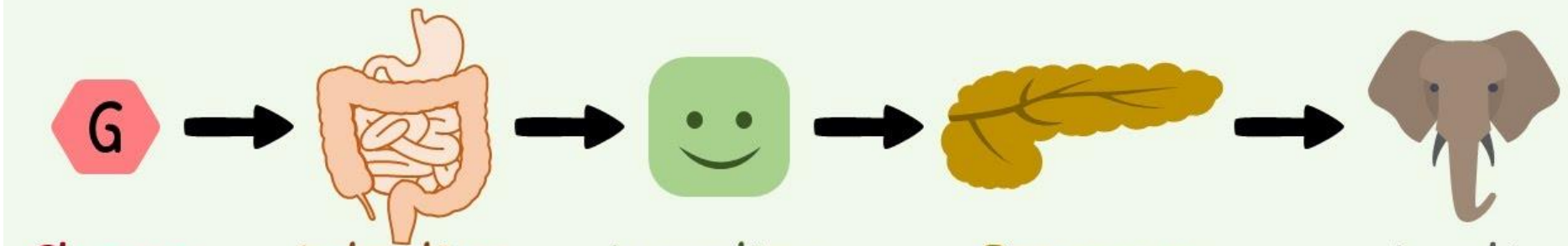
Semaglutide 처방부터 중단 후까지: 체중 유지 전략과 실전 노하우

CHA 의과학대학교 분당차병원

가정의학과 김 영 상

Incretin Effect

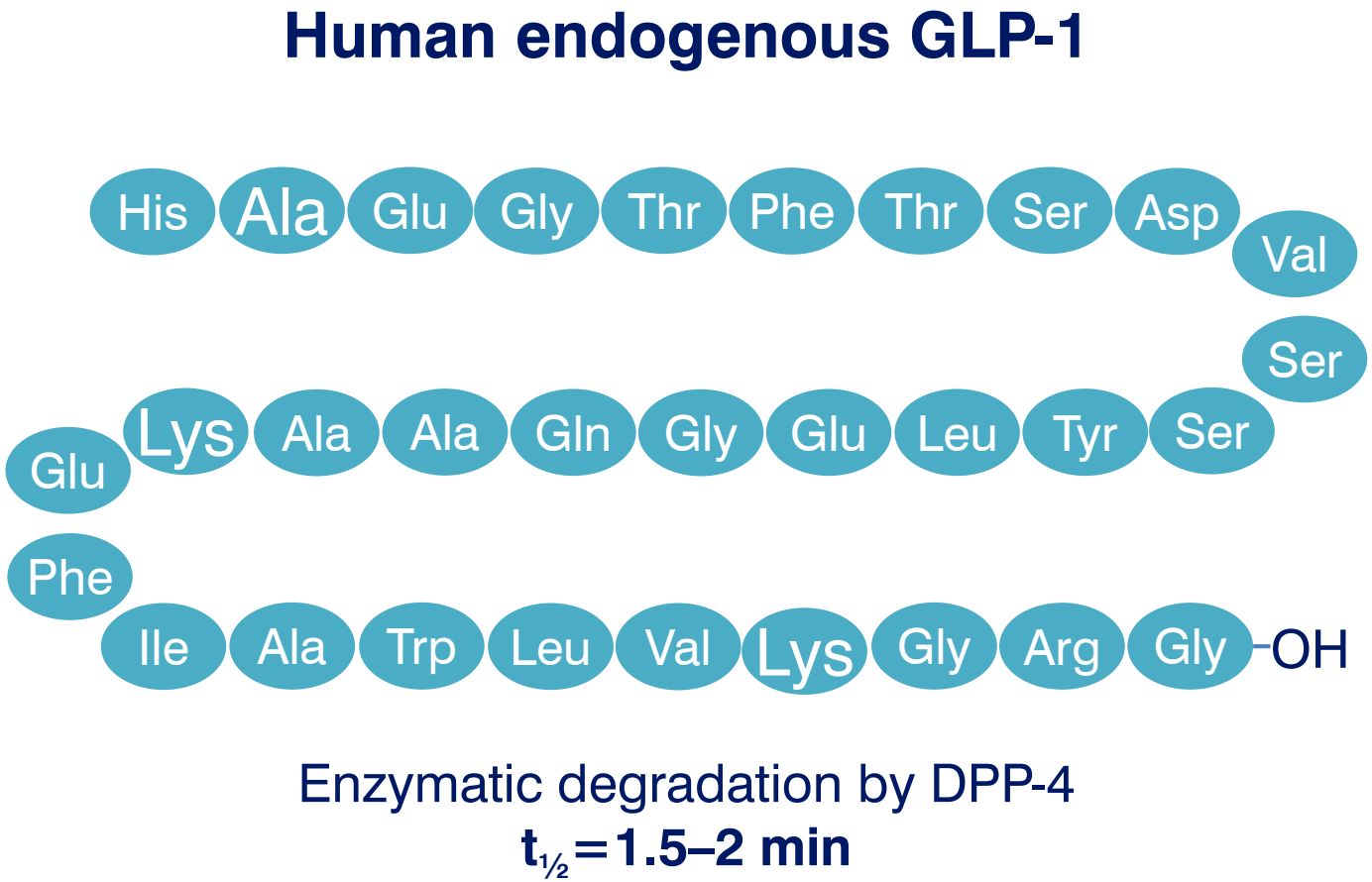


Incretin Family Members

- GLP-1:
  - Most clinically relevant; targeted by GLP-1 receptor agonists (e.g., semaglutide, liraglutide) for diabetes/obesity.
- GIP:
  - Secreted by K-cells in the duodenum.
  - Stimulates insulin secretion but has weaker effects on appetite/glucagon vs. GLP-1.
  - Dual GLP-1/GIP agonists (e.g., tirzepatide) show enhanced efficacy.
- Other peptides:
  - Oxyntomodulin (appetite suppression)
  - glicentin (from proglucagon cleavage)

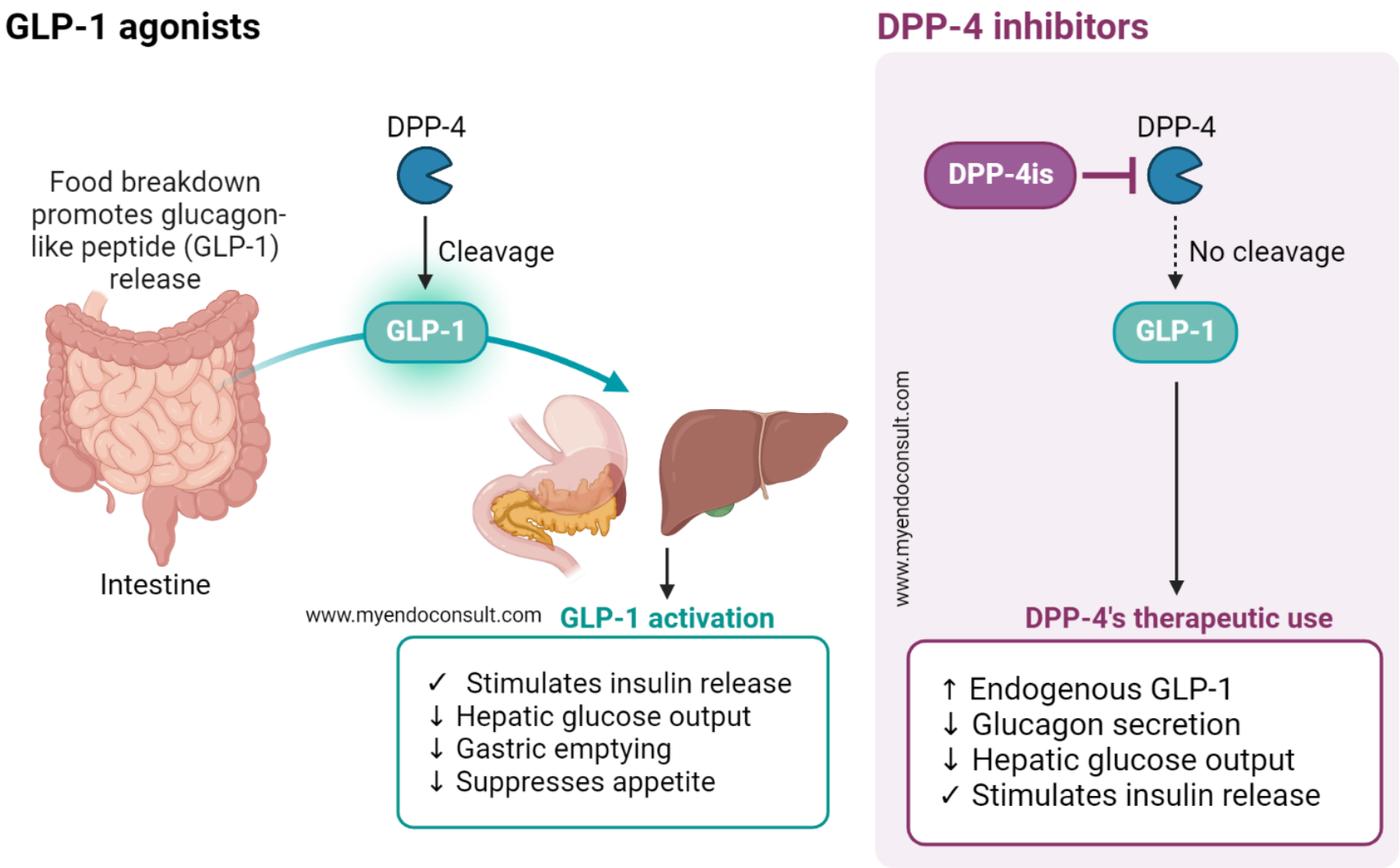
What is GLP-1?

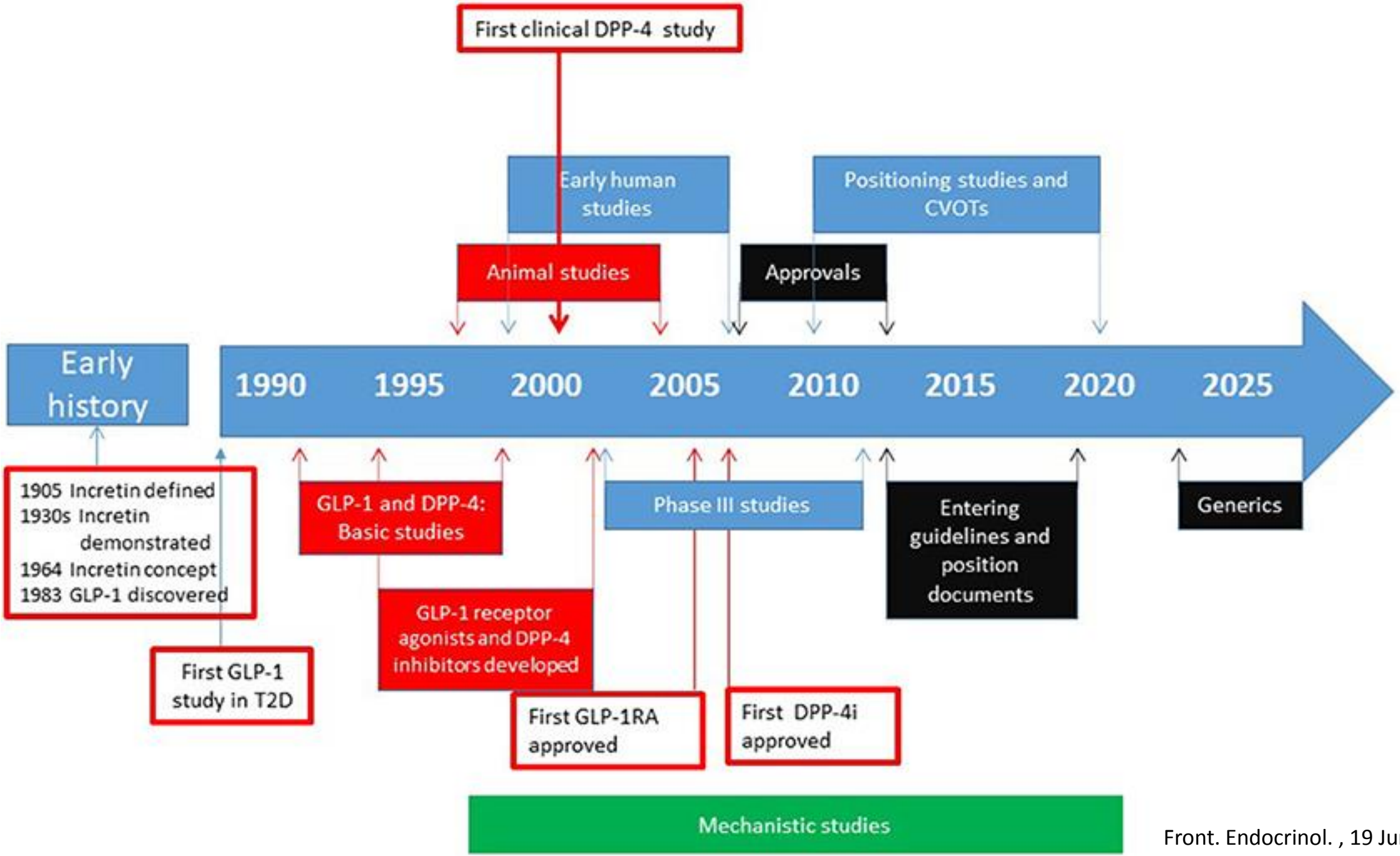
- GLP-1 is a peptide comprised of 31 amino acids
- Member of incretin family
- Secreted predominantly from L-cells in the gut, but also the brain (nucleus tractus solitarius)



DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; t½, half-life.
Merchenthaler et al. J Comp Neurol 1999;403:261–80; Baggio and Drucker. Gastroenterology 2007;132:2131–57; Drucker and Nauck. Lancet 2006;368:1696–705.

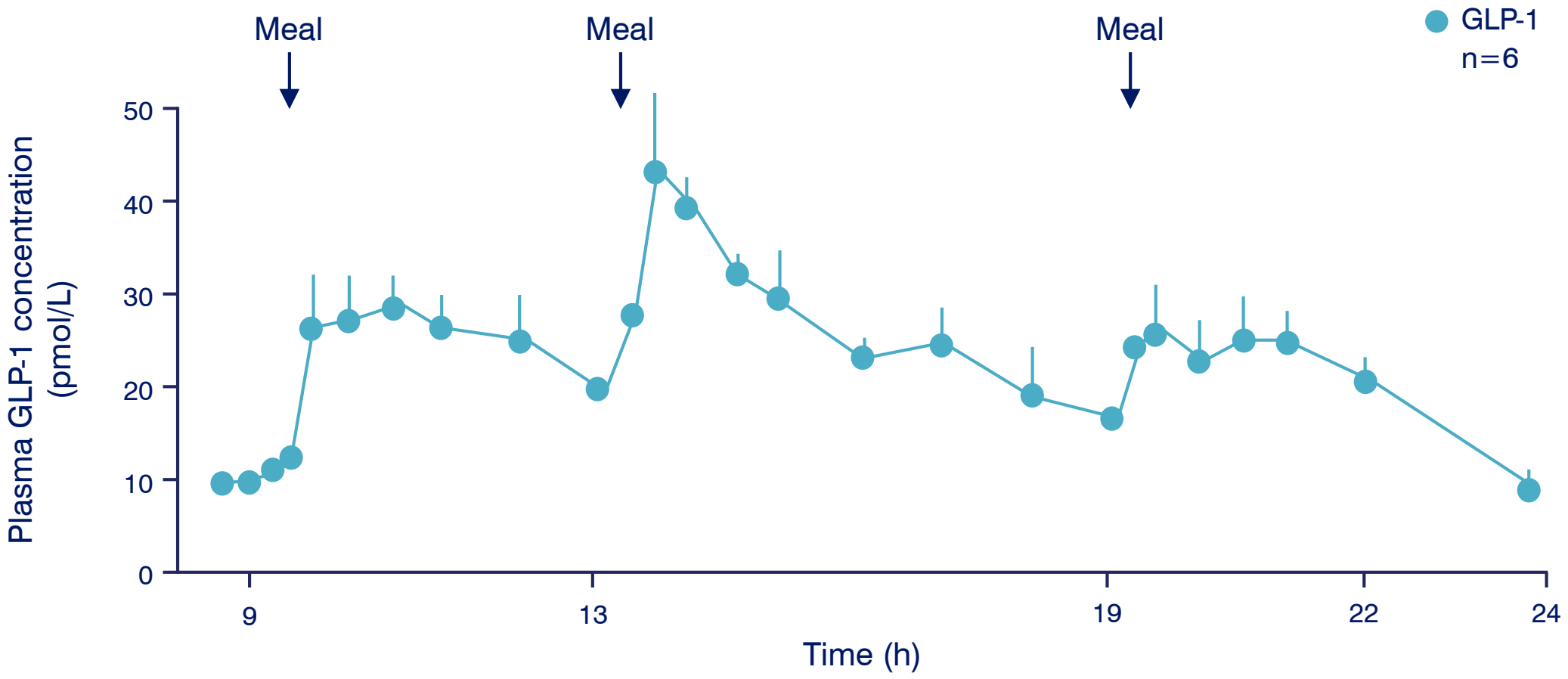
GLP-1 Agonists Dipeptidyl-Peptidase-4 Inhibitors (DPP-4's)





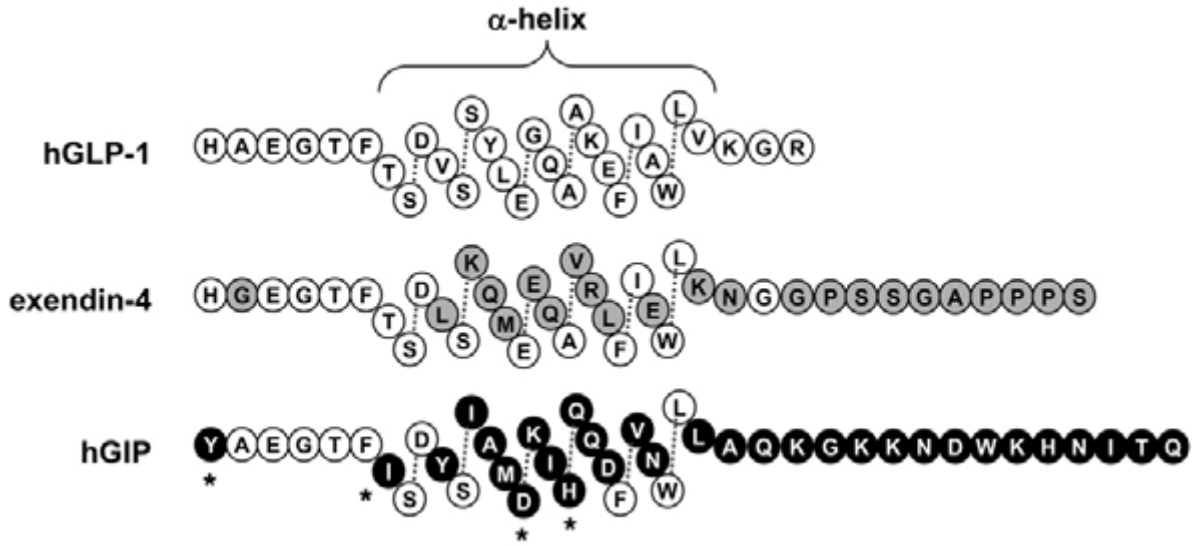
Front. Endocrinol. , 19 June 2019

GLP-1 is released in response to food intake



GLP-1, glucagon-like peptide-1.
Adapted from Orskov et al. Scand. Gastroenterol 1996;31:665–70.

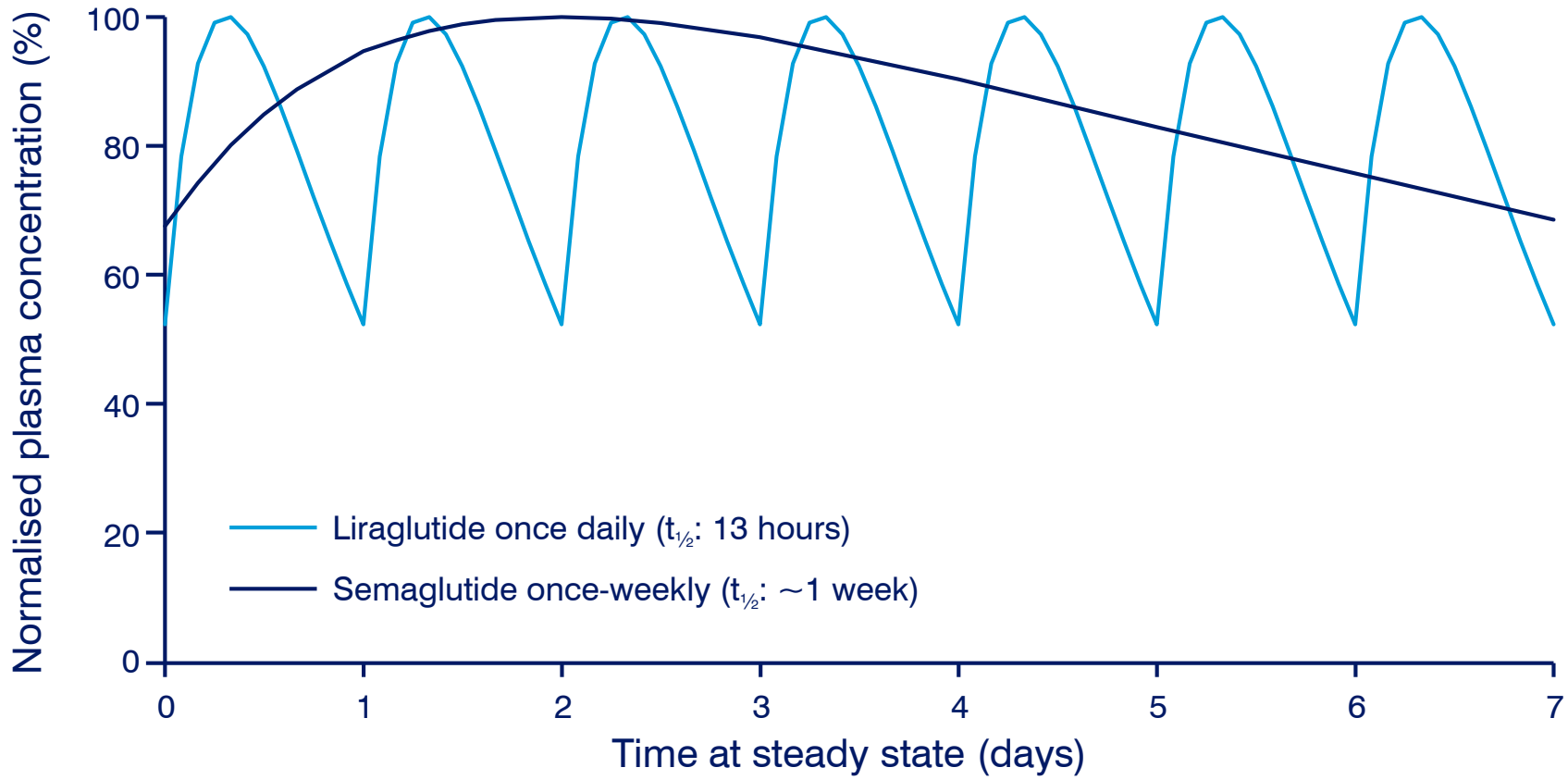
GLP-1 RA



Drug	Structure	Dosing	Half-Life	Key Use
Exenatide	Exendin-4 analog	Twice daily	2–4 hours	T2D
Lixisenatide	Exendin-4 analog	Once daily	~3 hours	T2D
Liraglutide	Human analog	Once daily	13 hours	T2D, Obesity
Semaglutide	Human analog	Once weekly/oral	~7 days	T2D, Obesity, CVD
Dulaglutide	Human analog	Once weekly	~5 days	T2D, CVD

Semaglutide concentration constant in the plasma

Semaglutide provides more constant plasma levels compared with liraglutide



Profiles were based on simulated modelling. Liraglutide is the only GLP-1RA that is approved by the US FDA and EMA for use in overweight/obese participants without T2D. It is dosed once daily.
EMA, European Medicines Agency; FDA, US Food and Drug Administration; GLP-1RA, glucagon-like peptide-1 receptor agonist; t½, half life.
Elbrønd et al. Diabetes Care 2002;25:1398–404; Marbury et al. Clin Pharmacokinet 2017;56:1381–90.

Semaglutide Treatment Effect in People with obesity STEP series

Common Characteristics Across STEP Trials

1. Inclusion Criteria:
   - Adults/adolescents with BMI ≥30 (obesity) or ≥27 + ≥1 comorbidity (e.g., hypertension, dyslipidemia, T2D).
   - Prior unsuccessful weight-loss efforts via diet/exercise.
   - Exclusions: History of pancreatitis, medullary thyroid carcinoma, or pregnancy.
2. Intervention:
   - Subcutaneous semaglutide 2.4 mg weekly (titrated over 16–20 weeks).
   - All trials included lifestyle counseling (calorie deficit, physical activity).
3. Primary Endpoint:
   - Percentage change in body weight from baseline.
   - Secondary endpoints: Proportion achieving ≥5%, ≥10%, or ≥15% weight loss.

Adverse Event Profiles

- Common AEs:
  - Gastrointestinal
    (nausea [~20–44%], diarrhea [~13–30%], vomiting [~5–15%]).
  - Mild-to-moderate severity; typically resolved over time.
- Serious AEs:
  - Gallbladder-related events (e.g., cholelithiasis: ~1.5–2.6%).
  - Rare pancreatitis (<1%) or hypoglycemia (in T2D trials with concomitant therapies).
- Discontinuation Rates: ~5–10% due to GI side effects.

Overview of STEP Trial Series

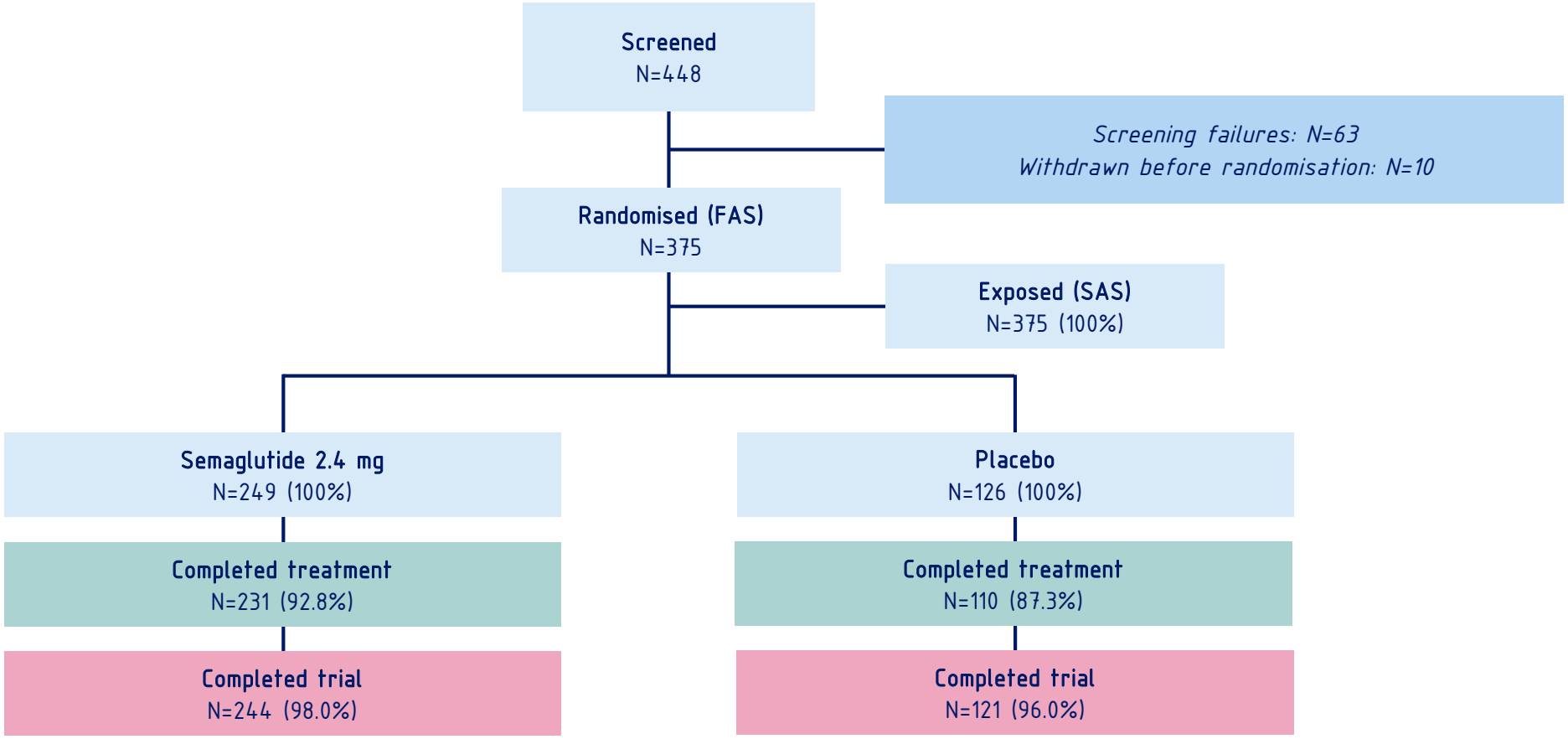
Trial	Population	Intervention	Duration	Key Findings
STEP 1	1,961 adults with obesity/overweight (BMI ≥30 or ≥27 + comorbidities), **without diabetes**	Semaglutide 2.4 mg vs. placebo + lifestyle intervention	68 weeks	**-14.9%** body weight loss (vs. -2.4% placebo). 86% achieved ≥5% weight loss.
STEP 2	1,210 adults with **T2D + obesity/overweight** (BMI ≥27)	Semaglutide 2.4 mg vs. 1.0 mg vs. placebo + lifestyle	68 weeks	**-9.6%** (2.4 mg) vs. **-7.0%** (1.0 mg) vs. **-3.4%** placebo. Improved HbA1c.
STEP 3	611 adults with obesity/overweight + intensive behavioral therapy (IBT)	Semaglutide 2.4 mg + IBT vs. placebo + IBT	68 weeks	**-16.0%** (sema + IBT) vs. **-5.7%** (placebo + IBT). Highest weight loss in series.
STEP 4	803 adults who completed 20-week run-in (semaglutide responders)	Continue semaglutide 2.4 mg vs. switch to placebo	48 weeks	**-7.9%** (continued) vs. **+6.9%** (placebo). Demonstrated need for long-term use.
STEP 5	304 adults with obesity/overweight (2-year extension)	Semaglutide 2.4 mg vs. placebo	104 weeks	**-15.2%** (sema) vs. **-2.6%** (placebo). Confirmed sustained efficacy.
STEP 6	401 Asian adults with obesity/overweight (BMI ≥27)	Flexible-dose semaglutide (1.7–2.4 mg) vs. placebo	68 weeks	**-13.2%** (sema) vs. **-2.1%** (placebo). Lower dose effective in Asian population.
STEP 8	338 adults with obesity/overweight, head-to-head vs. liraglutide 3.0 mg	Semaglutide 2.4 mg vs. liraglutide 3.0 mg vs. placebo	68 weeks	**-15.8%** (sema) vs. **-6.4%** (lira) vs. **-1.9%** (placebo). Superiority of sema.
STEP TEENS	201 adolescents (12–18 years) with obesity (BMI ≥95th percentile)	Semaglutide 2.4 mg vs. placebo	68 weeks	**-16.1%** BMI (sema) vs. **+0.6%** (placebo). FDA approved for adolescents.

Weight Loss Outcomes Summary

Trial	Semaglutide Group	Comparator	Key Takeaway
STEP 1	-14.9%	-2.4% (placebo)	Semaglutide nearly **6× more effective** than placebo in non-diabetic adults.
STEP 2	-9.6% (2.4 mg)	-3.4% (placebo)	Weight loss reduced in T2D patients but still significant.
STEP 3	-16.0%	-5.7% (placebo)	**Intensive behavioral therapy** amplified semaglutide’s effects.
STEP 8	-15.8%	-6.4% (liraglutide)	Semaglutide **doubled weight loss** vs. liraglutide.
STEP TEENS	-16.1% BMI	+0.6% (placebo)	First trial showing efficacy in adolescents.

STEP 7 for Asians

Patient disposition



%, proportion of patients in the FAS; FAS, full analysis set; SAS, safety analysis set.
Mu, Y., et al. The Lancet Diabetes & Endocrinology, 2024. 12(3): p. 184-195

Patients with T2DM taking semaglutide 2.4mg in combination with an insulin secretagogue (e.g., sulfonylurea) may have an increased risk of hypoglycemia, including severe hypoglycemia. When initiating semaglutide 2.4mg consider reducing the dose of concomitantly administered insulin secretagogue (such as sulfonylureas) to reduce the risk of hypoglycemia.

Demographics and baseline characteristics

Male | Female	Mean age	Asian | White | Black*
54.7% | 45.3%	41 years	90.7% | 8.3% | 1.1%

Mean body weight	Mean BMI	Mean waist circumference	Type 2 diabetes	Comorbidities‡ 0 | 1 | 2 | 3 | 4 | ≥5
96.4 kg	34.0 kg/m^2	108.0 cm	25.6% (Mean HbA_{1c} 8.0%†)	7.7|21.3|18.9|23.7|19.5|8.8%

*Black participants refer to Black participants or African American participants; †Mean HbA_{1c} is calculated for the subpopulation with type 2 diabetes only; ‡Comorbidities evaluated included dyslipidaemia, hypertension, coronary artery disease, cerebrovascular disease, obstructive sleep apnoea, type 2 diabetes, impaired glucose metabolism, reproductive system, liver disease, kidney disease, osteoarthritis, gout and asthma.
%, proportion of patients in full analysis set; BMI, body mass index; HbA_{1c}, glycated haemoglobi
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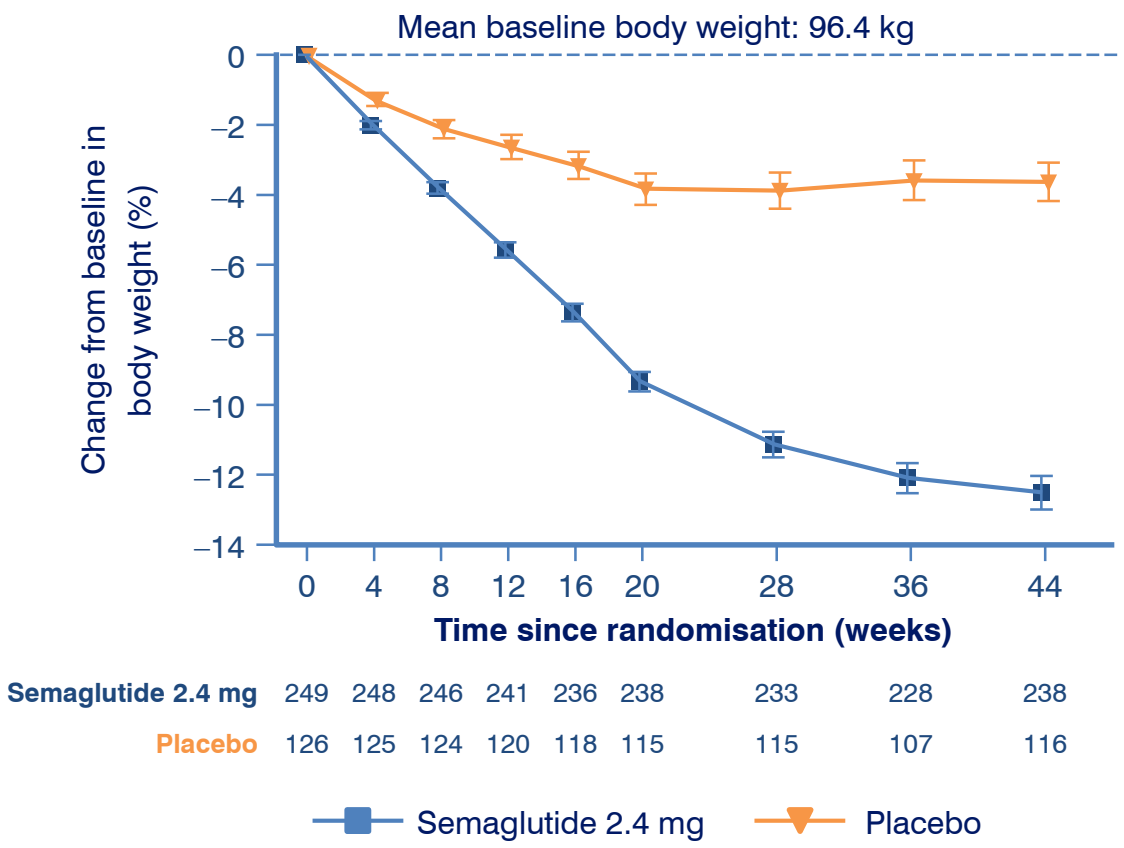
Semaglutide 2.4 mg (Wegovy®) is not approved as the treatment for weight-related comorbidity such as dysglycemia (pre-diabetes, T2DM), hypertension, dyslipidemia, OSA, and cardiovascular disease) by Ministry of Food and Drug Safety (MFDS) in Korea.

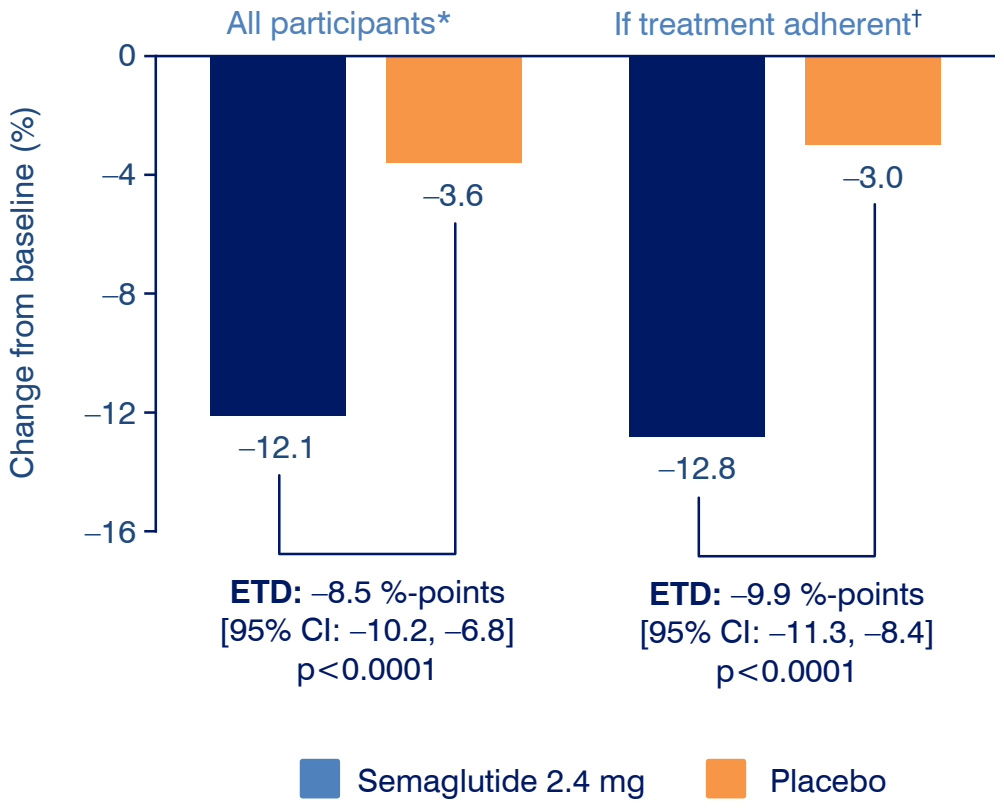
Change in body weight

Observed mean change over time

In-trial



Estimated mean change from baseline to week 44



*Treatment policy estimand (assesses treatment effect regardless of treatment discontinuation or rescue intervention); †Trial product estimand (assesses treatment effect if trial product was taken as intended). Error bars are +/- standard error of the mean. Numbers shown in the lower panel of the figure (left) are numbers of patients contributing to the mean.
CI, confidence interval; ETD, estimated treatment difference.
Mu, Y., et al. The Lancet Diabetes & Endocrinology, 2024. 12(3): p. 184-195

Patients with T2DM taking semaglutide 2.4mg in combination with an insulin secretagogue (e.g., sulfonylurea) may have an increased risk of hypoglycemia, including severe hypoglycemia. When initiating semaglutide 2.4mg consider reducing the dose of concomitantly administered insulin secretagogue (such as sulfonylureas) to reduce the risk of hypoglycemia.

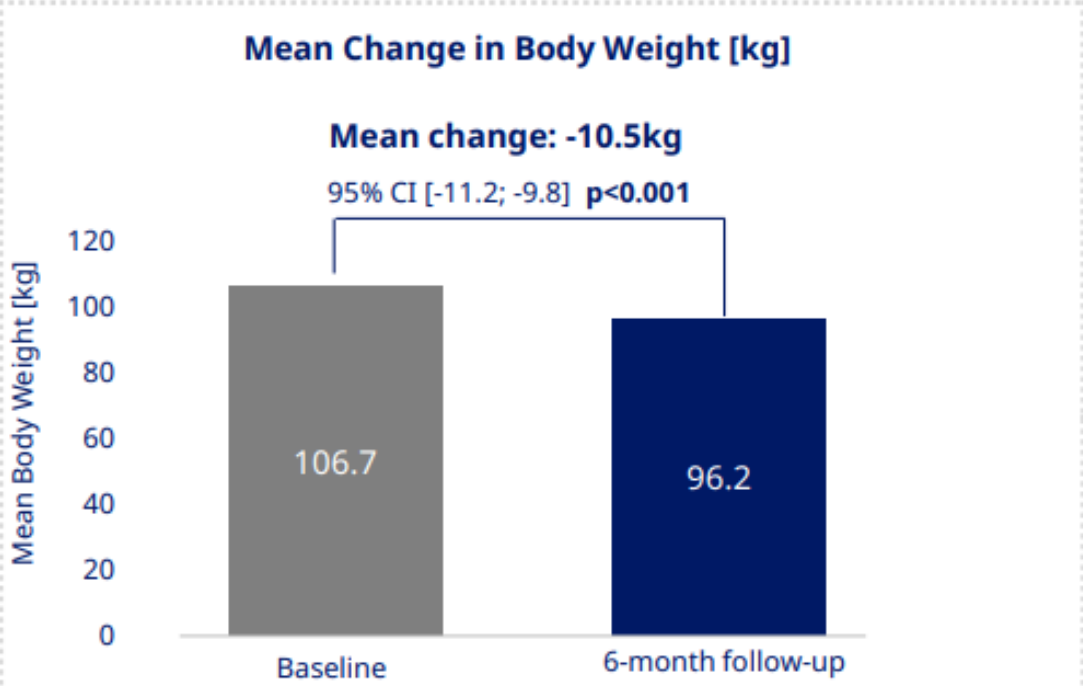
Real World Analyses based on SCOPE studies

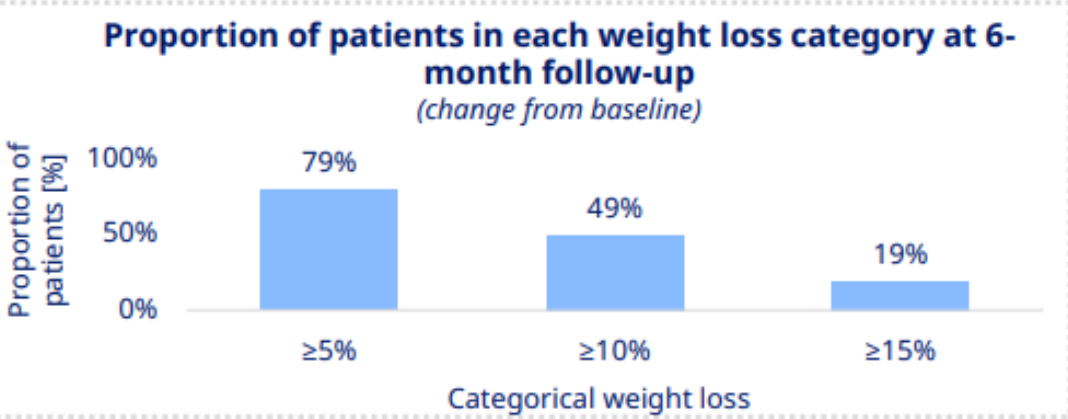
Semaglutide 2.4 mg clinical outcomes in patients with obesity or overweight **in a real-world setting: A 6-12month** retrospective study in the **United States**

Body weight change

SCOPE 6 Months

Finding: Patients with obesity or overweight had a mean reduction of 10.5 kg or 10% of initial body weight





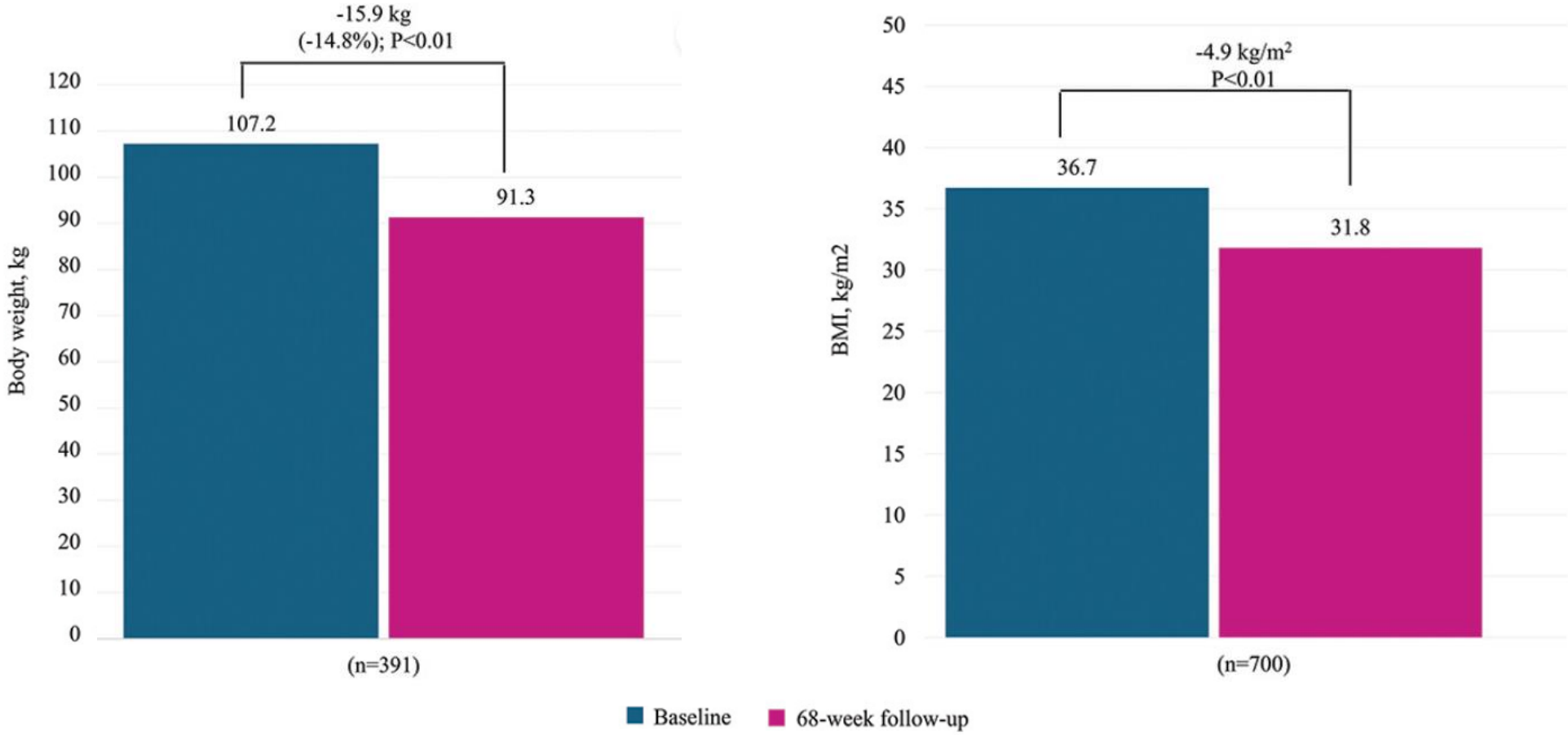
Mean Change in BMI [kg/m²] after 6 months

Mean change in BMI	Mean baseline measure	Mean follow-up measure	95% CI	p-value*
-3.7 kg/m²	37 kg/m²	33 kg/m²	-4.0 ; -3.4	p= 0.001

To evaluate the effectiveness of semaglutide 2.4 mg for weight reduction and **improvement in cardiometabolic biomarkers** at 52 and 68 weeks **in a real-world setting in the United States**

Change in body weight and BMI

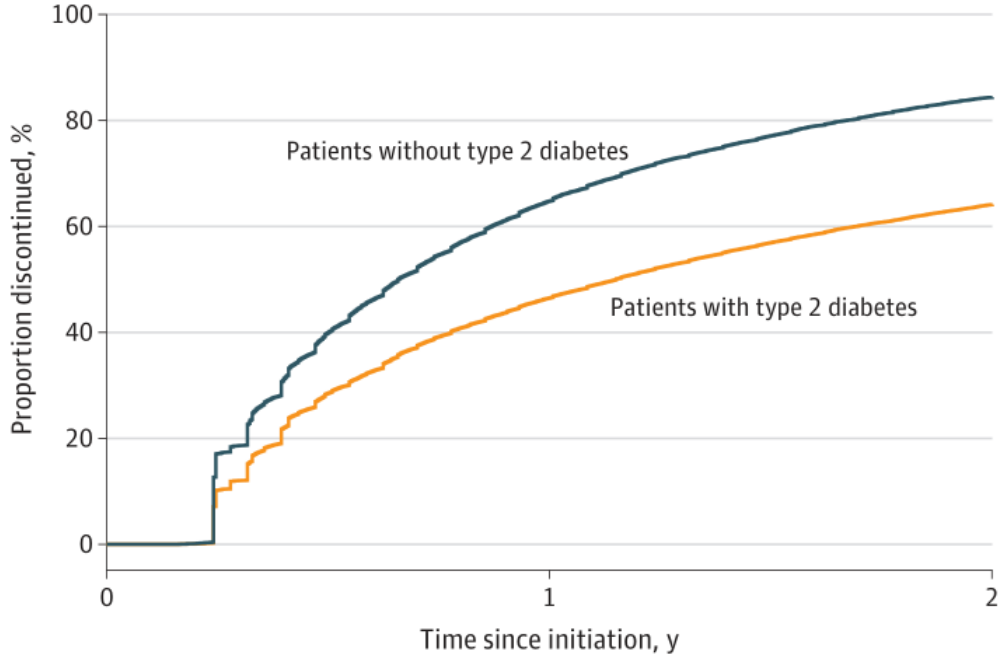
SCOPE 12 Months : from baseline to 68-week follow-up



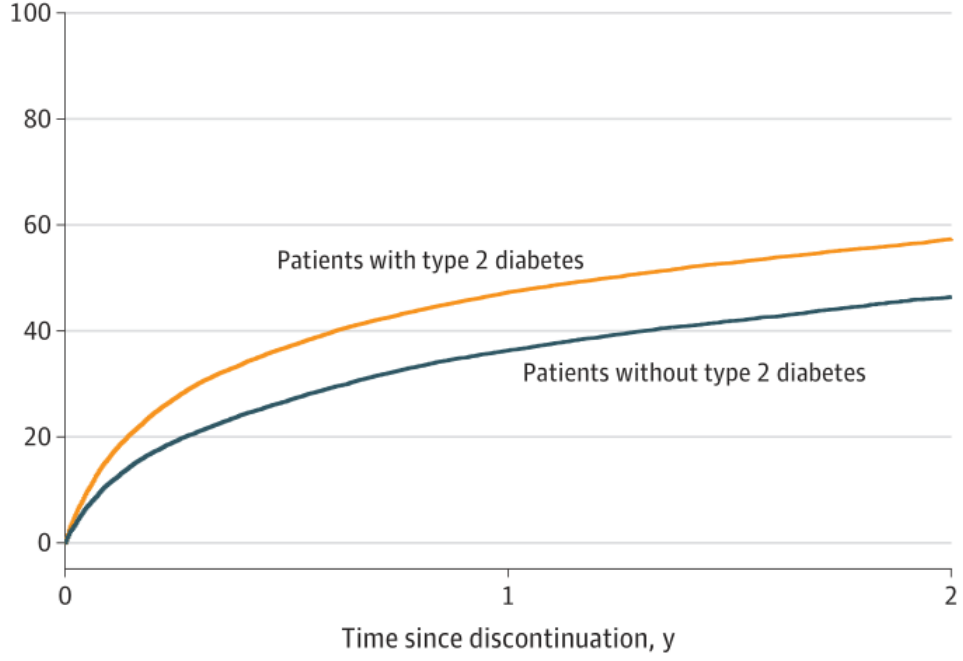
After Treatment Discontinuation

Discontinuation and Reinitiation of GLP-1 Receptor Agonists

Time to discontinuation of GLP1RA



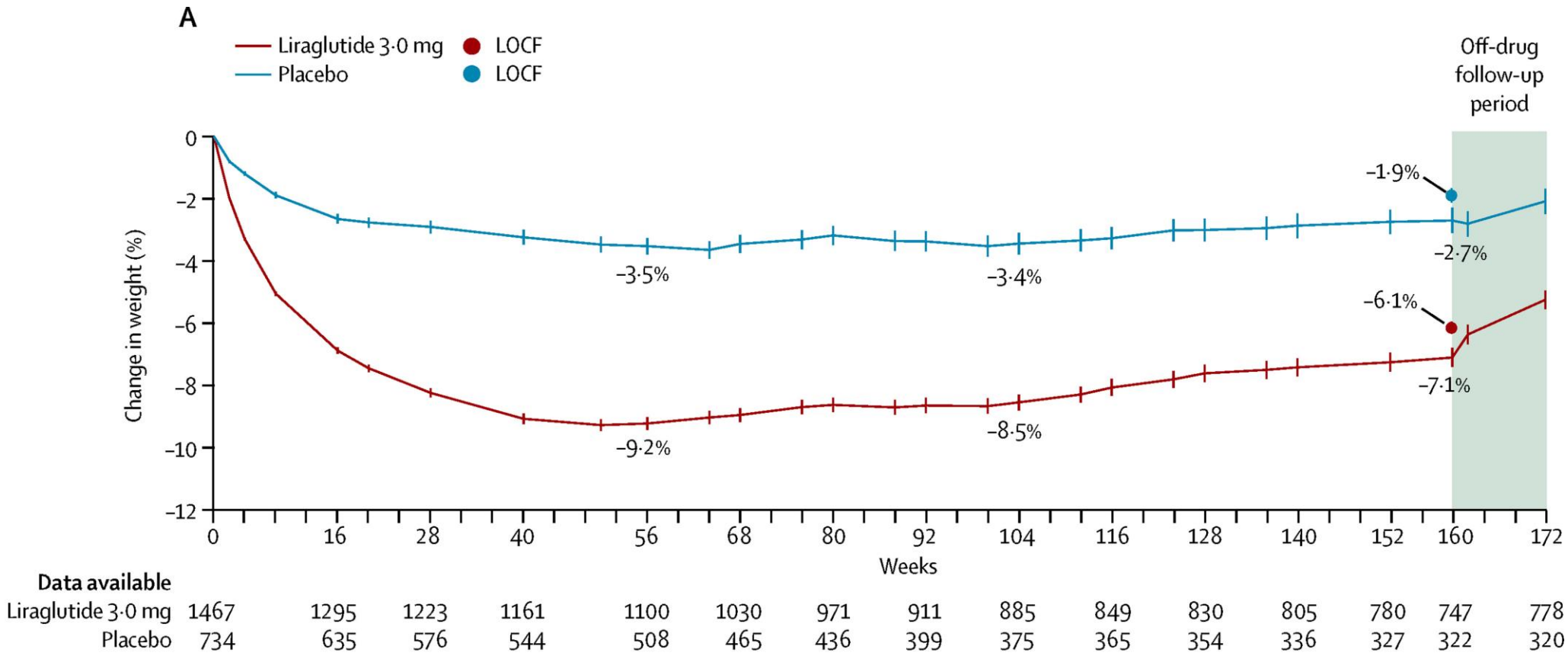
Time to Reinitiation of GLP1RA



No. at risk						
Patients with type 2 diabetes	76 524	36 709	10 774	22 869	7597	3368
Patients without type 2 diabetes	48 950	15 696	2750	18 923	7048	1592

Rodriguez, Patricia J., et al. JAMA Network Open 8.1 (2025): e2457349-e2457349.

3 years of liraglutide versus placebo



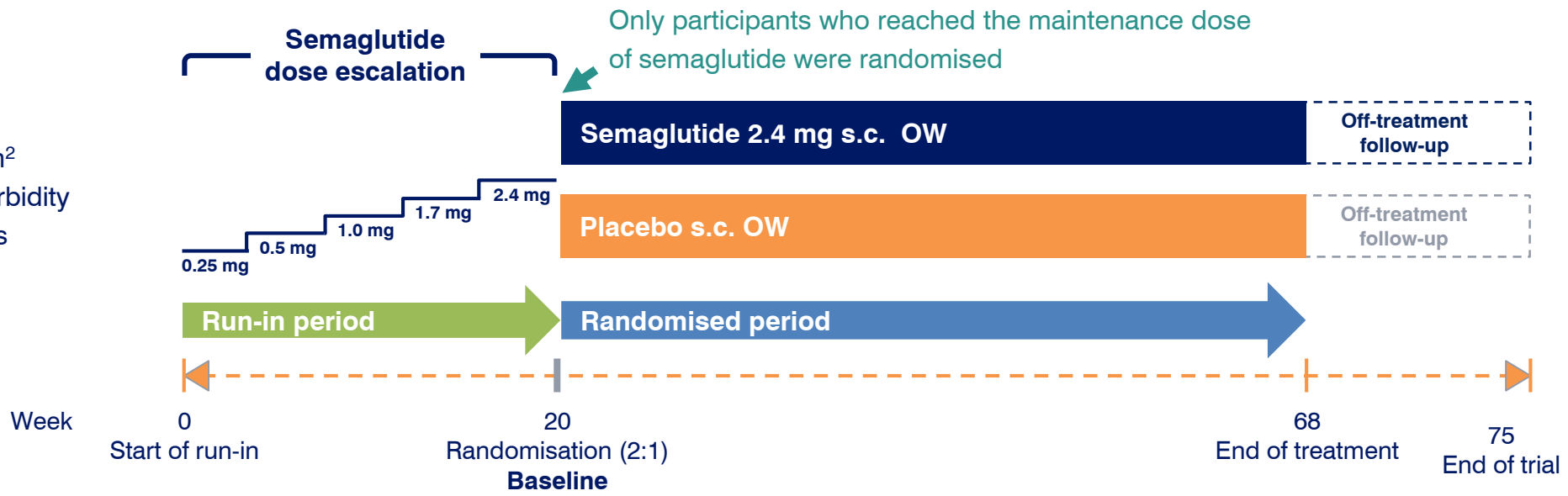
Le Roux, Carel W., et al. The Lancet 389.10077 (2017): 1399-1409.

Trial design

STEP 4: Randomised, double-blind, multicentre, placebo-controlled, withdrawal trial

902 participants
with overweight or obesity

- Male or female ≥18 years
- BMI: ≥30 kg/m^2 or ≥27 kg/m^2 and ≥1 weight-related comorbidity
- Stable body weight ≥90 days
- HbA_{1c} <6.5%



Trial objectives

Week 20 to week 68

- To compare the effect of continued semaglutide treatment versus a switch to placebo# on body weight, cardiovascular risk factors, COAs, glucose metabolism, and other factors related to body weight
- To compare the safety and tolerability of continued semaglutide treatment versus a switch to placebo#

Week 0 to week 68

- To evaluate the efficacy and safety of semaglutide during the entire 68 weeks of treatment

Primary endpoint *(Week 20 to week 68)*

- % weight loss

Confirmatory secondary endpoints *(Week 20 to week 68)*

- Waist circumference
- Systolic blood pressure
- SF-36 (Physical Functioning)

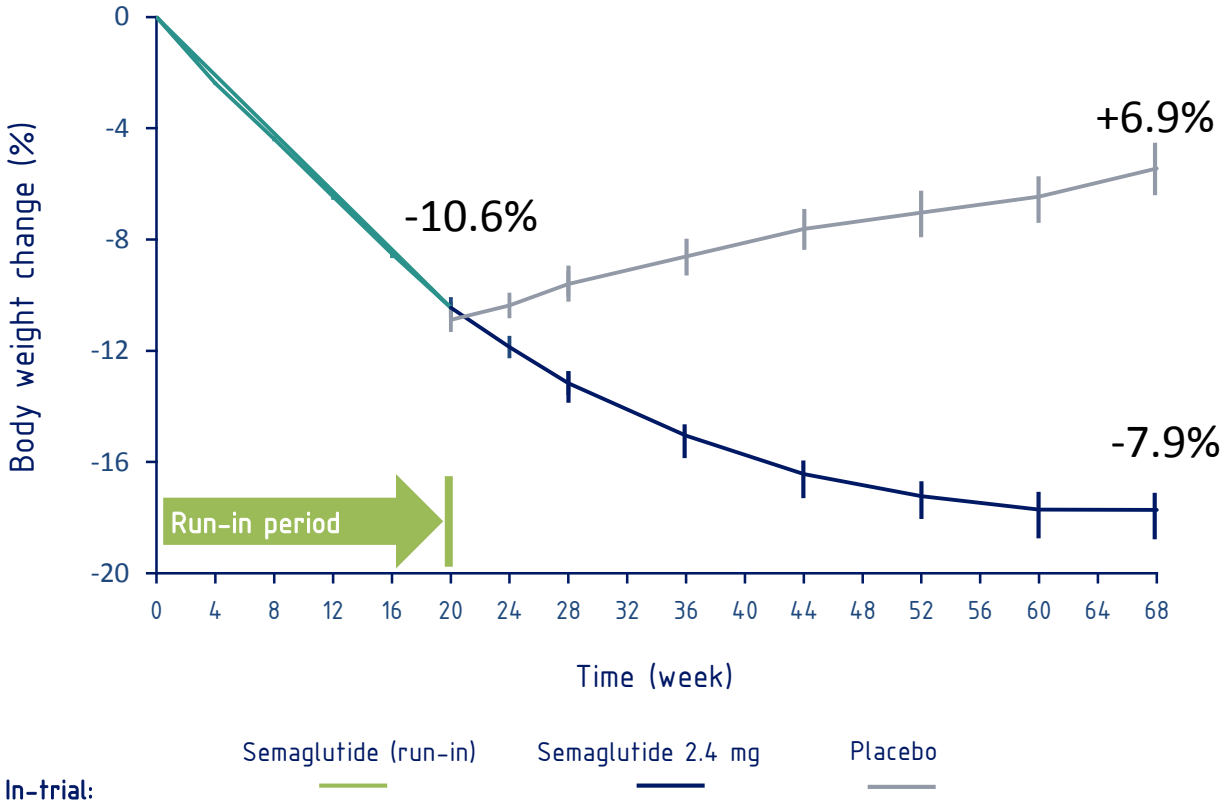
 # As an adjunct to lifestyle intervention (-500 kcal/day diet + 150 min/week physical activity).
BMI, body mass index; COAs, clinical outcome assessments; FU, follow-up; HbA_{1c}, glycated haemoglobin; IWQOL-Lite-CT, Impact of Weight on Quality of Life-lite; OW, once-weekly; s.c., subcutaneous; SF-36, Short Form 36-item Health Survey.
Rubino et al. JAMA. 2021;325:1414-25.

Body weight change (week 0–68)

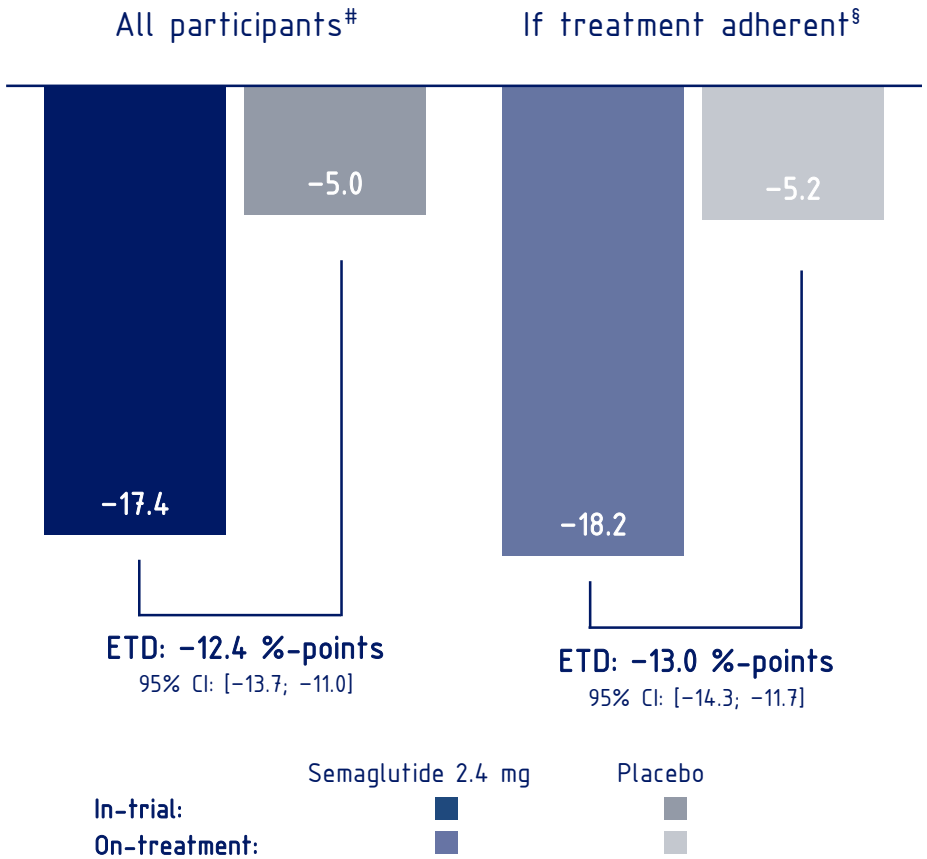
STEP 4

Observed body weight change over time

(Mean at week 0: 107.2 kg)

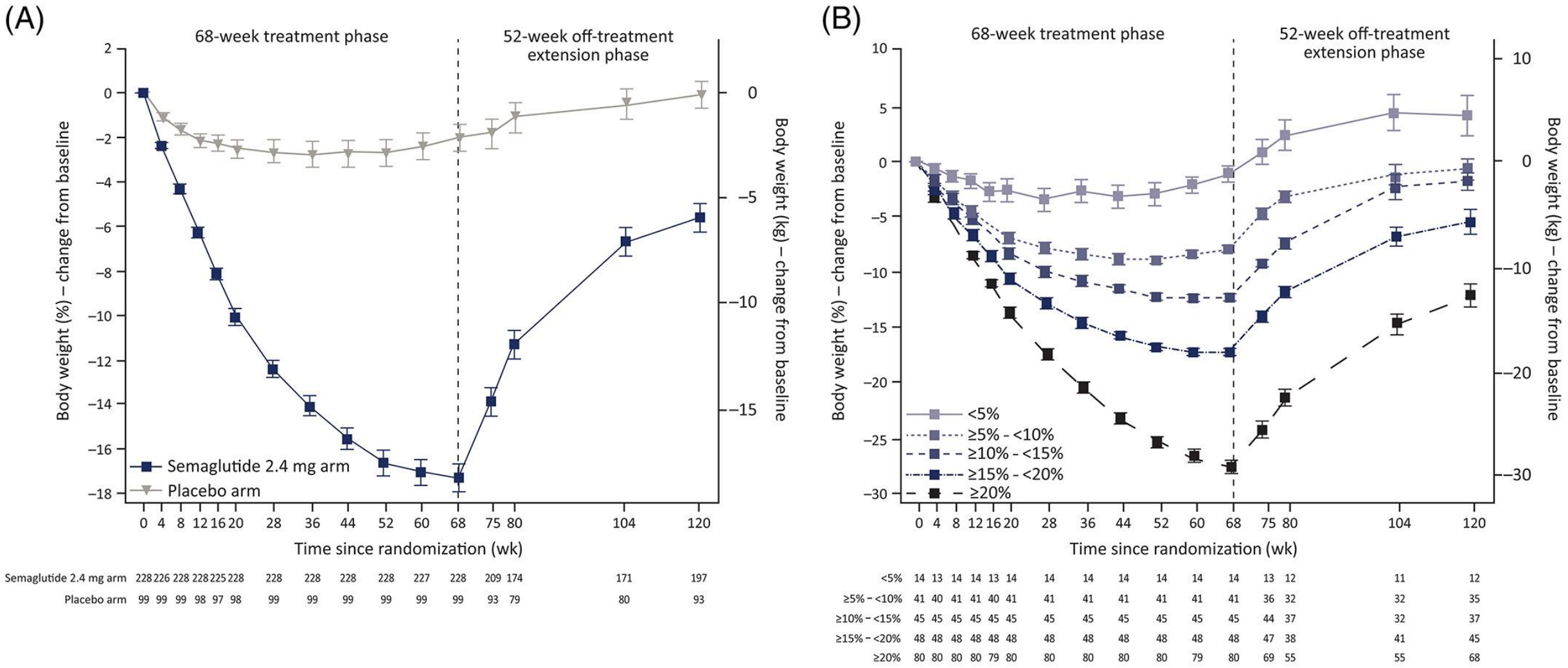


Estimated change from week 0 to week 68



#Treatment policy estimand (regardless of treatment adherence). §Trial product estimand.
Error bars are +/- standard error of the mean.
CI, confidence interval; ETD, estimated treatment difference; IT, in-trial; OT, on-treatment.
Rubino et al. JAMA. 2021;325:1414–25.

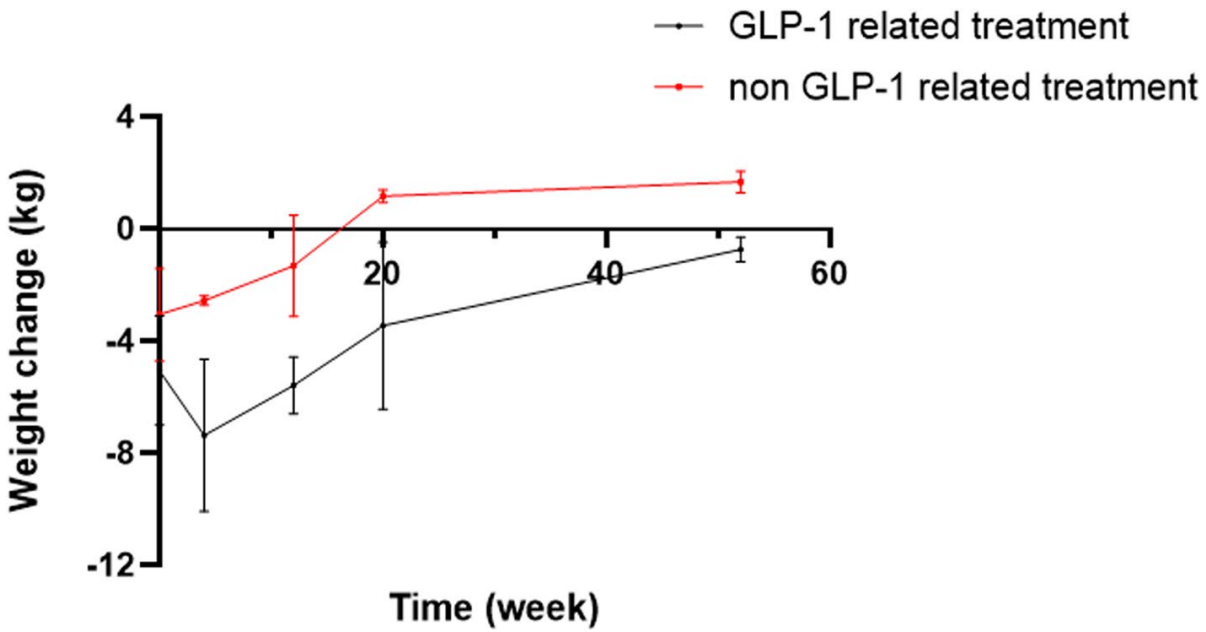
Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension

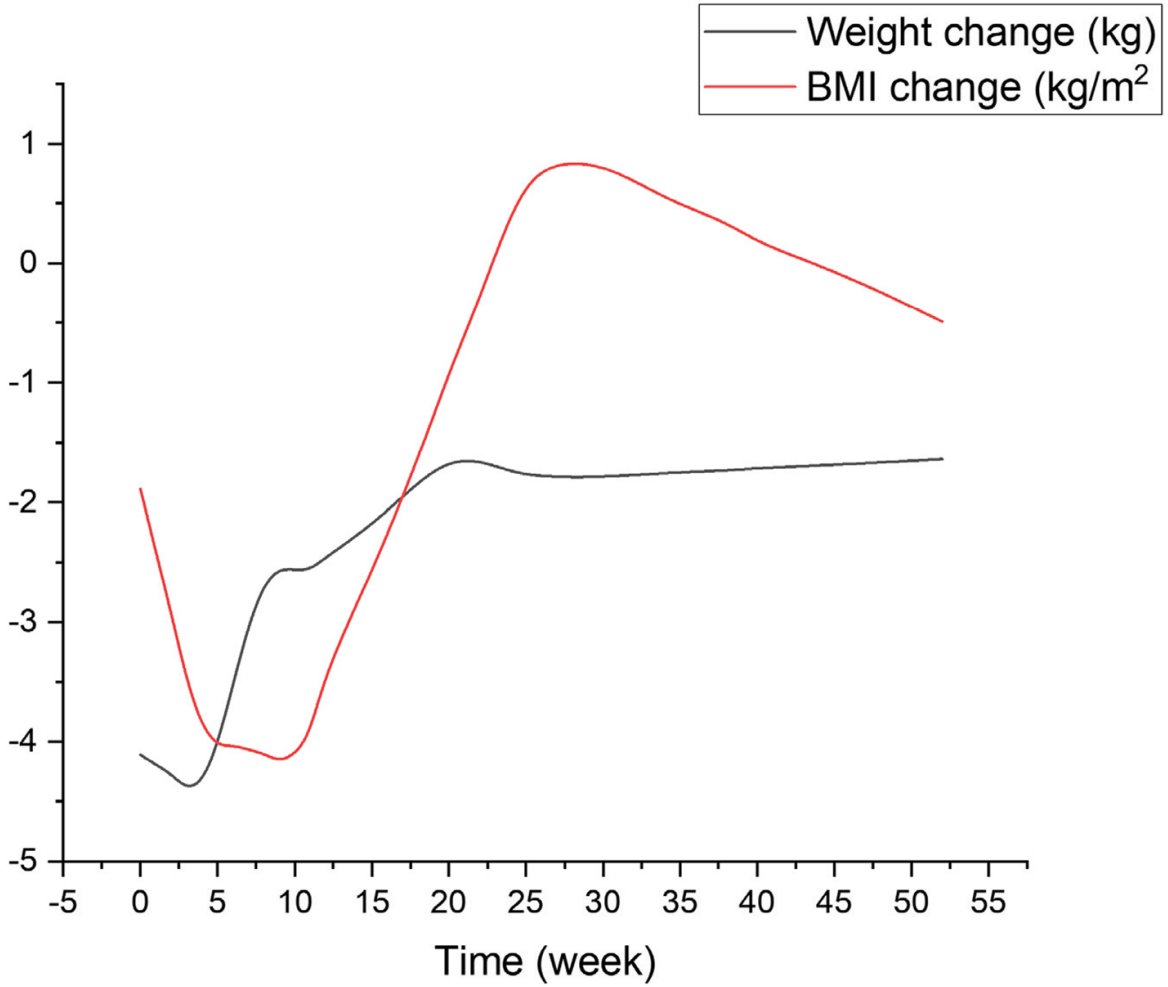


Diabetes Obesity Metabolism, Volume: 24, Issue: 8, Pages: 1553-1564, First published: 19 April 2022, DOI: (10.1111/dom.14725)

Trajectory of the body weight after drug discontinuation in the treatment of anti-obesity medications

중국 베이징대 연구진은 전 세계 비만치료제 임상시험 데이터 11건을 종합해 치료군 1,574명과 대조군 893명을 분석

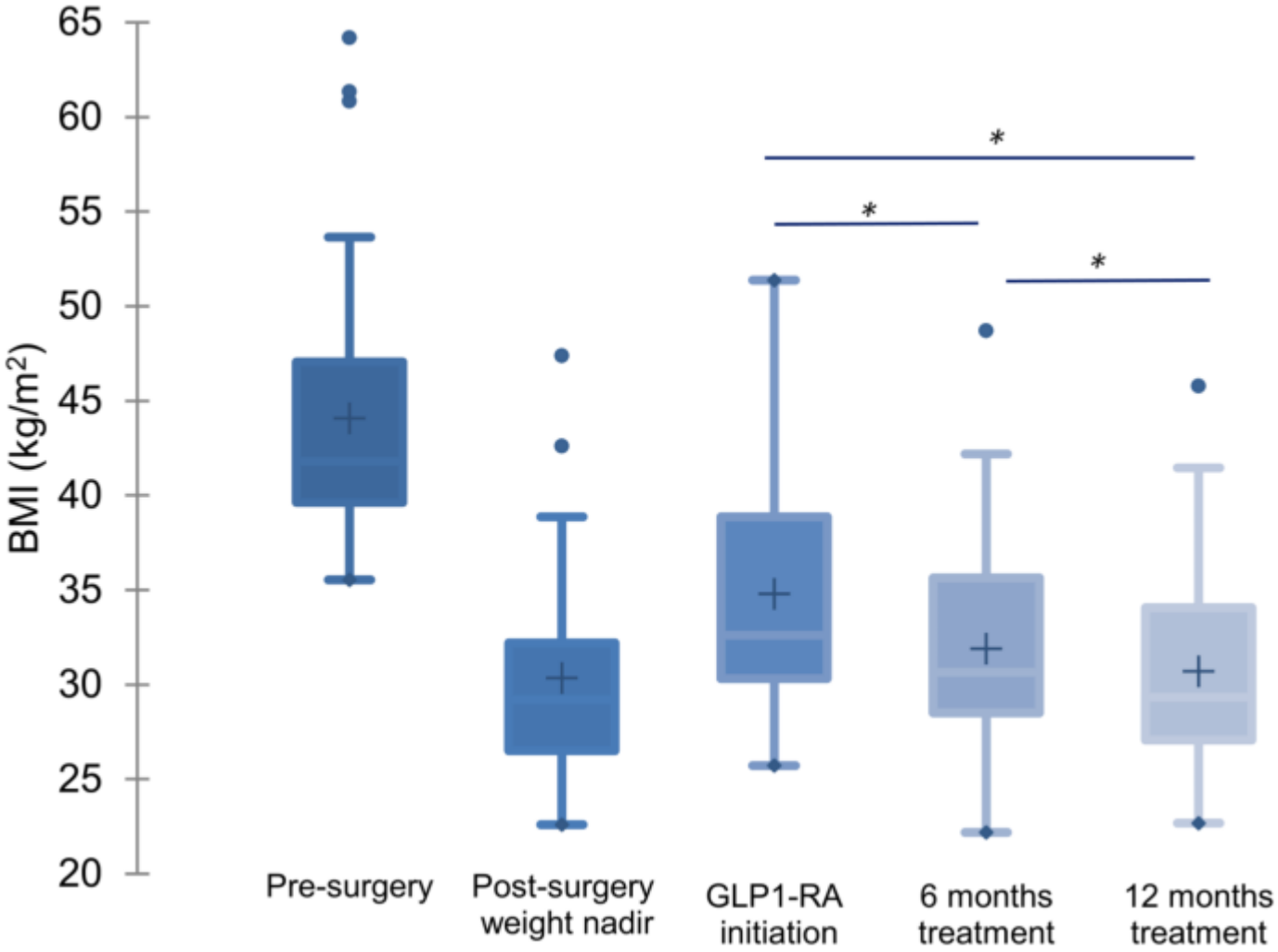




BMC medicine 23.1 (2025): 398.

GLP1RA after bariatric surgery

- 스위스 세인트 갈렌 주립병원 안데르스 보이젠 젠슨 등 연구진이 진행한 리라글루타이드와 세마글루타이드를 사용한 비만 수술 후 체중 재증가 치료 연구 결과
- 총 40명의 환자(여성 80%)가 분석에 포함
- 비만수술 이후 체중이 다시 증가한 환자에게 GLP-1 수용체 작용제(GLP-1 RA)를 12개월간 투여한 결과, 재증가한 체중의 99%가량을 감량하는 효과가 나타남
- The observed reduction in BMI was significantly lower with liraglutide than with semaglutide, 3.1 (2.0, 4.7) vs. 4.7 (3.7, 6.0) kg/m2 (P-value = 0.04).



BMC Endocrine Disorders volume 25, Article number: 93 (2025)

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pISSN 2951-0333 eISSN 2951-0597

비만대사연구학술지
Archives of Obesity and Metabolism

종 설

체중감량 이후 장기적인 유지를 위한 다양한 행동전략

조영혜[1,2]

[1]부산대학교 의과대학 가정의학교실, [2]양산부산대학교병원 가정의학과

- 체중유지에 효과적인 단 하나의 식사방법은 없으며 칼로리 제한, 탄수화물, 단백질, 지방의 건강한 비율, 식사대체요법 등의 다양한 식사조절 방법을 이용해 통합적으로 적절한 식사습관에 목표를 두어야 한다.
- 신체 활동량 증가는 체중감량과 유지를 위해 도움이 되지만 과도한 운동량을 권고하기보다는 현실 가능하고 장기적으로 실행 가능한 목표를 설정하는 것이 좋겠다.
- 체중 유지 단계에 맞게 목표를 재설정하고 자가 모니터링, 스트레스 관리 등의 행동요법을 지속적으로 적용해야 한다.

Thank You for Your Attention