Author's response to reviews

Title: A phase 1 study evaluating the pharmacokinetics, safety and tolerability of repeat dosing with a human IL-13 antibody (CAT-354) in subjects with asthma

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Author's response to reviews: see over
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Dear Dr. Graham:

We thank you and the reviewers for their comments, and have made changes to the manuscript as outlined below.

**General Comment**

1) We have noticed that you are reporting a controlled clinical trial but have not cited a trial registration number. This must be attained BEFORE we can publish your manuscript.

**Reviewer 1**

1) A minor criticism is that a reduced number of subjects (n=3) received the highest dose (10 g/Kg).

RESPONSE: We agree, and this is already stated in the discussion (page 14) as follows: “Although only 3 subjects received the 10 mg/kg repeat dose, no additional safety concerns were identified at this dose compared to the lower doses. Future studies could test repeated doses up to 10 mg/kg.”

2) Data on the safety profile of subcutaneously administered CAT-354 would be of considerable interest and if the authors have this data then I suggest that it be included in the manuscript. If the data is not available then the authors should comment in the discussion on the likely formulation (SC or IV) of CAT-354 that will be used in future clinical studies.

RESPONSE: This data is not available, as of course it requires new studies. We have inserted discussion to state that SC may be the route for the future (see page 14) as follows:

“Future studies may also focus on the development of subcutaneous administration, as this will have practical advantages for administration.”
Reviewer 2

1) *This is an acceptable report on a phase 1 trial of a humanized monoclonal to IL-13 emphasizing safety and pharmacokinetics. No data of biologic plausibility for this agent is evident from the report.*

RESPONSE: We agree that we did not study efficacy. This is discussed already on page 14 as follows:
“The current study used pulmonary function as a safety measure, and was not properly powered to assess clinical benefits due to the low number of subjects. “

2) *The dominance of IL-13, even over IL-4 as well as other mediators, in human asthma is less established and certainly not proven so that it’s place as a therapeutically effective strategy is still untested even with this study.*

RESPONSE: We agree. This point is discussed on page 14-15 as follows:
“The relative contributions of blocking IL-13 as opposed to IL-4 function to these results is not known, although animal studies suggest that IL-13 plays a dominant role in TH2 inflammation [10-14]. Human proof-of-concept studies using CAT-354 are required to confirm these animal findings.”

3) *The sentence at the top of page 3 lacks punctuation.*

RESPONSE: Thank you for catching this typographical error. We have added the punctuation at the end of the sentence.

Thank you for your consideration. Please do not hesitate to contact me, if I can be of further assistance.

Sincerely,

Nestor Molfino