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:** 2 January 2011

Reviewer: Andrew Östör

Reviewer's report:

The authors present important, early trial data regarding a novel biologic agent and is important information which contributes to the field. I do have a number of queries/suggetions:

Major Compulsory Revisions

Despite prior dose ranging studies the higher doses of canakinumab in this trail were not as good as the lowest dose. This is very surprising and I feel the authors need to try to explain this finding further.

The result that no significant difference between any of the canakinumab dosage groups and the placebo group was observed with regard to the ACR70 response rates at 12 weeks is very disappointing. Does this mean that this drug is not particularly effective for RA, this requires exploration in the discussion (see comment below).

In the discussion the authors state that the patients were suffering from relatively low disease activity however greater than or equal to 6 swollen and tender joints plus a significantly raised inflammatory response is not low disease activity in my practice. The conclusion that this may have had an impact on response magnitude needs to be readdressed.

I feel the paper would benefit greatly from one to two paragraphs in the discussion regarding the rationale for blocking IL-1 in RA and the fate of anakinra following its use in RA. Perhaps this is not the ideal target for the majority of RA patients but will be best suited to a subset (especailly if biomarkers of reponse are identified).

Minor Essential Revisions

The conclusion should state specifically the dose which was beneficial (150 mg s/c 4 weekly) as in the abstract conclusion.

Discretionary Revisions

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:

Andrew Ostor has received support from (including attendance at conferences), undertakes clinical trials and acts as a consultant to Roche, Chugai, Schering-Plough/MSD, Abbott, Wyeth, BMS, GSK, MerckSorono and UCB.