

Title: Using PANSS Score Profiles to Predict Early Termination in a Study on Acute Exacerbation of Schizophrenia

Authors:

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The Methodological Question Being Addressed: Is it possible to predict early termination using score profiles on the Positive and Negative Syndrome Scale (PANSS)?

Introduction (Aims): Early termination in clinical trials, especially in those involving schizophrenia, is a significant concern, with some studies showing early discontinuation rates of over 50% (Rabinowitz and Davidov, 2008). Missing data due to early dropouts can compromise the results of a trial, thereby wasting valuable resources. While this area has been identified as an issue in antipsychotic clinical trials, there is little research on understanding the factors that lead to early termination (Mocks et al., 2002). One strategy that may be useful is to identify subjects who present with atypical symptom profiles. Atypical symptom profiles may represent subjects who are inappropriate for the clinical trial.

Methods: These analyses were aimed to determine how different PANSS score profiles were able to predict early termination. Inpatient adults with a diagnosis of schizophrenia (N=137) receiving randomly-assigned treatment (including placebo) and identified as experiencing an acute exacerbation within the last 60 days were evaluated with the PANSS by raters. Five different atypical PANSS item relationships were examined (one related to anxiety symptoms, three related to psychosis symptoms, and one related to negative symptoms) at both the screening and baseline visits. Sensitivity and specificity analyses were run using Microsoft Excel.

Results: A total of 19 (13.87%) subjects who early terminated from the study were assessed in this preliminary blinded analysis prior to database lock. Using sensitivity and specificity analyses, we determined that the score profile with the highest specificity examined the relationship between two anxiety items (G2 [Anxiety] and G4 [Tension]; Sensitivity=0.00, Specificity=96.61, Positive Predictive Value [PPV]=0.00, Negative Predictive Value [NPV]=85.71). The score profile that showed the highest sensitivity looked at the relationship between P3 (Hallucinatory Behavior) and G15 (Preoccupation) (Sensitivity=100.00, Specificity=6.78, PPV=14.73, NPV=100.00). The item relationship that showed the greatest positive predictive value looked at atypical presentations of negative symptoms on the PANSS (N1, Blunted Affect and N5, Difficulty in Abstract Thinking) (Sensitivity=52.63, Specificity=65.25, PPV=19.61, NPV=89.53).

Conclusions: These data provide preliminary evidence that atypical score profiles on the PANSS can be used to predict early termination. Results also point to the possibility of using different strategies to maximize the effectiveness of identifying subjects who are likely to early terminate. For instance, if one wants to pursue a strategy that has the highest sensitivity (but also highest likelihood of false positives), it may be more useful to look at the atypical relationship between P3 (Hallucinatory Behavior) and G15 (Preoccupation). Planned analyses to follow include updating analyses to reflect the complete end of study dataset, the addition of demographic covariates, as well as a hierarchical regression model to examine the cumulative effect of using each of the atypical score profiles.

Disclosures:

Mark Opler, Jonathan Lam, and Jennifer Lord-Bessen are employees of ProPhase LLC, New York, NY, and consultants to Takeda Development Center Americas, Inc., Deerfield, IL.

Elizabeth Hanson, Atul Mahableshwarkar, Xinxin Dong, Maggie McCue, and Thomas A. Macek are employees of Takeda Development Center Americas, Inc., Deerfield, IL.

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