**Abstract**

**BACKGROUND:** Patient-reported outcomes, such as quality of life (QOL), are increasingly used as secondary endpoints in clinical trials. We report changes in weight and QOL in a double-blind, randomized, placebo-controlled trial of combination therapy with topiramate and phentermine in obese adults.

**METHODS:** Two hundred (159 women, 41 men) obese adults (mean BMI of 38.6 kg/m²) received placebo (PBO), topiramate (TPM), phentermine (PHN), or the combination (COM) in conjunction with dietary counseling for 24 weeks. Weight-related QOL was assessed using the Impact of Weight on Quality of Life-Lite (IWQOL-Lite). Differences between treatments were evaluated by Analyses of Covariance (ANCOVA) conducted on the intent-to-treat (ITT) sample with last observation carried forward.

**RESULTS:** Of the 200 randomized subjects, 158 (79%) completed the full 24-week treatment, with individuals in the COM group having the highest retention rate (92%). Mean changes in body weight (kg) for PBO, TPM, PHN, and COM were –2.2, –6.6, –5.3, and –11.4, respectively (p<0.0001). Overall QOL (mean change in total score) improved with all treatments over time; however, the groups differed significantly (PBO 5.5; TPM 4.4; PHN 9.2; COM 11.1; p<0.0001). The COM group experienced significantly greater improvements in QOL than PBO and TPM on 3 of the 5 domains (Physical Function, Self-Esteem, and Public Distress) compared to the PBO and TPM groups (p<0.02), with the greatest improvement occurring in the COM group (p<0.0001). The COM group trended toward greater improvement compared to the PHN group (p=0.09), but was similar to PHN for other domains.

**CONCLUSIONS:** Combination therapy (topiramate plus phentermine) and phentermine alone were associated with greater improvements in weight-related quality of life. Treatment with topiramate alone was not associated with appreciable improvements in quality of life relative to placebo. Positive changes in quality of life during treatment with the combination of phentermine and topiramate may be primarily influenced by phentermine.

**Methods**

- **24-week, randomized, double-blind, placebo-controlled trial**
- **4 treatment groups**
  - Placebo (PBO)
  - Phentermine (PHN)
  - Topiramate (TPM)
  - Combination (COM)
- **Ancillary intervention of 500 kcal/day deficit diet and lifestyle counseling for all treatment groups**

**SUBJECTS:** 200 obese subjects (159 women, 41 men, mean [SE] BMI 38.6 [0.4] kg/m²)

**INCLUSION CRITERIA:**
- Age 18-60 years
- BMI 30-50 kg/m²

**KEY EXCLUSION CRITERIA:**
- Serious or unstable medical illness
- Known history of primary pulmonary hypertension
- Significant cardiac, hepatic or renal disease
- Clinically significant valvular heart disease
- History of renal calculi; uncontrolled HTN; diabetes mellitus; hyperthyroidism; glaucoma
- Major psychiatric disorder or alcohol/drug abuse
- Other

**RESULTS**

- **Weeks 0, 2, 4, 8, 12, 16, 20, 24**

**KEY ASSESSMENTS**

- **Weight**
- **Impact of Weight on Quality of Life-Lite (IWQOL-Lite)**
  - The IWQOL-Lite is a 31-item self-report measure of weight-related quality of life that provides scores on five domains (physical function, self-esteem, sexual life, public distress, and work) plus a total score
  - The IWQOL-Lite has been shown to have good internal consistency (.90 to .96), good test-retest reliability (.83 to .94), and sensitivity to weight changes
- **Scores range from 0 to 100, with higher scores representing better quality of life**

**STATISTICAL ANALYSIS**

- **Intention-to-treat (ITT) sample with the last observation carried forward (LOCF)**
- **ANCOVA with baseline value as the covariate**

**Table 1. Subject Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PBO</th>
<th>PHN</th>
<th>TPM</th>
<th>COM</th>
<th>p-value</th>
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**Table 2. Weight Loss**

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<th>Treatment</th>
<th>Weight Loss (kg)</th>
<th>p-value</th>
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<tr>
<td>Placebo</td>
<td>–2.2 (0.9)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Phentermine</td>
<td>–5.3 (0.9)</td>
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<td>Combination</td>
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**Table 3. Weight Loss**

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**References**

CHANGES IN WEIGHT AND QUALITY OF LIFE IN OBESE ADULTS TREATED WITH TOPIRAMATE PLUS PHENTERMINE

KISHORE M. GADDE1, RONETTE L. KOLOTKIN1,2, CRAIG A. PETERSON3, WESLEY W. DAY3

1Duke University Medical Center, Durham, NC, 2Obesity and Quality of Life Consulting, Durham, NC, 3Vivus, Inc., Mountain View, CA
Abstract

**BACKGROUND:** Patient-reported outcomes, such as quality of life (QOL), are increasingly used as secondary endpoints in clinical trials. We report changes in weight and QOL in a double-blind, randomized, placebo-controlled trial of combination therapy with topiramate and phentermine in obese adults.

**METHODS:** Two hundred (159 women, 41 men) obese adults (mean BMI of 38.6 kg/m²) received placebo (PBO), topiramate (TPM), phentermine (PHN), or the combination (COM) in conjunction with dietary counseling for 24 weeks. Weight-related QOL was assessed using the Impact of Weight on Quality of Life-Lite (IWQOL-Lite). Differences between treatments were evaluated by Analyses of Covariance (ANCOVA) conducted on the intent-to-treat (ITT) sample with last observation carried forward.

**RESULTS:** Of the 200 randomized subjects, 158 (79%) completed the full 24-week treatment, with individuals in the COM group having the highest retention rate (92%). Mean changes in body weight (kg) for PBO, TPM, PHN, and COM were –2.2, –6.6, –5.3, and –11.4, respectively (p<0.0001). Overall QOL (mean change in total score) improved with all treatments over time; however, the groups differed significantly (PBO 5.5; TPM 4.4; PHN 9.3; COM 11.1; p<0.002). The COM group experienced significantly greater improvements in QOL than PBO and TPM on 3 of the 5 domains (Physical Function, Self-Esteem, and Public Distress) (p<0.02), with the greatest improvement occurring in Self-Esteem (effect size = 0.86). The COM group trended toward greater improvement compared to the PHN group for Self-Esteem (p=0.09), but was similar to PHN for other domains.

**CONCLUSIONS:** Combination therapy (topiramate plus phentermine) and phentermine alone were associated with greater improvements in quality of life than placebo or topiramate. Topiramate treatment yielded more weight loss than phentermine, but without any appreciable improvements on QOL. This suggests that phentermine in the presence of topiramate may play an important role for maintaining positive QOL outcomes.
Background

- Obesity is associated with decreased health- and weight-related quality of life (QOL).\textsuperscript{1,2}
- With the increasing prevalence of obesity, QOL may be affecting significantly more people, both those seeking treatment or non-treatment seeking people.
- Treatments targeted to promote weight loss in obese patients should ideally lead to improved quality of life.
- We examined the impact of weight loss achieved with a novel combination therapy of topiramate and phentermine on quality of life in obese patients.

Methods

**DESIGN**
- 24-week, randomized, double-blind, placebo-controlled trial

**INTERVENTIONS**
- 4 treatment groups
  - Placebo (PBO)
  - Phentermine (PHN)
  - Topiramate (TPM)
  - Combination (COM)
- Ancillary intervention of 500 kcal/d deficit diet and lifestyle counseling for all treatment groups

**SUBJECTS**
- 200 obese subjects (159 women, 41 men, mean [SE] BMI 38.6 [0.4] kg/m\textsuperscript{2})

**INCLUSION CRITERIA**
- Age 18-60 years
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VISITS
- Weeks 0, 2, 4, 8, 12, 16, 20, 24

KEY ASSESSMENTS
- Weight
- Impact of Weight on Quality of Life-Lite (IWQOL-Lite)³
  - The IWQOL-Lite is a 31-item self-report measure of weight-related quality of life that provides scores on five domains (physical function, self-esteem, sexual life, public distress, and work) plus a total score
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STATISTICAL ANALYSIS
- Intention-to-treat (ITT) sample with the last observation carried forward (LOCF)
- ANCOVA with baseline value as the covariate

Results

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ITT-LOCF analysis. Data shown as mean (SE) values
Figure 1. Changes in IWQOL-Lite Quality of Life

- Combination therapy (topiramate plus phentermine) and phentermine alone were associated with greater improvements in weight-related quality of life.
- Treatment with topiramate alone was not associated with appreciable improvements in quality of life relative to placebo.
- Positive changes in quality of life during treatment with the combination of phentermine and topiramate might be primarily influenced by phentermine.

References