Title: ***Don't Change the Subject! The Changing Nature of Screened Subjects During Phase 3 Clinical Trials***

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Methodological Question: Do subjects entered early into Phase 3 CNS studies differ from those entered later?

Introduction: Clinical trial recruitment and enrollment are affected by a number of factors, such as use of recruitment vendors, the use of sites known to the sponsor and subjects known to the site early in the recruitment process, and addition of sites and pressure to increase enrollment later in the study. Previous reports describe placebo response increasing later in enrollment; we seek to understand more about how subjects enrolled early in a clinical trial might differ from those enrolled later in the same study. Our registry, which seeks to track and eliminate duplicate and professional subjects in clinical trials, has collected data on over 40,000 subjects screened or prescreened for clinical trials, especially for Phase 2-4 studies of CNS indications.

Methods: We looked at pooled study data for all subjects screened for Phase 3 studies that have used CTSdatabase and are completed or at least 75% enrolled (n = 4352). Only *actionable* matches that occurred at unique sites were included in the analysis. Actionable matches are exclusionary per protocol and include concurrent enrollment, participation in another study less than the number of days required by I/E criteria or previously enrolled in a study for a prohibited indication (eg. Bipolar in an ADHD study). For each study, total subjects screened were divided into four equal quartiles based on enrollment and the results were pooled for analysis. Study indications included Schizophrenia (n=2), Binge Eating Disorder (BED, n=1) and Adult ADHD (n=2).

Results: 103 Actionable Matches were found among 4227 subjects screened through December 29, 2017. The overall percentage of actionable matches in these studies was 2.4%. When investigated by quartile, the percentages of excluded subjects were different: 1.6%, 2.1%, 3.2% and 2.8% in quartiles 1-4, respectively. There were fewer subjects excluded (inappropriate subjects who are likely duplicate and/or professional) in the 1st quartile and a greater number in the 3rd quartile of enrollment. The percentage of exclusionary matches in the second half of enrollment (3.0% in quartiles 3+4) was significantly higher than in the first half (1.8% in quartiles 1+2), p =.028).

Conclusions: Subjects excluded from studies by a registry are a marker for inappropriate or professional subjects. Our data support a hypothesis that subjects enrolled later in Phase 3 studies are more likely to be study inappropriate. These findings should be investigated further in larger samples and for other indications. Correlation with recruitment data and PK data would be helpful to determine if rates of these inappropriate subjects correlate with enrollment efforts or rates of nonadherence. In addition, Phase 3 data on inappropriate subjects could be compared to Phase 2 data. If the type of subjects enrolled later in Phase 3 trials differ from those entered in successful Phase 2 studies, and they are not accounted for, they may contribute to study failure.

Disclosures: Dr. Shiovitz has ownership interest in CTSdatabase.

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