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Response to Dr. Okumura

RESPONSE TO DR. OKUMURA

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Dr. Okumura (Okumura, 2017) criticized our paper (Yamanouchi et al., 2015) for misleading readers as we had modified our hypothesis from that in the original study protocol, and because of a decrease in the number of patients studied, there was inadequate statistical power. Also, there was selective reporting of outcomes. However, we modified our protocol before we analyzed our data (Sukegawa et al., 2014). Originally, the Safe Correction of Antipsychotic Polypharmacy and High-Dose Prescriptions Study aimed to verify improvements in health-related quality of life by improving side effects without major deterioration of mental conditions through dose reduction and simplification. For this study, we attempted to secure 400 patients (Iwata et al., 2011). However, the recruitment process did not succeed as anticipated, and we were only able to secure a total of 163 patients during the 3-year study period. We could have aimed to secure 400 patients by extending the research period; however, we were unable to do so, as the Safe Correction of Antipsychotic Polypharmacy and High-Dose Prescriptions Study was funded by the Japanese Ministry of Health, Labour and Welfare, which would not allow the study to be extended beyond a fourth year. Thus, we had to conduct the study with 163 patients.

For these reasons, the protocols, including the analysis methods, were revised from those described in the paper. Based on the revised plan, a protocol paper was drafted prior to the publication of the paper in question (Sukegawa et al., 2014). In the initial sample size design, we set the significance threshold to an effect size of $\Delta = 0.3$ in either direction when comparing the reduced-dose group and the control group. We used a size of n = 176, and added a drop-out group to obtain 200 cases. We wanted to verify noninferiority under these revised conditions. To do so, we added a noninferiority margin of $\Delta = 0.2$ to the previous threshold. The number of cases was n = 176 x (0.3/(0.3 + 0.2)) ^ 2 = 63. Using the same percentage for the addition of the drop-out subject, the case number rose to n = 71. These circumstances should have been specified in the paper, but it was not. The reduced number of subjects is why we changed our hypothesis from one emphasizing superiority to one of noninferiority.

As for the primary endpoint, we have used EQ5D consistently in the calculation and did not use the Manchester scale. Therefore, simply for the clinical meaning, we wrote both the Manchester scale and the EQ5D as "primary endpoint." However, there was a lack of explanation concerning the absence of this description in the protocol paper.

Therefore, we acknowledge the lack of explanation concerning the reasons for the changes in protocol. This led to misunderstandings for which we are at fault. However, we do not agree with the criticism that the paper presents unreliable results; as such, we do not believe that our paper should be retracted.

References

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