Frequency of rater-based efficacy assessments correlated with magnitude of placebo response in generalized anxiety disorder trials

Submitter Michaela Gold

Affiliation Seaport Therapeutics

SUBMISSION DETAILS

I agree to provide poster pdf for attendee download. Yes

I have used the poster abstract template to develop my abstract. Yes

Methodological Issue Being Addressed Multiple clinical trial design factors are hypothesized to impact the magnitude of the placebo response in generalized anxiety disorder (GAD) clinical trials. Here, data from GAD trials completed in the past 20 years that met the criteria outlined below were investigated to identify associations between clinical trial design factors and magnitude of placebo change from baseline.

Introduction Participants in randomized, placebo-controlled GAD trials of anxiolytics often show a strong response to placebo on clinical endpoints. Clinical trial design factors, such as number of site visits and baseline HAM-A scores, may contribute to the placebo response, increasing the challenge of demonstrating a treatment effect. The impact of these factors on placebo response in recently completed GAD trials has not been well studied.

Methods A systematic search of unique randomized, placebo-controlled trials with the following analysis inclusion criteria was conducted: Phase 2-4, conducted in adults with GAD, completed within the past 20 years using primary endpoint of HAM-A, with ≥100 total participants enrolled and ≥25 participants enrolled in the placebo arm, and funded by industry. A total of 22 trials, 6 Phase 2 and 16 Phase 3, met the above criteria and had necessary data available via public sources, predominantly from clinicaltrials.gov and publications. Of the 22 trials, 13 met the primary outcome on at least one of the treatment arms. Placebo response was measured by placebo group change from baseline of HAM-A total score.

Results Linear regression analyses demonstrated that while study length did not impact the placebo response, the frequency (number per week) of efficacy assessments was strongly associated with a greater placebo change ($p<0.005$; frequency range: 1.3-5.5; $\beta= -0.93$). Investigating the different types of efficacy assessments showed that this association was likely driven primarily by the frequency of rater-based assessments (clinician-administered assessments e.g., HAM-A, MADRS, CGI-I) ($p<0.005$; $\beta= -1.3$) and not the frequency of self-reported efficacy assessments (e.g., PGI-I, SDS) ($\beta= -0.75$).

Further, the total number of efficacy assessments conducted during these clinical trials trended toward an association with greater placebo group change from baseline ($p<0.07$; $\beta= -0.12$). Examining the types of efficacy assessments showed that the number of rater-based efficacy

assessments also trended toward a correlation with greater placebo response ($p<0.09$; $\beta= -0.12$) while self-reported efficacy assessments did not ($\beta= -0.033$).

We also explored additional factors that could potentially impact placebo response, such as number of trial sites, baseline HAM-A score, number of site visits, and the ratio of placebo to active arm sizes. These factors were not strongly correlated with placebo response. There was no strong correlation between whether the trials met the primary outcome and the placebo group change.

Conclusion Our results show that the frequency of efficacy assessments is an important factor associated with the magnitude of placebo group change in GAD trials conducted over the past 20 years. Regression analyses highlighted a strong association of frequency of efficacy assessments, primarily rater-based assessments, with placebo response. These findings are similar to our previous meta-analysis of placebo response in major depressive disorder trials and suggest that clinician-patient interaction could increase the placebo response in GAD trials.

Co-Authors

Michaela Gold[1], Brianna Bisson[1], Haiyuan Zhu[1], Antony Loebel[1], Michael Chen[1]

[1] Seaport Therapeutics

Keywords

Keywords
placebo
generalized anxiety disorder
meta-analysis

Guidelines I have read and understand the Poster Guidelines

Disclosures Research sponsored by Seaport Therapeutics. MG, BB, HZ, AL, and MC are employed by and hold stock in Seaport Therapeutics.