

Site ratings versus site-independent ratings of PANSS interviews in a schizophrenia study

Submitter Steven Targum

Affiliation Clintara

SUBMISSION DETAILS

What is the Methodological Question Being Addressed? Can blinded, site-independent scoring of audio recorded site-based PANSS interviews of acutely psychotic patients replicate site-based scores and affirm treatment outcome results?

Introduction One approach to the confirmation of site-specific research assessments in multicenter trials has been to conduct paired site-independent ratings of audio-recorded site-based assessments such that the independent rating is blind to other clinical and research evaluations conducted on site. We applied this blinded assessment method to confirm data obtained from site-based raters administering the Positive and Negative Syndrome Scale (PANSS) during a clinical trial of acute exacerbation of psychosis in subjects with schizophrenia.

Methods Data derived for this analysis came from a 5-week, phase 2, randomized, double-blinded study to assess the safety, tolerability, and efficacy of the investigational antipsychotic KarXT in hospitalized adults with an acute exacerbation of schizophrenia enrolled in a Phase 2 placebo-controlled double-blind randomized clinical trial (ClinicalTrials.gov Identifier: NCT03697252). KarXT is a fixed combination of xanomeline and trospium chloride being investigated for the treatment of subjects with schizophrenia.

The site-independent PANSS ratings were derived from audio recordings of site-based PANSS interviews with accompanying digital notes that provided corroborative informant information. The paired PANSS scoring data was used for quality assurance to independently confirm the site based PANSS ratings. The study plan anticipated a review all PANSS interviews for completeness and independent scoring of 100% of interviews conducted at the baseline and endpoint visits and 20% at the other visits.

We conducted concordance analyses of the paired site-based and site-independent PANSS interviews and compared the PANSS treatment outcome at the study endpoint between these two methods of assessment.

Results There were 553 pairs of paired PANSS scores available for analysis from the full study data. There were 142 subjects with paired site-based and site-independent PANSS data available from both the baseline and end of study (week 5) visits.

Concordance analyses of the paired site-based and site-independent PANSS ratings revealed a high correlation ($ICC = 0.746$; $p < 0.001$) with minimal scoring discordance. Paired scoring differences were positively correlated with the PANSS total score (Spearman's $\rho = 0.35$, $p < 0.001$).

The site based PANSS total scores revealed a significantly greater improvement from baseline in the KarXT treatment group compared to placebo ($p < 0.0001$). The blinded site-independent PANSS total scores derived from listening to and scoring the recorded site-based PANSS interviews

replicated this finding ($p=0.0005$).

Conclusion Blinded site-independent scoring of audio-digital recordings of site-based PANSS interviews confirmed the primary PANSS findings in this schizophrenia study and obviated any concerns about possible functional unblinding. This method of blinded assessment via audio-digital recordings may have utility for other studies concerned with ratings precision and/or functional unblinding.

Co-Authors

* Presenting Author

First Name	Last Name	Affiliation
Steven *	Targum *	Clintara
Stephen	Brannan	Karuna Therapeutics Inc
Christopher	Murphy	Signant Health
David	Daniel	Signant Health
Alan	Breier	Karuna Therapeutics Inc

Keywords

Keywords
paired ratings
site-independent PANSS scoring
schizophrenia
audio recording surveillance

Guidelines I have read and understand the Poster Guidelines

Disclosures if applicable Support for this report was provided by Karuna Therapeutics Inc., and Signant Health. One of more authors report potential conflicts which are described in the program: Dr.'s Targum, Murphy, and Daniel are employees of Signant Health; Dr.'s Brannon is an employee and Dr. Breier is chair of the Scientific Advisory Board at Karuna Therapeutics Inc.

Related tables <blank>