Reviewer’s report

Title: Safety of intravenously applied mistletoe extract - results from a phase I dose escalation study in patients with advanced cancer

Version: 0 Date: 23 Feb 2017

Reviewer: Panagiotis Balermpas

Reviewer’s report:

The authors present a phase-I-prospective, monocentric trial examining the safety of intravenous application of misteltoe extract.

The manuscript is very well written in flawless language, the methods and the statistics very well described.

A standard dose escalation regimen is used and the results are presented in a comprehensive way.

This is a very interesting topic and there is a need for serious Trials about alternative cancer therapies, as many of the data existing are not reliable.

I have some minor remarks:

- page 3, lines 62-65 Background: "Some VaE are approved in Germany..use in cancer patients" please add a reference or explain why does this happen in Germany. And: "..activity is limited by this route of application" Please add a reference! Are there any data supporting this Statement

- line 66: "..in humans immunomodulatory effects" Is the supposed effect of misteltoe immune mediated or not? This Statement does not support the cell line data. Please add a comment

- page 14 (clinical observations): regarding the 56-y-old-patient with peritoneal carcinomatosis: is the treatment still ongoing to this day? was it paused or continued the whole time? that is very interesting, please explain it better.

Finally, I think that your data pave the way for a standardized, randomized, placebo-controlled, phase-III-trial testing efficacy of misteltoe, which is more than urgently needed and essential. Please add this remark to the end of your discussion or under "Conclusions"

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:

Acceptable

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