Reviewer's report

Title: Inability to Achieve a Therapeutic Dose of Tacrolimus in a Pediatric Stem Cell Transplant Patient due to Generic Substitution

Version: 3 Date: 7 October 2014

Reviewer: Staffan Rosenborg

Reviewer's report:

Dear Authors,

Thank you for your revision. I think it got a lot better this way, but still has some opportunities for improvement.

MINOR ESSENTIAL REVISIONS

1) The abstract would benefit from some further refinement. For example ‘Conclusions’ should be focused on what could be learnt from this case report, not on regulatory guidelines or the lack of evidence. Such statements are part of the background and I’m not convinced that they belong in the abstract.

2) I’m still not convinced that it is the change in formulation from brand to generic that caused the drop in tacrolimus levels. How would we differ between the contribution brand and generic products and hospital and community pharmacies? Were the subsequent Prograf solutions prepared at the hospital pharmacy or at the community pharmacy?

3) Page 9: What do you mean by “their bioequivalencies are comparable”? Bioequivalence is a statistical conception; either you have or you don’t. How do you compare things considered to be equivalent? I’m aware that I didn’t comment on this wording in my previous review, but I still thought it was odd and had hoped for it to be rephrased during your major revision.

DISCRETIONARY REVISIONS

1) I do not agree with your statement of steady state being reached after 2-3 administrations (12-36 hours) for a drug with a half-life of 15-45 hours. The elimination half-life would be even longer in the presence of an inhibitor. Thus it could take up to 2-3 weeks to reach steady state after a dose change.

2) Page 6: “pruritis” should be “pruritus”

3) Page 7: “tacroliumus” should be “tacrolimus”

4) There are extra spaces and punctuations at some places in the manuscript. Please check and edit.

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

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

Declaration of competing interests:

I received an unrestricted grant from the Swedish subsidiary of Astellas Pharma in 2012.