IMPACT OF SUBCUTANEOUS VK2735 ON WEIGHT, PREDIABETES, AND CARDIOMETABOLIC STATUS: THE VENTURE STUDY

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INTRODUCTION

- Nearly 75% of US adults have overweight or obesity, with approximately 42% having obesity[1,2]
- Obesity / overweight is associated with increased comorbidities and negative health outcomes
- Prediabetes (FPG 100 – 125 mg/dL or HbA1c 5.7 – 6.4% inclusive) is associated with increased risk of progression to type 2 diabetes, poor cardiovascular outcomes, and chronic kidney disease[3]
- Metabolic syndrome (MetS) is a clustering of cardiometabolic risk factors (e.g., increased waist circumference, increased blood glucose, increased blood pressure, increased triglyceride blood levels, and decreased high density lipoprotein cholesterol blood levels) that is associated with an increase in cardiovascular disease risk, and facilitated by genetic predisposition, excess body fat, insulin resistance, unhealthful nutrition, physical inactivity, certain medications, and aging[4,5]
- Cardiovascular-Kidney-Metabolic (CKM) syndrome is a complex health condition involving the interconnected risks of heart disease, kidney disease, and metabolic disorders, like type 2 diabetes and obesity[6]
- VK2735 is a GIP/GLP-1 inhibitor in development for treatment (tx) of obesity/overweight and related complications

OBJECTIVE

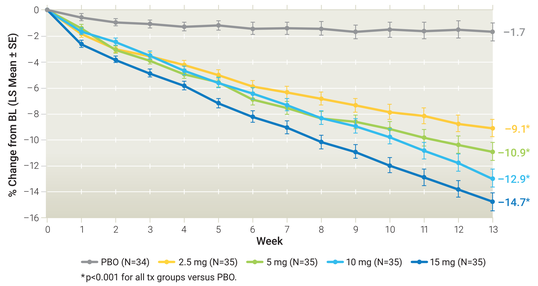
- The objective of this analysis was to assess the impact of VK2735 on cardiometabolic parameters, including prediabetes and MetS

METHODS

- VENTURE was phase 2 study (NCT06068946)
- Adults with a BMI ≥30 kg/m², or BMI ≥27 kg/m² and ≥1 weight-related comorbid condition, received once-weekly subcutaneous injections of VK2735 or matched placebo (PBO) for 13 weeks
- Primary endpoint was the percentage change in body weight from baseline (BL) to week 13
- Exploratory analyses included change in prediabetes and MetS status from BL to week 13

VK2735 SIGNIFICANTLY REDUCED BODY WEIGHT AND DECREASED THE PREVALENCE OF PREDIABETES AND METS OVER 13 WEEKS

Every VK2735 Group had Significant Weight Loss by Week 13

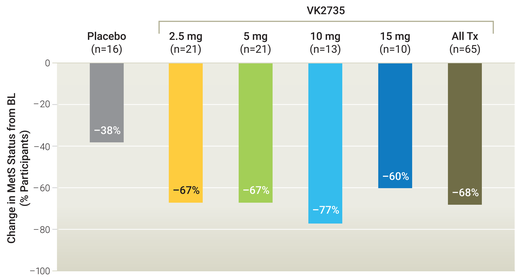


*p<0.001 for all tx groups versus PBO.

Weight Loss

- Participants in every VK2735 tx group had significant weight loss from BL within 13 weeks
- No weight loss plateau was observed at week 13

VK2735 Groups were Less Likely to Have Metabolic Syndrome at Week 13

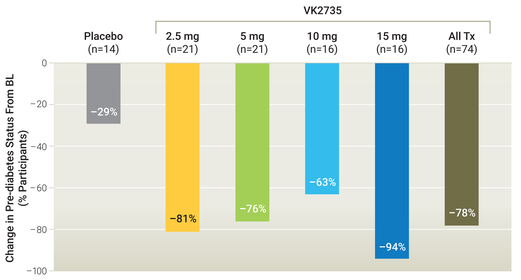


Includes all participants who had confirmed MetS at BL and enough MetS component Week 13 data collected to determine MetS status at end of study.

Decrease in Metabolic Syndrome

- Participants receiving VK2735 (combined tx groups) had significantly greater odds of transitioning from meeting MetS criteria at BL to not meeting them by week 13 compared to placebo (OR: 6.74; p=0.02)

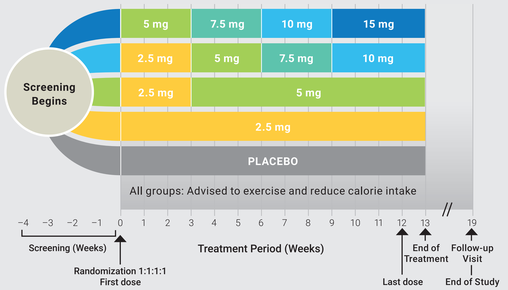
VK2735 Groups were Less Likely to Meet Criteria for Prediabetes at Week 13



Prediabetes Shift to Normoglycemia

- Participants receiving VK2735 (combined tx groups) had significantly greater odds of transitioning from prediabetes at BL to normoglycemia by week 13 compared to placebo (OR: 9.1; p=0.0008)

VENTURE Was A 5-Arm, 13-Week, Randomized, PBO-Controlled Study



Demographics Were Well Matched Across Groups (N=176)

Characteristic	Placebo (n=35)	2.5 mg (n=35)	5.0 mg (n=35)	10 mg (n=36)	15 mg (n=35)	All VK2735 (n=141)
Age, years, mean (SD)	47.6 (16.4)	49.7 (13.9)	51.8 (14.1)	47.1 (13.4)	51.3 (15.4)	49.9 (14.2)
Female, n (%)	29 (83)	27 (77)	23 (66)	24 (67)	27 (77)	101 (72)
Race, n (%)						
White	26 (74)	28 (80)	31 (89)	26 (72)	28 (80)	113 (80)
Black or African American	8 (23)	7 (20)	2 (6)	10 (28)	6 (17)	25 (18)
Ethnicity, n (%)						
Not Hispanic or Latino	28 (80)	29 (83)	28 (80)	30 (83)	30 (86)	117 (83)
Weight, kg, mean (SD)	104 (22.2)	103(19.0)	98 (13.2)	103 (18.3)	101 (18.9)	101 (17.4)
BMI, kg/m², mean (SD)	38.88 (6.3)	38.03 (5.6)	35.86 (4.0)	36.62 (4.2)	36.63 (5.2)	36.78 (4.8)
Pre-diabetes,[a] n (%)	14 (40)	21 (60)	21 (60)	16 (44)	16 (45.7)	74 (52.5)
MetS,[b] n/N (%)	18/34 (53)	21/35 (60)	22/35 (63)	14/35 (40)	13/35 (37)	70/140 (50)

Abbreviations: BMI, body mass index; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; SD, standard deviation.

[a]Pre-diabetes defined as FPG 100 – 125 mg/dL or HbA1c 5.7 – 6.4%.

[b]Participants who met MetS criteria at BL. MetS criteria are having ≥3 of 5 factors: abdominal obesity (ie, waist circumference >40 inches [101.6 cm] in men and >35 inches [88.9 cm] in women), high blood pressure, high fasting blood sugar, high triglycerides, low HDL (good) cholesterol.

CKM Measures: Change from BL at Week 13

Measure	Placebo BL	Placebo Δ	VK2735 BL	VK2735 Δ
Change from baseline in absolute value				
hsCRP, mg/L, median (range)	4.50 (0.2-55.0)	0.20 (-34.6, 40.5)	3.60 (0.2-63.9)	-0.30 (-53.8, 11.0)
SBP, mmHg, mean (SE)	125.1 (13.96)	-4.4 (13.80)	125.1 (14.61)	-7.7 (12.92)
DBP, mmHg, mean (SE)	80.9 (9.17)	-2.2 (9.37)	80.4 (8.64)	-3.7 (8.34)
HbA1c, % (SD)	5.49 (0.361)	0.04 (0.207)	5.49 (0.355)	-0.29 (0.249)
Waist circumference, cm, mean (SD)	115.34(15.51)	-1.18 (5.86)	112.58 (11.66)	-9.49 (5.61)
ALT, IU/L, mean (SD)	23.1 (12.32)	-1.5 (8.87)	23.2 (15.66)	-2.5 (16.66)
AST, IU/L, mean (SD)	19.6 (5.23)	-0.1 (5.21)	20.0 (8.34)	-0.9 (8.37)
Albumin, g/L, mean (SD)	4.24 (0.208)	-0.04 (0.217)	4.27 (0.290)	0.02 (0.227)
Creatinine, mg/dl, mean (SD)	0.731 (0.1223)	-0.008 (0.0652)	0.801 (0.1961)	0.004 (0.1343)
eGFR, ml/min/1.73m², mean (SD)	102.7 (17. 70)	1.0(5.17)	97.0 (17.20)	-1.0 (9.36)
Percent change from baseline				
Total cholesterol, mg/dl, mean (SD)	204.1 (49.45)	-3.11 (12.35)	194.9 (40.69)	-7.91 (15.07)
Triglyceride, mg/dl, mean (SE)	140.7 (99.02)	2.74 (40.51)	120.9 (59.65)	-2.53(41.95)

CONCLUSIONS

- VK2735 significantly reduced body weight over the 13-week treatment period with no evidence of plateau
- VK2735 improved cardiometabolic parameters, reducing the prevalence of prediabetes and MetS by week 13
- Results suggest that treatment with VK2735 may reduce the risk of patients transitioning from pre-diabetic to diabetic status
- VK2735 demonstrated an encouraging safety and tolerability profile, with the incidence of GI AEs largely subsiding over time
- VK2735 may be an effective option for the treatment of individuals with overweight and obesity
- Phase 3 VANQUISH-1 (NCT07104500; see ObesityWeek Modesto poster) and VANQUISH-2 (NCT07104383) studies are currently enrolling participants with obesity or overweight

SAFETY & TOLERABILITY

- Among participants receiving VK2735, the majority (92%) reported drug-related TEAEs as mild or moderate in severity
- Most common TEAEs were GI related: nausea, constipation, vomiting and diarrhea, which substantially subsided after titration

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DISCLOSURES

The VENTURE study was supported by Viking Therapeutics, Inc (San Diego, CA). All authors are either principal site investigators for the VENTURE trial, and sites were given remuneration for conducting the trial, or are employees of Viking Therapeutics, Inc.