Reviewer’s report

Title: Pharmacokinetics comparison of two pegylated interferon alfa formulations in healthy volunteers

Version: 0 Date: 26 Feb 2017

Reviewer: Thomas Polasek

Reviewer's report:

1. Some sentences in the manuscript are poorly written. Please improve the English grammar prior to submitting the next version.

2. Background pg 2/27. This section is too long for an abstract. Please shorten since the majority of this information is provided in the Introduction.


4. Pg 5/27 line 56. Should read 'longer' rather than 'higher' half-life.

5. Pg 5 and 6/27. The following sentence does not make sense in the context of the preceding sentence. 'This factor does not affect the kinetics of the non-pegylated product, but it also does not rule out the possibility that this may affect the PEG bond, causing some kind of structural change.' In the preceding sentence the focus is on the difference in PK between the PEGylated and the non-PEGylated products in animal studies. Please correct.

6. Page 6/27 lines 5 to 12. Please comment on how the introduction of the new hepatitis C eradication medications will influence the clinical use of PEG IFN i.e., what will be the clinical role of PEG IFN and does this change the need to develop a product with longer half-life? This is important because the rationale behind the study and the development program would be the need of such new PEG IFNs with improved PK. Please comment.

7. Page 6/27 line 22. It is stated that the study was designed to evaluate 'pharmacodynamics' of PEF IFN, but there are no pharmacodynamic parameters in the manuscript.

8. Page 11/27 line 25. AUC should be the area under the plasma concentration time curve.

Page 10/27. What software package was used to calculate the pharmacokinetic parameters?

9. Page 12/27 lines 31-43. It states that a 'statistical model theory' and a mathematical model were both used to estimate PK parameters, but these two methods are not described in the Methods section.

10. Page 14/27 line 14. Please explain what is meant by 'induction of biological effects'?
11. Page 16/27 lines 29-34. You briefly describe that 3 subjects had samples that could not detect PEG-IFN plasma concentrations, but there is not an attempt to explain why.

12. Please comment on the PK/PD relationships for PEG-IFN, and whether the small changes in PK parameters are likely to be clinically relevant in terms of safety and/or efficacy.

13. Please comment on whether the PK of PEG-IFN is different between healthy volunteer and patients with hep C. Are the results in this study likely to be similar in patients?

14. Both figures are very poor quality and not of the standard for publication. Figure 2 includes text 'Figure 1', there is grey shading in the main graphs with measurement lines too. The presentation of these Figures should be improved.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?
2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal