Hypertension

RESEARCH LETTER

Tirzepatide Reduces 24-Hour Ambulatory Blood Pressure in Adults With Body Mass Index ≥27 kg/m^2: SURMOUNT-1 Ambulatory Blood Pressure Monitoring Substudy

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Obesity is a risk factor for hypertension and cardiovascular disease. In SURMOUNT-1, tirzepatide, the glucose-dependent insulinotropic polypeptide/GLP-1 (glucagon-like peptide-1) receptor agonist approved in the United States for treatment of type 2 diabetes and obesity, provided substantial weight loss and reduced office blood pressure (BP).[1] This study assessed the effect of tirzepatide on 24-hour BP, measured by ambulatory BP monitoring (ABPM), in people with the disease of obesity but without type 2 diabetes.

SURMOUNT-1 (N=2539; NCT04184622: https://clinicaltrials.gov/study/NCT04184622) was a randomized, placebo-controlled trial investigating the effects of once-weekly tirzepatide (5, 10, and 15 mg) in adults with a body mass index (BMI) ≥27 kg/m^2.[1] A subset of participants underwent 24-hour ABPM at baseline and week 36 as part of a prospectively planned substudy. Key inclusion criteria for the substudy were BP <140/90 mm Hg and stable (≥3 months) antihypertensive therapy, if used. BP was measured every 30 minutes during daytime (07:00–22:00 hours) and every 60 minutes during nighttime (22:00–07:00 hours) over a 24- to 27-hour period using an Oscar 2 Monitor (SunTech Medical). Only participants with ≥70% valid readings on ABPM and a minimum of 20 daytime and 7 nighttime readings were included in the analyses.[2]

Mixed model repeated measures were used to compare changes in ABPM parameters from baseline to week 36 between tirzepatide and placebo with an unstructured covariance matrix.

The substudy enrolled 600 participants (155 placebo, 145 tirzepatide 5 mg, 152 tirzepatide 10 mg, and 148 tirzepatide 15 mg); 68.7% female, 66.8% White, and 25.0% Hispanic. Mean (SD) age was 45.5 (12.9) years, and BMI was 37.4 (6.8) kg/m^2; 30.0% of participants reported hypertension at baseline, and 29.0% reported the use of ≥1 antihypertensive medication. Overall, 494 participants had valid ABPM data at baseline and week 36.

The baseline mean (SD) 24-hour systolic BP was 124.6 (10.4) mm Hg, with no significant between-group differences. Treatment with each tirzepatide dose reduced 24-hour systolic BP at 36 weeks compared with placebo. The placebo-adjusted systolic BP change from baseline was −7.4 (95% CI, −10.0 to −4.7) mm Hg for 5-mg tirzepatide, −10.6 (95% CI, −13.2 to −8.0) mm Hg for 10-mg tirzepatide, and −8.0 (95% CI, −10.6 to −5.4) mm Hg for 15-mg tirzepatide (Figure [A]). Results were consistent for both day and nighttime BP, with significant reductions versus placebo for each tirzepatide dose (Figure [A]). There were no significant interactions by baseline age, sex, BMI, systolic BP, the presence of hypertension, antihypertensive medication use, or glycemic status (prediabetes: yes/no) for the change in 24-hour mean systolic BP (Figure [C]). For pooled tirzepatide doses,

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Nonstandard abbreviations and acronyms

ABPM	ambulatory blood pressure monitoring
BMI	body mass index
BP	blood pressure
GLP-1	glucagon-like peptide-1

change in 24-hour systolic BP correlated with change in body weight (r=0.31; *P*<0.0001). Mediation analyses indicated that changes in ambulatory systolic BP were partially mediated by weight changes (percentage mediated, 70.0% [95% CI, 47.0–102.6]).

At baseline, the mean (SD) overall 24-hour diastolic BP from ABPM was 72.1 (7.7) mm Hg, with no between-group differences. At week 36, 24-hour diastolic BP decreased from baseline versus placebo in participants who received tirzepatide 5 mg (−2.0 [95% CI, −3.6 to −0.3] mm Hg) and 10 mg (−2.9 [95% CI, −4.5 to −1.3] mm Hg) but not 15 mg (−0.5 [95% CI, −2.0 to 1.1] mm Hg; Figure [B]).

The mean 24-hour heart rate was 77.4 (8.7) beats per minute at baseline and did not differ between treatment groups. At week 36, heart rate increased with tirzepatide versus placebo by 2.1 (95% CI, 0.3–3.9), 2.3 (95% CI, 0.6–4.1), and 5.4 (95% CI, 3.6–7.1) beats per minute, respectively, with tirzepatide 5, 10, and 15 mg.

This study demonstrated the BP-lowering effects of tirzepatide in people with BMI ≥27 kg/m^2, during both daytime and nighttime. Reductions in 24-hour systolic BP were consistent across subgroups of participants

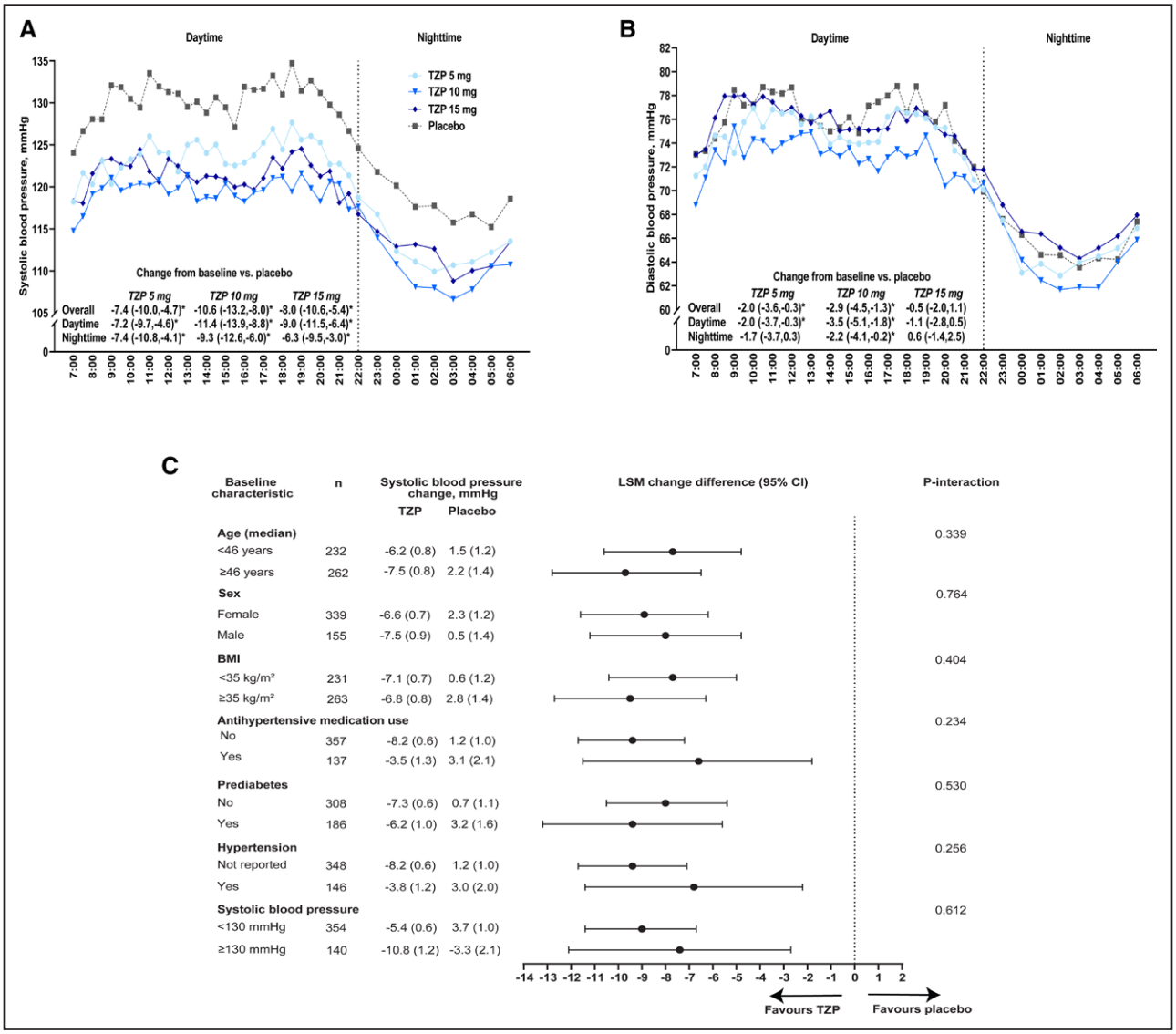

Figure. 24-hour ambulatory systolic and diastolic blood pressure at week 36 among SURMOUNT-1 participants.
Mean 24-hour ambulatory systolic (**A**) and diastolic (**B**) blood pressure with least squares mean (LSM; 95% CI) change difference from baseline vs placebo and (**C**) 24-hour ambulatory systolic blood pressure LSM (SE) and LSM difference (95% CI) between pooled tirzepatide (TZP) doses and placebo among subgroups at week 36. BMI indicates body mass index. n indicates the number of participants in the subgroup with baseline and week 36 value. *P<0.05 vs placebo.

stratified by clinically relevant factors, including age, sex, BMI, and hypertension-related factors. This study demonstrates that tirzepatide improves 24-hour BP in obesity-related hypertension. While being consistent with in-office measurement,[1] the current study uses a method that is superior to office BP alone for predicting cardiovascular risk.[3] Furthermore, nighttime systolic BP, which is a stronger predictor for cardiovascular death and all-cause death than daytime and 24-hour systolic BP, was also significantly reduced by tirzepatide.[3] Correlation and mediation analyses indicated that tirzepatide-induced body weight reduction effects were associated with BP reductions, but tirzepatide, as a GLP-1/glucose-dependent insulinotropic polypeptide receptor agonist, may also have effects on BP independent of weight loss.

An increase in the heart rate was observed, as expected from GLP-1 receptor agonist studies in people living with obesity.[4,5] In SURMOUNT-1, after 72 weeks, changes in pulse from baseline were 0.6, 2.3, and 2.6 beats per minute in tirzepatide 5-, 10-, and 15-mg groups, respectively, compared with 0.1 beats per minute in the placebo group.[1] This suggests that the heart rate increase may attenuate with continued treatment over a longer time frame than this 36-week data.

Strengths of this study include the use of 24-hour ABPM, providing a more comprehensive assessment of trends than in-office BP measurements. Limitations include that ABPM was only conducted in a subset of the SURMOUNT-1 population. Additionally, BP was only measured at baseline and 1 other time point, and measurements were only taken once per hour at night to minimize participant burden. Changes in food intake and 24-hour urine sodium excretion were not assessed. Thus, the contribution of dietary modifications, including salt intake, to BP changes cannot be estimated.

These data provide further evidence for the potential benefits of tirzepatide on cardiometabolic health and cardiovascular outcomes.

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