Standardization of EEG Enrichment Marker Acquisitions in a Randomized, Double-Blind, Placebo-Controlled Study of ALTO-300 in Adults with Major Depression Disorder

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Methodological Issue Being Addressed We present an innovative approach to standardizing the collection of high-quality resting-state EEG (rsEEG) across multiple clinical trial sites, enabling use of a reliable EEG enrichment marker for antidepressant response in patients with Major Depressive Disorder (MDD).

Introduction Antidepressants often show little to no differentiation from placebo, likely due to MDD's heterogeneity. Using biological markers to identify likely responders could enhance therapeutic outcomes by focusing on a more responsive subpopulation for a given drug. In this study, we analyzed resting-state EEG (rsEEG) data to classify participants as meeting (enrichment marker positive) or not meeting the enrichment marker threshold. Our primary goal is to evaluate the efficacy of ALTO-300 versus placebo in reducing MDD symptoms among enrichment-positive participants, as determined by their baseline EEG.

Methods We employed a multi-pronged approach to ensure standardization of rsEEG data acquisition in more than 40 sites consisting of: standardized EEG equipment and materials; sponsor-led training and qualification of site personnel; ongoing monitoring; and a centralized web application providing feedback to site personnel in real time. This approach provides a robust platform ensuring high quality and reliable acquisition of EEG data across sites. Trained site personnel collected rsEEG data from participants under eyes closed and eyes open conditions for 4 minutes each, repeated twice. rsEEG data were uploaded to the web application. Crucially, users received automated feedback within 2 minutes indicating if a session passed. Artifacts like muscle activity, movement, and flat lines can be identified. Data that passed quality-control checks were then processed using proprietary feature generation algorithms. The generated features were age/gender normalized and compared to threshold values to stratify participants into either an enrichment marker positive or negative group. To generate a reliable enrichment marker output, two passing eyes closed recordings were required. Results were generated within 24 hours and entered in the randomization system. Sites were blinded to enrichment status of the participant.

Results Our approach has resulted in the training of over 100 EEG-naive personnel across 45 clinical sites nationwide who have gathered data from more than 298 participants during screening by the date of this submission (the trial remains ongoing). Of those, 268 participants passed the stringent quality control standards set in our automated pipeline—resulting in a 90% success rate in the setting of variability in recording conditions and staff expertise expected in a large multi-site

clinical trial.

Conclusion We successfully developed and deployed a standardized EEG data acquisition and analysis platform to collect high quality data across large numbers of clinical trial sites for the purpose of EEG-based patient selection. The EEG platform supports a precision psychiatry drug development approach with the goal of identifying participants most likely to respond to treatment with ALTO-300.

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Keywords

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Guidelines I have read and understand the Poster Guidelines

Disclosures All authors are employees at and hold equity in Alto Neuroscience, Inc. Adam Savitz holds equity in Johnson & Johnson.

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