

Efficacy and Safety of Semaglutide 2.4 mg by Race and Ethnicity

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Plain Language Summary

- Why does it matter?** People living with obesity face physical, social, and financial burdens that impact their daily lives. Certain racial and ethnic groups are at greater risk for obesity, and new treatments may be helpful for these groups
- How does it work?** People (aged ≥18 years) from multiple countries were treated for obesity using a drug (semaglutide). Scientists gathered data on demographics, body weight, and side effects of treatment over the course of the study and processed it by racial and ethnic subgroups
- What did we find?** Semaglutide treatment was effective for reducing body weight within each racial and ethnic subgroup. The treatment appeared to be equally effective for every subgroup. There was no apparent impact on safety or side effects across subgroups

Introduction

- Globally, obesity is a chronic disease with few options for pharmacologic intervention^{1,2}
- Obesity is more prevalent in some racial and ethnic minority groups, which may be disproportionately affected by the negative physical, social, and financial effects of obesity³
- Semaglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist, tested for body weight reduction in the Semaglutide Treatment Effect in People with Obesity (STEP) clinical trials⁴⁻⁶
- The present analyses evaluated the tolerability and effect of semaglutide 2.4 mg treatment among participants in STEP 1 & 3 (people with obesity) and STEP 2 (people with obesity and type 2 diabetes) by race and ethnicity

Methods

- The STEP trials were US- or global-based, blinded, randomized, placebo-controlled, phase 3 clinical trials evaluating the safety and efficacy of once-weekly, subcutaneous semaglutide 2.4 mg in adults aged ≥18 years
- Given the similarity in study objectives, design, and population, STEP 1 & 3 results were pooled for analysis, and STEP 2 analyses were conducted separately
- Analyses of % weight change from baseline to week 68 were conducted separately by ethnicity (Hispanic or Latino, not Hispanic or Latino, or not applicable/unknown) and race (Asian, Black, White, or other [includes “not applicable” responses])
- The primary outcome was the estimated treatment difference (ETD) for % weight change with semaglutide 2.4 mg vs placebo
- Secondary outcomes included the odds ratio of achieving ≥5%, ≥10%, or ≥15% body weight loss vs placebo by week 68 and the occurrence of adverse events (AEs; analyzed descriptively)

- Analyses addressed the treatment policy estimand. Tests for interaction between treatment and subgroup were performed at 5% significance level; *P* values were not adjusted for multiplicity

Results

- In STEP 1 & 3 and STEP 2, the participants had an average body mass index (BMI) of 37.9 and 35.9 and a mean age of 46 and 55 years, respectively (**Table 1**)

Table 1: Participant demographics and baseline characteristics for STEP 1 & 3 and STEP 2

STEP 1 & 3				
	Asian	Black	White	Other
n (%)	272 (10.6)	227 (8.8)	1937 (75.3)	136 (5.3)
Sex, n (%)				
Female	148 (54.4)	207 (91.2)	1509 (77.9)	84 (61.8)
Male	124 (45.6)	20 (8.8)	428 (22.1)	52 (38.2)
Ethnicity, n (%)				
Not Hisp./Latino	272 (100)	223 (98.2)	1642 (84.8)	22 (16.2)
Hisp./Latino	0	4 (1.8)	295 (15.2)	58 (42.6)
NA/unknown	0	0	0	56 (41.1)
Age (SD), y	42 (12)	46 (12)	47 (13)	43 (13)
Weight (SD), kg	91.4 (16.9)	109.1 (22.3)	106.9 (21.8)	106.7 (25.8)
BMI (SD), kg/m²	34.5 (5.5)	39.1 (6.7)	38.2 (6.7)	38.1 (7.0)
HbA1c (SD), %	5.8 (0.3)	5.8 (0.4)	5.7 (0.3)	5.7 (0.4)
STEP 2				
	Asian	Black	White	Other
n (%)	220 (27.3)	72 (8.9)	479 (59.4)	36 (4.5)
Sex, n (%)				
Female	110 (50)	53 (73.6)	231 (48.2)	19 (52.8)
Male	110 (50)	19 (26.4)	248 (51.8)	17 (47.2)
Ethnicity, n (%)				
Not Hisp./Latino	220 (100)	72 (100)	388 (81.0)	31 (86.1)
Hisp./Latino	0	0	91 (19.0)	5 (13.9)
Age (SD), y	50 (10)	56 (9)	58 (10)	50 (12)
Weight (SD), kg	87.4 (16.3)	107.9 (21.7)	105.2 (21.7)	97 (17.3)
BMI (SD), kg/m²	32.9 (4.5)	38.7 (5.9)	36.9 (6.9)	35.2 (4.9)
HbA1c (SD), %	8.2 (0.8)	8.0 (0.7)	8.1 (0.8)	8.1 (0.9)

- In both populations, the majority of participants reported their race as White and ethnicity as not Hispanic or Latino
- The treatment effect of semaglutide 2.4 mg vs placebo ranged from 9.3% to 12.5% across all subgroups in the pooled sample (patients without type 2 diabetes) and 4.5% to 7.3% in the STEP 2 sample (patients with type 2 diabetes; **Figure 1**)
- There were no statistically significant interactions between the treatment efficacy and race or ethnicity in the pooled STEP 1 & 3 or STEP 2 populations

Figure 1: ETD for semaglutide vs placebo % body weight loss by race and ethnicity

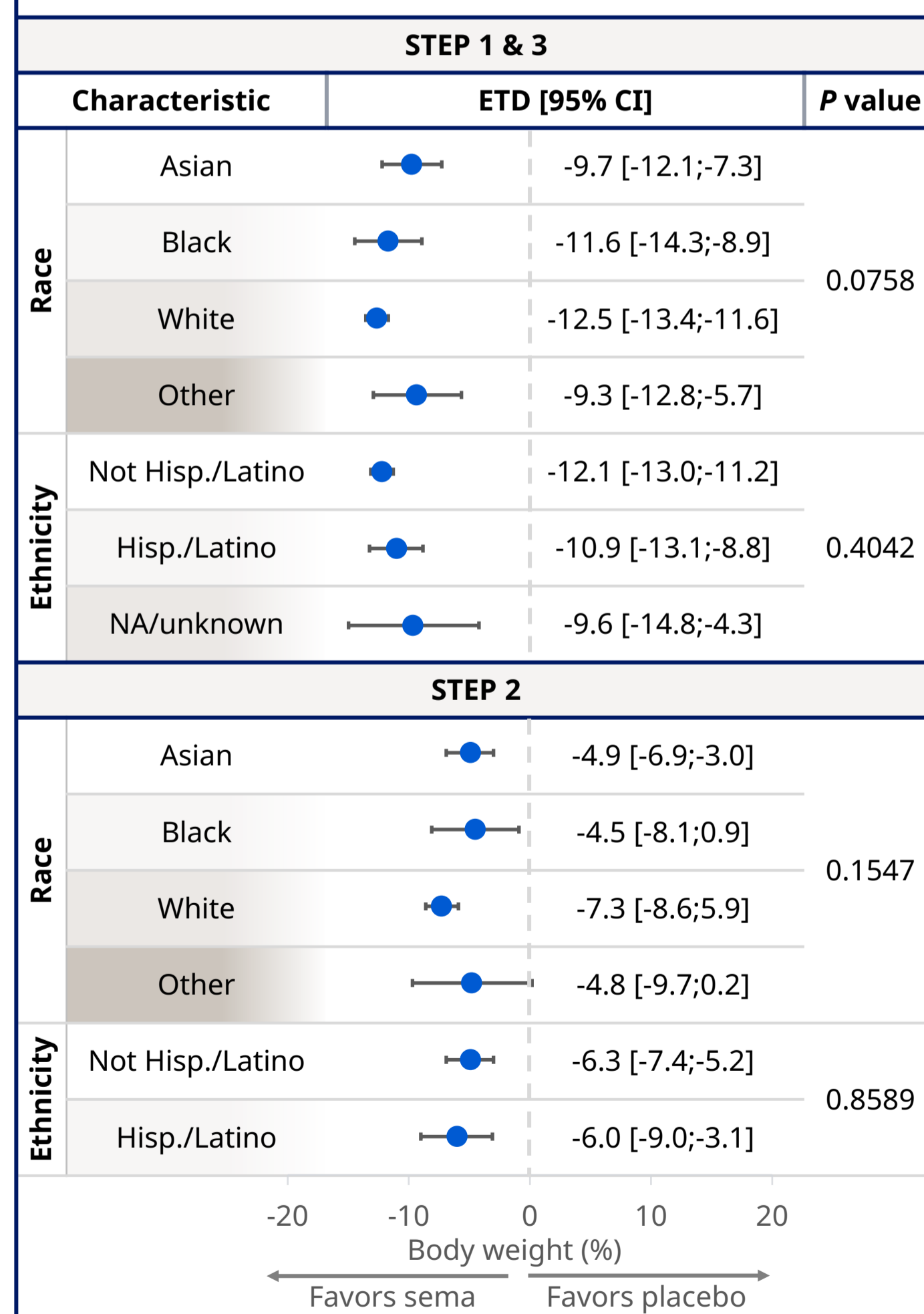
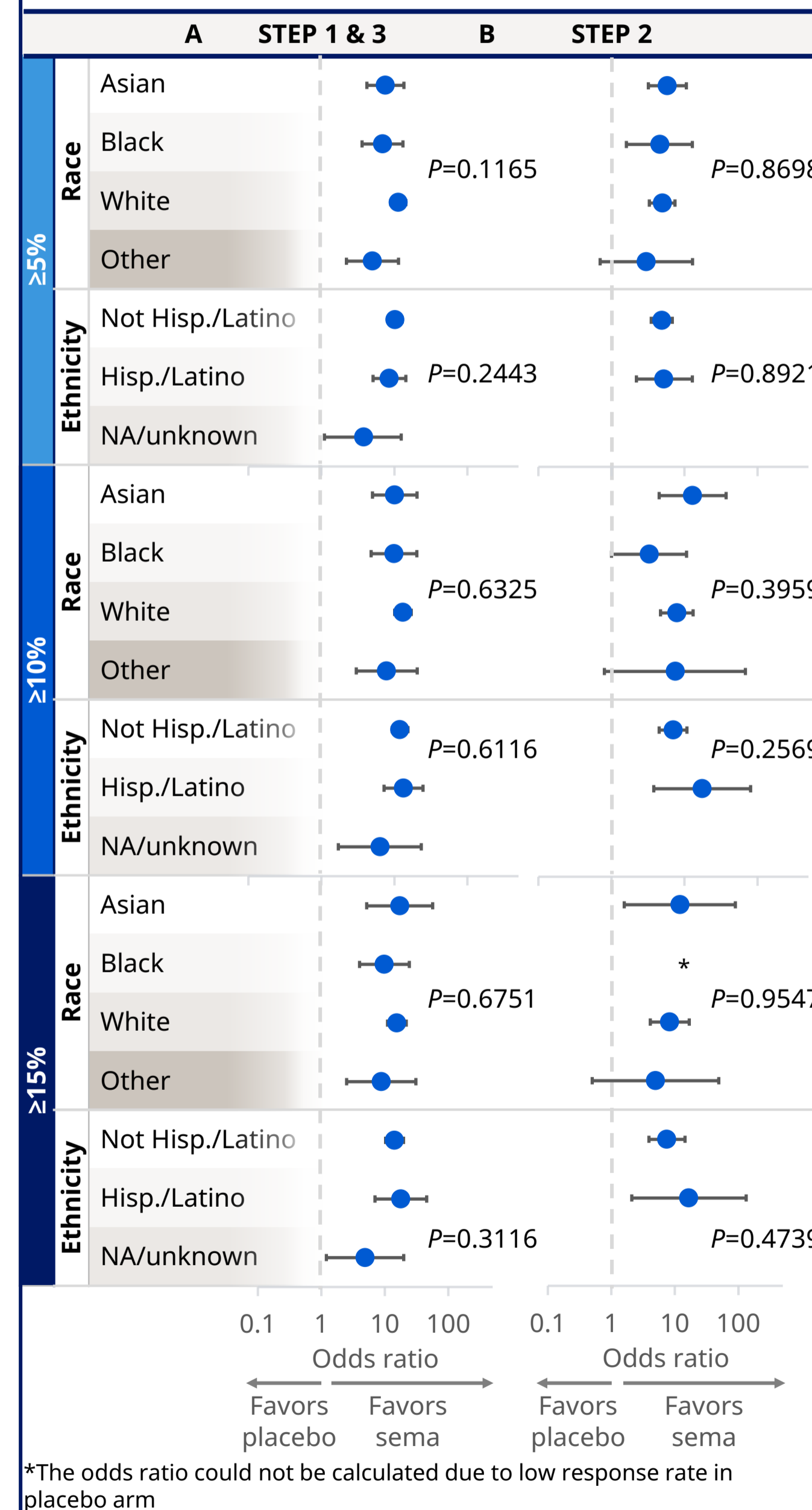


Figure 2: Odds ratio of ≥5%, ≥10%, or ≥15% weight loss for sema vs placebo in (A) STEP 1 & 3 or (B) STEP 2



- Across all subgroups, participants with semaglutide 2.4 mg had greater odds of achieving ≥5%, ≥10%, or ≥15% body weight loss by week 68 as compared to placebo in both STEP 1 & 3 and STEP 2 populations (**Figure 2**)
- The safety profile of semaglutide 2.4 mg was generally consistent across all subgroups in both populations (**Table 2**)

Table 2: AEs for STEP 1 & 3 and STEP 2

	STEP 1 & 3		STEP 2	
	Placebo	Sema	Placebo	Sema
Total AEs, n (%)				
Asian	163 (87.6)	70 (81.4)	96 (85.7)	78 (72.2)
Black	146 (96.1)	68 (90.7)	29 (85.3)	28 (75.7)
White	1163 (90.9)	585 (89)	209 (88.2)	188 (78)
Other	89 (93.7)	39 (95.1)	19 (95)	15 (93.8)
Not Hisp./Latino	1320 (91)	631 (89.0)	316 (88.8)	270 (76.5)
Hisp./Latino	203 (90.2)	113 (85.6)	37 (78.7)	39 (79.6)
NA/unknown	38 (100)	18 (100)	0	0
Serious AEs, n (%)				
Asian	8 (4.3)	3 (3.5)	8 (7.1)	9 (8.3)
Black	14 (9.2)	3 (4)	4 (11.8)	4 (10.8)
White	134 (10.5)	41 (6.2)	26 (11)	22 (9.1)
Other	9 (9.5)	1 (2.4)	2 (10)	2 (12.5)
Not Hisp./Latino	139 (9.6)	41 (5.8)	37 (10.4)	36 (10.2)
Hisp./Latino	19 (8.4)	6 (4.5)	3 (6.4)	1 (2)
NA/unknown	7 (18.4)	1 (5.6)	0	0

Conclusions

- Across all subgroups in both populations, the treatment effect of semaglutide 2.4 mg on body weight was statistically significant and clinically relevant
- There were no statistically significant differences in the treatment effect on body weight by race or ethnicity in either the pooled STEP 1 & 3 or STEP 2 populations
- Participants with semaglutide 2.4 mg had greater odds of achieving ≥5%, ≥10%, or ≥15% body weight loss vs placebo across all subgroups in both STEP 1 & 3 and STEP 2 populations
- Treatment was well tolerated for all subgroups in both populations

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