

# Impact of Tesamorelin on Cardiovascular Disease Risk Prediction Scores in Phase 3 Studies

## Treatment Arms: Subanalysis

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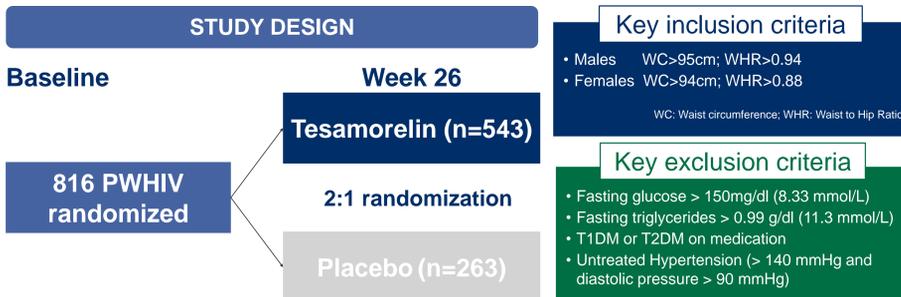
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### Background

- ▶ The risk of cardiovascular disease (CVD) is nearly twice as high for persons with HIV (PWH) as the general population.<sup>1</sup>
- ▶ Excess visceral abdominal fat (EVAF), the key characteristic of central adiposity, has also been associated with an increased risk of CVD in PWH.<sup>2</sup>
- ▶ Tesamorelin, a growth hormone-releasing hormone analog, has previously demonstrated significant reductions in EVAF in two phase 3 randomized controlled trials in PWH.<sup>3</sup>
- ▶ The impact of the reduction of EVAF from tesamorelin on CVD outcomes has been unknown.

Here, we aimed to determine the impact of reducing EVAF by tesamorelin on 10-year ASCVD risk scores.

### Methods



- ▶ Data from two Phase III trials of tesamorelin among PWH with excess VAT was leveraged, where participants were randomized to tesamorelin (2mg) vs placebo daily for 26 weeks.<sup>3-5</sup>
- ▶ Measurements of body composition, as assessed by computerized tomographic (CT) scan, and lipid and metabolic parameters were taken at baseline and 26 weeks.
- ▶ 10-year atherosclerotic cardiovascular disease (ASCVD) and Framingham risk scores were calculated for participants in treatment arms at baseline and 26 weeks.
- ▶ *Statistical analysis:* An effect analysis was conducted to characterize the significance of treatment impact via intermediate variables that factor into 10-year ASCVD risk prediction changes.
  - ▶ Modifiable variables included systolic and diastolic blood pressure, total cholesterol (TC), high-density and low-density lipoprotein (HDL, LDL).

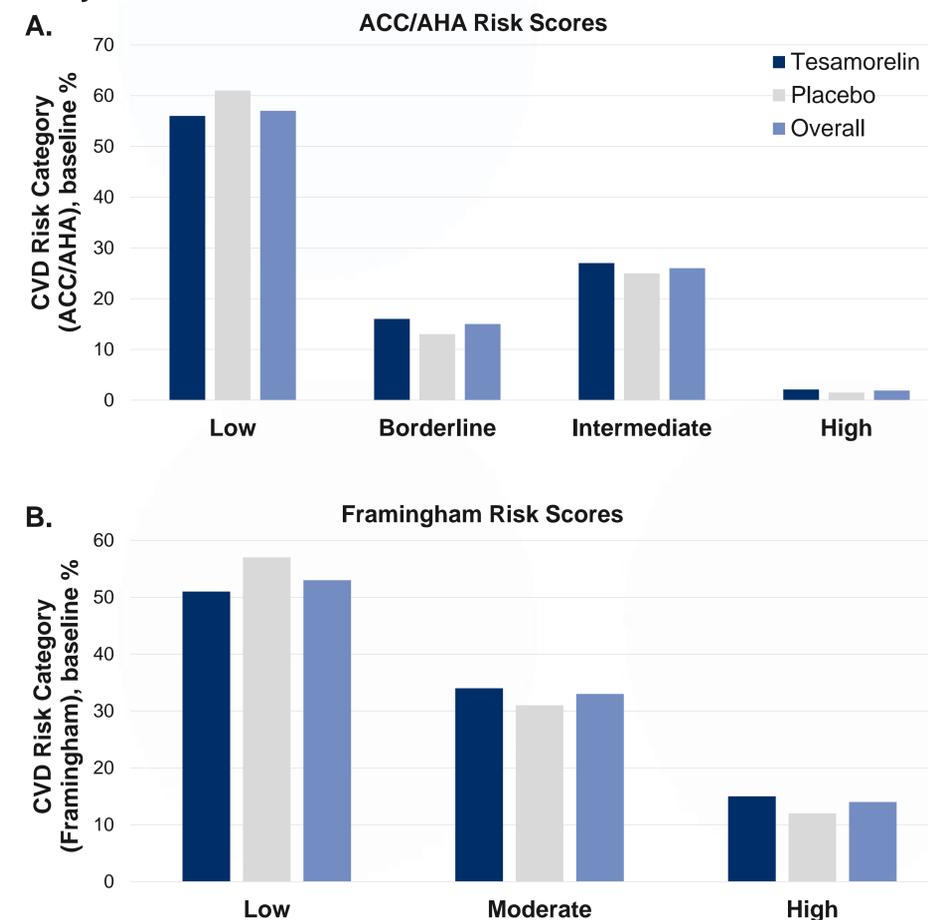
### Results

Table 1: Participant characteristics overall and by randomization arm.

	Tesamorelin (n=543)	Placebo (n=263)	Overall (n=806)
Age (years)	47 (43, 53)	48 (43, 54)	47 (43, 53)
Sex – Male†	465 (86%)	220 (84%)	685 (85%)
Race†			
White	418 (77%)	195 (74%)	613 (76%)
Black or African American	71 (13%)	34 (13%)	105 (13%)
Other/Unknown	54 (9.9%)	34 (13%)	88 (11%)
BMI mean (kg/m <sup>2</sup> )	28.4 (26.3, 31.0)	28.3 (26.2, 31.4)	28.4 (26.2, 31.1)
VAT (cm <sup>2</sup> )	171 (122, 236)	164 (119, 233)	168 (121, 234)
Total cholesterol (mg/dL)	188 (164, 220)	192 (167, 218)	188 (165, 218)
HDL cholesterol (mg/dL)	42 (36, 53)	44 (37, 52)	43 (36, 53)
Lipid-lowering medication†	238 (44%)	113 (43%)	351 (44%)
Blood pressure medication†	199 (37%)	89 (34%)	288 (36%)
Diabetes status†	97 (18%)	40 (15%)	137 (17%)

Values reported as Median (IQR); †: values reported as n.

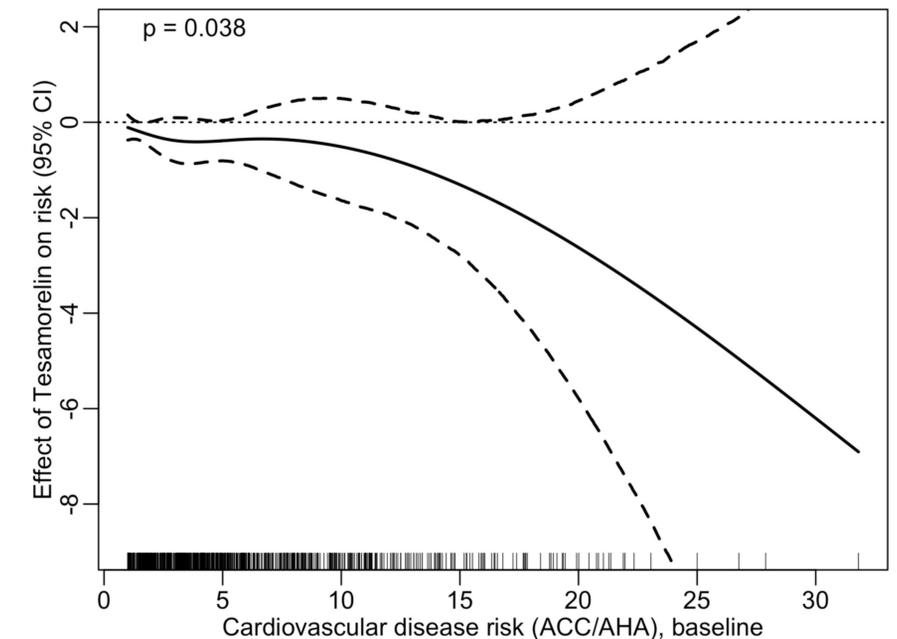
Figure 1: Cardiovascular risk classifications of study participants at study baseline.



Cardiovascular risk scores were calculated – both by ACC/AHA criteria (A) and Framingham risk calculations (B) - to assess baseline characteristics of the study population. Percentages within each risk category are shown.

### Results (continued)

Figure 2: Participants in the tesamorelin arm tended towards a modest reduction in 10-year ASCVD risk prediction.



Estimates of the effect of tesamorelin on average cardiovascular risk score, as calculated using 10-year ASCVD risk score (ACC/AHA), are presented as a figure that displays the estimated effect as a function of baseline risk. Pointwise 95% confidence intervals are displayed, along with a rug plot showing the distribution of the baseline 10-year ASCVD risk score.

- ▶ Tesamorelin was associated with an estimated decrease in ASCVD risk score of -0.40% (95% CI -0.89%, 0.05%).
- ▶ The reduction in CVD risk was relatively larger among subjects with higher CVD risk at baseline (p=0.038 for overall trend among all participants).
- ▶ Reductions in ASCVD risk score were driven predominantly by reductions in total cholesterol (TC), independent of lipid lowering therapies.

### Conclusions

- ▶ This analysis provides evidence that reductions in excess visceral fat with tesamorelin lead to a significant reduction in forecasted CVD risk in PWH, resulting from reduction in TC even among a group heavily treated with lipid-lowering therapy.
- ▶ Given the increasing prevalence of obesity and central adiposity in PWH, more attention should be given to targeting visceral fat when considering CVD risk management.

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<sup>1</sup>Shah et al, *Circulation* 2018; <sup>2</sup>Orlando et al, *JAIDS* 2012; <sup>3</sup>Falutz et al, *AIDS* 2008; <sup>4</sup>Falutz et al, *J AcquirImmuneDeficSyndr.* 2010; <sup>5</sup>Falutz et al, *J Clin Endocrinol Metab.* 2010.