How valid are the accusations of the review Commission?

MF: Firstly, it should be noted that this is a 'Final Statement' (FS) from the private organisation *Austrian Agency for Research Integrity* (OeAWI) and not a scientific report. The difference lies, among other things, in the fact that the authors were not given the opportunity to comment after publication of the FS, although we clearly indicated our willingness to do so.

With such an admonitory report, one would expect a flawless FS. However, the OeAWI Commission has published a chronology of its own activities on page 2 of the FS. Surprisingly, there are five incorrect time specifications, eg: *Re-analysis of part of the data of the Study and preliminary report on the inquiry by F. R. Rosendaal: 28 November 2022*: this would mean that the re-analysis was carried out 2 months AFTER the deadline, namely 21 September 2022. For scientists, these five timing errors shed a significant light on the FS, which was obviously prepared in great haste.

The Commission makes assertions that could have been clarified immediately and with minimal effort: the head of the Commission, Prof Dr Rosendaal, by his own admission, even went to Vienna in person without seeking an interview with the study authors, in particular with the statistician at the Medical University of Vienna (MUV) who planned the study. At the beginning of the FS, for example, the claim is made that the study was not performed double-blind from the outset. However, there are several control mechanisms that monitor and guarantee double-blinding, which are still easily verifiable today, eg. in the randomization program described in detail below or in the extensive documentation of the cooperating pharmacy. The committee obviously did not consider, or incorrectly interpreted, the submissions reported by the study authors to the MUV Ethics Committee and accepted by it.

All patients who participated in the study were treated double-blind. The blinding codes were stored by the independent statistician, who did not appear as a study author, in the randomization platform described in more detail below, to which the authors had no access. Therefore, no patients could have been removed (= 'post hoc exclusion') unnoticed from the dataset due to their outcome data: all inclusion and exclusion events are automatically logged and traceably registered in the audit trail to this day.

Due to the maintenance of blinding until the actual statistical analysis by a second, previously uninvolved statistician, selective data manipulation within one or the other study arm would not have been possible. Regarding blinding: the study medication was not handed over in person by the pharmacy, but by mail. This unique study design, which excluded any influence by the pharmacy, is another exceptional quality feature.

Further concerns: the study authors are accused of having embellished the results by subsequently removing patients from the analysis who did not show the hoped-for course of the disease. Is that true? If so, in what way? If not, how can the Commission's findings be explained?

MF: The study was accompanied and monitored by the planning statistician with the help of the computer-aided randomization program *Randomizer* from the Medical University of Graz, Austria. This internationally recognised, top-class programme automatically writes a protocol (= 'audit trail'), so that every process involving the study patients was recorded in a sustainable manner and was unable to be influenced. Therefore, 'post-hoc exclusion', as assumed by the Commission, is technically not possible, as every step was permanently monitored. Only the planning statistician had access to this randomization program so, both theoretically and practically, it is simply not possible for the study authors to intervene in this program, which proves the high quality of the study. The OeAWI Commission was obviously unaware of this unique innovative feature of the randomization program.

Further proof of top quality is that the study was analysed using a four-stage procedure, which is unusual for an academic study: The data were entered into the MUV's tamper-proof *Research, Documentation and Analysis* (RDA) platform, then forwarded by the planning statistician to the analysing statistician by means of an elaborate clearing process. This exceptional quadruple evaluation check proves the reliability of the results. This security check ensures that the integrity of the recorded data is maintained. We categorically state that there has been no *selective deletion of records* and our assertions are fully confirmed by the objective audit trail.

Manipulation would also have been difficult to achieve: Here, 16 deserving study authors, who monitored the study at all times, would have had to take part in falsification. Among them were two top scientists from the MUW. Manipulation would also have been difficult to achieve: 16 respected study authors, who monitored the study at all times, would have had to take part in falsification. Among them were two top scientists from the MUW with no connection to homeopathy and the first author is internationally recognised in all current textbooks and in the guidelines of the American Heart Association (AHA) and the Society of Anaesthesiologists (ASA) as a figurehead for alternative airway devices thanks to the life-saving invention of the Combitube® for securing the airway and for ventilation in emergencies. This cooperation between conventional and complementary study authors, the majority of whom have no affinity to homeopathy, guarantees constant mutual control and is a further seal of quality for the study.

The description of the survival curves as implausible in their progression is an arbitrary expression of opinion of the OeAWI without scientific support. Compared to other published Kaplan-Meier survival curves in lung cancer studies, our published data are well within the expected range. In particular, the prompt separation of the survival curves immediately after the start of the study is a frequently observed pattern. One can easily find examples of survival curves similar to those shown in our study. Entry dates into the study as well as deaths are known to be distinctive tamper-proof data.

The accusation of whitewashing or falsification of questionnaires on quality of life can be directly refuted by the facts and by statistical understanding: patients have, as is often the case with written questionnaires, re-evaluated one point or another and

corrected the previous evaluation by hand. With over 26,000 available data, this happened in only 90 cases. Every biometrician will confirm that these changes, which are spread over various parameters and are approximately 3.5% of all collected data, cannot have had any influence on the results. Any date changes on the questionnaires are due to the shifting of the examination dates, which may have been due to a shift in chemotherapy, an acute illness of the study patients, etc. These questionnaires were made available to the Commission upon request by the first author immediately and in full, which in turn proves that they were the unaltered original questionnaires that had been accepted 1:1 by the study patients without inspection or correction by the study authors.

The Commission criticises the fact that several patients who reported maximum health status died within a few months, which is highly implausible. However, the patients' perception of quality of life is explained by the process of coping: one of the study authors observed on the palliative care ward (outside the study) that, even in the advanced stages of the disease, patients experience and describe their situation as very satisfactory, apparently because they can spend their last days of life well-protected and pain-free.

The exclusion criteria described in the paper are standard in oncological treatment and were therefore naturally followed from the outset. The exclusion of the initially planned patients with glioblastoma and metastatic sarcoma was reported to and accepted by the MUW Ethics Committee due to inadequate recruitment. The change is also transparently recorded in the *History of Changes* on clinicaltrials.gov. These points are not described in the 26-page paper, as they would not have provided any additional information for the readership.

It must be recognised that this study, which was conducted at the highest level, was extremely complex and therefore underwent adaptations due to new medical findings. These adaptations, necessitated by the constant advances in conventional medicine and accepted by the MUV Ethics Committee and thus recognised by the highest ethical standards, are further proof of the quality of the study.

Conclusion: The OeAWI Commission made every effort to scrutinise the study, but was unable to grasp its complexity due to a lack of communication with the study authors and therefore came to incomprehensible conclusions. The FS is therefore a collection of unreliable assumptions and suspicions that can easily be refuted by the facts. The study is therefore valid and confirms earlier studies with regard to quality of life and survival.

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Comprehensive literature is available from the author