Reviewer’s report

Title: Clinical and Genomic Safety of Treatment with Ginkgo biloba L. leaf extract (IDN 5933, Ginkgoselect®Plus) in Elderly: A Randomised placebo-controlled clinical trial [GiBiEx].

Version: 0 Date: 29 Jun 2017

Reviewer: JOHNSON STANSLAS

Reviewer's report:

General comments

1. Too many acronyms in the text without providing their full names (definitions) at first mention. The list of abbreviations is only found almost close to end of the document.

2. It is good to get the language edited.

Specific comments

Abstract

1. NTP - in full.

2. Provide more details of Ginkgoselect®Plus such as
   a. how it was prepared.
   b. standardisation of the extract.

3. Elaborate further how clinical (adverse clinical effects, hepatotoxicity) end points were determined.

4. From which biological sample the genomic studies were conducted?

Introduction

1. "the compound has been.." - not a compound but rather best referred as extract!

2. Technical Report published by the US National Toxicology Program - provide the supporting literature.
Materials and Methods

1. Was the blood thinning effect of Ginkgoselect®Plus determined?

2. Is 6 months trial sufficient to provide the safety profile of this product when in reality it is consumed for a longer time? Do note that the toxicological study by US National Toxicology Program was done for 2 years!

3. State how randomization was performed.


5. NMT? 5 ppm

6. Provide the questionnaire as a supplementary file.

7. The numbers do not add up "A total of 19 subjects (28.8%), withdrew from the study for the following reasons: death (19), discharge (10), admission to another hospital for worsening state of health (4), and discontinued treatment (4)". I believe the correct number of death is 1.

8. State how many males and females in each group.

9. MR, GR, and RR?

10. SPSS version?

11. What is the cause of death of a patient in the Ginkgoselect®Plus group?

12. CBMN? assay.

Results

1. "Up-regulated in 3 out of 8 IDN 5933-treated patients, down-regulated in 3 other GBLE-treated patients - what is the difference between IDN5933 and GBLE"?

2. Why no statistical analysis is shown in "Table 5. Expression profiling of c-myb and p53 genes"? However, in the text it is mentioned that no significant difference was observed - what statistical test used for this purpose?
Discussion

1. A specific heading on Limitations of Study should be provided immediately after the "Discussion" section.

2. Upload raw data of MN, comet assay and gene expression studies as supplementary files.

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

No

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

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