Effects of Tirzepatide on Eating Behavior: A Phase 1 Study in People Living with Obesity

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BACKGROUND AND OBJECTIVE

• Tirzepatide is a first-in-class once-weekly glucose-dependent insulino-tropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist approved for treatment of people with type 2 diabetes (T2D) and under review for chronic weight management

• Tirzepatide is known to decrease body weight

Objective

• To test the effects of tirzepatide on energy intake (primary aim) and eating attitudes and behaviors (secondary aim) when compared to placebo and a GLP-1 receptor agonist (liraglutide)
**STUDY DESIGN**

*primary study objective at week 3

Phase 1, multicenter, randomized, partially blinded (LIR: open label, TZP/PBO: double blinded), placebo controlled, parallel arm study

LIR=liraglutide; PBO=placebo; PWO=people with obesity; QD=once daily; QW=once weekly; TZP=tirzepatide.

- **PBO** (N=39)
- **TZP** (N=37)
- **LIR** (N=38)

**Randomized 1:1:1 (Day -4)**

- **PWO** (N=114)

**6-Week Treatment Period**

- **PBO QW**
- **5 mg**
- **10 mg TZP QW**
- **0.6 mg**
- **1.2 mg**
- **1.8 mg**
- **2.4 mg**
- **3.0 mg LIR QD**

**Assessments at Baseline and Weeks 3 and 6**

- **Food intake** during ad libitum lunch
- **Appetite** via Visual Analog Scales (VAS) before lunch (“weekly” ratings were also assessed)
- **Food craving** via the Food Craving Inventory (FCI) and Food Craving Questionnaire-State (FCQ-S)
- **Disinhibition, hunger, and dietary restraint** via the Eating Inventory (EI)
- **Susceptibility to Food Environment** via the Power of Food Scale (PFS)
- **Impulsivity** via the Barratt Impulsiveness Scale (BIS)
# Baseline Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo (N=39)</th>
<th>Tirzepatide (N=37)</th>
<th>Liraglutide (N=38)</th>
<th>Overall (N=114)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
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<td>44.8 (10.2)</td>
<td>43.7 (11.9)</td>
<td>44.9 (10.5)</td>
</tr>
<tr>
<td>Male/female, n</td>
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<td>1/36</td>
<td>13/25</td>
<td>17/97</td>
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<tr>
<td>Race, n (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
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<tr>
<td>White</td>
<td>28 (71.8)</td>
<td>27 (73.0)</td>
<td>28 (73.7)</td>
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<td>Black or African American</td>
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<td>9 (24.3)</td>
<td>10 (26.3)</td>
<td>30 (26.3)</td>
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<tr>
<td>Weight, kg</td>
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<td>97.6 (16.0)</td>
<td>101.1 (19.5)</td>
<td>99.0 (18.8)</td>
</tr>
<tr>
<td>BMI, kg/m&lt;sup&gt;2&lt;/sup&gt;</td>
<td>36.2 (5.9)</td>
<td>36.1 (5.7)</td>
<td>36.2 (5.4)</td>
<td>36.2 (5.6)</td>
</tr>
<tr>
<td>27 - &lt;30, n (%)</td>
<td>6 (15.4)</td>
<td>5 (13.5)</td>
<td>4 (10.5)</td>
<td>15 (13.2)</td>
</tr>
<tr>
<td>30 - &lt;35, n (%)</td>
<td>12 (30.8)</td>
<td>12 (32.4)</td>
<td>13 (34.2)</td>
<td>37 (32.5)</td>
</tr>
<tr>
<td>35 – 50, n (%)</td>
<td>21 (53.8)</td>
<td>20 (54.1)</td>
<td>21 (55.3)</td>
<td>62 (54.4)</td>
</tr>
</tbody>
</table>

<sup>a</sup>1 patient in tirzepatide group identified with multiple races and was not counted in either race category.

Notes: Parameters are mean (SD) for continuous data unless otherwise noted.

BMI = body mass index; N = number of randomized patients; SD = standard deviation.
KEY RESULTS
Tirzepatide Significantly Decreased Food Intake at Lunch and Body Weight Compared to Placebo and Liraglutide at Week 3 and 6

Baseline mean: PBO = 893; TZP = 926; LIR = 1045

Baseline mean: PBO = 98; TZP = 98; LIR = 101

Throughout the slides:
- asterisks (*) reflect significant (p<0.05) differences when compared to placebo
- crosses (†) reflect significant (p<0.05) differences between tirzepatide and liraglutide

*p<0.05 vs. placebo. †p<0.05 vs. liraglutide.
Notes: Data are LSM (SE). Δ indicates change from baseline. Δ energy intake and Δ body weight were analyzed using MMRM with treatment, baseline BMI stratum, week and treatment-by-week interaction as fixed effects and baseline value as a covariate. BMI=body mass index; LIR=liraglutide; LSM=least squares mean; MMRM=mixed model for repeated measures; PBO=placebo; SE=standard error; TZP=tirzepatide.
Effects on Pre-Lunch Appetite

- Tirzepatide significantly decreased pre-lunch hunger and prospective food consumption, and increased satiety and fullness compared to placebo and liraglutide.

Notes: Data are LSM (SE). $\Delta$ indicates change from baseline. Scores (range 0-100) were analyzed using MMRM. Each question (satiety, fullness, prospective food consumption, and hunger) was rated from 0 (“not at all”) to 100 (“extremely”). Flint A et al, Int J Obes 2000;24:38-48. LIR=liraglutide; LSM=least squares mean; MMRM=mixed-model repeated measures; PBO=placebo; SE=standard error; TZP=tirzepatide; VAS=visual analog scale.
Effects on the Food Craving Inventory (FCI)

- The Food Craving Inventory (FCI) assesses **trait** cravings for specific types of foods (high fat foods, sweets, carbs/starches, fast food fats, fruits & vegetables, and overall cravings).
- Tirzepatide significantly decreased overall food cravings and cravings for sweets from baseline to week 3 and 6 compared to placebo and liraglutide.

*\( p<0.05 \) vs. PBO.
\( \dagger p<0.05 \) vs. LIR.

Notes: Data are LSM (SE). D indicates change from baseline. Each FCI item was scored on a 5-point Likert scale: 1=never, 2=rarely, 3=sometimes, 4=often, and 5=always. Overall score is mean from 5 items. White MA, et al. Obes Res. 2002;10(2):107-114. FCI=Food Craving Inventory; LIR=liraglutide; LSM=least squares mean; PBO=placebo; SE=standard error; TZP=tirzepatide.
Effects on the Food Craving Questionnaire - State (FCQ-S)

• Tirzepatide and liraglutide significantly decreased all FCQ-S subscales from baseline to week 6 compared to placebo.
• Tirzepatide significantly decreased all 5 FCQ-S subscales from baseline to week 3 compared to liraglutide.
• Tirzepatide significantly decreased the following 4 (of 5) FCQ-S subscales from baseline to week 6 compared to liraglutide (anticipation of negative reinforcement was nonsignificant):
  • Physiological state (e.g., hunger)
  • Lack of control over eating
  • Anticipation of positive reinforcement that may result from eating
  • Intense desire to eat

*p<0.05 vs. PBO. †p<0.05 vs. LIR.
Notes: Data are LSM (SE). ∆ indicates change from baseline. FCQ-S consists of 15 items. Each FCQ-S item was scored on a 5-point Likert scale: 1=strongly disagree to 5=strongly agree based on subject’s observations across the week. Subscale parameters are the means of associated questions. Cepeda-Benito A, et al. Behav Ther. 2000;31(1):151-173.
FCQ-S=Food Craving Questionnaire-State; LIR=liraglutide; LSM=least squares mean; PBO=placebo; SE=standard error; TZP=tirzepatide.
Effects on the Eating Inventory

- Compared to placebo and liraglutide, tirzepatide more effectively reduced hunger and disinhibition, which is the tendency to eat/overeat in response to external cues (e.g., the smell of food) and internal cues (e.g., anxiety).

- Interestingly and despite reduced food intake and body weight, tirzepatide and liraglutide did not statistically increase dietary restraint, which refers to the intention to limit food intake.
  - Both drugs increased restraint by ~2.5 points.

Notes: Data are LSM (SE). EI is a 51-item validated questionnaire assessing dietary restraint, disinhibition, and perceived hunger. Scores for restraint, disinhibition, and hunger range from 0-21, 0-18, and 0-14, respectively. A higher score indicates greater levels of the respective component. Stunkard AJ, et al. J Psychosom Res. 1985;29(1):71-83.

**EI=Eating Inventory; LIR=liraglutide; LSM=least squares mean; PBO=placebo; SE=standard error; TZP=tirzepatide.**
Effects on the Power of Foods Scale (PFS)

- Tirzepatide significantly decreased appetite for palatable foods at all 3 levels from baseline to week 3 and 6 compared to placebo and liraglutide.

*\(p<0.05\) vs. PBO.
†\(p<0.05\) vs. LIR.

Notes: Data are LSM (SE). \(\Delta\) indicates change from baseline. PFS measures the impact of living in a food-rich environment. Each item is scored on a 5-point Likert scale and subscale parameters are derived as the mean of each item. A higher score indicates a greater responsiveness to the food environment.


PFS=Power of Food Scale; LIR=liraglutide; LSM=least squares mean; PBO=placebo; SE=standard error; TZP=tirzepatide.
Effects on the Barratt Impulsiveness Scale (BIS)

- The BIS has six subscales and an overall score.
  - Higher scores indicate higher levels of impulsiveness.
- Tirzepatide significantly decreased overall impulsiveness and 2 BIS subscales from baseline to week 6 compared to placebo:
  - Cognitive Instability
  - Motor Impulsiveness
- Liraglutide did not demonstrate statistically significant differences in overall BIS or subscales compared to placebo

Notes: Data are LSM (SE). Δ indicates change from baseline. BIS is a 30-item self-reported measure describing impulsive behaviors and preferences. Items are rated on a 4-point scale ranging from 1=rarely/never to 4=almost always/always. Factors are derived as the mean of each item. Higher scores are indicative of higher impulsivity. Patton JH, et al. J Clin Psychol. 1995;51(6):768-774.

* p<0.05 vs. PBO. † p<0.05 vs. LIR.
CONCLUSIONS

• Compared to placebo and liraglutide, tirzepatide decreased:
  • Energy intake, body weight, appetite, food cravings, disinhibition, and reactivity to foods in the environment
  • Compared to placebo, tirzepatide, but not liraglutide, reduced some measures of impulsiveness

• Interestingly and at odds with most behavioral and dietary approaches to weight loss, tirzepatide and liraglutide had no significant effect on dietary restraint

• Limitations:
  • Liraglutide was open label (and had more men)
  • Longer therapy at maximum maintenance doses of both medications could elucidate further changes in eating attitudes and behaviors
BACKUP SLIDES
Patient Disposition

114 Enrolled and randomized

- 39 placebo
  - 2 adverse event
  - 3 withdrew consent
  - 34 Completed Study

- 37 Tirzepatide 5/10 mg QW
  - 3 adverse event
  - 3 withdrew consent
  - 31 Completed Study

- 38 Liraglutide 0.6 to 3 mg QD
  - 2 adverse event
  - 36 Completed Study
SAFETY

**Tirzepatide and liraglutide were generally well tolerated**

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N=39)</th>
<th>Tirzepatide (N=37)</th>
<th>Liraglutide (N=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AE</td>
<td>17 (43.6)</td>
<td>30 (81.1)</td>
<td>25 (65.8)</td>
</tr>
<tr>
<td>Mild</td>
<td>14 (35.9)</td>
<td>26 (70.3)</td>
<td>22 (57.9)</td>
</tr>
<tr>
<td>Moderate</td>
<td>6 (15.4)</td>
<td>14 (37.8)</td>
<td>5 (13.2)</td>
</tr>
<tr>
<td>Severe</td>
<td>0 (0)</td>
<td>2 (5.4)</td>
<td>1 (2.6)</td>
</tr>
<tr>
<td>Serious AE</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (2.6)</td>
</tr>
<tr>
<td>Discontinuation due to AE</td>
<td>2 (5.1)</td>
<td>3 (8.1)</td>
<td>2 (5.3)</td>
</tr>
<tr>
<td>AE related to study treatment</td>
<td>11 (28.2)</td>
<td>29 (78.4)</td>
<td>18 (47.4)</td>
</tr>
<tr>
<td>TEAE reported by &gt;10 participants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>2 (5.1)</td>
<td>19 (51.4)</td>
<td>11 (28.9)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1 (2.6)</td>
<td>11 (29.7)</td>
<td>4 (10.5)</td>
</tr>
<tr>
<td>Headache</td>
<td>3 (7.7)</td>
<td>7 (18.9)</td>
<td>3 (7.9)</td>
</tr>
<tr>
<td>Constipation</td>
<td>0 (0)</td>
<td>7 (18.9)</td>
<td>5 (13.2)</td>
</tr>
</tbody>
</table>

Data are number of participants (%) in all randomized participants who received ≥1 dose of study treatment. AE=adverse event, TEAE=treatment emergent AE
KEY RESULTS

Tirzepatide Significantly Decreased Food Intake Compared With Placebo and Liraglutide During Ad Libitum Lunch

Baseline mean: PBO = 893; TZP = 926; LIR = 1045

* p<0.05 vs. placebo. † p<0.05 vs. liraglutide. ‡ p<0.05 for week 6 vs. week 3.

Notes: Data are LSM (SE). Δ indicates change from baseline. LIR=liraglutide; LSM=least squares mean; PBO=placebo; SE=standard error; TZP=tirzepatide.
Tirzepatide Significantly Lowered Overall Appetite Compared to Placebo and Liraglutide

- At Weeks 3 and 6, tirzepatide significantly increased pre-lunch overall appetite VAS scores, indicating reduced appetite.

*\(p<0.05\) vs. PBO.
†\(p<0.05\) vs. LIR.

Notes: Data are LSM (SE). \(\Delta\) indicates change from baseline. Scores (range 0-100) were analyzed using MMRM. A higher overall score indicates less appetite; a lower overall score indicates more appetite. Overall score = (satiety + fullness + [100 - prospective food consumption] + [100 - hunger]) / 4. Each question (satiety, fullness, prospective food consumption, and hunger) was rated from 0 ("not at all") to 100 ("extremely"). Flint A et al, Int J Obes 2000;24:38-48. LIR=liraglutide; LSM=least squares mean; MMRM=mixed-model repeated measures; PBO=placebo; SE=standard error; TZP=tirzepatide; VAS=visual analog scale.
Tirzepatide Significantly Lowered Pre-lunch Appetite from Baseline to Week 3 Compared to Placebo and Liraglutide

- Tirzepatide significantly decreased pre-lunch hunger and prospective food consumption subscales, while increasing satiety and fullness compared to placebo and liraglutide

* *p<0.05 vs. PBO. †p<0.05 vs. LIR.

Notes: Data are LSM (SE). Δ indicates change from baseline. Scores (range 0-100) were analyzed using MMRM. A higher overall score indicates less appetite; a lower overall score indicates more appetite. Overall score = (satiety + fullness + [100 - prospective food consumption] + [100 - hunger]) / 4. Each question (satiety, fullness, prospective food consumption, and hunger) was rated from 0 ("not at all") to 100 ("extremely"). Flint A et al, Int J Obes 2000;24:38-48. LIR=liraglutide; LSM=least squares mean; MMRM=mixed-model repeated measures; PBO=placebo; SE=standard error; TZP=tirzepatide; VAS=visual analog scale.
Tirzepatide Significantly Improved Pre-lunch Appetite Ratings from Baseline to Week 6 Compared to Placebo and Liraglutide

- Tirzepatide significantly decreased pre-lunch hunger and prospective food consumption, and increased satiety and fullness compared to placebo and liraglutide.

*\( p<0.05 \) vs. PBO. †\( p<0.05 \) vs. LIR.

Notes: Data are LSM (SE). Δ indicates change from baseline. Scores (range 0-100) were analyzed using MMRM. A higher overall score indicates less appetite; a lower overall score indicates more appetite. Overall score = \( \frac{\text{satiety} + \text{fullness} + \text{prospective food consumption} + \text{hunger}}{4} \). Each question (satiety, fullness, prospective food consumption, and hunger) was rated from 0 ("not at all") to 100 ("extremely"). Flint A et al, Int J Obes 2000;24:38-48.

**LIR**=liraglutide; **LSM**=least squares mean; **MMRM**=mixed-model repeated measures; **PBO**=placebo; **SE**=standard error; **TZP**=tirzepatide; **VAS**=visual analog scale.
Tirzepatide Induced “Average” Weekly Appetite Changes from Baseline to Week 3

Analyses using retrospective VAS (average ratings over previous week) showed that tirzepatide reduced overall appetite and hunger compared to placebo and liraglutide.

Notes: Data are LSM (SE). Δ indicates change from baseline. Scores (range 0-100) were analyzed using MMRM. A higher overall score indicates less appetite; a lower overall score indicates more appetite. Overall score = (satiety + fullness + [100 - prospective food consumption] + [100 - hunger]) / 4. Each question (satiety, fullness, prospective food consumption, and hunger) was rated from 0 (“not at all”) to 100 (“extremely”). Flint A et al, Int J Obes 2000;24:38-48. LIR=liraglutide; LSM=least squares mean; MMRM=mixed-model repeated measures; PBO=placebo; SE=standard error; TZP=tirzepatide; VAS=visual analog scale.
Analyses using retrospective VAS (average ratings over previous week) showed that tirzepatide reduced overall appetite, hunger, and prospective food consumption compared to placebo and liraglutide.

Notes: Data are LSM (SE). Δ indicates change from baseline. Scores (range 0-100) were analyzed using MMRM. A higher overall score indicates less appetite; a lower overall score indicates more appetite. Overall score = (satiety + fullness + [100 - prospective food consumption] + [100 - hunger]) / 4. Each question (satiety, fullness, prospective food consumption, and hunger) was rated from 0 ("not at all") to 100 ("extremely"). Flint A et al, Int J Obes 2000;24:38-48. LIR=liraglutide; LSM=least squares mean; MMRM=mixed-model repeated measures; PBO=placebo; SE=standard error; TZP=tirzepatide; VAS=visual analog scale.
Tirzepatide significantly decreased food cravings from baseline to Week 3 compared with placebo.

<table>
<thead>
<tr>
<th>Baseline mean</th>
<th>Overall Score</th>
<th>High Fats</th>
<th>Sweets</th>
<th>CHO Starches</th>
<th>Fast Food Fats</th>
<th>Fruits and Vegetables</th>
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<tbody>
<tr>
<td></td>
<td>2.5</td>
<td>2.2</td>
<td>2.6</td>
<td>2.4</td>
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<td>2.3</td>
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<td>2.4</td>
<td>2.1</td>
<td>2.7</td>
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<td></td>
<td>2.7</td>
<td>2.5</td>
<td>2.6</td>
<td>2.6</td>
<td>3.2</td>
<td>2.4</td>
</tr>
</tbody>
</table>

* *p<0.05 vs. PBO.
† *p<0.05 vs. LIR.

Notes: Data are LSM (SE). Δ indicates change from baseline. Each FCI item was scored on a 5-point Likert scale: 1=never, 2=rarely, 3=sometimes, 4=often, and 5=always. Overall score is average from 5 items. White MA, et al. Obes Res. 2002;10(2):107-114. CHO=carbohydrates; FCI=Food Craving Inventory; LIR=liraglutide; LSM=least squares mean; PBO=placebo; SE=standard error; TZP=tirzepatide.

- Tirzepatide significantly decreased the overall FCI score, sweets, and fast food fats subscales at Week 3 compared with liraglutide.
Tirzepatide Significantly Decreased Food Cravings From Baseline to Week 6 Compared With Placebo

- Tirzepatide significantly decreased the overall FCI score and sweets subscale at Week 6 compared with liraglutide (results at week 3 were similar, with Fast Food Fats also significantly differing between tirzepatide and liraglutide).

Notes: Data are LSM (SE). \( \Delta \) indicates change from baseline. Each FCI item was scored on a 5-point Likert scale: 1=never, 2=rarely, 3=sometimes, 4=often, and 5=always. Overall score is average from 5 items. White MA, et al. Obes Res. 2002;10(2):107-114. CHO=carbohydrates; FCI=Food Craving Inventory; LIR=liraglutide; LSM=least squares mean; PBO=placebo; SE=standard error; TZP=tirzepatide.
Food Craving Questionnaire – State (FCQ-S)

• The FCQ-State measures cravings that occur in the moment and that are responsive to specific situations (e.g., food deprivation, eating).

• The FCQ-State has 5 subscales that reflect:
  1. an intense desire to eat
  2. anticipation of positive reinforcement from eating (e.g., pleasure)
  3. anticipation of negative reinforcement from eating (e.g., removal of an aversive state, such as depressed mood)
  4. lack of control over eating (e.g., difficulty eating just one)
  5. craving as a physiological state (e.g., hunger)
Tirzepatide Significantly Decreased State Food Cravings from Baseline to Week 3 Compared to Placebo and Liraglutide

*P<0.05 vs. PBO.
†P<0.05 vs. LIR.

Notes: Data are LSM (SE). ∆ indicates change from baseline. FCQ-S consists of 15 items. Each FCQ-S item was scored on a 5-point Likert scale: 1=strongly disagree to 5=strongly agree based on subject’s observations across the week. Subscale parameters are the means of associated questions. Cepeda-Benito A, et al. Behav Ther. 2000;31(1):151-173.
FCQ-S=Food Craving Questionnaire-State; LIR=liraglutide; LSM=least squares mean; PBO=placebo; SE=standard error; TZP=tirzepatide.
Tirzepatide Significantly Decreased Intensity of Momentary Food Cravings from Baseline to Week 6

*\(p<0.05\) vs. PBO. †\(p<0.05\) vs. LIR.

Notes: Data are LSM (SE). \(\Delta\) indicates change from baseline. FCQ-S consists of 15 items. Each FCQ-S item was scored on a 5-point Likert scale: 1=strongly disagree to 5=strongly agree based on subject’s observations across the week. Subscale parameters are the means of associated questions. Cepeda-Benito A, et al. Behav Ther. 2000;31(1):151-173.

\(FCQ-S=\)Food Craving Questionnaire-State; LIR=liraglutide; LSM=least squares mean; PBO=placebo; SE=standard error; TZP=tirzepatide.
Tirzepatide Significantly Decreased Tendency to Overeat and Perceived Hunger from Baseline to Week 3 Compared to Placebo and Liraglutide

Baseline mean:

<table>
<thead>
<tr>
<th></th>
<th>PBO</th>
<th>TZP 5 mg</th>
<th>LIR 1.8 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary Restraint</td>
<td>9.6</td>
<td>10.2</td>
<td>6.8</td>
</tr>
<tr>
<td>Tendency to Overeat (Disinhibition)</td>
<td>9.3</td>
<td>9.5</td>
<td>7.1</td>
</tr>
<tr>
<td>Perceived Hunger</td>
<td>9.4</td>
<td>9.2</td>
<td>6.5</td>
</tr>
</tbody>
</table>

*p<0.05 vs. PBO. †p<0.05 vs. LIR.

Notes: Data are LSM (SE). Δ indicates change from baseline. EI is a 51-item validated questionnaire assessing dietary restraint, disinhibition, and perceived hunger. Scores for restraint, disinhibition, and hunger range from 0-21, 0-18, and 0-14, respectively. A higher score indicates greater levels of the respective component. Stunkard AJ, et al. J Psychosom Res. 1985;29(1):71-83.

EI=Eating Inventory; LIR=liraglutide; LSM=least squares mean; PBO=placebo; SE=standard error; TZP=tirzepatide.
Tirzepatide Significantly Decreased Disinhibition and Perceived Hunger from Baseline to Week 6 Compared to Placebo and Liraglutide

• Interestingly and despite reduced food intake and body weight, Tirzepatide and Liraglutide did not increase dietary restraint or the cognitive intention to limit food intake.
  • Both drugs increased restraint by only ~2.5 points.

• Compared to placebo and Liraglutide, Tirzepatide more effectively reduced hunger and disinhibition, which is the tendency to eat/overeat in response to external cues (e.g., the smell of food) and internal cues (e.g., anxiety, depressed mood).

Baseline mean:

<table>
<thead>
<tr>
<th></th>
<th>PBO</th>
<th>TZP 10 mg</th>
<th>LIR 3.0 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disinhibition</td>
<td>9.6</td>
<td>10.2</td>
<td>6.8</td>
</tr>
<tr>
<td>Hunger</td>
<td>9.3</td>
<td>9.5</td>
<td>7.1</td>
</tr>
<tr>
<td>Body Weight</td>
<td>9.4</td>
<td>9.2</td>
<td>6.5</td>
</tr>
</tbody>
</table>

*↑p<0.05 vs. PBO. †p<0.05 vs. LIR.

Notes: Data are LSM (SE). △ indicates change from baseline. EI is a 51-item validated questionnaire assessing dietary restraint, disinhibition, and perceived hunger. Scores for restraint, disinhibition, and hunger range from 0-21, 0-18, and 0-14, respectively. A higher score indicates greater levels of the respective component. Stunkard AJ, et al. J Psychosom Res. 1985;29(1):71-83.

EI=Eating Inventory; LIR=liraglutide; LSM=least squares mean; PBO=placebo; SE=standard error; TZP=tirzepatide.
Power of Foods Scale (PFS) Results

• The PFS assesses the impact of living in a food-rich environment.

• The PFS measures appetite for palatable foods at three levels of proximity:
  1. **Food available**, reflecting reactions to an environment where food is always available but not present.
  2. **Food present**, reflecting reactions to foods when they are present but not yet tasted.
  3. **Food tasted**, reflecting reactions to foods when they are first tasted but not yet consumed.

Tirzepatide Significantly Decreases Appetite for Palatable Food in Proximity From Baseline to Week 3 Compared to Placebo and Liraglutide

Baseline mean:

<table>
<thead>
<tr>
<th></th>
<th>PBO</th>
<th>TZP 5 mg</th>
<th>LIR 1.8 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.0</td>
<td>3.2</td>
<td>2.9</td>
<td>3.6</td>
</tr>
<tr>
<td>2.8</td>
<td>2.9</td>
<td>2.6</td>
<td>3.7</td>
</tr>
<tr>
<td>3.6</td>
<td>3.7</td>
<td>3.4</td>
<td>3.0</td>
</tr>
</tbody>
</table>

Notes: Data are LSM (SE). Δ indicates change from baseline. PFS measures the impact of living in a food-rich environment. Each item is scored on a 5-point Likert scale and subscale parameters are derived as the mean of each item. A higher score indicates a greater responsiveness to the food environment. Lowe MR, et. al. Appetite. 2009;53(1):114-118.

*Δp<0.05 vs. PBO. †p<0.05 vs. LIR.

PFS=Power of Food Scale; LIR=liraglutide; LSM=least squares mean; PBO=placebo; SE=standard error; TZP=tirzepatide.
Tirzepatide Significantly Decreased Appetite for Palatable Foods at All 3 Levels from Baseline to Week 6 Compared to Placebo and Liraglutide

Baseline mean:

<table>
<thead>
<tr>
<th></th>
<th>Placebo (Mean)</th>
<th>Liraglutide (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Score</td>
<td>3.0</td>
<td>2.8</td>
</tr>
<tr>
<td>Food Available</td>
<td>3.2</td>
<td>2.9</td>
</tr>
<tr>
<td>Food Present</td>
<td>3.6</td>
<td>3.7</td>
</tr>
<tr>
<td>Food Tasted</td>
<td>3.0</td>
<td>3.1</td>
</tr>
</tbody>
</table>

* p<0.05 vs. PBO. † p<0.05 vs. LIR.

Notes: Data are LSM (SE). Δ indicates change from baseline. PFS measures the impact of living in a food-rich environment. Each item is scored on a 5-point Likert scale and subscale parameters are derived as the mean of each item. A higher score indicates a greater responsiveness to the food environment. Lowe MR, et. al. Appetite. 2009;53(1):114-118.

PFS=Power of Food Scale; LIR=liraglutide; LSM=least squares mean; PBO=placebo; SE=standard error; TZP=tirzepatide.
Tirzepatide Significantly Decreased Impulsiveness From Baseline to Week 3 Compared to Placebo

Notes: Data are LSM (SE). Δ indicates change from baseline. BIS is a 30-item self-reported measure describing impulsive behaviors and preferences. Items are rated on a 4-point scale ranging from 1=rarely/never to 4=almost always/always. Factors are derived as the mean of each item. Higher scores are indicative of higher impulsivity. Patton JH, et al. J Clin Psychol. 1995;51(6):768-774.

BIS=Barratt Impulsiveness Scale; LIR=liraglutide; LSM=least squares mean; PBO=placebo; SE=standard error; TZP=tirzepatide.
Tirzepatide Significantly Decreased Impulsiveness From Baseline to Week 6 Compared to Placebo

*\(p<0.05\) vs. PBO. †\(p<0.05\) vs. LIR.

Notes: Data are LSM (SE). \(\Delta\) indicates change from baseline. BIS is a 30-item self-reported measure describing impulsive behaviors and preferences. Items are rated on a 4-point scale ranging from 1=rarely/never to 4=almost always/always. Factors are derived as the mean of each item. Higher scores are indicative of higher impulsivity. Patton JH, et al. J Clin Psychol. 1995;51(6):768-774.

BIS=Barratt Impulsiveness Scale; LIR=liraglutide; LSM=least squares mean; PBO=placebo; SE=standard error; TZP=tirzepatide.