SIGNANT HEALTH
THE EVIDENCE GENERATION COMPANY™

CASE STUDY:

SIGNANT SMARTSIGNALS eCOA – CENTRAL RATINGS

Leveraging central clinician ratings to assess and improve the reliability of site-rating of major depressive disorder patients

OVERVIEW:

Signant's expert central raters performed an evaluation of site-based Montgomery-Asberg Depression Rating Scale (MADRS) ratings produced in five major depressive disorder (MDD) clinical trials. They compared paired, site-independent scores derived from audio recordings of the site-based MADRS assessment interviews to the original site-based ratings to provide insight into the reliability of site ratings and to provide feedback to site raters to ensure consistent and accurate scoring throughout the study.

EVALUATION SUMMARY:

Number of studies: 5

Study Phases: Phase 2 and Phase 3

Therapeutic area: Major depressive disorder (MDD)

Patient population: Adults, aged 18 – 75

Primary endpoint: Montgomery-Asberg Depression Rating Scale (MADRS)

Number of patients: 500+

Number of site raters: 390+

Countries: USA, Canada, Russia, Serbia, Ukraine, UK, Australia

INTRODUCTION

Primary endpoints in psychiatric trials are commonly comprised of the scores derived from clinician ratings using standardized rating instruments. To optimize the power of the clinical trial to detect treatment-related differences, it is important to consider approaches to limiting inter-rater and intra-rater variability. In addition to comprehensive rater training and qualification programs, the use of site-independent central raters to assess and mitigate ongoing rater accuracy and reliability can improve the through-study accuracy and consistency of ratings and improve signal detection.

This evaluation served to demonstrate the value of central ratings for quality control in reference to five phase 2 and 3 studies in MDD using the MADRS to measure severity of depressive symptoms.

METHODS

All raters (397 site raters, and 42 site-independent raters) involved in the studies underwent comprehensive rater training and qualification. Each study included central ratings based on audio recordings of the site interview, for quality control performed by qualified site-independent raters. Central ratings were performed in a randomized manner, and blinded to site, study visit, and site-rater score. Site-independent and site-based ratings were compared to provide quality control of site-based clinician ratings. Site-based raters who were frequently associated with divergent scores compared to the site-independent ratings were provided additional telephone-based training to remediate.

RESULTS

Site and central ratings were available for 3,736 MADRS assessments, and were highly correlated across all study visits. There were 249 paired interviews (6.7%) with total score deviations exceeding 6 points. The reason for most rating discrepancies was usually a failure to apply scoring conventions, or interviews of insufficient length to conduct a comprehensive assessment. Subsequent review of site-based rater performance following telephone remediation revealed greater scoring concordance with the central rater in almost every case.

CONCLUSIONS

This analysis confirms the value of audio recording of site-based interviews as a surveillance strategy for quality assurance using central site-independent raters to identify rating deviations and enable in-study remediation training where needed.

PUBLICATION

Targum SD, Catania CJ. Audio-digital recordings for surveillance in clinical trials of major depressive disorder. Contemp Clin Trials Commun. 2019; 14: 100317.

ABOUT SIGNANT HEALTH

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