Exploring Novel Behavioral Tasks and Digital Phenotyping Technologies as Adjuncts to a Clinical Trial of BTRX-246040

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The Methodological Question Being Addressed

What are the benefits, challenges and best practices of implementing quantitative, objective behavioral measures of reward and affective processing and innovative, objective "digital phenotyping" technologies in clinical trials for major depressive disorder (MDD)?

Introduction (Aims)

Rating scales for diagnosing psychiatric disorders and evaluating treatment response in psychiatric clinical trials are subjective and may be unreliable for identifying patient subtypes or accurately quantifying outcomes (Insel et al., 2010; Clementz et al., 2016). Patients with MDD are heterogeneous in disease etiology, clinical presentation and treatment response. A precision medicine strategy using quantitative, objective measures to target brain-behavior symptom domains that are disrupted in MDD, such as anhedonia, rather than the non-specific categorical construct of MDD, may deepen insights into patient phenotypes, enable patient stratification and reliable detection of treatment response.

An aim of the present study is to identify, adapt and implement a strategic battery of quantitative, objective behavioral tasks and "digital phenotyping" technologies as complements to rating scales in a Phase 2 clinical trial in patients with MDD. A key goal is to determine whether these measures improve insight into patient heterogeneity and treatment response.

Methods

In a randomized, multi-center, double-blind placebo-controlled study assessing the safety and efficacy of BTRX-246040, a potent and selective nociceptin-1 receptor antagonist, approximately 100 adult patients with MDD are evaluated using active and passive measures at baseline and continuously or at regular intervals over an 8-week treatment phase. Assessments include quantitative behavioral tasks that measure dysfunction in anhedonia and reward processing (Probabilistic Reward Task, PRT; Effort Expenditure for Reward Task, EEfRT) or social-emotional (Facial Emotional Recognition Task, FERT) symptom domains, smartphone technologies to predict affect and cognition from vocal features and continuous passive human-computer interaction (Mindstrong), and rating scales of anhedonia (Snaith-Hamilton Pleasure Scale, SHAPS; Dimensional Anhedonia Rating Scale, DARS) and depression (Montgomery-Asberg Depression Rating Scale, MADRS).

Results

The study commenced recently and is ongoing. Results and insights from implementing novel phenotyping and pharmacodynamic endpoints in a phase 2 clinical trial will be presented and include 1) strategy for the selection of tasks, technologies and quantitative endpoints to meet the objectives of the study, 2) real and perceived risks, benefits, challenges and solutions for adapting experimental computerized behavioral tasks and novel technologies for use in clinical trials, and 3) consideration of best practices and regulatory issues.

Conclusions

Quantitative, objective endpoints and passive, continuous measurement technologies have the potential to synergize with rating scales and improve insights into patient heterogeneity and treatment response. Promising new tasks and technologies need to be optimized and validated to meet drug development goals and regulatory requirements. Collaboration between sponsors, inventors and patients is critical. Addressing privacy and data security concerns is tantamount. Rigorous data analytical methods are critical to the value proposition of these approaches.

Disclosures: DGS, KS and AM are employees of BlackThorn Therapeutics; SAH is a paid biostatistics consultant for BlackThorn Therapeutics; PD is an employee of Mindstrong Health.