Using Active and Passive Digital Phenotyping to Increase Signals in Early Stage Drug Development Trials

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Methodological Issue Being Addressed Early stage drug development requires balancing cost and optimization of data collection. Blinded trials may not be feasible because of cost/benefit. Assuming risks of placebo effects in order to not miss beneficial elements of a novel compound is required. One strategy to reduce this risk, increasing the volume of data collected and collecting data that is less susceptible to placebo effects, is technology-based approaches collecting densely sampled data actively and passively. Passively collected data are less likely to manifest a participant-driven placebo effect. Some actively sampled data are not transparently related to efficacy measures, such as engagement in activities that are common when participants are in a better emotional state, such as social and physical activities. This presentation addresses whether such strategies can collect credible data to support efficacy inferences in an open-label study.

Introduction These are the results of an open-label treatment study of participants with Major Depressive Disorder. The study drug was a “ANC-501”, a V1b receptor antagonist. Sampling with passive and active technology-based assessments occurred daily and clinical ratings were more widely dispersed.

Methods In this study, 13 participants were treated with ANC-501 50mg adjunctive to ongoing AD medication in a non-blinded design for 8 weeks,examined with in-person clinical ratings of depression (MADRS) anxiety (HAM-A) at days 1, 8, 15, 29, 43, and 56. During the protocol, participants also answered ecological momentary assessment (EMA) surveys, 3 times per day, 7 days per week, as well as wearing an actigraph which measured steps and sleep. EMA surveys examined reports of depression (HAM-D 6) and Anxiety (GAD7) [AM and PM] as well as a responses to a previously validated survey of daily activities, including location (Home vs away), social context (alone vs. with someone), productive and unproductive home-based activities and away from home activities. Data analyses included changes in symptoms based on in-person and EMA assessments of symptoms and EMA-based assessments of activities and daily steps. Concurrent and lagged analyses were used to determine if EMA and actigraphy-based assessments both converged with and predicted in-person symptom assessments.

Results A total of 658 EMA surveys were collected over 8 weeks from the 13 participants.. The effect sizes for improvements in depression to day 56 were d=1.8 for in person ratings and d=1.3 for EMA (all p<.004). Nighttime sleep increased over the protocol, p<.001. EMA depression ratings correlated concurrently with clinical ratings at days 8, 15, 29, 43, and 56 (all p’s < .05) and clinical

and EMA depression ratings correlated with concurrent step counts (p<.05). Importantly, changes in EMA-rated depression up to days 15 and 29 predicted changes in MADRS ratings at days 43 and 56 (all r>.45). Productive activities increased over time (all p<.004) and increases in productive activities from baseline to days 8, 15, and 29 correlated with concurrent EMA depression ratings (p=.02) and predicted MADRS ratings of depression at the later assessments (all p<.03).

Conclusion Even in a small unblinded trial, passive and active digital phenotyping assessments converged with and predicted later clinical ratings with high levels of adherence observed. To obtain 658 datapoints in an in-person study with 6 assessments, over 100 participants would be required. Most importantly, digital phenotyping content that is not an obvious element of an efficacy assessment (productive activities, nighttime sleep, step counts) correlates with concurrent ratings and anticipates later clinical ratings confirming that these clinical ratings are truly sampling the stream of behavior that leads up to the dispersed ratings. These data suggest that lower-cost, technology-based assessments can efficiently provide high volumes of information that could never be collected by an in-person assessment strategy.

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Guidelines I have read and understand the Poster Guidelines

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