Randomized Placebo-Controlled Clinical Trial of Lorcaserin for Weight Loss in Type 2 Diabetes Mellitus: The BLOOM-DM Study

BACKGROUND:

- Lorcaserin has caused significant weight loss in overweight and obese individuals who did not have diabetes, and weight loss was accompanied by generally favorable changes in lipids, blood pressure, anthropometric measures, and insulin sensitivity. However, the efficacy and safety of lorcaserin in people with type 2 diabetes mellitus had not been previously evaluated. Also, excess body weight is a key contributor to type 2 diabetes and over 85% of adults diagnosed with type 2 diabetes are classified as overweight or obese

OBJECTIVE

- The objective of the Behavioral Modification and Lorcaserin for Obesity and Overweight Management in Diabetes Mellitus Study, or BLOOM-DM study, was to evaluate the efficacy and safety of lorcaserin for weight loss and glycemic control in adults with type 2 diabetes treated with metformin and/or a sulfonylurea.

METHODS

- **Design**: This study was a 1-year, randomized, double-blind, parallel, placebo-controlled study.
- **Duration:** 12 months
- **Inclusion criteria**: Eligible patients had type 2 diabetes mellitus that was treated with metformin, a sulfonylurea, or both. They had an A_{1C} at baseline of 7-10%; were 18-65 years old with a BMI of 27-45 kg/m^2, and were able to participate in a moderate intensity exercise program.
- **Exclusion criteria**: Exclusion criteria included use of insulin in any form, use of exenatide or pramlintide (due to effects on body weight); had prior bariatric surgery; had a change in weight of greater than or equal to 5kg within 3 months; had a binge eating scale score of greater than 17; had a significant change in cigarette smoking within 3 months; had a malignancy within 5 years; had a recent major surgery; had a history of seizure disorder within 5 years; had depression or other major psychiatric disease requiring treatment with prescription medication within 1 year; had a Beck Depression Inventory-II score of greater than or equal to 20 or an individual response suggesting suicidal thoughts; were pregnant or lactating; had a history of cardiac valve disease or pulmonary artery hypertension, myocardial infarction or stroke within 6 months, or unstable angina; had a prior administration of lorcaserin or drugs associated with cardiac valvulopathy, use of selective dserotonin reuptake inhibitors or selective norepinephrine reuptake inhibitors, topiramate, and drugs for wieth loss/ had clinically significant thyroid stimulating hormone and/or T4 abnormalities; had triglycerides greater than 499 mg/dl; had an LDL greater than or equal to 160 mg/dl; had an aspartat aminotransferase or alanine aminotransferase greater than 2.5 times the upper limit of normal; bilirubin or creatinine greater than 1.5 times the upper limit of normal; or a positive HIV, hepatitis B or hepatitis C screen.

- **Primary outcome measure**: There were 3 co-primary endpoints and they were: the proportion of patients achieving greater than or equal to 5% reduction in baseline body weight at the end of 1 year, change in weight, and the proportion of patients achieving greater than or equal to 10% reduction in baseline body weight.
- **Secondary outcome measures**: Secondary endpoints included changes from baseline in glycemic control using A_{1C}, fasting plasma glucose, fasting insulin, homeostatic model assessment-insulin resistance, total cholesterol, LDL, HDL, triglycerides, waist circumference, BMI, systolic blood pressure, diastolic blood pressure, and quality of life as assessed by the Impact of weight on Quality of Life-LITE questionnaire.
- 256 patients were allocated to receive lorcaserin 10 mg twice daily, 95 patients were allocated to receive lorcaserin 10 mg once daily and placebo once daily, and 253 patients were allocated to receive placebo twice daily. A lifestyle modification program was also administered to all patients at each visit, and included advice about exercise, behavior modification techniques, calorie restriction, and food choices.
- Based on a two-sample test of equality of binomial proportions at the 0.05 level of significance, a sample size of 147 patients per group would provide 84% power.
- Both an intent-to-treat and a per-protocol analyses were done

RESULTS

- 87 patients in the lorcaserin BID group dropped out, 20 patients in the lorcaserin QD group dropped out and 96 patients in the placebo group dropped out.
- **Primary outcome measure**: 37.5% of patients on lorcaserin BID, 44.7% on lorcaserin QD, and 16.1% of patients on placebo lost at least 5% of baseline body weight. The p-value for this primary outcome measure was <0.001. 16.3% of patients on lorcaserin BID, 18.1% of patients on lorcaserin QD, and 4.4% of patients on placebo lost at least 10% of baseline body weight. The p-value for this primary outcome measure was <0.001.
- **Author's conclusion:** The authors conclusion was that lorcaserin use for up to 1 year in obese and overweight patients with type 2 diabetes was associated with statistically significant and clinically meaningful weight reduction. Because significant improvements in glycemic control were also observed, lorcaserin could represent a useful weight management tool for overweight and obese type 2 diabetic patients.

STRENGTHS

- Study duration was of a sufficient amount of time
- Controlled study
- Orlistat dosed appropriately
- Power of the study was appropriate for the lorcaserin BID and the placebo groups

LIMITATIONS

- No data provided to account for adherence to diet, exercise, and medication regimen.
- Lack of data regarding sustained effects after cessation of study
- Did not explain randomization fully
- Inclusion and exclusion criteria did not allow for extrapolation to the population of interest

- Power of the study for the lorcaserin QD group was not appropriate
- Hard to ensure standardization across 58 sites

CONCLUSION

- The fact that this study was conducted at 58 different sites makes it hard to determine if standardization among all patients was accomplished, also the lack data regarding long term weight loss after treatment discontinuation, and the limitations that the authors provided, all lead me to believe that lorcaserin could have a place in therapy for weight loss, but before it becomes a standard of treatment among overweight and obese populations with type 2 diabetes mellitus, further research is necessary into the safety and efficacy of lorcaserin in a broader diabetic population and the long term effects such as weight loss need to be evaluated as well.

Reference:

O'Neil, Patrick, Steven Smith, et al. "Randomized Placebo-Controlled Clinical Trial of Lorcaserin for Weight Loss in Type 2 Diabetes Mellitus: The BLOOM-DM Study." *Obesity Journal*. 20.7 (2012): 1426-36. Web. 14 Sep. 2012.

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