Impact of Protocol Design on Between Scale Discrepancies in Early AD Clinical Trials

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SUBMISSION DETAILS

What is the Methodological Question Being Addressed? For this poster, we expanded on our prior research and analyzed the impact of both of these protocol designs (where inclusion criteria need to be met at Screen alone or at both Screen and Baseline) on the presence of discrepancies between the MMSE, ADAS-Cog and CDR scales between Screen and Baseline and then 6 months post-randomization.

Introduction We previously presented the impact of protocol design on the MMSE changes observed in the screening period. Protocols requiring inclusion criteria be met at Screening alone had significantly more large MMSE changes between Screening and Baseline than did protocols where the criteria needed to be met at both Screening and Baseline. [Kott,2020]. In the current analysis we explore the impact of protocol design on the presence of between scale change discrepancies at baseline and 6 months after randomization.

Methods Data were pulled from multi-national clinical trials in early AD where MMSE and ADAS-Cog and/or CDR were collected at screening, baseline and 6 months after baseline. Subjects were categorized into 2 groups depending on whether inclusion criteria were required at screening alone or at screening and baseline. We defined discordance as occurring when at least 2 of the 3 instruments showed a clinically meaningful change from the prior visit but the changes were in opposite directions. Chi-square test was used to compare the distribution of discordances between the protocols at baseline and at month 6.

Results Our dataset consisted of 4,862 subjects with data available from screening, baseline and month 6. At Baseline, we saw significantly more instances of discordance from Screening in studies requiring criteria be met at Screening alone (5%) vs 2% when the requirement needed to be met at both Screen and Baseline ($chi2 = 20.4$, $P < 0.001$). At month 6, no difference between the protocol types was identified – (12.3% vs. 12.3%, $chi2 = 0.003$, $p = 0.955$).

Conclusion Our analyses indicate a significant impact of protocol design on the presence of between scale change discrepancies. Protocols requiring criteria be met at baseline only had a significantly increased number of discordances at baseline but this difference disappeared by month 6. Among the potential explanations for such between scale discordances, score manipulations to comply with inclusion criteria needs to be considered. These findings should be considered when designing protocol inclusion criteria. Further research is necessary to understand the impact of these discrepancies on drug-placebo separation.

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Keywords

Keywords
Protocol Design
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Guidelines I have read and understand the Poster Guidelines

Disclosures if applicable Both Drs. Miller and Kott are full-time employees of Signant Health.

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