What's New in Incretin based Therapies in 2024

GLMS Symposium

February 2024

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Nutrient –stimulated hormones and hormone based treatments

1. Gut hormones (GLP1, GIP, Glucagon, Amylin)
2. GLP1 agonists (Dulaglutide and Semaglutide)
3. Dual and triple agonists (Tirzepatide and others)
4. Monoclonal AB for treatment of obesity

Development of exenatide: an incretin mimetic (1980 and 90's)

- Synthetic version of salivary protein found in the Gila Gila monster[1]
- More than 50% overlap with human GLP-1[1]
  - Binds GLP-1 receptors on β-cells (*in vitro*)[2]
  - Resistant to DPP-IV inactivation[3]
    - Following injection, exenatide is measurable in plasma for up to 10 hours[4]

[1]**Eng J, et al. *J Biol Chem* 1992;267:7402–7405**; Adapted from [2]Nielsen LL, et al. *Regul Pept* 2004;117:77–88; [3]Drucker DJ. *Diabetes Care* 2003;26:2929–2940; [4]Calara F, et al. *Clin Ther* 2005;27:210–215.

Incretin Therapies: Effects Beyond Glycemic Control

Mudaliar S, Henry RR Eur J Intern Med. 2009 Jul; 20 Suppl 2: p 319-28 (Review)

The incretin hormones

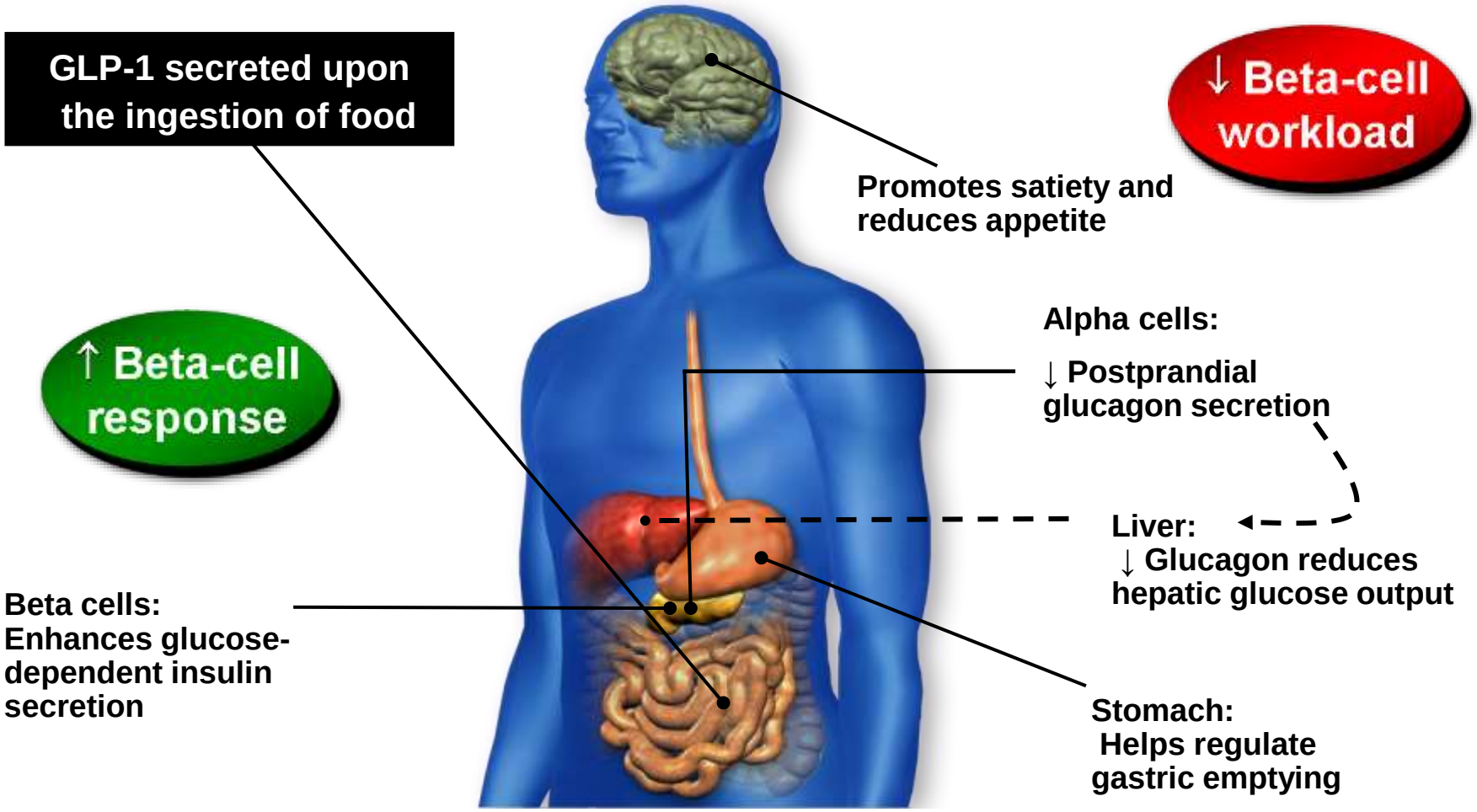
1. **glucagon-like peptide-1 (GLP-1)**
2. glucose-dependent insulinotropic polypeptide (GIP)

- peptide hormones produced by the gastrointestinal tract (L cells in the ileum and colon) in response to nutrient entry

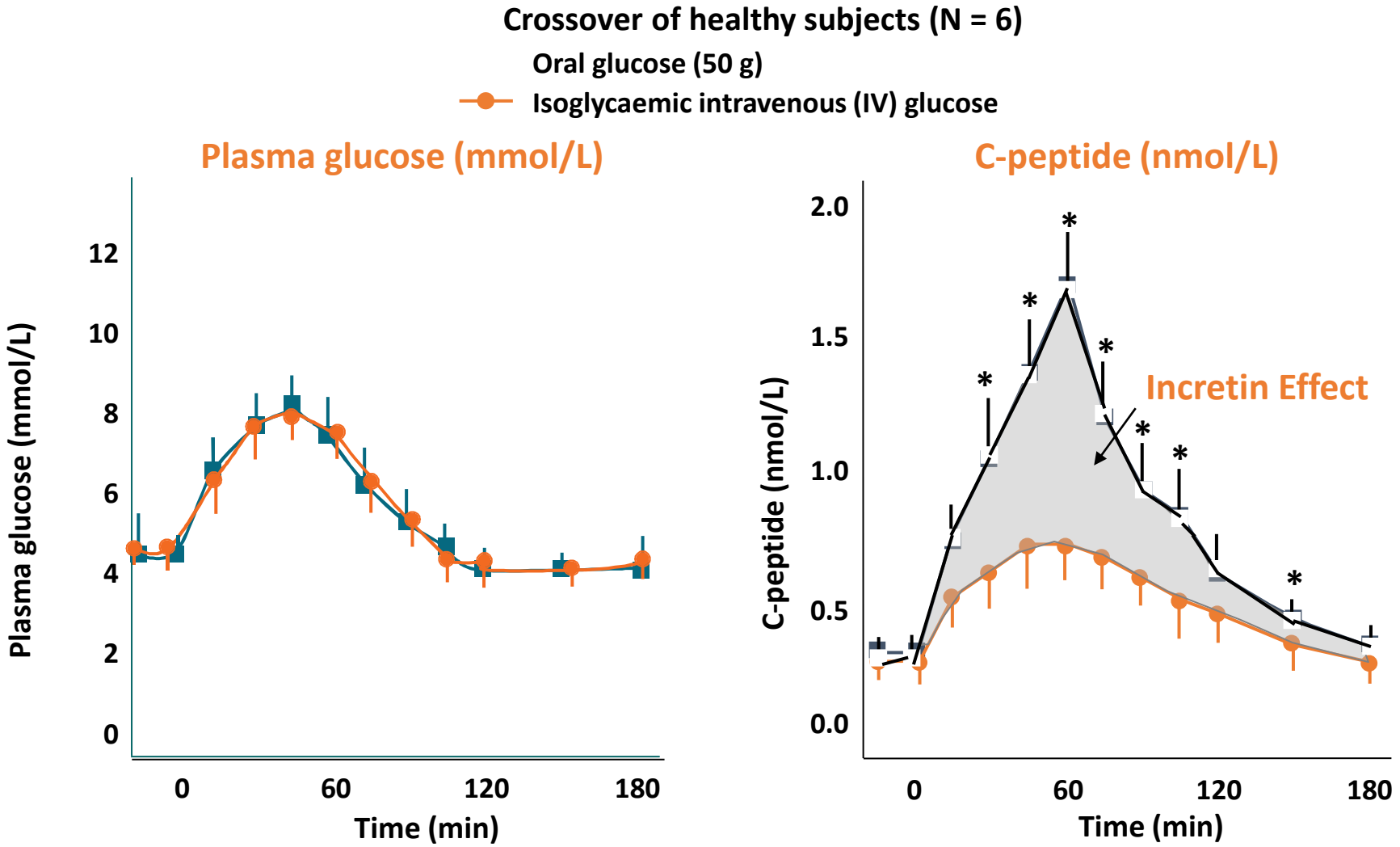
- **play a major role in glucose homeostasis**

    1. stimulate insulin secretion
    2. suppress glucagon secretion
    3. inhibit gastric emptying
    4. reduce appetite and food intake

GLP-1 Effects in Humans: Understanding the Glucoregulatory Role of Incretins



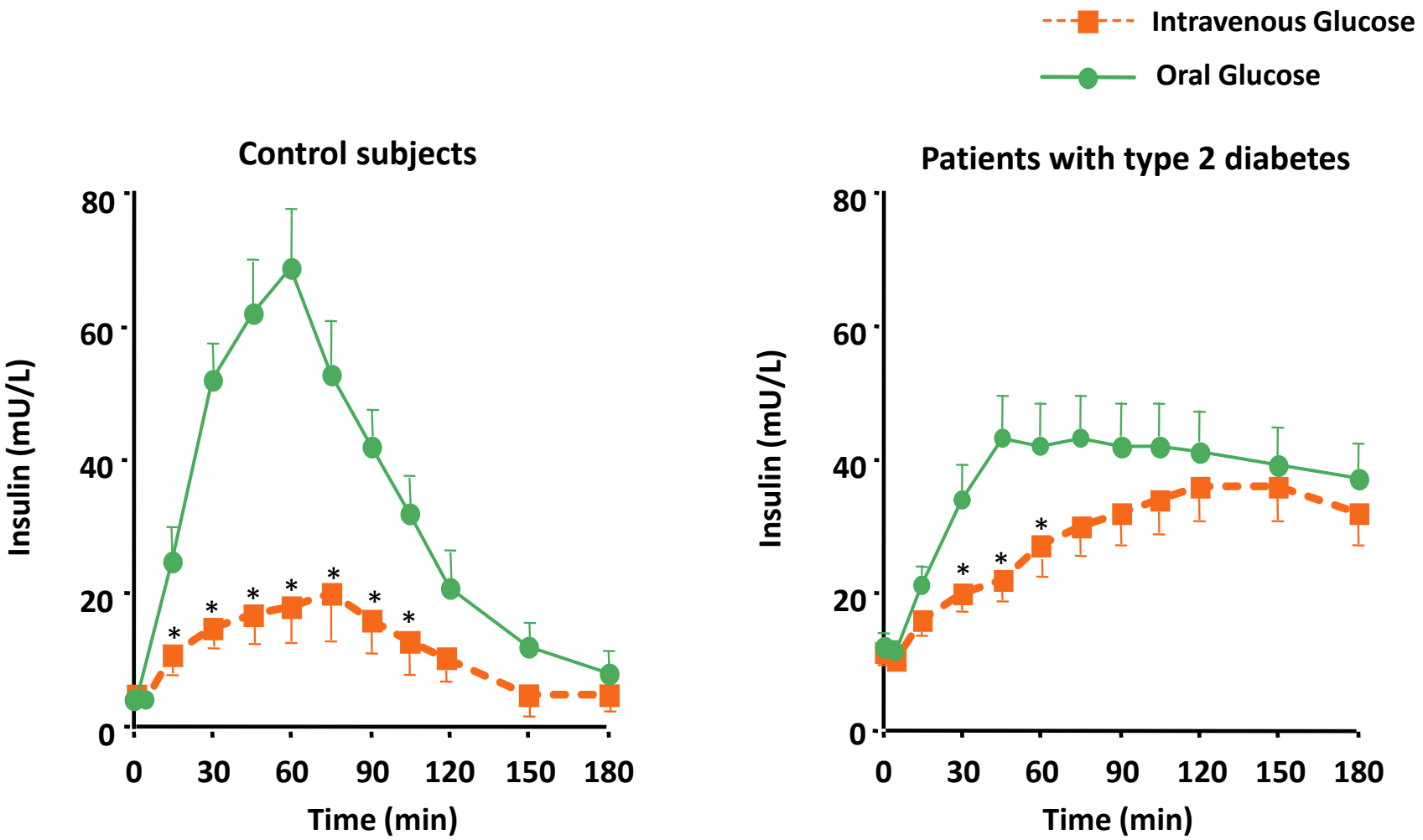
The incretin effect
β-cell response to oral vs IV glucose



Mean (SE); *$P \leq 0.05$

Data from Nauck MA, et al. *J Clin Endocrinol Metab* 1986;63:492–498. Plasma glucose values converted to mmol/L from mg/dL using conversion factor of 0.0555; C-peptide values converted to nmol/L from ng/mL using conversion factor 0.333.

The incretin effect is reduced in patients with type 2 diabetes



*$P \leq .05$ compared with respective value after oral load.
Nauck MA, et al. *Diabetologia* 1986;29:46–52.

Different GLP1 agonists

Available in NZ

- Liraglutide 1.8 mg (for DM2)
- Liraglutide 3mg (for weight management)

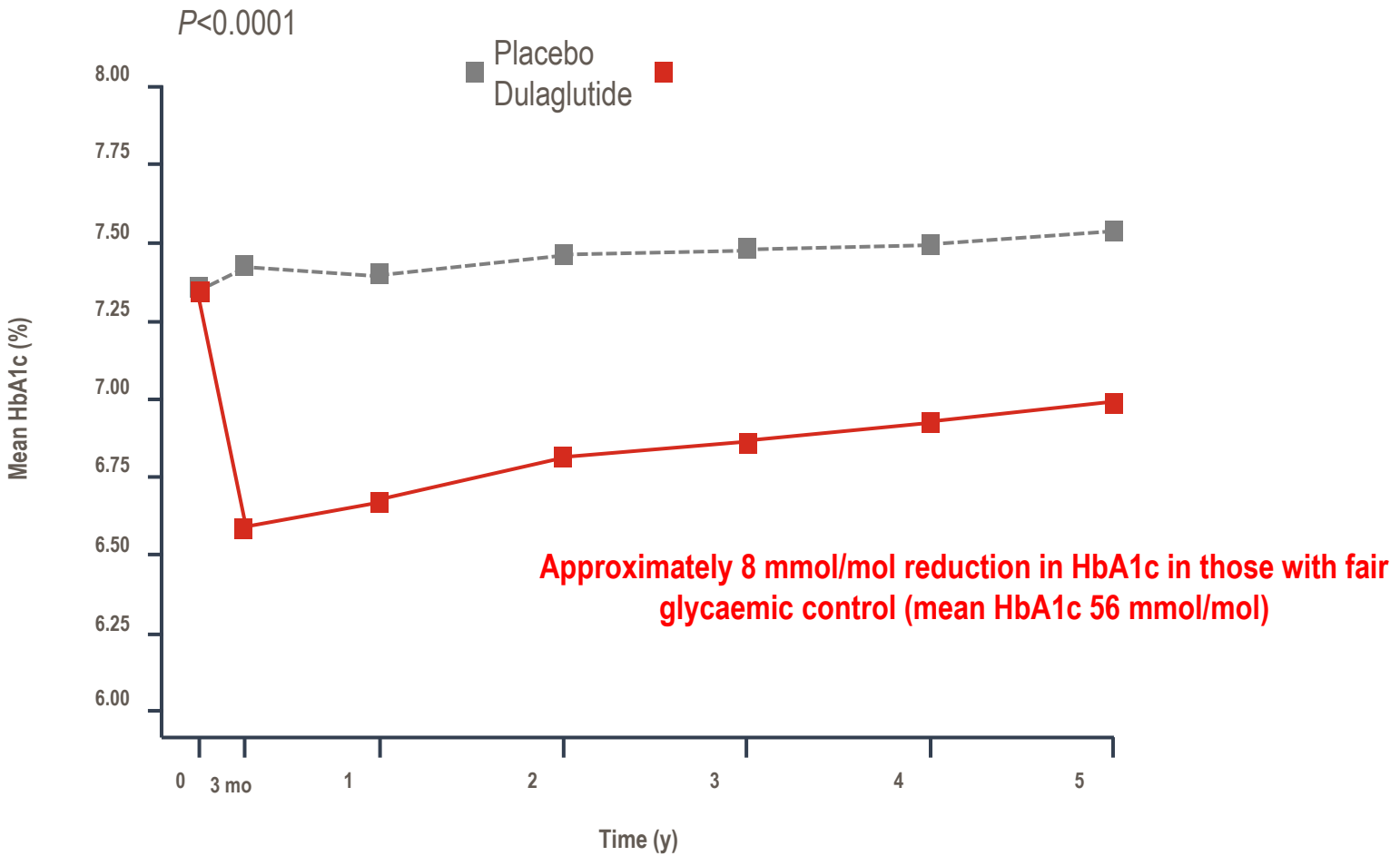
- **Dulaglutide (1x week)**

- **International**
- Exenatide bd
- Exenatide LAR (1x week)
- Liraglutide 1.8 mg
- Liraglutide 3mg (for weight management)
- Semaglutide s/c and **oral**
- Lixisenatide s/c
- Dulaglutide s/c
- Tircepatide (dual GLP1/GIP)

REWIND Trial

- Multinational study of **9901 patients** with T2D + either known CVD or ≥ risk factors randomized to:
  - Placebo (n = 4952)
  - Dulaglutide 1.5 mg weekly **(n = 4949)**
- Powered for 3-point MACE with median follow up **5.4 years**
- Baseline characteristics:
  - Mean age 66 years (57% male) with mean **BMI 32.3 kg/m^2**
  - 31.5% had had prior CVD
- Treatment was additional to standard management:
  - 82% on ACEi/ARB + 46% on β-blockers
  - 66% on statins
  - 54% on antiplatelet therapy

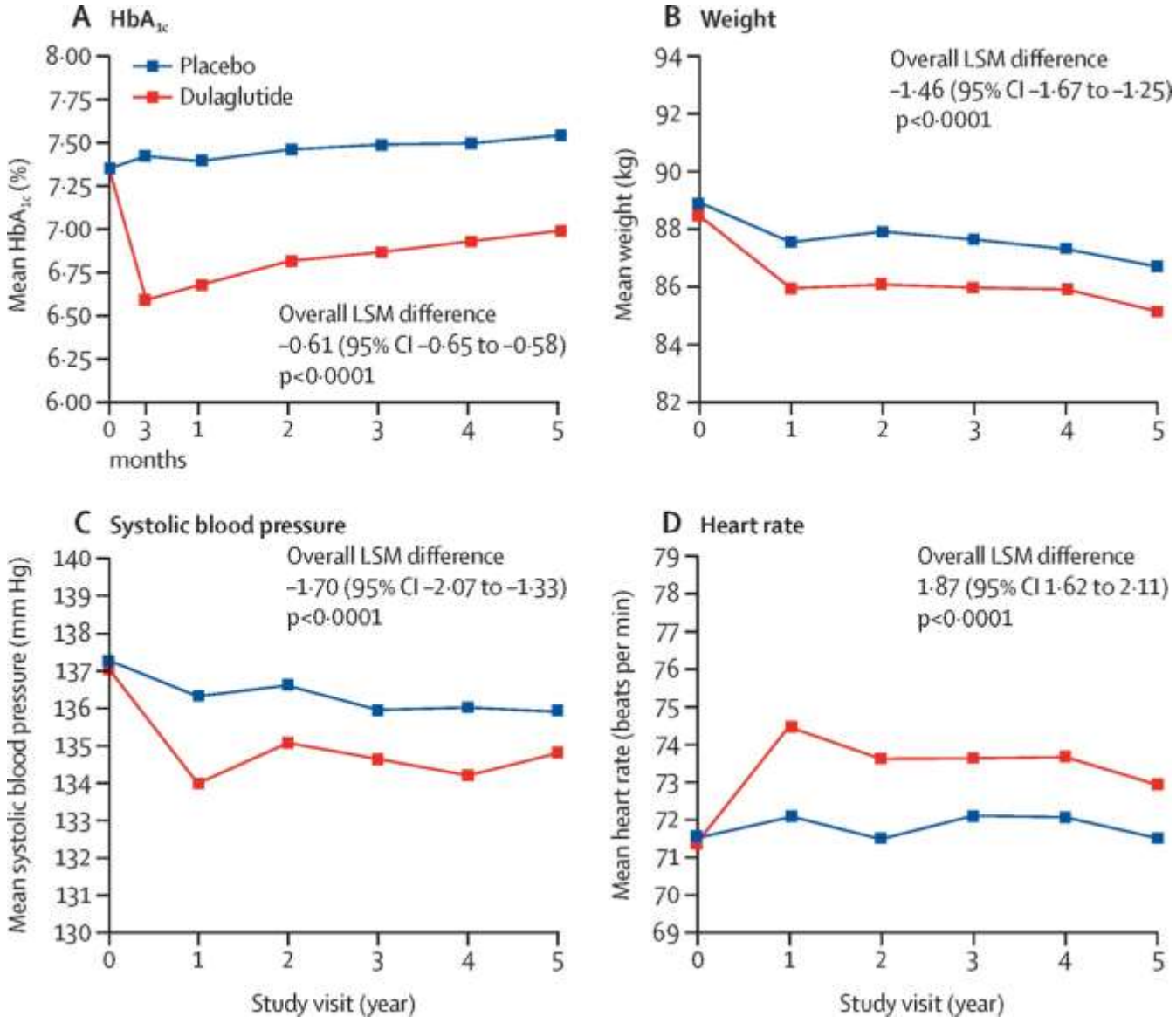
Reduction in HbA1c with dulaglutide



Associated with mean reductions in weight of 2 kg, SBP of 2 mmHg + LDLc 0.05 mmol/L (P all < 0.001)

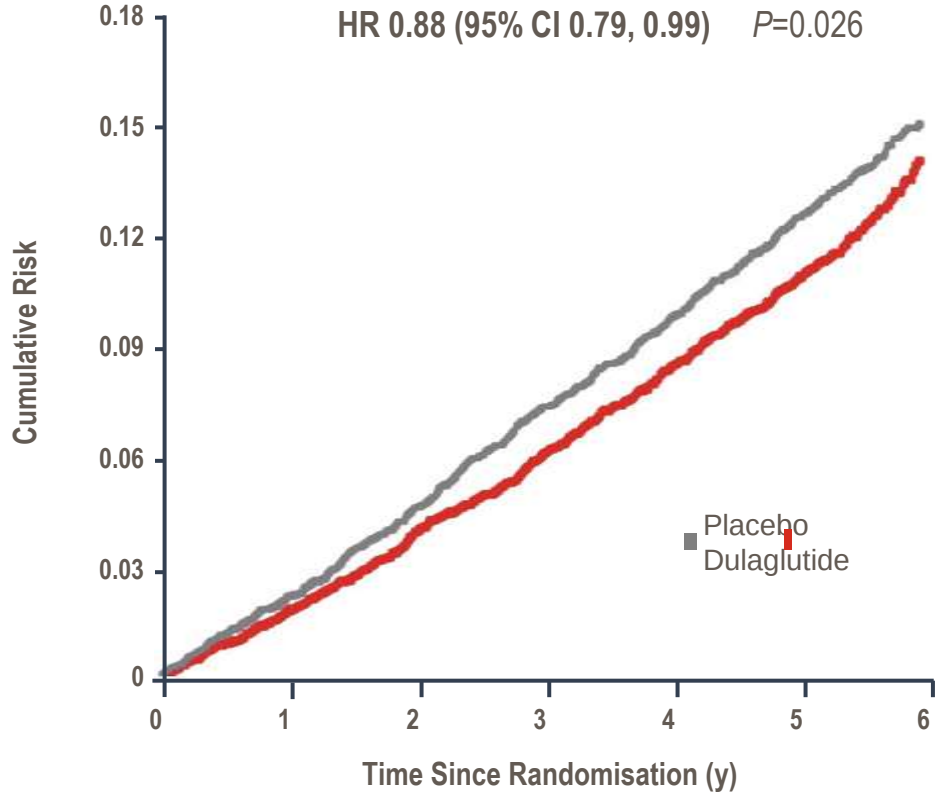
Adapted from Gernstein H *et al*. *Lancet* 2019; 394:121-130

Dulaglutide – REWIND trial



Gerstein et al 2019. Lancet

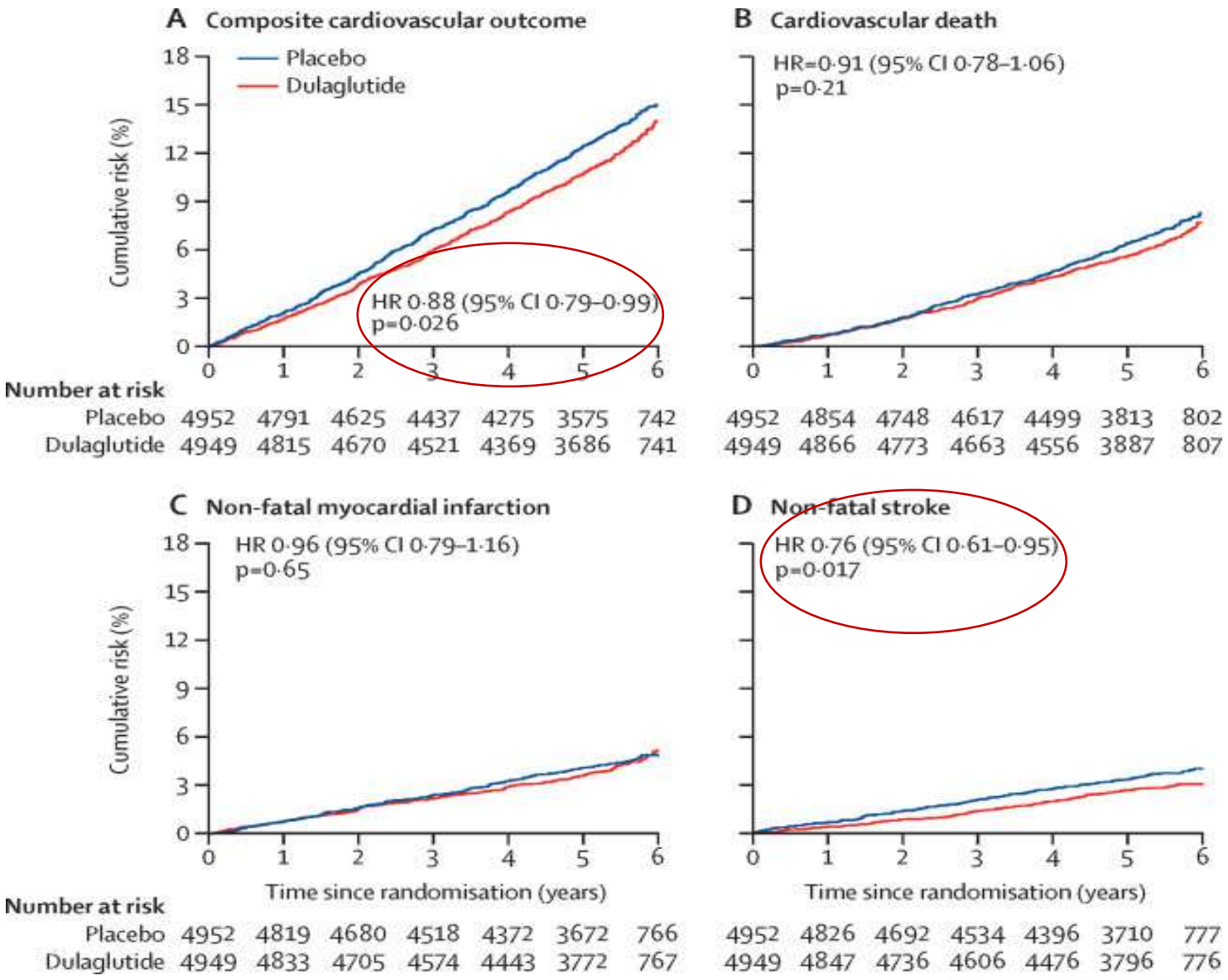
Reductions in CV death, non-fatal MI + stroke with dulaglutide



NNT = 18 for 5.4 years in established CVD
NNT = 60 for 5.4 years in subclinical vascular disease or ≥ 2 CVD risk factors

Adapted from Gernstein H *et al*. *Lancet* 2019; 394:121-130

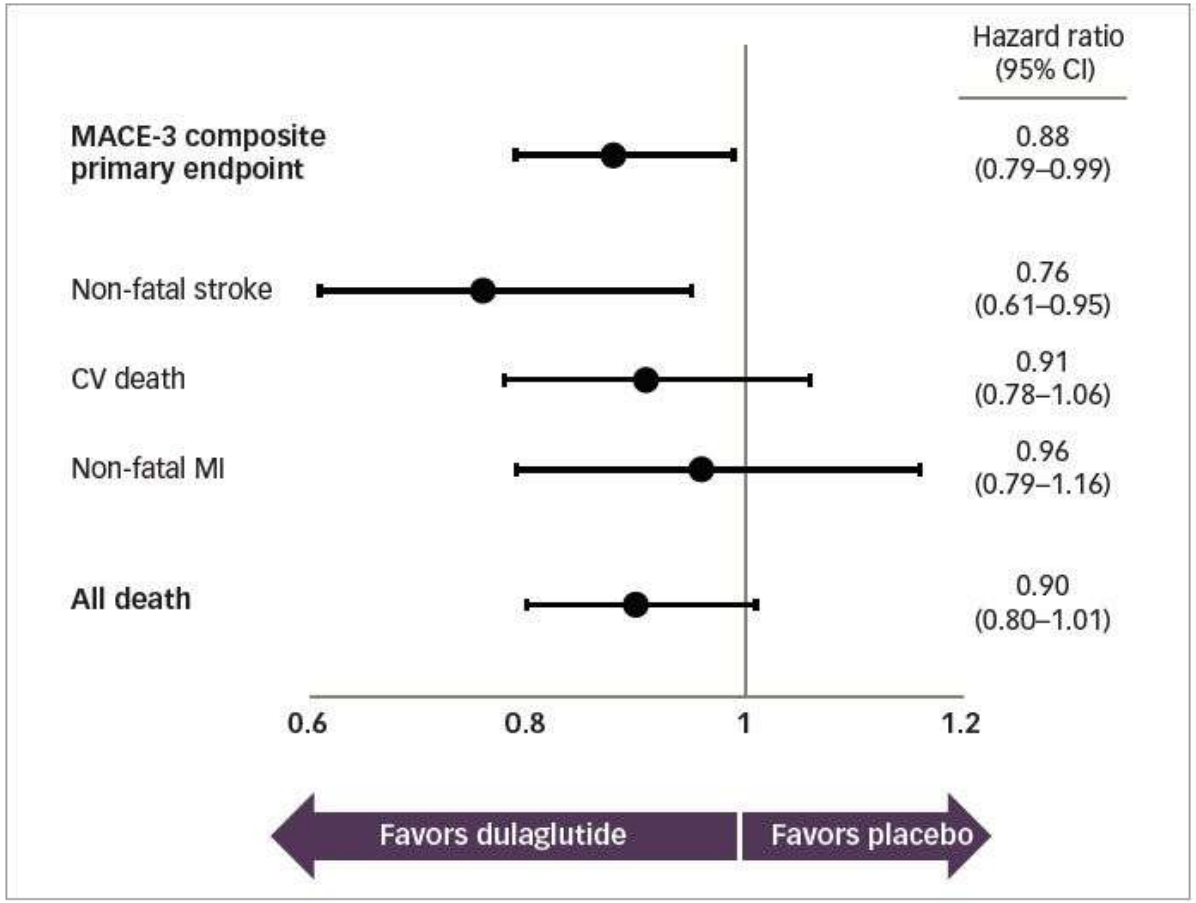
Dulaglutide – REWIND trial



Gerstein et al 2019. Lancet

Dulaglutide – REWIND trial

Figure 2: Individual cardiovascular outcomes of the REWIND trial

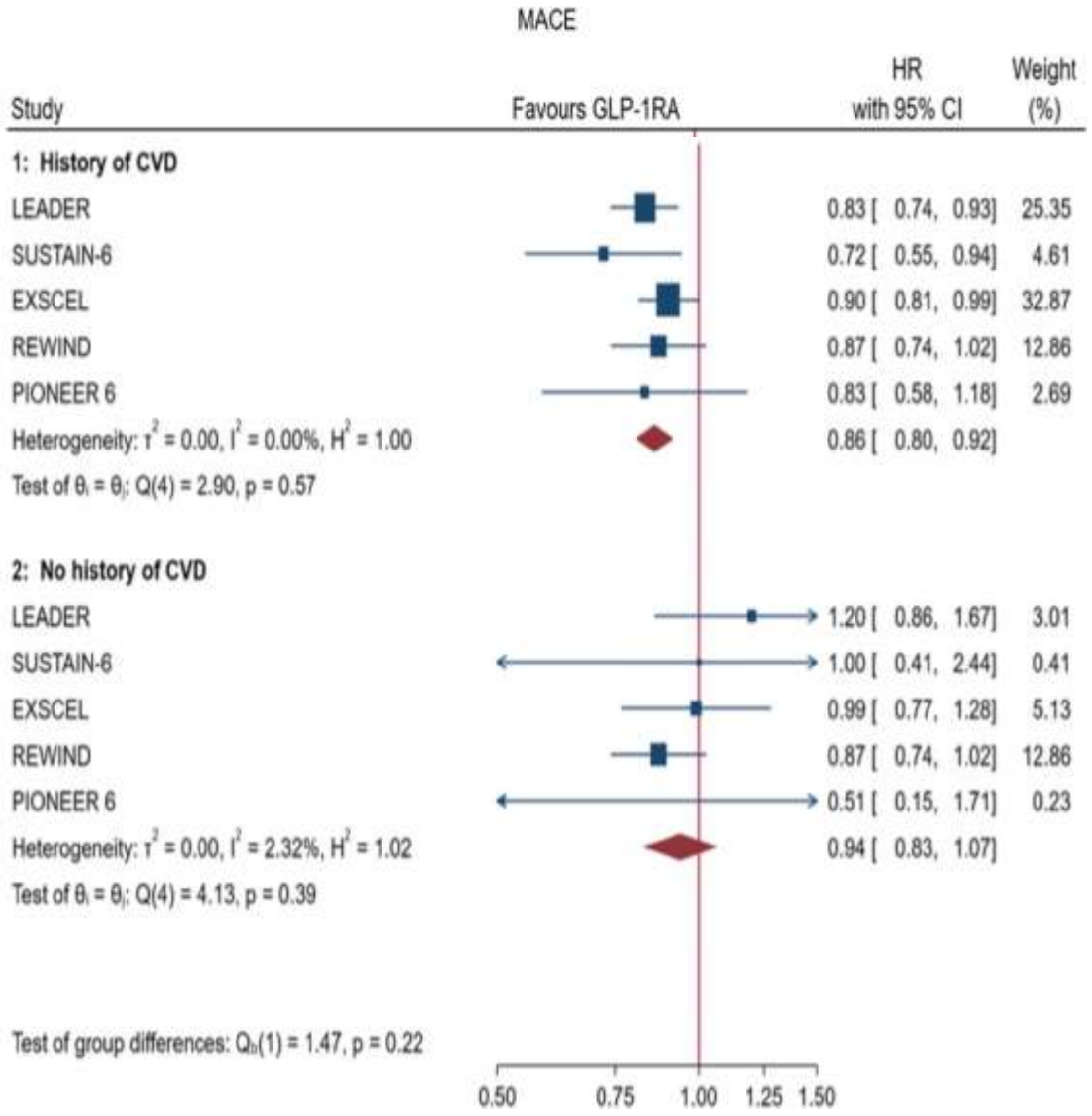


CI = confidence interval; CV = cardiovascular; MACE = major cardiovascular events; MI = myocardial infarction.

Reused with permission from The Lancet. *Source: Gerstein et al. 2019.*[10]

Gerstein et al 2019. Lancet

But clear class effect of GLP1RA on MI, stroke + CVD death



Data for potential role in primary prevention only for dulaglutide at present

LEADER = liraglutide

SUSTAIN-6 = semaglutide

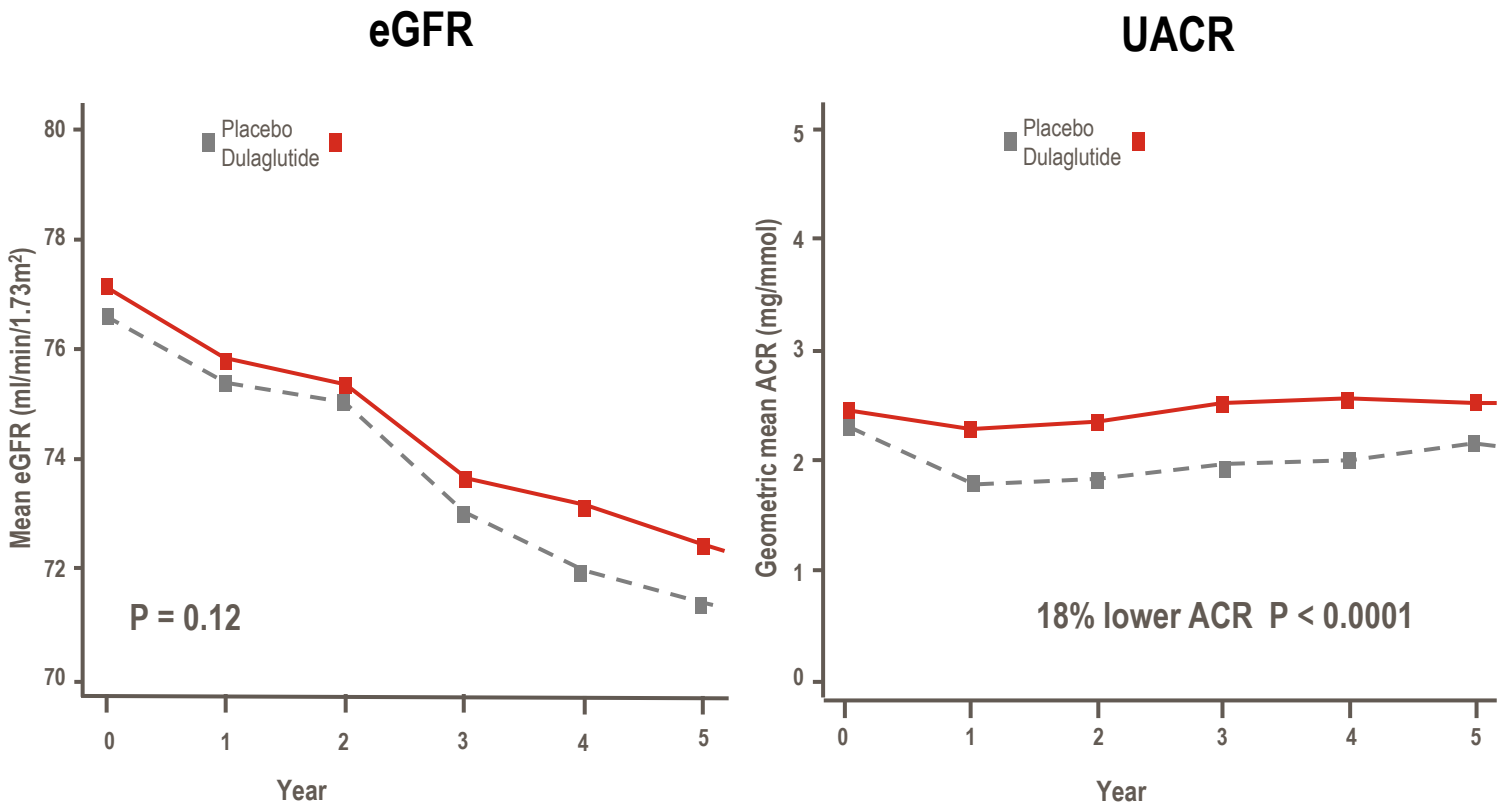
EXSCEL = exenatide

REWIND = dulaglutide

PIONEER-6 = semaglutide

Giugliano et al. Diabetes, Obesity + Metabolism. 2019; 21(11):2576

Effects of dulaglutide on diabetic renal disease



No evidence to date the improvements result in a significant reduction in RRT or renal death

Adapted from Gernstein H *et al*. *Lancet* 2019; 394:121-130

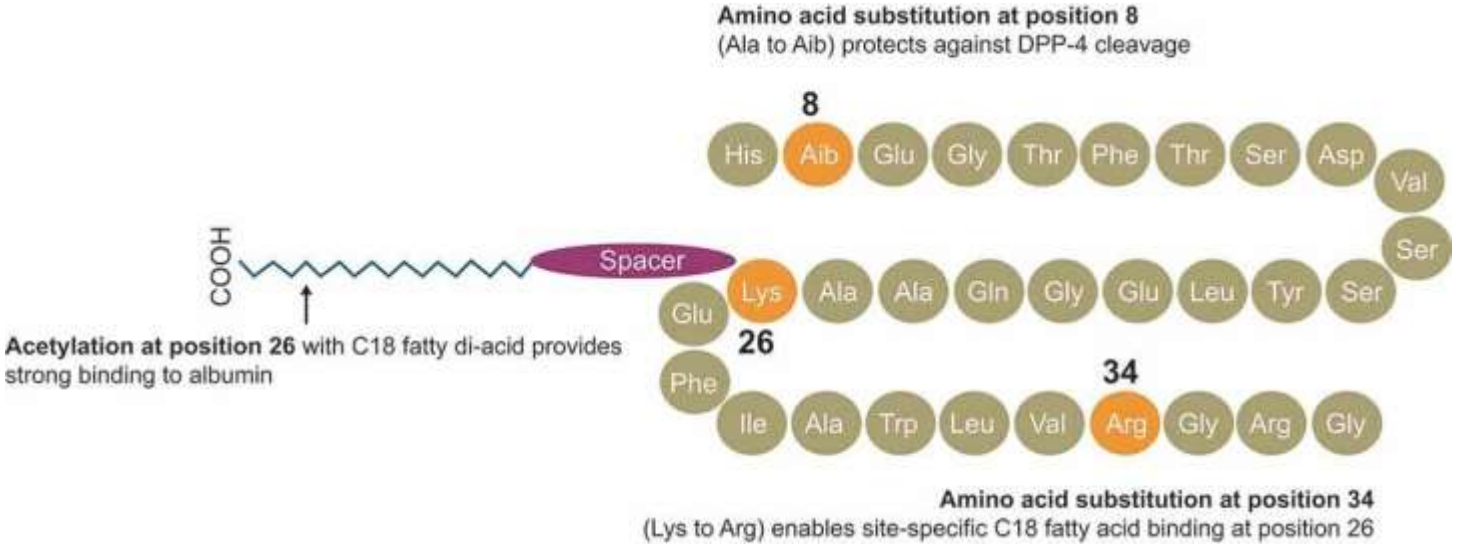
Precautions with use of dulaglutide

- No safety data so **not recommended** for use in:
  - Pregnancy/breast feeding
  - Children < 18 years of age
  - **eGFR < 15 mL/min**
  - Type 1 diabetes

- Due to risk of volume depletion be cautious in those > 75 years of age
  - Particularly those on diuretics, ACEi/ARBs + NSAIDs

- Due to risk of other potential adverse effects not recommended for use in:
  - Significant gastrointestinal disease – especially gastroparesis or **severe GORD**
  - Previous pancreatitis
  - History of medullary thyroid carcinoma or multiple endocrine neoplasia 2 (MEN2) syndrome

Semaglutide



- Semaglutide - human GLP-1 analog with
- 94% amino acid homology to native GLP-1
- half-life of approximately 1 week
- Three important structural modifications - to the semaglutide molecule that extend its half-life to approximately 1 week

Semaglutide – available evidence

STEP trials – primary **obesity** (2.4mg weekly)

- STEP-Teens (12-18 years)
- STEP 1 to 5 trials

SUSTAIN trials (1-7) – primarily **diabetes** (0.5 and 1.0mg weekly)

- 2,3,4 – combination with other DM medications
- Sustain 7- Sema vs. Dulagutide
- Sustain 6 Sema vs Liraglutide

SELECT CVOT trial

OASIS & PIONEER - oral semaglutide

- **Combination:**
  - Cargri-sema (Cargrilintide 2.4mg and Sema 2.4mg)

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Once-Weekly Semaglutide in Adults with Overweight or Obesity

John P.H. Wilding, D.M., Rachel L. Batterham, M.B., B.S., Ph.D., Salvatore Calanna, Ph.D., Melanie Davies, M.D., Luc F. Van Gaal, M.D., Ph.D., Ildiko Lingvay, M.D., M.P.H., M.S.C.S., Barbara M. McGowan, M.D., Ph.D., Julio Rosenstock, M.D., Marie T.D. Tran, M.D., Ph.D., Thomas A. Wadden, Ph.D., Sean Wharton, M.D., Pharm.D., Koutaro Yokote, M.D., Ph.D., Niels Zeuthen, M.Sc., and Robert F. Kushner, M.D., for the STEP 1 Study Group*

N ENGL J MED 384;11 NEJM.ORG MARCH 18, 2021

STEP 1 trial

Once-Weekly Semaglutide in Adults with Overweight or Obesity

- **1961 adults** with a body-mass index >30kg/m2, 2:1 ratio, **68 weeks**
- once-weekly *subcutaneous* semaglutide (**dose of 2.4 mg**) or placebo, plus lifestyle intervention.
- **The co-primary end points:** percentage **change in body weight** and weight **reduction of at least 5%** (ITT analysis)

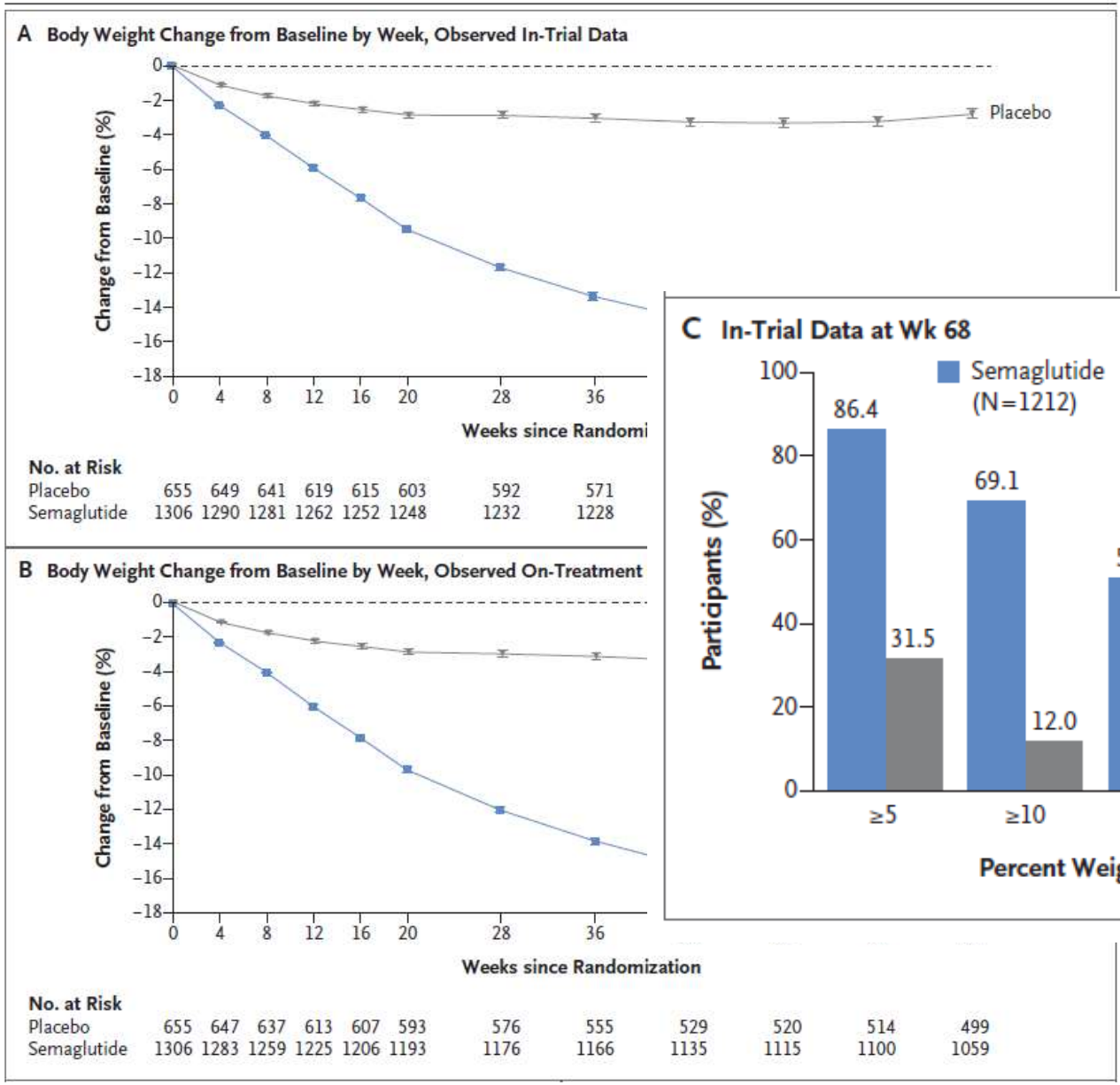
- **Results:** The mean change in body weight from baseline to week 68 was **-14.9%** in the semaglutide group as compared with **-2.4%** with placebo, for an estimated treatment difference of **-12.4** % (95% confidence interval [CI] -13.4 to -11.5; P<0.001).

- Participants who received semaglutide had a greater improvement in cardiometabolic risk factors and a greater increase in physical functioning

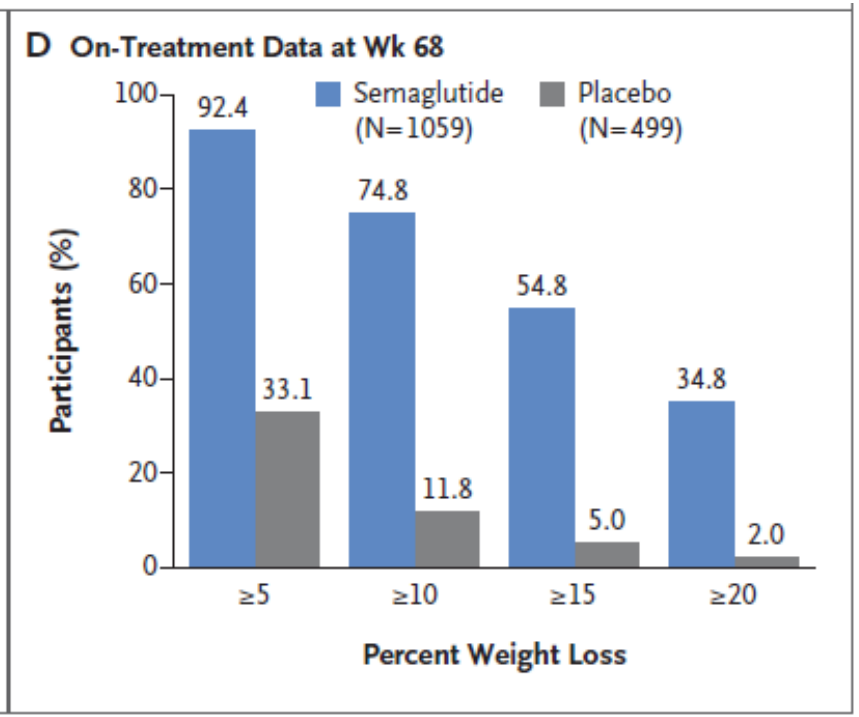
- *Nausea and diarrhea were the most common adverse events, typically transient and mild-to-moderate and subsided with time*

- **Conclusions:** 2.4 mg of semaglutide - associated with **sustained, clinically relevant** reduction in weight

- (Funded by Novo Nordisk; STEP 1)


A Body Weight Change from Baseline by Week, Observed In-Trial Data
Change from Baseline (%)
0
−2
−4
−6
−8
−10
−12
−14
−16
−18
Placebo
0 4 8 12 16 20 28 36
Weeks since Randomi
No. at Risk
Placebo 655 649 641 619 615 603 592 571
Semaglutide 1306 1290 1281 1262 1252 1248 1232 1228
B Body Weight Change from Baseline by Week, Observed On-Treatment
Change from Baseline (%)
0
−2
−4
−6
−8
−10
−12
−14
−16
−18
0 4 8 12 16 20 28 36
Weeks since Randomization
No. at Risk
Placebo 655 647 637 613 607 593 576 555 529 520 514 499
Semaglutide 1306 1283 1259 1225 1206 1193 1176 1166 1135 1115 1100 1059

C In-Trial Data at Wk 68
Semaglutide (N=1212)
Placebo (N=577)
Participants (%)
100
80
60
40
20
0
86.4
31.5
69.1
12.0
50.5
4.9
32.0
1.7
≥5 ≥10 ≥15 ≥20
Percent Weight Loss


D On-Treatment Data at Wk 68
Semaglutide (N=1059)
Placebo (N=499)
Participants (%)
100
80
60
40
20
0
92.4
33.1
74.8
11.8
54.8
5.0
34.8
2.0
≥5 ≥10 ≥15 ≥20
Percent Weight Loss

Risks and side effects - Semaglutide

- **pancreatitis** have been described in connection with the use of GLP-1RAs
  - STEP 1 to 5 trials - history or presence of chronic pancreatitis or acute pancreatitis within the past 180 days **excluded**
  - consensus statement: GLP-1RAs should be used cautiously (if at all) in patients with a history of pancreatitis (due to a lack of clinical trial data), and that treatment should be discontinued if acute pancreatitis develops

- Weight loss is known to increase the risk of **cholelithiasis,** prevalence reaching **12%** after 8 - 16 weeks of a low-calorie diet and reaching greater than **30%** within 12 - 18 months after gastric bypass surgery
  - GLP-1RA treatment has been linked with an increase in gallbladder AEs, including cholelithiasis and cholecystitis
  - In STEP 1, 3, and 5, gallbladder-related disorders were reported in a higher proportion of participants in semaglutide 2.4 mg groups

- The prescribing information for semaglutide state that they have been reported to cause **thyroid C-cell tumors in rodents**
  - A meta-analysis of 11 cardiovascular outcomes studies of GLP-1RAs including over **55,000 patients** identified **no increased risk** of MTC with GLP-1RAs
  - No cases of MTC were reported in STEP 1 to 5, no imbalances in calcitonin levels between semaglutide 2.4 mg and placebo

STEP trial programme (primary Obesity)

- **In STEP 1** - 52-week **off-treatment extension** phase of STEP 1 - **weight regain in both treatment** arms
- weight loss of 5.6% with semaglutide and 0.1% with placebo

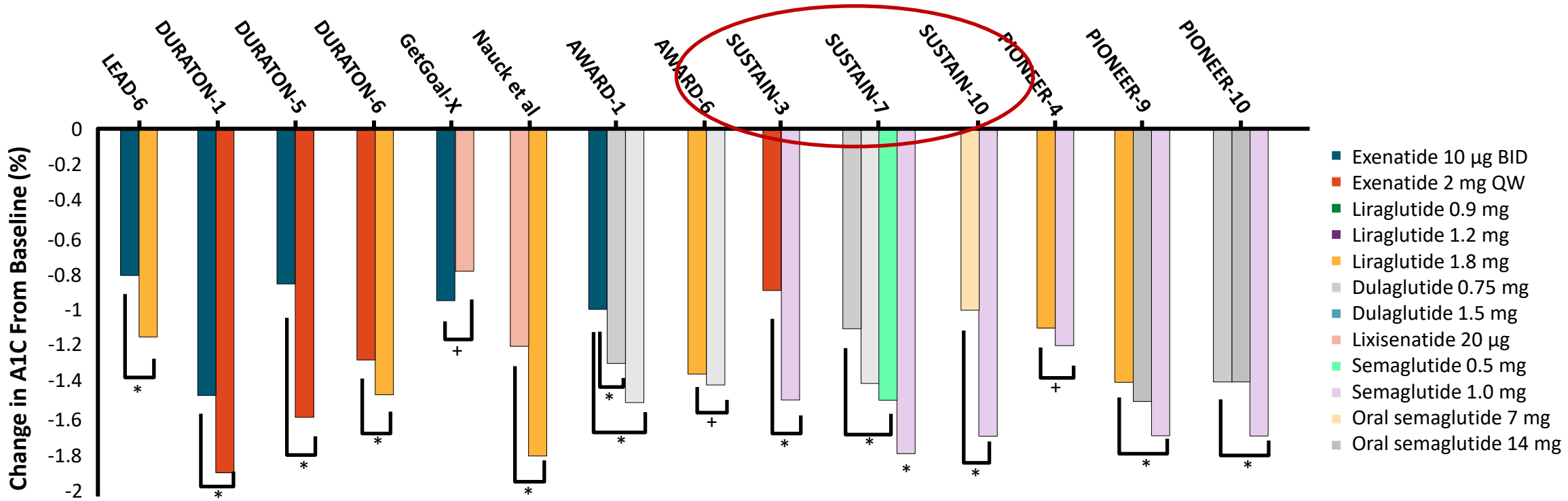
- **STEP 3 - IBT +** semaglutide and an initial **low-calorie diet**

*STEP 3 (placebo-subtracted weight loss **10.3%)** vs. STEP 1 (placebo-subtracted weight loss **12.4%)***

the inclusion of an intensive lifestyle intervention (including a partial meal replacement program and 30 treatment sessions) no additional weight loss beyond that achieved with semaglutide and less intensive lifestyle intervention.

- In **STEP 5,** once-weekly semaglutide resulted in substantial initial body weight reductions that were then **maintained over 104 weeks** compared to placebo.
- There **was no additional weight loss between weeks 52–104;** weight loss was maintained during this period. The mean weight loss in the semaglutide group was **–15.2%,** compared to –2.6% in the placebo group

GLP-1 RA Comparative **Studies in T2D**: Change in A1C



*P <.05. †P <.05, meeting predefined noninferiority margin.

Figure adapted from: Trujillo. Ther Adv Endocrinol Metab. 2021;12:2042018821997320. Note that direct comparisons between clinical trials cannot be made. Ahmann. Diabetes Care. 2018;41:258. Blevins. J Clin Endocrinol Metab. 2011;96:1301. Buse. Lancet. 2009;374:39. Buse. Lancet. 2013;381:117. Capehorn. Diabetes Metab. 2020;46:100. Drucker. Lancet. 2008;372:1240. Dungan. Lancet. 2014;384:1349. Nauck. Diabetes Care. 2016;39:1501. Pratley. Lancet. 2019;394:39. Pratley. Lancet Diabetes Endocrinol. 2018;6:275. Rosenstock. Diabetes Care. 2013;36:2945. Wysham. Diabetes Care. 2014;37:2159. Yabe. Lancet Diabetes Endocrinol. 2020;8:392. Yamada. Lancet Diabetes Endocrinol. 2020;8:377.

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes

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CVOT in DM2

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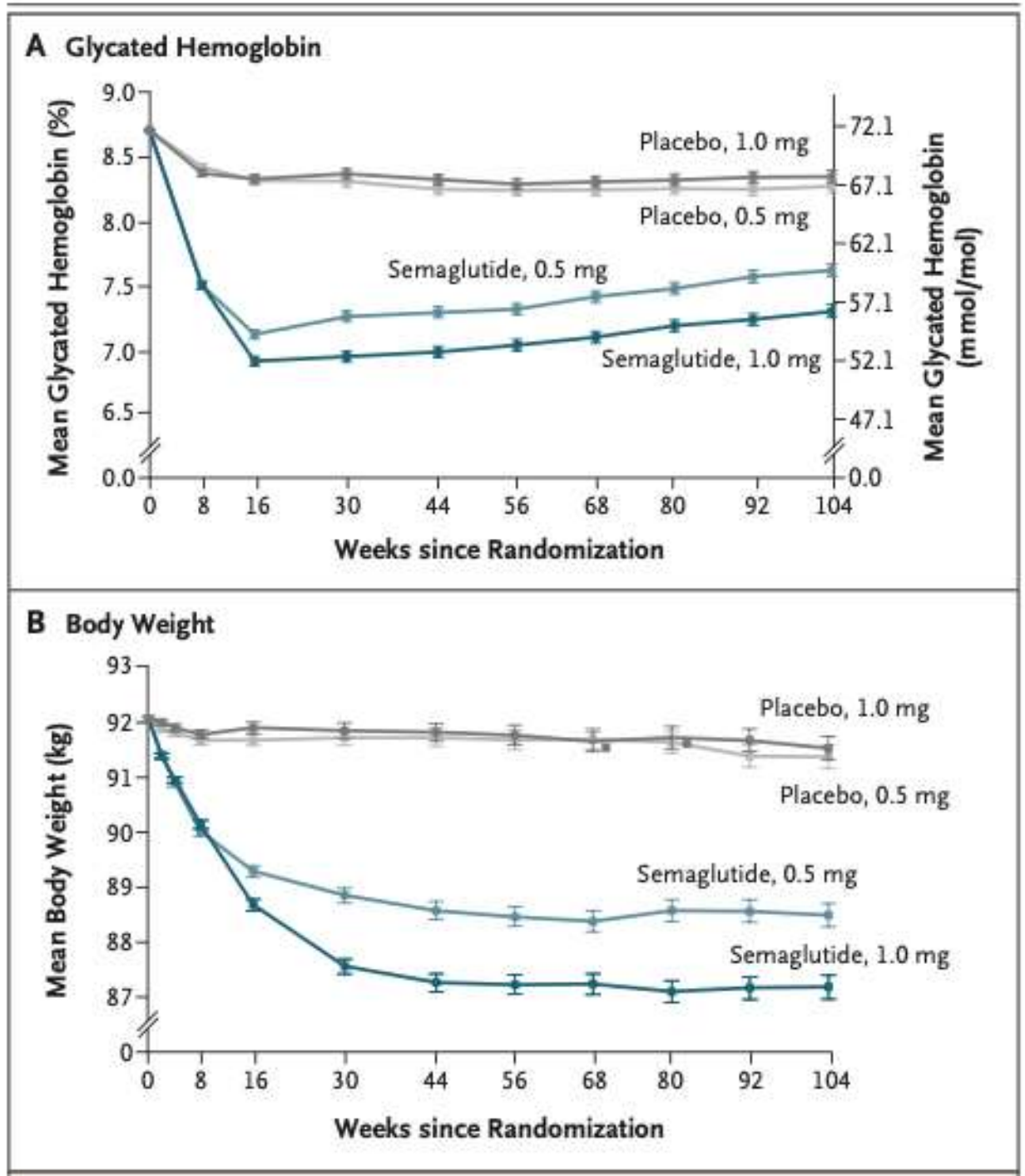
- **3297** patients with **type 2 diabetes** - once-weekly semaglutide
- randomized either **0.5 mg or 1.0 mg or placebo**
- *fixed dose-escalation procedure was used, with a starting dose of 0.25 mg for 4 weeks that escalated to 0.5 mg for 4 weeks until the maintenance dose (0.5 mg or 1.0 mg) was reached*
- primary composite outcome - first occurrence of **cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke**
- Cox proportional-hazards model (semaglutide vs. placebo)
- median observation time was **2.1 years**

- The primary outcome occurred in **108 of 1648 patients (6.6%) in the semaglutide group** and in **146 of 1649 patients (8.9%)** in the placebo group (hazard ratio, 0.74; **0.58 to 0.95;** P<0.001)
- Nonfatal myocardial infarction occurred in 2.9% (hazard ratio, 0.74; 95% CI, **0.51 to 1.08;** P=0.12);
- Nonfatal stroke occurred in 1.6% (hazard ratio, 0.61; 95% CI, **0.38 to 0.99**; P=0.04)

  - worsening nephropathy were lower in the semaglutide group,
  - **rates of retinopathy complications** (vitreous hemorrhage, blindness, requiring treatment with an intravitreal agent or photocoagulation) **were significantly higher**


A Glycated Hemoglobin
Mean Glycated Hemoglobin (%)
9.0
8.5
8.0
7.5
7.0
6.5
0.0
72.1
67.1
62.1
57.1
52.1
47.1
0.0
Mean Glycated Hemoglobin (mmol/mol)
Placebo, 1.0 mg
Placebo, 0.5 mg
Semaglutide, 0.5 mg
Semaglutide, 1.0 mg
0 8 16 30 44 56 68 80 92 104
Weeks since Randomization
B Body Weight
Mean Body Weight (kg)
93
92
91
90
89
88
87
0
Placebo, 1.0 mg
Placebo, 0.5 mg
Semaglutide, 0.5 mg
Semaglutide, 1.0 mg
0 8 16 30 44 56 68 80 92 104
Weeks since Randomization

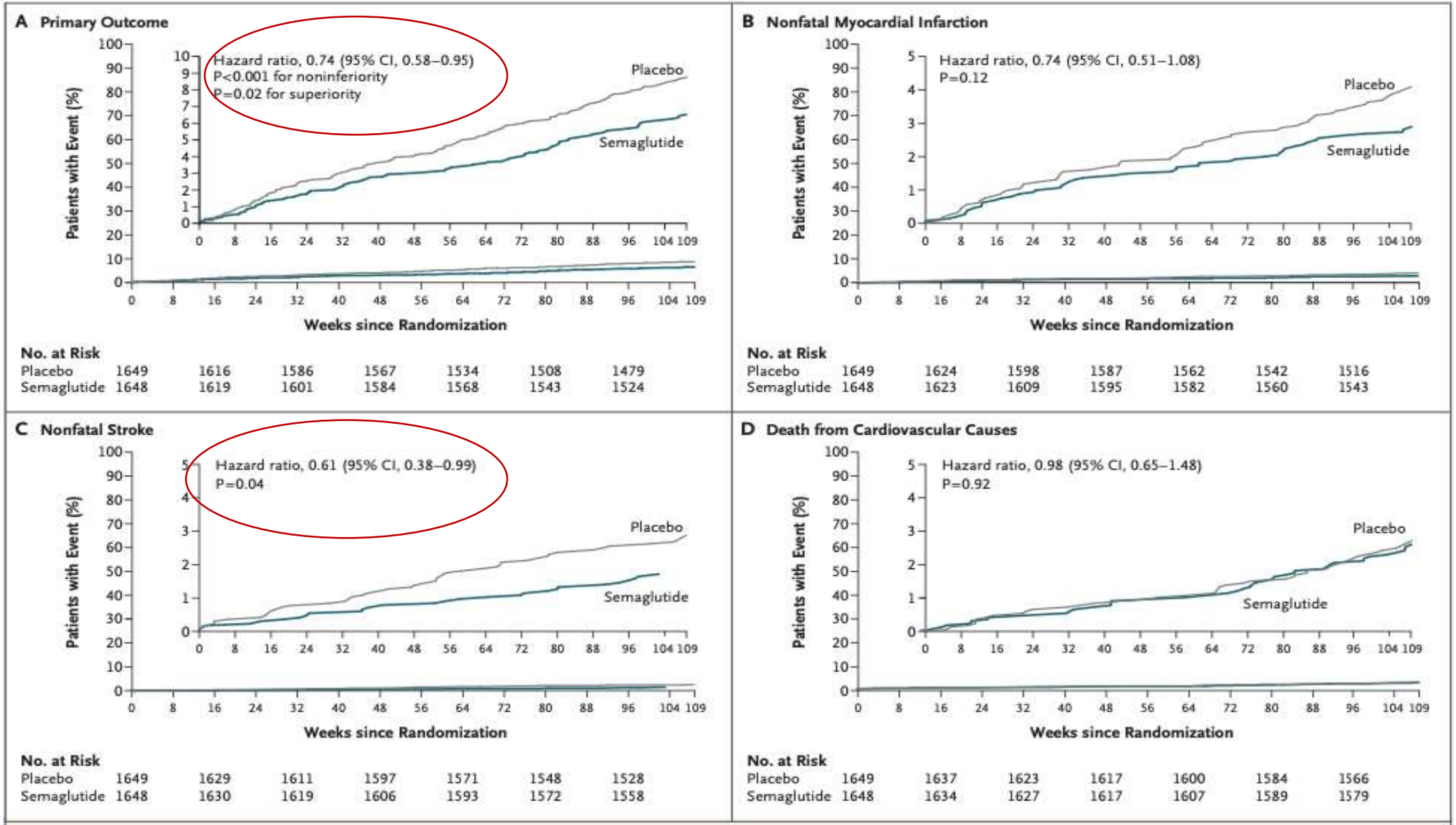
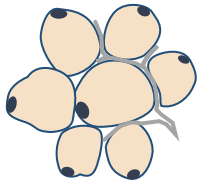


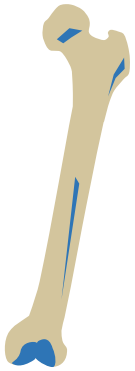
Figure 1. Cardiovascular Outcomes.

Shown are Kaplan–Meier plots of the primary outcome (a composite of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke) (Panel A), nonfatal myocardial infarction (Panel B), nonfatal stroke (Panel C), and death from cardiovascular causes (Panel D). The trial included a planned observation period of 109 weeks for all patients (a 104-week treatment period with a 5-week follow-up period). In Panel C, there were no events in the semaglutide group after week 104. Insets show the same data on an expanded y axis.

The Evolving GIP–GLP-1 Partnership in Metabolism

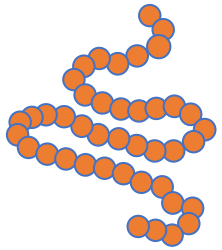


↑ LPL activity
↑ adipose tissue accretion

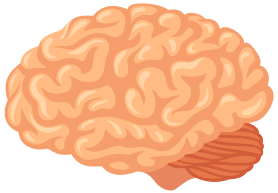


↓ bone resorption

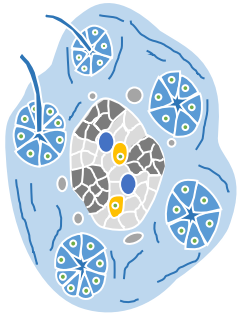
GIP



↑↓ glucagon secretion

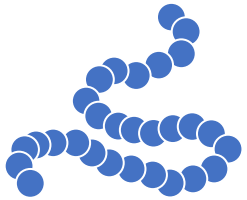


↓ Food intake
↑ Weight loss

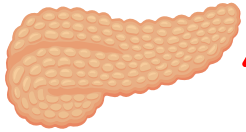


↑ insulin secretion

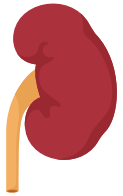
GLP-1



↓ glucagon secretion

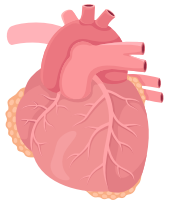


↑ enzyme secretion



↑ natriuresis
↑ diuresis

↓ gastric emptying



↑ cardioprotection

Baggio. J Mol Metabolism. 2020;46:101090.

Glucagon-like Peptide-1 Receptor Agonism

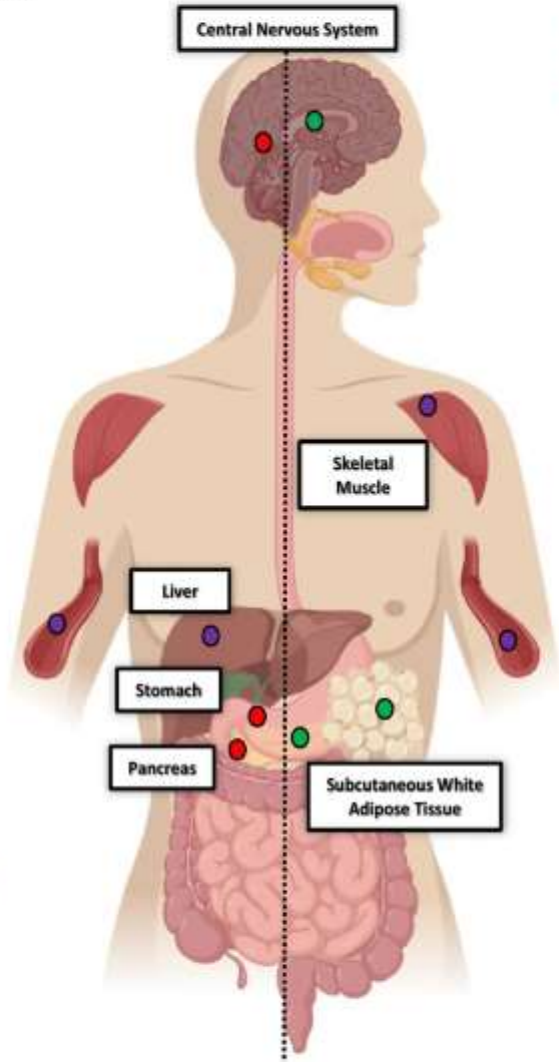
Central Nervous System
- ↑ Satiety
- ↓ Food Intake
- ↑ Nausea
- ↓ Body Weight

Pancreas
- ↑ Insulin
- ↓ Glucagon

Stomach
- ↓ Gastric Emptying

Systemic
- ↓ Hyperglycemia

Liver
- ↑ Insulin Sensitivity
- ↓ Hepatic Glucose Production
- ↓ Ectopic Lipid Accumulation



Glucose-dependent Insulinotropic Polypeptide Receptor Agonism

Central Nervous System
- ↓ Food Intake
- ↓ Nausea
- ↓ Body Weight

Pancreas
- ↑ Insulin
- ↑ Glucagon

Subcutaneous White Adipose Tissue
- ↑ Insulin Sensitivity
- ↑ Lipid Buffering Capacity
- ↑ Blood Flow
- ↑ Storage Capacity
- ↓ Proinflammatory Immune Cell Infiltration

Systemic
- ↓ Hyperglycemia
- ↓ Dietary Triglyceride

Skeletal Muscle
- ↑ Insulin Sensitivity
- ↑ Metabolic Flexibility
- ↓ Ectopic Lipid Accumulation

Glucose-dependent Insulinotropic Polypeptide Receptor Agonism
Glucagon-like Peptide 1 Receptor Agonism
Indirect Action

Tirzepatide: Novel Dual GIP and GLP-1 Receptor Agonist

- Tirzepatide is 39 amino acid peptide based on **native GIP peptide** sequence and modified to **bind to GIP or GLP-1 receptors**

- Administered as once-weekly injection as **half-life of 5 days**
  - Starting dose 2.5 mg weekly, titrated at 2.5-mg increments monthly to **max dose of 15 mg**

- Contraindications and AEs similar to GLP-1 RAs (dulaglutide)
  - Contraindications: personal or family history of MTC or MEN2
  - Precautions: pancreatitis, AKI, diabetic retinopathy, gallbladder disease
  - Adverse events: GI including nausea, vomiting, diarrhea, constipation, abdominal pain

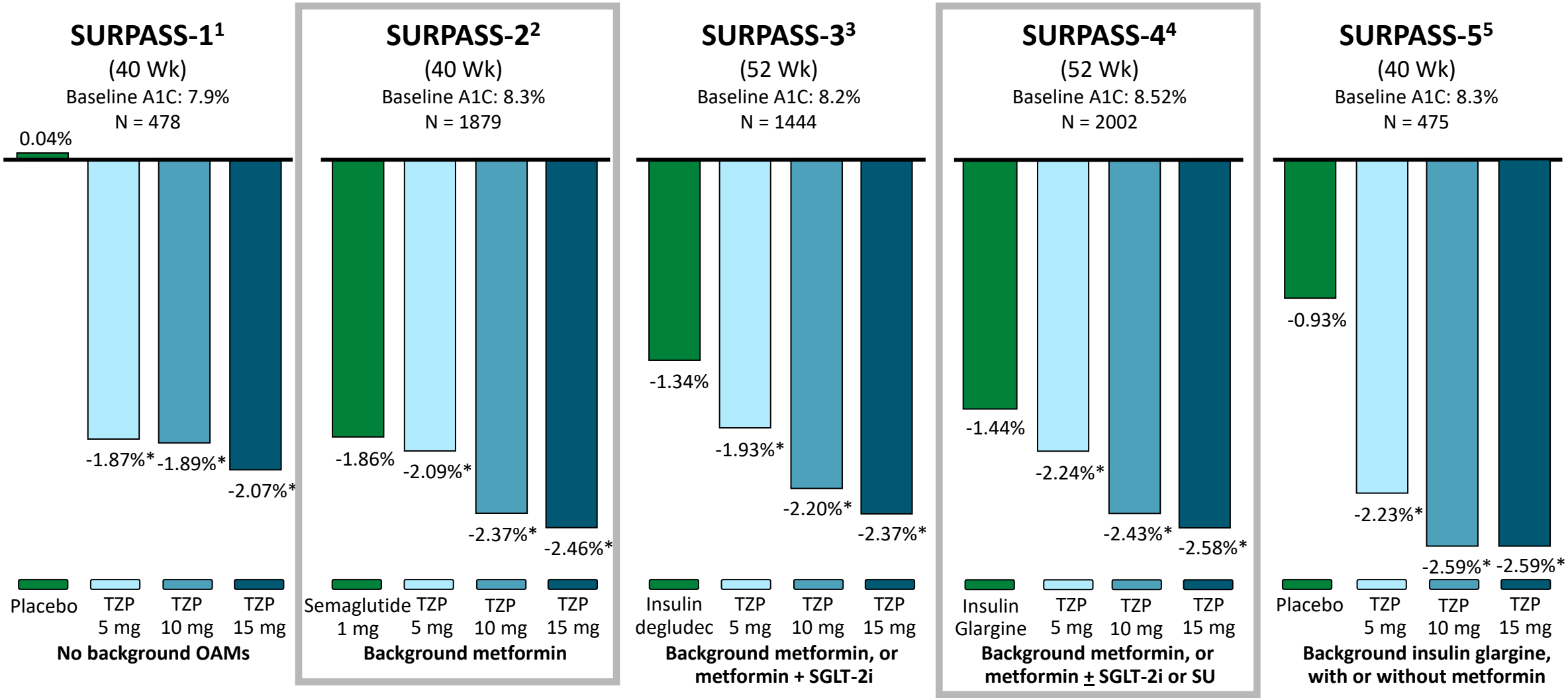
Min. Diabetes Ther. 2021;12:143. Coskun. Mol Metab. 2018;18:3. Tirzepatide PI.

Tirzepatide trials

- SURPASS – for DM – 7 + 1 CVOT

- SURMOUNT – for weight loss
  - 1= weight
  - 2 = DM2
  - 4 = maintenance
  - MMO-CV = CV outcome trial

SURPASS: Tirzepatide Reduces A1C in Type 2 Diabetes

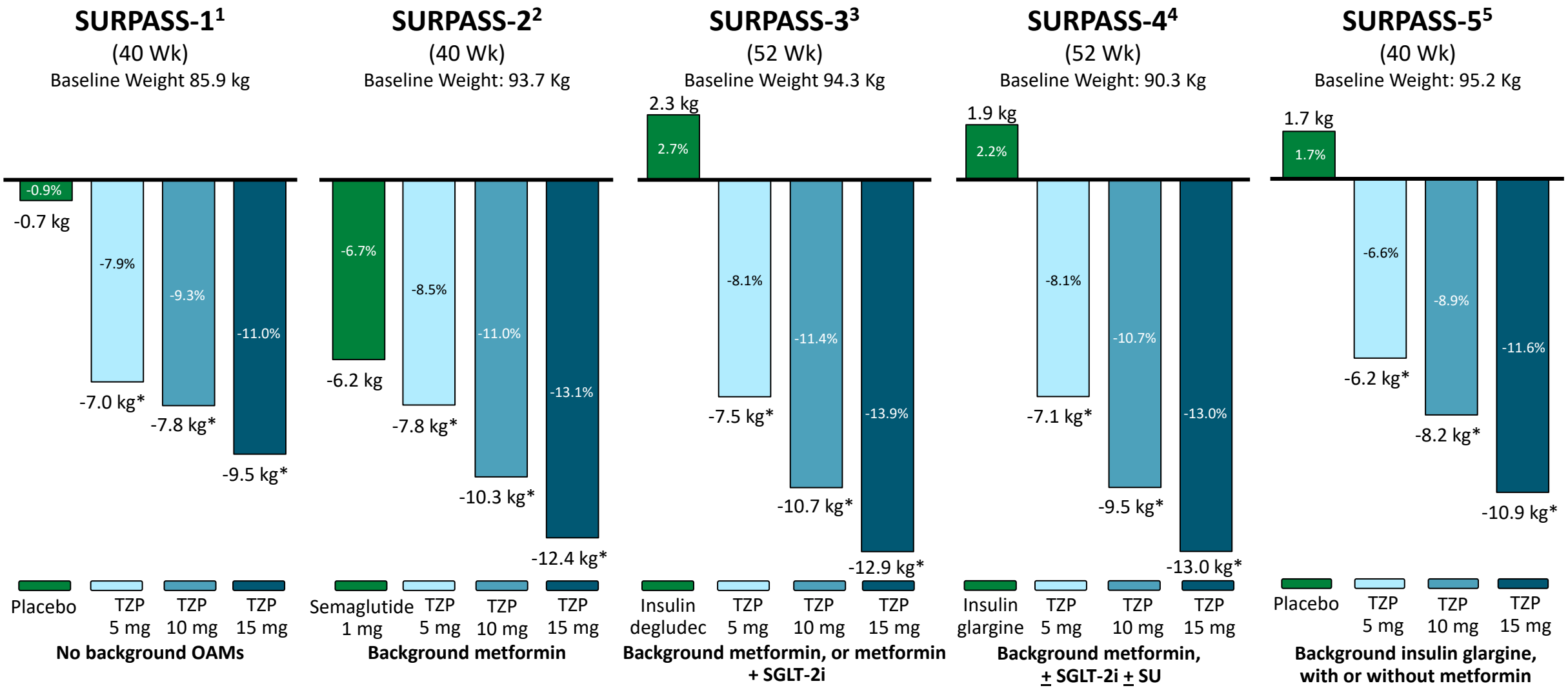


1. Rosenstock. Lancet. 2021;398:143. 2. Frias. NEJM. 2021;385:503. 3. Giorgino. ADA 2021. Abstr 78-LB. 4. Del Prato. Lancet. 2021;398:1811. 5. Dahl. ADA 2021. Abstr 80-LB.

*Denotes statistical significance to comparator.

Slide credit: clinicaloptions.com

SURPASS: Weight Loss With Tirzepatide in T2D

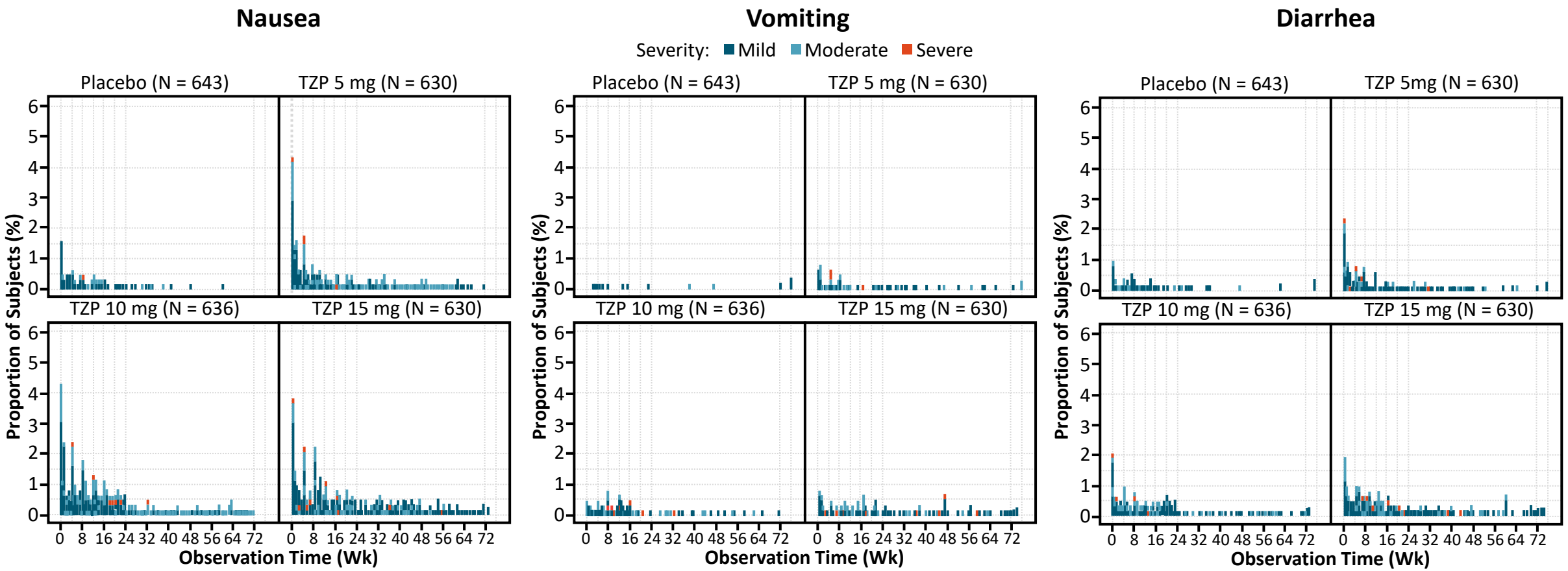


*Denotes statistical significance to comparator.

1. Rosenstock. Lancet. 2021;398:143. 2. Frias. NEJM. 2021;385:503. 3. Giorgino. ADA 2021. Abstr 78-LB. 4. Del Prato. Lancet. 2021;398:1811. 5. Dahl. ADA 2021. Abstr 80-LB.

Slide credit: clinicaloptions.com

SURMOUNT 1: GI Adverse Events With Tirzepatide



Jastreboff. NEJM. 2022;387:205.

Slide credit: clinicaloptions.com

Other upcoming medications

- **Cagrilintide** – amylin receptor agonist
- Cargri-Sema – REDEFINE 1 (2026) 3 arms 2.4 +2.4mg

- Glucagon + GLP1 = **Pemvidutide & Mazdutide**
- Glucagon + GLP1 + GIP = **Retatrutide** (phase 2 published NEJM 08/23)

- **Danuglipiron and Orfoglipiron –** orally administrated, small molecule GLP1 R agonist
- **Monthly GIP and GLP1**

- **Bimagrumab**
  - Monoclonal AB for Activin type 2 receptors
  - 20% fat loss and 3.6% increase in muscle mass

- **Setmelanotide** – MCR4R agonist

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

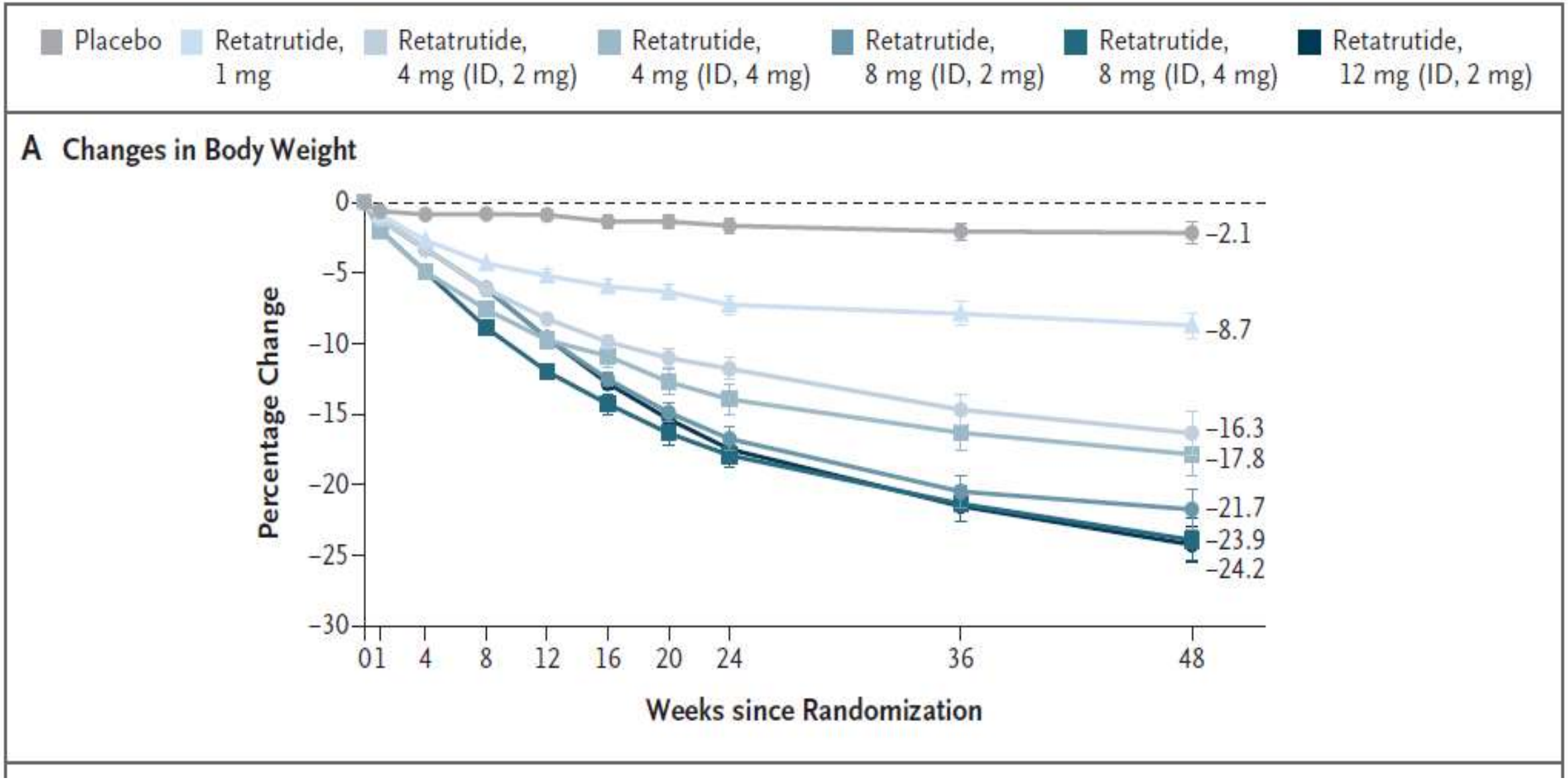
Triple–Hormone-Receptor Agonist Retatrutide for Obesity — A Phase 2 Trial

Ania M. Jastreboff, M.D., Ph.D., Lee M. Kaplan, M.D., Ph.D., Juan P. Frías, M.D., Qiwei Wu, Ph.D., Yu Du, Ph.D., Sirel Gurbuz, M.D., Tamer Coskun, M.D., Ph.D., Axel Haupt, M.D., Ph.D., Zvonko Milicevic, M.D., and Mark L. Hartman, M.D., for the Retatrutide Phase 2 Obesity Trial Investigators*

Triple-Hormone-Receptor Agonist Retatrutide for Obesity

- Retatrutide = **agonist** of the **GIP, GLP1, glucagon receptors**
- phase 2, BMI >30, 338 adults, 51.8% men
- *subcutaneous* Retatrutide (**1 mg, 4 mg, 8 mg or 12 mg** or placebo **once weekly** for 48 weeks)
- The primary end point was the **percentage change in body** weight from baseline **to 24 weeks.**
- Secondary end points included the **percentage change in body** weight from baseline **to 48 weeks**
- The most common adverse events in the retatrutide groups were **gastrointestinal**, dose-related, were mostly mild to, *partially mitigated with a lower starting dose (2 mg vs. 4 mg).*
- **Conclusions:** In adults with obesity, retatrutide treatment for 48 weeks **resulted in substantial reductions in body weight**.

(Funded by Eli Lilly)



Retatrutide associated with improvements in cardio-metabolic measures including systolic and diastolic blood pressure, **glycated hemoglobin**, fasting glucose, insulin and lipids at weeks 24 and 48

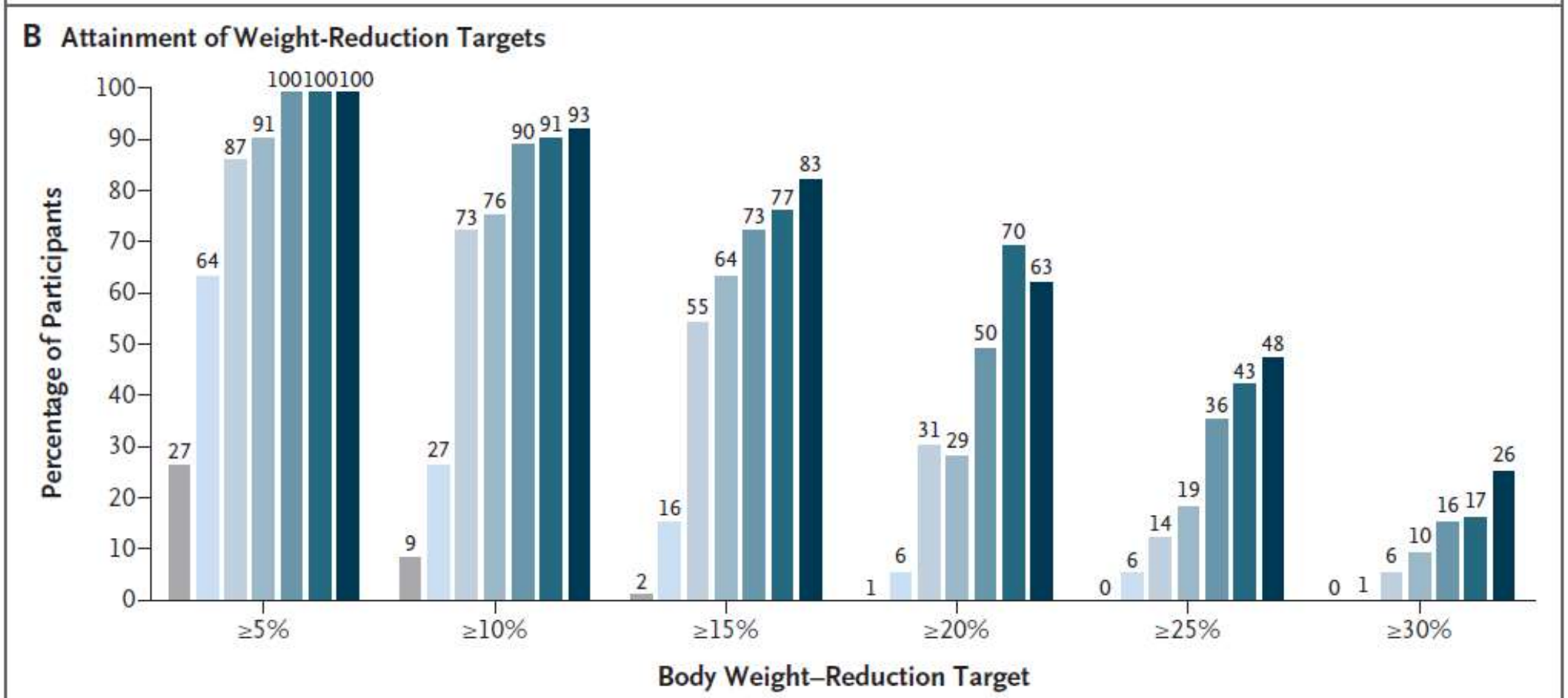
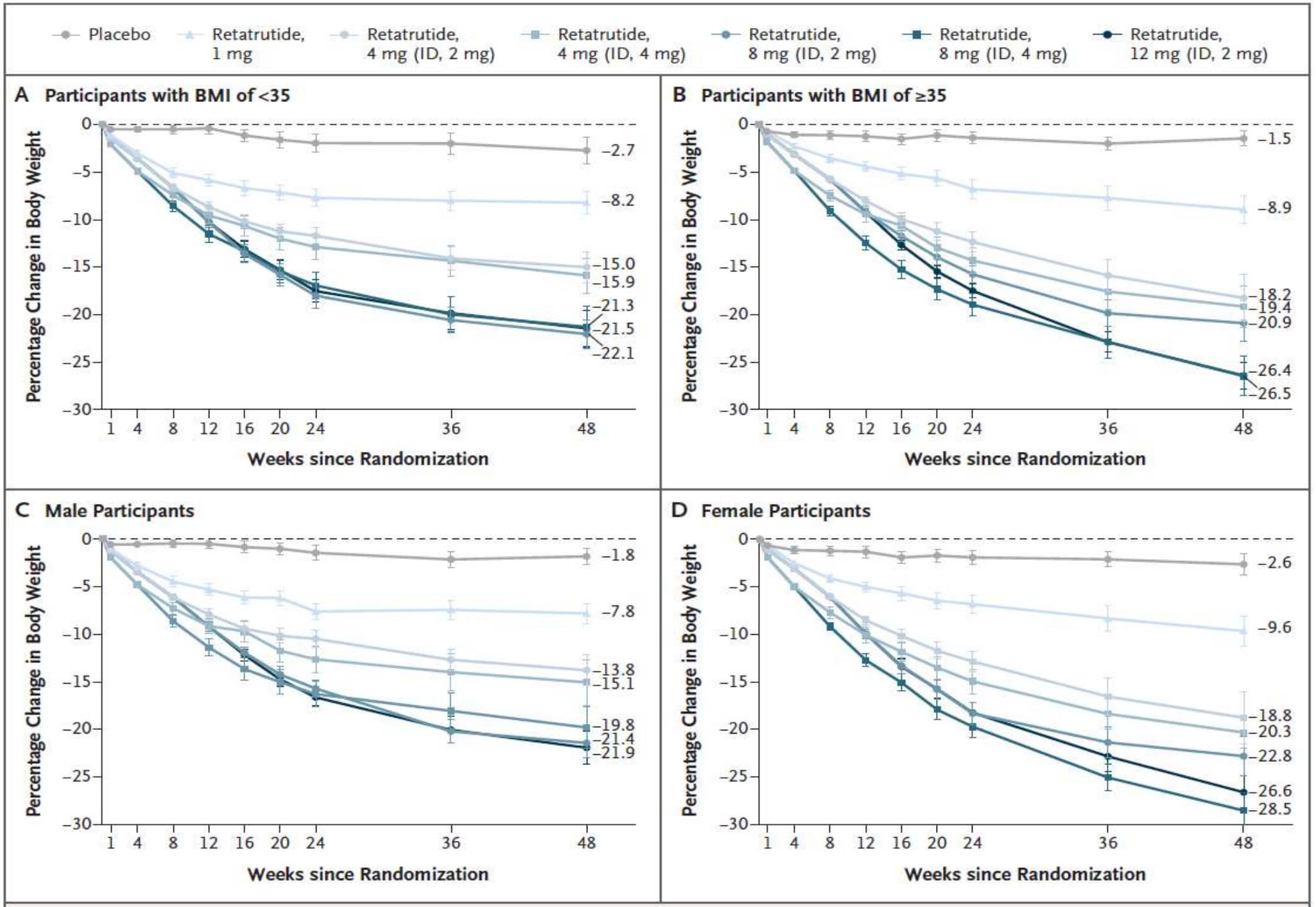


Figure 1. Changes in Body Weight with Retatrutide as Compared with Placebo.

Panel A shows the percentage change in body weight from baseline to week 48, derived from a mixed model for repeated measures (MMRM) analysis for the efficacy estimand. The values shown are least-squares means; I bars indicate standard errors. Panel B shows the percentages of participants with percentage body-weight reductions of at least 5%, 10%, 15%, 20%, 25%, and 30% from baseline to week 48. Efficacy end points were analyzed with data from all the participants who underwent randomization, excluding those who discontinued treatment because of inadvertent enrollment. ID denotes initial dose.


Placebo
Retatrutide, 1 mg
Retatrutide, 4 mg (ID, 2 mg)
Retatrutide, 4 mg (ID, 4 mg)
Retatrutide, 8 mg (ID, 2 mg)
Retatrutide, 8 mg (ID, 4 mg)
Retatrutide, 12 mg (ID, 2 mg)
A Participants with BMI of <35
Percentage Change in Body Weight
0
−5
−10
−15
−20
−25
−30
1 4 8 12 16 20 24 36 48
Weeks since Randomization
−2.7
−8.2
−15.0
−15.9
−21.3
−21.5
−22.1
B Participants with BMI of ≥35
Percentage Change in Body Weight
Weeks since Randomization
−1.5
−8.9
−18.2
−19.4
−20.9
−26.4
−26.5
C Male Participants
Percentage Change in Body Weight
Weeks since Randomization
−1.8
−7.8
−13.8
−15.1
−19.8
−21.4
−21.9
D Female Participants
Percentage Change in Body Weight
Weeks since Randomization
−2.6
−9.6
−18.8
−20.3
−22.8
−26.6
−28.5

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Original Investigation | Nutrition, Obesity, and Exercise

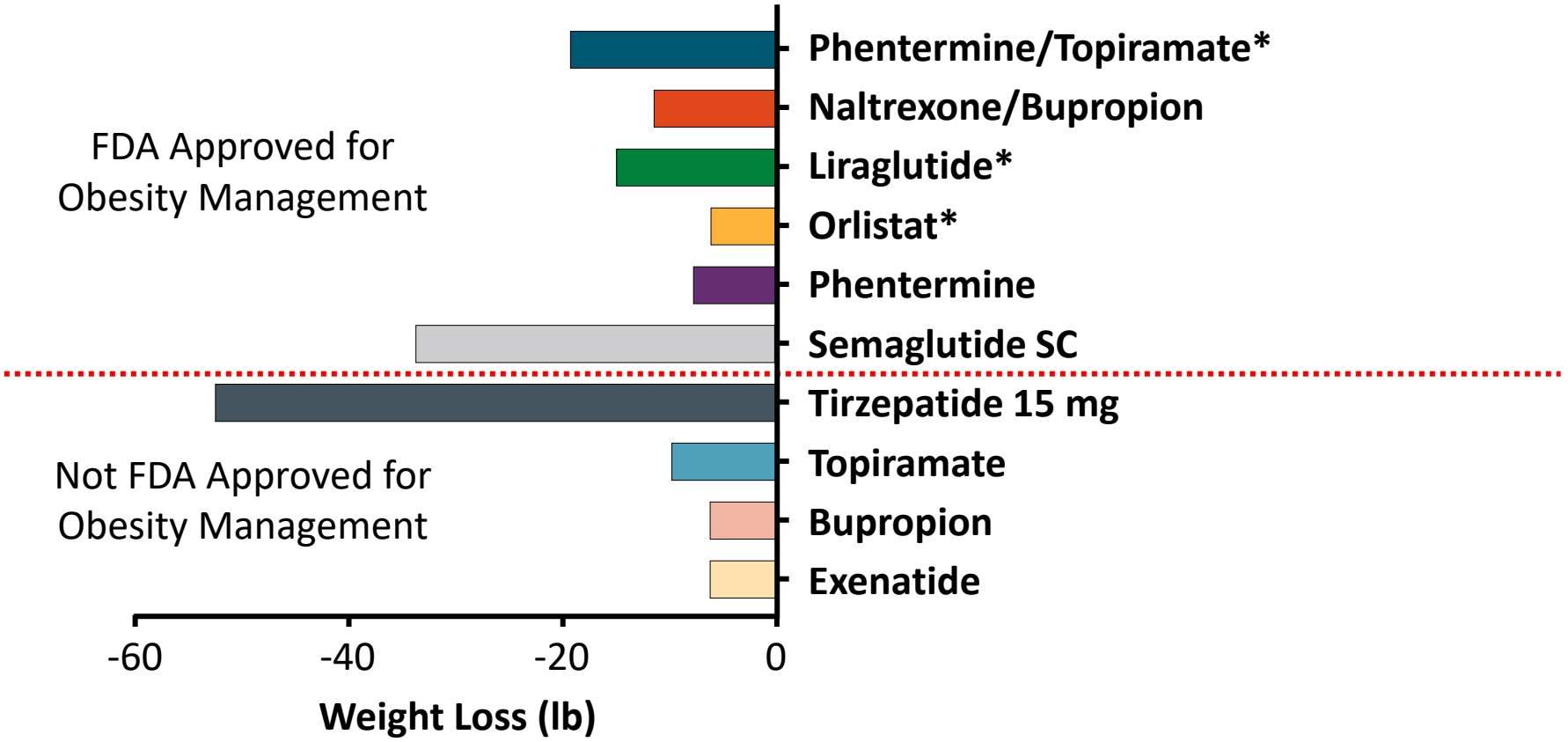
Effect of Bimagrumab vs Placebo on Body Fat Mass Among Adults With Type 2 Diabetes and Obesity

A Phase 2 Randomized Clinical Trial

Steven B. Heymsfield, MD; Laura A. Coleman, PhD, RD; Ram Miller, MD; Daniel S. Rooks, PhD; Didier Laurent, PhD; Olivier Petricoul, PhD; Jens Praestgaard, PhD; Therese Swan, PharmD; Thomas Wade, MD; Robert G. Perry, MD; Bret H. Goodpaster, PhD; Ronenn Roubenoff, MD, MHS

Bimagrumab blocks activin type II receptors associated with growth of skeletal muscle

Average Weight Loss With Pharmacotherapy



*Approved in pediatrics.

Adapted from Jastrebof. NEJM. 2022;383:205. Wilding. NEJM. 2021;384:989. Butch ABOM Course 2016.

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