Exploring Discordant Data in Dementia Clinical Trials

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SUBMISSION DETAILS

What is the Methodological Question Being Addressed? In the current analysis we explore the presence of clinically meaningful discordances between cognitive measures in dementia clinical trials and their association with administration or scoring errors.

Introduction We have observed numerous apparent inconsistencies in direction of scale (eg – MMSE, ADAS-Cog and CDR) change between visits across multiple dementia clinical trials. While all instruments are not expected to move in the same direction, clinically meaningful changes in opposite directions may signal scoring and/or administration errors in one or more scales. In this analysis, we explore a) the extent to which such discordances between the MMSE, ADAS-Cog and CDR occur in dementia clinical trials, and b) whether any associations between the presence of such discordances and scoring and/or administration errors exist.

Methods Blinded data were obtained from multi-national dementia clinical trials in early AD. Visit-to-visit point change was calculated for the MMSE, ADAS-Cog and CDR-SB. Clinically meaningful changes were defined as ≥ 4 points for the ADAS-Cog, 3 points for the MMSE and 1 point for the CDR-SB. We defined discordance occurring when at least 2 of 3 instruments showed clinically meaningful change, but in opposite directions. We also evaluated data from the corresponding Endpoint Quality reviews of both the worksheet and audio recordings of these assessments. These were performed by calibrated, independent Clinicians and assessed whether there were any administration and/or scoring errors. Descriptive statistics and logistic regression analyses were used to address our questions.

Results Data were collected from 5,452 randomized subjects. Visit-to-visit discordances were identified in 2,262 out of 20,127 (11.24%) collected visits. Discordances were significantly less likely at baseline than after randomization (OR=0.57; CI=0.51-0.64). The presence of baseline discordances significantly increased the odds of post-baseline discordances (OR = 1.41; CI=1.14-1.75). No association between the presence of discordances and administration or scoring errors was identified (OR = 1.00; CI=0.92-1.10).

Conclusion We have identified over 11% of study visits affected by clinically meaningful discordances between the visit-to-visit changes between the MMSE, ADAS-Cog and CDR-SB. Despite the expected lower presence of baseline than post-baseline discordances, discordances at baseline affected almost 8% of randomized subjects. The lack of association between the discordances and administration or scoring errors is surprising and we plan further analyses to understand this phenomenon better.

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Keywords

Keywords
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Guidelines I have read and understand the Poster Guidelines

Disclosures if applicable Both authors are full time employees of Signant Health. The poster was financially supported by Signant Health.

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