

Word count/limit: 907/1,500

Display items: 0

References: 13

## Commentary

### Could homeopathy improve survival in advanced non-small-cell lung cancer?

Harald H. Sitte<sup>1</sup>, Viktor Weisshäupl<sup>2</sup>, Norbert Aust<sup>3</sup>, Jutta Hübner<sup>4</sup>, Edzard Ernst<sup>5</sup>

<sup>1</sup>Institute of Pharmacology, Medical University of Vienna, Vienna, Austria

<sup>2</sup>Initiative Wissenschaftliche Medizin (Scientific Medicine Initiative)

<sup>3</sup>Informationsnetzwerk Homöopathie (Homeopathy Information Network)

<sup>4</sup>Universitätsklinikum Jena, Klinik für Innere Medizin II, Jena, Germany

<sup>5</sup>University of Exeter, Exeter, United Kingdom

Address correspondence to: [harald.sitte@meduniwien.ac.at](mailto:harald.sitte@meduniwien.ac.at)

In 2020, “The Oncologist” published a paper by Frass et al [1] showing that adding homeopathy to conventional oncological treatments improves the quality of life and prolongs survival in patients with advanced non-small cell lung cancer.

Homeopathy is defined as “a therapeutic method using preparations of substances whose effects when administered to healthy subjects correspond to the manifestations of the disorder in the individual patient” [1a]. Homeopathic preparations undergo a process called ‘potentization’ which is defined as “a multi-step process developed by Hahnemann by which the medicinal power of a homeopathic medicine is release or increased, involving serial dilution with succussion, or using trituration or fluxion” [1a]. Most homeopathic remedies use dilutions beyond the Avogadro number, e.g. a C30 dilution would result in 30 consecutive dilutions in steps of 1:100, resulting in a  $10^{-60}$  fold dilution. Such dilutions result in the absence of molecules from the starting material in the resulting solution. Hence, such homeopathic remedies are indistinguishable from placebo formulations, which *per definition* are devoid of any active ingredients.

It is therefore not surprising that the study by Frass et al was criticized as soon as it was published [3]. A working group of the “Informationsnetzwerk Homöopathie” (INH; “Homeopathy information network”) and the “Initiative Wissenschaftliche Medizin” (IWM; “Initiative Scientific Medicine”) then conducted a thorough analysis of the available data which raised serious questions about the trustworthiness of the paper [4]. In addition, all co-authors of the study and the lead author’s employer (the Medical University of Vienna) were informed about the concerns. Furthermore, a “letter to the editor” was submitted to “The Oncologist” expressing the concerns (but never published by “The Oncologist”).

Our actions prompted the Medical University of Vienna to request an independent investigation by the Austrian Agency for Scientific Integrity (OeAWI). In 2022, the OeAWI published its analysis of the study stating that *“In a very time-consuming and comprehensive investigation, requiring—among other things—an on-site inspection of original documents, the Commission was able to substantiate the suspicion of data falsification, fabrication, and manipulation”* [5]. Based on these findings both the Medical University of Vienna and the OeAWI urged “The Oncologist” to retract the study. These actions triggered firstly the publication of an “Expression of Concern” [6] and secondly an investigation by “The Oncologist”. The result of the latter was a correction of the original study [7], accompanied by an editorial by the chief editor of “The Oncologist” [8]. Regrettably, the correction did not even attempt to address many of the most serious concerns of scientific misconduct by OeAWI, INH and IWM. In particular, it failed to deal with any of the issues that lead to the conclusion of data manipulation and falsification.

These main issues that are still unresolved include:

- Important details of the study provided in the first registration [9] differ significantly from those in the published paper. No explanation was given for these discrepancies.
- The first study protocol version [10] was uploaded to clinicaltrials.gov *after* completion of the study in 2019 and backdated to 2011, i.e. before the first patient was enrolled in 2012. This manipulation creates the false impression that the protocol was established before the study began. Details in the text prove that the protocol was written much later than 2011 [9,10], e.g. SSPS

version 25 was planned to be used which was not released until July 2017. Several details of the study as described in this first protocol differ considerably from those in the first registration but agree with those of the published paper.

- After the authors were informed about the concerns of the INH in May 2021, a second version of the protocol [11] was uploaded to clinicaltrials.gov in June 2021 with corrections and backdated to February 6, 2014 [11,12]. This might have been done to alleviate our concerns. In this second version, the details proving that the previous version was written later but backdated to 2011, were removed. The previous protocol version was not mentioned at all; yet, this would be essential for transparency.
- Up to June 14, 2021, only one exclusion criterion (pregnancy) had been registered at clinicaltrials.gov. After the completion of the study on July 31, 2019, twenty exclusion criteria were added. None of this was discussed in the published paper [13]. In the correction, the exclusion criteria were claimed to be “standard for treatment trials” but no explanation was given why the change was made post hoc and without mentioning the excluded patients.
- The patients who were eliminated according to the added exclusion criteria are neither listed in the CONSORT diagram nor mentioned in the text of the paper. The correction does not provide an explanation for this.
- The homeopathic preparations used in the study are not specified. This renders the study irreproducible and is therefore not acceptable.

In view of these concerns, we draw five conclusions:

1. The published corrections do not address the concerns that have been voiced by various parties.
2. The suspicions regarding data manipulation and falsification have not been refuted.
3. The lack of relevant information about the nature and potency of the employed homeopathic preparations renders the study irreproducible and scientifically useless.
4. The study does nothing to change the principle that homeopathic remedies which are indistinguishable from placebo cannot possibly affect the natural history of cancer.

5. As presently published, this study endangers the lives of patients who might believe its unreliable conclusion.

We therefore strongly suggest that the study be retracted.

## References

1. Swayne J, International Dictionary of Homeopathy. Churchill Livingstone, 2000.
2. Frass M, Lechleitner P, Gründling C, Pirker C, Grasmuk-Siegl E, Domayer J, Hochmair M, Gaertner K, Duscheck C, Muchitsch I, Marosi C, Schumacher M, Zöchbauer-Müller S, Manchanda RK, Schrott A, Burghuber O. Homeopathic Treatment as an Add-On Therapy May Improve Quality of Life and Prolong Survival in Patients with Non-Small Cell Lung Cancer: A Prospective, Randomized, Placebo-Controlled, Double-Blind, Three-Arm, Multicenter Study. *Oncologist*. 2020 Dec;25(12):e1930-e1955. doi: 10.1002/onco.13548. Epub 2020 Nov 7. Erratum in: *Oncologist*. 2021 Mar;26(3):e523. doi: 10.1002/onco.13693.
3. Homeopathy prolongs survival of lung cancer patients ... Can it be true? (<https://edzardernst.com/2020/10/homeopathy-prolongs-survival-of-lung-cancer-patients-can-it-be-true/>)
4. Aust & Weisshäupl (2023) Homeopathy research hits new low. *Sceptical Inquirer* 47, No.3 (<https://skepticalinquirer.org/2023/05/homeopathy-research-hits-new-low/>)
5. The OEAWI Annual report 2022 (page 4, A 2021/10): [https://oeawi.at/wp-content/uploads/2024/05/OeAWI-AnnualReport\\_2022.pdf](https://oeawi.at/wp-content/uploads/2024/05/OeAWI-AnnualReport_2022.pdf)
6. "Expression of Concern: Homeopathic Treatment as an Add-On Therapy May Improve Quality of Life and Prolong Survival in Patients with Non-Small Cell Lung Cancer: A Prospective, Randomized, Placebo-Controlled, Double-Blind, Three-Arm, Multicenter Study." *The Oncologist* 27, no. 12 (December 9, 2022): e985. DOI: 10.1093/oncolo/oyac221.
7. Correction to: Homeopathic Treatment as an Add-On Therapy May Improve Quality of Life and Prolong Survival in Patients with Non-Small Cell Lung

Cancer: A Prospective, Randomized, Placebo-Controlled, Double-Blind, Three-Arm, Multicenter Study. *Oncologist*. 2024 Sep 24;oyae253. DOI: 10.1093/oncolo/oyae253

8. Figg WD, Bates SE. Clinical trial results: each patient's participation should count. *Oncologist*. 2024 Sep 24;oyae252. DOI: 10.1093/oncolo/oyae252
9. <https://www.clinicaltrials.gov/study/NCT01509612?term=frass%20&rank=2&a=1&tab=history#version-content-panel>
10. [https://cdn.clinicaltrials.gov/large-docs/12/NCT01509612/Prot\\_SAP\\_000.pdf](https://cdn.clinicaltrials.gov/large-docs/12/NCT01509612/Prot_SAP_000.pdf)
11. [https://cdn.clinicaltrials.gov/large-docs/12/NCT01509612/Prot\\_SAP\\_001.pdf](https://cdn.clinicaltrials.gov/large-docs/12/NCT01509612/Prot_SAP_001.pdf)
12. <https://clinicaltrials.gov/study/NCT01509612?term=frass%20homeopathy%20cancer&rank=1&tab=history&a=10#version-content-panel>
13. <https://www.clinicaltrials.gov/study/NCT01509612?term=frass%20&rank=2&tab=history&a=9&b=10#version-content-panel>