

## **Author's response to reviews**

**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

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**Version:** 4 **Date:** 18 May 2011

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**Dear Professor John Isaacs**

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We would like to get back to you regarding the final two points raised on the manuscript MS 2063903084916479

**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**

Clarification on no of patient with ALT on page 12:

“In the group receiving canakinumab 300 mg SC q2wk, one patient (1.6%) had an ALT  $\geq 5$  times the ULN and an AST  $\geq 3$  times the ULN, another patient (1.6%) had an ALT  $\geq 5$  times ULN. The latter patient discontinued the study due to the ALT elevation and, for this patient, an elevated ALT of 1.5 times ULN at baseline was noted.

Was changed to:

In the group receiving canakinumab 300 mg SC q2wk, two patients had ALT/ AST elevations: one patient (1.6%) had an ALT  $\geq 5$  times the ULN and an AST  $\geq 3$  times the ULN, another patient (1.6%) had an ALT  $\geq 5$  times ULN. The patient with ALT  $\geq 5$  times ULN discontinued the study due to the ALT elevation, for this patient, an elevated ALT of 1.5 times ULN at baseline was noted.

“A DAS28 of 5.8-5.9 with 11 to 12 swollen joints equates to high disease activity and therefore discussion should be changed”

The sentence “The still-unexplained fact that higher doses of canakinumab did not result in a greater response (dose-response relationship) cannot be accounted for by the relatively low DAS and swollen and tender joint counts “ has been deleted from the discussion section of the manuscript following reviewers comments and we have indicated this on page 16 of the manuscript.

We hope with those final edits the manuscript will be acceptable for publication.

With best wishes

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