Reviewer's report

Title: Adjuvant Interferon Gamma in Patients with Pulmonary Atypical Mycobacteriosis: a Randomized, Double-blind, Placebo-Controlled Study.

Version: 3 Date: 3 August 2007

Reviewer: Leslie W Huson

Reviewer's report:

General

One general issue is the effectiveness of the blinding in the presence of flu-like symptoms typical of IFN treatment, but I leave this to a physician to decide whether or not this is enough of a problem to render the study uninterpretable. Also, the English language is not fluent enough at the moment and needs to be edited.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The statistical aspects of this MS are not satisfactory and need to be revised and/or explained further before this MS is considered for publication.

Taking things in order of the presentations within the results tables:

(1) Table 2 – all p-values for comparisons of baseline data should be removed. It is not acceptable to use p-values as a basis for deciding whether or not baseline differences are large enough to have affected the trial results. This should either be based on clinical judgment, or in the case of any doubt, the baseline measurement(s) should be included as covariate(s) in the relevant analysis.

(2) Table 3. Remove all p-values from Month 0 comparisons. Several additional problems also:

(2a) there are some apparent discrepancies between the way endpoints are defined on Pages 8/9/10 and the way the endpoints are presented in Table 3. For example, overall response is described as “complete”, “partial” or “none” on Page 8, but is treated as binary in Table 3. Similarly, General Clinical Status is defined as good, moderate or bad on Page 8 - but treated as binary in Table 3. Dyspnea perception is defined on a scale OF 0-4 on Page 9 but seems to be reported just as presence/absence in Table 3. The analyses should reflect the nature of he endpoint, or, if the endpoint is collapsed from categorical into binary, a justification for this must be given.

(2b) It is not clear what "improvement" is in the final row of “Clinical” section in Table 3 – this does not appear to be general status, nor overall response – what is it?
(2c) no need to use switch between using Chisq and Fisher Exact for binary data - stick to Fisher Exact throughout for comparisons of binary endpoints.

(2d) All binary analyses in Table 3 should be shown as ITT with any missing responses classified as failures.

(2e) The bacilli counts could be compared directly between groups using a Poisson regression analysis or similar technique, which would avoid the loss of information resulting from coding which has been defined on Page 9.

Bacilli counted 0-9 (definition Page 9)

(2f) Pulmonary lesions are defined as minimum, moderate, advanced on Page 9. It is not acceptable to combine moderate/minimum for the month 6 analysis and moderate-advanced for the month 18 analysis – the combination should be dictated clinically and hence should be same.

3. Table 4 – time-to-response is usually summarized as median and confidence interval – means should not be presented as in Table 4.

4. Page 12/Table 2 – the abbreviation IQR is more conventional than QR. This is also mis-spelled in Table as “RQ”

5. Table 5. These data would be better presented by removing the p-values – it is not at all clear that a valid p-value can be obtained by comparing these trial patients with a reference set of healthy subjects.

6. Table 6 – it is not clear why these analyses are paired - why not simply compare the change from baseline between the two groups – in a two-arm randomized trial, all comparison should normally be done between groups unless there is good justification for doing otherwise.

7. Table 7 – remove p-values – it is generally not acceptable to compare safety data using p-values: the implication that a non-significant p-value indicates no difference between adverse event rates is not valid. Better to present confidence intervals either for the individual event rates, or for the rate differences.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

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Discretionary Revisions (which the author can choose to ignore)

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What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions
**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests