**Reviewer's report**

**Title:** Nasal administration of the neuroprotective candidate NeuroEPO to healthy volunteers: A randomized, parallel, open-label safety study

**Version:** 0  **Date:** 02 Apr 2017

**Reviewer:** Alberto Lazarowski

**Reviewer's report:**

The manuscript describe a simple but very elegant and significant study, which clearly demonstrates that intranasal administration of neuro-EPO is widely tolerated, does not produce significant adverse effects, nor does it activate erythropoiesis.

The manuscript can be published however I suggest authors include a paragraph in the discussion that takes into account the following comments:

1- Text page 5: "Neuroprotective actions of recombinant human erythropoietin (rHu-EPO) have been evaluated both in vitro and in vivo, demonstrating antiapoptotic, antioxidative, antiinflammatory, neurotrophic and angiogenic properties [3, 4]. However, its action on erythropoiesis could be inconvenient by triggering an increase in cardiovascular and thromboembolic events [5]."

Comment: It has been demonstrated that intranasal administration of rHu-EPO was able to recovery spontaneous motor activity, producing neuroprotection without induction of peripheral erythropoiesis


Author should add this information.

1- Text page 9: "The subjects were put to bed in decubitus supine position, with the head dorsally bowed 45 degrees from the axis of the body to guarantee arrival of the product to the third cornet, cross BBB and reach their site of action".
Comment: The mechanism by which the intranasal administration of EPO reaches the CNS is not fully understood, and it has been postulated that the flow of this compound does not use a vasogenic pathway, and so it would not cross the BBB, but it would access the CNS via a retrograde axonal transit path.

See references:


Author should consider this information's.

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.

No

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:

Acceptable

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