



## Answer to the letter to the editors by Matthes and colleagues regarding our systematic reviews on mistletoe

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We thank the authors for their comments, yet, none of the arguments is substantial.

First of all, a meta-analysis was not conducted due to the highly heterogeneous data from studies with mostly high risk of bias. To aggregate these data would insinuate a capacity of the data which is not supported by the evidence. In fact, even the Cochrane Review of Horneber et al. (2008) refrained from doing a meta-analysis.

With respect to overall survival, not the number of statistically significant results but their scientific and methodological reliability is decisive. As we describe in our reviews, none of these studies stands up to a thorough scientific assessment. In fact, the meta-analysis by Ostermann et al. (2009) did not report the data for only randomized studies but summarized also other types of studies.

Assessment of risk of bias was based on the Cochrane risk of Bias tool, which does not mean that we should avoid a look at other fallacies of the included studies. For the reader and physician, a comprehensive evaluation of the published data is important.

The publications by Grossarth-Maticek and Ziegler have been discussed controversially by other authors as well. Considering the large collective of patients, the selection process of the matched pair patients who were included in the randomized studies is insufficiently described, which makes the whole process non-transparent and insufficient as randomization of the whole collective would have been

the much better alternative. Furthermore, the randomization only elected the patients to asking their general practitioners to prescribe mistletoe and those who were not asked to do so.

In fact the study by Tröger et al. (2013, 2014) which has been published in two parts (one on survival and one on quality of life) has a high number of patients who were not evaluable. For this second publication, the authors used multiple testing with respect to parameters of quality of life.

Considering the power analysis in the studies by Longhi et al. (2014) and Tröger et al. (2014), recruiting less patients may be part of a study concept if an interim analysis had been planned. Last but not least, we do not agree that best supportive care was thoroughly described by Tröger et al. (2014) as only the fact of individual adaptation is mentioned.

To sum up, the demand of a revision of our manuscript is unjustified.

### Compliance with ethical standards

**Conflict of interest** The authors declare no conflict.

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