PORTICO – A Case Study in Overcoming Methodological Challenges in Borderline Personality Disorder Clinical Development

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SUBMISSION DETAILS

What is the Methodological Question Being Addressed? Previously ISCTM panel presentations (Ropacki, 2020) highlighted the methodological challenges in conducting Borderline Personality Disorder (BPD) clinical trials including: lack of a 'gold standard' measure, uncertain but high placebo rate, large sample sizes, difficult and non-adherent patient population, endpoint timing challenges, and the fact that a large percentage of BPD patients are receiving psychotherapy.

Introduction To-date there have been over 17 industry-sponsored clinical trials in Borderline Personality Disorder (BPD), but no approved drug treatment. The purpose of this presentation is to provide an overview of the methodology and design of PORTICO, a double-blind, randomized, placebo-controlled, adaptive 14-week Phase IIb trial to evaluate the efficacy and safety of vafidemstat in an adult BPD population. PORTICO is the first clinical trial specifically designed to address many of the methodological challenges in BPD clinical development.

The question is whether novel methodological approaches employed in PORTICO will facilitate enrollment and help enroll a more representative BPD population, as well as increase treatment adherence, decrease dropout rate and result in cleaner data that will hopefully lead to a treatment option in a population with high unmet need and no approved drug therapy. The novel approaches employed includes an adaptive design that employs multiple primary, secondary and exploratory endpoints, selection of a small number of specialized BPD sites with established clinician-patient relationships, blinding the primary endpoint timing, implementing less restrictive inclusion/exclusion criteria but only in stable and/or treated participants, and allowing flexibility around alcohol and marijuana use, but removal of non-adherent substance abusing subjects.

Methods Up to 156 participants will be enrolled and randomized in a 1:1 ratio (78 subjects per arm) to active treatment with vafidemstat (1.2 mg) or placebo to yield an expected 124 completed study subjects, since it is anticipated that 20% of subjects will drop out of the trial. PORTICO will involve 9 study visits, a blinded protocol where some information related to the study design has been blinded to reduce the risk of bias in the assessment of the study endpoints. Inclusion and exclusion criteria designed to address BPD clinical development challenges will be discussed in the poster.

There is a one-week screening period to ensure study eligibility criteria, followed by 14 weeks where subjects receive vafidemstat or placebo. The multiple primary endpoints include the Clinician's Global Impression – Severity focused on agitation and aggression (CGI-S A/A), as well as the Borderline Personality Disorder Checklist (BPDCL). Participants and Investigators are blinded to treatment allocation, as well as the timing of all the efficacy endpoints.

Results As a methodological poster, the results will be forthcoming. The primary efficacy analysis compares active treatment to placebo. Both primary endpoints (CGI S A/A and BPDCL) will be analyzed for significance as the difference between active treatment and placebo from baseline to specific week. The post-baseline results for both primary endpoints will be analyzed using a mixed model repeated measures (MMRM), including as fixed factors: visit, treatment arm, psychotherapy at baseline, the interaction between treatment and visit as well as the baseline value (last measurement prior to treatment initiation) for the endpoint.

Conclusion PORTICO is BPD clinical trial that encourages enrollment of a real-world BPD population allowing common comorbidities and concomitant medications that are typically exclusionary, as well subjects to receive psychotherapy.

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Keywords

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Borderline Personality Disorder
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Guidelines I have read and understand the Poster Guidelines

Disclosures if applicable Michael Ropacki - Employee of Oryzon & SGR&D
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