

## Peer-review Comments and Author Responses

### Reviewer 1

1. *The title of the manuscript identifies the design, but I would suggest adding some indication that it is a protocol and not the trial itself.*

We added that it is a phase III trial protocol.

2. *Abstract: please, define the abbreviation OT, before its first use in the text.*

Occupational Therapy (OT) is now being introduced.

3. *Abstract: the sample size is described as 276, but in the Methods section, the sample size is described as 278 subjects. Could the authors clarify?*

We corrected the sample size to 278.

4. *Abstract: in the Discussion subtopic, the sentence "The DECREASE trial aims to assess the effectiveness of a cognitive-based OT intervention amongst AD patients" seems out of place. Usually, the purpose is described at the end of the Introduction. The authors could consider moving this sentence to the Introduction subtopic of the abstract.*

We moved the sentence from the discussion to the introduction.

5. *Introduction: the third paragraph, describing the Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS-Cog), seems to break the flow of ideas. In the previous paragraph, the authors explain pharmacological treatments for Alzheimer and in the following one, they describe occupational therapy. It seems that this paragraph about the outcome measure is out of place, in the middle of 2 paragraphs describing treatment modalities for AD. Maybe the authors could consider presenting this background information about this scale in the Methods section when they present the outcome.*

We moved the paragraph about the outcome measures to the methods section.

6. *Introduction: the sentence "The aforementioned data appear promising" at the end of the seventh paragraph, seems ambiguous and it is not clear what the authors are referring to.*

We deleted the sentence "the aforementioned (...)".

7. *Introduction: the eighth paragraph brings redundant information that was already mentioned in previous paragraphs.*

We deleted the 8th paragraph with abundant information.

8. *Introduction: the information described in the tenth paragraph, with the scales to measure secondary endpoints, seems a little too much for this section. The authors could mention which are the secondary outcomes, but the scales can be presented in the Methods section.*

Scales are presented in the methods section now.

9. *Introduction: the last paragraph of the Introduction relates to the relevance of the study and ideally, should be presented earlier in this section, before the study objectives, and not be the last paragraph.*

The last paragraph concerning the relevance of the study has been moved upwards.

10. *Methods: Does the SMART intervention have a reference that they could mention?*

A reference to the SMART intervention (Griffin et al., 2022) has been added.

11. *Methods: Since this is a trial proposal, in the second paragraph, I suggest changing the sentence "We allocated our patients in a 1:1 ratio to each group" to "We will allocate our patients in a 1:1 ratio to each group".*

Allocation has been reformulated in the future tense.

12. *Methods: the third paragraph seems redundant, bringing information already mentioned in previous paragraphs.*

The redundant paragraph has been deleted.

13. *Methods: in inclusion/exclusion criteria (paragraph 9), it seems confusing that the participant will be included only if the diagnosis was made less than 2 years, but he/she must have been taking the standard medications for more than 2 years. Could the authors clarify that? If they could not have a diagnosis for more than 2 years to be enrolled, how can they be taking the medications for more than 2 years?*

In the inclusion criteria we deleted the part that medications will have to be taken for more than 2 years.

14. *Methods: the seventh paragraph seems out of place. It describes the enrollment process, but the authors describe it again only in paragraphs 10 and 11.*

The redundant paragraph has been deleted.

15. *Methods: about the adherence-enhancing strategies mentioned in paragraphs 15 and 16, who will be responsible for the phone calls?*

Phone calls will be done by study nurses.

16. *Methods: the information provided in paragraph 18 ("Recruited participants will be randomized in two groups...") is redundant and was already mentioned in previous paragraphs. In paragraphs 19 e 20, the authors provide information about the SMART intervention, but they already mentioned that in the first paragraph of Methods. They are repeating information already provided. Also, when the authors describe the SMART protocol, in the Week 1 description, they again mention information about the recruitment that they already provided: "During the first visit the recruitment will be performed by physicians and nurses in charge at each research center."*

The redundant information in paragraph 18, 19 and 20 and about the SMART protocol was deleted.

17. *Methods: could you clarify at which points the primary outcome measure (ADAS-Cog) will be assessed? And by whom? How will you ensure that the outcome assessor is blinded?*

The ADAS-cog will be assessed at baseline and six months follow-up, it will be assessed by an outcome assessor that is blinded to study allocation.

18. *The authors state that the primary outcome is the global value of ADAS-Cog after the intervention, but they used the mean change in the ADAS-Cog to calculate the sample size. Could they clarify that?*

The primary outcome has been corrected to the mean change in ADAS-cog.

19. *Discussion: in the fourth paragraph, about limitations, I suggest changing the verb "was" to "will" in "Lastly, our study is an open-label RCT as blinding patients and caregivers through a sham OT in the control group was not feasible."*

20. *Discussion: I suggest also adding that, despite being an open-label, the outcome assessor will be blinded.*

We added that the outcome assessor will be blinded.

21. *Discussion: in the last paragraph, in "Therefore, our study will add information to determine cognitive-based OT usefulness in AD patient care, even if our results are inconclusive", what do you mean by inconclusive? Is it not conclusive of the positive effects of OT? Or doubtful results?*

The part "even if our results are inconclusive" was deleted. It referred to there not being previous literature really showing clear effects of cognitivebased OT. However, since the goal of our study is to show that there is na effect, this part of the sentence is redundant.

## **Reviewer 2**

22. *It is important that the intervention does not put in danger patients because you are using OT as intervention and not a drug. Also, I highly recommend using subtitles because will be easier to read the whole article.*

23. *Introduction: in the first paragraph the citation does not match with APA style, meanwhile in the rest of the introduction's text is correct.*

The citation was changed to APA;

24. *Introduction: the second paragraph is a little bit to read, I think because there is lack of connectors. This paragraph sound like only sentences. In paragraph three, the first and second sentences are not connected or correlated. I mean, the first one talks about the scale and the second describes early symptoms of AD*

The style of the second and third paragraph has been adapted;

25. *Introduction: I think the introduction could be shorter*

The introduction was shortened.

26. *Methods: some parts could be erased because at some point of the reading there are some sentences which have been repeated or used twice.*

Redundant information has been erased.

27. *Discussion: it would be nice to compare your trial with something similar from bibliography. I think, you will not find the exact OT type like smart, but it would be interesting to compare results with other articles which used OT and AD.*

We compare our suggested trial to the already existing SMART trial (Griffin et al., 2022). We also compare to other occupational therapy trials (Ham et al., 2021, Alvarez et al., 2017).