Cardiac- renal-metabolic update

- **Kim Connelly MBBS, PhD**
- *Executive Director Keenan Research Centre for Biomedical Science*
- *Division head – Department of Cardiology St Michael's Hospital*
- *Keenan chair in research Leadership*
- *Brazilian Ball chair*
- *Toronto, Canada*

Faculty/Presenter Disclosure

- **Faculty: Kim Connelly**
- **Relationships with financial sponsors:**
  - **Any direct financial relationships including receipt of honoraria:** Merck, Astra Zeneca, Boehringer Ingelheim, Janssen, Servier, Eli Lilly and Novo Nordisk
  - **Memberships on advisory boards or speakers' bureau:** Merck, Astra Zeneca, Boehringer Ingelheim, Janssen, Servier, Eli Lilly and Novo Nordisk
  - **Patents for drugs or devices**: Boehringer Ingelheim - linaglitpin
  - **Other: financial relationships/investments**

Learning objectives

- To review latest evidence in Cardiac, Kidney and Metabolism trials (and obesity – CKOM)!

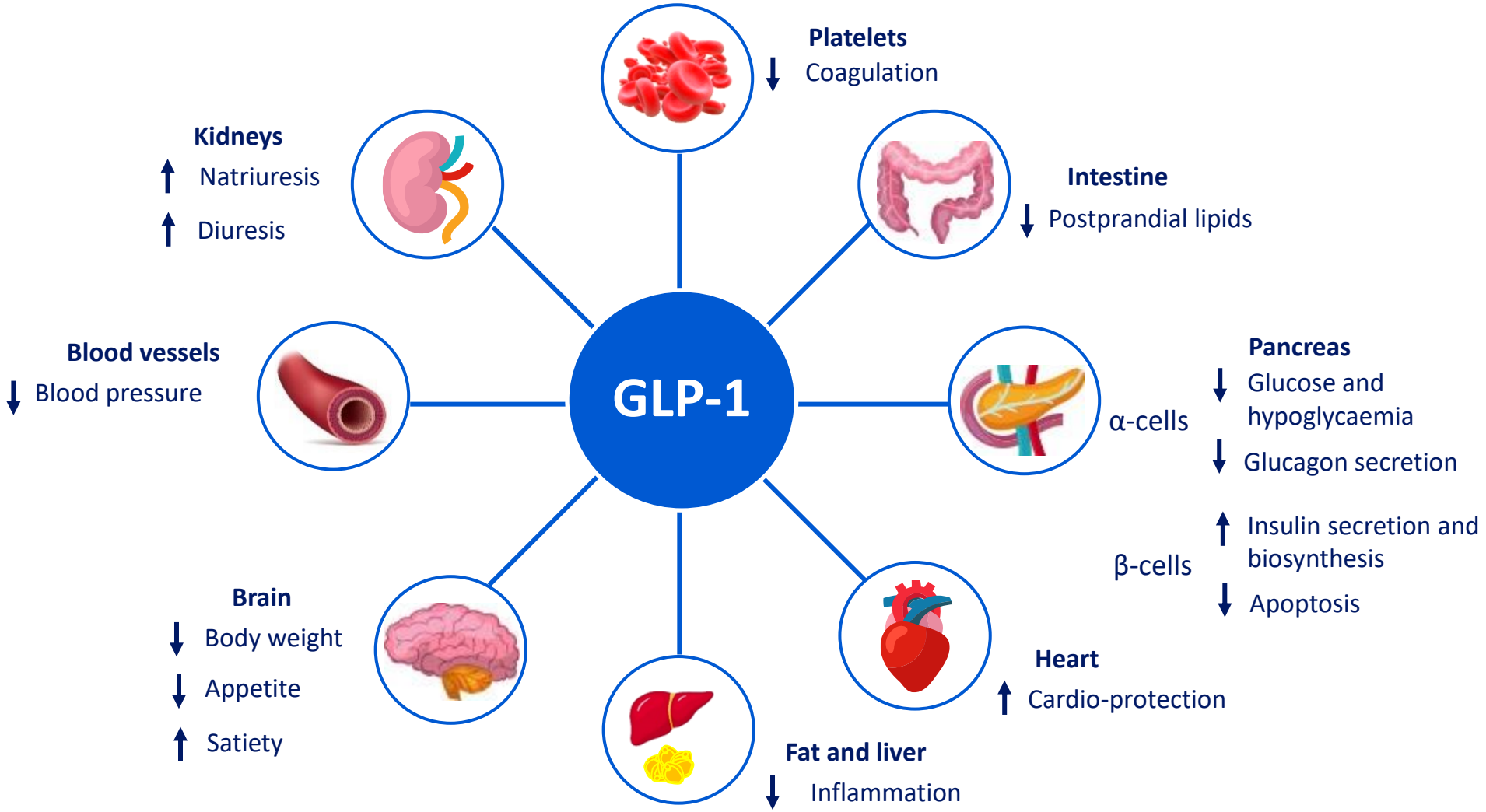
Let's start with a case!

Mrs. A.C.

- 66-year-old female with chronic stable hypertension and prior PCI of the mid-LAD for NSTEMI 2 years ago. She is referred because of atypical exertional symptoms of dyspnoea on exertion.
- Medications: ASA 81mg, ramipril 10 mg, rosuvastatin 20 mg, ezetimibe 10 mg, PCSK9i injected every 2 weeks. Dapa 10mg daily, metformin 500mg BID
- Physical examination: BMI 35, BP 136/84, JVP is difficult to assess but appears mildly elevated, normal S1 and S2, there is no edema.

	Age 66
EKG	NSR 65/min, QS V1, V2
A1C	6.7
TC	3.4
HDL-C	1
LDL-C	1.25
TG	1.24
apoB	0.55
eGFR/ UACR	47 32

Role of GLP-1[1–3] in metabolism, inflammation and CV protection

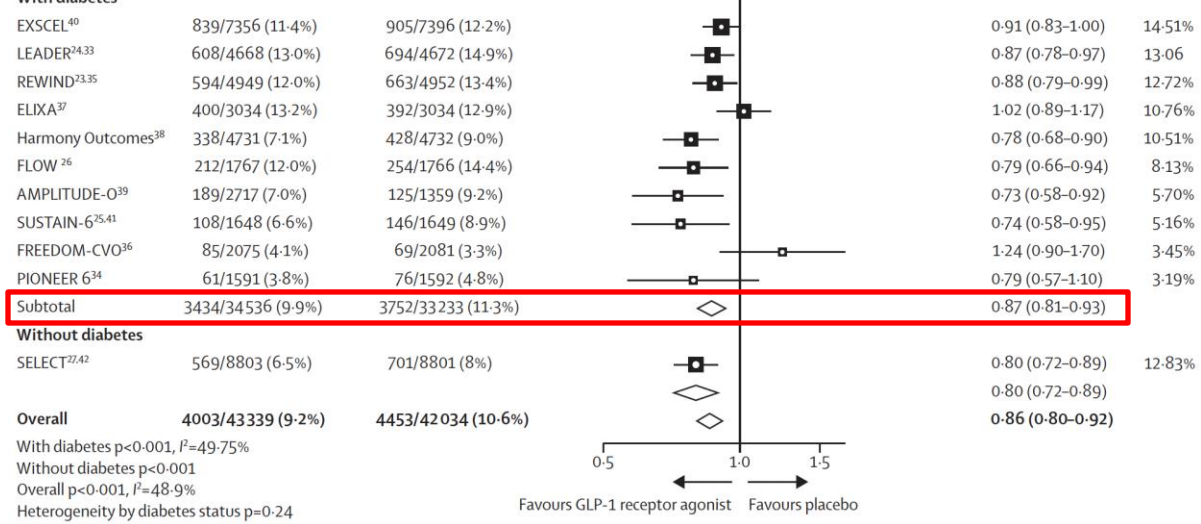


GLP-1, glucagon-like peptide

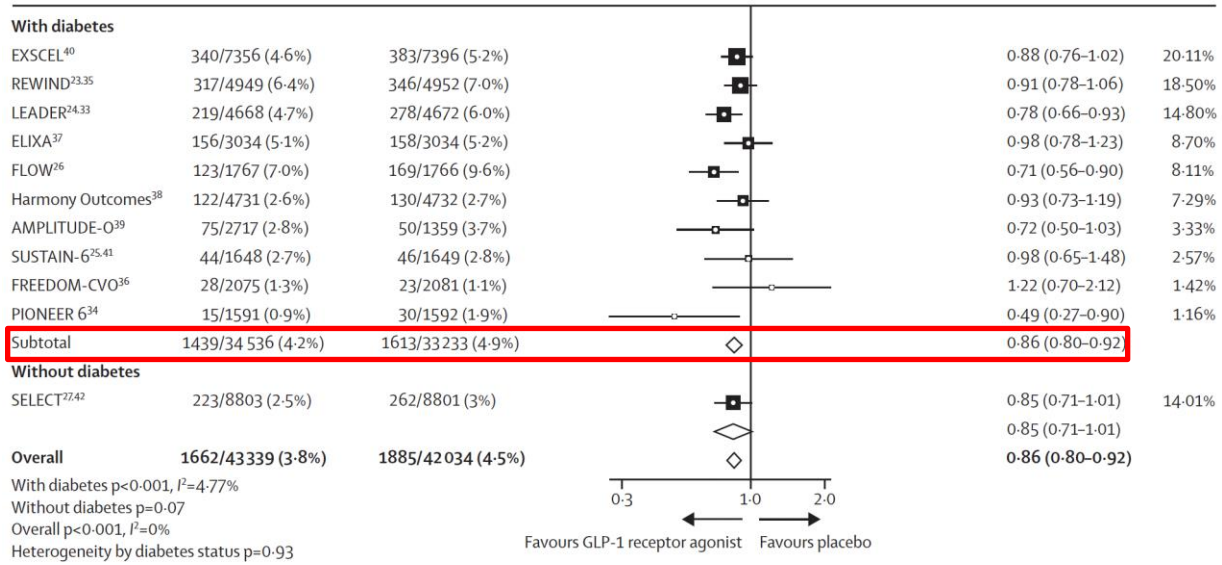
1. Wang XC et al. World J Gastroenterol 2014;20:14821–14830; 2. Lee J et al. Diabetes Metab J 2012;36:262–267; 3. Sharma S et al. PLoS One 2011;6:e25269

GLP-1 RA meta-analysis

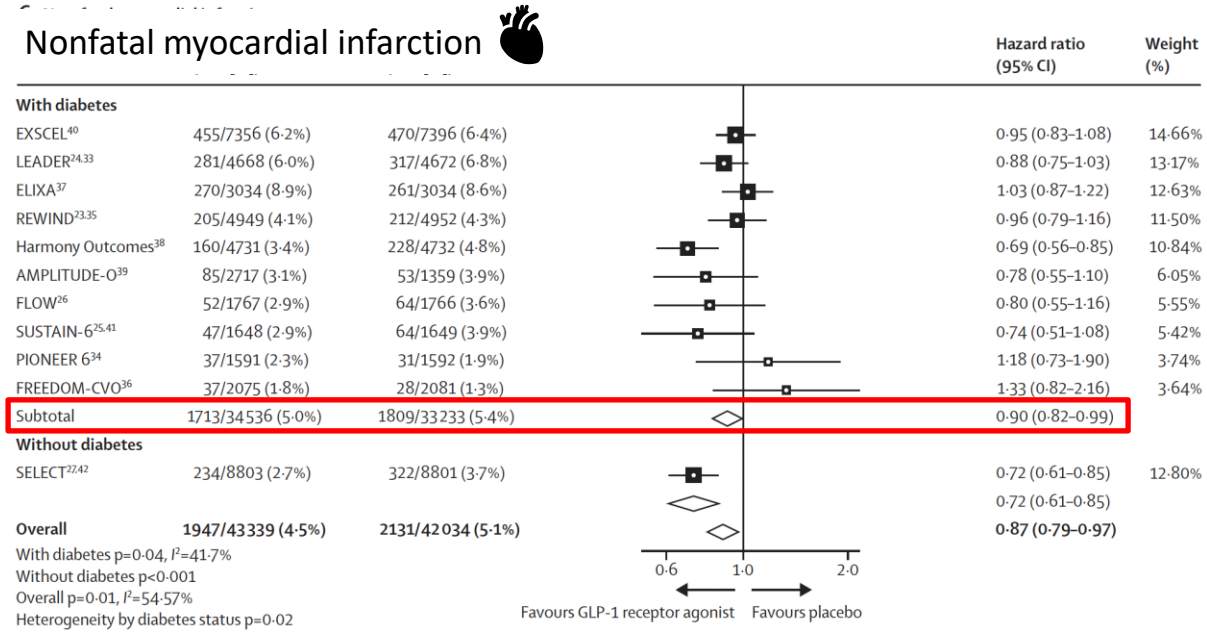
Major adverse CV events



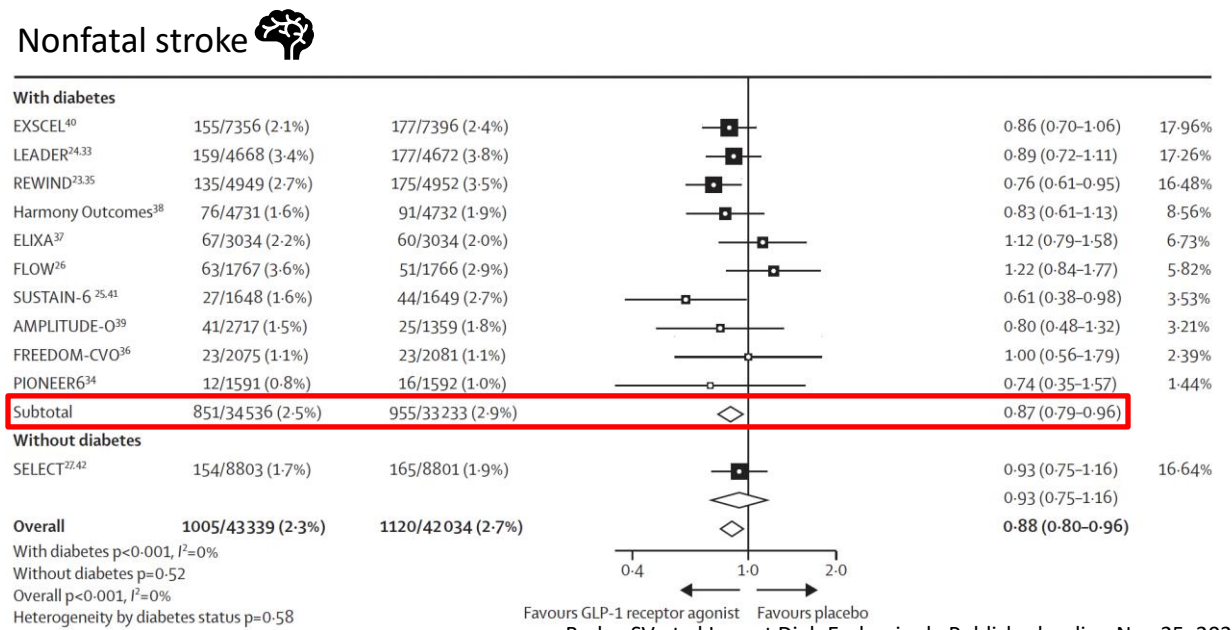
Cardiovascular death



Nonfatal myocardial infarction



Nonfatal stroke



Badve SV et al Lancet Diab Endocrinol. Published online Nov 25, 2024

GLP-1 Receptor Agonists in Cardiovascular Disease & Diabetes

Guideline Alignment: ESC/EASD • Diabetes Canada • Canadian Cardiovascular Society

ESC / EASD (2023)

Class I recommendation for GLP-1RA in T2DM with ASCVD
Agents with CV benefit: semaglutide, liraglutide, dulaglutide
Independent of HbA1c or metformin use
Primary goal: reduction in MACE

Diabetes Canada

GLP-1RA or SGLT2i recommended in T2DM with ASCVD
GLP-1RA preferred when ASCVD or obesity predominate
Agents: semaglutide, liraglutide, dulaglutide
May start regardless of A1c when CV benefit desired

Canadian Cardiovascular Society

GLP-1RA recommended in T2DM with ASCVD
Reduces major adverse CV events
SGLT2i preferred if HF or CKD predominates
Part of comprehensive cardiometabolic care

Key Message: *Major international and Canadian guidelines align—GLP-1 receptor agonists with proven CV benefit should be used early in T2DM with ASCVD to reduce cardiovascular events.*

FLOW trial design

A multinational, randomized controlled clinical trial

Key eligibility criteria

- Adults with T2D, HbA_{1c} ≤10%
- RAS inhibitor
- eGFR ≥50 and ≤75 mL/min/1.73 m^2 and UACR >300 and <5000 mg/g
  OR
  eGFR ≥25 and <50 mL/min/1.73 m^2 and UACR >100 and <5000 mg/g

R
1:1

N=3533

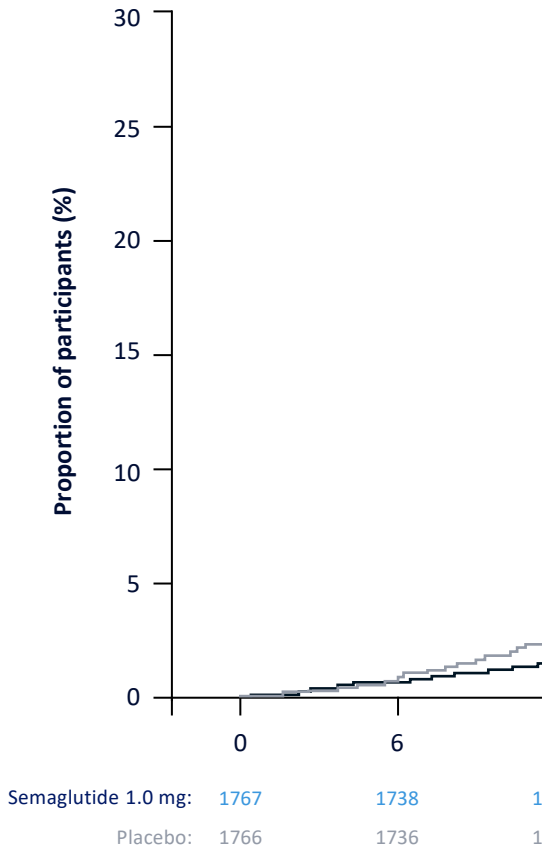
Once-weekly s.c. **semaglutide** 1 mg
+ standard of care

Placebo
+ standard of care

Early trial cessation was recommended at a pre-specified **interim** analysis for efficacy at **~570 events**

eGFR was calculated using the CKD-EPI formula. Randomization was stratified according to SGLT2 inhibitor use at baseline.
CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; HbA_{1c}, glycated hemoglobin; R, randomization; RAS, renin–angiotensin–aldosterone system; s.c., subcutaneous; SGLT2, sodium–glucose co-transporter 2; T2D, type 2 diabetes; UACR, urine albumin:creatinine ratio.
Perkovic V et al. *N Engl J Med* 2024;391:109–121.

Primary kidney o



press release

Health Canada approves Ozempic® to reduce the risk of sustained eGFR decline, end-stage kidney disease, and cardiovascular death in adults with type 2 diabetes and chronic kidney disease

- *Ozempic® is the first-and-only medication indicated for both the once-weekly treatment of adult patients with type 2 diabetes mellitus to improve glycemic control and to reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end-stage kidney disease, and cardiovascular death in adults with type 2 diabetes and chronic kidney disease.*[1]
- *Chronic kidney disease in patients with type 2 diabetes is associated with an elevated risk of end-stage kidney disease, cardiovascular disease, and death.*[2]

MISSISSAUGA, ON, August 19, 2025 – Novo Nordisk announced today that Ozempic® (semaglutide injection) is now approved as the first-and-only medication indicated for both the once-weekly treatment of adult patients with type 2 diabetes mellitus to improve glycemic control and to reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end-stage kidney disease, and cardiovascular death in adults with type 2 diabetes (T2D) and chronic kidney disease (CKD).[1]

Novo Nordisk Canada Inc.
Corporate Communications
101-2476 Argentia Road
Mississauga, Ontario L5N 6M1
Tel: 905-629-4222
www.novonordisk.ca

FLOW
semaglutide | kidney outcomes trial

acebo 23.2%
l0/1766)

emaglutide 18.7%
31/1767)

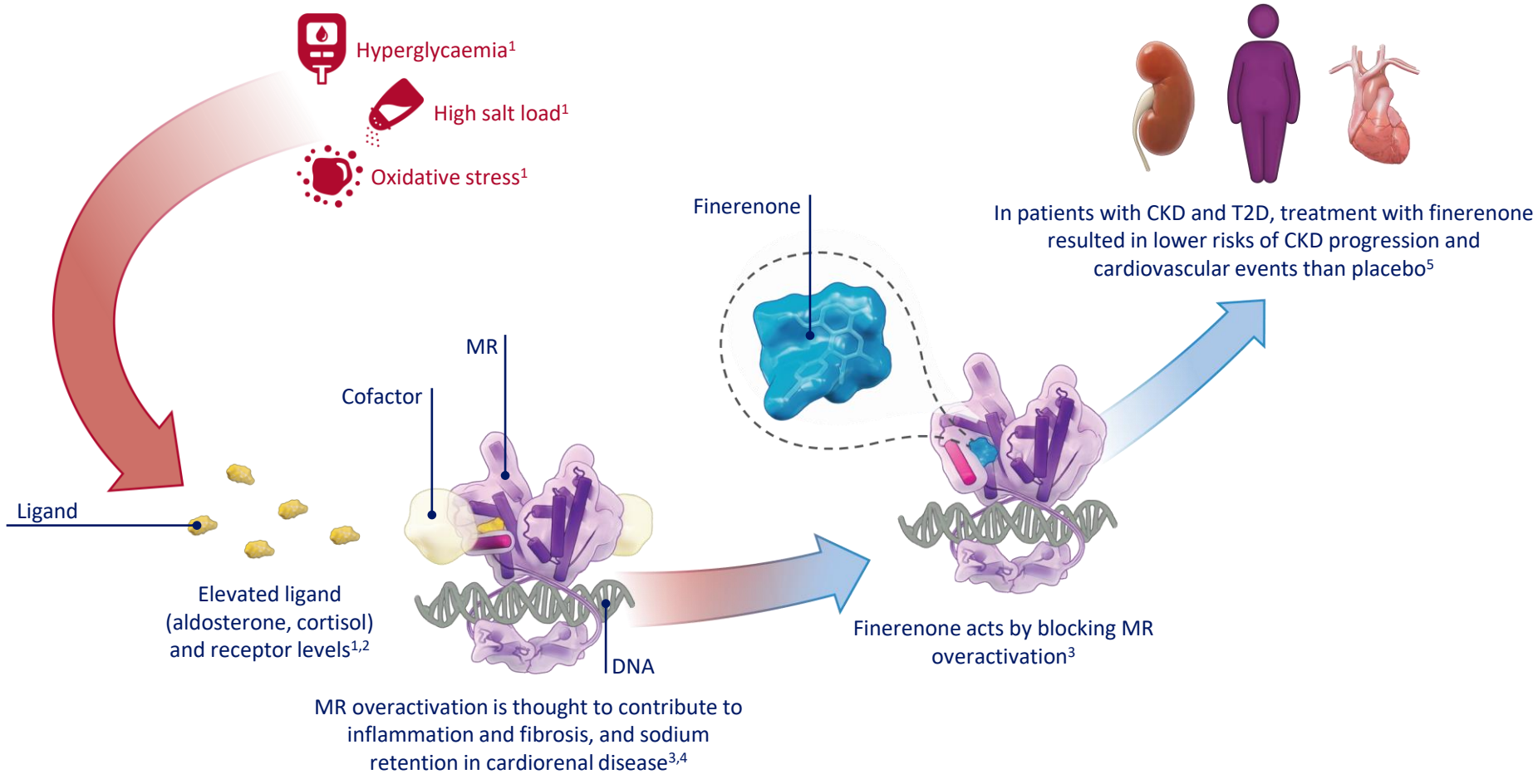
R 0.76 (95% CI 0.66, 0.88)
=0.0003

Superiority if
two-sided p value is <0.0322

Full analysis set. Data from the in-trial period. Numbers shown in the l
confidence interval; HR, hazard ratio.
Perkovic V et al. *N Engl J Med* 2024;391:109–121.

nts receiving semaglutide and placebo, respectively. CI,

Finerenone, a novel, selective, nonsteroidal MRA, blocks MR overactivation



Finerenone is approved by the FDA and is indicated to reduce the risk of sustained eGFR decline, ESKD, CV death, non-fatal MI, and HHF in adult patients with CKD associated with T2D. Finerenone is currently under review by other health authorities, including the EMA

1. Buonafine M, *et al. Am J Hypertens* 2018;31:1165–1174; 2. Buglioni A, *et al. Hypertension* 2015;65:45–53; 3. Agarwal R, *et al. Nephrol Dial Transplant* 2020; doi: 10.1093/ndt/gfaa294; 4. Khan NUA & Movahed A. *Rev Cardiovasc Med* 2004;5:71–81; 5. Bakris GL, *et al. N Engl J Med* 2020;383:2219–2229

Finerenone phase III program[1–4] including patients with CKD and T2D across the spectrum of CKD severity

Patients

T2D and CKD, pretreated with either an ACEi or ARB at maximum tolerated dose and serum [K^+] ≤4.8 mmol/l

FIDELIO-DKD (N=5734)

CKD eligibility criteria

- UACR 30–<300 mg/g and eGFR ≥25–<60 ml/min/1.73 m^2 and a history of diabetic retinopathy
- **Or** UACR ≥300–≤5000 mg/g and eGFR ≥25–<75 ml/min/1.73 m^2

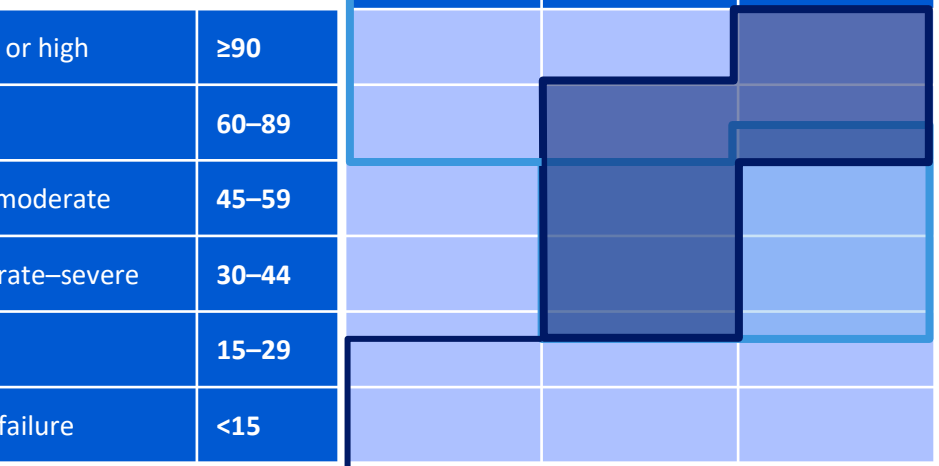
FIGARO-DKD (N=7437)

CKD eligibility criteria

- UACR 30–<300 mg/g and eGFR 25–≤90 ml/min/1.73 m^2
- **Or** UACR ≥300–≤5000 mg/g and eGFR ≥60 ml/min/1.73 m^2

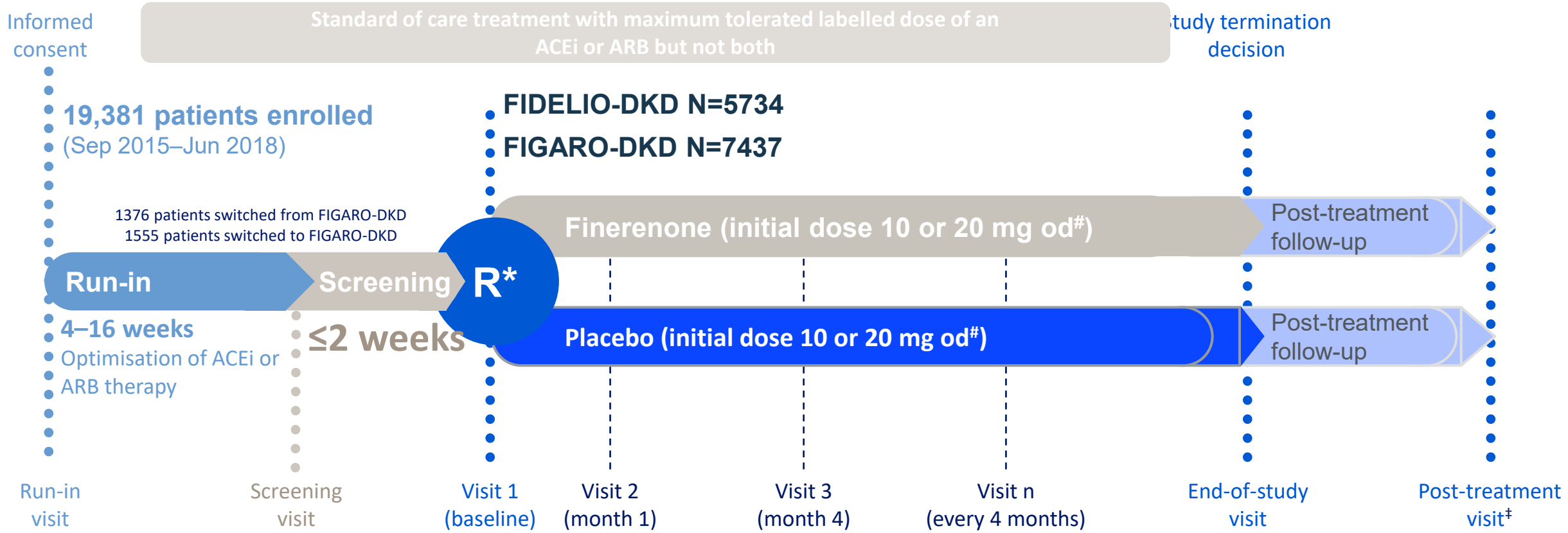
GFR stages description and range[5] (ml/min/1.73 m^2)		
	G1 Normal or high	≥90
	G2 Mild	60–89
	G3a Mild–moderate	45–59
	G3b Moderate–severe	30–44
	G4 Severe	15–29
	G5 Kidney failure	<15

Albuminuria categories Description and range[5] (UACR, mg/g)		
A1 Normal–mildly increased	**A2** Moderately increased	**A3** Severely increased
<30	**30–300**	**>300**



1. Bakris GL, *et al. Am J Nephrol* 2019;50:333–344; 2. Bayer. https://clinicaltrials.gov/ct2/show/NCT02540993 [accessed 9 Jun 2021]; 3. Ruilope LM, *et al. Am J Nephrol* 2019;50:345–356; 4. Bayer. https://clinicaltrials.gov/ct2/show/NCT02545049 [accessed 9 Jun 2021]; 5. KDIGO. *Kidney Int Suppl* 2013;3:1–150

FIDELIO-DKD[1] and FIGARO-DKD[2] phase III clinical trial design



*Randomisation was stratified by region (North America, Latin America, Europe, Asia or Other), eGFR category at screening visit (25–<45, 45–<60 or ≥60 ml/min/1.73 m²) and albuminuria category at screening visit (moderately increased or severely increased); #up-titration of study drug was encouraged after visit 2 provided serum [K⁺] value was ≤4.8 mmol/l and eGFR was stable; down-titration was allowed any time after treatment initiation for safety reasons; ‡4 weeks and 5 days after last dose of study drug

1. Bakris GL, *et al*. *Am J Nephrol* 2019;50:333–344; 2. Ruilope LM, *et al*. *Am J Nephrol* 2019;50:345–356

Summary: FIDELIO-DKD and FIGARO-DKD results

D [2,3]
ular

Patients

1–2 CKD

1 Primary endpoint

mortality and
bidity by **13%**
; 95% CI 0.76–0.98)

2 Secondary endpoint

rogression
y **13%**
ically significant)
5% CI 0.76–1.01)

Safety

dies

Finerenone (brand name Kerendia) is listed under Limited Use (LU) code

700 in Ontario for treating chronic kidney disease (CKD) associated with type 2 diabetes (T2D). It is approved for adults with an eGFR ≥ 25 mL/min/1.73 m^2 and albuminuria

≥ 30 mg/g, used alongside maximized ACE inhibitor/ARB and SGLT2 inhibitor therapy.

ontario.ca

Key Details for Code 700:

- **Indication:** Reduction of risk for end-stage kidney disease, sustained eGFR decrease, cardiovascular death, nonfatal myocardial infarction, and hospitalization for heart failure.
- **Criteria:** Patients must be 18+ with T2D and CKD, and it must be used as an adjunct to standard-of-care (specifically, maximized doses of ACE inhibitors/ARBs and SGLT2 inhibitors, unless contraindicated).

Adding to the evidence from the FIDELIO-DKD trial, FIGARO-DKD results indicate that finerenone is an effective investigational treatment option for CV and kidney protection in patients with CKD stage 1–4 and T2D

1. Bakris GL, *et al. N Engl J Med* 2020;383:2219–2229; 2.Ruilope LM, *et al. Am J Nephrol* 2019;50:345–356; 3. [FIGARO primary-placeholder]

Can J Diabetes 49 (2025) 73–86

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journal homepage: www.canadianjournalofdiabetes.com

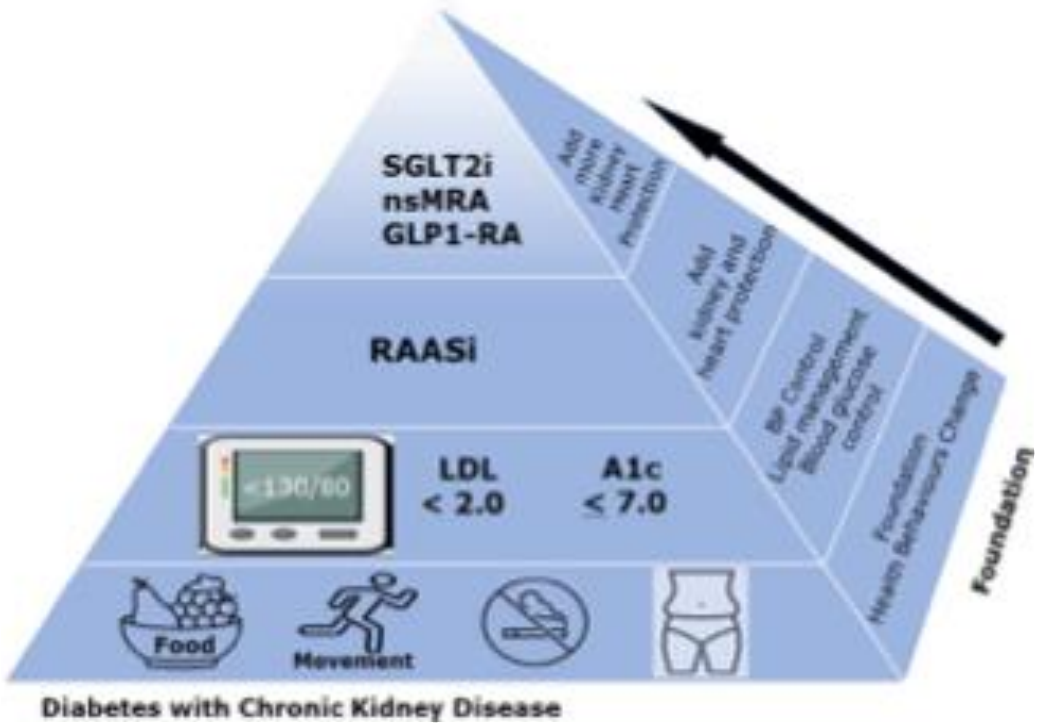
Special Article

Chronic Kidney Disease in Diabetes: A Clinical Practice Guideline

Sheldon W. Tobe MD, MScCH, FRCPC, FACP, FAHA; Harpreet S. Bajaj MD, MPH; Navdeep Tangri MD, PhD, FRCPC; Rahul Jain MD, CCFP, MScCH, FCFP; Thuy Pham NP, MN, MScCH; Valerie Beaudin RN; Phil McFarlane MD, PhD, FRCPC

On behalf of the Diabetes Canada Clinical Practice Guideline Steering Committee

8. Adults with type 2 diabetes and CKD defined by eGFR between 20 and 45 mL/min per 1.73 m^2 regardless of uACR, or eGFR between 45 and 90 mL/min per 1.73 m^2 with uACR >20 mg/mmol, on maximally tolerated, or maximally prescribed doses of RAASis, should be recommended an SGLT2i to delay progression of CKD and progression to dialysis, and to reduce likelihood of cardiovascular events [57,58,75,76] [Grade A, Level 1A].
9. Adults with type 2 diabetic nephropathy defined by eGFR between 25 and 50 mL/min per 1.73 m^2 with uACR between 10 and 500 mg/mmol, or if eGFR is >50 mL/min per 1.73 m^2 with uACR between 30 and 500 mg/mmol, on maximally tolerated, or maximally prescribed doses of RAASi, should be recommended a GLP1-RA with proven kidney benefit to reduce proteinuria and risk of worsening kidney function [72] [Grade A, Level 1A for subcutaneous semaglutide].
10. Adults with type 2 diabetic nephropathy defined by eGFR between 25 and 90 mL/min per 1.73 m^2 with uACR between 3 and 30 mg/mmol with or without diabetic retinopathy, for those with eGFR between 25 and 60 mL/min per 1.73 m^2, or if eGFR is >25 mL/min per 1.73 m^2 with uACR between 30 and 500 mg/mmol, on maximally tolerated, or maximally prescribed doses of RAASi, with serum potassium ≤4.8 mmol/L, should be recommended a nsMRA with proven efficacy alongside potassium monitoring to improve kidney and cardiovascular outcomes [64,66,70,71] [Grade A, Level 1A for finerenone].



GLP1 RA and Peripheral vascular disease: The STRIDE trial

Semaglutide and walking capacity in people with symptomatic peripheral artery disease and type 2 diabetes: A phase 3b, double-blind, randomized, placebo-controlled trial

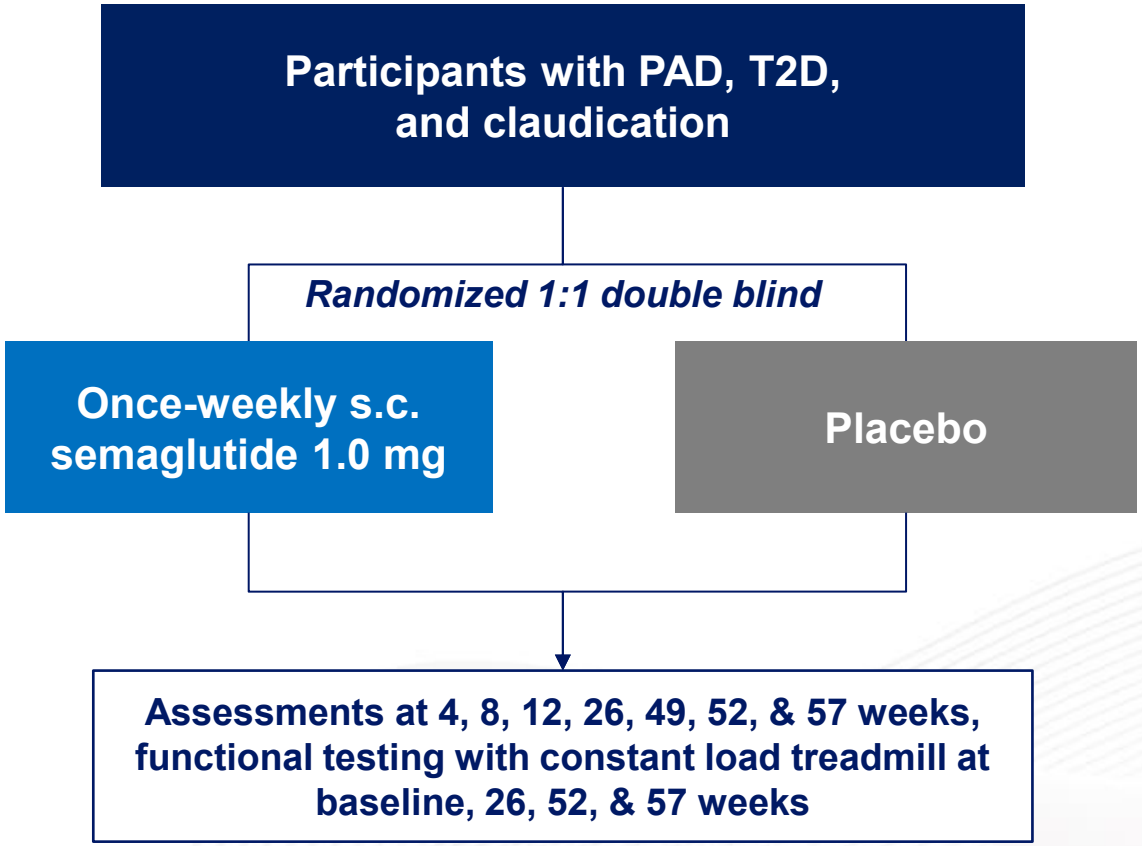
Marc P. Bonaca, Andrei-Mircea Catarig, Kim Houlind, Bernhard Ludvik, Joakim Nordanstig, Chethana Kalmady Ramesh, Neda Rasouli, Harald Sourij, Alex Videmark, and Subodh Verma, for the STRIDE Trial Investigators

American College of Cardiology Scientific Sessions 2025
Late-Breaking Clinical Trial
March 29, 2025

CPC Clinical Research
An Affiliate of:
University of Colorado Anschutz Medical Campus

Objectives and Trial Design

Objective: To demonstrate the effect of once weekly semaglutide 1.0 mg vs. placebo on functional capacity in people with T2D and symptomatic PAD



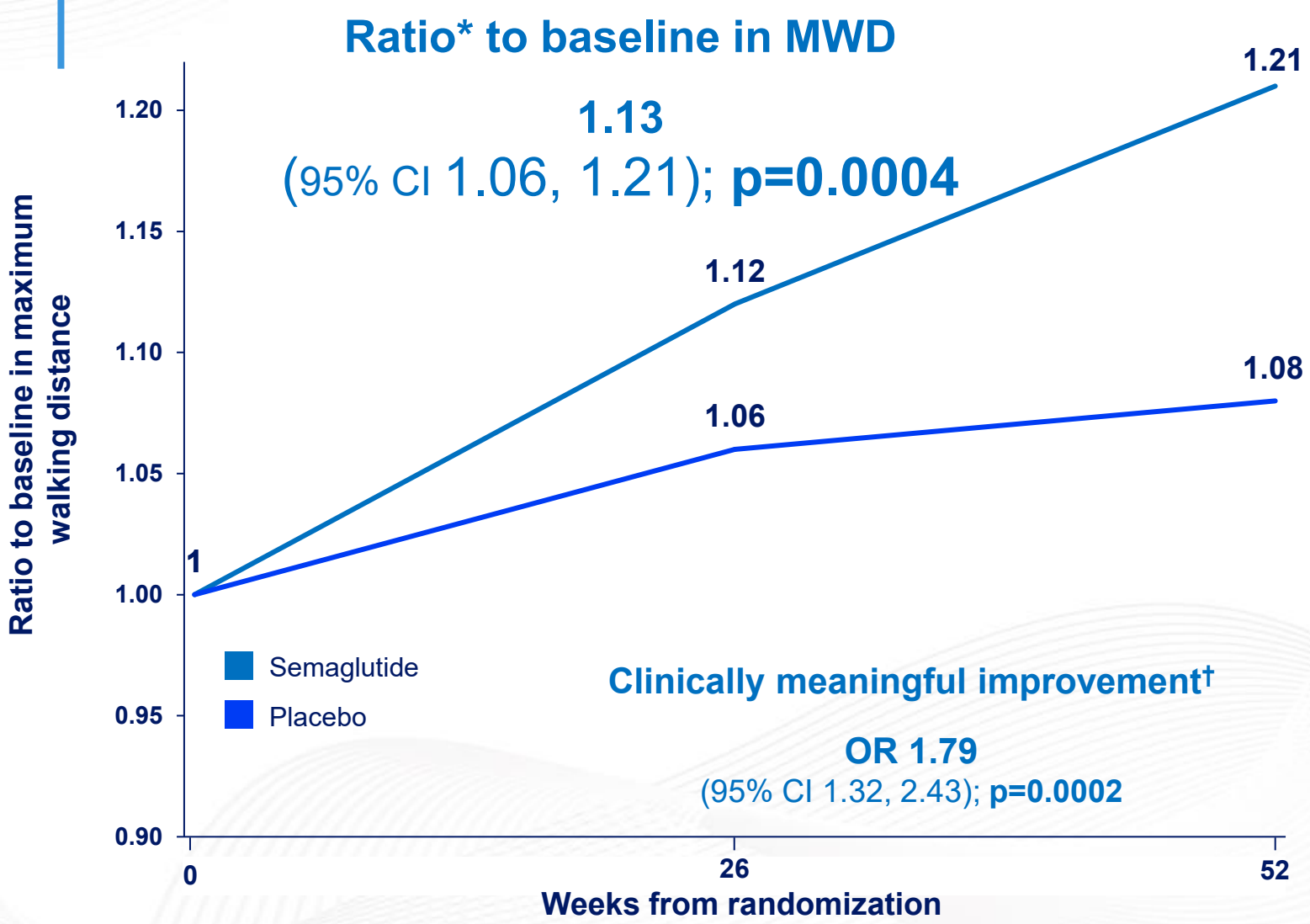
Inclusion criteria

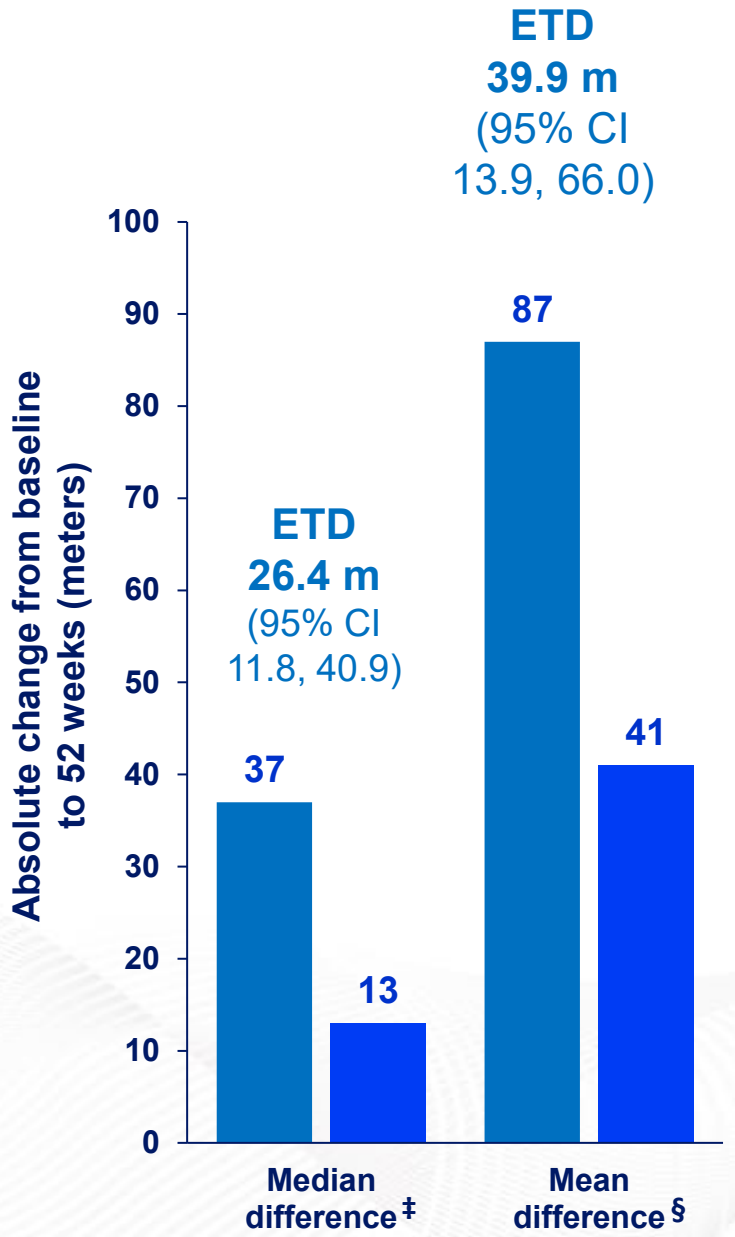
- Age ≥18 years old
- T2D diagnosis ≥180 days prior to screening
- HbA_{1c} ≤10%
- Early-stage symptomatic PAD (Fontaine stage IIa)
- PFWD ≥200 m (flat treadmill test)
- MWD ≤600 m (constant load treadmill test)
- ABI ≤0.9 or TBI ≤0.7

Exclusion criteria

- Conditions other than PAD that limit walking
- Vascular revascularization ≤180 days prior to screening or planned arterial revascularization
- Heart failure (NYHA Class III–IV)
- MI, stroke, hospitalization for unstable angina, or TIA within 180 days prior to screening

Primary Outcome





*Estimated treatment ratio; †Using a prespecified anchor measure to assess clinical meaningfulness of change with semaglutide versus placebo; ‡Treatment policy estimand; §Trial product (hypothetical) estimand. Absolute change from baseline to 52 weeks was an exploratory outcome, based on the in-trial observation period for the median difference estimate, and the on-treatment without rescue (revascularization or medication) observation period for the mean difference.
CI, confidence interval; ETD, estimated treatment difference; MWD, maximum walking distance; OR, odds ratio.

Oral Semaglutide Reduces Cardiovascular Events in People with Type 2 Diabetes with Atherosclerotic Cardiovascular and/or Chronic Kidney Disease: Primary Results From the SOUL Randomized Trial

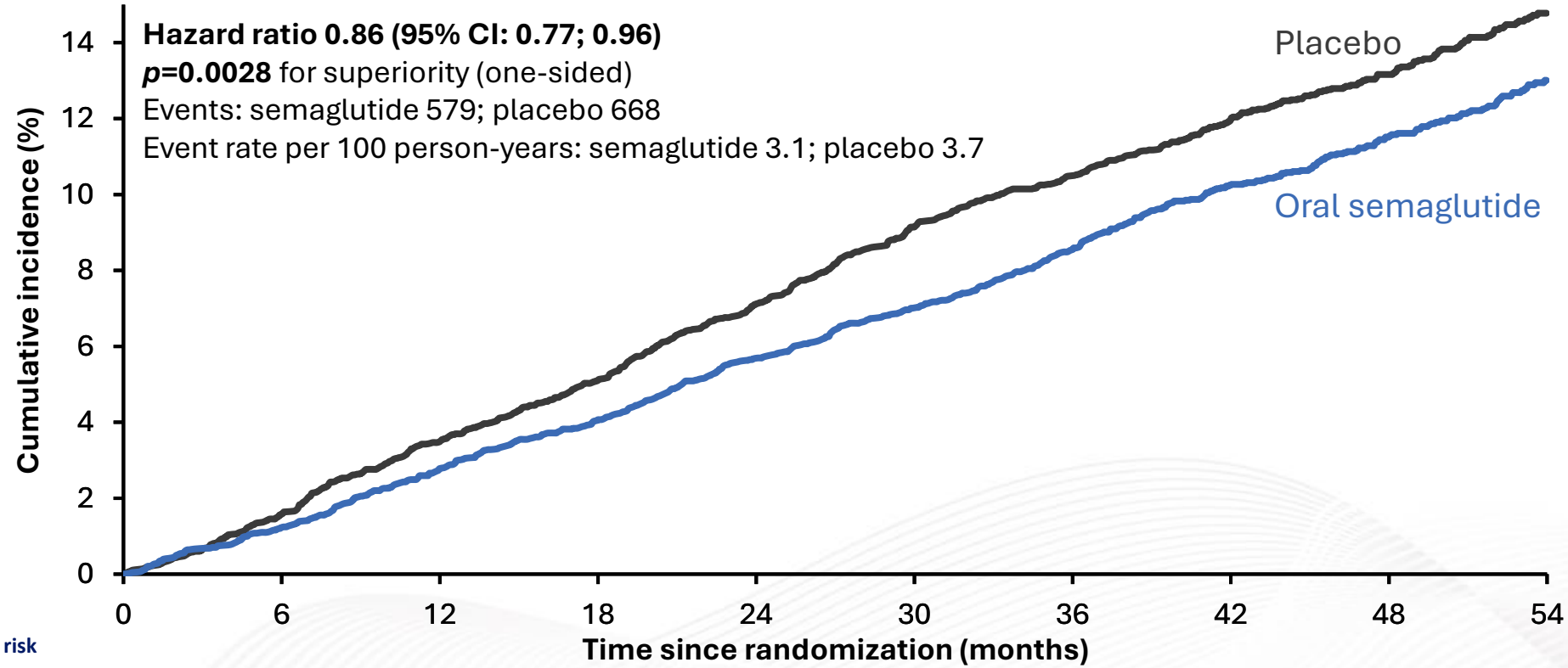
Darren K. McGuire, M.D., MHSc

on behalf of the SOUL study group

University of Texas Southwestern Medical Center, and
Parkland Health System, Dallas, Texas, USA

3-point MACE composite

Primary outcome



No. at risk										
Placebo	4825	4718	4583	4455	4322	4194	4101	3727	2517	1346
Semaglutide	4825	4743	4835	4542	4438	4346	4239	3831	2555	1346

Components:

- CV death
- Nonfatal MI
- Nonfatal stroke

- Results consistent across pre-specified sensitivity analyses
- Absolute risk reduction 2% over 3 years
- **NNT = 50**

Cumulative incidence estimates are based on time from randomization to first MACE with non-CV death modelled as competing risk using the Aalen-Johansen estimator. Time from randomization to first MACE was analysed using a Cox proportional hazards model with treatment as categorical fixed factor. Adjustment for group sequential design was done using likelihood ratio ordering.
CI, confidence interval; CV, cardiovascular; MACE, major adverse cardiovascular event; MI, myocardial infarction; NNT, number needed to treat.

Conclusions

- Oral semaglutide was superior to placebo in reducing the incidence of 3-point MACE in people with T2D a
- There was age, BMI, eGFR and concomit

- The overa ved in previous clinical trials witl
- The trial r his population

- Oral sem

press release

Health Canada approves RYBELSUS® (semaglutide tablets) to reduce the risk of major adverse cardiovascular events (MACE) in adults with type 2 diabetes

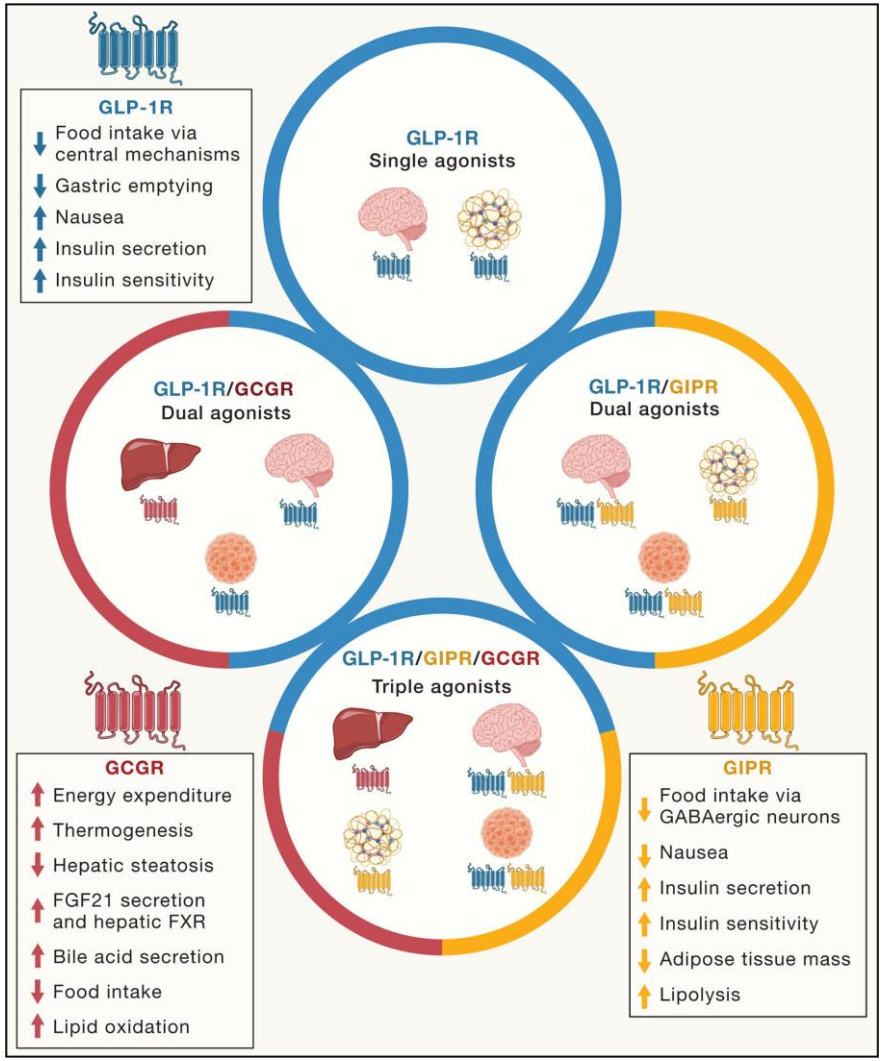
- *RYBELSUS® (semaglutide tablets) is the first glucagon-like peptide-1 (GLP-1) approved in Canada to reduce the risk of major adverse cardiovascular events (MACE).*[1]
- *RYBELSUS® (semaglutide tablets) is approved to reduce the risk of major adverse cardiovascular (CV) events (CV death, non-fatal myocardial infarction or non-fatal stroke) in adults with type 2 diabetes mellitus who have established cardiovascular disease or are at high risk for these events.*[1,2]
- *The indication expansion is based on positive outcomes observed in the cardiovascular outcomes (SOUL) trial data, which demonstrated that RYBELSUS® decreased the risk of major adverse cardiovascular events.*[1]
- *Cardiovascular disease is the second-leading cause of death in Canada.*[3]

ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide-1 receptor agonist; MACE, major adverse cardiovascular event; T2D, type 2 diabetes.

1. Aroda *et al. Diabetes Obes Metab* 2023;25:1385–97.

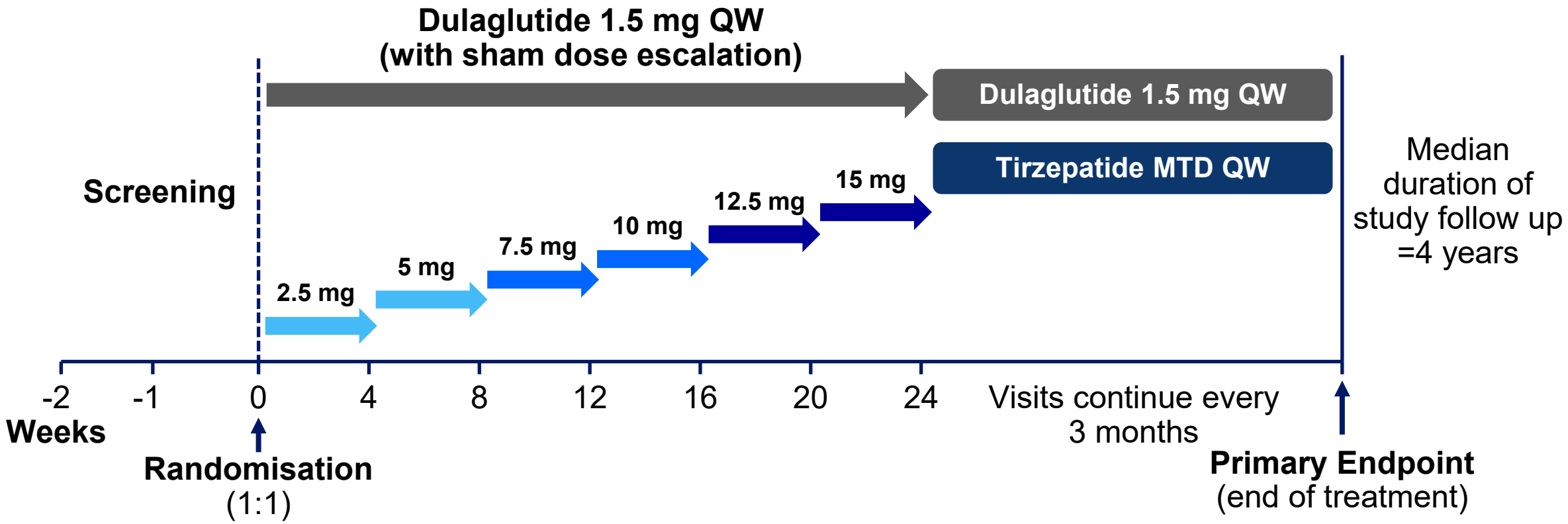
Major new “G” targets!

- **GIP Receptor Agonist (GIP-RA):**
  Agents that activate the GIP receptor to boost insulin release and improve metabolic control; often combined with GLP-1 action for additive effects.



The Cardiovascular Outcomes in Participants on Tirzepatide Versus Dulaglutide of the SURPASS-CVOT

Study Design



- Study drug added to standard of care for underlying ASCVD
- Glucose-control regimen adjusted during the trial, using open-label non-incretin agents
- Adjustment of study medication dose permitted

SURPASS-CVOT scientific disclosure, oral presentation at EASD Congress Vienna, Austria, on 18th September 2025

Baseline Characteristics

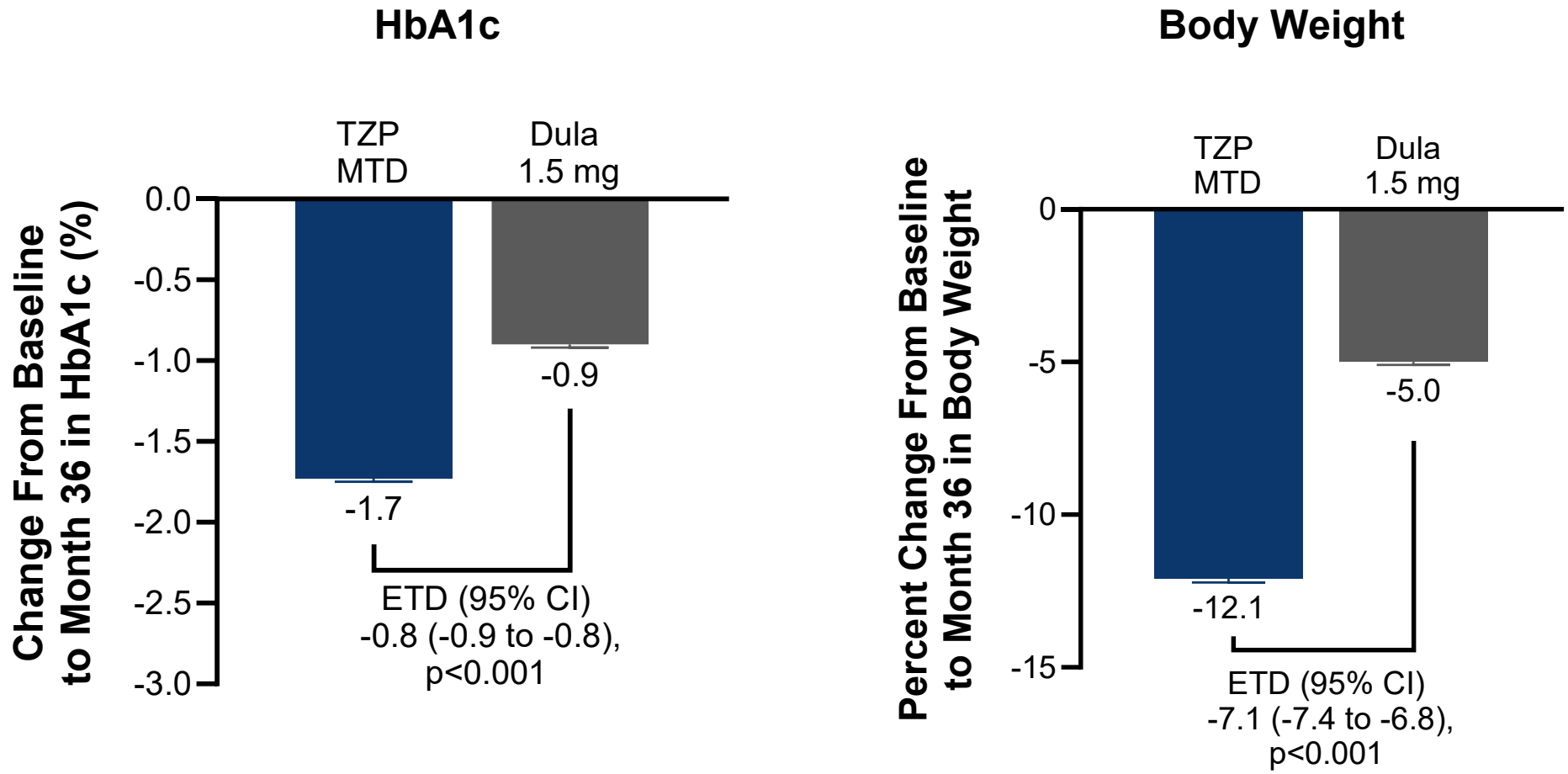
Parameter	TZP MTD (N=6586)	Dula 1.5 mg (N=6579)
Age, mean, years	64.0	64.1
Female, %	28.7	29.3
Race, %		
White	81.5	81.4
Asian	8.8	9.1
Native Hawaiian or Other Pacific Islander	0.1	0.1
Ethnicity, %		
Hispanic or Latino	30.2	30.1

Parameter, %	TZP MTD (N=6586)	Dula 1.5 mg (N=6579)
Statin	86.0	85.6
Antihypertensive medications		
ACE inhibitor	40.3	39.4
ARB	40.0	40.9
Mineralocorticoid receptor antagonist	9.7	9.3
Antihyperglycaemic medications		
Metformin	81.1	81.7
SGLT-2 inhibitor	30.4	30.8
Sulfonylurea	21.3	22.0
DPP-4 inhibitor	5.8	5.7
Thiazolidinedione	2.4	2.7
Alpha-glucosidase inhibitor	1.7	1.6
Insulin	49.4	48.3

Note: Data are from the mITT population.

SURPASS-CVOT scientific disclosure, oral presentation at EASD Congress Vienna, Austria, on 18th September 2025

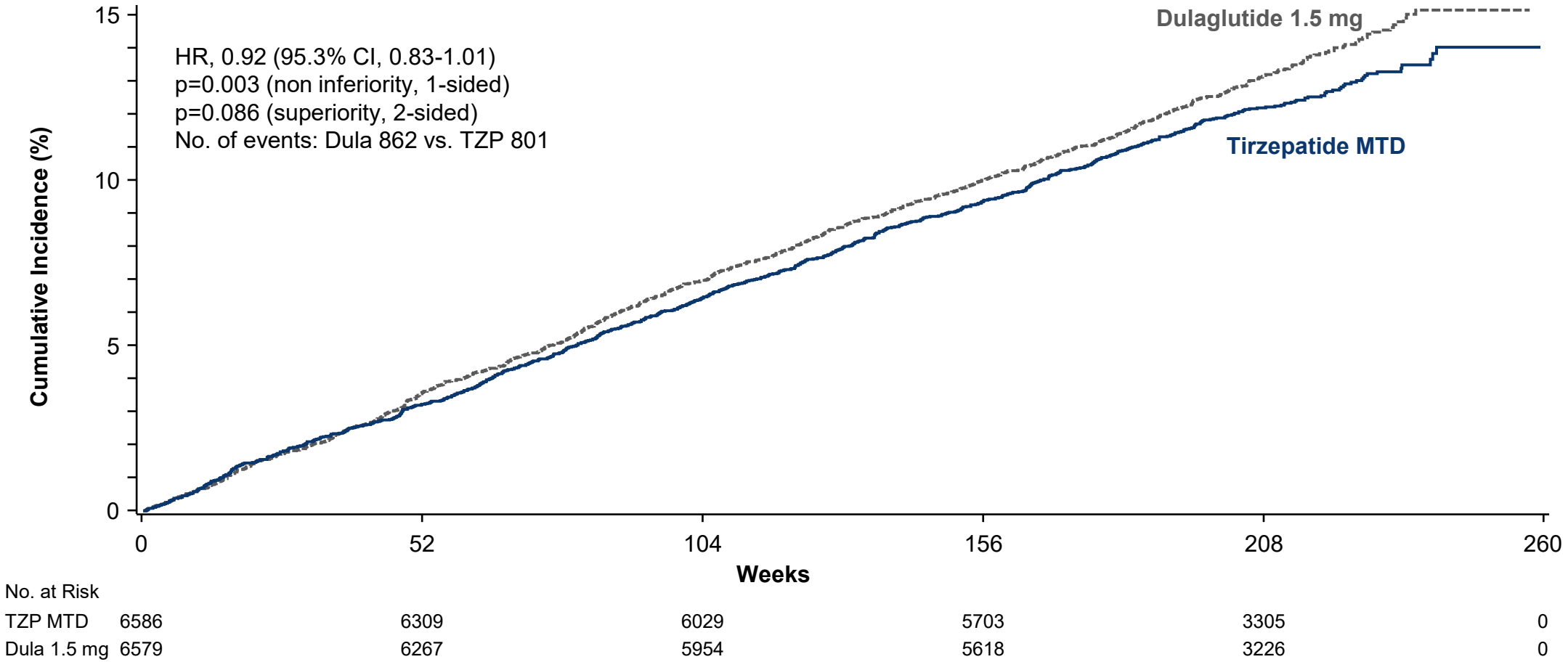
Change From Baseline in HbA1c and Weight



Notes: Data are mean estimates (SE). Change from baseline to Month 36 were analysed using an ANCOVA model with treatment, SGLT-2 inhibitor use at baseline and country as fixed factors and baseline value as a covariate, with multiple imputation of missing values.

SURPASS-CVOT scientific disclosure, oral presentation at EASD Congress Vienna, Austria, on 18th September 2025

Primary Endpoint: CV Death, MI or Stroke



Note: HR and 95.3% CI were derived from a Cox proportional hazards model with treatment as a fixed effect, stratified by SGLT-2 inhibitor use at baseline.

Key Secondary Efficacy Endpoints

Outcome	TZP MTD (N=6586)	Dula 1.5 mg (N=6579)	HR (95% CI)
Key Secondary Efficacy Endpoints, % of Participants With Event			
MI	4.7	5.4	0.86 (0.74-1.00)
Stroke	3.5	3.8	0.91 (0.76-1.09)
CV death	5.6	6.2	0.89 (0.77-1.02)
CV death, MI, stroke, coronary revascularisation	16.5	18.5	0.88 (0.81-0.96)
CV death or hospitalisation or urgent visits for HF	7.8	8.5	0.91 (0.81-1.03)
All-cause death	8.6	10.2	0.84 (0.75-0.94)

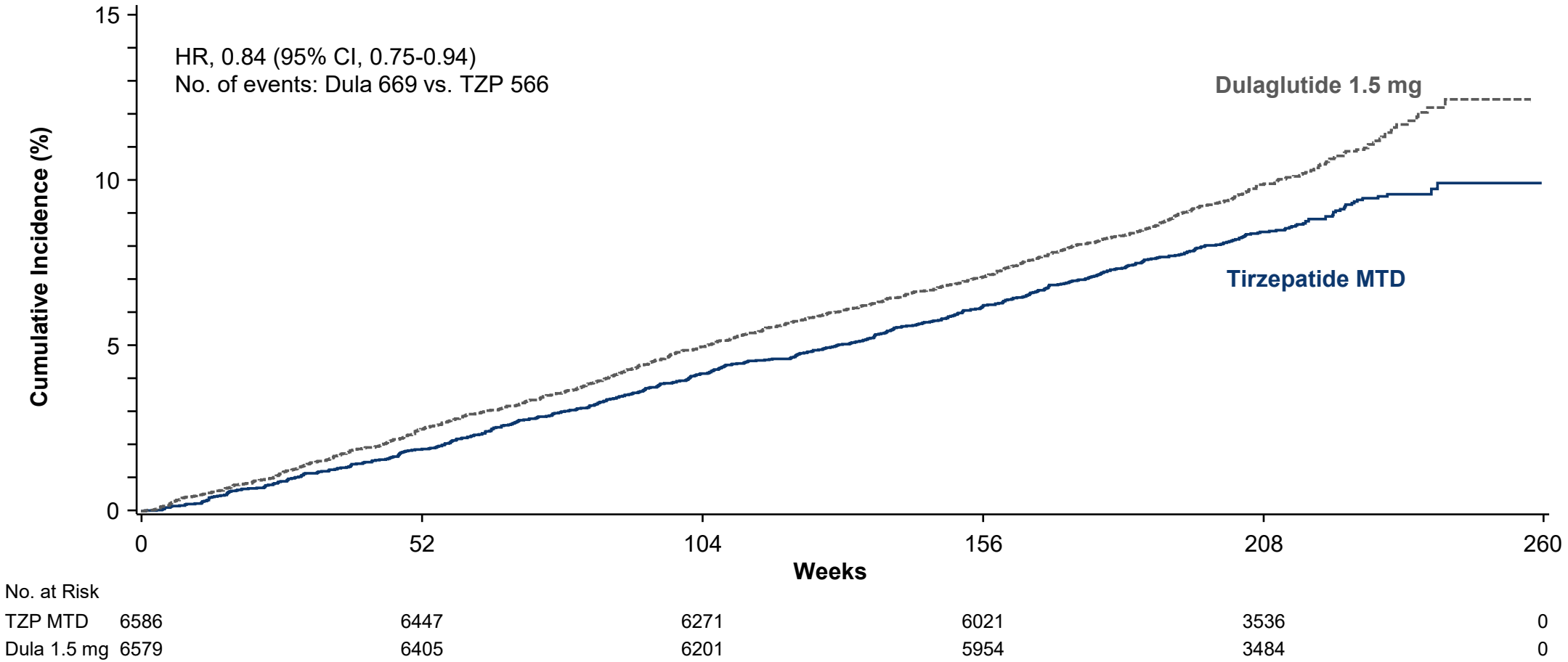
Outcome	TZP MTD (N=1520)	Dula 1.5 mg (N=1403)	Difference (95% CI)
Key Secondary Endpoint: Change in eGFR in high-risk CKD group[a]			
Change from baseline to 36 months in eGFR, mL/min/1.73 m^2, estimate	-5.0	-8.5	3.5 (2.6-4.5)

[a]In participants with high or very high-risk CKD as defined by KDIGO guidelines 2025 definition, identified as having eGFR ≥60 mL/min/1.73 m^2 and UACR >300 mg/g, eGFR 45-<60 mL/min/1.73 m^2 and UACR >30 mg/g, or eGFR <45 mL/min/1.73 m^2 at baseline.

Notes: Data are percentage of participants with event unless stated otherwise. HR and 95% CI were derived from a Cox proportional hazards model with treatment as a fixed effect, stratified by SGLT-2 inhibitor use at baseline. Change from baseline to Month 36 was analysed using an ANCOVA model with treatment, SGLT-2 inhibitor use at baseline, and country as fixed factors and baseline value as a covariate, with multiple imputation of missing values.

SURPASS-CVOT scientific disclosure, oral presentation at EASD Congress Vienna, Austria, on 18th September 2025

All-Cause Mortality



No. at Risk						
TZP MTD	6586	6447	6271	6021	3536	0
Dula 1.5 mg	6579	6405	6201	5954	3484	0

Note: HR and 95% CI were derived from a Cox proportional hazards model with treatment as a fixed effect, stratified by SGLT-2 inhibitor use at baseline.

SURPASS-CVOT scientific disclosure, oral presentation at EASD Congress Vienna, Austria, on 18th September 2025

MOUNJARO (tirzepatide injection) is indicated for once-weekly administration as an adjunct to diet and exercise to improve glycemic control for the treatment of adult patients with type 2 diabetes mellitus.

- As **monotherapy** when metformin is inappropriate due to contraindication or intolerance.
- In **combination with**:
  - metformin, or
  - metformin and a sulfonylurea (see 4.1 Dosing Considerations and 7 WARNINGS AND PRECAUTIONS), or
  - metformin and a sodium-glucose cotransporter 2 inhibitor (SGLT2i), or
  - basal insulin with or without metformin (see 4.1 Dosing Considerations and 7 WARNINGS AND PRECAUTIONS).

Upcoming CVOT's

Receptor	# of patients	Inclusion Criteria	Duration	Main Findings
GLP-1/GIP SURMOUNT-MMO	Total: 15,374 Tirzepatide vs placebo	≥40 years, overweight or obese and established CVD ≥3 months or CVD risk factors	5 years	Incidence of MACE
GLP-1/Amylin REDEFINE-3	Total: 7,000 CagriSema (2.4mg cagrilintide and 2.4mg semaglutide) vs placebo	≥55 years, BMI ≥25 and prevalent ASCVD	TBD	Time to first occurrence of MACE
GLP-1/GIP/ glucagon TRIUMPH-OUTCOMES	Total: 10,000 Retatrutide vs placebo	≥45 years, BMI ≥27 and established ASCVD and/or CKD	TBD	Incidence of MACE Kidney function
GLP-1/glucagon SYNCHRONIZE-CVOT	Total: TBD Survodutide	Overweight or obese and established CVD, CKD, or CVD risk factors	TBD	Time to first occurrence of 5P-MACE: death, non-fatal MI, non-fatal stroke, ischemia-related coronary revascularization and HF events

Let's end with the case!

Mrs. A.C.

- 66-year-old female with chronic stable hypertension and prior PCI of the mid-LAD for NSTEMI 2 years ago. She is referred because of atypical exertional symptoms of dyspnoea on exertion.
- Medications: ASA 81mg, ramipril 10 mg, rosuvastatin 20 mg, ezetimibe 10 mg, PCSK9i injected every 2 weeks. Dapa 10mg daily, metformin 500mg BID
- Physical examination: BMI 35, BP 136/84, JVP is difficult to assess but appears mildly elevated, normal S1 and S2, there is no edema.

Step wise plan

1) Added GLP1RA Ozempic

Then add

2) finenerone 10mg, and careful K+ monitoring, aiming for 20mg if 2 K+ <4.8 and eGFR stable after 4 weeks

	Age 66
EKG	NSR 65/min, QS V1, V2
A1C	6.7
TC	3.4
HDL-C	1
LDL-C	1.25
TG	1.24
apoB	0.55
eGFR/	47
UACR	32
K+	4.2

Summary

- s/c GLP1RA show benefits in persons with T2DM, CAD, CKD, HF
- Oral GLP1RA show CV benefit in persons with T2DM
- ”new” therapies include GLP1RA + GIP or glucagon agonist (Double G or triple G) with multiple new trials underway across a wide variety of conditions

Thank you