Author's response to reviews

Title: Early postoperative cognitive dysfunction and postoperative delirium after anaesthesia with various hypnotics: a double blind, prospective, randomized, controlled clinical trial - The PINOCCHIO trial -

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Author's response to reviews: see over
Dear Dr. Goldsmith

Thank you for the peer-review feedback and the opportunity to resubmit this protocol entitled “Early postoperative cognitive dysfunction and postoperative delirium after anaesthesia with various hypnotics: a double blind, prospective, randomized, controlled clinical trial - The PINOCCHIO trial”. The feedback was extremely useful.

We have revised the manuscript according with your suggestion, modifying reference list and statistical analysis. All corrections made in the text are in bold.

Sincerely,

Federico Bilotta
1. Page 11, paragraph 2, line 8. Replace [stratified] by [blocked]. The comments provided make it clear that the study is NOT stratified; but blocked. We have changed it accordingly.

2. P 13, p 1, l 2. Replace [ranging] by [varying]. We have replace the term [ranging] with [varying].

3. P 15, p 1, last 2 lines. The Aldrete score software should be referenced “Every anaesthesiologist involved in patient evaluation will be trained and certified with a dedicated software course developed to use the Aldrete score.” We have removed this sentence from the text.

4. P 16, p 1, l 4,5. It is now clear that the authors are testing 2 correlated hypotheses. It would be best to compute their statistical significance with a variant of Dunnett’s test because of the correlation. Also, it would have been best to use a 2:2:3 allocation ratio and so block sizes as a multiple of 7 to handle the correlation. However, since the study has recruited many patients it does not make sense to change the blocking factor in the middle of the trial. We have added the use of Dunnett’s test in our statistical analysis and we have also specify the use of 2:2:3 allocation ratio.

5. P 16, p 1, l 9, 10, 11, 13. The text on the sample size uses the term [proportion] or [proportions] while the numbers used are percentages. This should be made consistent. We have changed it accordingly.
6. P 16, p 1, l 15. The Farrington and Manning reference is NOT contained in the reference list. Please add it.
We have added this reference in the Reference list

We have added this reference in reference list

8. P 16, p 2, l 1,2. There is no need to specify the block size in this publication. It runs the risk that clinicians who make decisions to put patients into the trial will be encouraged to anticipate the next allocation with the knowledge of the last few allocations and so break the concealment of the randomization list. It is soon enough to inform clinicians at the time of the publication as to what the block size indeed was. The sentence needs to state it was blocked, but not specify the block sizes.

“Patients will be randomly assigned in consecutive order (in allocation blocks of 6 for the first 750 patients and of 3 for the last three patients).” We have removed this sentence.

We have changed it accordingly

10. P 23, Symptoms 2,3 on line 1. Since [or] includes [and] logically, there is no need to use [and/].
We have changed it accordingly