**Reviewer's report**

**Title:** Efficacy and safety of the human anti-IL-1beta monoclonal antibody canakinumab in rheumatoid arthritis: results of a 12-week, phase II, dose-finding study

**Version:** 1 **Date:** 22 December 2010

**Reviewer:** Peter Taylor

**Reviewer's report:**

This study reports the findings of a double blind, placebo-controlled, parallel group study investigating the effects of a mAb with specificity for IL-1beta in patients with active RA despite methotrexate therapy.

Discretionary revisions

The puzzling absence of a dose response is rather reminiscent of early anakinra trial data in RA. In particular, the cohort receiving the intravenous loading dose seems to behave very much like placebo treated patients. Although it is stated that pharmacokinetic data will be published elsewhere, it seems reasonable to ask whether there is a pharmacological explanation for this, for example, an increase in clearance associated with intravenous dosing? Or alternatively, is there any evidence that a subgroup flare after iv canakinumab and that this drives the relatively low response rate at a cohort level?

Was blood sampling for biomarkers undertaken at a consistent time of day to allow for known diurnal variation in biomarkers such as IL-6?

Minor essential revisions

P12. The sentence given as follows “In the group receiving canakinumab 300 mg SC q2wk, one patient(1.6%) had an ALT #5 times the ULN and an AST #3 times the ULN, and one patient (1.6%) had an ALT #5 times ULN” the latter part of the sentence appears to have been repeated in error or is it referring to a second patient with an ALT rise exceeding 5 times ULN?.

The baseline Tender and swollen joint counts are missing from the placebo group reported in Table 1.

**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:**

I declare that I have no competing interests