

WCG Improves PANSS Data Quality and Signal Detection in a Global Schizophrenia Trial, Leading to Approval

By improving site and rater performance and increasing signal detection, WCG helped Noven Pharmaceuticals and Hisamitsu Pharmaceutical win approval for the asenapine transdermal system (HP-3070), the first antipsychotic patch approved in the United States for treatment of adults with schizophrenia. ¹



The Challenge: Risk of Placebo Effect

Noven Pharmaceuticals and Hisamitsu Pharmaceutical were conducting a global Phase III randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of an asenapine transdermal system in schizophrenia.

The study faced several challenges, including:

- a failure-prone therapeutic area: psychiatry.
- a condition with one of the highest placebo-response rates: schizophrenia.
- a delivery method – dermal patch – associated with higher placebo response.
- a global trial involving multiple countries: variabilities in ratings.
- three treatment arms design.
- a potential reduction in treatment effect size due to measurement error and noise in clinical trials.

For the sponsors, use of rater training to establish adequate rater reliability and outstanding clinical oversight to ensure data quality were paramount, so they turned to WCG.

Symptom manifestations and changes in psychiatric illnesses can be subtle. However, consistency checks can be used to flag instances of possible rating error, regardless of source.²

¹Suzuki K, Castelli M, Komaroff M, Starling B, Terahara T, Citrome L. Pharmacokinetic Profile of the Asenapine Transdermal System (HP-3070). J Clin Psychopharmacol. 2021;41(3):286-294. doi:10.1097/JCP.0000000000001383
²Rabinowitz J, Schooler NR, Anderson A, et al. Consistency checks to improve measurement with the Positive and Negative Syndrome Scale (PANSS). Schizophr Res. 2017;190:74-76. doi:10.1016/j.schres.2017.03.017



The Solution: Better Signal Detection

The question WCG answered affirmatively was: *Can data quality flags and risk signals be applied to manage site and rater performance to improve data quality and efficacy signal detection?*³

Algorithms for Positive and Negative Syndrome Scale (PANSS) and Clinical Global Impression Scales – Severity and Improvement (CGI-S/I) monitoring included flags developed by the International Society for CNS Clinical Trials and Methodology (ISCTM) Algorithms/Flags workgroup, along with other in-study performance indicators, such as numbers of raters per patient and PANSS-CGI correlations, were implemented as part of the clinical data monitoring for this study.

WCG reviewed discrepancies identified in the data and implemented a series of interventions, including scoring inquiries, clinical review, and remedial training, to improve data quality.



The Results: Regulatory Approval

WCG's unique combination of clinical oversight, data quality monitoring, technology and project management improved signal detection, which led to a successful trial and regulatory approval.

This success suggests:

- The methodology described by the ISCTM workgroup, when carefully implemented through a data analytics approach, can improve signal detection.
- Certain ISCTM flags, PANSS-CGI-S correlation and rater consistency can be translated into actionable items to improve data quality

More research is needed, but these findings hold tremendous potential for future schizophrenia and other CNS trials.

³Opler M, Negash S, Tatsumi K, et al. Application of a Novel Analytic Methodology to Improve PANSS Data Quality and Signal Detection in a Global Clinical Trial of Schizophrenia. https://isctm.org/public_access/Autumn2021/Posters/Opler_Poster.pdf