Placebo Response Assessed by Site and Remote Blinded Centralized Ratgrpcers in a GAD Trial

ABSTRACT

Results: Site raters admitted 122 subjects to the placebo arm of the study. At baseline, remote centralized raters selected 59 (48%) of these admitted subjects at or above the HAM-A entry criterion and rated 63 (52%) of the admitted subjects below the entry criterion. At baseline, site raters' mean HAM-A score was 24.9 (SD: 3.2; N = 122), compared to 19.9 (SD: 3.3; N = 119) for the remote centralized raters. In addition, site raters' mean scores were higher than remote raters on all of the individual HAM-A items at baseline. At endpoint, however, site raters' scores were similar to remote raters' scores.

Methods: This double-blind, placebo-controlled, multi-center study examined the efficacy and safety of two doses of an experimental compound to treat Generalized Anxiety Disorder. The primary outcome measure was the Hamilton Anxiety Scale (HAM-A). Site raters assessed subjects six times over an 8-week period. Remote centralized raters independently rated the same subjects on the HAM-A at baseline and week 6. 119 site raters were trained and calibrated by MedAvante, and maintained high interrater reliability throughout the study with quarterly group recalibrations and regular observations by trainers. Remote centralized raters were trained and calibrated by MedAvante, and maintained high interrater reliability throughout the study with quarterly group recalibrations and regular observations by trainers. At baseline, site raters' scores were truncated at the inclusion score of 20, as expected. Remote centralized raters' baseline scores were normally distributed, even though site raters scored all subjects as having a HAM-A ≥ 20.

Results: Blinded remote raters showed a 36% reduction in placebo response compared to site raters. This may be due to the blinded remote ratings being independent from the study enrollment process. A decrease in placebo response assessed by site vs. central raters in the same group of subjects.

Placebo response rate was -5.9, 36% lower for these same subjects when assessed by remote centralized raters. At endpoint, site raters' and remote raters' scores were similarly distributed.