

FOCUS ON CARDIOLOGIA CLINICA

Dallo studio SELECT al SOUL: nuove evidenze, solita consistenza per semaglutide

*Gianturco Luigi, MD
IRCCS Fondazione Ca' Granda, Ospedale Maggiore Policlinico, Milano*

Modulo Biomedico Nazionale AIA-FIGC





DICHIARO

ai sensi e per gli effetti dell'art. 48, comma 25, del D.L. 269/2003, convertito in legge 25 novembre 2003 nr. 326

che l'attività professionale e scientifica svolta nell'ambito dell'evento citato non configura in alcun caso conflitto di interessi con l'organizzatore dell'evento formativo

DICHIARO altresì

ai sensi dell'art. 76 «Conflitto di Interessi ECM» sul Conflitto di Interessi, dell'Accordo Stato-Regione del 2 febbraio 2017

BAYER - consulenza



Futuro

Guidelines

Nota 100

Safety

Diabete

Weight

SUSTAIN - PIONEER

SELECT

STEP

FLOW

CKM

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Diabete

Weight

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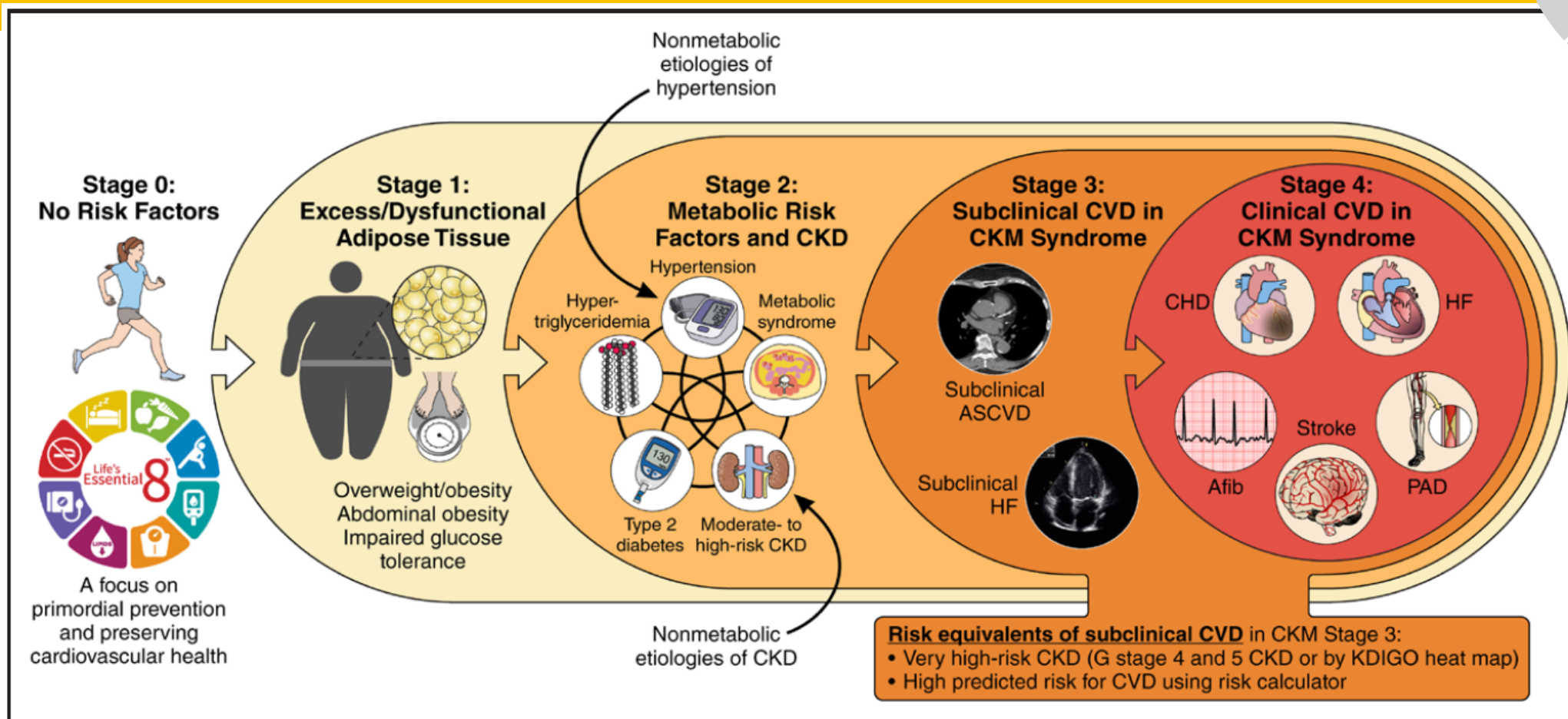
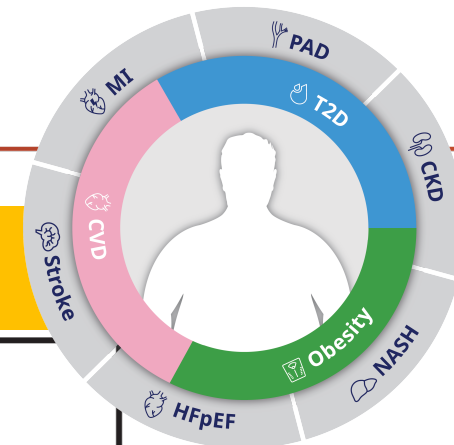
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FLOW

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Cardiovascular-Kidney-Metabolic (CKM) Syndrome



Ndumele CE, et al. *Circulation*. 2023 Nov 14;148(20):1606-1635.



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Guidelines

Nota 100

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Weight

SUSTAIN - PIONEER

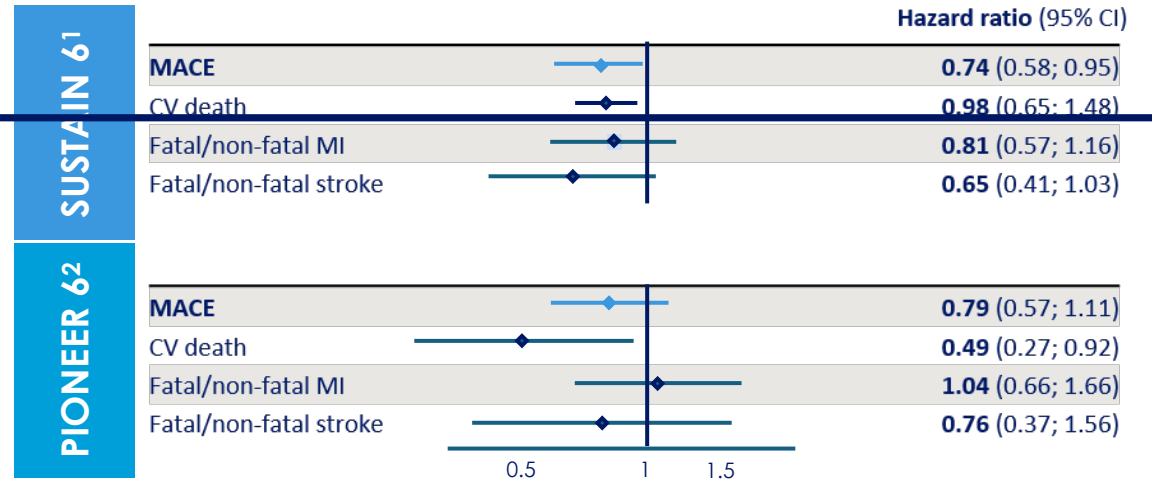
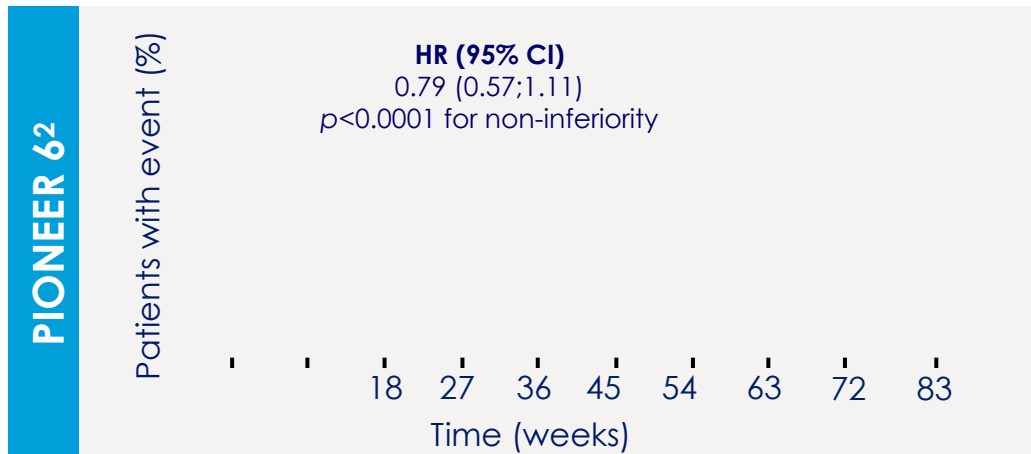
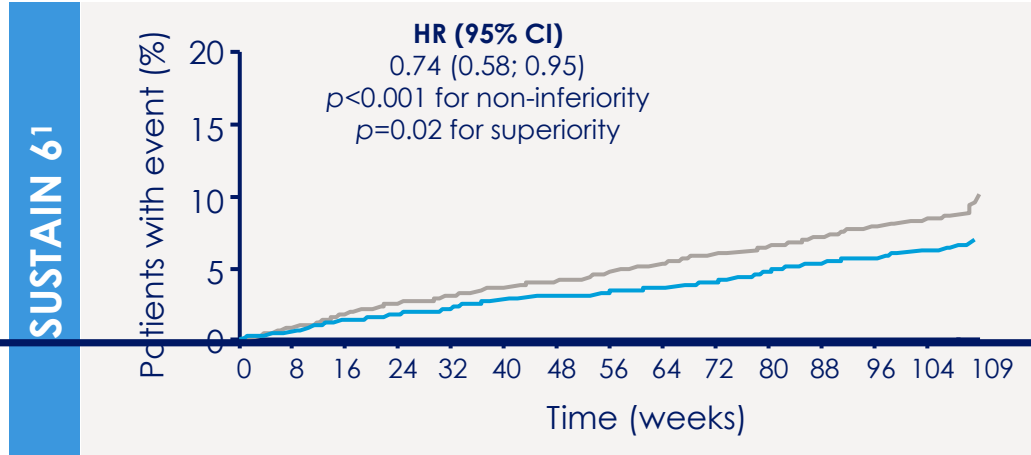
SELECT

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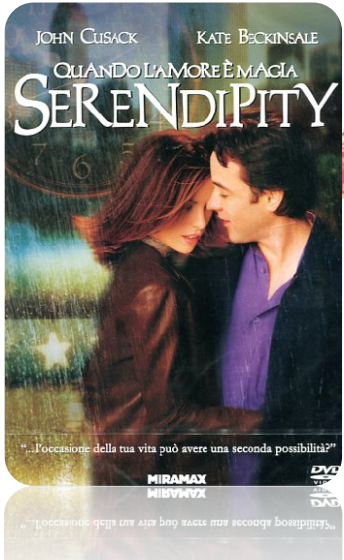
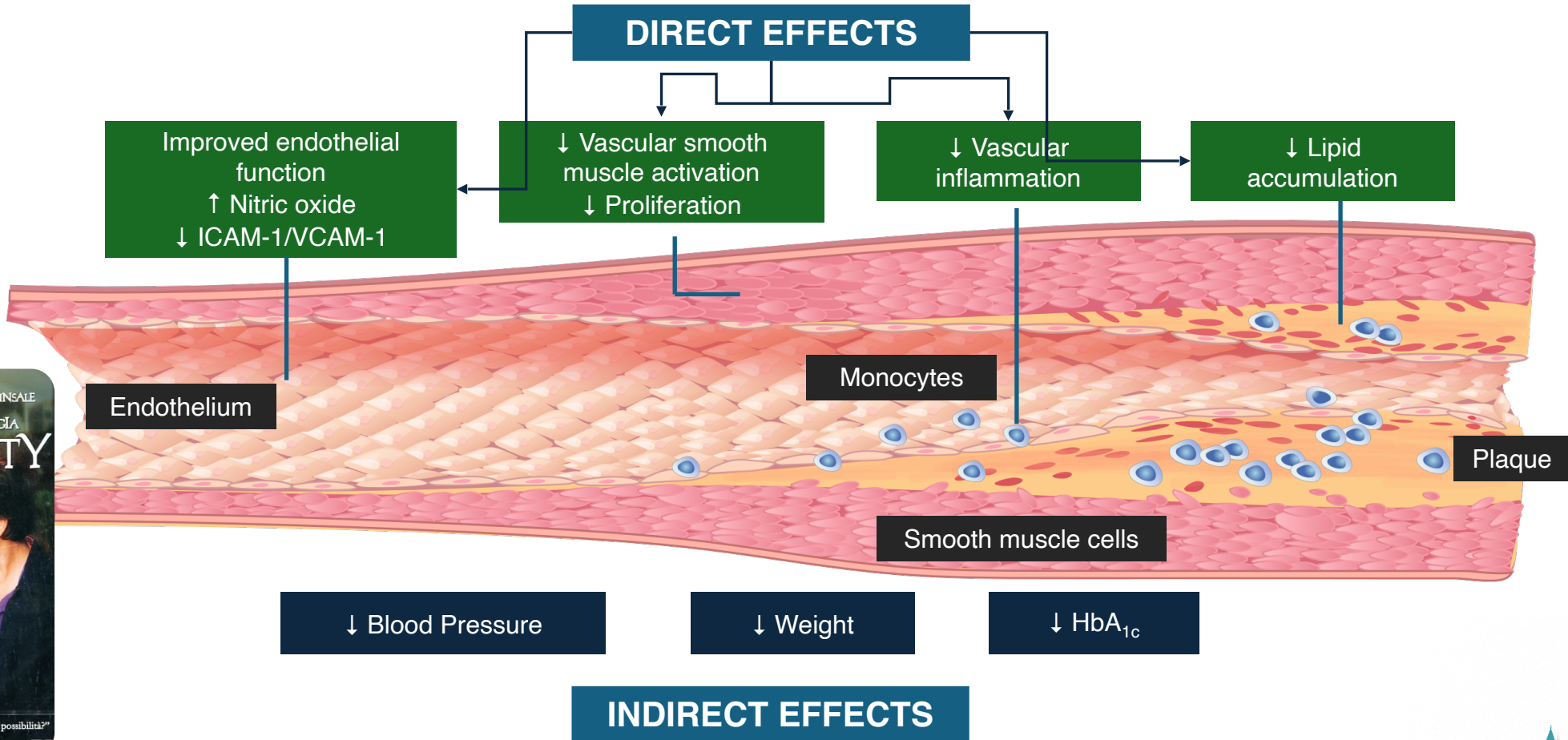
The risk of MACE was reduced by semaglutide in high-risk CV patients with T2D



CI, confidence interval; CV, cardiovascular; CVOT, cardiovascular outcomes trial; HR, hazard ratio; MACE, major adverse cardiovascular events; MI, myocardial infarction.
1. Marso S, et al. N Engl J Med. 2016;375:1834-44. 2. Husain M, et al. Diabetes Obes Metab. 2020;22:442-51.



CVOTs & Anti-Atherosclerotic Effects GLP-1



GLP-1RA, glucagon like peptide receptor agonist; HbA_{1c}, glycated haemoglobin; ICAM-1, intercellular adhesion molecule 1; VCAM-1, vascular cell adhesion protein 1
Sharma A and Verma S. Can J Diabetes 2020;44:93–102



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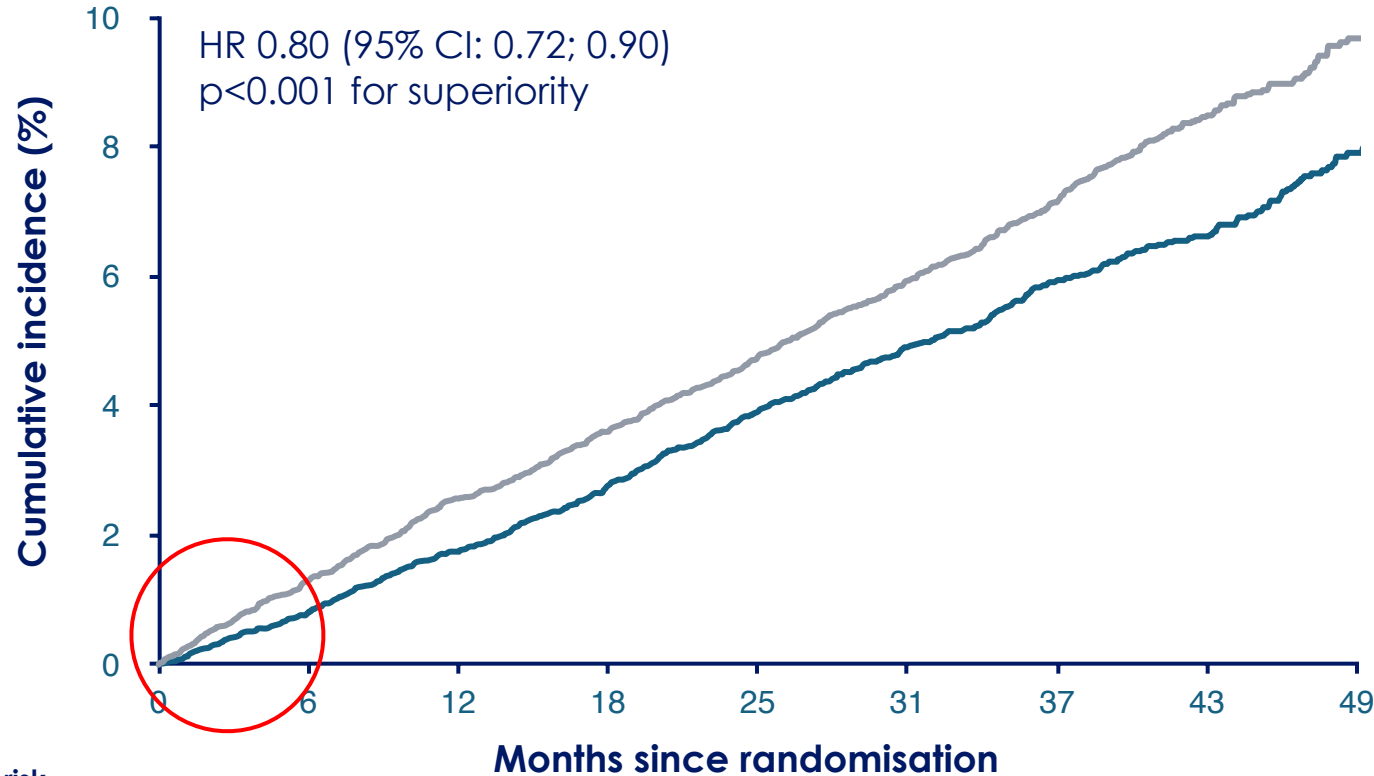
STEP

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Cumulative incidence of MACE

SELECT: Primary cardiovascular composite endpoint



No. at risk									
Semaglutide	8,803	8,695	8,561	8,427	8,254	7,229	5,777	4,126	1,734
Placebo	8,801	8,652	8,487	8,326	8,164	7,101	5,660	4,015	1,672

— Semaglutide 2.4 mg — Placebo

20%
reduction in
risk of MACE*

Semaglutide 2.4 mg significantly reduced the risk of MACE by 20% compared with placebo in people with obesity and established CVD, without T2D^{1,2}



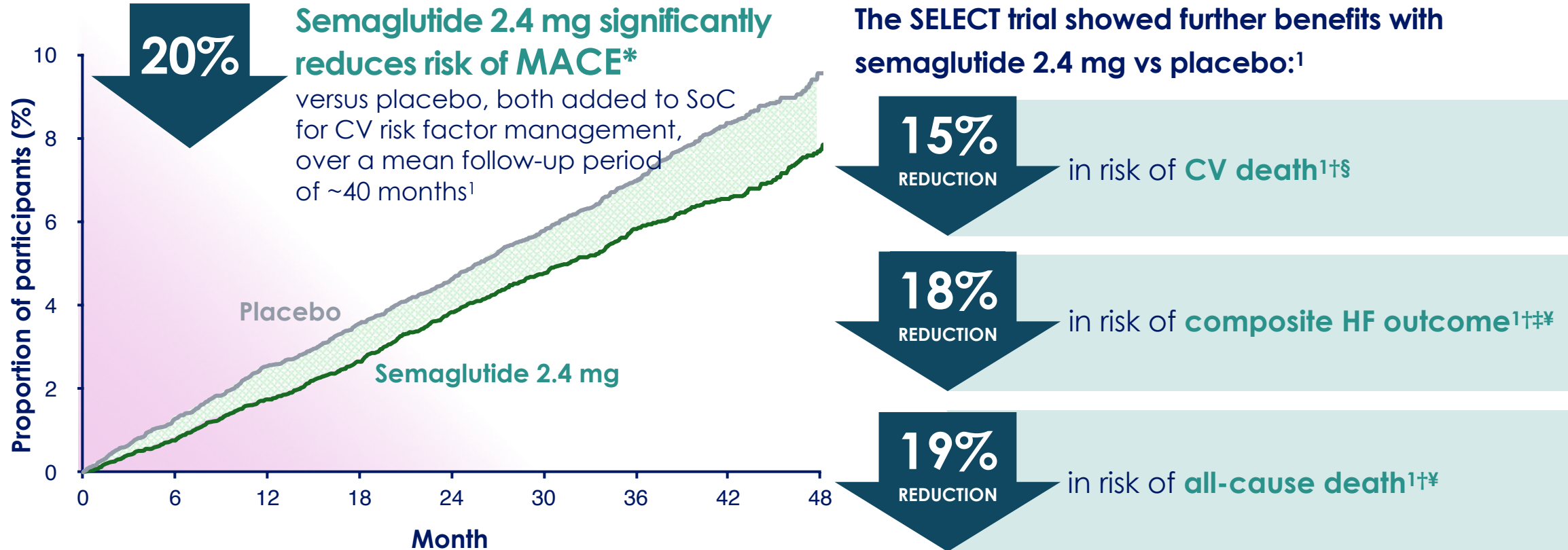
All three components (death from CV causes, non-fatal MI and non-fatal stroke) contributed to MACE risk reduction



Mean follow-up time was 39.8 months

Cumulative incidence (using the Aalen-Johansen method) of the composite MACE primary endpoint. The HR was estimated using a Cox proportional hazards regression model. The proportion of participants with MACE was 6.5% with semaglutide 2.4 mg and 8.0% with placebo. MACE was defined as death from CV causes, non-fatal myocardial infarction, or non-fatal stroke. CI, confidence interval; HR, hazard ratio; MACE, major adverse cardiovascular events; MI, myocardial infarction. 1. Lincoff AM et al. N Engl J Med 2023;DOI:10.1056/NEJMoA2307563; 2. American College of Cardiology, SELECT: Semaglutide Reduces Risk of MACE in Adults With Overweight or Obesity. Accessed October 2023. <https://www.acc.org/Latest-in-Cardiology/Articles/2023/08/10/14/29/SELECT-Semaglutide-Reduces-Risk-of-MACE-in-Adults-With-Overweight-or-Obesity>





*Time from randomisation to first occurrence of CV death, non-fatal MI, or non-fatal stroke. [†]Treatment with semaglutide 2.4 mg or placebo was as an adjunct to SoC for CV risk reduction. [‡]HF hospitalisation/urgent HF visit or CV death. [§]Superiority of semaglutide 2.4 mg versus placebo for time from randomisation to CV death was not confirmed; [¥]Superiority of semaglutide 2.4 mg versus placebo for time from randomisation to first composite HF outcome and to all-cause death was not tested.

CKM, cardiovascular-kidney-metabolic; CV, cardiovascular; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HbA_{1c}, haemoglobin A_{1c}; MACE, major adverse cardiovascular event; MI, myocardial infarction; SoC, standard of care.

1. Lincoff AM, et al. N Engl J Med. 2023;DOI:10.1056/NEJMoa2307563.



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STEP-HFpEF and STEP-HFpEF DM trial design

STEP-HFpEF Trial Design^{1,2}

N=529



NYHA II-IV

Ejection fraction $\geq 45\%$



BMI ≥ 30 kg/m²



Semaglutide OW 2.4 mg + SoC

Placebo + SoC



Trials Objective

To investigate the effects of semaglutide 2.4 mg s.c. once weekly on **physical function, symptoms** and **body weight** compared with placebo, both added to SoC, in people with the obesity phenotype of HFpEF with/without T2D

STEP-HFpEF-DM Trial Design³

N=616



NYHA II-IV

Ejection fraction $\geq 45\%$



BMI ≥ 30 kg/m²



T2D
HbA_{1c} $\leq 10\%$



Semaglutide OW 2.4 mg + SoC

Placebo + SoC

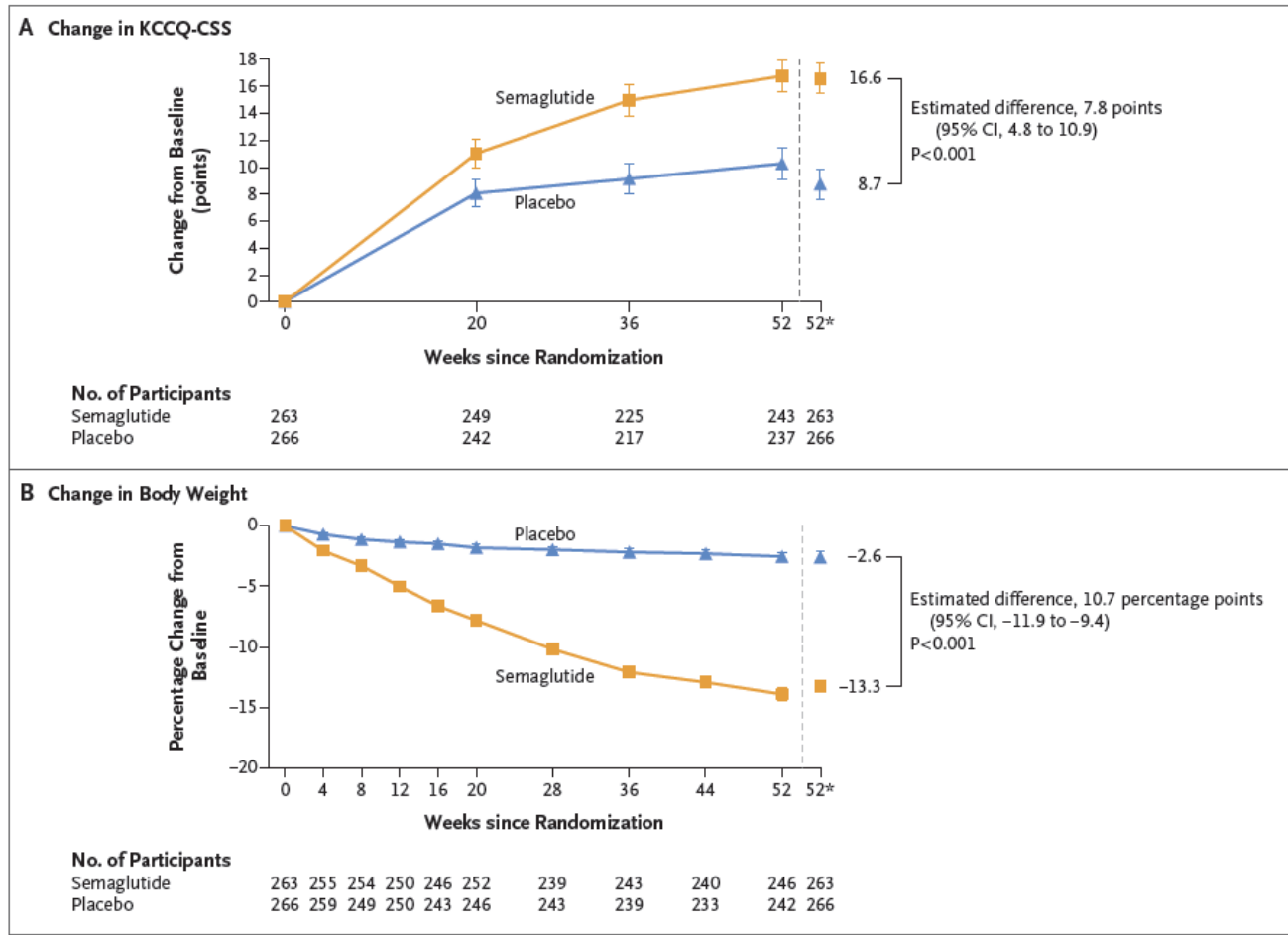


Key Endpoints

- **Dual primary endpoints:** KCCQ-CSS and body weight
- **Confirmatory secondary endpoints:** 6MWD, hierarchical composite endpoint*, hs-CRP
- **Key exploratory endpoints:** loop diuretic medication, NT-proBNP, NYHA class, time to first HF event (hospitalisation or urgent visit)

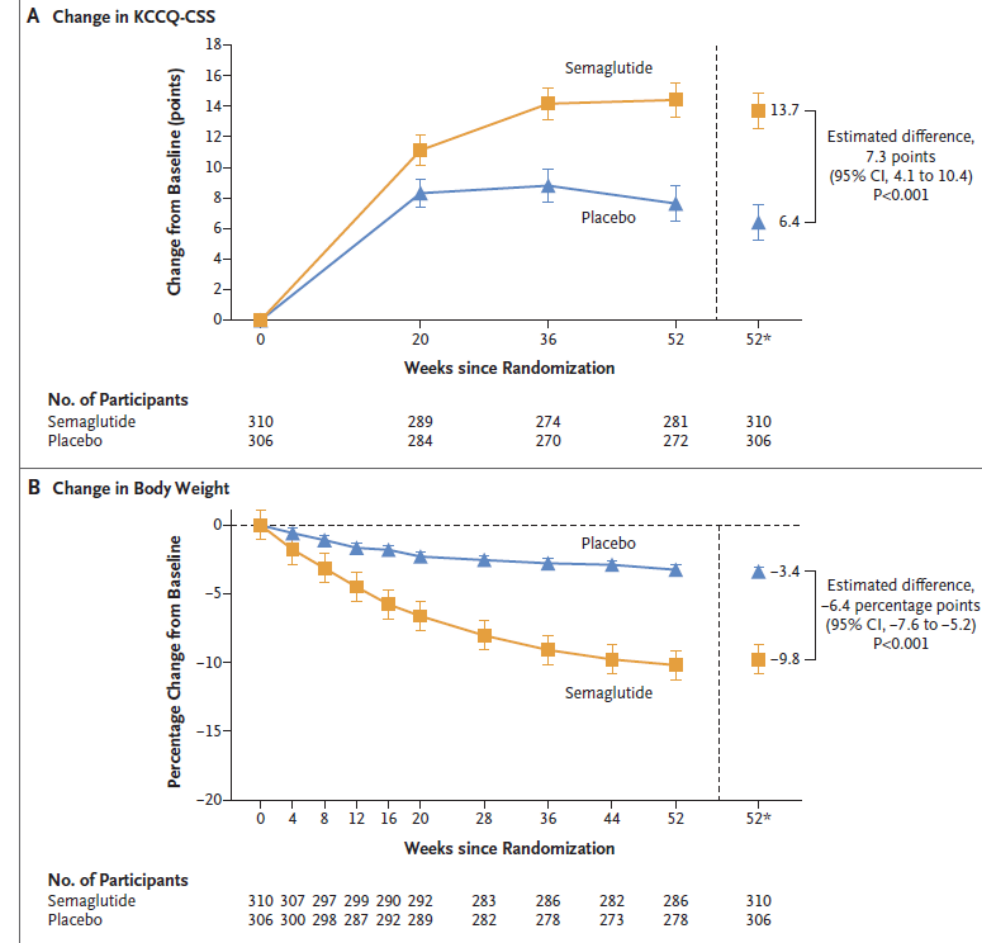
*Comprising time to all-cause death, time to and number of HF events, changes in KCCQ-CSS and 6MWD
6MWD, 6-minute walk distance; BMI, body mass index; CRP, C-reactive protein; HbA_{1c}, glycated haemoglobin; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; KCCQ-CSS, Kansas City Cardiomyopathy Questionnaire Clinical Summary Score; KCCQ-OSS, Kansas City Cardiomyopathy Questionnaire Overall Summary Score; NT-proBNP, N-terminal pro B-type natriuretic peptide; NYHA, New York Heart Association; SBP, systolic blood pressure; s.c., subcutaneous; SoC, standard of care; T2D, type 2 diabetes
1. NCT04788511. Available at: <https://clinicaltrials.gov/ct2/show/NCT04788511> (accessed August 2023); 2. Kosiborod MN et al. JACC HF 2023;11(8_Part_1):1000-1010. 3. Kosiborod MN et al. N Engl J Med 2024;390(15):1394-1407

STEP HFpEF



1. Kosiborod MN et al. JACC HF 2023;11(8_Part_1):1000-1010.

STEP HFpEF DM



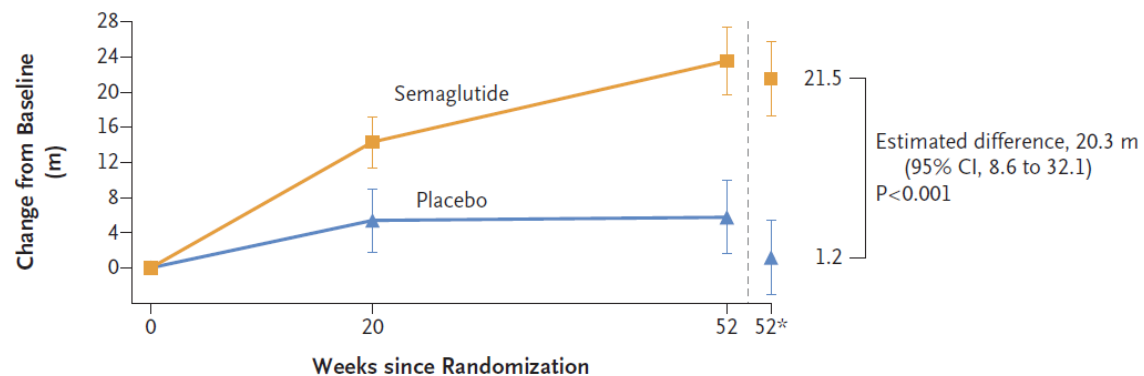
2. Kosiborod MN et al. N Engl J Med 2024;390(15):1394-1407

*Estimated mean changes from baseline to week 52 based on analysis of covariance (ANCOVA) and an imputation approach for missing data. In the left figure, error bars are $\pm$ standard error of the mean. Numbers shown in the lower panel are numbers of patients contributing to the mean



STEP HFpEF

Change in 6-Minute Walk Distance



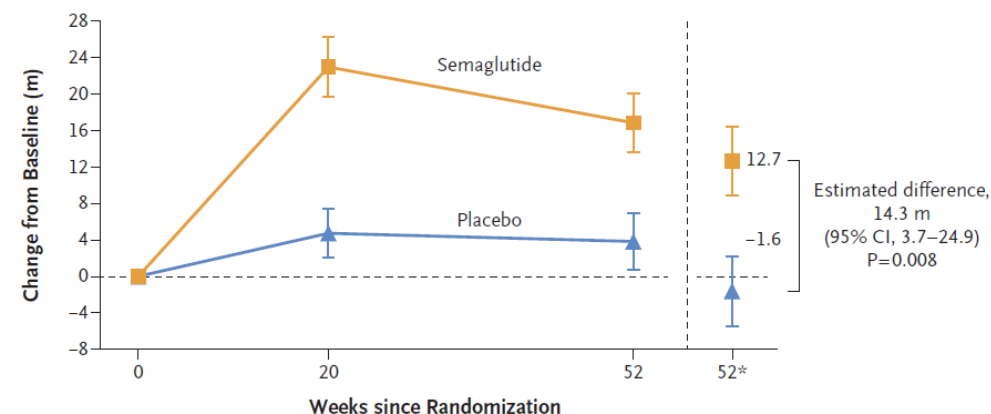
No. of Participants

Semaglutide	263	245	240	263
Placebo	266	232	225	266

1. Kosiborod MN et al. JACC HF 2023;11[8_Part_1]:1000–1010.

STEP HFpEF DM

Change in 6-Minute Walk Distance



No. of Participants

Semaglutide	310	284	281	310
Placebo	306	277	265	306

2. Kosiborod MN et al. N Engl J Med 2024;390(15):1394–1407

6MWD

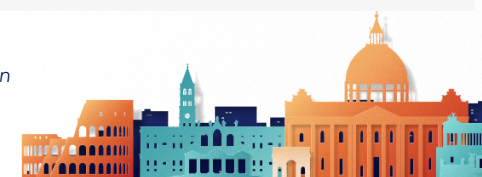
320.0 m
(240.0; 389.0)

Baseline

6MWD (m)

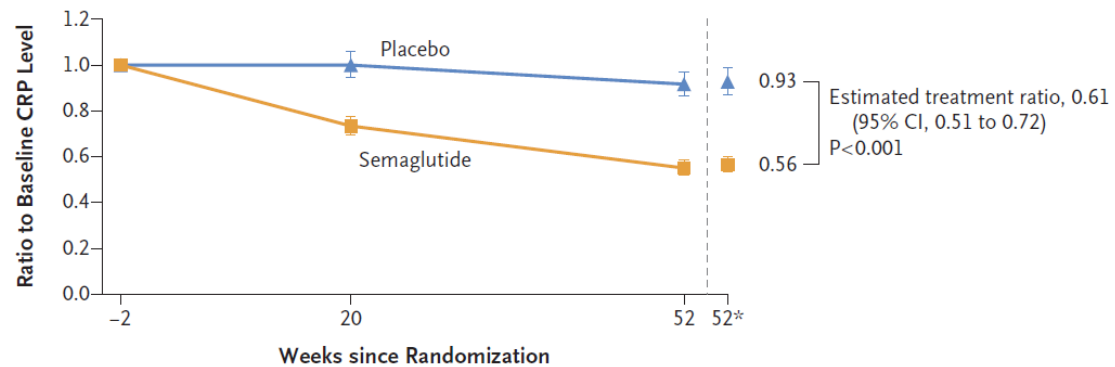
280.0 (205.1–357.6)
280.0 (200.0–345.0)

*Estimated mean changes from baseline to week 52 based on analysis of covariance (ANCOVA) and an imputation approach for missing data. In the left figure, error bars are $\pm$ standard error of the mean. Numbers shown in the lower panel are numbers of patients contributing to the mean



STEP HFpEF¹

Change in C-Reactive Protein Level



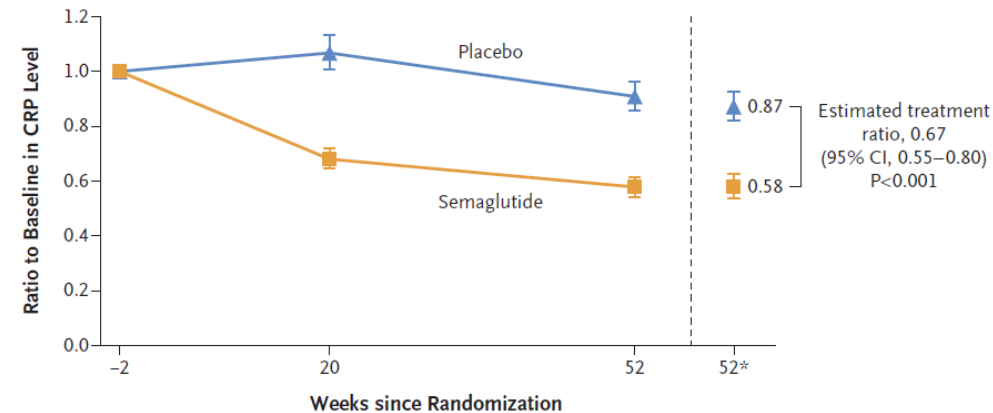
No. of Participants

Semaglutide	263	245	240	263
Placebo	266	232	225	266

1. Kosiborod MN et al. JACC HF 2023;11(8_Part_1):1000-1010.

STEP HFpEF DM²

Change in C-Reactive Protein Level



No. of Participants

Semaglutide	310	288	286	310
Placebo	306	285	277	306

2. Kosiborod MN et al. N Engl J Med 2024;390(15):1394-1407

Semaglutide, semaglutide 2.4 mg

*Estimated mean changes from baseline to week 52 based on analysis of covariance (ANCOVA) and an imputation approach for missing data.

In the left figure, error bars are $\pm$ standard error of the mean. Numbers shown in the lower panel are numbers of patients contributing to the mean

1. Kosiborod MN, et al. N Engl J Med. 2023;389(12):1069-1084. 2. Kosiborod MN, et al. N Engl J Med. 2024;390(15):1394-1407.



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Guidelines

Nota 100

Safety

Diabete

Weight

SUSTAIN - PIONEER

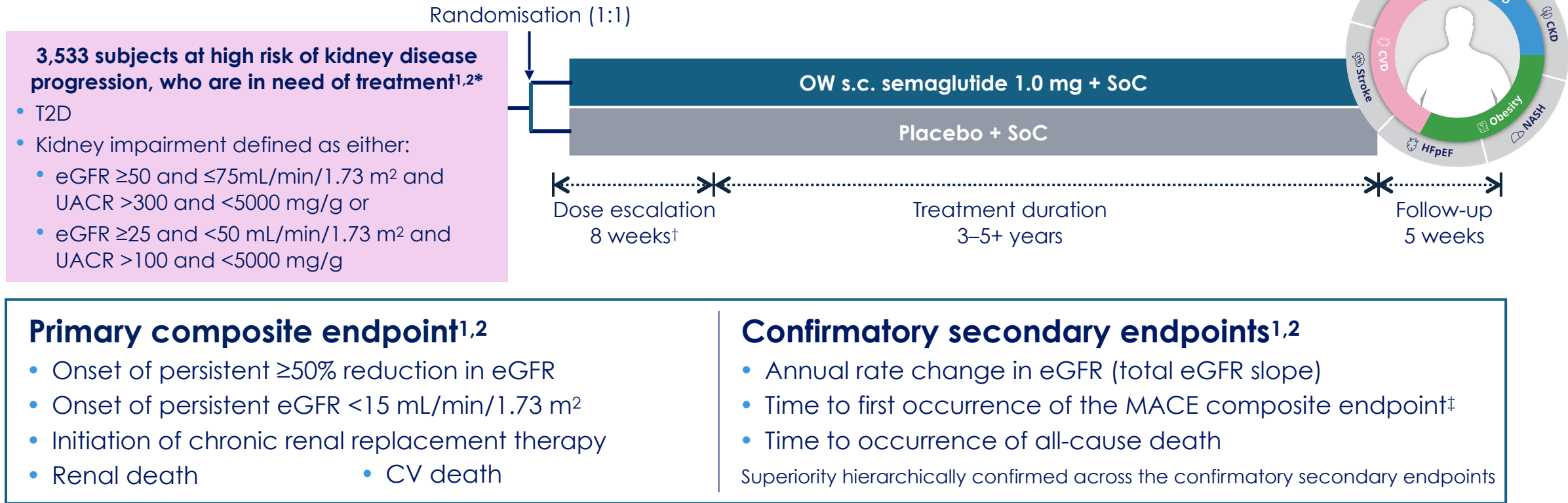
SELECT

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FLOW

CKM

FLOW assessed the effect of semaglutide versus placebo on kidney, cardiovascular and mortality outcomes



FLOW investigated OW semaglutide's potential as a new kidney-protective treatment option for people with T2D and CKD^{1,2}

*Additional inclusion criteria: age ≥ 18 years (≥ 20 years in Japan); HbA_{1c} $\leq 10\%$ (≤ 86 mmol/mol); RAAS blocker (4 weeks' stable dose of maximum tolerated dose). [†]OW semaglutide dose escalation from starting dose of 0.25 mg; dose doubled every 4 weeks until trial maintenance dose achieved. [‡]MACE endpoint consisted of time to first CV death, non-fatal MI, or non-fatal stroke.

CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; MACE, major adverse cardiovascular events; MI, myocardial infarction; OW, once weekly; RAAS, renin-angiotensin-aldosterone system; s.c., subcutaneous; SoC, standard of care; T2D, type 2 diabetes; UACR, urinary albumin to creatinine ratio.

1. Rossing P, et al. Nephrol Dial Transplant. 2023;38(9):2041-2051. 2. Perkovic V, et al. Published online 6 May, 2024. N Engl J Med. DOI: 10.1056/NEJMoa2403347.



93% of the participants at **high** or **very high risk** for **CKD progression**

According to KDIGO guideline categorisation, 68.2% were at very high risk for CKD progression

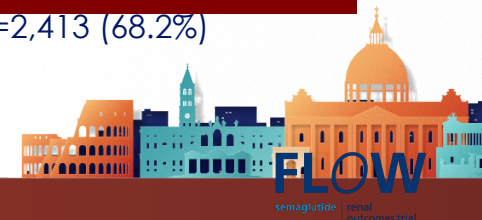
Baseline data

KDIGO risk categories among FLOW participants, n (%)

		UACR categories (mg/g)		
		<30	≥30—<300	≥300
eGFR categories (mL/min/1.73 m ²)	≥90	1 (<0.1)	7 (0.2)	23 (0.6)
	≥60—<90	24 (0.7)	173 (4.9)	431 (13.9)
	≥45—<60	37 (1.0)	324 (9.2)	694 (19.6)
	≥30—<45	40 (1.1)	414 (11.7)	1003 (25.6)
	≥15—<30	7 (0.2)	87 (2.5)	306 (8.6)
	<15	NA	NA	NA
		Low risk n=25 (0.7%)	Moderate risk n=217 (6.1%)	High risk n=878 (24.8%)
				Very high risk n=2,413 (68.2%)

FLOW population

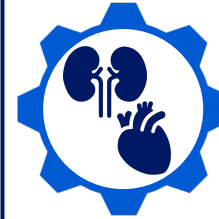
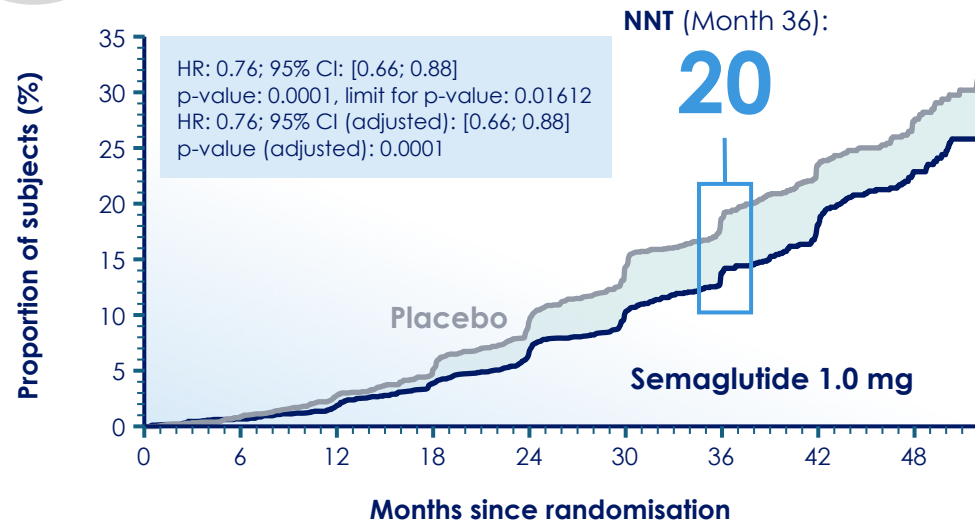
Adapted from KDIGO Diabetes Work Group. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease; Kidney International (2022) 102 (Suppl 5S), S1–S127. CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease: Improving Global Outcomes; UACR, urine albumin-creatinine ratio. Rossing P et al. Nephrol Dial Transplant 2023;38:2041–2051; Perkovic V, et al. N Engl J Med. 2024; DOI: 10.1056/NEJMoa2403347



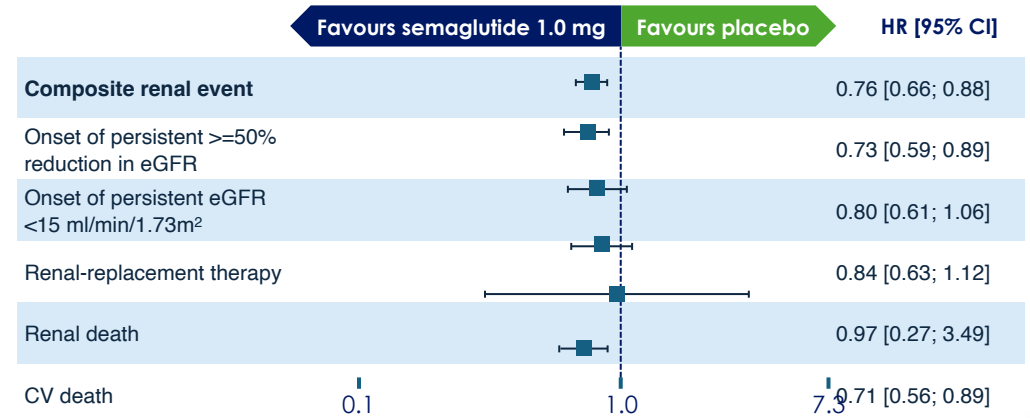
In FLOW, semaglutide showed a 24% risk reduction of the primary kidney composite endpoint

24%

risk reduction of first composite kidney event in people with T2D and CKD^{1*}
OW s.c. semaglutide 1.0 mg versus placebo in addition to SoC



Hazard ratios suggest that both **kidney** and **CV** components contributed to **risk reduction**, and that risk reduction was **consistent** across kidney components of the primary endpoint:^{1†}



*Cumulative incidence estimates are based on time from randomisation to first composite renal event with non-cardiovascular and non-renal death modelled as competing risk using the Aalen-Johansen estimator. Subjects without events of interest were censored at the end of their in-trial observation period. Events not related to eGFR are EAC-confirmed. eGFR was calculated using the CKD-EPI formula. The x-axis is truncated at 52 months where approximately 5% of the population was still in the trial. Time from randomisation to first composite renal event was analysed using a Cox proportional hazards model with treatment as categorical fixed factor and stratified by use of SGLT-2 inhibitor (yes/no) at baseline. Based on the available number of events for analysis, the nominal significance level was updated to 0.01612 using the Lan-DeMets alpha spending function. Adjustment for group sequential design was done using likelihood ratio ordering. Event rates are events per 100 years of observation. †All endpoints were analysed using a Cox proportional hazards model with treatment as categorical fixed factor and stratified by use of SGLT-2 inhibitor use (yes/no) at baseline. Subjects without events of interest were censored at the end of their in-trial observation period. For the primary composite kidney event endpoint, the hazard ratio and confidence interval are adjusted for the group sequential design using the likelihood ratio ordering. The eGFR is estimated using the CKD-EPI formula. Persistent is defined as having two consecutive measurements at least 4 weeks apart fulfilling the criteria. Reduction in eGFR is reduction in eGFR compared to baseline. CI, confidence interval; CKD, chronic kidney disease; CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration; CV, cardiovascular; EAC, event adjudication committee; eGFR, estimated glomerular filtration rate; GLP-1RA, glucagon-like peptide 1 receptor agonist; HR, hazard ratio; NNT, number needed to treat; OW, once weekly; p-value, one-sided p-value for the test of no difference; s.c., subcutaneous; SGLT-2, sodium-glucose cotransporter-2; SoC, standard of care; T2D, type 2 diabetes. 1. Perkovic V, et al. Published online 6 May, 2024. N Engl J Med. DOI: 10.1056/NEJMoa2403347.

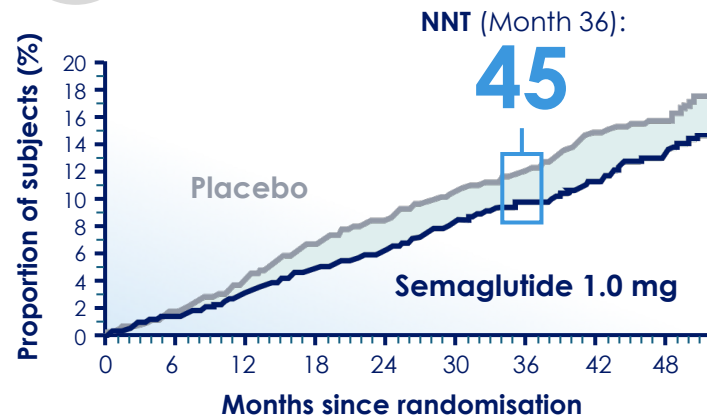
Annual rate change in eGFR (total eGFR slope)

↓ 1.16 mL/min/1.73m²/year **less decline in eGFR** (95% CI: [0.86; 1.47])^{1*}



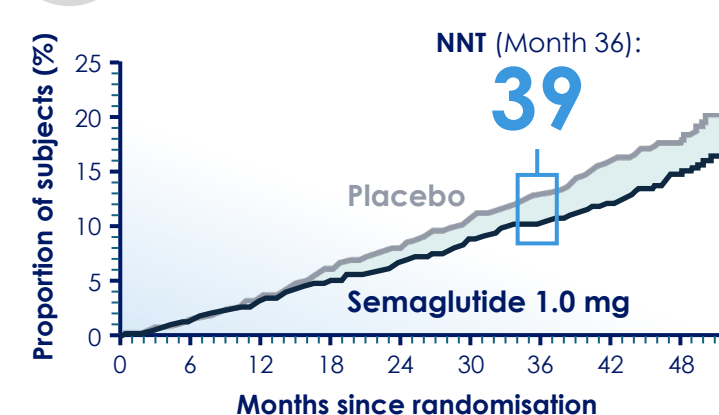
MACE

18% risk reduction in the time to **first MACE** vs placebo (95% CI: [0.68; 0.98])^{1†}



All-cause death

20% risk reduction in time to occurrence of **all-cause death** vs placebo (95% CI: [0.67; 0.95])^{1‡}



Superiority of OW s.c. semaglutide 1.0 mg in people with CKD and T2D on top of SoC was **hierarchically confirmed** across the confirmatory secondary endpoints^{1,2}

*Data from visits with scheduled eGFR assessment in the in-trial period. Annual rate of change in eGFR was analysed using a linear random effects model with treatment, use of SGLT-2 inhibitors (yes/no) at baseline, time (as a continuous variable) and treatment time interaction as fixed effects and including subject effect as a random intercept and time as a random slope. Based on the available number of events for analysis, the nominal significance level was updated using the Lan-DeMets alpha spending function. eGFR was calculated using the CKD-EPI formula. †Cumulative incidence estimates are based on time from randomisation to first EAC-confirmed MACE with non-cardiovascular death modelled as competing risk using the Aalen-Johansen estimator. Subjects without events of interest were censored at the end of their in-trial observation period. Time from randomisation to first EAC-confirmed MACE was analysed using a Cox proportional hazards model with treatment as categorical fixed factor and stratified by use of SGLT-2 inhibitor (yes/no) at baseline. Based on the available number of events for analysis, the nominal significance level was updated using the Lan-DeMets alpha spending function. The x-axis is truncated at 52 months where approximately 5% of the population was still in the trial. ‡Cumulative incidence estimates are based on time from randomisation to EAC-confirmed all-cause death using the Aalen-Johansen estimator. Subjects without events of interest were censored at the end of their in-trial observation period. Time from randomisation to EAC-confirmed all-cause death was analysed using a Cox proportional hazards model with treatment as categorical fixed factor and stratified by use of SGLT-2 inhibitor (yes/no) at baseline. Based on the available number of events for analysis, the nominal significance level was updated using the Lan-DeMets alpha spending function. The x-axis is truncated at 52 months where approximately 5% of the population was still in the trial. CI, confidence interval; CKD, chronic kidney disease; CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration; EAC, event adjudication committee; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide 1 receptor agonist; MACE, major adverse cardiovascular event; NNT, number needed to treat; OW, once weekly; s.c., subcutaneous; SGLT-2, sodium-glucose cotransporter-2; SoC, standard of care; T2D, type 2 diabetes.

1. Perkovic V, et al. Published online 6 May, 2024. N Engl J Med. DOI: 10.1056/NEJMoa2403347.





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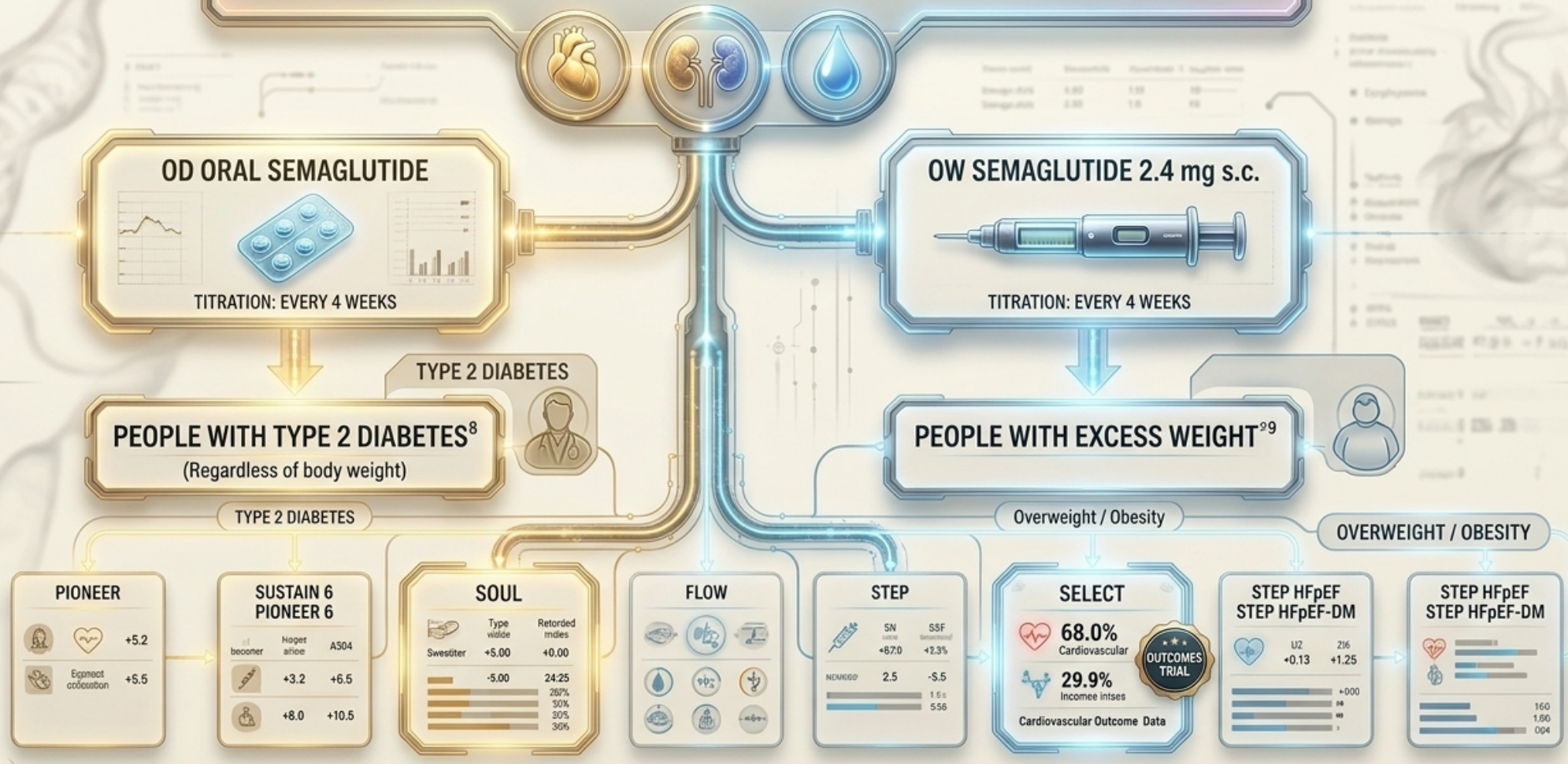
SELECT

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SEMAGLUTIDE: A REVOLUTION IN CARDIO-RENO-METABOLIC HEALTH¹⁻⁷

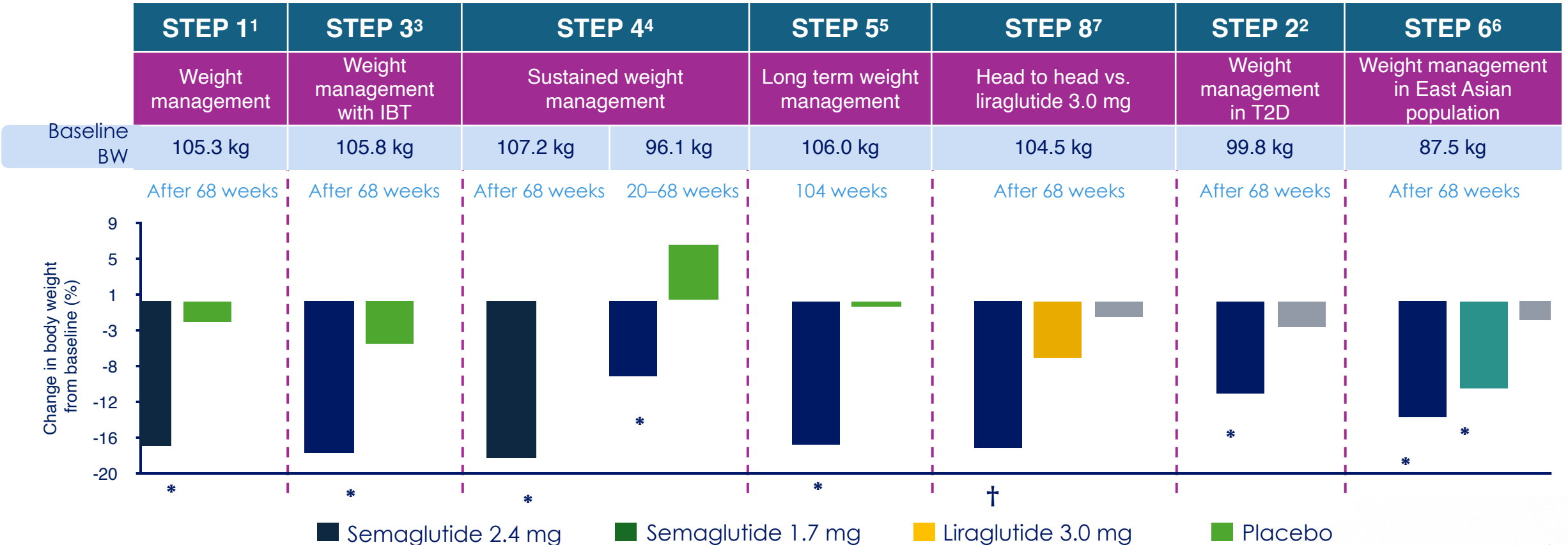


GO, once daily, OW, once weekly, e.c., subcutaneous. *Excess weight defined as: BMI ≥ 30 kg/m² or BMI ≥ 27 and < 30 kg/m² in the presence of at least one weight comorbidity e.g. dyslipidemia, hypertension, dysglycemia, as well as obesity. 1. Mario S. et al. N. Engl. J. Med. 381:131-141, 2019. 2. Teusler N. et al. N. Engl. J. Med. 381:131-141, 2019. 3. Kovil 201/9/10-1084-4. 4. Kossprad-V/R. et al. N. Engl. J. Med. 381:131-141, 2019. 5. Renouard et al. Published online May, 2023. 6. Engl / Napi cast. H614HNCR 280502.272, Published online 25, 2023, def. 7. Kossprad-V/R. et al. N. Engl. J. Med. 381:131-141, 2019. 8. Oti Oral semaglutide - Summary of main characteristics, last revised March 2024. 9. OW semaglutide 2.4 mg s.c. - Summary of main characteristics, last revised June 2024.

7. Dysglycemia, excess weight comorbidity, e.g. dyslipidemia (pretreatment (prediabetes or type 2 diabetes) and collected as a comorbidity). 8. Cathorn H. H. 1 Eng 20235378N2550537.21. Calhoun HIV, nuv. 9 eaf. Published online 25, 2024, del. 9. OW semaglutide 2.4 mg s.c. 4 mg s.c.: Summary of main characteristics, last revised June 2024.

Weight loss across STEP trials

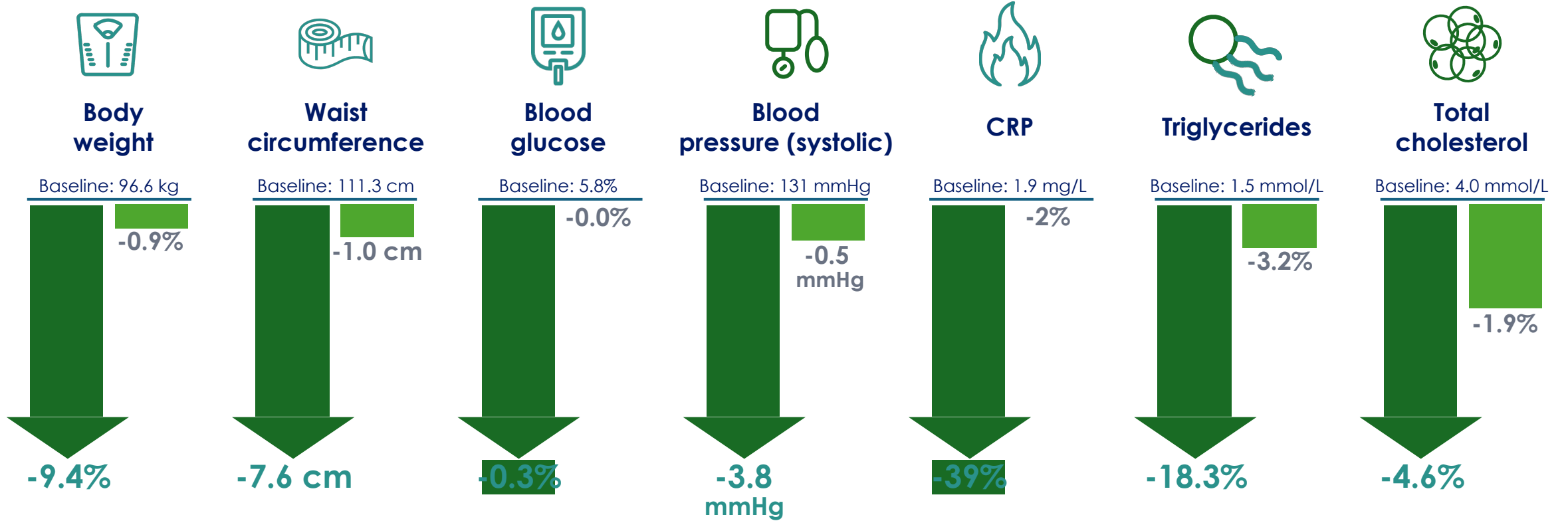
Semaglutide 2.4 mg once-weekly in participants with overweight or obesity



*Statistically significant vs placebo; † Statistically significant vs. liraglutide 3.0 mg
BW, body weight; IBT, intensive behavioural therapy.
1. Wilding et al. N Engl J Med 2021; doi:10.1056/NEJMoa202183; 2. Davies et al. Lancet. 2021; doi.org/10.1016/S0140-6736(21)00213-0; 3. Wadden et al. JAMA. doi:10.1001/jama.2021.1831; 4. Rubino et al. JAMA. 2021 Apr 13;325(14):1414-1425. doi: 10.1001/jama.2021.3224.
5. Garvey et al. Nat Med 26, 2085–2091 (2022); 6. Kadowaki et al. The Lancet Diabetes & Endocrinology 2022; 7. Rubino et al. JAMA 2022; 327(2): 136-150



Change from baseline to Week 104 in semaglutide 2.4-mg and placebo groups¹



CRP, C-reactive protein; CV, cardiovascular; SELECT, semaglutide effects on cardiovascular outcomes in people with overweight or obesity.

1. Lincoff AM, et al. N Engl J Med. 2023;DOI:10.1056/NEJMoa2307563.



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Most frequent adverse events are gastrointestinal, but most events were mild to moderate in severity and of short duration

The most frequently reported adverse reactions in clinical trials were gastrointestinal disorders, including



Nausea



Diarrhoea

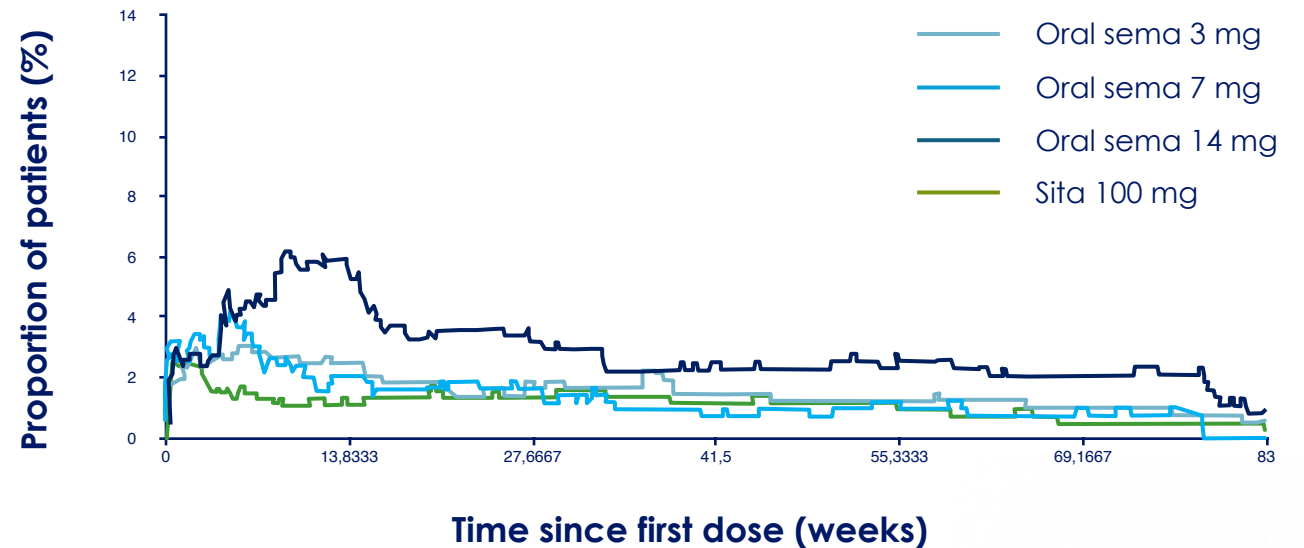


Vomiting

Most events were mild to moderate and most frequently reported during the first months on treatment.

The most common gastrointestinal adverse event, nausea, is transient and generally reduces after dose escalation

PIONEER 3



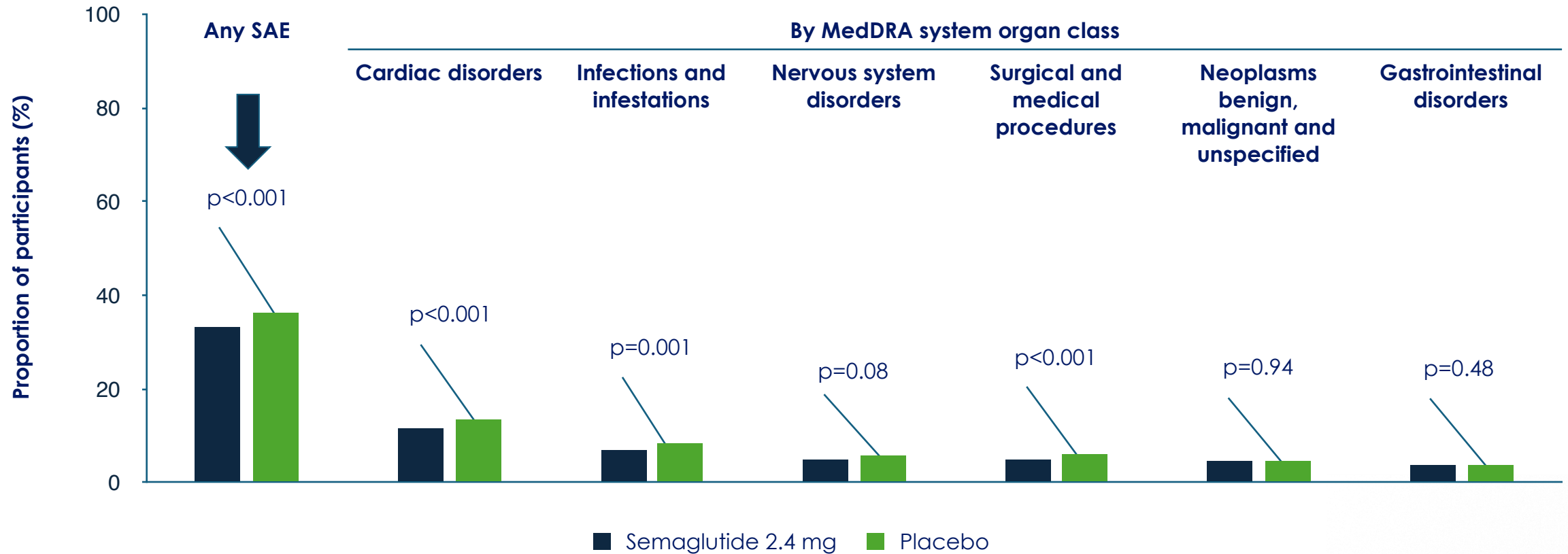
Sema, semaglutide; Sita, sitagliptin.

Oral semaglutide summary of product characteristics. Available at: <https://www.medicines.org.uk/emc/product/11507/smpc>. Accessed August 2021; Rosenstock J et al. JAMA 2019;321:1466–80.



Serious adverse events

SELECT



Two-sided p-values from Fisher's exact test for test of no difference.
MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event.
Lincoff AM et al. N Engl J Med 2023;DOI:10.1056/NEJMoa2307563.





RESEARCH ARTICLE

Evaluating the safety profile of semaglutide: an updated meta-analysis

Frederick Berro Rivera^a , Eloise Arias-Aguirre^b, Zedrick Aguirre^b , Mc John C. Ybañez^b, Janos Marc M. Rubia^b, Danica Janine Galang^b, Grace Nooriza Lumbang^b, Jade Monica Marie J. Ruyeras^b , John Vincent Magalong^c, Polyn Luz Pine^d, John Andrew C. Amigo^d, Marie Francesca M. Ansay^e, Nenad Zelenkov^e, Steve Samuel Thomas^f, and Krishnaswami Vijayaraghavan^g

^aDepartment of Medicine, Lincoln Medical Center, New York, NY, USA; ^bCebu Institute of Medicine, Cebu City, Philippines; ^cCollege of Medicine, San Beda University, Manila, Philippines; ^dAteneo School of Medicine and Public Health, Manila, Philippines; ^eDepartment of Family Medicine, University of Pittsburgh Medical Center (UPMC) McKeesport, McKeesport, PA, USA; ^fArizona State University, Tempe, AZ, USA; ^gUniversity of Arizona, Tucson, AZ, USA

ABSTRACT

Background: Semaglutide is increasingly used in the management of type 2 diabetes mellitus and obesity. Ensuring the safety of this medication is crucial for its clinical use. This meta-analysis evaluates the safety profile of semaglutide across patient populations and treatment durations.

Methods: Randomized controlled trials assessing the safety of semaglutide vs. placebo, with specified treatment durations were identified. The primary outcome was occurrence of any cardiovascular adverse events. Secondary outcomes included sudden cardiac death, adverse events leading to death, adverse events, gastrointestinal side effects, occurrence of hypoglycemia, and new-onset neoplasm.

Results: A total of 23 studies met the inclusion criteria with a combined sample size of 57,911 participants. The meta-analysis revealed that the adverse event associated with semaglutide is gastrointestinal in nature (nausea and vomiting). No significant differences were observed between semaglutide and comparator groups.

Conclusion: Semaglutide appears to have a favorable safety profile across diverse patient populations and treatment durations, supporting its continued use in the management of type 2 diabetes mellitus and obesity. It is generally well-tolerated, with a low incidence of adverse events. Clinicians should be aware of these findings and monitor patients accordingly. Further long-term studies are warranted to assess the safety of semaglutide in clinical practice.

ARTICLE HISTORY

Received 10 May 2024
Revised 16 July 2024
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KEYWORDS

Semaglutide; safety profile; adverse events; meta-analysis; glucagon-like peptide-1 receptor agonist; type 2 diabetes mellitus; obesity



Futuro

Guidelines

Nota 100

Safety

Diabete

Weight

SUSTAIN - PIONEER

SELECT

STEP

FLOW

CKM

Recommendation Table 1 — Recommendations for diagnosing diabetes

Recommendations	Class ^a	Level ^b
Screening for diabetes is recommended in all individuals with CVD, ^c using fasting glucose and/or HbA1c. ^{5-7,36,37,39}	I	A
It is recommended that the diagnosis of diabetes is		B

~~glucose tolerance~~

, atrial fibrillation,

glucose levels and

C GUIDELINES

nt of diabetes

Developed by the task force on the management of cardiovascular disease in patients with diabetes of the European Society of Cardiology (ESC)

Authors/Task Force Members: Nikolaus Marx [†], (Chairperson) (Germany), Massimo Federici [†], (Chairperson) (Italy), Katharina Schütt [‡], (Task Force Co-ordinator) (Germany), Dirk Müller-Wieland [‡], (Task Force Co-ordinator)

Cardiovascular disease

Type 2 diabetes mellitus

Patient presentation

Evaluation

Diagnosis

Treatment

To reduce independent risk of ASCVD

GLP-1 RA^a (Class I)

SGLT2 inhibitor^b (Class I)

SGLT2 inhibitor^c (Class I)

SGLT2 inhibitor^d (Class I)

Finerenone (Class I)

Atherosclerotic cardiovascular disease risk reduction by glucose-lowering therapies in patients with T2DM

Empagliflozin, canagliflozin, or dapagliflozin are recommended in patients with T2DM and CVD, or at very high/high CV risk to reduce CV events.

Liraglutide, semaglutide, or dulaglutide are recommended in patients with T2DM and CVD, or at very high/high CV risk to reduce CV events.

I

A

I

A

SGLT2 inhibitor^e (Class I)

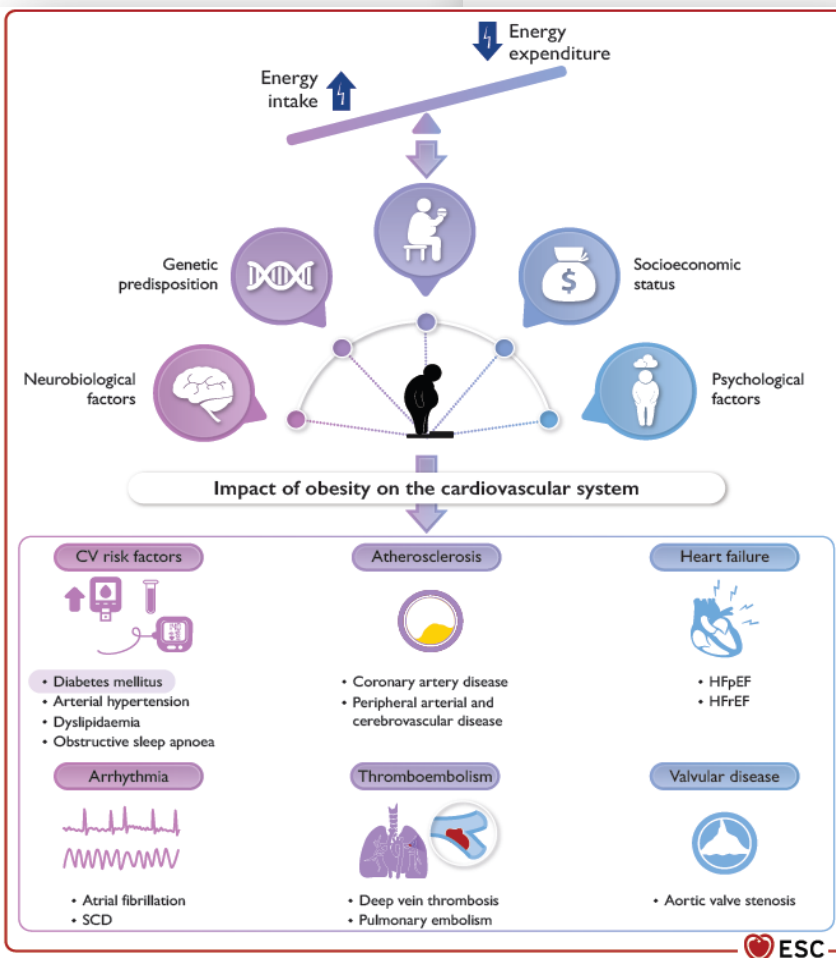
GLP-1 RA^f (Class I)

Finerenone (Class I)

All therapies are recommended independent of glucose control and in addition to standard of care

Obesity and cardiovascular disease: an ESC clinical consensus statement

Koskinas KC, et al. *Eur J Prev Cardiol.* 2024 Aug 30;zwae279.
doi: 10.1093/eurjpc/zwae279.



Lifestyle interventions		Pharmacological treatment					Intra-gastric and surgical interventions	
Dietary changes	Physical activity	Orlistat	Naltrexone/ Bupropion	Liraglutide 3 mg sc	Semaglutide 2.4 mg sc	Tirzepatide 5–15 mg sc	Intra-gastric procedures**	Bariatric surgery***
Blood pressure								
 —↓*	↓	↓	↑	↓	↓	↓	n/a	↓
LDL-cholesterol								
 ↓	↓	↓	↓	↓	↓	↓	n/a	↓
HDL-cholesterol								
 ↑	↑	—	↑	↑	↑	↑	n/a	↑
Triglycerides								
 ↓	↓	—	↓	↓	↓	↓	n/a	↓
% Weight reduction								
 3–10%	 1–3% Effective for weight loss maintenance	 4.1%	 4.8%	 5.4%	 12.5%	 17.8%	 7–12.8%	 25–30%

*Hypocaloric Mediterranean or low-carbohydrate diet
**Intra-gastric balloons; endoscopic sleeve gastroplasty
***Roux-en-Y gastric bypass; laparoscopic sleeve gastrectomy

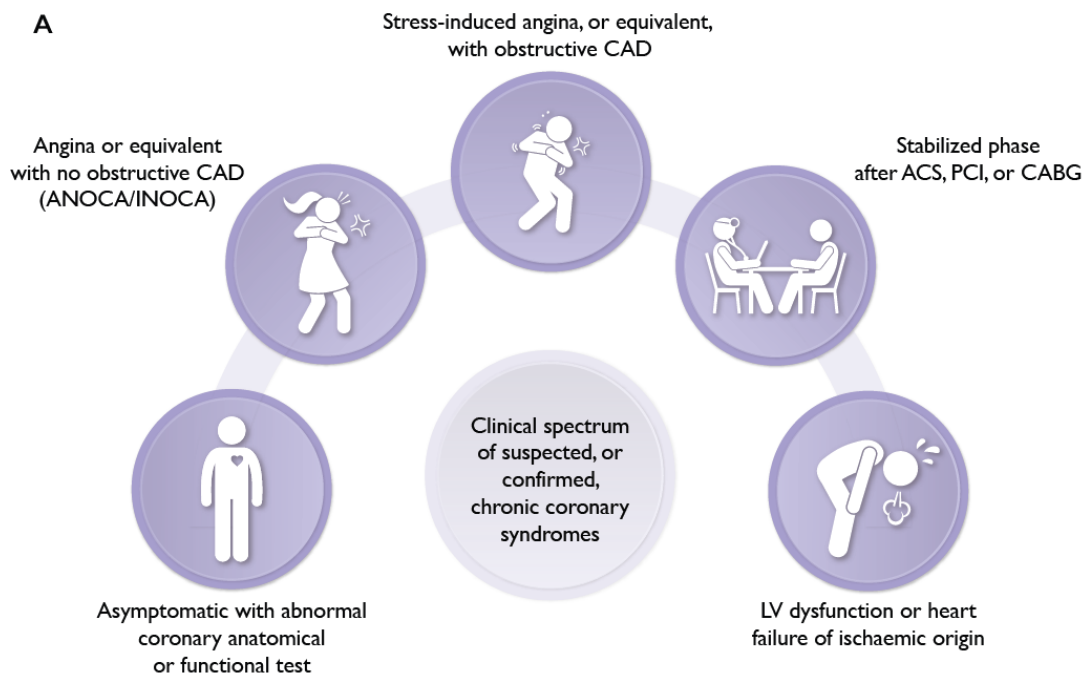


Among anti-obesity drugs, **semaglutide 2.4 mg once weekly** showed **clinical benefit** in a dedicated **CV outcome trial** involving **overweight or obese patients with pre-existing CVD** and **without diabetes**.

Developed by the task force for the management of chronic coronary syndromes of the European Society of Cardiology (ESC)

Vrints C, et al. Eur Heart J. 2024 Aug 30;ehae177. doi: 10.1093/eurheartj/ehae177.

Chronic Coronary Syndromes (CCS) are a range of clinical presentations or syndromes that arise due to **structural** and/or **functional alterations** related to **chronic diseases** of the **coronary arteries** and/or **microcirculation**.



Although **stable for long periods**, chronic coronary diseases are frequently **progressive** and may **destabilize** at any moment with the development of an **ACS**

Recommendation Table 19 — Recommendations for sodium–glucose cotransporter 2 inhibitors and/or glucagon-like peptide-1 receptor agonists in patients with chronic coronary syndrome (see also Evidence Table 19)

Recommendations	Class ^a	Level ^b
CCS patients with type 2 diabetes		
SGLT2 inhibitors with proven CV benefit ^c are recommended in patients with T2DM and CCS to reduce CV events, independent of baseline or target HbA1c and independent of concomitant glucose-lowering medication. ^{86,688,695,697,700}	I	A
GLP-1 receptor agonists with proven CV benefit ^d are recommended in patients with T2DM and CCS to reduce CV events, independent of baseline or target HbA1c and independent of concomitant glucose-lowering medication. ^{710,711}	I	A

^aClass of recommendation.

^bLevel of evidence.

^cCanagliflozin, dapagliflozin, empagliflozin, sotagliflozin (listed in alphabetical order).

^dDulaglutide, efpeglenatide, liraglutide, semaglutide (listed in alphabetical order).



Futuro

Guidelines

Nota 100

Safety

Diabete

Weight

SUSTAIN - PIONEER

SELECT

STEP

FLOW

CKM

SCHEDA PRESCRITTIVA

Nota AIFA 100

Scheda di prima prescrizione (versione del 23 febbraio 2025)

DI INIBITORI DEL SGLT2, AGONISTI RECETTORIALI DEL GLP1, INIBITORI DEL DPP4 E DOPPI AGONISTI RECETTORIALI GIP/GLP1 NEL TRATTAMENTO DEL DIABETE MELLITO TIPO 2

Da compilare a cura del prescrittore che seguirà il paziente nella gestione del trattamento e del follow-up periodico (Specialista SSN, Medico di Medicina Generale).

Scheda di prima prescrizione

Medico prescrittore _____ Tel _____

Specificare se: ☐ Medico di Medicina Generale ☐ Specialista in _____

U.O. _____ Az. Sanitaria _____

Paziente (nome e cognome) _____

Sesso: ☐ M ☐ F Data di Nascita _____ Codice Fiscale _____

Residenza _____

Valutazione

Paziente in trattamento con metformina: ☐ Sì ☐ No, per controindicazione o intolleranza

Mancato raggiungimento/mantenimento degli obiettivi glicemici individuali prefissati o necessità di modificare la terapia in corso anche nel caso di HbA1c a target: ☐ Sì

Indicare le principali motivazioni della strategia terapeutica che si propone di prescrivere:

☐ prevenzione CV secondaria*

☐ rischio CV elevato**

☐ scompenso cardiaco (solo se SGLT2i)

☐ malattia renale cronica*** (solo se SGLT2i)

☐ mancato raggiungimento/mantenimento degli obiettivi glicemici individuali prefissati****

☐ solo per DPP4i: controindicazione o intolleranza a SGLT2i e GLP1-RA (nel paziente a rischio CV elevato o con malattia CV, malattia renale cronica o scompenso cardiaco)

☐ altra motivazione (specificare) _____

*per prevenzione CV secondaria si intende la presenza di malattia cardiovascolare (cardiopatia ischemica, IMA, bypass aortocoronarico, angioplastica, procedura di rivascolarizzazione coronarica, coronaropatia), malattia cerebrovascolare (pregresso ictus o TIA, rivascolarizzazione carotidea) o arteriopatia periferica sintomatica.

**per rischio CV elevato, nel paziente senza malattia CV conclamata, si intende: presenza di danno vascolare aterosclerotico documentato (es. malattia coronarica multivasale o stenosi carotidea >50%); presenza di danno in un organo target; presenza di almeno tre fattori di rischio CV (tra età >50 anni, ipertensione, dislipidemia, obesità, fumo di sigaretta).

***per malattia renale cronica si intende la presenza di GFR <60 mL/min e/o di albuminuria (micro o macro).

****per i DPP4i: solo nel paziente non a rischio CV elevato o senza malattia CV, malattia renale cronica o scompenso cardiaco.

Doppi agonisti recettoriali GIP/GLP1

Al momento per il *first in class* tirzepatide sono disponibili soltanto i risultati degli studi clinici randomizzati che ne hanno valutato primariamente il beneficio in termini di riduzione dell'HbA1c mentre è in corso lo studio, di confronto vs dulaglutide 1.5 mg OAW, sulla sicurezza ed efficacia cardiovascolare. In attesa delle evidenze su *hard endpoint* e nonostante i risultati sulla riduzione dell'HbA1c e del peso corporeo, i doppi agonisti recettoriali GIP/GLP1 dovrebbero rappresentare farmaci di seconda scelta nei soggetti con malattia renale cronica, malattia cardiovascolare o rischio cardiovascolare particolarmente elevato (multipli fattori di rischio o con un danno d'organo subclinico). Alla luce dei risultati finora ottenuti, questa classe di farmaci può rappresentare una opzione di prima scelta quando la principale necessità clinica consiste in una sostanziale riduzione dell'emoglobina

Nei pazienti di cui ai punti 1, 2, 3 e 4 gli inibitori del DPP4 e i doppi agonisti recettoriali GIP/GLP1 dovrebbero essere considerati soprattutto quando i farmaci per i quali esiste una dimostrazione di un beneficio clinico su esiti *hard* (eventi cardiovascolari maggiori o mortalità cardiovascolare) siano controindicati/non tollerati; in particolare, i doppi agonisti recettoriali GIP/GLP1 dovrebbero essere considerati quando sia necessaria una maggiore riduzione dell'emoglobina glicata oppure una importante riduzione del peso corporeo.



Futuro

Guidelines

Nota 100

Safety

Diabete

Weight

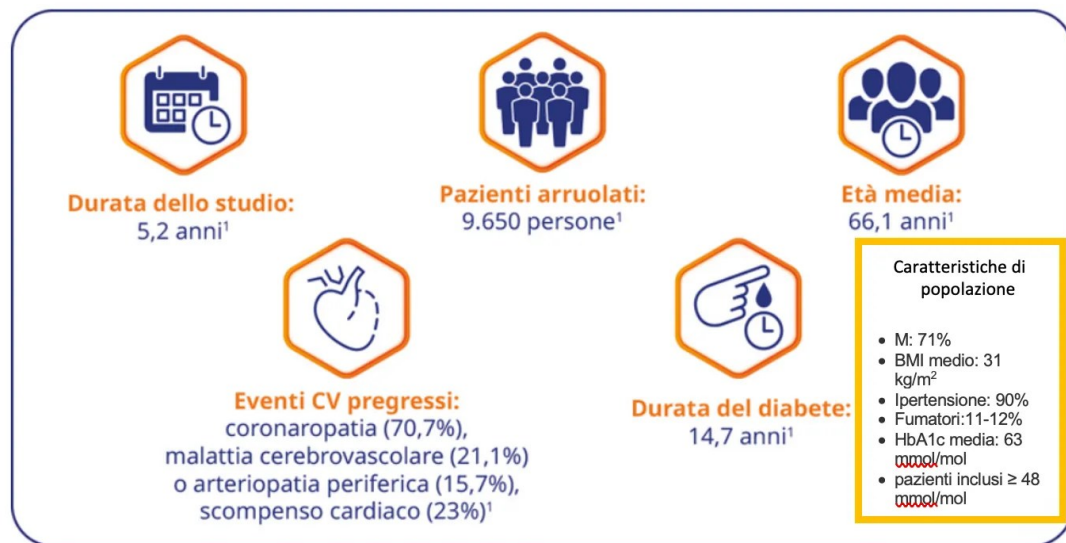
SUSTAIN - PIONEER

SELECT

STEP

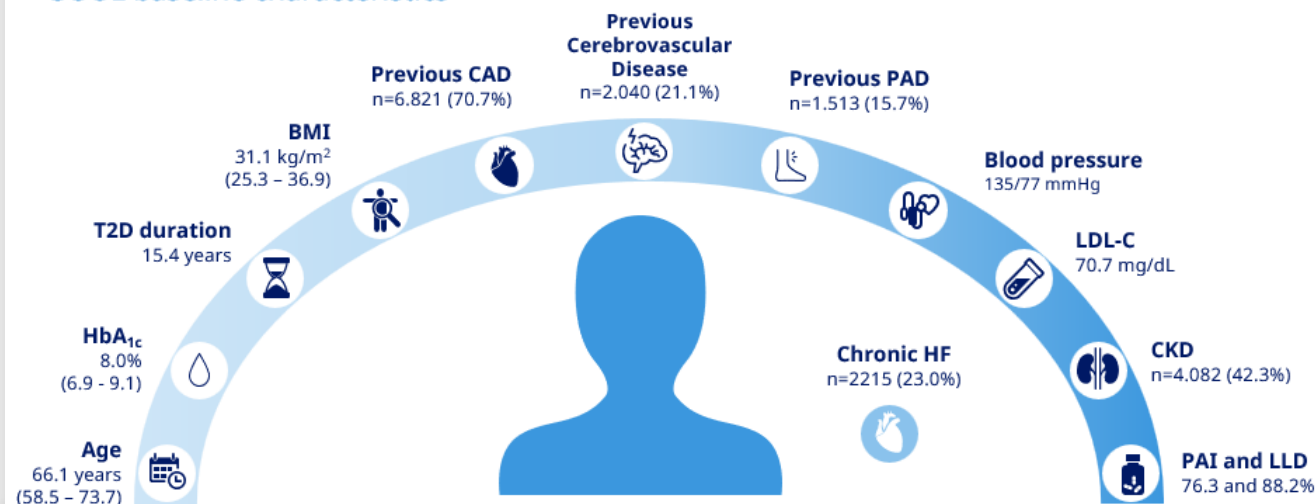
FLOW

CKM



Typical SOUL participant

SOUL baseline characteristics¹



Le analisi statistiche di superiorità rispetto al placebo hanno confermato il beneficio della semaglutide orale sulla riduzione dei classici MACE (eventi cardiovascolari maggiori) a tre punti (morte cardiovascolare, infarto miocardico non fatale e ictus non fatale) per un periodo di osservazione di 3.7 anni (HR 0,86; IC 95% 0,77-0,96; $p = 0,006$), *con una riduzione pertanto del rischio relativo del 18% e assoluto del 2%*. In particolare la riduzione più pronunciata si è osservata sulla riduzione dell'infarto miocardico (4 vs 5,2%, HR 0,73; IC 95% 0,61-0,88). L'effetto favorevole della semaglutide orale è risultato inoltre presente e omogeneo in tutti i diversi possibili sottogruppi (per età, sesso, con o senza obesità, con o senza malattia renale cronica) con un Number Needed to Treat (NNT) di 50 pazienti per 3 anni per prevenire un MACE, effetto coerente con la sua controparte iniettiva, con NNT sovrapponibile.



Dimensioni delle compresse: Le compresse della nuova formulazione sono di dimensioni più piccole e hanno una forma diversa (rotonda). I dosaggi sono impressi sulle compresse.

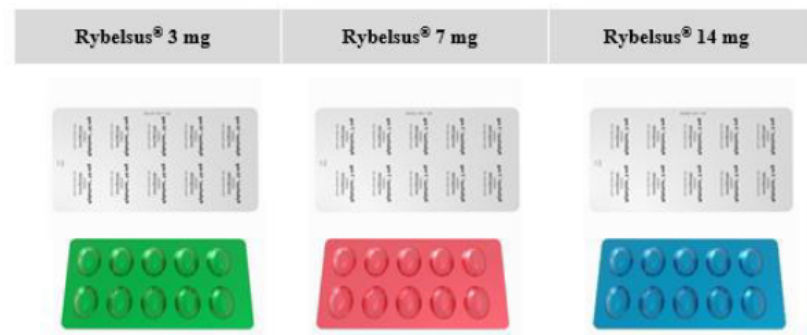
Iniziale

Nuovo



Confezionamento primario: i blister della nuova formulazione sono argentati sia sul fronte che sul retro e sono più piccoli rispetto ai blister della formulazione iniziale

Formulazione iniziale



Nuova formulazione

Rybelsus® 1.5 mg

Rybelsus® 4 mg

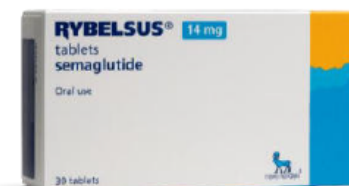
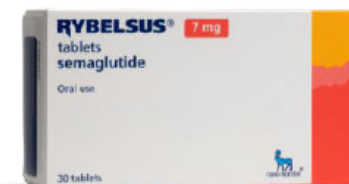
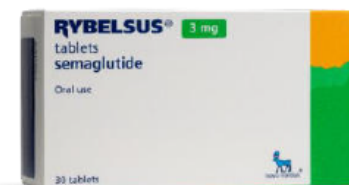
Rybelsus® 9 mg



Confezionamento secondario: le confezioni della nuova formulazione sono più piccole

Confezione della formulazione iniziale

Confezione della nuova formulazione





TO BE

CONTINUED...



STRIDE: Effects of 1 mg once-weekly semaglutide on functional capacity in patients with type 2 diabetes and peripheral artery disease



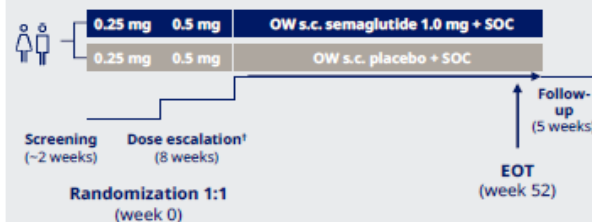
BACKGROUND

- Lower extremity peripheral artery disease (PAD) is a severe form of atherosclerotic cardiovascular disease.
- The classical symptom is intermittent claudication (IC), associated with limited walking ability and poor health-related quality of life (QoL)
- Type 2 diabetes is one of the leading causes of PAD; ~30% of patients with PAD have T2D.
- While anti-atherosclerotic drugs and lifestyle changes are recommended, there are no effective drugs to specifically improve functional outcomes in PAD and T2D.
- Semaglutide is a glucagon-like peptide-1 receptor agonist (GLP-1RA) approved as an adjunct to diet and exercise for glycemic control in patients with T2D. In the T2D SUSTAIN clinical trial program, once-weekly (OW) subcutaneous semaglutide 0.5 and 1.0 mg was superior for glycemic control and weight loss vs placebo and a range of approved antidiabetic drugs.
- In SUSTAIN 6, a dedicated CV outcomes trial, OW semaglutide resulted in a 26% reduction in three-point major adverse CV events (MACE) compared with placebo in patients with T2D at high CV risk, leading to its approval for MACE risk reduction in those with T2D and CV disease in the USA.
- Evidence suggests this may be partly attributable to the anti-inflammatory and anti-atherosclerotic effects of semaglutide, which may also apply to PAD

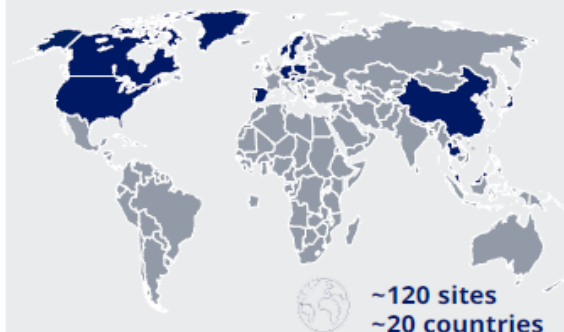
STUDY DESIGN

STRIDE is a 52-week, randomized, double-blind, placebo controlled, phase 3b trial.

- | 800 participants | And without |
|--|--|
| <ul style="list-style-type: none"> Adults with T2D PAD with IC ABI ≤ 0.90 or TBI ≤ 0.70 MWD ≤ 600m | <ul style="list-style-type: none"> Heart failure (NYHA III-IV) Other conditions that limit walking |



STRIDE is a Global Trial across Asia, Europe and North America



ENDPOINTS²

PRIMARY ENDPOINT



Change in **maximum walking distance** on a constant load treadmill test from baseline to week 52

SECONDARY CONFIRMATORY ENDPOINTS



Change in **pain-free walking distance** from baseline to week 52



Change in **Vascular QoL Questionnaire-6** from baseline to week 52

SUMMARY

STRIDE is the first and only dedicated PAD outcomes trial with a GLP-1RA and thus presents a unique trial design. While major adverse limb events typically occur in the later stages of PAD, STRIDE instead measures the effect of OW semaglutide on functional outcomes such as walking ability and QoL, which affect everyday living in patients with PAD and IC. STRIDE data will provide important clinical insights regarding the role of OW semaglutide in patients with T2D and PAD



Conclusion

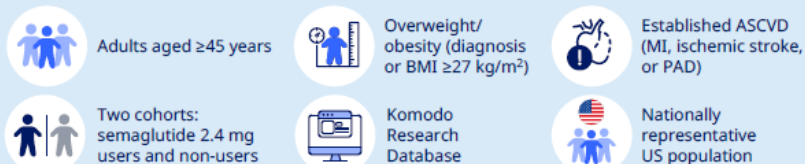
Semaglutide 2.4 mg was associated with a significantly lower risk of MACE-3 in this real-world study.

Real-world evidence cannot be directly compared to randomized control trial data

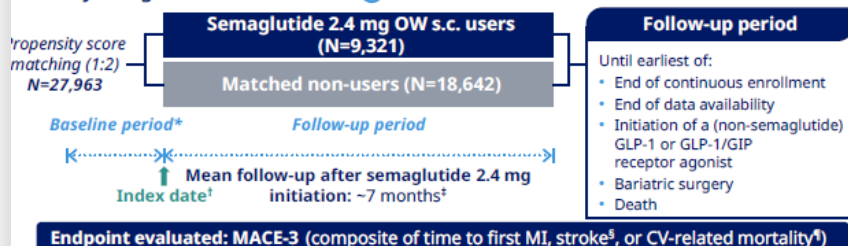
Objective

To evaluate semaglutide 2.4 mg effectiveness in reducing the risk of CV events in US adults with ASCVD and overweight or obesity without T2D in clinical practice.

Study population



Study design and outcomes



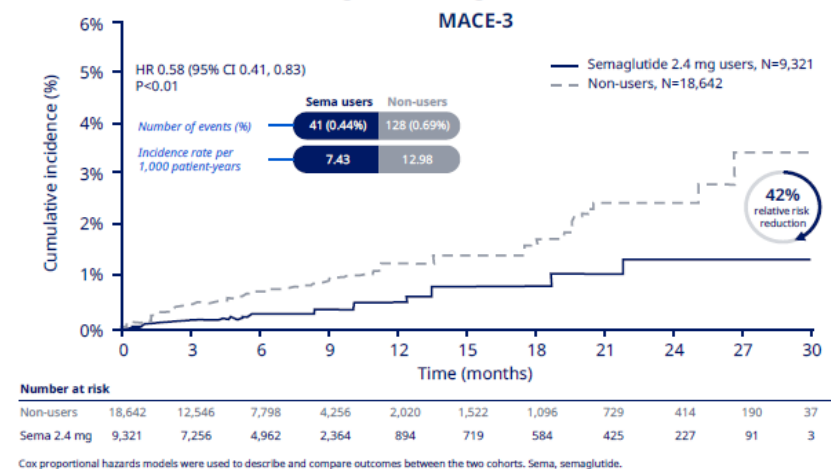
Key baseline demographics and characteristics*

Age (years, mean)	Female	Living with obesity	BMI (kg/m ² , mean) [†]
56.8 57.1	68.3% 67.5%	93.3% 93.7%	37.3 37.1
White	Black / African American	Hispanic / Latino	Other ethnicities [‡]
49.4% 48.6%	12.8% 12.7%	10.5% 10.6%	27.3% 28.0%
Prevalence of ASCVD	Myocardial infarction	Ischemic stroke	PAD
	34.1% 34.2%	30.9% 30.1%	44.6% 44.2%

Standardized mean difference ≤ 0.10 for all demographics and characteristics. *Baseline is data at index date. †Among those with available BMI data (n=6,032 for semaglutide 2.4 mg users; n=12,103 for non-users); ‡Includes Asian or Pacific Islander and patients without ethnicity data reported (i.e. 'unknown').

● Semaglutide 2.4 mg users, N=9,321
● Non-users, N=18,642

Lower risk of MACE-3 with semaglutide 2.4 mg



Conclusions

In this real-world study of patients in the US with overweight or obesity and ASCVD without T2D, semaglutide 2.4 mg was associated with significantly lower relative risk of MACE-3 (nonfatal MI, nonfatal stroke, or CV death)

Limitations

- Administrative data such as ICD-10 or procedure codes may be subject to coding inaccuracies or lack clinical detail, and laboratory and clinical assessments reflected routine clinical practice, which may result in variability in data.
- Caution should be exercised when interpreting the results of observational studies due to the potential of bias from unmeasured or residual confounding.
- The approval of semaglutide 2.4 mg in 2021 resulted in a relatively short duration of follow-up, limiting the assessment of long-term outcomes, and COVID-19 pandemic may have impacted data.
- Patients were required to have ≥ 12 months of continuous enrollment, which excluded patients who were treated with semaglutide 2.4 mg but experienced a change in insurance coverage during this period.

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; CI, confidence interval; CV, cardiovascular; ESKD, end-stage kidney disease; GLP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1; HR, hazard ratio; ICD, International Classification of Diseases; MACE, major adverse cardiovascular events; MACE-3, 3-point MACE; MI, myocardial infarction; OW, once weekly; PAD, peripheral artery disease; s.c., subcutaneous; SD, standard deviation; sema, semaglutide; T2D, type 2 diabetes; US, United States.

Reference: Zhao Z et al. Poster presented at the American College of Cardiology Scientific Session, March 29-31, 2025, Chicago, IL, USA.

Conclusions

From the STEER Real-World Study



In this real-world study of US patients with overweight or obesity and ASCVD but without diabetes, the primary endpoint demonstrated **a lower risk of CV events with semaglutide compared with tirzepatide**



Our findings support growing evidence that the established **CV benefit of semaglutide is molecule specific** and cannot be generalized to the GLP-1 or GIP/GLP-1 receptor agonist classes



Significantly lower risk of revised 3-point MACE with semaglutide vs tirzepatide

29%

ITT analysis
7.6 vs 10.8 incidence
per 1000 patient-years
HR, 0.71; $P = 0.046$

57%

Per-protocol analysis
4.4 vs 10.3 incidence
per 1000 patient-years
HR, 0.43; $P = 0.005$

ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1; HR, hazard ratio; ITT, intention to treat; MACE, major adverse cardiovascular event.

Wilson L, et al. Presented at the European Society of Cardiology (ESC) Congress together with World Congress of Cardiology; Madrid, Spain; August 29 - September 1, 2025.

Semaglutide 2.4 mg in participants with metabolic dysfunction-associated steatohepatitis: baseline characteristics and design of the phase 3 ESSENCE trial

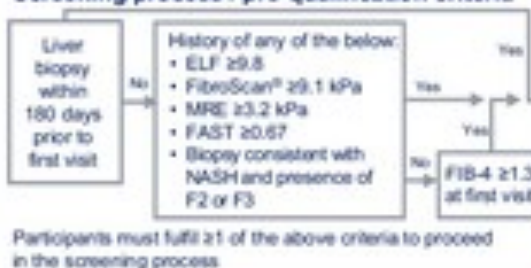
Key inclusion criteria

- Age ≥ 18 years old
- Biopsy-confirmed steatohepatitis stages F2/F3*
- NASH $\geq 4^1$

Key exclusion criteria

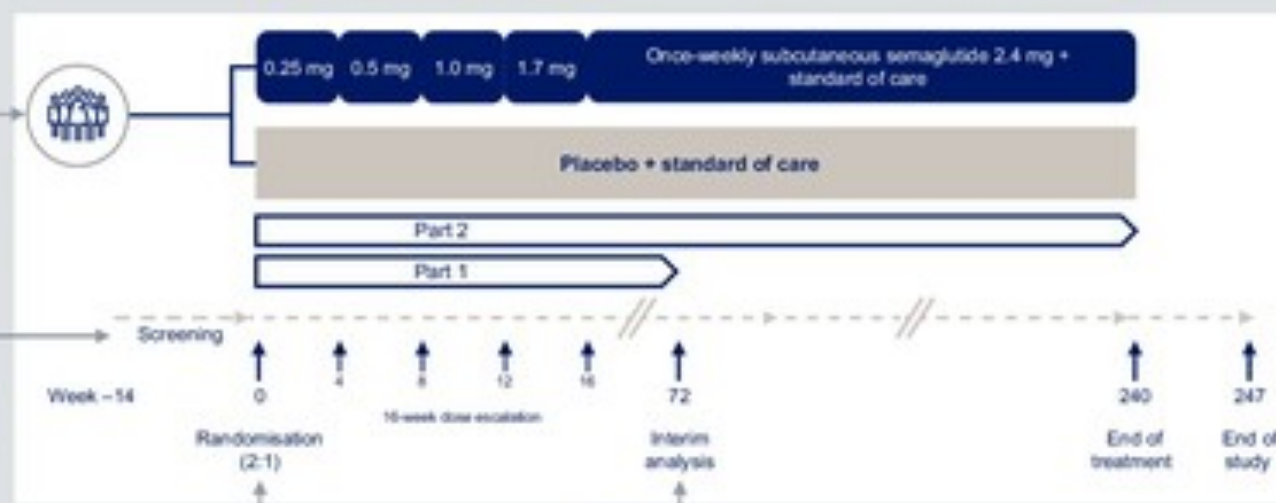
- Chronic liver diseases other than NAFLD
- Known or suspected excessive consumption of alcohol (>20 g/day for women or >30 g/day for men)
- Treatment with GLP-1RAs, or unstable use (based on investigator opinion) of glucose-lowering agents other than GLP-1RAs, lipid-lowering or weight loss medications during the 90-day period prior to screening

Screening process / pre-qualification criteria



ESSENCE is an ongoing, two-part, phase 3, randomised, multicentre, double-blind, parallel-group trial with Part 1 conducted at 253 sites in 37 countries.

Baseline characteristics of the first 800 randomised participants are reported, which includes demographics, laboratory parameters, liver histology, non-invasive tests and presence of MASLD cardiometabolic criteria.



Baseline characteristics



Endpoints

- Co-primary endpoints at 72 weeks:
- Resolution of steatohepatitis and no worsening of liver fibrosis
 - Improvement in liver fibrosis and no worsening of steatohepatitis

Results from Part 1 include the first 800 participants randomised between 27th May 2021 and 16th April 2023, and results from Part 2 will include an estimated 1200 participants. In Part 2 of the trial, the primary endpoint is cirrhosis-free survival at week 240.

Conclusion

The ESSENCE baseline population includes participants with clinically significant fibrosis stages 2 and 3.

Approximately 91% of participants had ≥ 1 positive NIT



Although recently defined MASLD cardiometabolic criteria¹ were not a requirement for study enrolment, almost all participants ($>99\%$) had at least one MASLD cardiometabolic criteria.

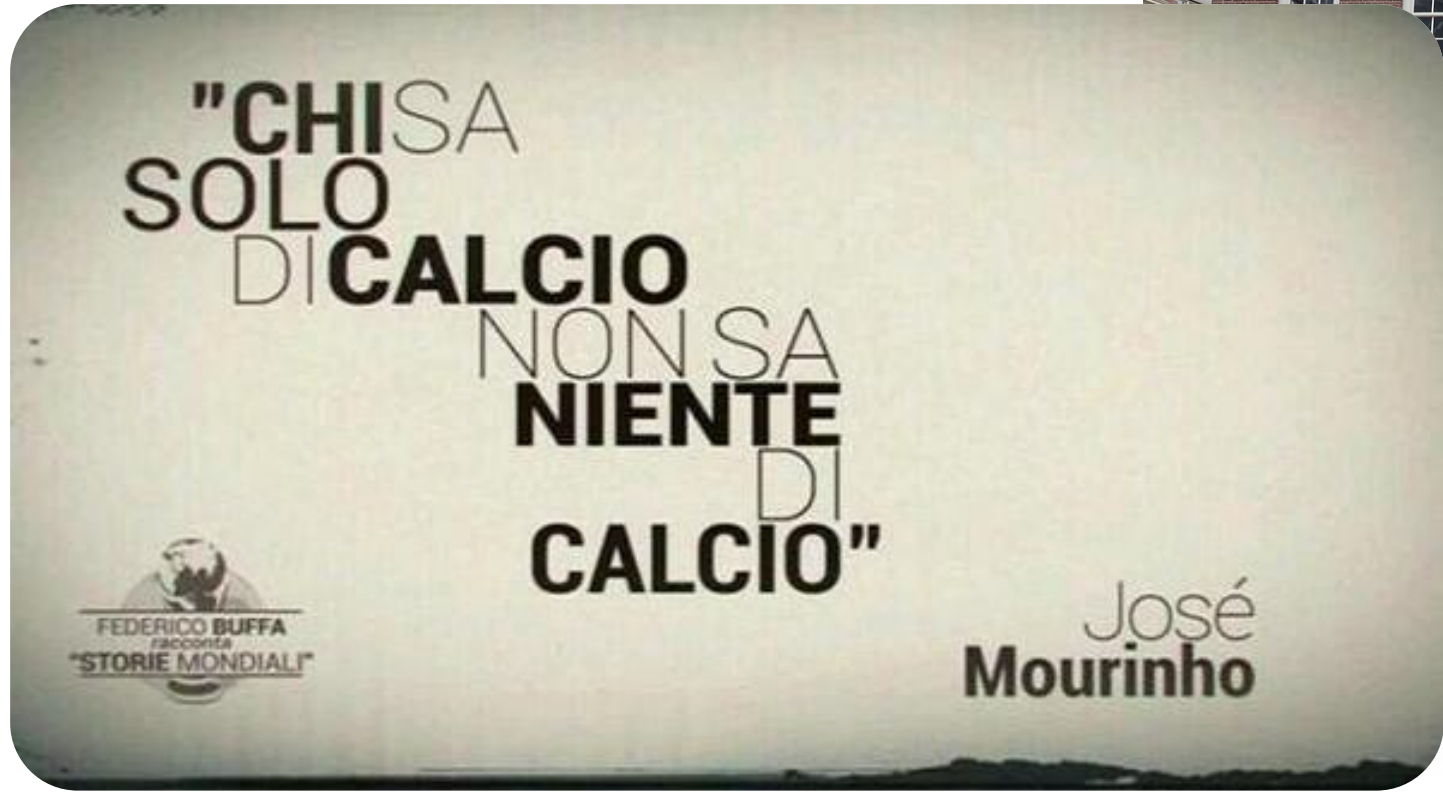
*According to NASH Clinical Research Network classification

¹With a score of ≥ 1 in steatosis, lobular inflammation and hepatocyte ballooning, based on central pathologist evaluation

Newsome, et al. *Aliment Pharmacol Ther*.

ELF, body mass index; ELF, enhanced liver fibrosis; F, fibrosis; FAST, FibroScan[®]-aspartate transaminase; FIB-4, fibrosis-4 index; GLP-1RA, glucagon-like peptide-1 receptor agonist; MASLD, metabolic dysfunction-associated steatotic liver disease; MRE, magnetic resonance elastography; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; NIT, non-invasive test; SD, standard deviation.

1. Rinella ME, et al. *J Hepatol* 2023;79(5):1542-56.



Visualizza tutti i formati ed edizioni

di Luigi Gianturco (Autore)

Una storia avvincente che vi catturerà sin dalle prime pagine. Un viaggio attraverso l'Italia ed il Nord Europa con tanti sviluppi come se fosse un thriller, anche se molto più patinato. Il lettore si immedesimerà con i protagonisti e proverà a suggerire mosse o tifare, come nello sport, per una soluzione ai tanti enigmi. Jennifer o Ilaria? Jennifer o Jennifer? Chi la spunterà alla fine della complicata e tanto articolata trama sempre piena di colpi di scena? Ognuno di voi avrà l'opportunità di muoversi assieme al protagonista principale, Luigi, alla ricerca della sua donna del mistero, alla ricerca del più minuscolo indizio e del profondo dettaglio, alla ricerca anche di se stessi. Sarà una lunga partita a scacchi con un fantomatico "avvocato Vita" con un finale quasi inimmaginabile e da assaporare a papille piene. Buona lettura!

 Segnala un problema con questo prodotto

Lunghezza stampa

1.
127 pagine

Lingua



Italiano

Data di pubblicazione



29 agosto 2024

Età di lettura



16 - 18 anni

Scorri sopra l'immagine per ingrandirla



LUIGI GIAN TURCO

SORRISI NASCOSTI

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Collana: Nuove voci Strade
Pagine: 62
ISBN-9788830679054

...i reali desideri e aspirazioni. C'è anche tanta frustrazione e rimorso in questo
uomo: il rapporto con la figlia, non coltivato negli anni più belli della vita, è ora
tenuto in scacco da una relazione che per forza di cose deve essere più matura.
Il lettore di questo romanzo dagli echi autobiografici viene accompagnato in un
viaggio intenso e conturbante, con un finale che crea ancora più disorien-
to. Ingredienti essenziali di una storia che vuole colpire (e attac-

Gruppo
Albatros Il Filo

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Trial	Popolazione	Intervento	Outcome Principale	Riduzione Mortalità CV	Riferimento
4S (1994)	CHD e ipercolesterolemia	Simvastatina vs placebo	Mortalità totale e CV	↓ 42% mortalità CV	Lancet 1994
CARE (1996)	Post-infarto, LDL moderato	Pravastatina vs placebo	Eventi coronarici maggiori	↓ 24% eventi coronarici	NEJM 1996
HOPE (2000)	Alto rischio CV	Ramipril vs placebo	Mortalità CV	↓ 26% mortalità CV	NEJM 2000
HPS (2002)	Alto rischio CV	Simvastatina vs placebo	Mortalità totale e CV	↓ 12% mortalità CV	Lancet 2002



PARADIGM-HF (2014)	Scompenso HFrEF	Sacubitril/valsartan vs enalapril	Mortalità CV e ospedalizzazioni	↓ 20% mortalità CV	NEJM 2014
HOPE-3 (2016)	Rischio CV intermedio	Rosuvastatina 10 mg	Morte CV, infarto, ictus	↓ 24% eventi CV	NEJM 2016
FOURIER / ODYSSEY (2017)	ASCVD e LDL elevato	Inibitori PCSK9	MACE (infarto, ictus, morte CV)	↓ significativa	NEJM 2017
DAPA-HF (2019)	Scompenso HFrEF	Dapagliflozin vs placebo	Mortalità CV e ospedalizzazioni	↓ significativa	NEJM 2019
EMPEROR-Reduced (2020)	Scompenso HFrEF	Empagliflozin vs placebo	Mortalità CV e ospedalizzazioni	↓ significativa	NEJM 2020



USO CONSOLIDATO

Sacubitril/valsartan

Rosuvastatina

Inibitori PCSK9

Dapagliflozin

Empagliflozin

co ...



Riduzione Mortalità CV

Farmaco

↓ 42% mortalità CV

SIMVA

↓ 24% eventi coronarici

PRAVA

↓ 26% mortalità CV

RAMIPRIL

↓ 12% mortalità CV

SIMVA

↓ 20% mortalità CV

ARNI

↓ 24% eventi CV

ROSU

↓ significativa

PCSK9-i

↓ significativa

DAPA

↓ significativa

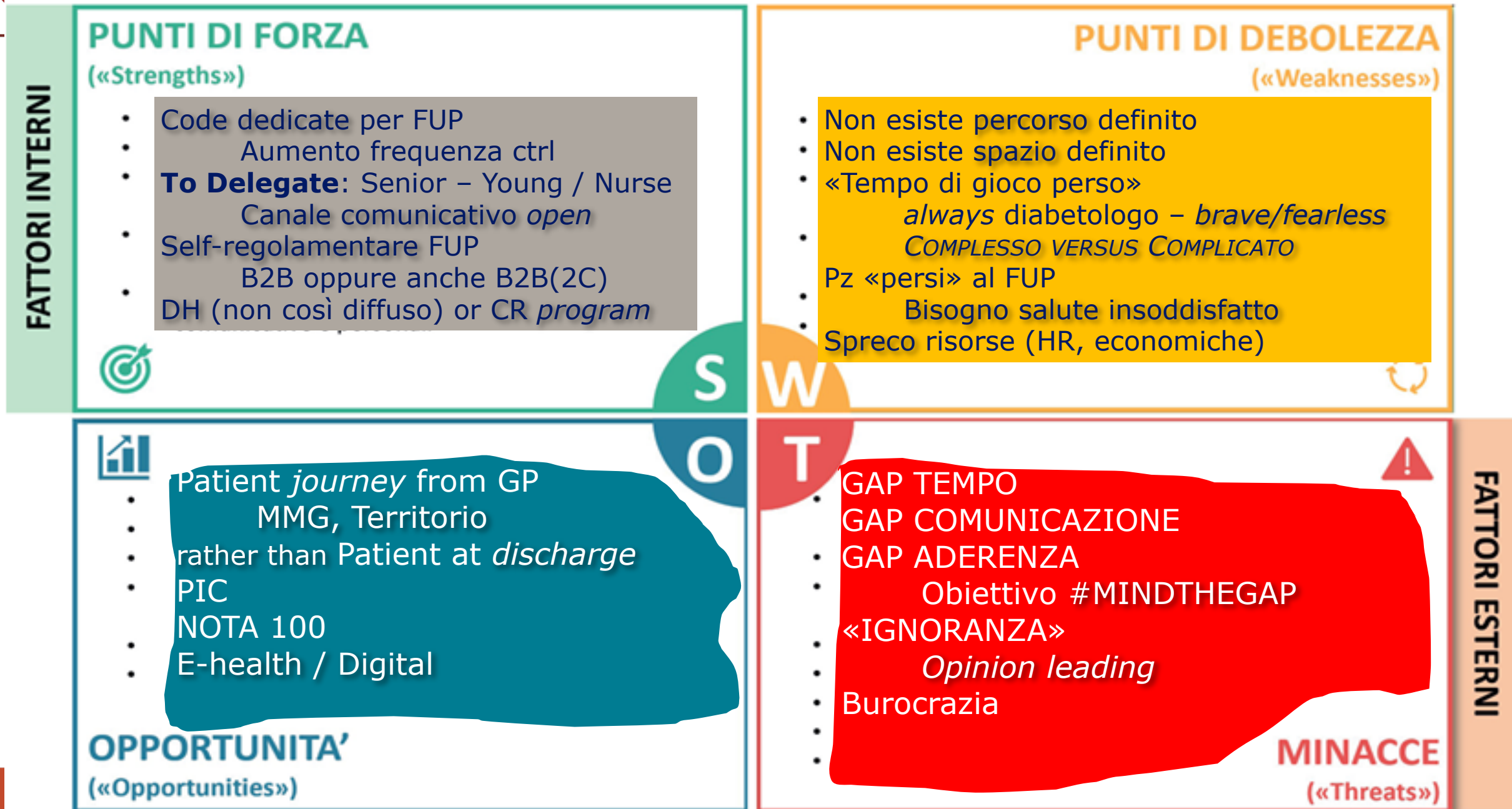
EMPA





Trial (Anno)	Formulazione / Dose	Popolazione Principale	Endpoint Primario (CV)	Risultato Principale
SUSTAIN 6 (2016)	Iniettabile (0.5 mg, 1.0 mg)	Pazienti con Diabete Tipo 2 (T2D) ad alto rischio CV (CV stabilita e/o malattia renale cronica).	MACE (Morte CV, Infarto non fatale, Ictus non fatale)	Riduzione del 26% del rischio relativo di MACE (HR 0.74, (p<0.001) per non-inferiorità e (p=0.02) per superiorità). Dimostra la sicurezza e il beneficio CV.
PIONEER 6 (2019)	Orale (14 mg)	Pazienti con T2D ad alto rischio CV.	MACE	Non-inferiorità di semaglutide orale rispetto al placebo per MACE (HR 0.79). Suggerisce un beneficio CV, ma lo studio era di sicurezza.
STEP Program (2021)	Iniettabile (2.4 mg)	Pazienti con Obesità o Sovrappeso (senza T2D in alcuni studi, con T2D in altri).	Variazioni di peso corporeo e parametri metabolici	Significativa e sostenuta perdita di peso (es. circa -15% vs placebo nello studio STEP 1). Ha portato all'approvazione per la gestione cronica del peso.
SELECT (2023)	Iniettabile (2.4 mg)	Pazienti con Obesità o Sovrappeso e Malattia CV stabilita , ma SENZA T2D .	MACE	Riduzione del 20% del rischio relativo di MACE (HR 0.80). Dimostra il beneficio CV anche nella popolazione non diabetica (prevenzione secondaria).
FLOW (2024)	Iniettabile (1.0 mg)	Pazienti con T2D e Malattia Renale Cronica (CKD) .	Composito di eventi renali maggiori e morte CV	Riduzione del 24% del rischio di progressione della CKD e morte renale/CV (HR 0.76). Dimostra la protezione renale.
SOUL (2025)	Orale (14 mg)	Pazienti con T2D ad alto rischio CV (CV stabilita e/o CKD).	MACE	Riduzione del 14% del rischio relativo di MACE (HR 0.86). Conferma l'efficacia CV anche della formulazione orale .







Caso 1

Pz in visita ambulatoriale cardiologica

Presenza di fattori di rischio CV

Identificazione di diabete di tipo 2

Alla visita
inizio terapia
Metformina +



Semaglutide orale



Caso 2

Pz ricoverato per evento cardiovascolare

Presenza di malattia ischemica

Identificazione di diabete di tipo 2

Alla dimissione
inizio terapia
Metformina +



Semaglutide orale



Caso 3

Pz DT2 in visita ambulatoriale cardiologica o post evento

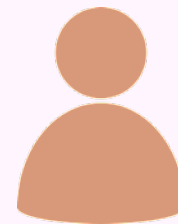
Trattamento con **METFORMINA**

Identificazione di fattori di rischio aterosclerotico o ASCVD

Add-on



Semaglutide orale



Caso 4

Pz DT2 in visita ambulatoriale cardiologica o post evento

Trattamento con **METFORMINA** e **DPP4i** o **SULFANILUREE**

Identificazione di fattori di rischio aterosclerotico o ASCVD

Sostituire con



Semaglutide orale



Caso 5

Pz DT2 in visita ambulatoriale cardiologica

Trattamento con **METFORMINA** e **SGLT2i**

Identificazione di fattori di rischio aterosclerotico o ASCVD

Valutazione indicazione SGLT2i

Sostituire con / Add-on

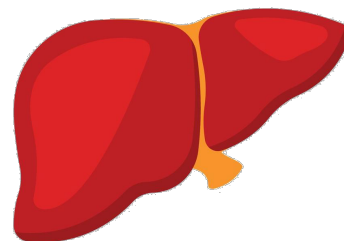


Semaglutide orale



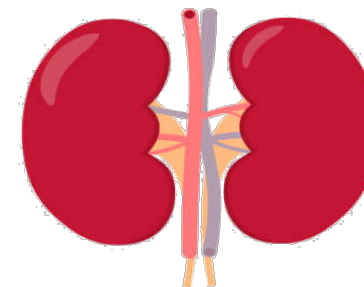
Paziente Anziano

Non è richiesta la
correzione della dose
in base all'età



Paziente con malattia epatica

Non è richiesta la correzione
della dose per i pazienti con
compromissione della
funzionalità epatica

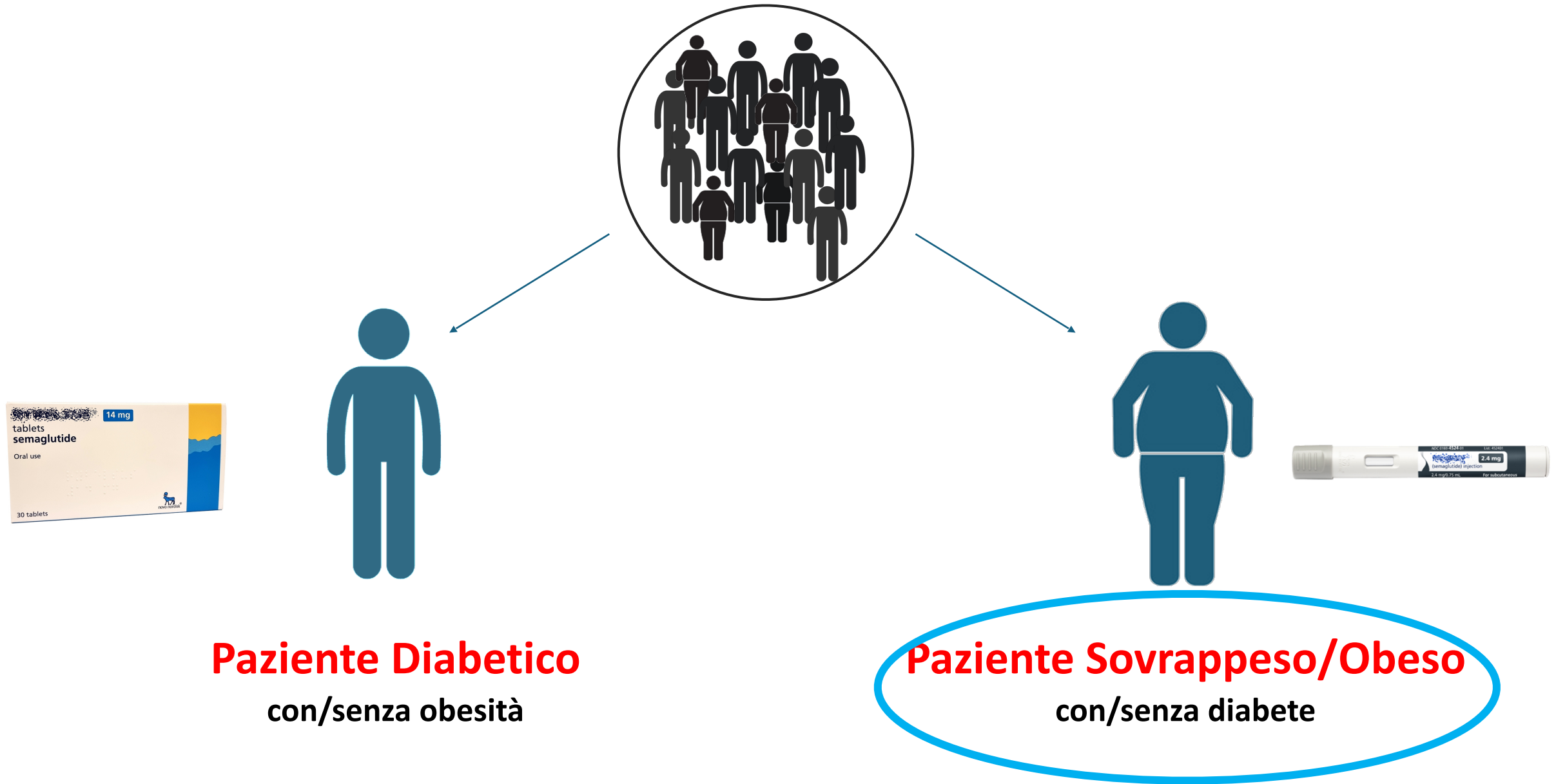


Paziente con malattia renale

Non è richiesta la correzione
della dose per i pazienti con
compromissione della
funzionalità renale lieve,
moderata o severa. [...]
Semaglutide non è raccomandato
nei pazienti con malattia renale
allo stadio terminale



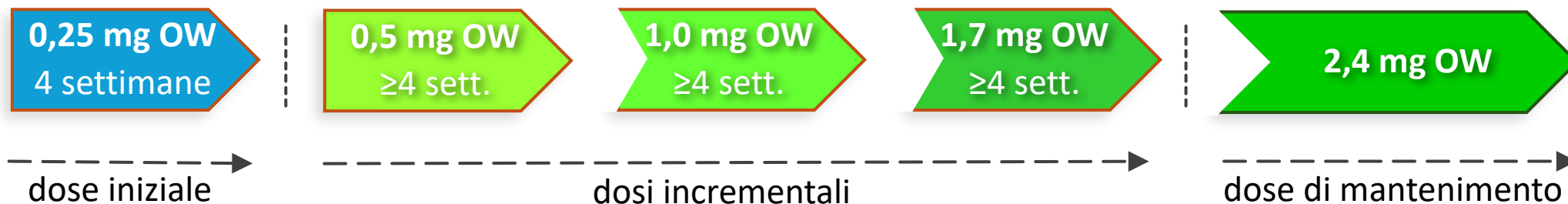
Due popolazioni ad elevato rischio CV – ad ognuno la «propria» semaglutide



Semaglutide sc – Scheda tecnica: posologia e modo d'assunzione



● Posologia:



● Modo d'assunzione: **1 volta alla settimana** per via **sottocutanea** nell'addome, coscia o braccio

La somministrazione può avvenire in qualsiasi ora del giorno, indipendentemente dai pasti

Se una dose viene saltata, assumere la dose appena possibile ed entro 5 gg dalla dose dimenticata
Se oltre 5 giorni la dose successiva deve essere somministrata nel giorno regolarmente pianificato



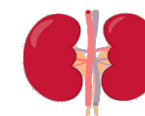
Paziente Anziano

Non è richiesta
correzione della dose in
base all'età



Paziente con malattia epatica

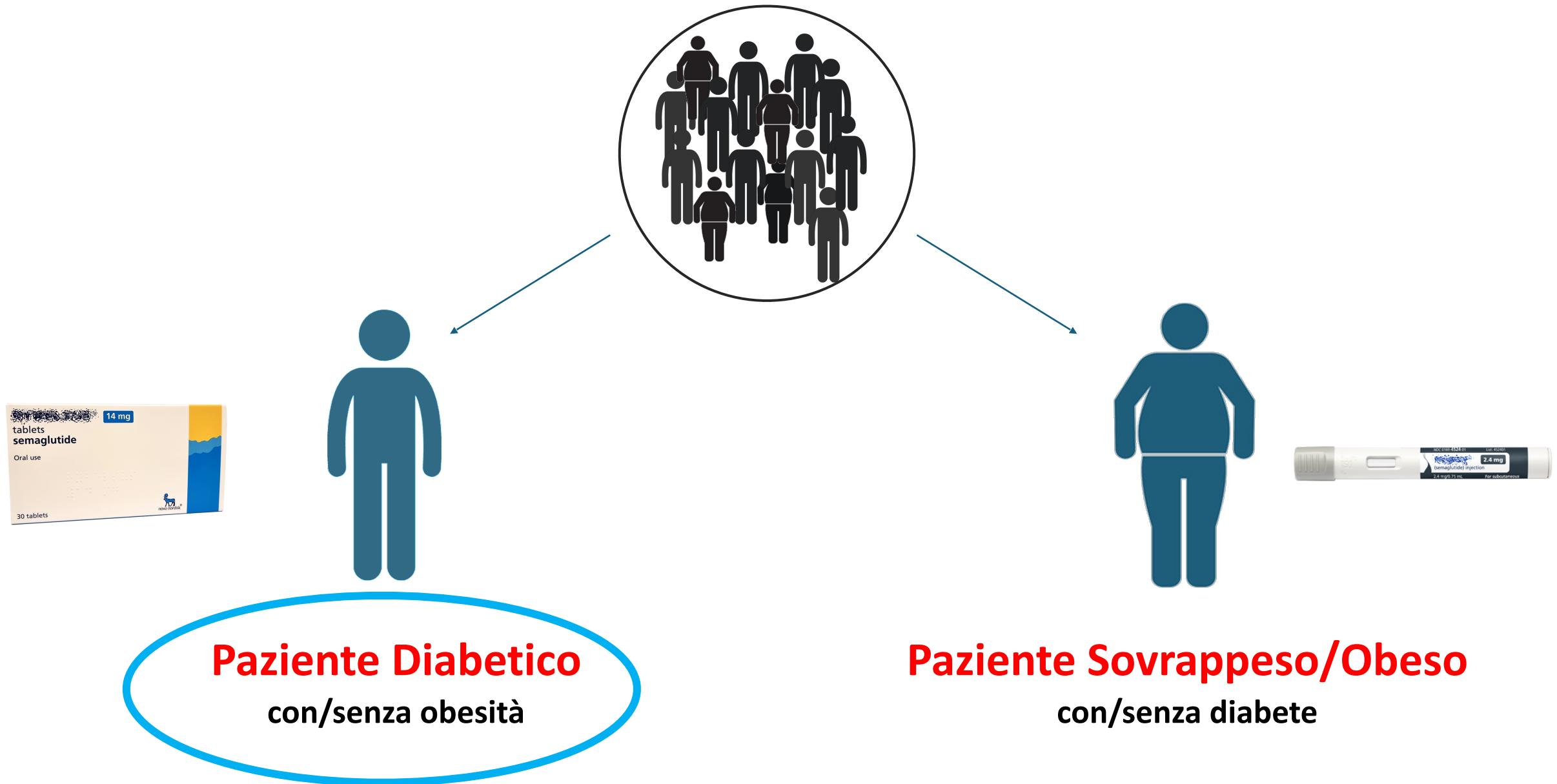
Non è richiesta correzione della dose
per pazienti con compromissione della
funzionalità epatica lieve o moderata



Paziente con malattia renale

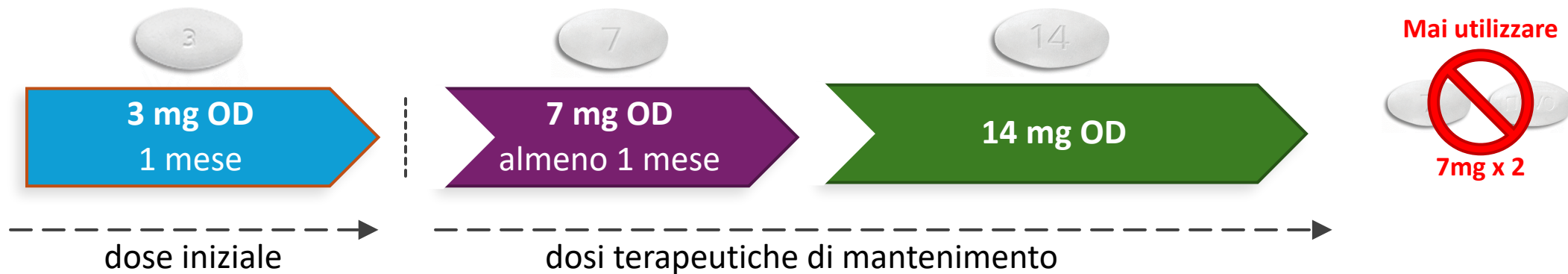
Non è richiesta correzione della dose per pazienti con
compromissione della funzionalità renale lieve o
moderata. Semaglutide non è raccomandato nei pazienti
con malattia renale severa (eGFR <30 ml/min/1.73m²) o
terminale

Due popolazioni ad elevato rischio CV – ad ognuno la «propria» semaglutide



Semaglutide orale – Scheda tecnica: posologia e modo d'assunzione

● Posologia:



● Modo d'assunzione: 1 volta al giorno a digiuno con mezzo bicchiere d'acqua



Attendere **almeno 30 min** prima di assumere cibo, bevande o altri medicinali

Le compresse non devono essere suddivise, frantumate o masticate

Se una dose viene saltata, assumere la dose successiva il giorno dopo all'ora indicata

● Background therapy: metformina e/o SGLT2i e/o tiazolidindioni → mantenere dosi iniziali

insulina o sulfanilurea → considerare possibile riduzione dosi iniziali





Applicazioni come **Shotsy - GLP-1 Tracker**, **SlimShot**, o **Wegovy Weight Loss Tracker** (disponibili sugli store iOS e Android) offrono funzionalità specifiche, come:



Tracciamento del Peso e dei Progressi: Permettono al paziente di visualizzare graficamente i risultati ottenuti. **Questo è fondamentale per gestire le aspettative:** vedere i progressi, anche se lenti, aiuta a mantenere alta la motivazione e a riconoscere che il farmaco *sta funzionando* in modo efficace.



Monitoraggio Dosi e Siti di Iniezione: Alcune app permettono di annotare il sito dell'ultima iniezione per evitare di iniettare sempre nello stesso punto. Esistono anche tutorial sul come farlo (es. click ON www.wegovy.com)



Promemoria Settimanale:

Aiutano a superare l'ostacolo della formulazione iniettiva, assicurando la corretta aderenza alla terapia con la somministrazione settimanale.



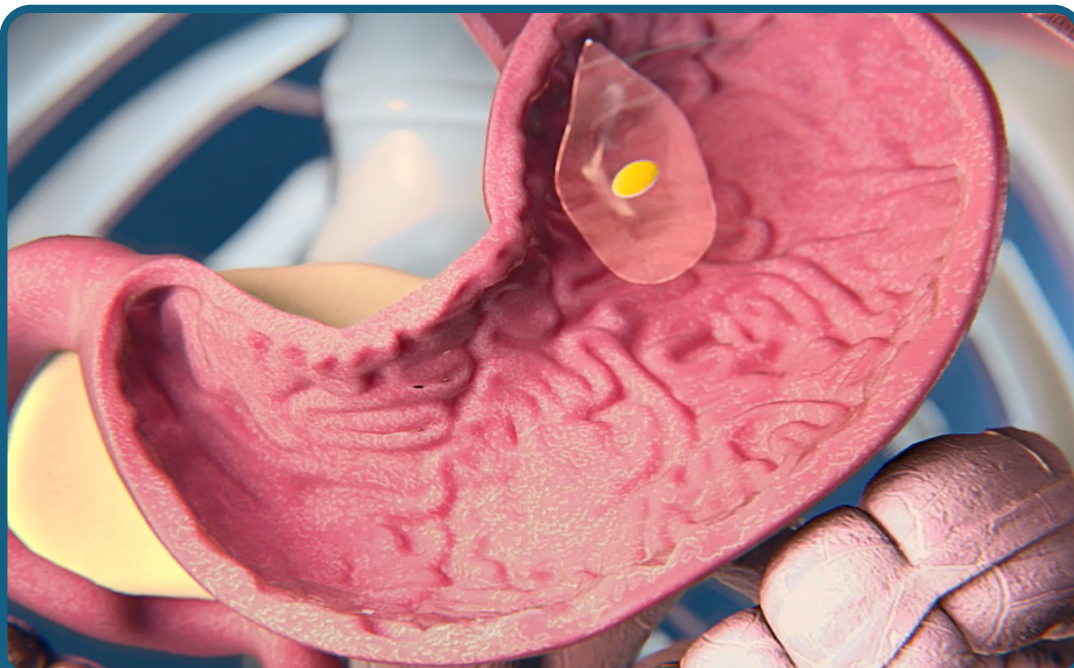
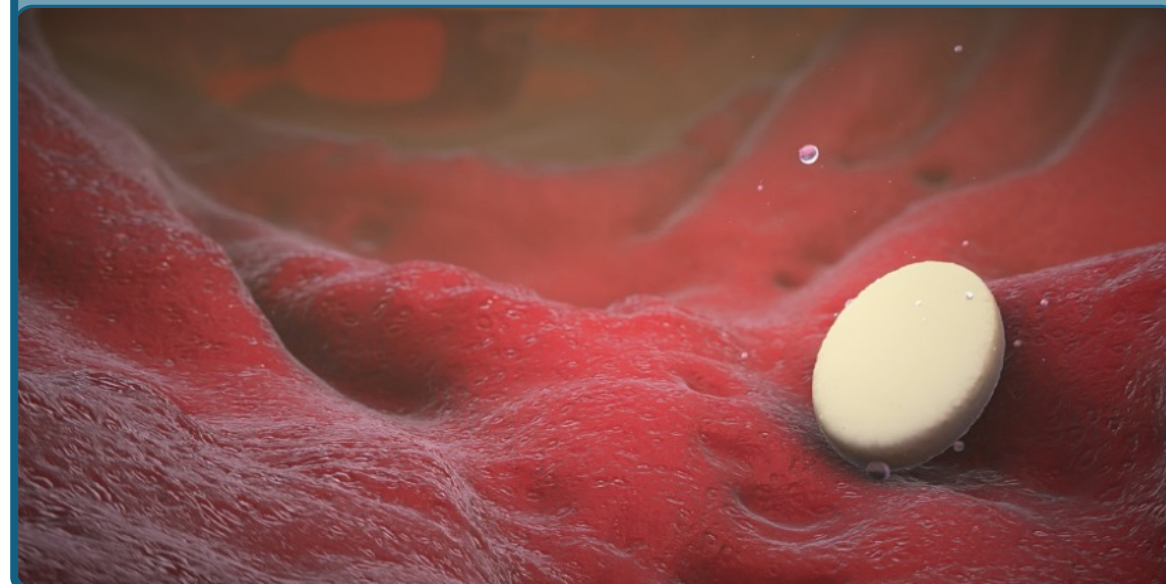
Diario Sintomi/Effetti Collaterali: Il paziente può registrare la nausea o altri effetti collaterali (comuni all'inizio e al cambio di dose), fornendole dati precisi per il *follow-up*.



Suitability and Usefulness of a Flexible Dosing Timing of Oral Semaglutide to Maximize Benefit in Clinical Practice: An Expert Panel

Riccardo Candido · Chiara Di Loreto · Paolo Desenzani · Paola Pantanetti ·
Cristina Romano · Silvio Settembrini · Sebastiano Bruno Solerte · Gian Paolo Fadini 

SNAC causes a local increase of pH leading to higher solubility and protection from proteolytic degradation



Absorption of semaglutide requires co-formulation with SNAC

