

Efficacy of Lisdexamfetamine in Adults With Moderate to Severe Binge-Eating Disorder: A Randomized Clinical Trial

BACKGROUND

- Lisdexamfetamine is FDA approved to treat moderate to severe binge eating disorder (BED).
- Previous studies have examined the efficacy of lisdexamfetamine in binge-eating disorder in the short-term, but it's ability to be effective long-term has not been evaluated.

OBJECTIVE

- To assess lisdexamfetamine maintenance of efficacy in adults with moderate to severe binge-eating disorder

METHODS

- **Design:** Multinational, phase 3, double-blind, placebo-controlled randomized withdrawal study
 - Open Label Phase: 12 weeks; 4 weeks for dose optimization and 8 weeks for dose maintenance
 - Randomized Withdrawal Phase: 26 weeks
- **Inclusion criteria:**
 - Adults: 18-55
 - Meet the Diagnostic and Statistical Manual of Mental Disorders IV – Text Revision (DSM-IV-TR) Binge Eating Disorder criteria
 - Moderate to severe binge eating disorder
 - Greater than or equal to 3 binge-eating days per week for 14 days before open label based on participant reported binge eating diaries
 - Clinical Global Impression-Severity (GCI-S) scores greater than or equal to 4 (moderately ill).
 - BMI = 18-45 at screening and open-label baseline
 - Negative serum pregnancy test at screening, open-label baseline, 4-week intervals, and treatment termination.
- **Exclusion criteria:**
 - Anorexia nervosa or bulimia nervosa
 - Comorbid psychiatric disorders (uncontrolled and associated with significant symptoms)
 - Psychotherapy or weight loss support for BED initiated less than 3 months before screening
 - Psychostimulant use for BED initiated 6 months or less before screening
 - Montgomery-Asberg Depression Rating Scale score of 18 or higher

- Past suicide attempt
- Current active suicidal ideation
- History of cardiovascular health problems
- Clinically significant ECG abnormalities at screening
- Moderate or severe hypertension
- History of stimulant abuse or dependence
- Substance abuse or dependence within the past 6 months
- Use of prohibited medications
 - sedatives/hypnotics, benzodiazepines, anxiolytics, antipsychotics, antidepressants, monoamine oxidase inhibitors, clonidine, guanfacine, atomoxetine, over-the-counter or prescription weight loss therapies, or narcotics (within 30 days of screening), sedating antihistamines, herbal preparations, or melatonin (within 7 days of screening), or sympathomimetics or appetite suppressants (within 6 months of screening)
- **Primary outcome measure:** Time to relapse
 - **Secondary outcome measures:** Binge-eating days per week, CGI-S scores, Yale-Brown Obsessive Compulsive Scale modified for Binge Eating (Y-BOCS-BE), and safety and tolerability assessments
- **Power:** 90% power with an alpha equal to 0.05 to detect a 25% difference between relapse rates; total participants required: 214
- **Data Handling Method:** Intent to Treat
- 411 participants in open-label phase
 - Starting dose: Lisdexamfetamine 30 mg
 - Dose titrated to 50-70 mg; no changes were made to the dose after week 3
- 275 completed open-label phase and were randomized to receive lisdexamfetamine or placebo
 - 138 placebo
 - 137 Lisdexamfetamine

RESULTS

- **Primary outcome:** participants meeting relapse criteria was 32.1% in the placebo group and 3.7% in the lisdexamfetamine group; p value <0.001.
- **Secondary outcomes**
 - The least squares mean treatment difference for the change from randomization withdrawal baseline in binge-eating days per week was -0.61 with a 95% CI ranging from -0.81 to -0.42 and p value < 0.001 indicating a statistically significant greater increase for placebo compared to lisdexamfetamine.
 - CGI-S score distributions differed between treatment groups; p <0.001

- The least squares mean treatment difference for the change from randomization withdrawal baseline in Y-BOCS-BE scores was -5.6 with a 95% CI ranging from -7.2 to -3.9 indicating a statistically significant greater increase for placebo compared to lisdexamfetamine; p value < 0.001

STRENGTHS

- Appropriate statistical tests used
- Sufficient background and rationale
- Acceptable effort to enroll a diverse population
- Outcome measures were appropriate to meet the study objective

LIMITATIONS

- The significant involvement of Shire, the study drug manufacturer, in the study
- Failure to admit the significance of the low relapse rate in the placebo group
- Lack of diverse study population
- Risk of unblinding
- Exclusion of comorbidities that may be common in patients with Binge Eating Disorder
- Insufficient method used to account for missing diary entries

CONCLUSION

- Although the relapse rate of the placebo group was higher than the lisdexamfetamine group, it was much lower than anticipated. The authors gloss over this finding likely due to their affiliations with Shire. The limited number of patients relapsing in the placebo group does not support the long-term use of lisdexamfetamine in patients with BED; however, it proposes new areas of research. Further studies could evaluate the efficacy of preventing relapse by closely monitoring post short-term pharmacologic therapy.

Reference: Hudson JI, McElroy SL, Ferreira-Cornwell MC, Radewonuk J, Gasior M. Efficacy of Lisdexamfetamine in Adults with Moderate to Severe Binge-Eating Disorder. *JAMA Psyc.* 2017;74(9).

Beka McCutcheon, Pharm. D. Candidate
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