

OASIS 4: Efficacy of oral semaglutide 25 mg in obesity treatment targets and low-risk outcomes for cardiometabolic risk factors

Carel W. le Roux¹, Oscar Birkhan², Naveen Rathor², Domenica Rubino³,
Chaithra Shaji⁴, Luca Busetto⁵

¹Diabetes Complications Research Centre, Conway Institute, University College Dublin, Dublin, Ireland; ²Novo Nordisk A/S, Søborg, Denmark;

³Washington Center for Weight Management and Research, Arlington, VA, USA; ⁴Novo Nordisk Global Business Services, Bangalore, India;

⁵Department of Medicine, University of Padova, Padova, Italy.

Introduction



A treat-to-target approach in obesity management, using a **BMI of $\leq 27 \text{ kg/m}^2$** and **WHtR of ≤ 0.53** may help to improve outcomes by reducing the risk of obesity-related complications¹



In a phase 3 trial of participants randomised to received once-weekly subcutaneous semaglutide 2.4 mg or tirzepatide 15 mg, achieving BMI $< 27 \text{ kg/m}^2$ and WHtR < 0.53 treatment targets resulted in achievement of low-risk thresholds for cardiometabolic outcomes.² These cardiometabolic outcomes included glycaemic measures, HDL cholesterol, systolic and diastolic blood pressure and triglycerides



In the **OASIS 4** trial, participants with overweight/obesity treated with once-daily oral semaglutide 25 mg had greater percentage body weight reductions (**-13.6%**) than those who received placebo (**-2.2%**)³

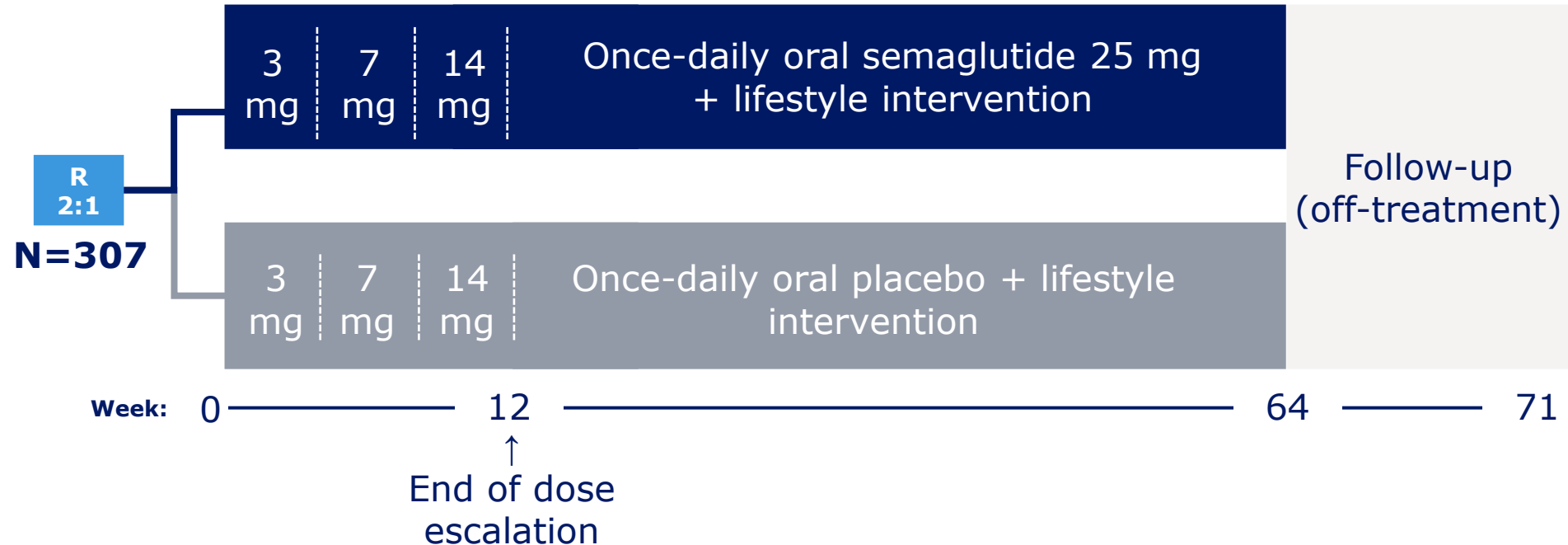


This secondary analysis of the OASIS 4 trial assessed the proportion of participants who achieved a BMI of $< 27 \text{ kg/m}^2$, WHtR of < 0.53 and low-risk thresholds for cardiometabolic outcomes after 64 weeks of treatment

BMI, body mass index; WHtR, waist to height ratio.

1. Busetto L et al. *Obes Sci Pract* 2025;11:e70094; 2. Le Roux C et al. *Diabetes Obes Metab* 2026;28:3355–3366; 3. Wharton S et al. *N Engl J Med* 2025;393:1077–1087.

OASIS 4 (NCT05564117) trial design



Lifestyle intervention involved counselling on diet (500 kcal deficit per day) and physical activity (150 minutes of physical activity per week) provided by a dietician or a similarly qualified healthcare professional at each study visit

OASIS 4 trial design

Population



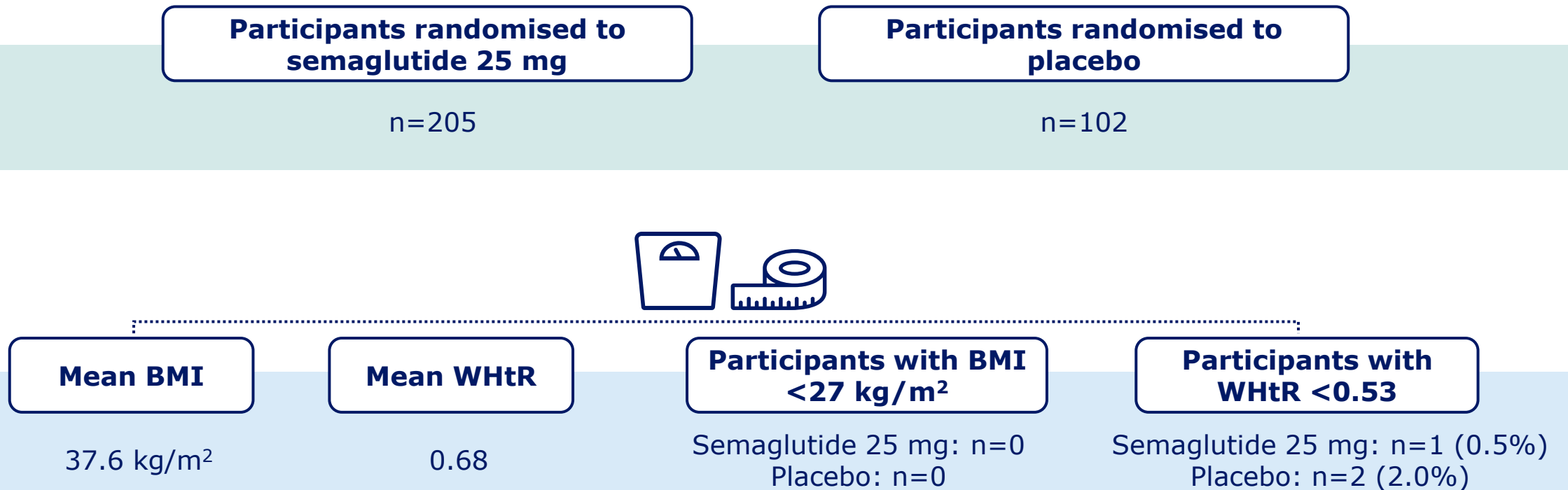
- **Key inclusion criteria:** aged ≥ 18 years; BMI ≥ 30 kg/m² (or ≥ 27 kg/m² with ≥ 1 obesity-related complication); ≥ 1 self-reported unsuccessful dietary effort to lose weight
- **Key exclusion criteria:** HbA_{1c} ≥ 48 mmol/mol ($\geq 6.5\%$) or history of diabetes; treatment with any medication indicated for weight management or any glucose lowering agent within 90 days prior to screening; history of MI, stroke, hospitalisation for unstable angina, TIA or HF; presence of acute pancreatitis within 180 days prior to screening; history or presence of chronic pancreatitis

Outcomes



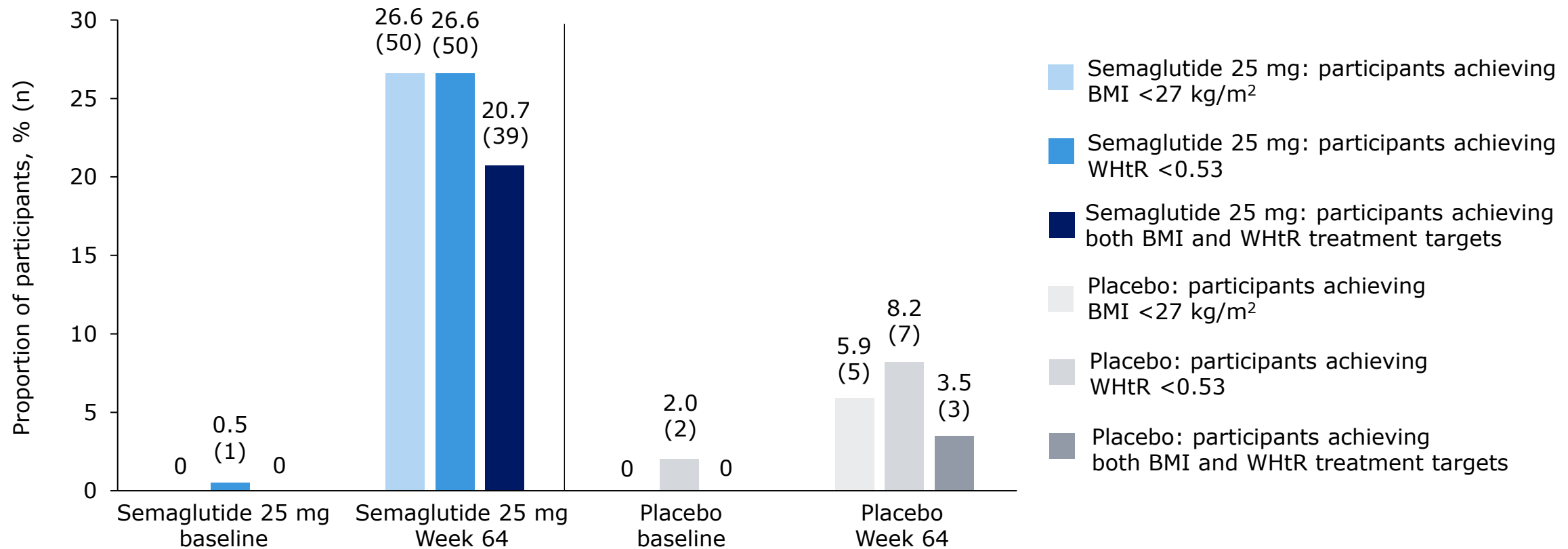
- This secondary analysis assessed the proportion of participants who achieved a BMI of < 27 kg/m², WHtR of < 0.53 and low-risk thresholds for cardiometabolic outcomes:
 - Glycaemia (normoglycaemia: glycated haemoglobin $< 5.7\%$ and fasting plasma glucose < 5.6 mmol/L)
 - HDL cholesterol (> 1.3 mmol/L [female] or > 1.0 mmol/L [male])
 - Systolic and diastolic blood pressure ($< 130/80$ mmHg)
 - Triglycerides (< 1.7 mmol/L)

Baseline characteristics



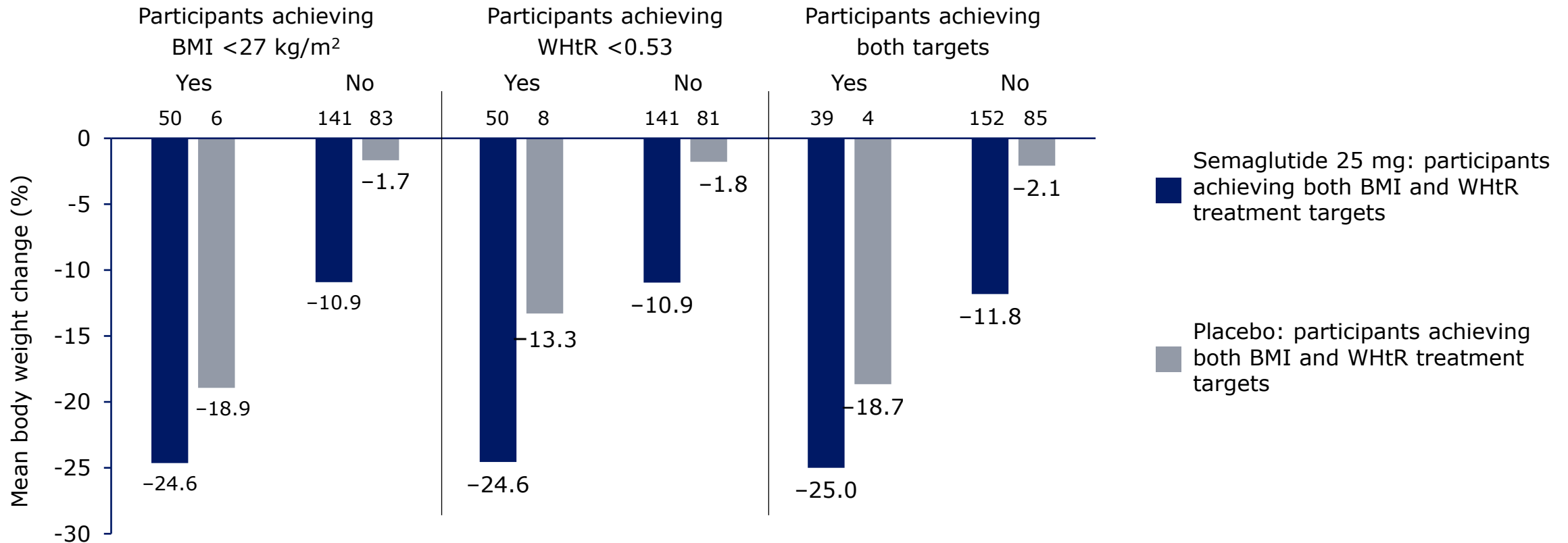
BMI, body mass index; WHtR, waist to height ratio.

Proportion of participants achieving BMI and WHtR treatment targets at week 64



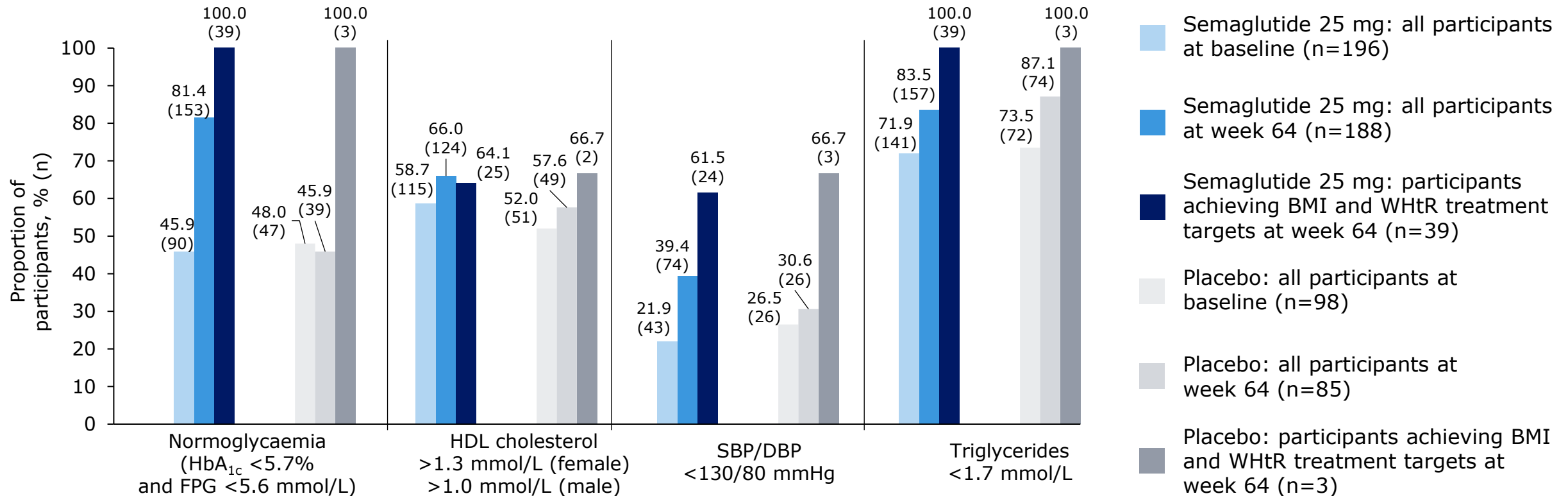
Data are from the in-trial period for participants with observed BMI and WHtR data during weeks 0 to 64.
BMI, body mass index; WHtR, waist to height ratio.

Change in bodyweight (%) from baseline to week 64 according to attainment of treatment targets



Data are from the in-trial period for participants with observed BMI and WHtR data during weeks 0 to 64.
BMI, body mass index; WHtR, waist to height ratio.

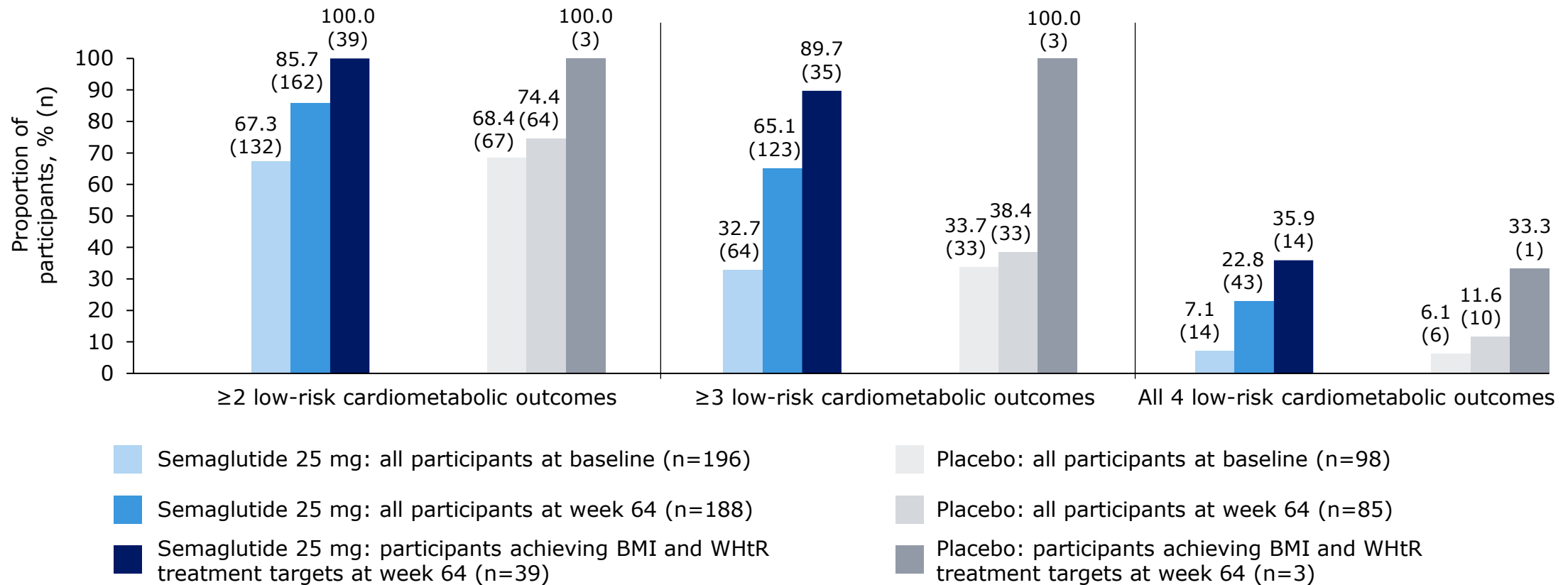
Proportions of participants achieving low-risk thresholds for cardiometabolic outcomes at week 64



Data are from the in-trial period for participants with observed data during weeks 0 to 64. Overall, 294 and 280 participants had data available for all cardiometabolic outcomes at baseline and week 64, respectively.

BMI, body mass index; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HbA_{1c}, glycated haemoglobin; HDL, high-density lipoprotein; SBP, systolic blood pressure; WHtR, waist to height ratio.

Number of low-risk thresholds for cardiometabolic outcomes achieved at week 64



Data are from the in-trial period for participants with observed data during weeks 0 to 64. Overall, 294 and 280 participants had data available for all cardiometabolic outcomes at baseline and week 64, respectively.

BMI, body mass index; WHtR, waist to height ratio.

Conclusions



In this analysis of the OASIS 4 trial, a greater proportion of participants achieved BMI and/or WHtR targets in the semaglutide 25 mg group compared with placebo



A greater proportion of participants treated with semaglutide 25 mg achieved low-risk thresholds for cardiometabolic outcomes compared with those who received placebo



Of those who achieved BMI and WHtR targets, a greater proportion of participants also met low risk outcomes for cardiometabolic risk factors, regardless of treatment. However, the absolute numbers of participants in the placebo group who achieved these targets and outcomes were lower compared with the semaglutide 25 mg group