LOUISIANA DEPARTMENT OF HEALTH

2025 American Diabetes Association National Conference Updates

Dragana Lovre, MD

11/13/2025

Disclaimer

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Speakers

Dragana Lovre, MD

Associate Professor of Medicine

Disclosures

- Co-PI for “REDEFINE-3: A Research Study to See the Effects of CagriSema in People Living With Diseases in the Heart and Blood Vessels” (Novo Nordisk)
- PI of “Study of Hypercortisolism in Patients with Difficult to Control Type 2 Diabetes Despite Receiving Standard-of-Care Therapies: Prevalence and Treatment with Korlym® (Mifepristone) (CATALYST)
- PI for “Semaglutide cardiovascular outcomes trial in patients with type 2 diabetes (SOUL)” (Novo Nordisk)
- Advisory Board, Novo Nordisk 2024 (Obesity)

VA U.S. Department of Veterans Affairs

Tulane University

TULANE UNIVERSITY BIRCWH BUILDING INTERDISCIPLINARY RESEARCH CAREERS IN WOMEN'S HEALTH

TCESBM Tulane Center of Excellence Sex-Based Biology & Medicine

NIH National Institutes of Health *Turning Discovery Into Health*

LA CaTS LOUISIANA CLINICAL & TRANSLATIONAL SCIENCE CENTER

Addressing health disparities & improving health outcomes in the underserved

The views expressed are my own and do not necessarily reflect the position or policy of VA or the US government.

Objectives

- **Highlight key scientific and clinical advances** presented at the 2025 ADA Scientific Sessions.
- **Discuss the impact of new evidence** on diabetes prevention, treatment, and outcomes.
- **Apply emerging research and guidelines** to enhance clinical practice and education.

How I Selected the Topics Presented

- While I have been involved in some of the clinical trials discussed, the data presented here were chosen **based on their relevance and practical value**, not personal involvement.

I focused on:

- **Clinically relevant findings** that can be applied in practice today
- **Topics familiar to our group**, allowing us to build on existing knowledge
- **Advances with direct clinical implications**, not distant from real-world use
- **New FDA indications and updated safety data** that impact patient care

Here are several session titles from the 85th Scientific Sessions of the American Diabetes Association (2025) that appeared in ADA Meeting News: https://www.adameetingnews.org/category/scientific-sessions/2025/session-coverage-2025/

- Experts debate relevance of bariatric surgery in the era of GLP-1 RAs.
- Panel shares ideas to augment traditional study approaches.
- Standards of Care in Overweight and Obesity updates help optimize care for patients and clinicians.
- Investigators spotlight innovative bioengineering efforts for beta cell replacement therapy.
- Specialists explain how to maximize impact of AI-enabled diabetes-related retinopathy screening.
- Diabetes Care Symposium examines how to fix a health care system driven by drug prices.
- Monoclonal antibody-peptide conjugate demonstrates efficacy as once-monthly treatment for obesity.
- BELIEVE spotlights quality and quantity approach to weight management with combo therapy.
- Add-on therapy improves glycemic outcomes and weight loss in adults living with type 1 diabetes and obesity.
- Experts contrast heart and kidney diseases in type 1 and type 2 diabetes.
- Debate will tackle optimal method for tracking burden and severity of hypoglycemia.
- Scientists to discuss multi-faceted approach to managing CV risk in people with diabetes and ASCVD.

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85TH SCIENTIFIC SESSIONS | ADA MEETING NEWS

American Diabetes Association.

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The official news source of the 85th Scientific Sessions

JUNE 20–23, 2025 | CHICAGO, IL

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LATEST NEWS FROM THE SCIENTIFIC SESSIONS

August 7, 2025

Specialists explain how to maximize impact of AI-enabled diabetes-related retinopathy screening

August 7, 2025

Experts debate relevance of bariatric surgery in the era of GLP-1 RAs

August 7, 2025

Panel shares ideas to augment traditional study approaches

August 7, 2025

Standards of Care in Overweight and Obesity updates help optimize care for patients and clinicians

Louis J. Aronne, MD, DABOM, and Kim Gudzune, MD, MPH, led an overview of the newly developed guidance, which provides clinicians, researchers, policy makers, and others with the components of obesity care, general treatment goals, and tools to evaluate the quality of care.

August 7, 2025

Investigators spotlight innovative bioengineering efforts for beta cell replacement therapy

Michael R. Rickels, MD, MS, and others shared results from FORWARD-101, which studied an investigational stem cell-derived, fully differentiated islet cell therapy for people with type 1 diabetes with impaired hypoglycemic awareness and severe hypoglycemic events.

VIEW ARCHIVES

Select Year

POPULAR ARTICLES

ADA President, Medicine & Science: Closing the circle from progress to promise is our unfinished journey

Banting Medalist explains how beta cells hold the key to type 2 diabetes

Standards of Care in Diabetes—2025 brings updates to practice

2025 Outstanding Educator in Diabetes Award honoree focuses on nutrition

Celebrity advocate promotes awareness for diabetes in session where ADA President, Health Care & Education touts multidisciplinary approach to care

June 23, 2025

STRIDE is a first step in addressing unmet needs in comorbid PAD and type 2 diabetes

Walking Further Toward the Future: Semaglutide and Functional Recovery in PAD

Bonaca et al., Lancet

STRIDE Trial

- Semaglutide 1.0 mg weekly vs placebo
- Symptomatic peripheral artery disease and type 2 diabetes

↑ **Maximum Walking Distance**
+26,4 m vs. placebo

↑ **Pain-Free Walking Distance**
+29,8 m vs. placebo

↑ **Quality of Life** (VascuQoL-6)

Fewer Limb Events

Semaglutide and walking capacity in symptomatic peripheral artery disease and type 2 diabetes (STRIDE)

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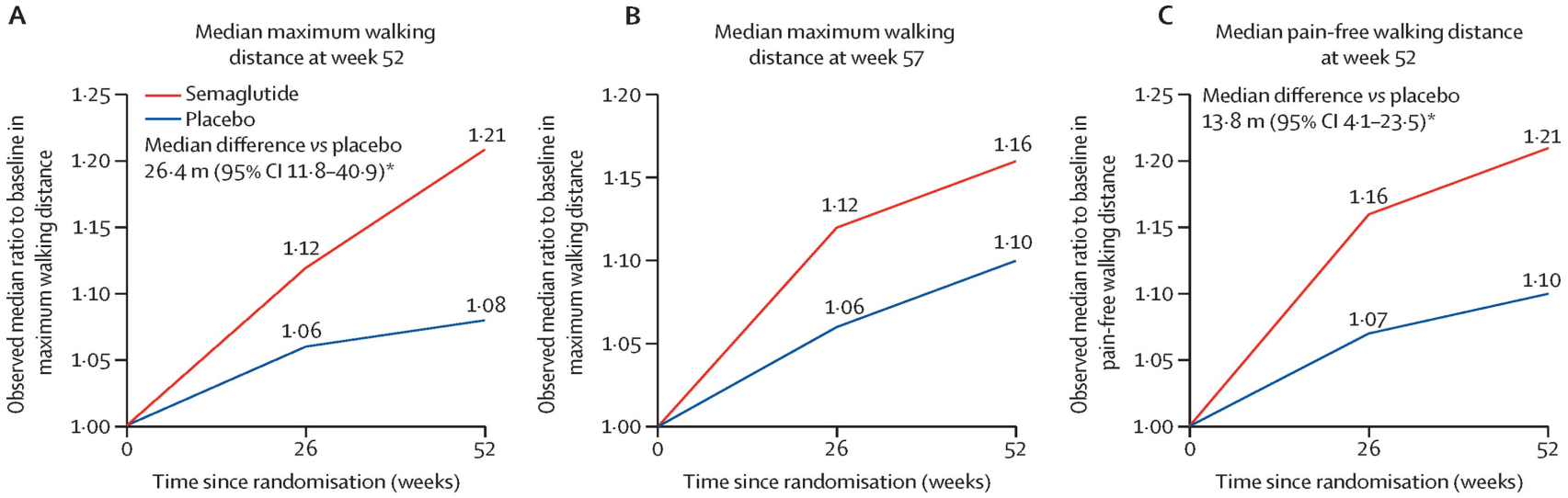


D

	Semaglutide (n=396)		Placebo (n=396)		ETR (95% CI) semaglutide *vs* placebo
	Number of participants	Median (IQR) ratio to baseline	Number of participants	Median (IQR) ratio to baseline	
Maximum walking distance at week 52	338	1·21 (0·95 to 1·55)	345	1·08 (0·86 to 1·36)	1·13 (1·06 to 1·21) p=0·0004
Maximum walking distance at week 57	329	1·16 (0·92 to 1·48)	333	1·10 (0·87 to 1·40)	1·08 (1·00 to 1·16) p=0·038
Pain-free walking distance at week 52	338	1·21 (0·92 to 1·52)	334	1·10 (0·86 to 1·44)	1·11 (1·03 to 1·20) p=0·0046
	Total (IQR) change from baseline				
VascuQoL-6 total score at week 52	362	2·0 (0·0 to 4·0)	362	1·0 (–1·0 to 4·0)	1·00 (0·48 to 1·52) p=0·011

Bonaca MP et al. The Lancet; 2025: 405, 1580-1593

JAMA Network | Open

RCT: Liraglutide for Lower Limb Perfusion in People With Type 2 Diabetes and Peripheral Artery Disease

POPULATION

43 Men, 12 Women

Adults with T2D and peripheral artery disease with transcutaneous oxygen pressure ($TcPo_2$) of the foot from 30 to 49 mm Hg

Mean age 67.5 y

INTERVENTION

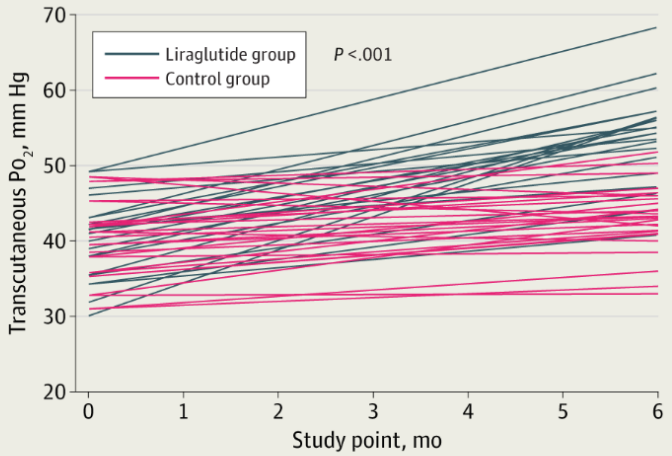
60 Patients randomized, 55 analyzed

30 Liraglutide
Once daily liraglutide subcutaneous injection

30 Control
Therapies to manage blood glucose levels and cardiovascular risk factors

FINDINGS

Liraglutide was associated with a higher TcPO2 increase over time, with a higher proportion of patients reaching at least a 10% increase compared with control therapy



Participants with 10% increase in $TcPo_2$:
Liraglutide, 24 (89%); control, 13 (46%)

Estimated treatment difference, liraglutide vs control:
11.2 mm Hg; 95% CI, 8.0-14.5 mm Hg; *P* <.001

SETTINGS / LOCATIONS

University hospital in Italy

PRIMARY OUTCOME

Coprimary outcomes were the change from baseline of $TcPo_2$ between groups at the end of trial and the comparison of the proportion of individuals who reached a 10% increase of $TcPo_2$ from baseline

Caruso P, Maiorino MI, Longo M, et al. Liraglutide for lower limb perfusion in people with type 2 diabetes and peripheral artery disease: the STARDUST randomized clinical trial. *JAMA Netw Open*. 2024;7(3):e241545. doi:10.1001/jamanetworkopen.2024.1545

- Go CC, Annie F, Drabish K, Eslami MH. **Glucagon-like peptide-1 receptor agonists** are associated with fewer major adverse cardiovascular and limb events in patients with moderate peripheral arterial disease. J Vasc Surg. 2025 Sep;82(3):1024-1032.e2. doi: 10.101
  - **Conclusions:** The use of GLP-1RAs in patients with moderate PAD is associated with a decreased rate of MACEs and MALEs. Patients on GLP-1RAs are at a decreased risk of mortality, inpatient hospitalizations, and inpatient complications.

- Geng L, Sun B, Chen Y. **A meta-analysis** of randomized controlled studies examining the effects of **sodium-glucose co-transporter-2 inhibitors** on peripheral artery disease and risk of amputations. Diabetes Obes Metab. 2024 Nov;26(11):5376-5389. doi: 10.1111/dom.15901. Epub 2024 Sep 12. PMID: 39267269.6/j.jvs.2025.05.037. Epub 2025 Jun 6. PMID: 40484062
  - **Conclusions:** The results of the meta-analysis showed no significant association between SGLT-2i use and PAD and amputation risks in diabetic patients when used for shorter treatment durations.

Cardiovascular Outcomes Trials (CVOTs) in Diabetes Medications

- **Background:**
  Concerns over **rosiglitazone's cardiovascular risk** in the mid-2000s prompted the **FDA (2008)** to mandate that all new glucose-lowering drugs demonstrate **cardiovascular safety** before approval.
- **Purpose:**
  Ensure therapies for diabetes do not increase CV risk and ideally improve outcomes.
- **Key Findings:**
  - **SGLT2 inhibitors** (empagliflozin, canagliflozin, dapagliflozin) → ↓ heart failure hospitalization, ↓ CV and renal events.
  - **GLP-1 receptor agonists** (liraglutide, semaglutide, dulaglutide) → ↓ MACE, stroke, and mortality.
  - **DPP-4 inhibitors** → CV *neutral*; some (saxagliptin) ↑ heart failure risk.
- **Clinical Impact:**
  Shift from glucose-centric to **cardiorenal outcome–driven** diabetes care.
- **Next Step:**
  Broader trials to assess **diverse populations** and **long-term real-world effects**.

STUDY DESIGN

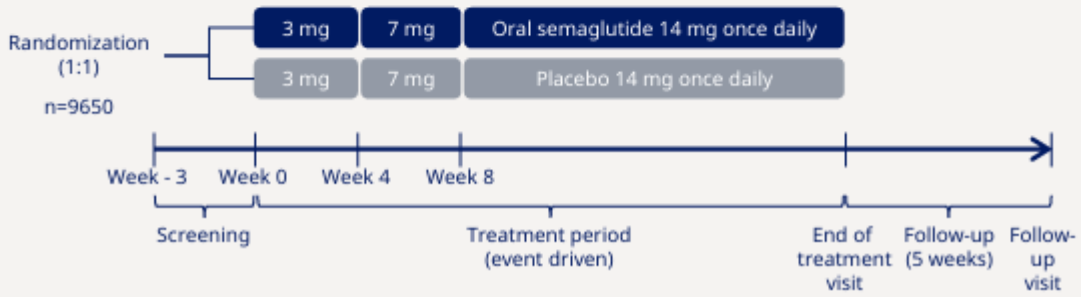
Randomized, double-blind, parallel-group, placebo-controlled

Adults ≥50 years, with T2D

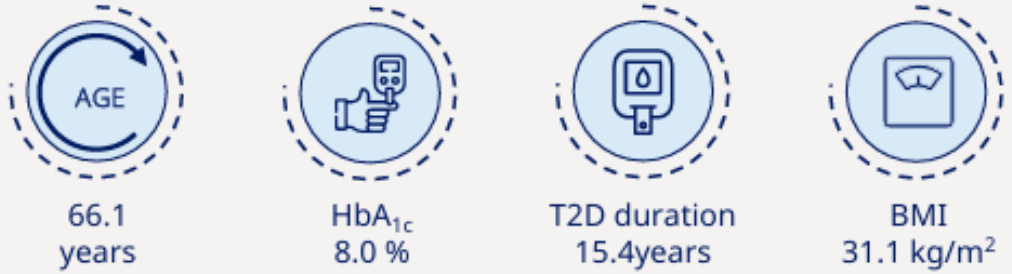
- HbA_{1c} between 6.5%–10.0%

And at least one of the following conditions:

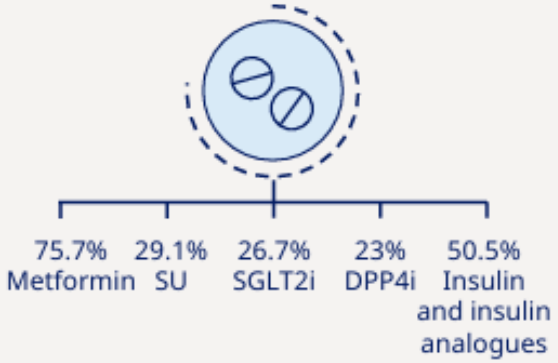
- CAD
- Cerebrovascular disease
- Symptomatic PAD
- CKD



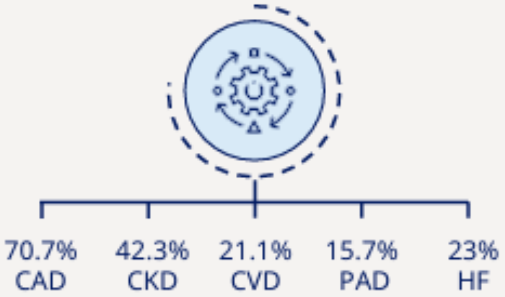
BASELINE CHARACTERISTICS



Oral glucose lowering drugs



Comorbidities at randomization



ENDPOINTS

Primary outcome

- Time to first occurrence of MACE, a composite outcome consisting of:
  - CV death
  - Nonfatal MI
  - Nonfatal stroke

Confirmatory secondary outcome

- Time to first occurrence of a composite CKD outcome consisting of:
  - CV death
  - Kidney-related death
  - Persistent ≥50% reduction in eGFR (CKD-EPI)‡
  - Persistent eGFR (CKD-EPI) <15 ml/min/1.73 m2
  - Initiation of chronic kidney replacement therapy (dialysis or kidney transplantation)
- Time to occurrence of CV death
- Time to first occurrence of major adverse limb events, a composite outcome consisting of:
  - Acute limb ischemia hospitalization
  - Chronic limb ischemia hospitalization

Oral Semaglutide and Cardiovascular Outcomes in High-Risk Type 2 Diabetes

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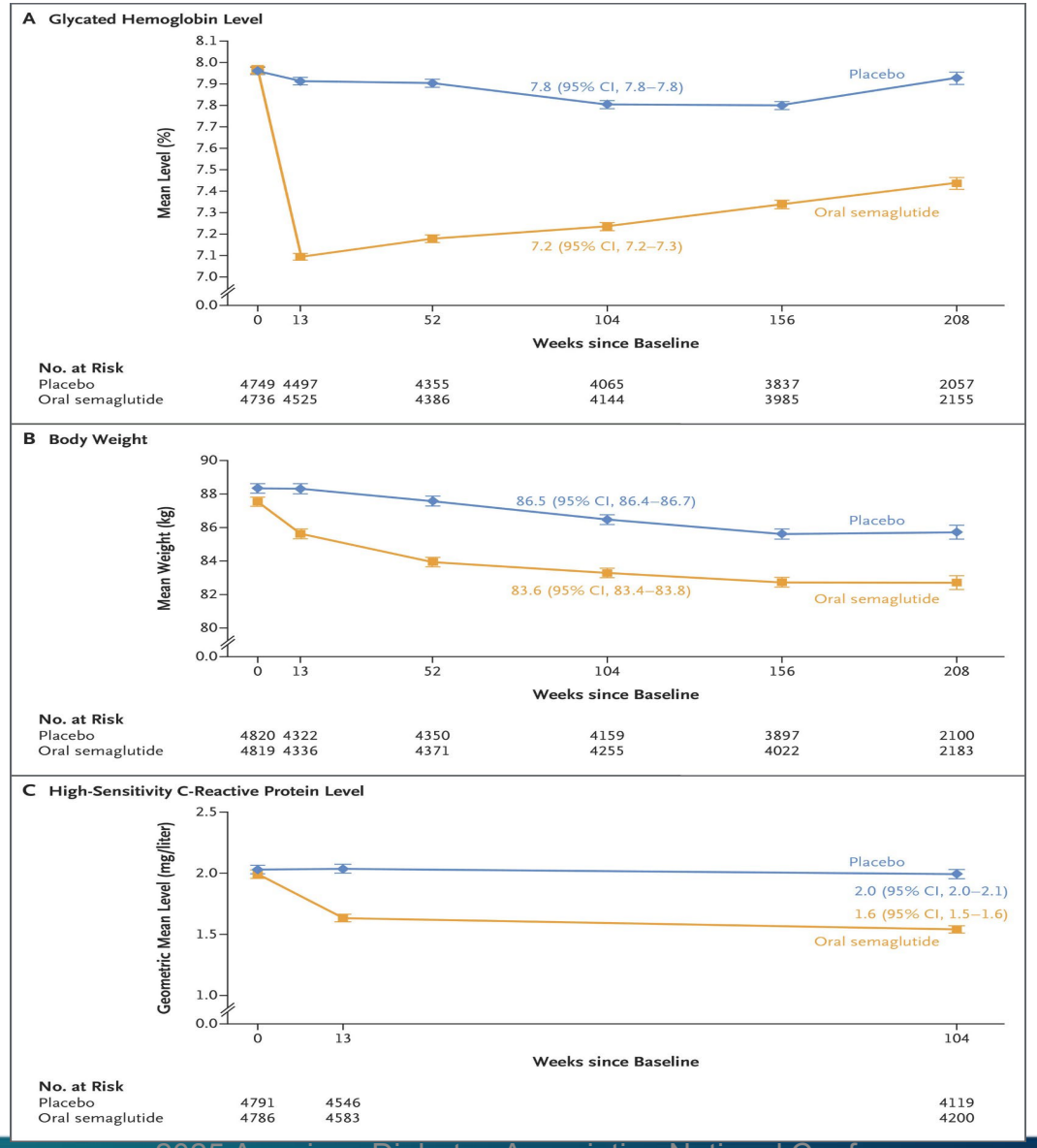
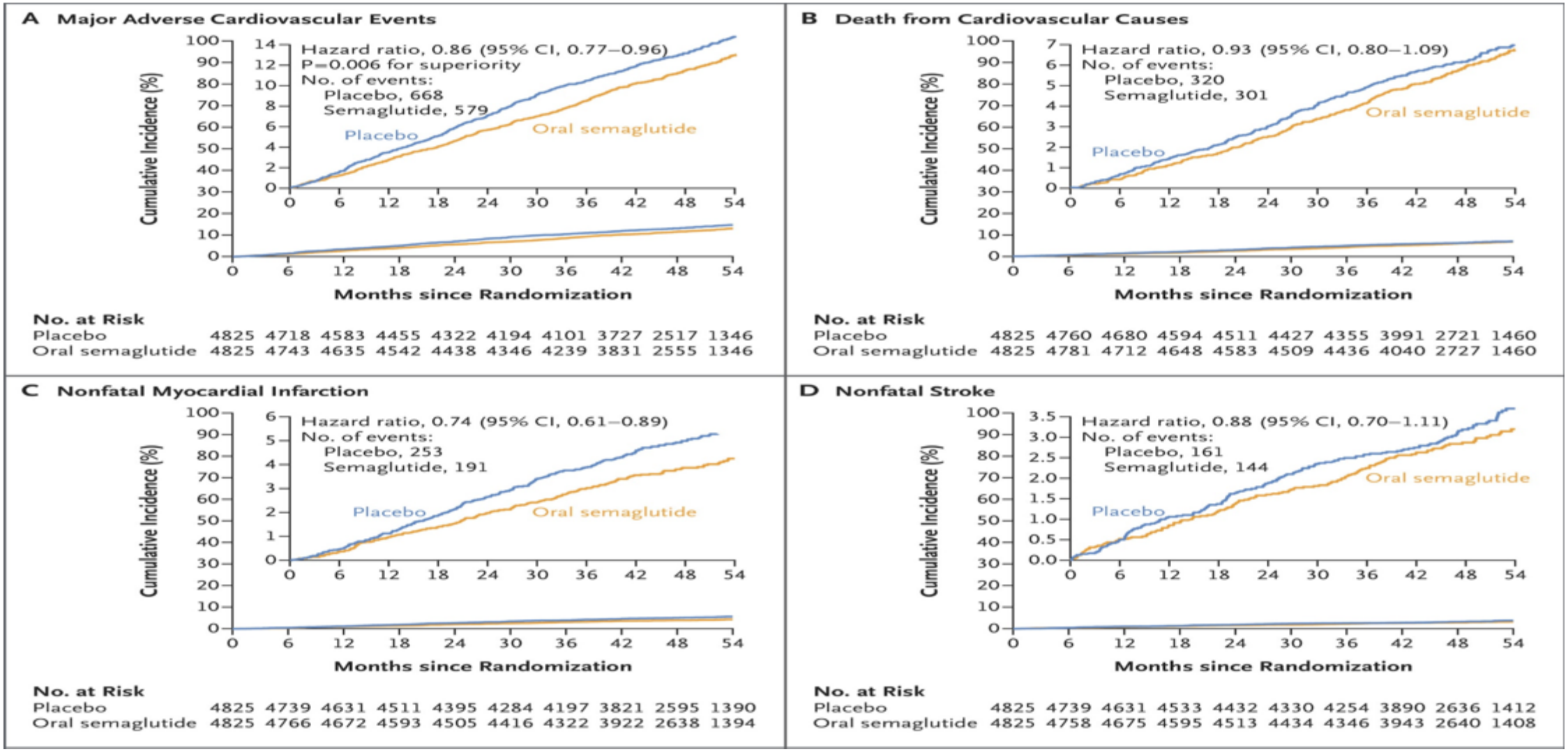


2025 American Diabetes Association National Conference Updates

McGuire et al N Engl J Med 2025;392:2001-2012



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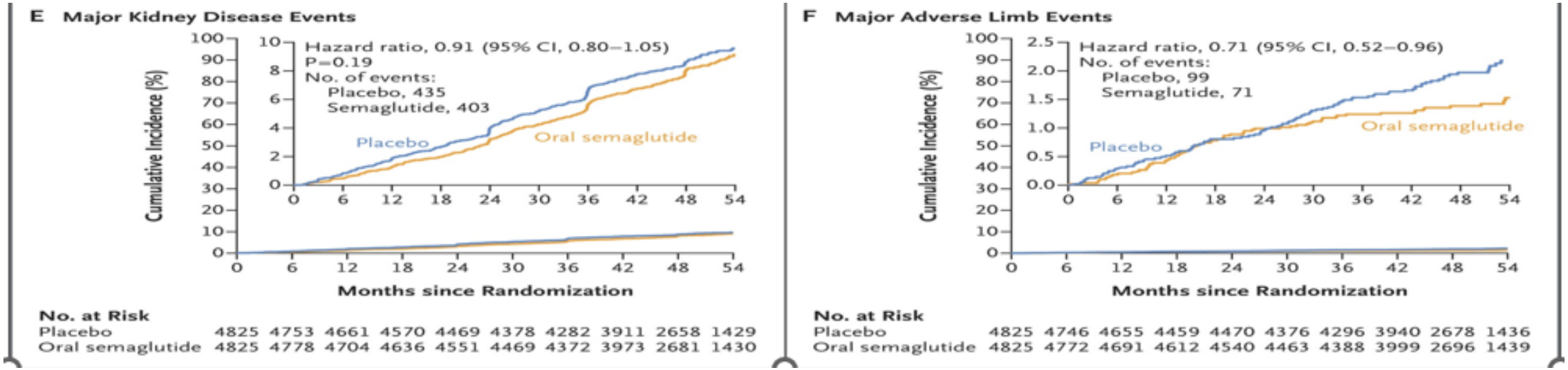


N Engl J Med 2025;392:2001-2012

Cardiology > General Cardiology

FDA Approves GLP-1 Pill for Primary, Secondary Cardiovascular Protection

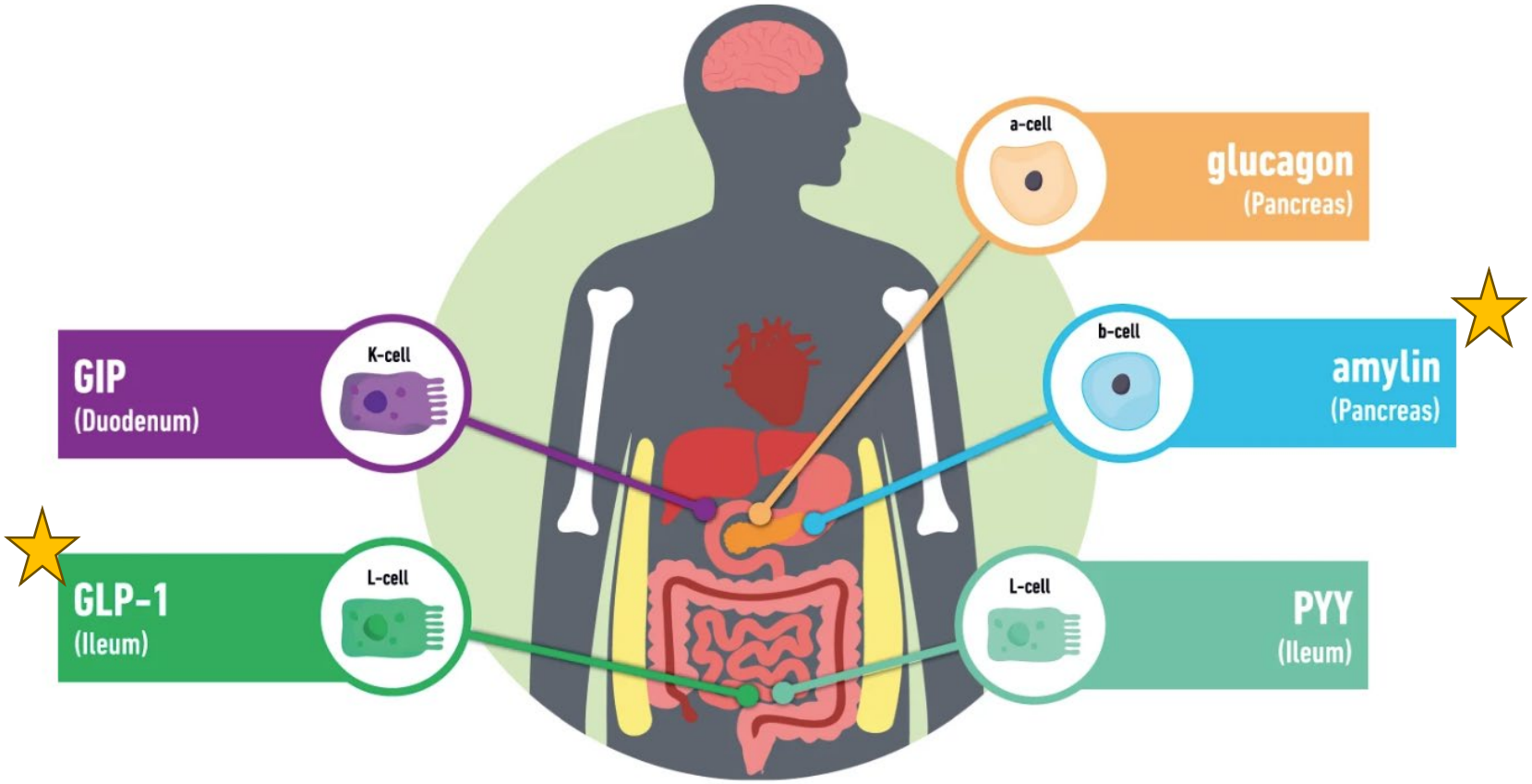
— Oral semaglutide achieves a first for this drug class

by Nicole Lou, Senior Staff Writer, MedPage Today

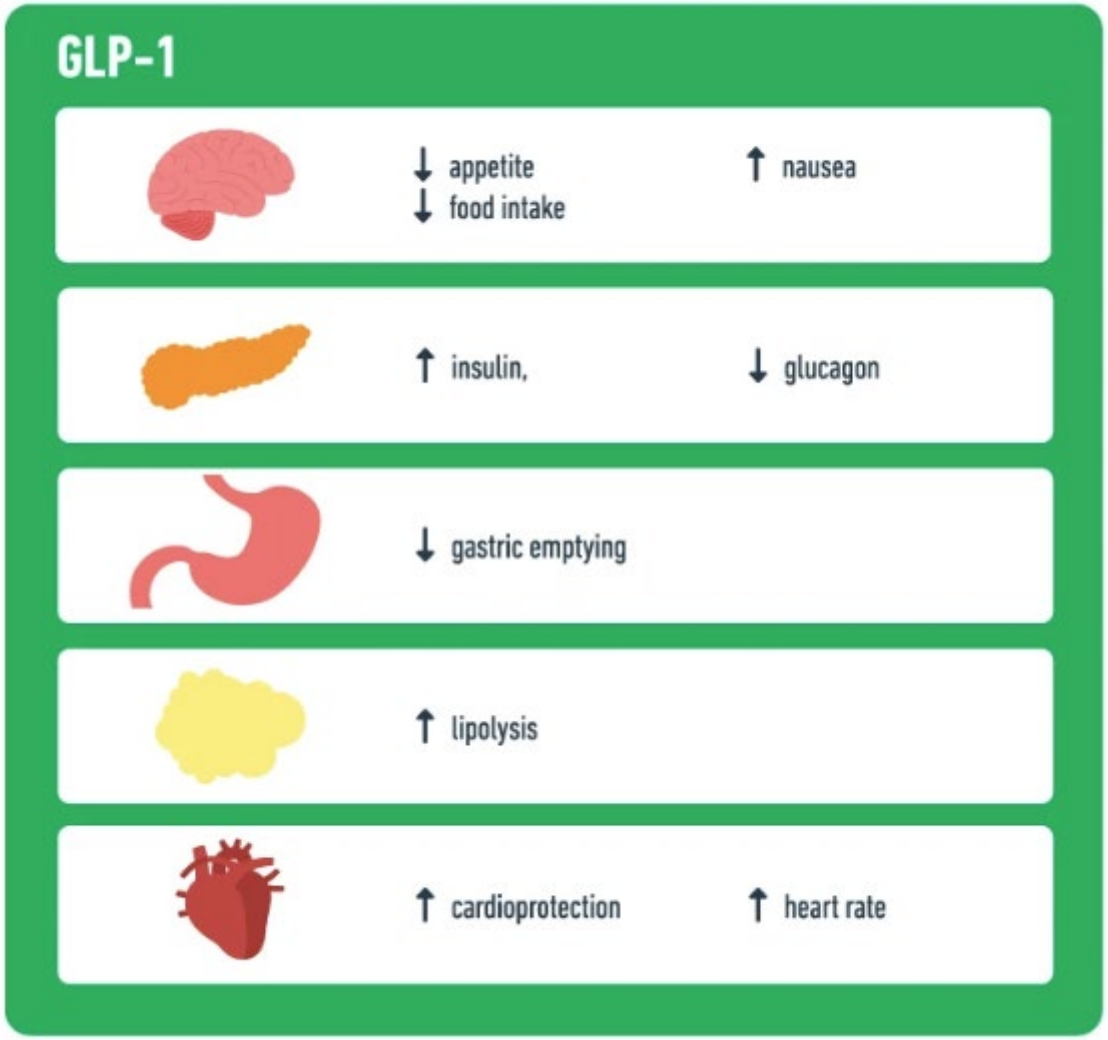
October 20, 2025 · 2 min read

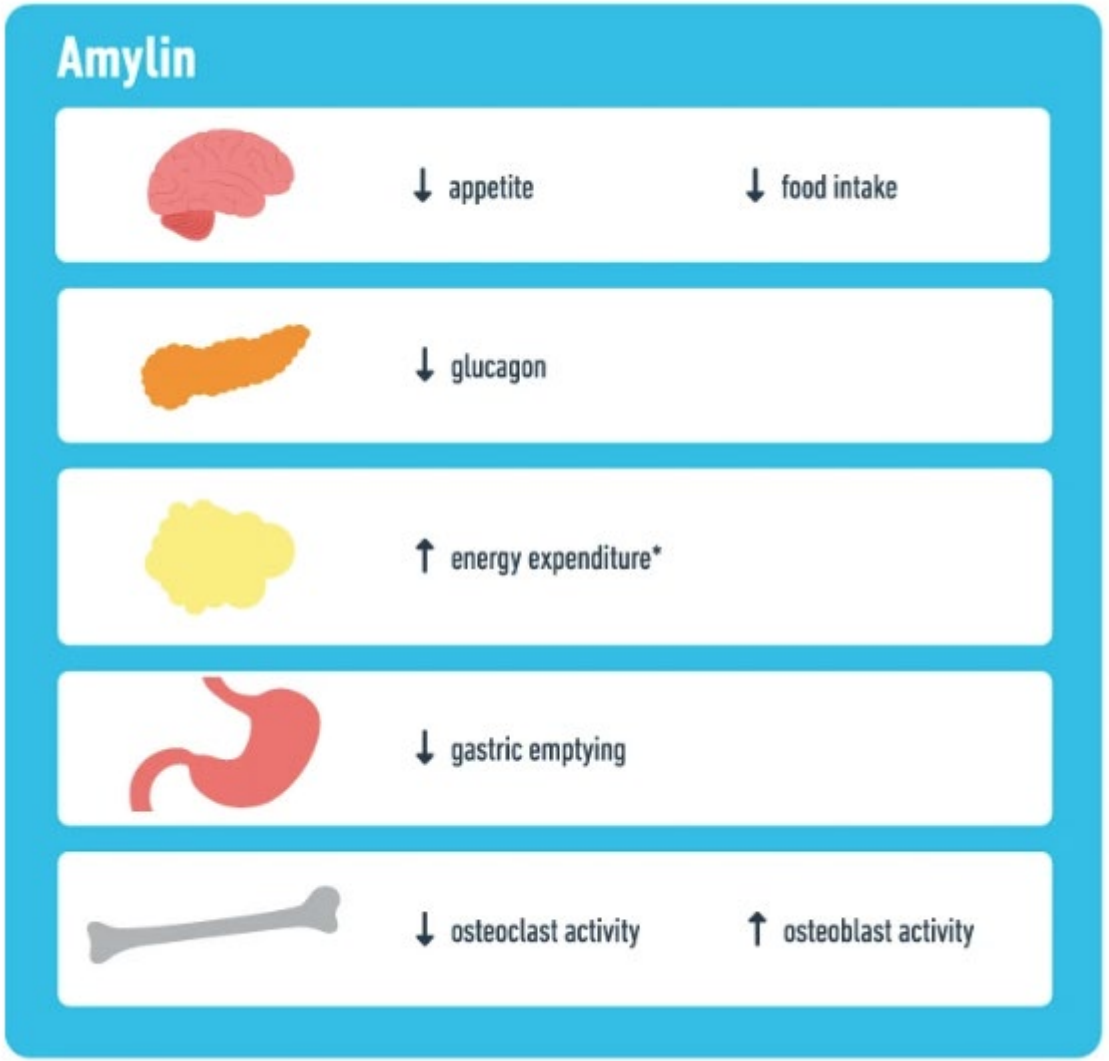
Fig. 1: Secretion and main actions of the gut hormones used in the pipeline obesity treatments.

From: What is the pipeline for future medications for obesity?



Melson, E., Ashraf, U., Papamargaritis, D. *et al.* What is the pipeline for future medications for obesity?. *Int J Obes* **49**, 433–451 (2025).





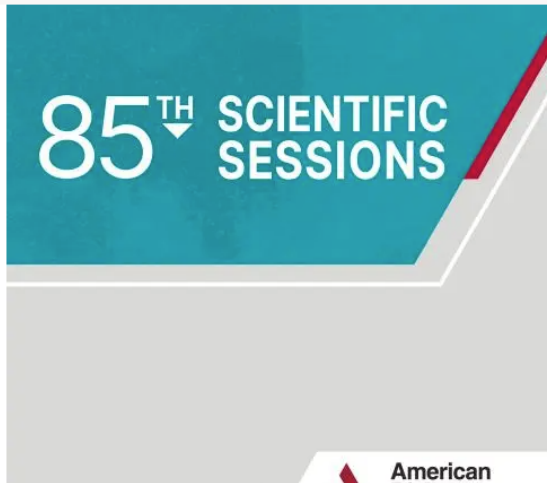
Melson, E., Ashraf, U., Papamargaritis, D. *et al.* What is the pipeline for future medications for obesity?. *Int J Obes* **49**, 433–451 (2025).

PRESS RELEASE

CagriSema Demonstrates Significant Weight Loss in Adults with Obesity

June 22, 2025 | Chicago, IL

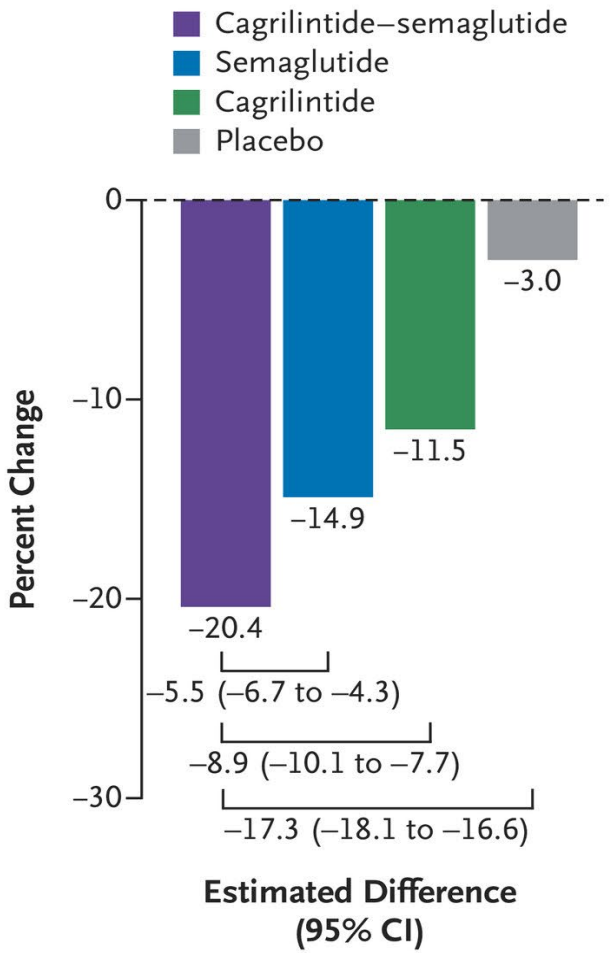
Download Press Materials



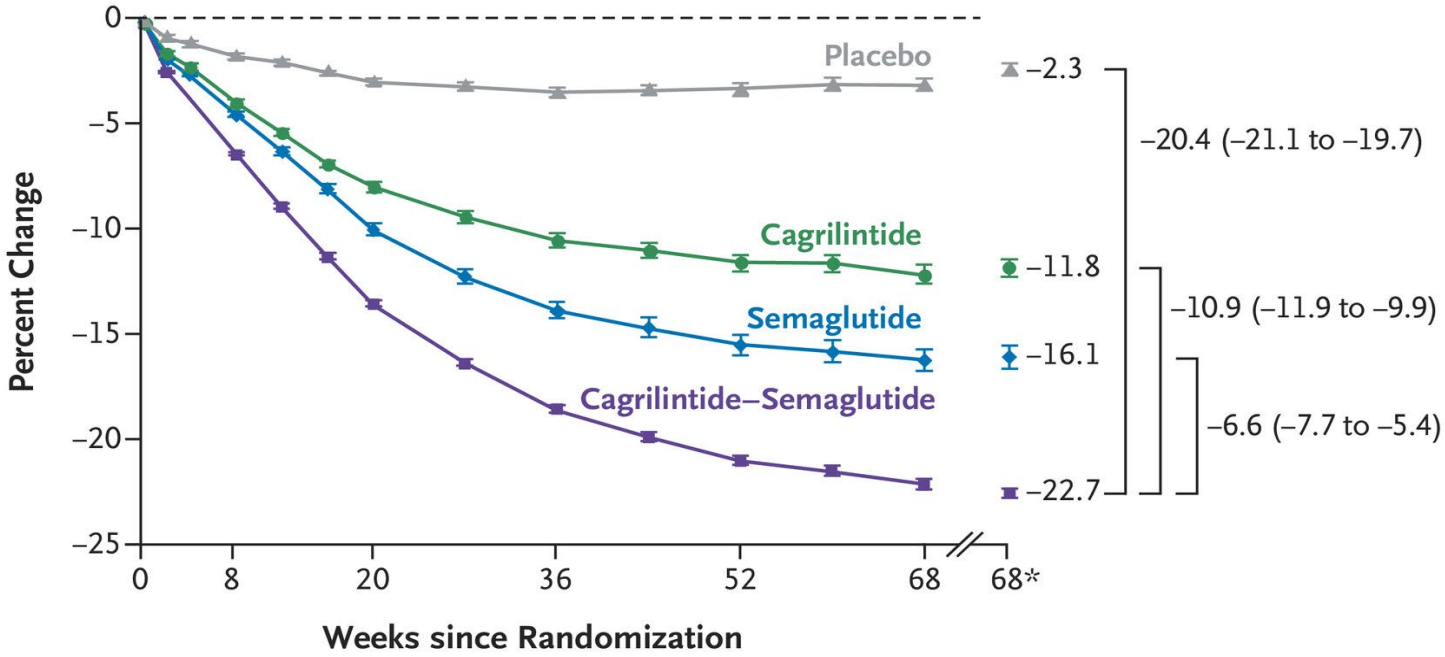
Drs. Davies and Garvey will present the findings at the following symposium:

- Efficacy and Safety of CagriSema 2.4mg/2.4mg in Adults with Overweight/Obesity—The REDEFINE 1 and REDEFINE 2 Clinical Trials
- Presented on June 22 at 8:00 a.m. CT

A Mean Change from Baseline in Body Weight (treatment-policy estimand)



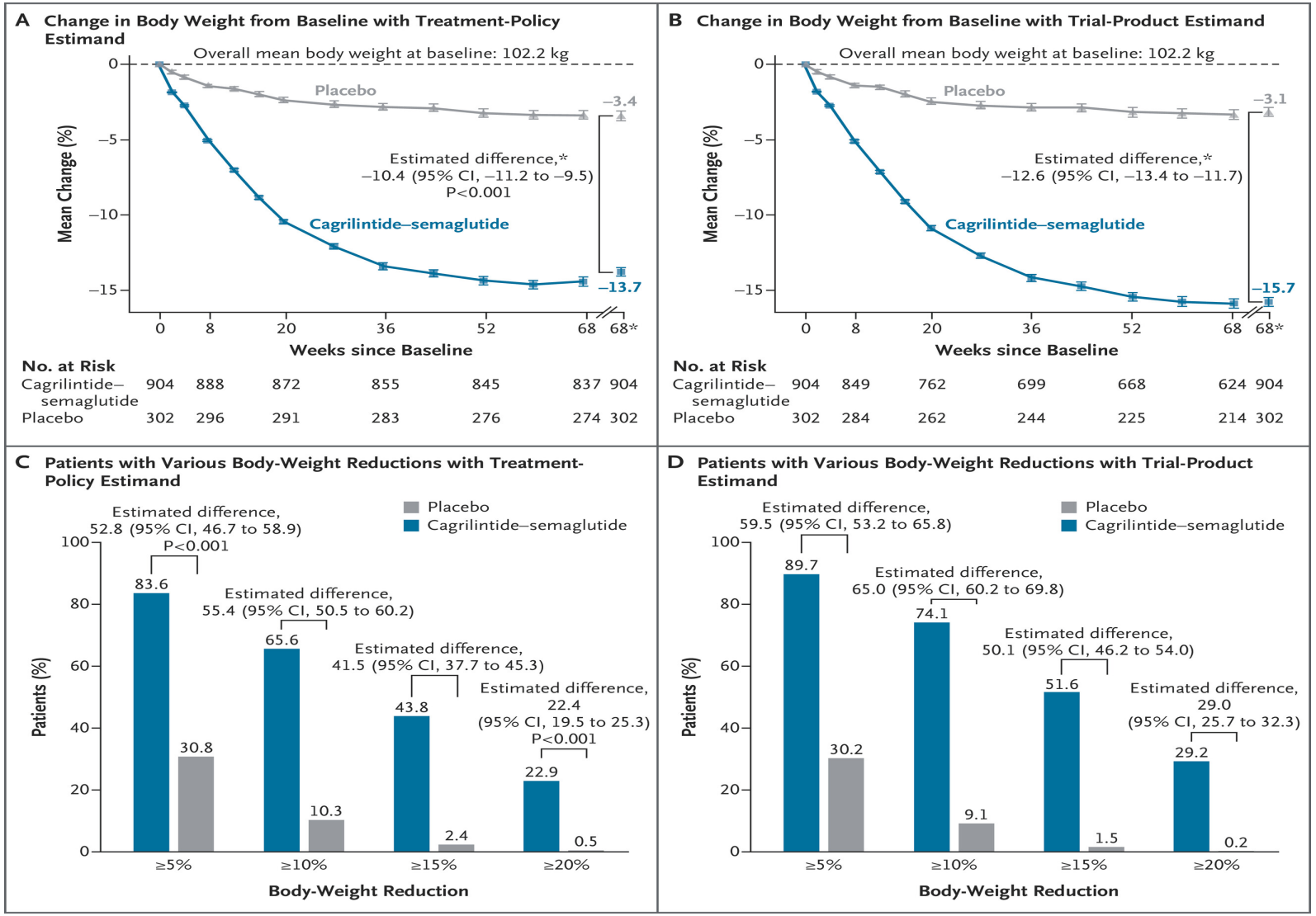
B Change in Body Weight from Baseline to Week 68 (trial-product estimand)



No. at Risk

Placebo	705	672	619	551	487	452	705
Cagrilintide	302	290	275	262	250	223	302
Semaglutide	302	290	269	253	238	220	302
Cagrilintide–semaglutide	2108	2016	1837	1691	1586	1455	2108

Diabetes : Effect of Once-Weekly Cagrilintide–Semaglutide, as Compared with Placebo, on Body Weight



REDEFINE-2, enrolled 1,200 adults with type 2 diabetes living with obesity or overweight,

Davies et al., N Engl J Med 2025;393:648-659

Diabetes : Effect of Once-Weekly Cagrilintide–Semaglutide, as Compared with Placebo, on Glycemic Control

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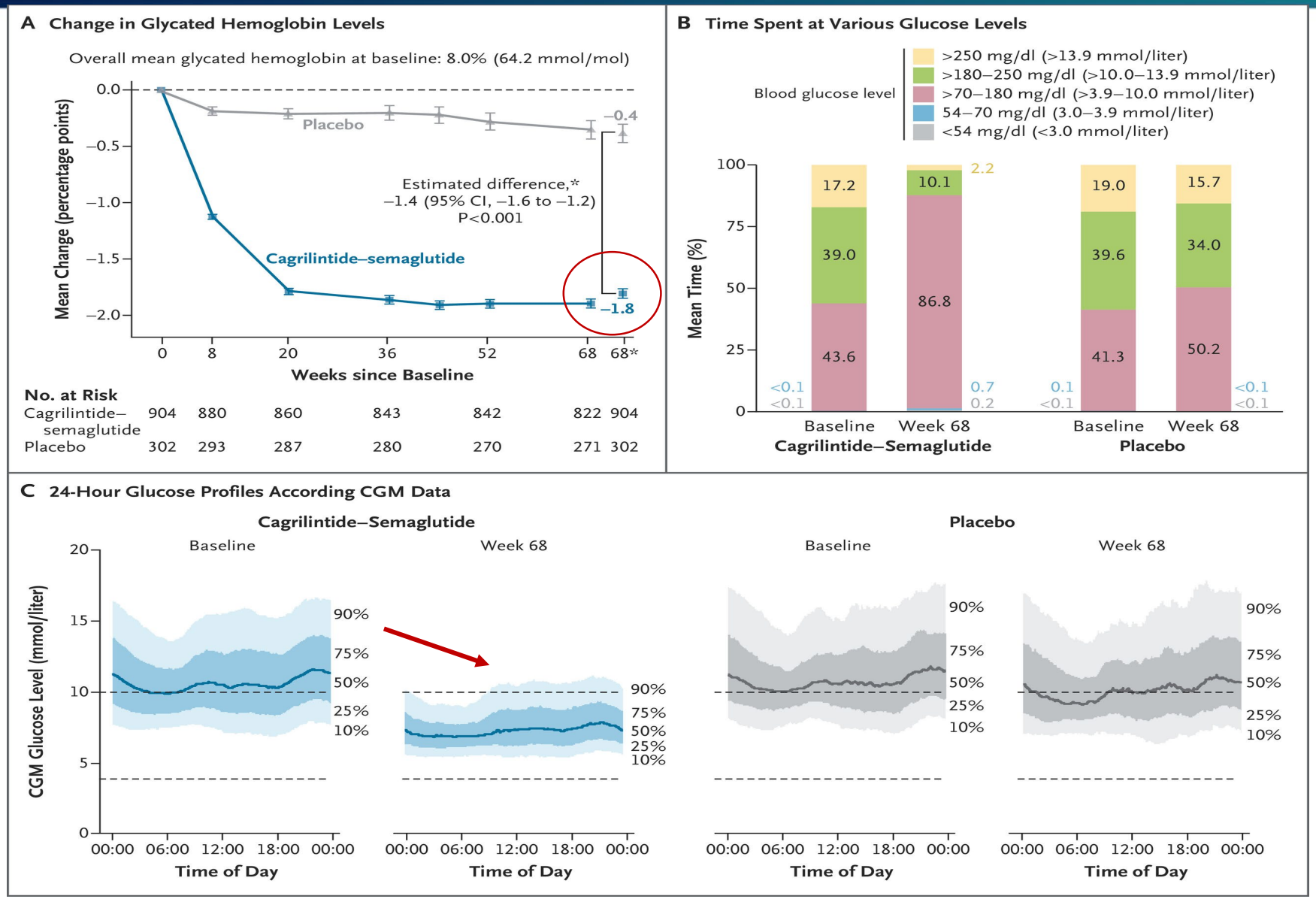
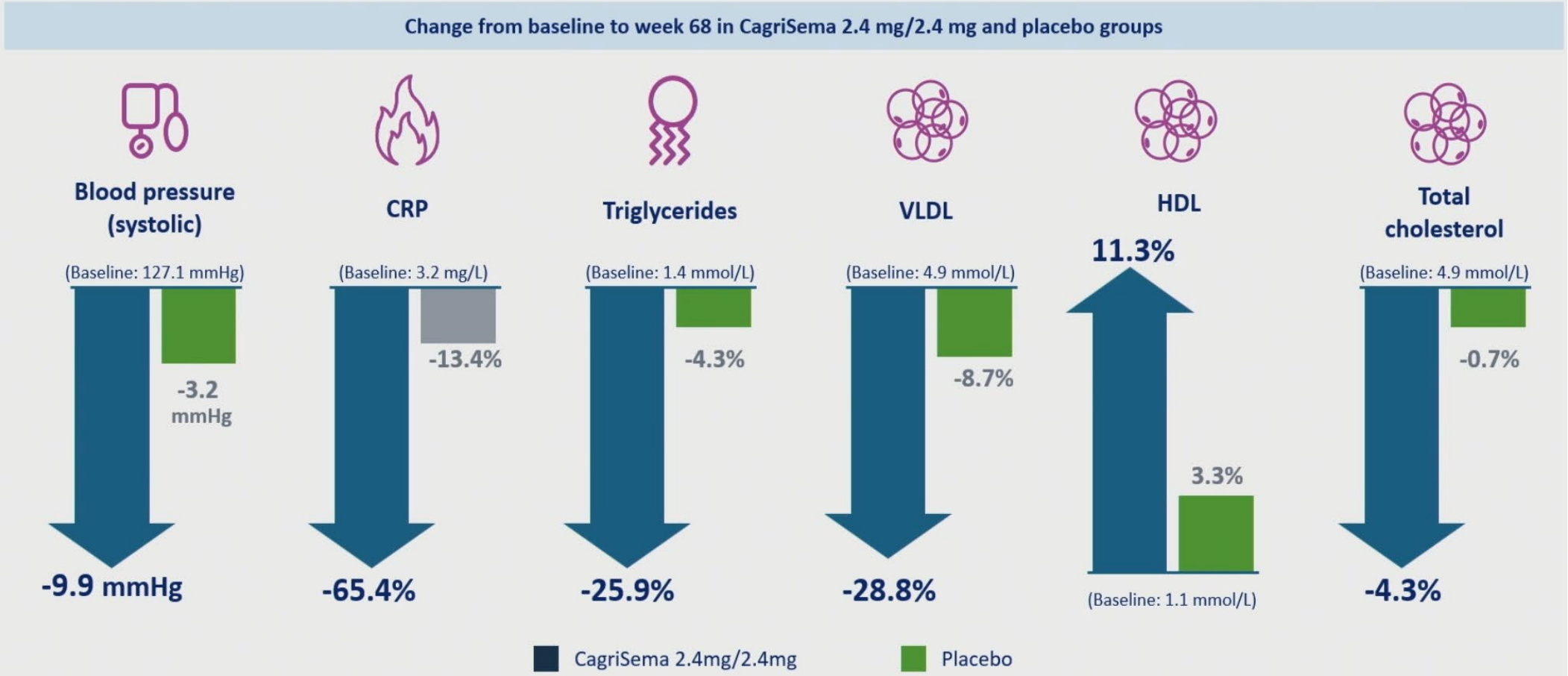


REDEFINE 2

Davies et al., N Engl J Med 2025;393:648-659

Overview of cardiometabolic endpoints in Redefine 2



What is next with this combo?

CVOT with cagrilintide + semaglutide estimated completion date October 2027

- **REDEFINE-3:**
  - **A Research Study to See the Effects of CagriSema in People Living With Diseases in the Heart and Blood Vessels**

Experts to explore future of emerging non-peptide, small molecule GLP-1 receptor agonists

JUNE 21, 2025 | ESTIMATED READ TIME: 2 MINUTES

A morning symposium on Saturday, June 21, will feature the first report of a phase 3 trial of the oral GLP-1 receptor agonist, orforglipron.

Julio Rosenstock, MD, Senior Scientific Advisor for Velocity Clinical Research, Director of Velocity's site at Medical City Dallas, and Clinical Professor of Medicine at the University of Texas Southwestern Medical Center, will present data from ACHIEVE-1 during Emerging Non-Peptide, Small Molecule GLP-1 Receptor Agonists—Can They Become Players?, which will take place from 8:00–9:30 a.m., in Room W375 A of the McCormick Place Convention Center. The randomized controlled trial is studying orforglipron as monotherapy in drug-naïve type 2 diabetes with inadequate glycemic management.

JULIO ROSENSTOCK, MD

In topline results, once-daily orforglipron was shown to be superior to placebo in A1C reduction, the study's primary endpoint. Participants in the orforglipron arm also experienced weight loss, a secondary endpoint. Ongoing studies are evaluating orforglipron for the treatment of type 2 diabetes, for weight management in adults with obesity or overweight and at least one weight-related medical problem, and for the treatment of obstructive sleep apnea and hypertension in adults with obesity.

The symposium also will feature Denise Wootten, PhD, Professor at Monash University, Australia, who will address how better understanding of GLP-1 receptors facilitates improved understanding of where and how small nonpeptide GLP-1 receptor agonists work. She will examine whether all these agents are equally effective.

Tina Vilsbøll, MD, DMSc, Clinical Professor and Head of Clinic at Steno Diabetes Center, Denmark, will discuss the data from currently available phase 2 clinical trials of small nonpeptide GLP-1 receptor agonists and what this research means for the outlook of diabetes treatment.

The NEW ENGLAND JOURNAL of MEDICINE

Orforglipron in Early Type 2 Diabetes

A Research Summary based on Rosenstock J et al. | 10.1056/NEJMoa2505669 | Published on June 21, 2025

WHY WAS THE TRIAL DONE?

For patients with type 2 diabetes, subcutaneous glucagon-like peptide-1 (GLP-1) receptor agonists are well-established, effective treatments. However, many patients prefer oral formulations over injectables. In a phase 2 trial, orforglipron — an oral, small-molecule, nonpeptide GLP-1 receptor agonist — led to meaningful reductions in the glycated hemoglobin level and body weight in patients with type 2 diabetes. However, additional data are needed.

HOW WAS THE TRIAL CONDUCTED?

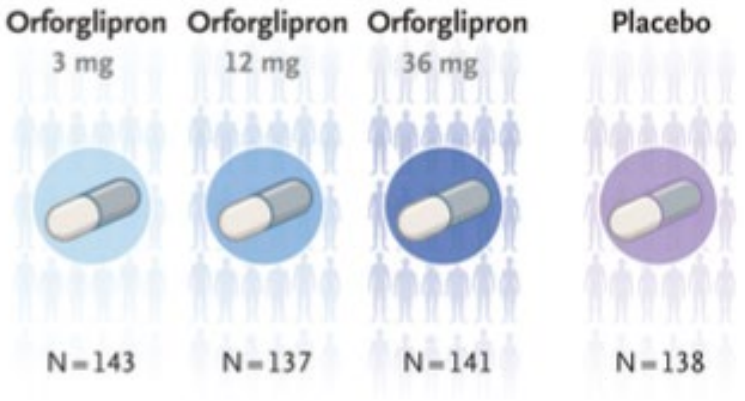
Adults with type 2 diabetes that was inadequately controlled with diet and exercise alone, a glycated hemoglobin level between 7.0% and 9.5%, and a body-mass index of at least 23.0 were assigned to receive oral orforglipron at one of three maintenance doses (3 mg, 12 mg, or 36 mg) or placebo once daily for 40 weeks. The primary end point was the change in the glycated hemoglobin level from baseline to week 40.

TRIAL DESIGN

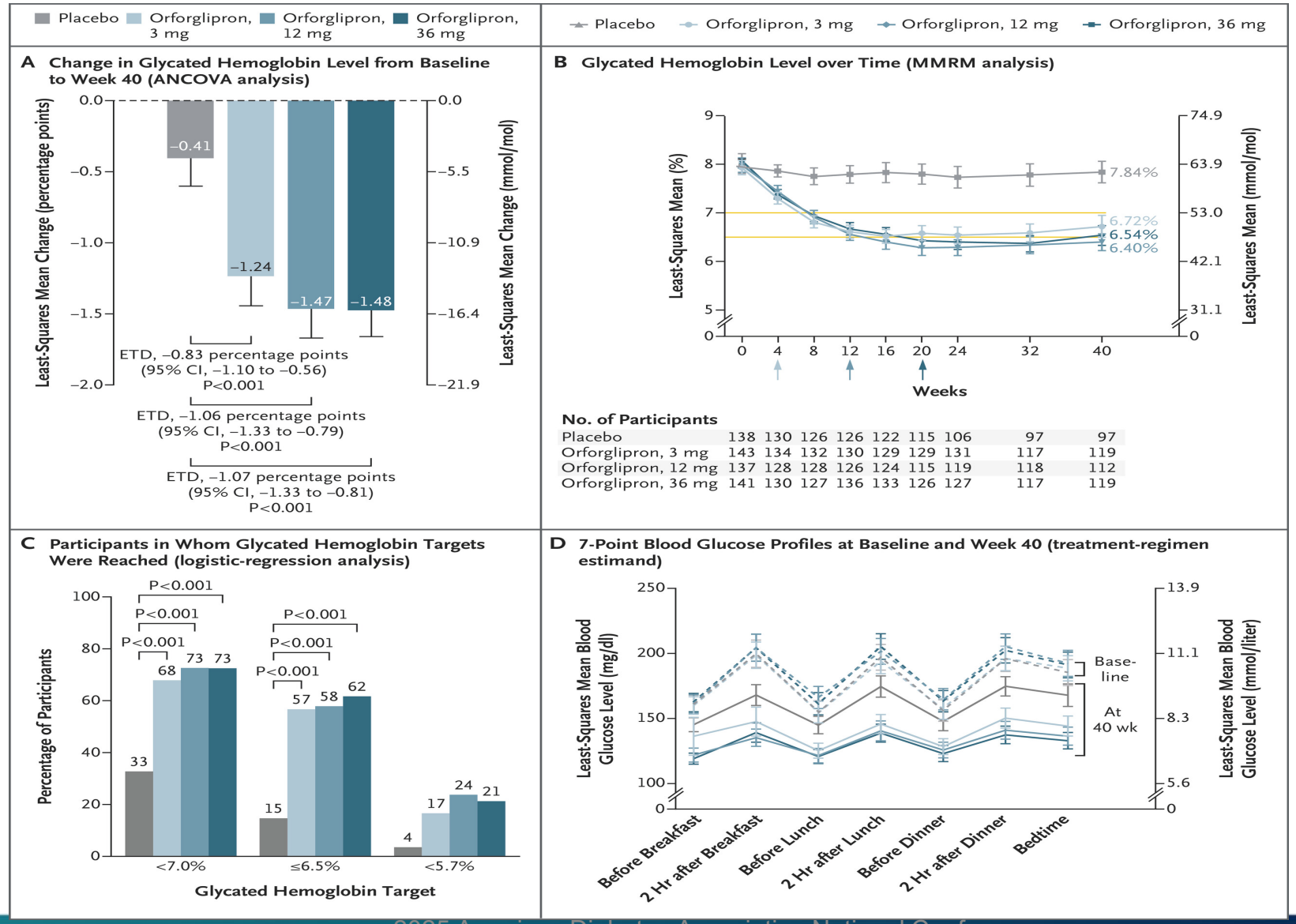
- Phase 3
- Double-blind
- Randomized
- Placebo-controlled
- Location: China, India, Japan, Mexico, and the United States

Participants

- 559 adults
- Mean age, 53 years
- Men: 52%; Women: 48%



Orfoglipron
Glycated Hemoglobin Levels and Participant-Monitored Blood Glucose Profiles



Rosenstock et al., NEngl J Med 2025;393:1065-1076

Orforglipron: Body Weight, Body-Weight Reduction Thresholds, and Lipid Profiles

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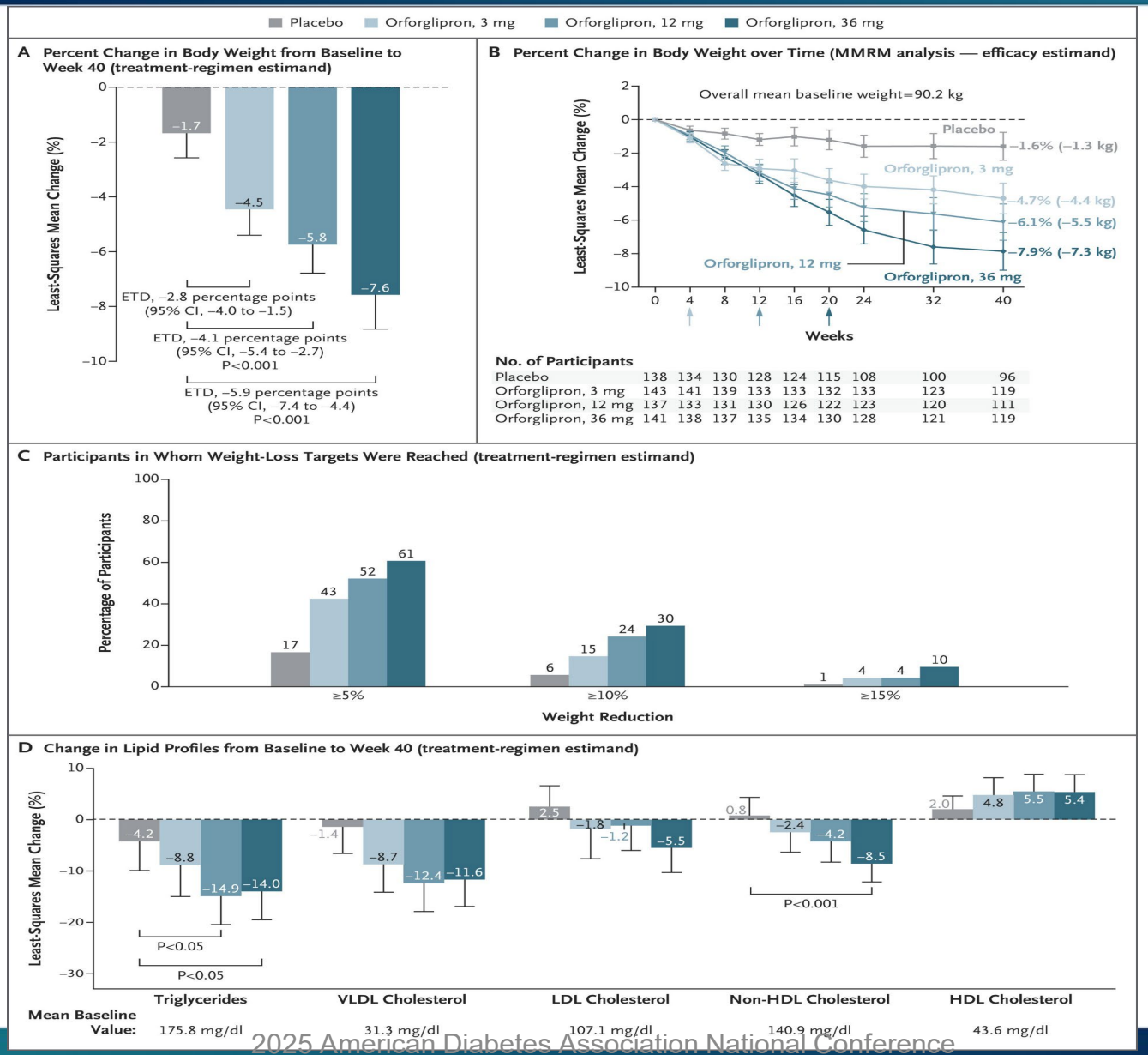


BELIEVE spotlights quality and quantity approach to weight management with combo therapy

JULY 10, 2025 | ESTIMATED READ TIME: 6 MINUTES

While the broad benefits of weight loss, even with modest reductions, have long been appreciated in obesity medicine, concomitant sarcopenia—loss of muscle mass—is often a collateral effect.

The phase 2 BELIEVE trial showed that the addition of bimagrumab, an activin type II receptor-targeted antibody that promotes muscle hypertrophy, could preserve the weight reduction seen with the glucagon-like peptide-1 receptor agonist (GLP-1 RA), semaglutide, while also improving body composition, preserving lean muscle mass, and boosting physical function in adults living with obesity without concomitant diabetes.

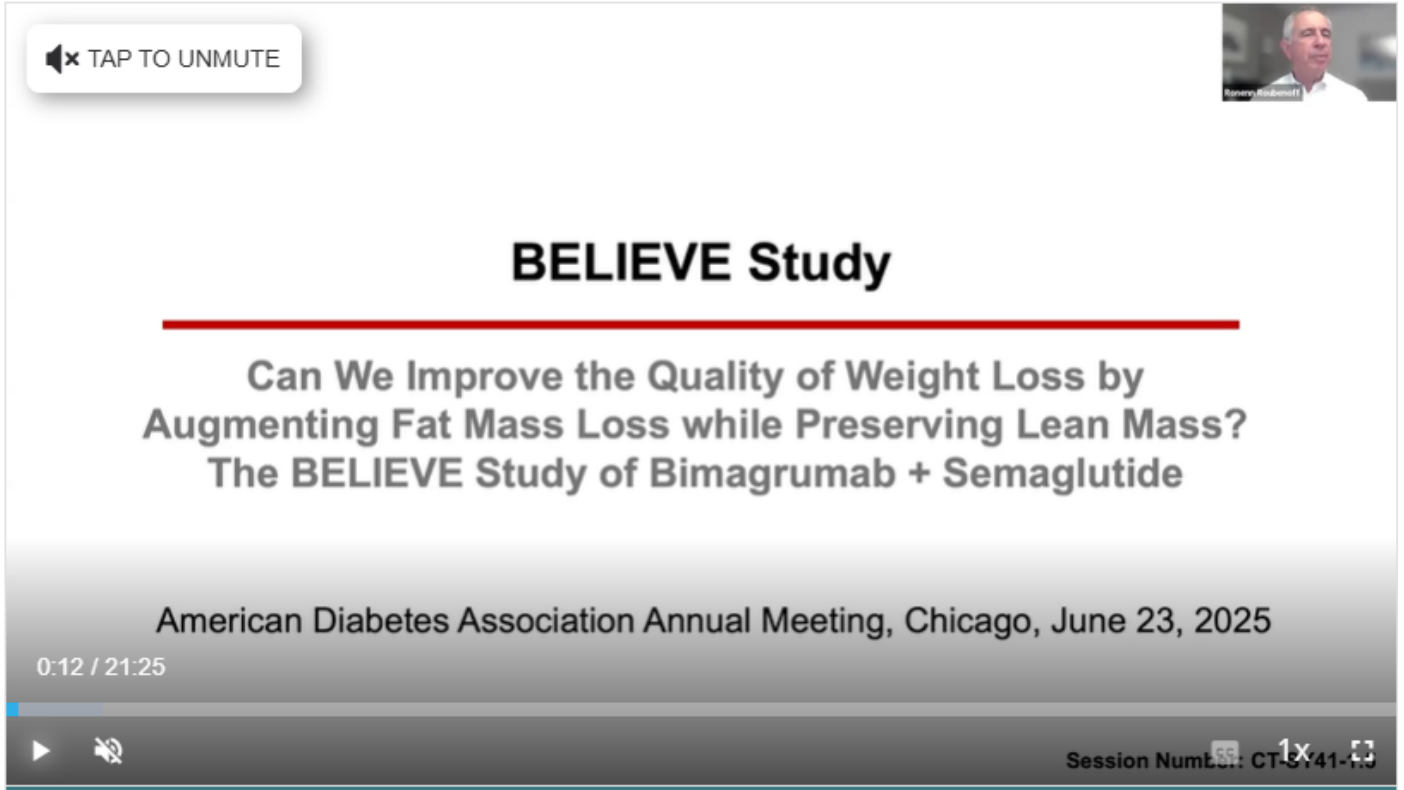
Steven B. Heymsfield, MD, Professor of Medicine at the Pennington Biomedical Research Center, summarized the key efficacy data from BELIEVE on Monday, June 23, at the 85th Scientific Sessions symposium, Can We Improve the Quality of Weight Loss by Augmenting Fat Mass Loss while Preserving Lean Mass? The BELIEVE Study of Bimagrumab + Semaglutide.

STEVEN B. HEYMSFIELD, MD

"We all know that obesity is a disease of excess adiposity, and the optimal treatment would be to promote mainly fat loss," Dr. Heymsfield said. However, with caloric restriction, and with other weight loss approaches, there is a risk of some degree of obligatory loss of lean muscle. "The goal of treatment, therefore, would be to optimize the quality of weight loss, maximize fat loss, and minimize lean muscle loss."

Ronenn Roubenoff, MD, MHS, Roubenoff Consulting, LLC, explained why bimagrumab, which blocks the activin/myostatin signaling in muscle and adipose tissues, was the rational choice of partner for the incretin semaglutide in the BELIEVE study.

"The mechanisms of action of the incretins and the activin pathway drugs are quite distinct," Dr. Roubenoff said, highlighting previous clinical data showing fat loss, especially visceral and hepatic fat, and muscle gain during weight loss in people treated with bimagrumab.



EMAIL RONENN

This video is featured in the ADA 2025 Insights

Can We Improve the Quality of Weight Loss by Augmenting Fat Mass Loss While Preserving Lean Mass? The BELIEVE Study of Bimagrumab + Semaglutide

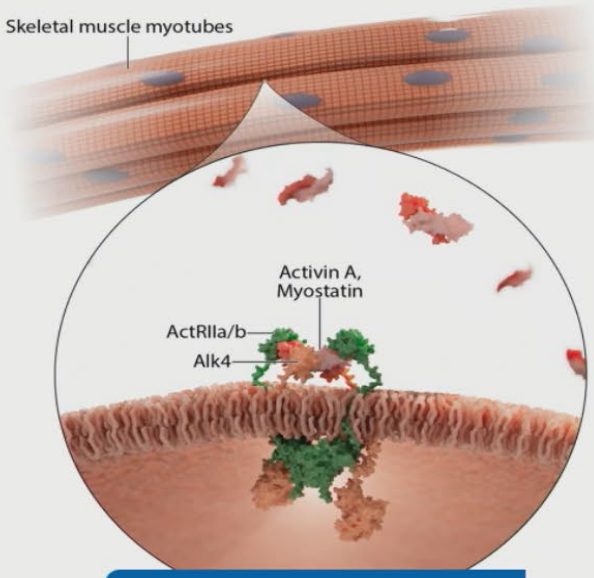
By **ADA 2025 INSIGHTS** FEATURING **RONENN ROUBENOFF**

Bimagrumab is a monoclonal antibody that blocks signaling of activins/GDFs in muscle and adipose tissue

- **Activin signaling pathways (myostatin [GDF8], activins A/B/E, GDF11, GDF3)**
  - inhibit muscle growth in skeletal muscle via ActRIIA/B and ALK4
  - increase lipid storage in adipose tissue via ActRIIA/B and ALK7
- **Bimagrumab** blocks these pathways, leading to increased muscle mass and decreased fat mass
- Mechanism is not dependent on effect in CNS, appetite or satiety

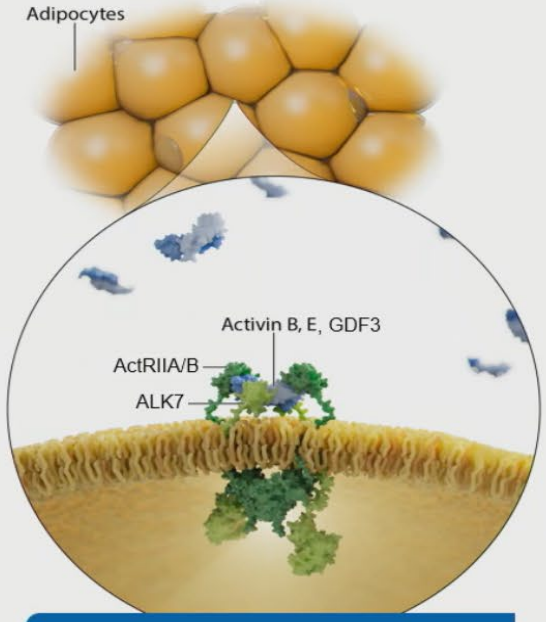
MUSCLE

Bhima



Inhibits Muscle Growth

FAT

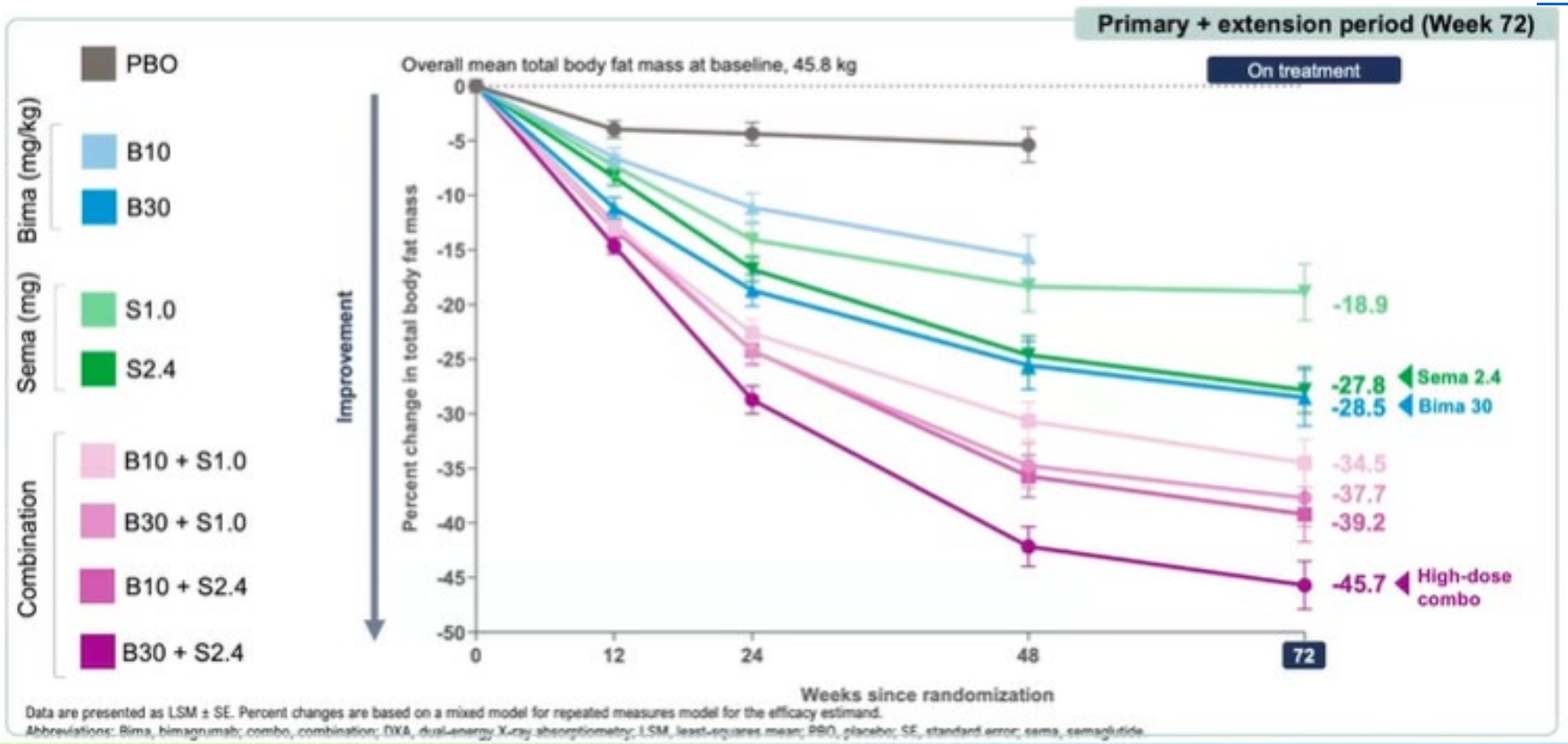


Drives Lipid Storage

Total Body Fat Mass: % Change from Baseline (DXA, Week 72)

High-dose combination group achieved 46% mean decrease in total body fat mass

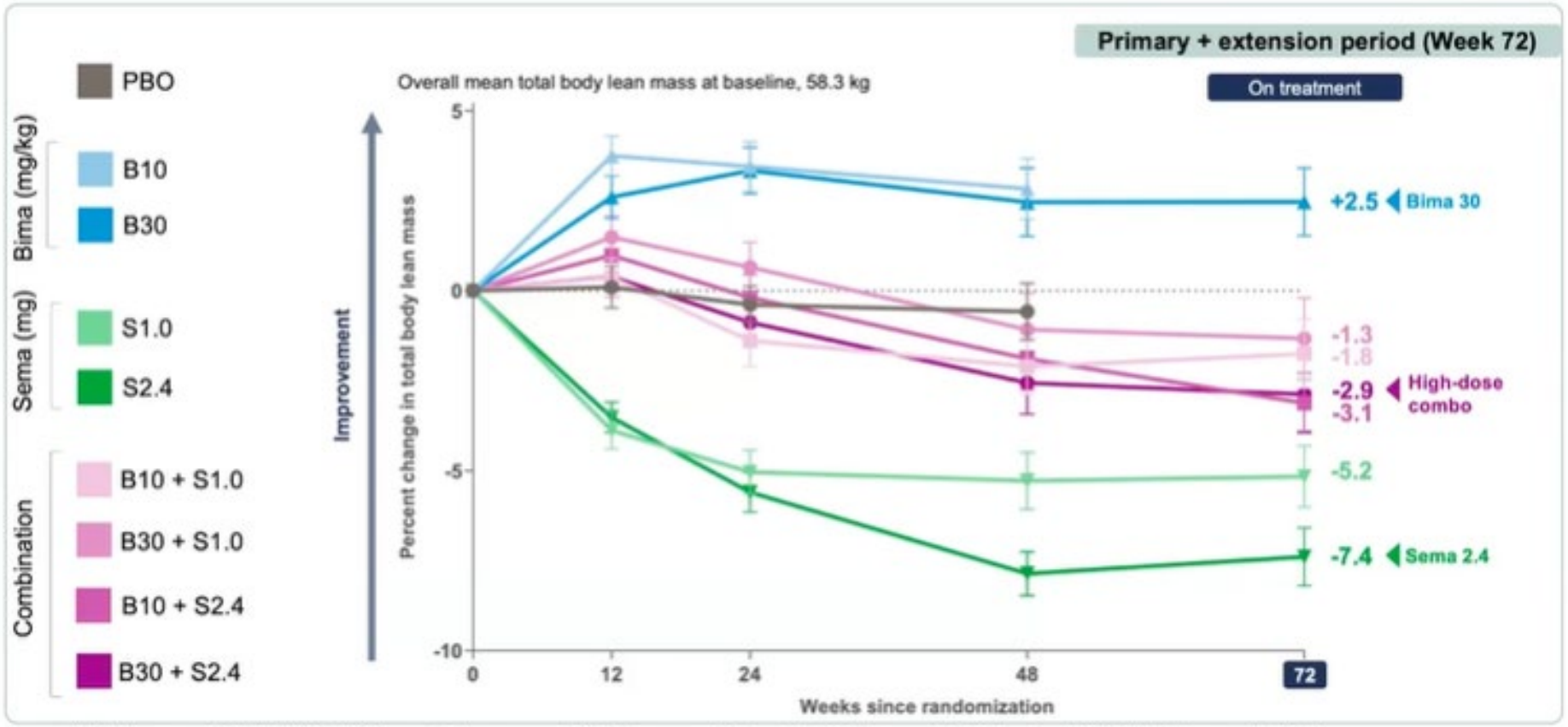
FEATURING RONENN ROUBENOFF



https://www.vumedi.com/video/can-we-improve-the-quality-of-weightloss-by-augmenting-fat-mass-loss-while-preserving-lean-mass-the-b/

Total Body Lean Mass: % Change from Baseline (DXA, Week 72)

Lean mass largely preserved with combination therapy



Appendicular lean mass (Week 72): The LSM percent changes were +2.3% (bimagrumab 30 mg/kg), −9.2% (semaglutide 2.4 mg), and −2.6% (high-dose combination).

Data are presented as LSM ± SE. Percent changes are based on a mixed model for repeated measures model for the efficacy estimand.
Abbreviations: Bima, bimagrumab; combo, combination; DXA, dual-energy X-ray absorptiometry; LSM, least-squares mean; PBO, placebo; SE, standard error; sema, semaglutide.

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Active, not recruiting

A Study to Investigate Weight Management With Bimagrumab (LY3985863) and Tirzepatide (LY3298176), Alone or in Combination, in Adults With Obesity or Overweight

ClinicalTrials.gov ID NCT06643728

Sponsor Eli Lilly and Company

Information provided by Eli Lilly and Company (Responsible Party)

Last Update Posted 2025-09-26

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Study Details | Researcher View | No Results Posted | Record History

On this page

- Study Overview
- Contacts and Locations
- Participation Criteria
- Study Plan
- Collaborators and Investigators

Study Overview

Brief Summary

The main purpose of this study is to evaluate the efficacy and safety of Bimagrumab and Tirzepatide, alone or in combination, in adults with obesity or overweight, with at least one obesity related comorbidity, without Type 2 Diabetes. The study will last about 70 weeks.

Official Title

Study Start (Actual)

2024-10-21

Primary Completion (Estimated)

2026-04

VIEW MORE SESSION COVERAGE

QWINT signals paradigm shift for basal insulin dosing in type 2 diabetes

JUNE 23, 2025 | ESTIMATED READ TIME: 5 MINUTES

The novel once-weekly insulin analog efsitora alfa (efsitora) improved glucose control, compared to daily insulin, without a concomitant increase in severe hypoglycemia, across three phase 3 trials focused on people living with type 2 diabetes within the QWINT clinical program.

Findings from three QWINT studies were shared on Sunday, June 22, during the symposium, Advancing and Facilitating Basal Insulin Therapy in Type 2 Diabetes—Breaking News on the QWINT 1, 3, and 4 Trials with Once-Weekly Insulin Efsitora Alfa!

"We are living in the most exciting time for type 2 diabetes therapy," said Chantal Mathieu, MD, PhD, Professor of Endocrinology at Katholieke Universiteit Leuven, Belgium, and President of the European Association for the Study of Diabetes. "We have all these new therapies for type 2 diabetes, but insulin is still on this list. Until now, none of the drugs have been shown to protect against beta cell failure. So, most patients with type 2 diabetes will eventually need insulin treatment."

With the new data from QWINT, efsitora is now the second long-acting, once-weekly insulin analog that has been evaluated in robust phase 3 studies and proven to be non-inferior to daily insulins. The other once-weekly insulin, icodec, was approved for use in both type 1 and 2 diabetes by the European Medicines Agency.

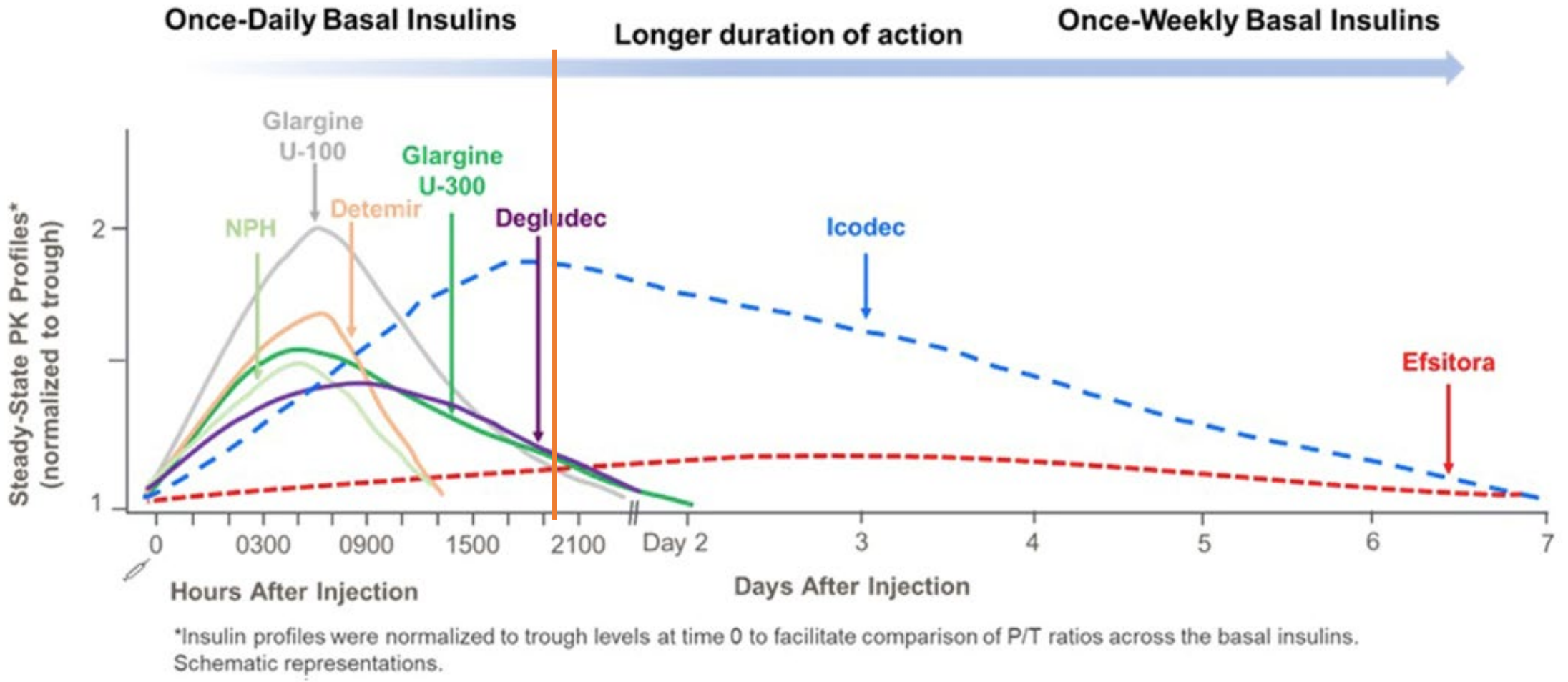

Fig. 2. Schematic representations of exposure profiles of daily and weekly basal insulins at steady state. *Insulin profiles were normalized to trough levels at time 0 to facilitate comparison of P/T ratios at steady state across the basal insulins when dosed daily (NPH, glargine, detemir and degludec) or weekly (icodec and efsitora). *NPH*, neutral protamine Hagedorn; *P/T*, peak-to-trough ratio.

Pieber TR, Leohr J, Bue-Valleskey JM, Juneja R, Chien J, Syring K, Buse JB. Understanding the Pharmacokinetics and Glucodynamics of Once Weekly Basal Insulins to Inform Dosing Principles: An Introduction to Clinicians. Endocr Pract. 2024 Sep;30(9):863-869. Epub 2024 Jun 14. PMID:

Fixed-Dose Regimen for Efsitora

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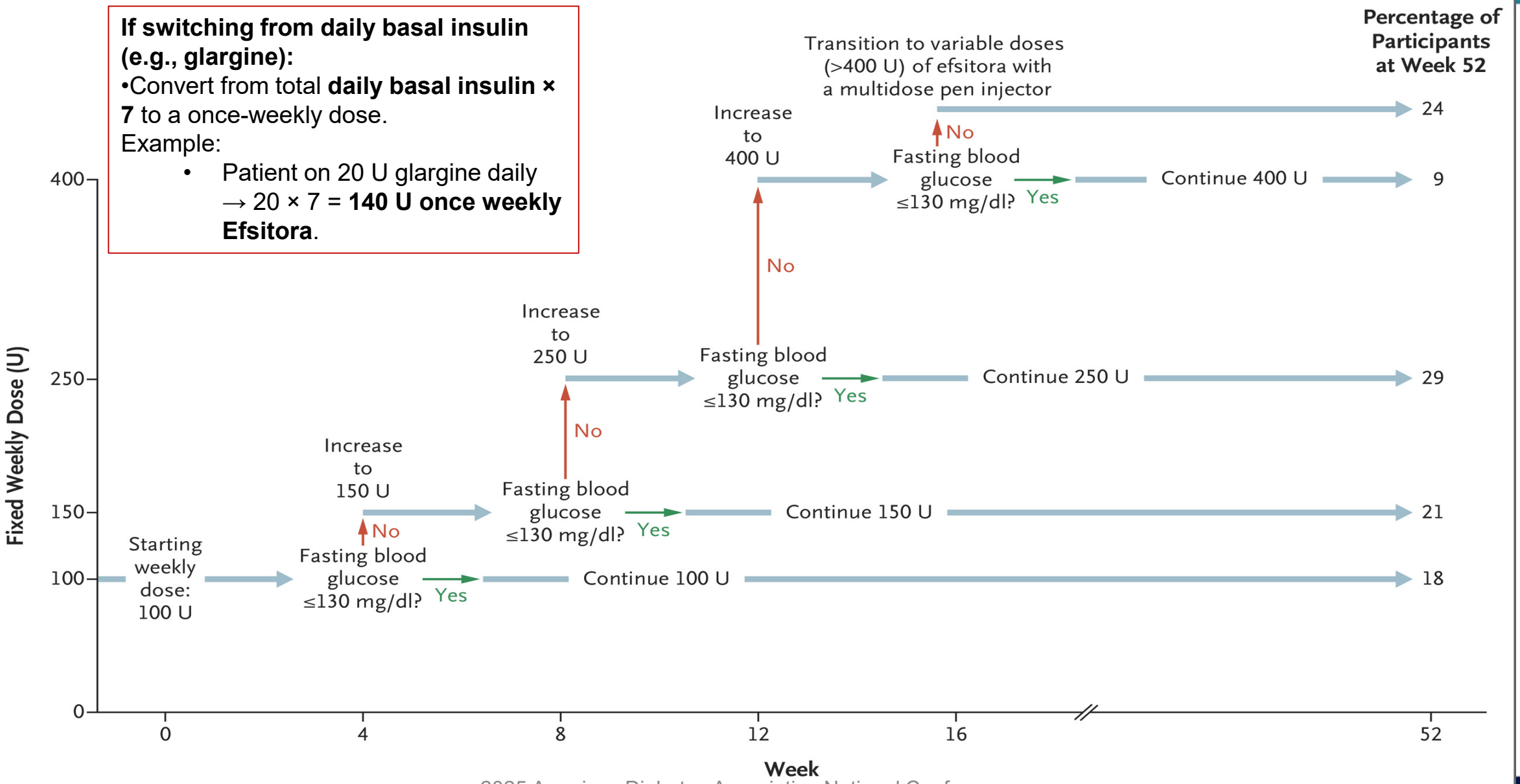
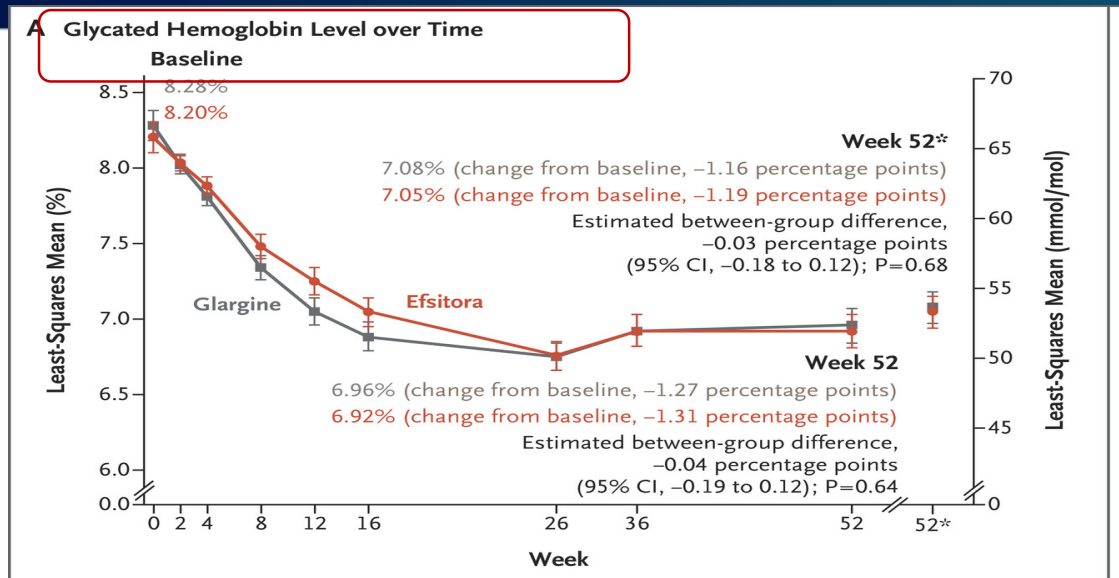
If switching from daily basal insulin (e.g., glargine):
- Convert from total **daily basal insulin × 7** to a once-weekly dose.

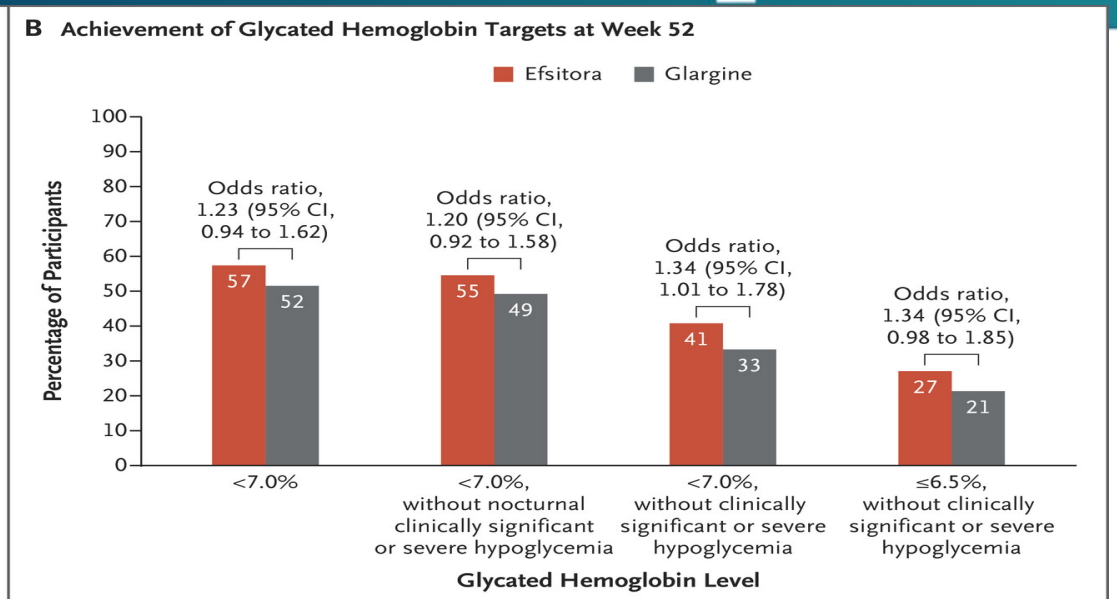
Example:
- Patient on 20 U glargine daily → 20 × 7 = **140 U once weekly Efsitora**.

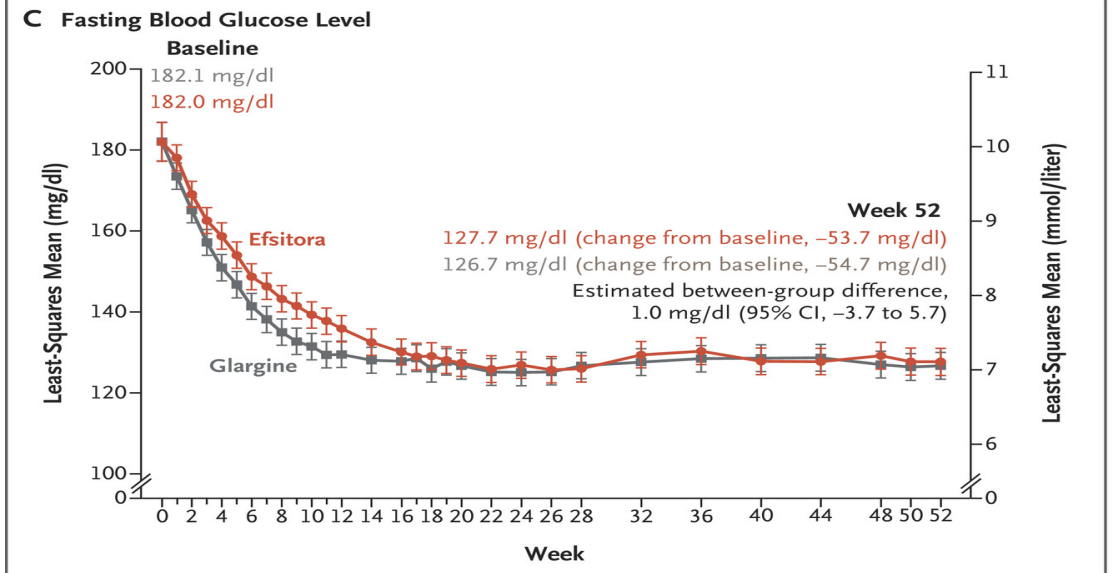


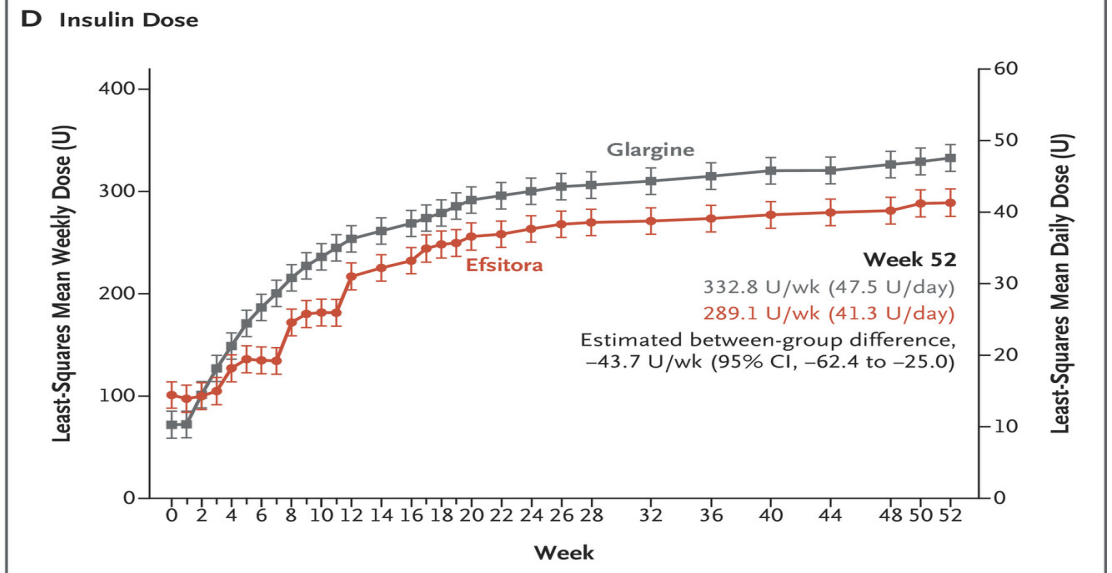
N Engl J Med 2025;393:325-335

Efficacy Outcomes among Participants Who Received Once-Weekly Efsitora or Once-Daily Glargine









Also presented at ADA were

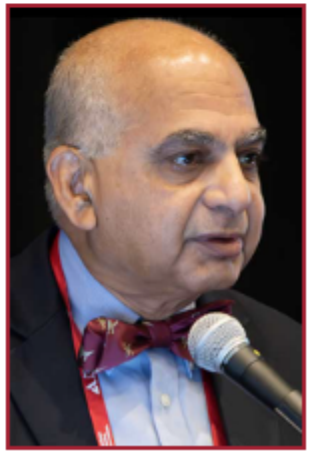
- QWINT-3 was a basal insulin switch study of flexible efsitora dosing, compared with degludec, over 78 weeks.
- QWINT-4, focused on individuals with type 2 diabetes on basal and mealtime insulin therapy, compared flexible efsitora dosing to insulin glargine over 26 weeks.
- Across the three QWINT studies discussed at the symposium, efsitora met the primary endpoint—non-inferiority to the comparator in inducing glycemic control, as measured by change in A1C from baseline to week 26 (QWINT-3 and QWINT-4) or week 52 (QWINT-1).

CATALYST shows mifepristone for hypercortisolism in type 2 diabetes reduces A1C, weight

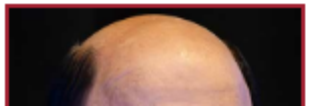
JULY 10, 2025 | ESTIMATED READ TIME: 3 MINUTES

Hypercortisolism has emerged as a common and largely unrecognized contributor to type 2 diabetes that is difficult to manage despite multiple medications. The CATALYST trial of mifepristone in individuals living with difficult-to-treat type 2 diabetes reduced A1C by 1.32% versus placebo. The A1C reductions came despite diabetes medication dose reductions in half the mifepristone participants during the 24-week trial.

"There was a discontinuation of some [diabetes medications], especially fast-acting insulin and sulfonylureas, and reductions in dose of long-acting insulin," said Vivian Fonseca, MD, Professor of Medicine and Pharmacology, Chief of the Section of Endocrinology, and Assistant Dean for Clinical Research at Tulane University School of Medicine. "This is a more precise way of treating diabetes than giving any drug that comes along," he continued. "You identify an abnormality and treat that abnormality."


VIVIAN FONSECA, MD

Dr. Fonseca delivered the findings during Treatment of Hypercortisolism in People with Difficult-to-Control Type 2 Diabetes—Final Results of the CATALYST Trial on Monday afternoon, June 23, at the 85th Scientific Sessions. CATALYST data suggest hypercortisolism contributes to difficult-to-treat type 2 diabetes in at least 1.125 million people in the U.S. alone. The U.S. Food and Drug Administration (FDA) has approved mifepristone to treat hyperglycemia secondary to hypercortisolism in adults with Cushing syndrome and living with type 2 diabetes or glucose intolerance.



Hyperglycemia secondary to hypercortisolism is a commonly missed diagnosis of difficult-to-treat type 2 diabetes, explained Ralph A. DeFronzo, MD, Professor of Medicine, Chief of the Diabetes Division, and Deputy Director of the Texas Diabetes Institute, University of Texas Health Science Center at San Antonio. Few individuals with hypercortisolism present with the

CATALYST

Study of Hypercortisolism in Patients with Difficult-to-Control Type 2 Diabetes

Prevalence of hypercortisolism in patients with difficult-to-control type 2 diabetes

CATALYST Part 1 Study Design (NCT05772169)

Adults with difficult -to- control type 2 diabetes (*N* = 1,057)

1-mg DST

Primary end point

Hypercortisolism prevalence

Post-DST cortisol >1.8 µg/dL[a]

Known causes of false-positive DSTs excluded

Further evaluation

- Clinical and laboratory characteristics
- Adrenal CT scan

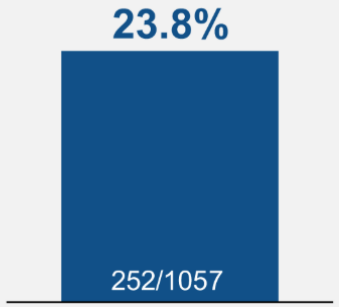
"Difficult-to-control" type 2 diabetes defined as:

HbA_{1c} 7.5 –11.5% and at least 1 of:

- Taking ≥3 DM drugs
- Taking insulin & other DM drugs
- Taking ≥2 DM drugs and ≥1 micro- or macrovascular complications
- Taking ≥2 DM and ≥2 BP drugs

Hypercortisolism Prevalence

Overall population

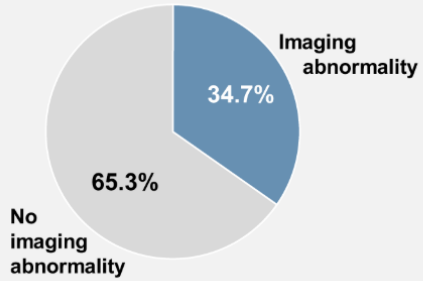


Prevalence among participants taking ≥3 BP drugs: 36.6%

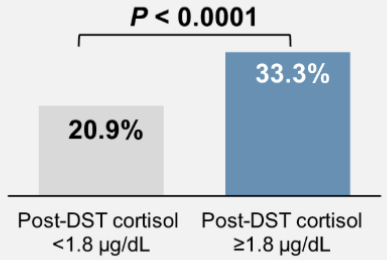
Key Takeaway: The prevalence of hypercortisolism in this population is higher than generally recognized

Other Key Findings

Adrenal imaging abnormality on CT scan[b]



More cardiac disorders in participants with hypercortisolism

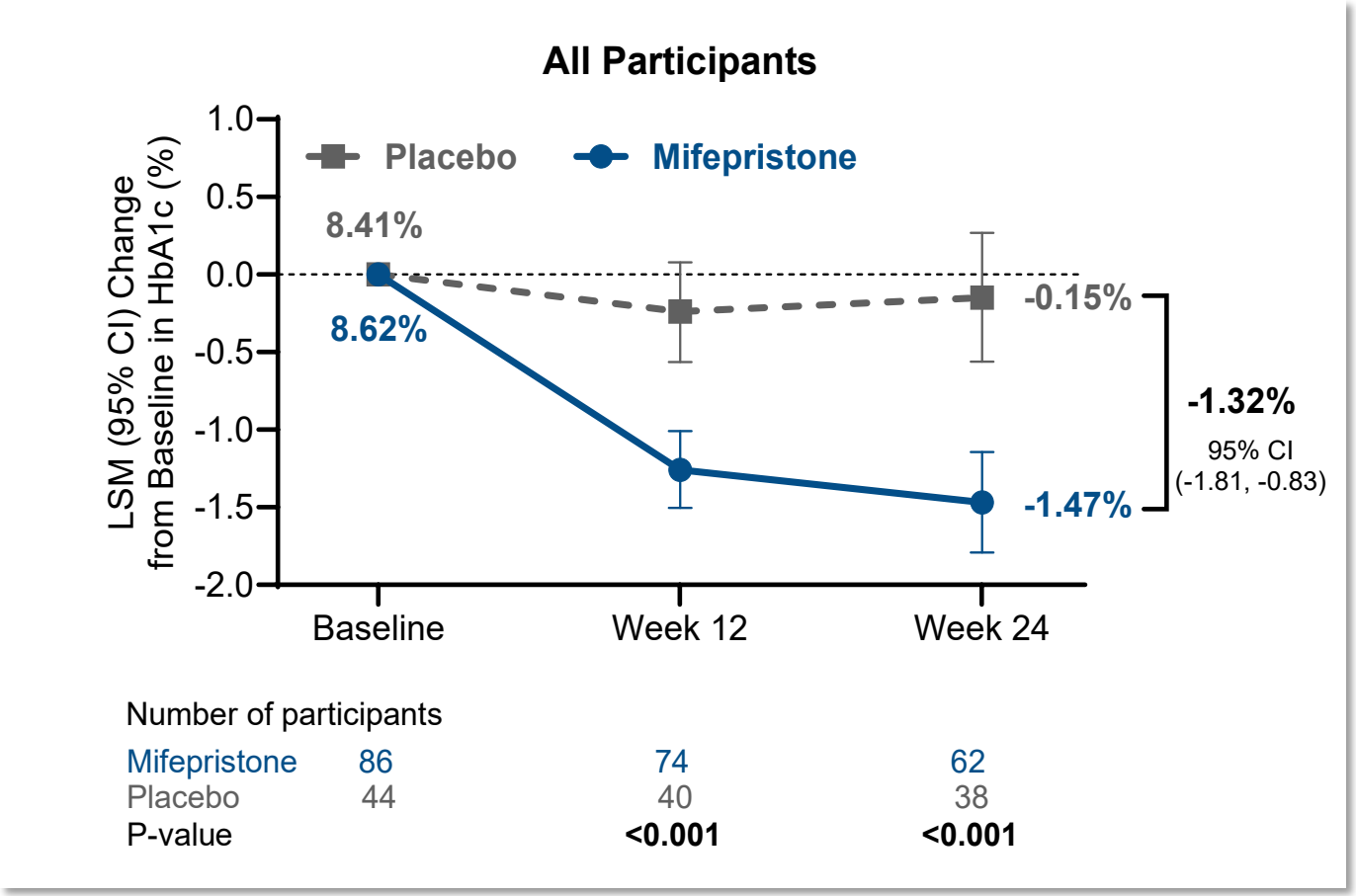


Factors independently associated with hypercortisolism

- Older age
- BMI <30 kg/m^2
- Non-Hispanic/Latino ethnicity
- Taking SGLT2 inhibitors, maximum-dose GLP-1 analogs, or tirzepatide
- Taking more BP drugs
- Taking fibrates or analgesics

[a]With dexamethasone ≥140 ng/dL. [b]In patients with hypercortisolism. BP, blood pressure; CT, computed tomography; DM drug, glucose-lowering drug; DST, dexamethasone suppression test; GLP-1, glucagon-like peptide 1.

Primary Endpoint: Significant Reduction in HbA1c Despite Medication Reduction/Discontinuation



Discontinuations/Dose Reductions in Glucose-Lowering Medications by Week 12

No. (%)	Mifepristone	Placebo
Long-acting insulin	32 (49.2)	3 (13.0)
Fast-acting insulin	10 (30.3)	2 (10.5)
Sulfonylureas	4 (22.2)	2 (10.5)
GLP-1 RAs	4 (12.1)	0
Tirzepatide	2 (10.5)	0
Metformin	1 (1.5)	0
SGLT2 inhibitors	0	1 (3.7)
Total, No.	**53**	**8**

What Do We Do With This Information today?

- **In addition to screening for PAD consider using GLP-1RA as means of treatment** for glucose lowering, CV risk reduction and PAD symptoms
- **Consider oral GLP-1 RA (semaglutide) in a similar way to sc GLP-1RAs** in the right patient setting
- **Share the new advances in medications with patients considering bariatric surgery** especially if they are hesitant to have surgery and not planning it soon
- **Maintain a high index of suspicion** for possible hypercortisolism in patients requiring multiple antihypertensive and glucose lowering medications without clear control, consider testing or refer to endocrinology to test for hypercortisolism

Questions?

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