the antigenemia were positive prior to symptoms. In another the antigenemia was positive at the time of symptoms. In the third patient, the antigenemia only was positive prior to symptoms. In general both assays were considered acceptable for use in monitoring patients.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. For the data that is presented on page 7. Looking at the detection by antigenemia vs. COBAS and the correlations between antigenemia and COBAS - the data should also be assessed using only the samples in which the patient is not on therapy. The rate of decline in antigen and DNA, as the authors state later in the paper, is not the same. So this could influence the results, and what would helpful is to know when the patient is not on pre-emptive therapy how well do the DNA and Ag agree.

2. Would analyze all data, and then those samples collected on therapy when assessing the sensitivity of the PCR and antigenemia, the authors compare the tests to each other. It would be helpful to see the data defining any positive test, either antigenemia or PCR as the gold standard and then comparing the antigenemia and PCR tests to this gold standard.

3. In the discussion, there needs to be some comment made about the difficulties in interpreting the “clinical” sensitivity of the PCR assay when pre-emptive therapy was based on antigenemia. It may be that with the antigenemia test the additional positives just lead over to treatment and do not actually prevent disease. The design of this study can not assess that possibility. The three patients with disease leads one to believe that there may be patients that will have disease that are PCR negative, as have been shown in the literature. However, a discussion of the limitation of the study design needs to be included.

4. Figure 1, Both the antigenemia and the PCR should be log transformed when analyzing the correlation between the two tests.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. The criteria on page 5, - In the method/section - criteria for the diagnosis of CMV disease “the sentence is a little confusing as written, is it a positive biopsy or a positive culture or are we doing PCR on
the biopsy material? Not clear as written. Also is infection defined as a positive antigenemia or as a positive antigenemia or PCR?

2. Patient 0138.1 who developed CMV disease, “Could the authors provide some comment as to why the PCR antigenemia was positive weeks after therapy was stopped. Details would be helpful. Also similarly do the authors have an explanation for the disconnect between the antigenemia and PCR as the antigenemia is coming down from weeks +49 to +63, the PCR is actually increasing quite dramatically.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No