Exploring the Phenomenon of Erratic Ratings in Schizophrenia Clinical Trials

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SUBMISSION DETAILS

What is the Methodological Question Being Addressed? What is the prevalence and phenomenology of erratic ratings in schizophrenia clinical trials?

Introduction We have previously described an association between erratic ratings and increased response to placebo in schizophrenia negative symptom studies. In the current analysis we wanted to explore the phenomenon of erratic ratings beyond our prior analyses and to 1) compare the frequency of erratic ratings by study population (acutely psychotic subjects vs. subjects affected by predominant negative symptoms vs. non-acute non-negative subjects) and 2) understand the pattern of erratic ratings (timing of occurrence, pattern of change, i.e. improvement followed by worsening or vice versa), on a dataset of blinded data pooled from 22 multicentric placebo controlled schizophrenia clinical trials.

Methods Post-baseline PANSS data were pooled from 9,773 subjects collected across 11 acute, 5 negative symptom and 6 non-acute non-negative studies. Erratic ratings were operationally defined as ratings where the absolute PANSS change from prior visit was at or above 90th percentile at two consecutive visits and the changes were in opposite direction. Erratic patterns were classified as improvement first if subjects initially improved. Data were analyzed using logistic regression models.

Results Erratic ratings affected a total of 574 out of 33,860 possible visits (1.70%).
In acute studies erratic ratings affected 1.33% of visits, in negative symptom studies 1.61% of visits and in non-acute non-negative studies 2.70% of visits. When correcting for number of study visits, the odds of erratic ratings were significantly increased in negative symptom trials compared to acute trials (OR = 1.26) and significantly increased in non-negative non-acute compared to acute (OR = 2.28) and negative symptom (OR = 1.81) trials.
Out of 574 erratic ratings, 114 (19.9%) happened at the first possible instance, that is the second post-baseline visit where PANSS was administered. Acute trials were significantly less likely to record an erratic rating in the first possible instance compared to non-acute non-negative trials (OR = 0.56). The improvement first erratic pattern was identified in 274 subjects out of 474 (57.8%). No difference between study types was identified. Improvement first was more likely to be identified if erratic ratings happened at the first possible instance (OR=1.57).

Conclusion Our analyses of a dataset consisting of 22 double blind placebo controlled clinical trials identified significant differences between study types in the proportion of visits affected by erratic pattern. The reason for this difference is currently unclear, but most likely results from an interplay of subject characteristics, expectation bias and measurement error. The fact that we see an

association of the improvement first erratic pattern with the occurrence at the first possible post-baseline instance, irrespective of study type, may be a marker of an increased placebo response. To further understand the mechanisms through which erratic ratings affect placebo response and drug placebo separation, we plan to analyze unblinded data sets as those become available.

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Keywords

Keywords
Clinical Trials
Data Quality
Schizophrenia
Erratic ratings

Guidelines I have read and understand the Poster Guidelines

Disclosures if applicable Both authors are full time employees of Signant Health.

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