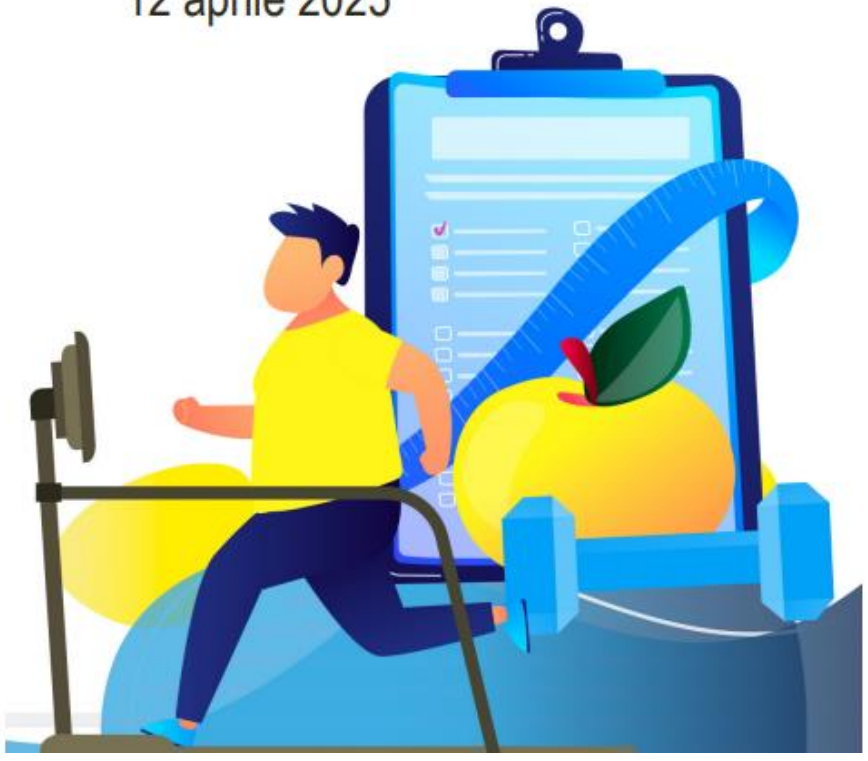
LA GESTIONE DEL SOGGETTO OBESO CON E SENZA DIABETE

Da Kennedy ad Obama:
dal sogno alle opportunità terapeutiche

TORINO
12 aprile 2025



Terza Sessione – "The best is yet to come"

Opportunità di terapia farmacologica

Moderatori: R. Fornengo, A.R. Pia

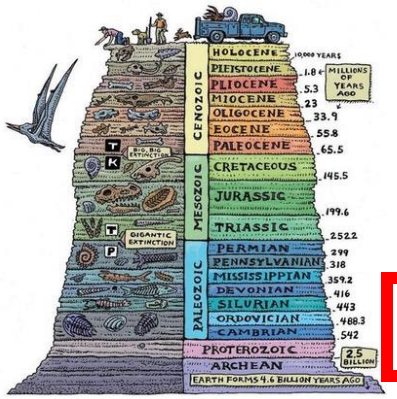
14.00 Effetto sul peso dei farmaci diabetologici
G. Margiotta

14.20 Agonisti GLP-1 e doppi agonisti:
ruolo nel paziente diabetico e non diabetico
M. Pellegrino

14.40 La remissione del diabete: un sogno divenuto realtà
M. Valenzano

15.00 Discussione sui temi trattati
Discussants: R. Fornengo, A.R. Pia

Ai sensi dell'art. 3.3 sul conflitto di interessi, pag. 17 del Regolamento Applicativo Stato-Regioni del 5/11/2009, dichiaro che negli ultimi 2 anni NON ho avuto rapporti diretti di finanziamento con soggetti portatori di interessi commerciali in campo sanitario.



ERE «DIABETOLOGICHE»

Benefit

Time

Containment	Management	Advanced optimization	Future
Pre 1922 Pre-insulin Limited/NO management Limited/NO monitoring	1923-1980s Basic insulin Non insulin – oral therapies Limited SMBG HbA1c for monitoring	1980-2016 Refined insulins Antidiabetic drugs in cardiorenal protection Broad SMG HbA1c for monitoring	2016-Now Advanced insulins Cardiorenal and Hepatic protection drugs Obesity management Increasing use F/CGM use Advanced hardware Algorhitmic assistance HbA1c for monitoring Emerging use of TIR	? Policy Prescriptions for Affordable Diabetes and Obesity Medications

EFFETTO INCRETINICO

- TREAT TO TARGET
- TREAT TO SATISFACTION
- TREAT TO BENEFIT
- TREAT TO PREVENT
- TREAT TO REMISSION

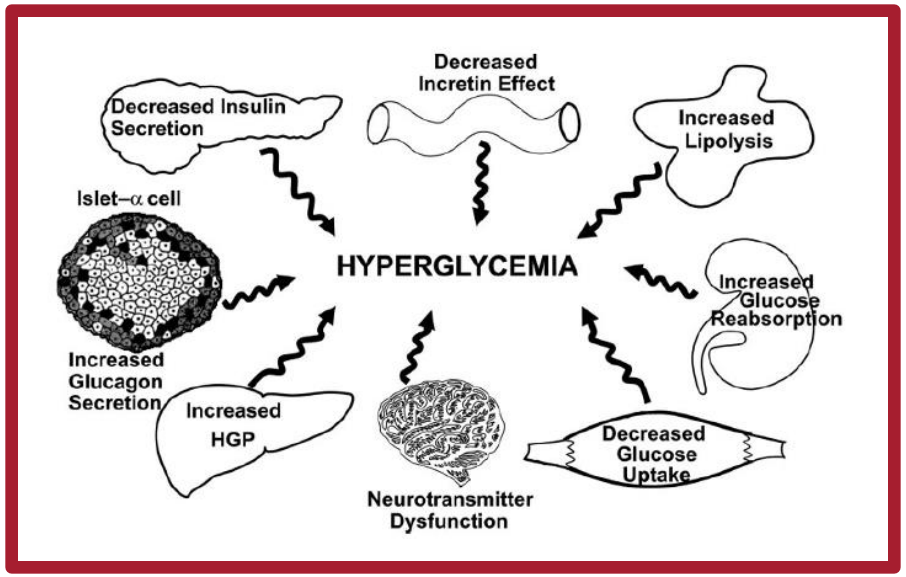
GLP1-BASED THERAPY

American Diabetes Association

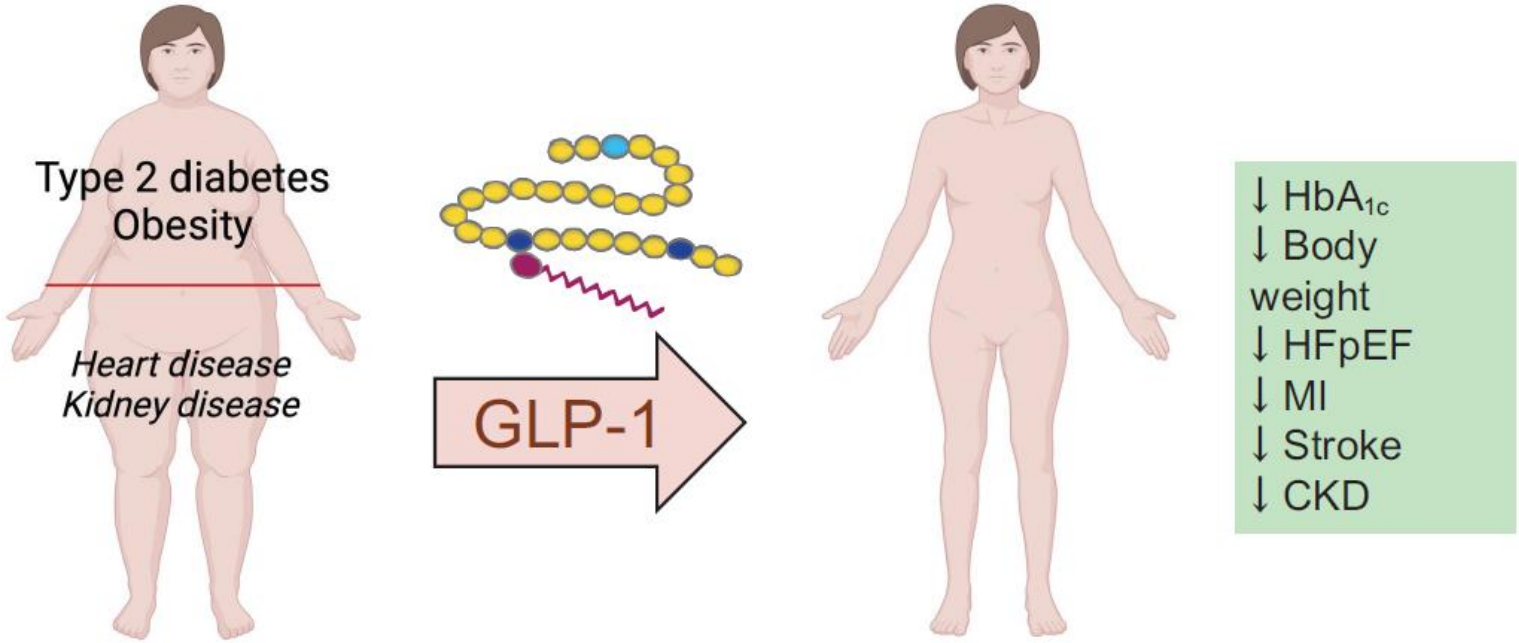
Efficacy and Safety of GLP-1 Medicines for Type 2 Diabetes and Obesity

Daniel J. Drucker

Diabetes Care 2024;47(11):1873–1888 | https://doi.org/10.2337/dci24-0003



GIP e “concetto incretinico”. Una breve storia
Umberto Goglia, Riccardo Fornengo
JAMD 2023 | VOL. 26 | N° 3



Adverse Events
Nausea, vomiting, constipation, diarrhea, abdominal discomfort, fatigue, gallbladder disease, acute kidney injury

CKD, chronic kidney disease; GLP-1, glucagon-like peptide 1; HFpEF, heart failure with preserved ejection fraction; MI, myocardial infarction.

Diabetes Volume 68, May 2019 897

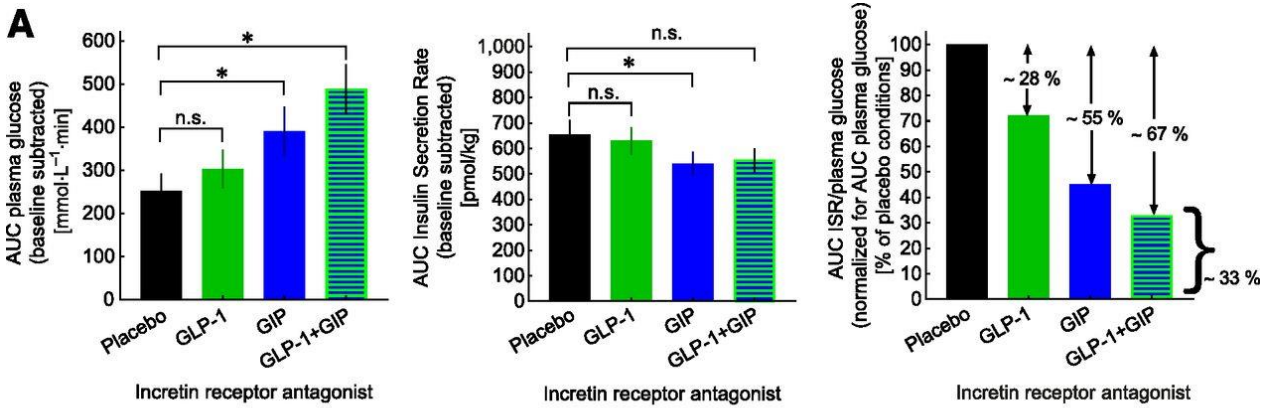
Check for updates

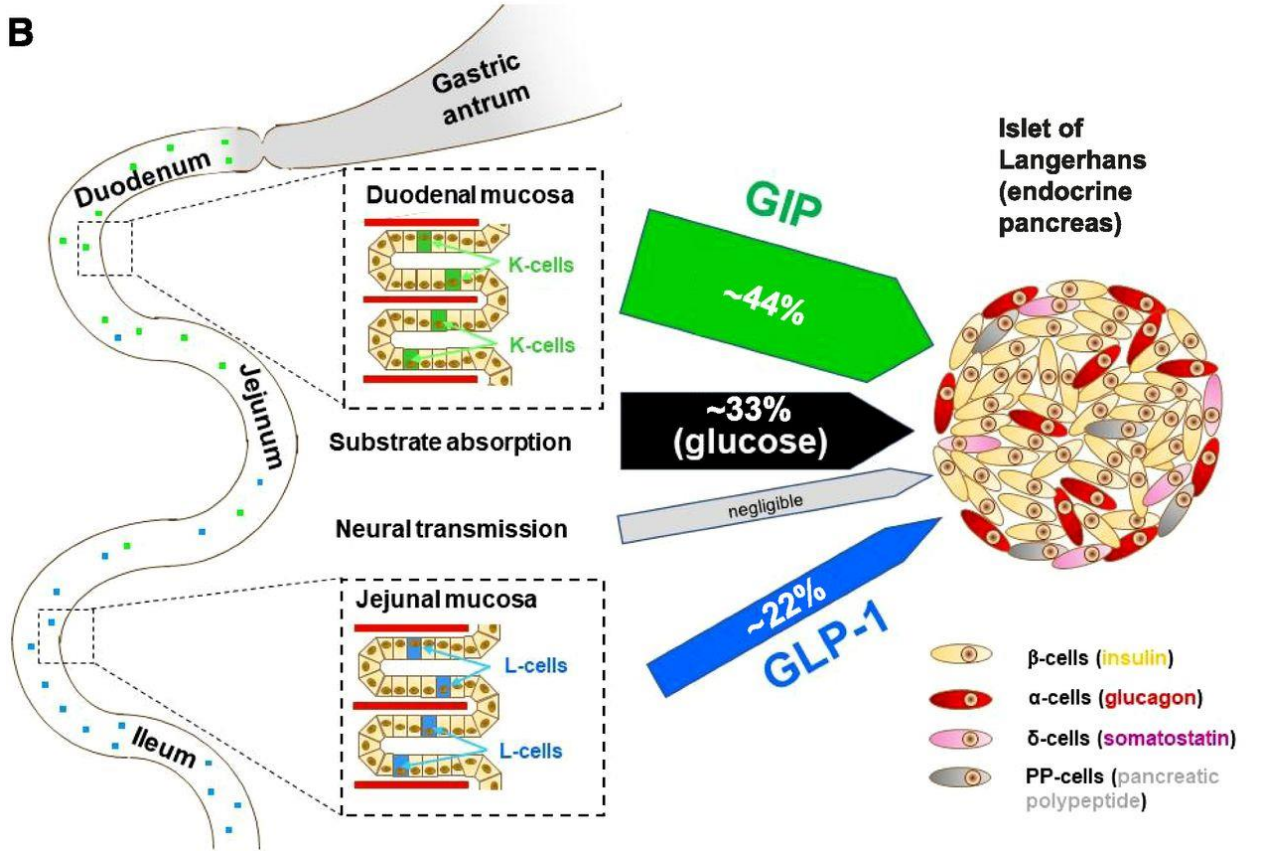
GIP and GLP-1: Stepsiblings Rather Than Monozygotic Twins Within the Incretin Family

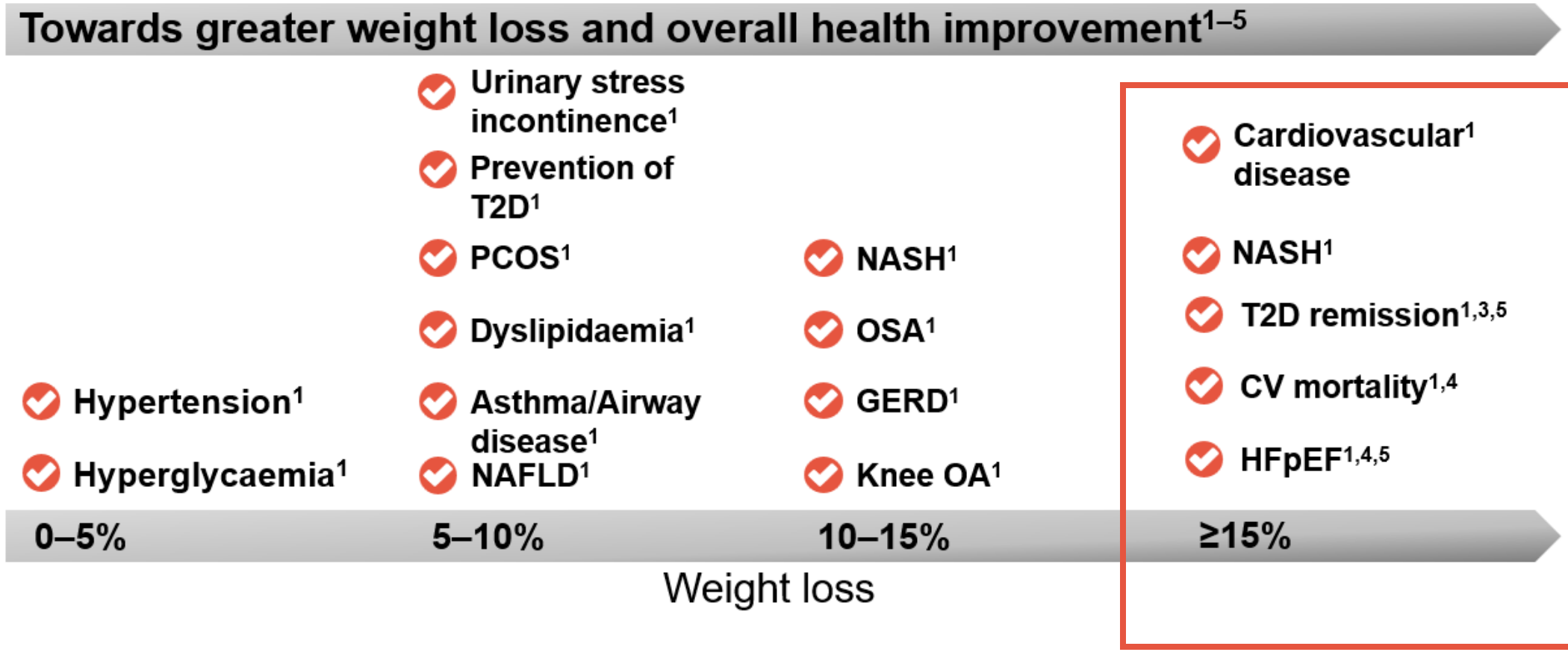
Michael A. Nauck and Juris J. Meier

Diabetes 2019;68:897–900 | https://doi.org/10.2337/dbi19-0005

GLP1-BASED THERAPY
UN UNICUUM TERAPEUTICO





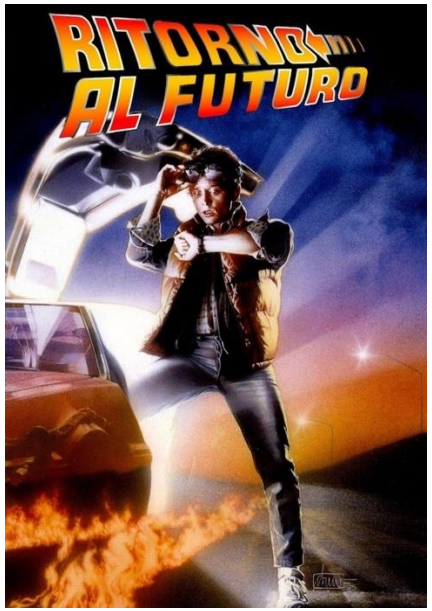


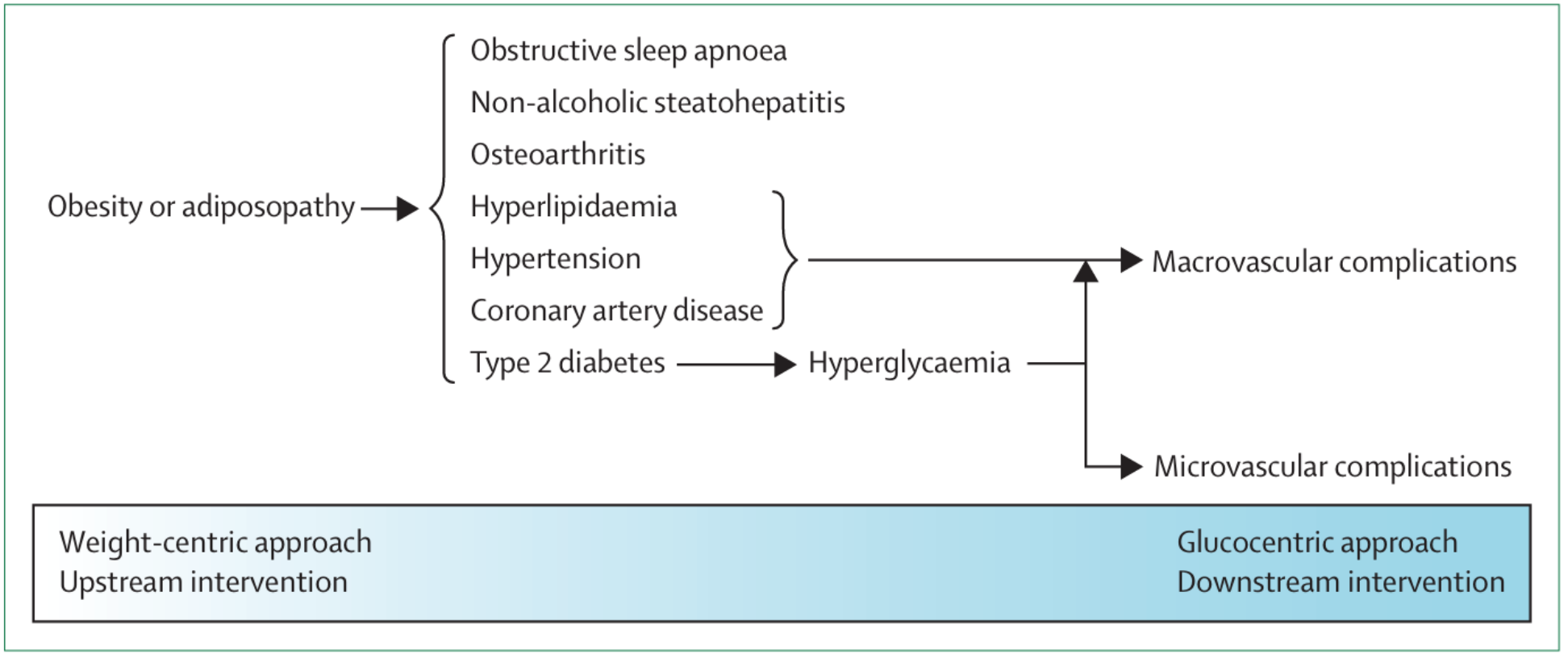
REVIEW · Volume 399, Issue 10322, P394-405, January 22, 2022 Download Full Issue

Obesity management as a primary treatment goal for type 2 diabetes: time to reframe the conversation

Prof Ildiko Lingvay, MD [a] · Priya Sumithran, PhD [b,c] · Ricardo V Cohen, MD [d] · Prof Carel W le Roux, MD [e,f]

APPROCCIO «KILOCENTRICO»





- tessuto adiposo come fattore chiave alla base del continuum tra obesità, diabete di tipo 2 e malattie cardiovascolari

- benefici terapeutici metabolici oltre la glicemia

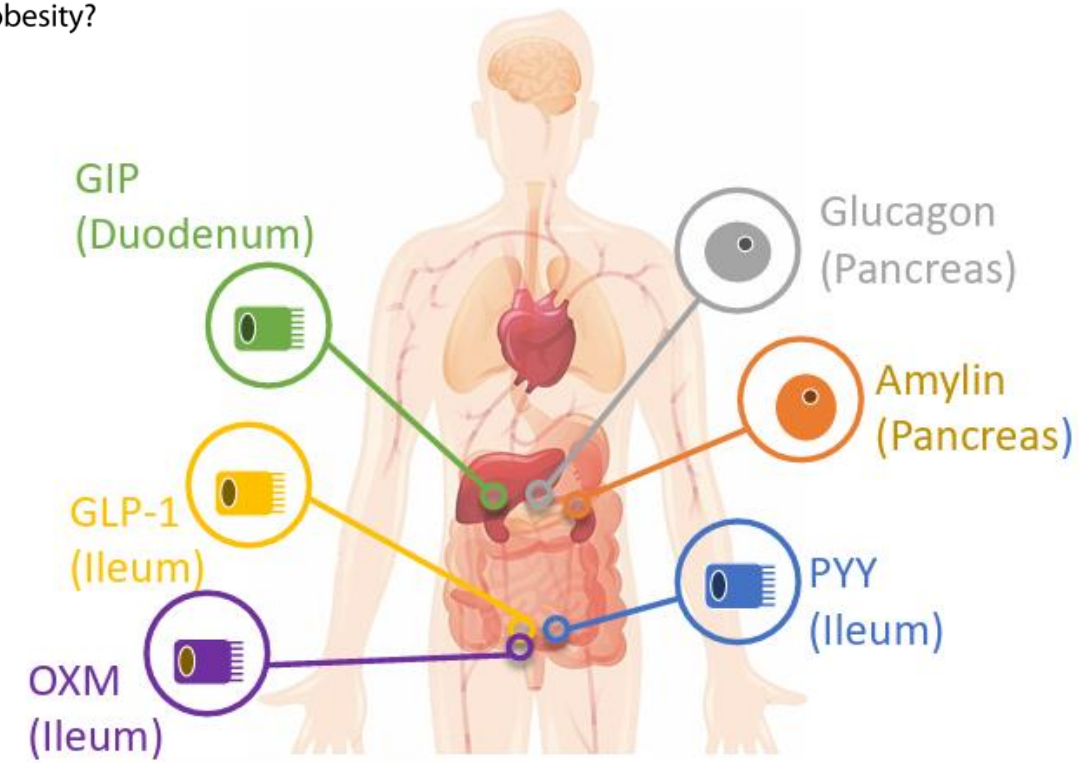
International Journal of Obesity www.nature.com/ijo

REVIEW ARTICLE OPEN

Clinical Research

What is the pipeline for future medications for obesity?

Eka Melson[1,4], Uzma Ashraf[1,4], Dimitris Papamargaritis[1,2,3]✉ and Melanie J. Davies[1,2]



GIP

- ↓ appetite ↓ nausea
- ↑ insulin ↑ glucagon
- ↓ gastric acid secretion
- ↑ lipid deposition
  ↑ lipogenesis
- ↓ bone resorption

GLP-1

- ↓ appetite ↑ nausea
  ↓ food intake
- ↑ insulin ↓ glucagon
- ↓ gastric emptying
- ↑ lipolysis
- ↑ cardioprotection
  ↓ heart rate

OXM

- ↓ appetite ↑ nausea
  ↓ food intake
- ↑ insulin
- ↓ gastric emptying
- ↑ energy expenditure

PYY

- ↓ appetite ↑ nausea
  ↓ food intake
- ↓ gastric emptying
- ↑ energy expenditure

Glucagon

- ↓ appetite ↑ nausea
  ↓ food intake
- ↑ insulin
- ↑ hepatic glucose production
  ↑ lipid oxidation
  ↓ hepatic lipid synthesis
- ↓ gastric emptying
- ↑ energy expenditure
- ↑ heart rate

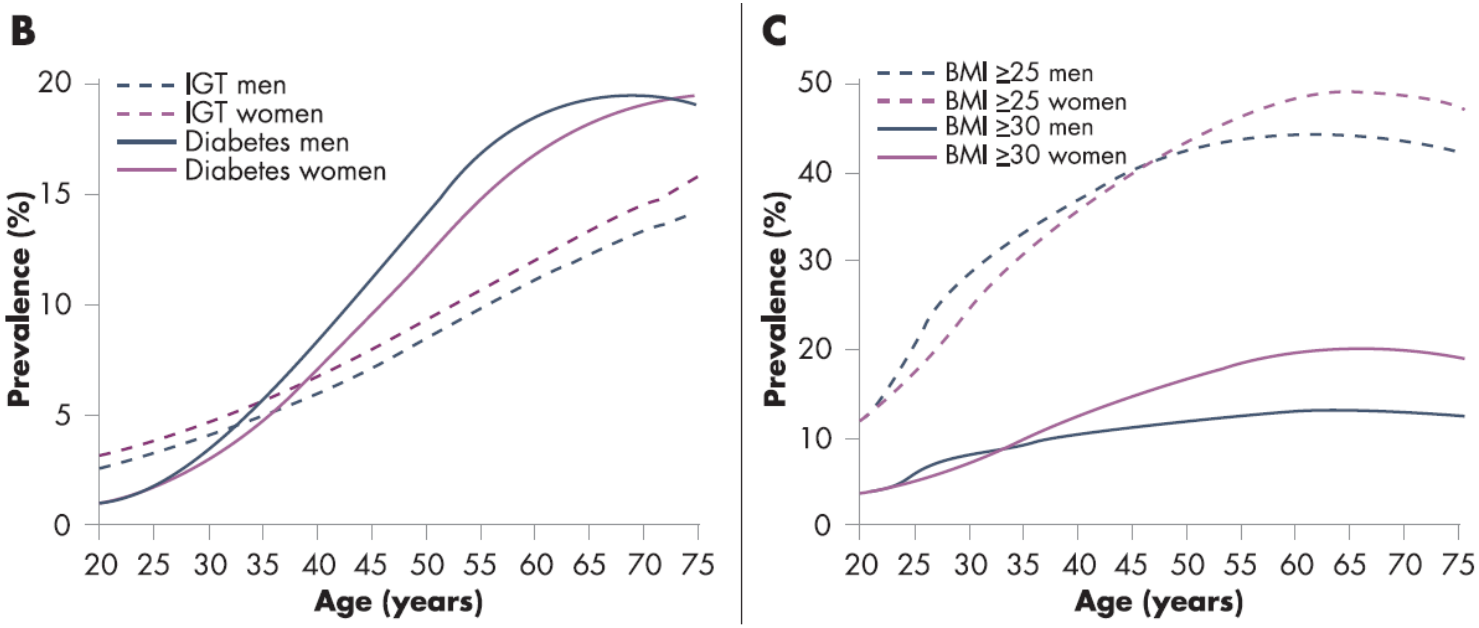
Amylin

- ↓ appetite ↓ food intake
- ↓ glucagon
- ↑ energy expenditure
- ↓ gastric emptying
- ↓ osteoclast activity
  ↑ osteoblast activity

Sex and Gender Differences in Risk, Pathophysiology and Complications of Type 2 Diabetes Mellitus

***Endocrine Reviews* 37: 278–316, 2016**

Alexandra Kautzky-Willer, Jürgen Harreiter, and Giovanni Pacini



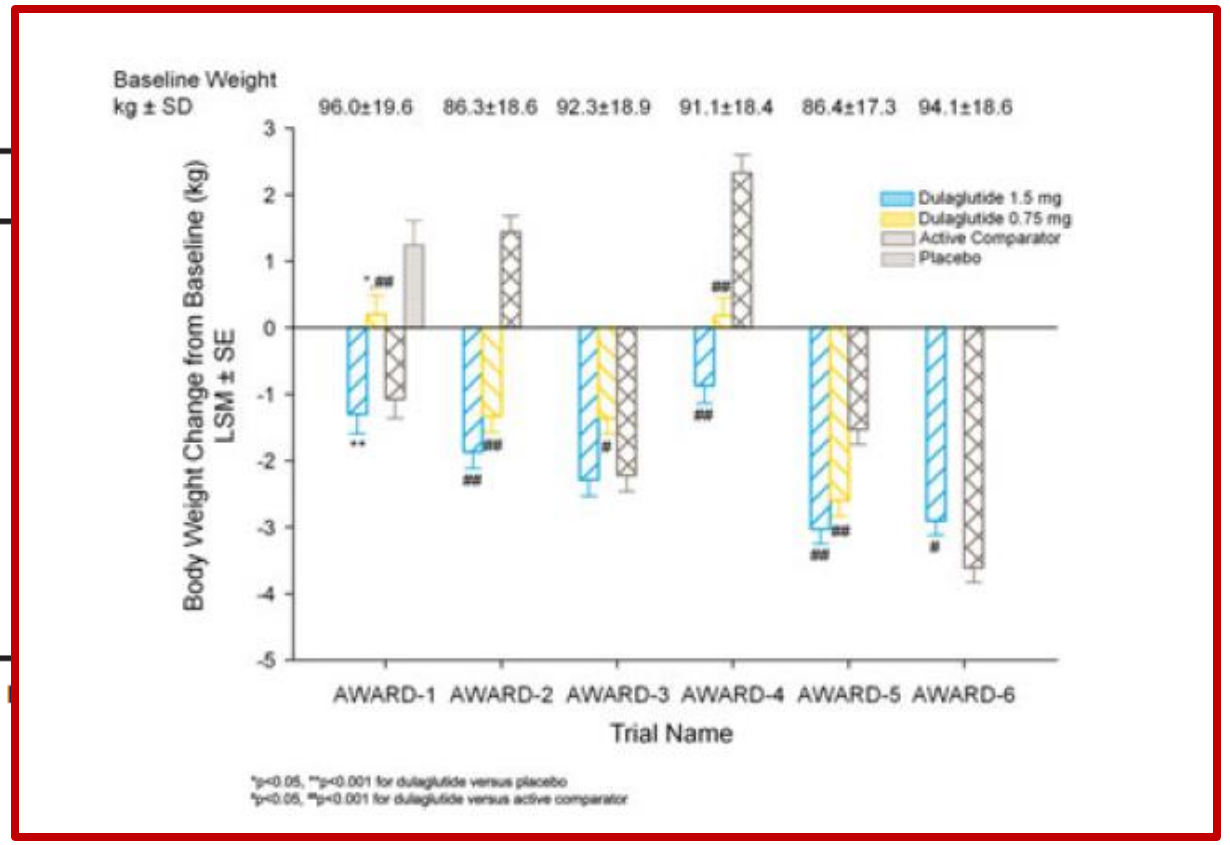
- **UOMINI**: aumentata incidenza di diabete in età più precoce (A) e con un BMI inferiore
- **DONNE** diabetiche più obese degli uomini diabetici nella maggior parte degli studi (B)

DULAGLUTIDE: AWARD Clinical Trial Program

Table 1. Dulaglutide clinical trial program for data analysis

Study	Primary objective	Comparator(s) (dose)
AWARD-1	ΔHbA1c 26 weeks	Exenatide (10 μg BID) Placebo (to week 26)
AWARD-2	ΔHbA1c 52 weeks	Insulin Glargine (titrated to target)
AWARD-3	ΔHbA1c 26 weeks	Metformin (1500–2000 mg QD)
AWARD-4	ΔHbA1c 26 weeks	Insulin Glargine (titrated to target)
AWARD-5	ΔHbA1c 52 weeks	Sitagliptin (100 mg QD) Placebo (to week 26)
AWARD-6	ΔHbA1c 26 weeks	Liraglutide (1.8 mg QD)

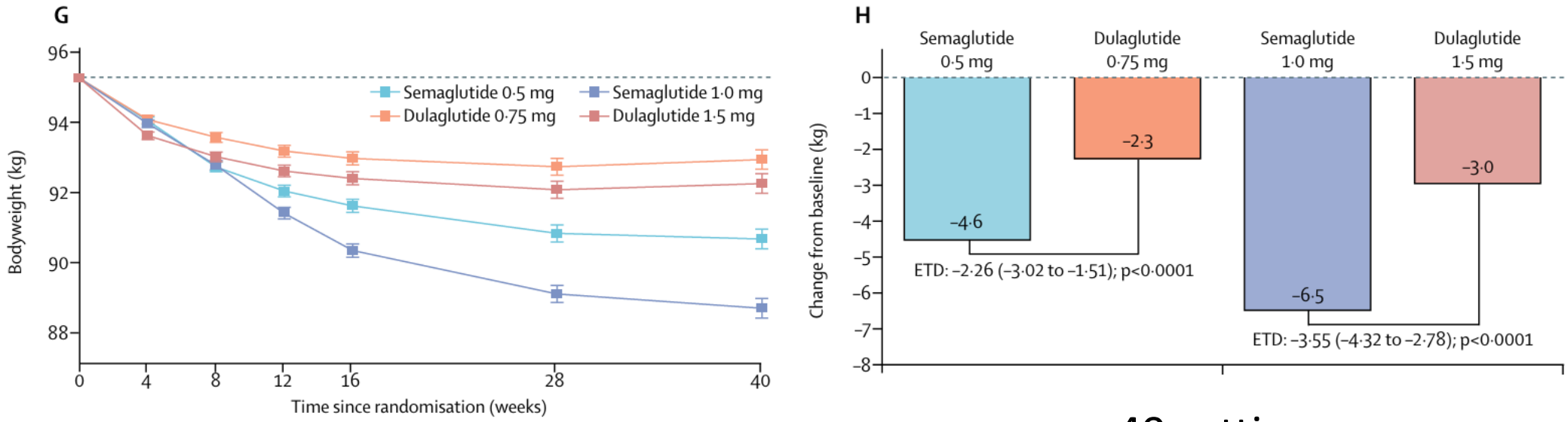
[a]Additional 104 patients were discontinued because the treatment dose was



Semaglutide versus dulaglutide once weekly in patients with type 2 diabetes (SUSTAIN 7): a randomised, open-label, phase 3b trial

Lancet Diabetes Endocrinol 2018; 6: 275–86

Richard E Pratley, Vanita R Aroda, Ildiko Lingvay, Jörg Lüdemann, Camilla Andreassen, Andrea Navarria, Adie Viljoen, on behalf of the SUSTAIN 7 investigators

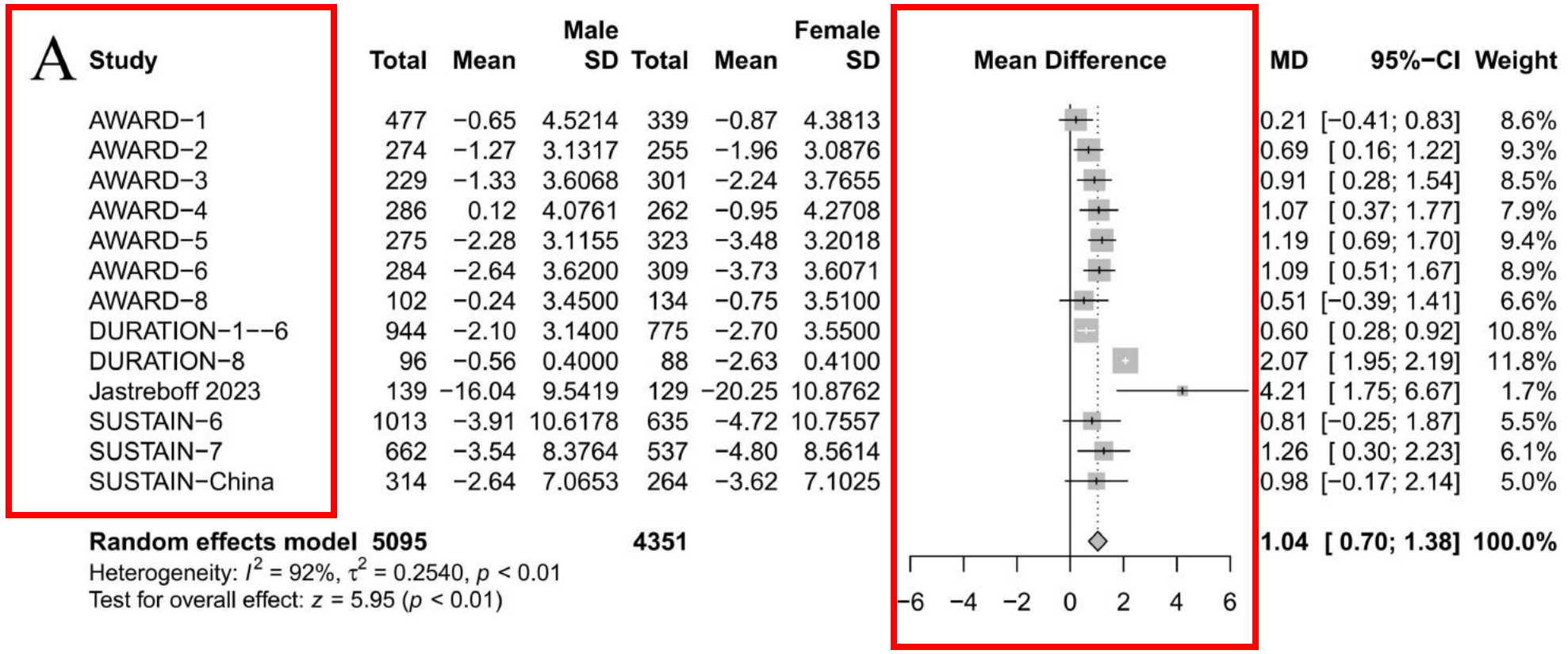


40 settimane

Journal of Diabetes, 2025; 17:e70063

Sex Differences in the Efficacy of Glucagon-Like Peptide-1 Receptor Agonists for Weight Reduction: A Systematic Review and Meta-Analysis

Yucheng Yang[1,2] | Liyun He[1,2] | Shumeng Han[1,2] | Na Yang[1,2] | Yiwen Liu[1,2] | Xuechen Wang[1,2] | Ziyi Li[1,2] | Fan Ping[1,2] | Lingling Xu[1,2] | Wei Li[1,2] | Huabing Zhang[1,2] | Yuxiu Li[1,2]



Journal of Diabetes, 2025; 17:e70063

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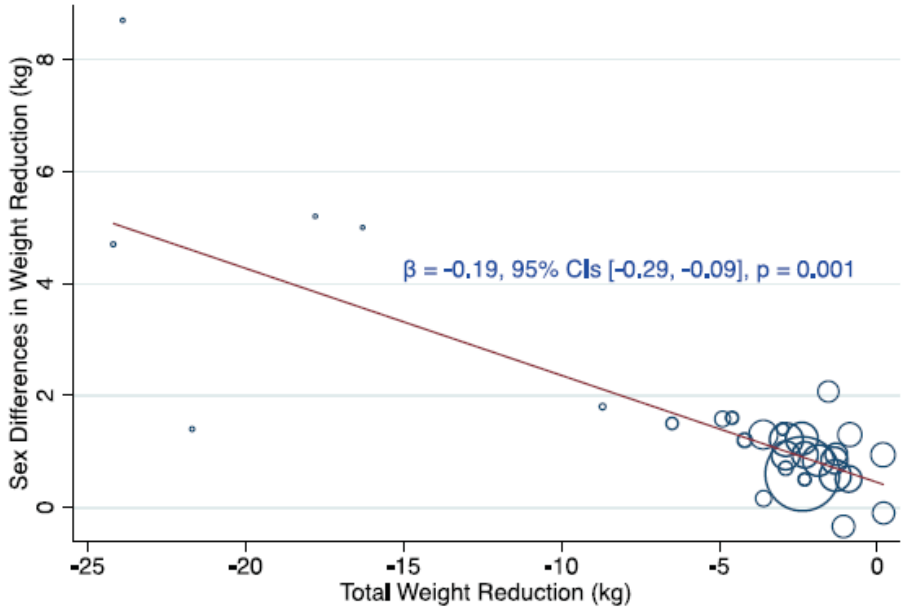
- Le donne hanno perso più peso rispetto agli uomini (MD 1,04 kg [IC 95% 0,70-1,38], p < 0,01)
- anche in termini di percentuale di variazione ponderale (MD 1,69% [IC 95% 0,78-2,61], p < 0,01)

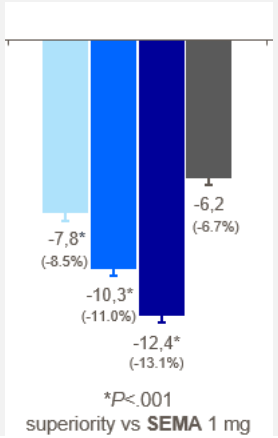
- La differenza nella riduzione del peso tra uomini e donne è positivamente correlata alla riduzione del peso complessivo



- L'indicazione «obesità» acuisce questa differenza (nella persona obesa la risposta in termini di calo peso è aumentata rispetto alla persona diabetica). Gli uomini perdono più peso in seguito a interventi sullo stile di vita

TIRZEPATIDE SURPASS Clinical Trial Program

Monotherapy	Combination With OAMs			Combination With Insulin
SURPASS-1 **vs placebo**[1] (mean T2D duration: 4.7 y)	**SURPASS-2** **vs semaglutide**[2] **Add-on to metformin** (mean T2D duration: 8.6 y)	**SURPASS-3** **vs insulin degludec**[3] **Add-on to metformin with or without SGLT2i** (mean T2D duration: 8.4 y)	**SURPASS-4** **vs insulin glargine**[4] **Add-on to ≥1 and ≤3 OAMs (metformin, SGLT2i, or SU)** (mean T2D duration: 11.8 y)	**SURPASS-5** **vs placebo**[5] **Add-on to insulin glargine with or without metformin** (mean T2D duration: 13.3 y) **SURPASS-6**[7] **vs insulin lispro (TID)** **Add-on to insulin glargine with or without metformin (ongoing)**



SURPASS-CVOT vs dulaglutide (ongoing)[6]

OAM = oral antihyperglycaemic medication; SGLT2i = sodium-glucose co-transporter-2 inhibitor; SU = sulphonylurea; TID = thrice daily; T2D = type 2 diabetes.

1. Rosenstock J, et al. *Lancet*. Published online June 26, 2021. 2. Frias JP, et al. *N Engl J Med*. Published online June 25, 2021. 3. Ludvik B, et al. *Lancet*. 2021; In press. 4. Eli Lilly and Company, 2021. Accessed 5 June 2021. https://investor.lilly.com/news-releases/news-release-details/lillys-tirzepatide-achieves-all-primary-and-key-secondary-study 5. Dahl D, et al. Presented at the 81st Scientific Sessions of the ADA. 2021. 6. SURPASS-CVOT. Accessed 1 April 2021. Available at: https://clinicaltrials.gov/ct2/show/NCT04255433 7. SURPASS-6. Accessed 1 April 2021. Available at: https://clinicaltrials.gov/ct2/show/NCT04537923

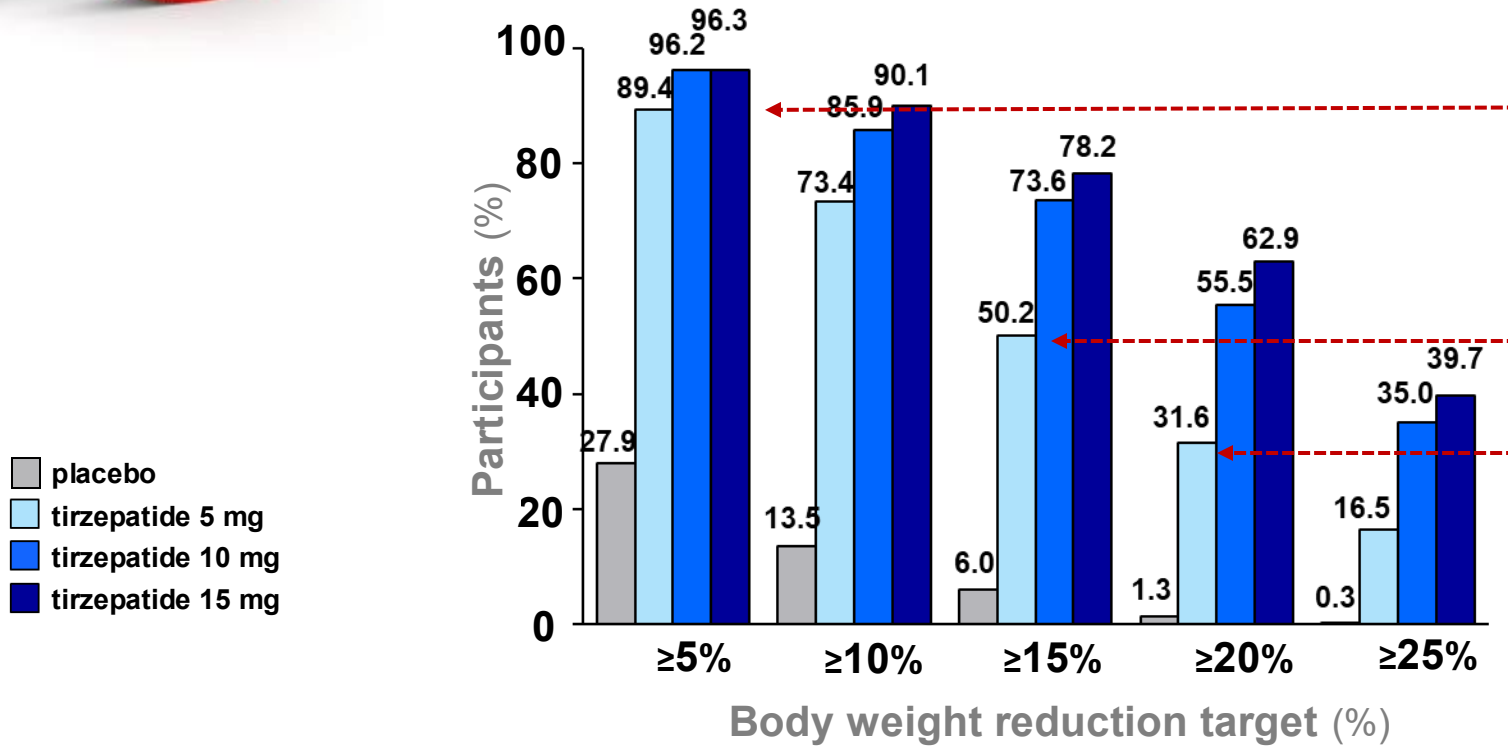
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 21, 2022 VOL. 387 NO. 3

Tirzepatide Once Weekly for the Treatment of Obesity

Ania M. Jastreboff, M.D., Ph.D., Louis J. Aronne, M.D., Nadia N. Ahmad, M.D., M.P.H., Sean Wharton, M.D., Pharm.D., Lisa Connery, M.D., Breno Alves, M.D., Arihiro Kiyosue, M.D., Ph.D., Shuyu Zhang, M.S., Bing Liu, Ph.D., Mathijs C. Bunck, M.D., Ph.D., and Adam Stefanski, M.D., Ph.D., for the SURMOUNT-1 Investigators*

tirzepatide 5 mg



90% achieved ≥5%

50% achieved ≥15%

30% achieved ≥20%

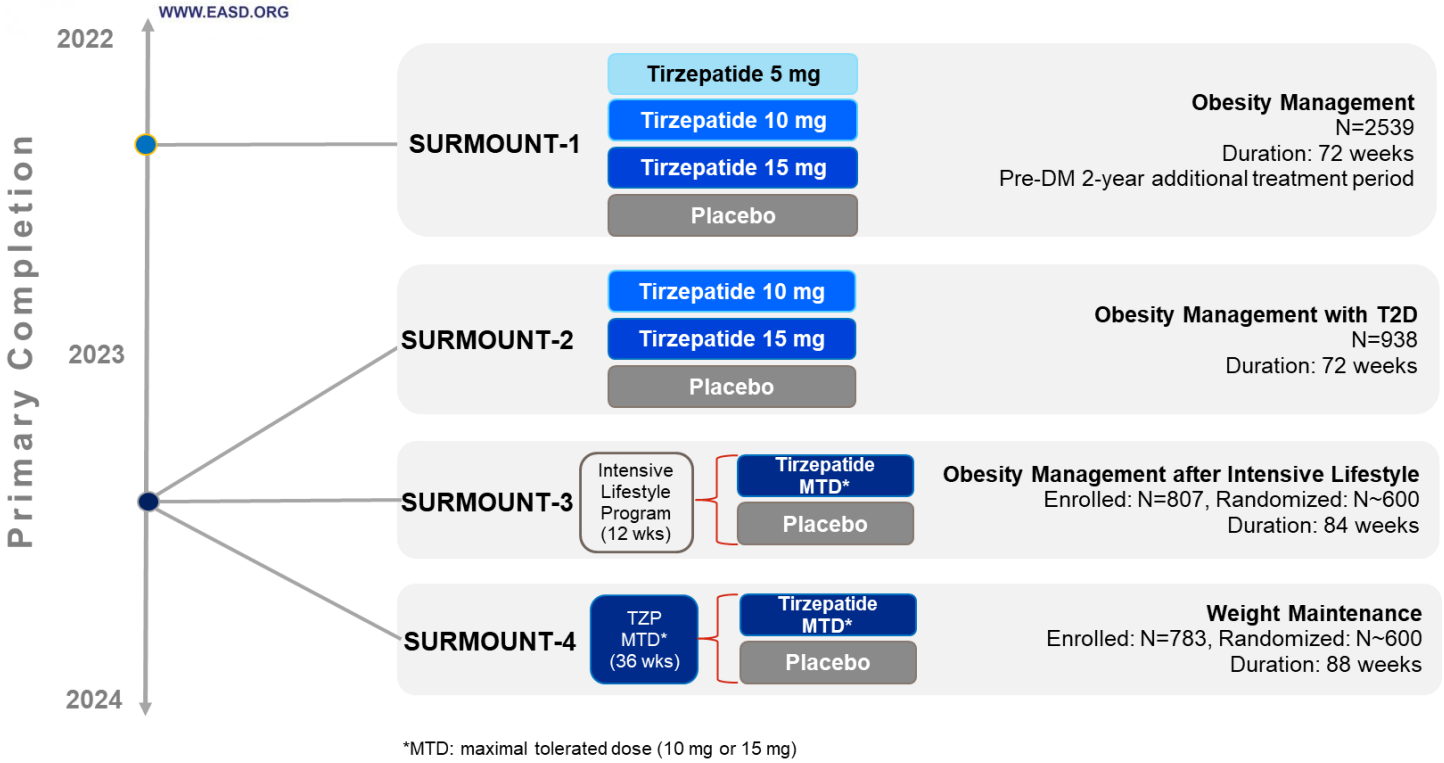
60th ANNUAL MEETING
EASD
9-13 SEPTEMBER 2024
MADRID

Meeting Coverage > EASD

Tirzepatide Yields Greater Weight Loss in Women Than Men

— But significant weight loss reported for both

by Kristen Monaco, Senior Staff Writer, MedPage Today
September 12, 2024



L'analisi post hoc, che includeva i quattro studi SURMOUNT, ha confrontato il tirzepatide con placebo per un periodo fino a 72-88 settimane in 4.677 adulti (2.999 femmine, 1.678 maschi) con obesità, evidenziando potenziali differenze di genere

Contents lists available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.journals.elsevier.com/diabetes-research-and-clinical-practice

Diabetes Research and Clinical Practice 212 (2024) 111689

Real-world sex differences in type 2 diabetes patients treated with GLP-1 receptor agonists

Sara Piccini [a], Giuseppe Favacchio [a], Emanuela Morenghi [b], Gherardo Mazziotti [a,c], Andrea G. A. Lania [a,c], Marco Mirani [a,*]

..POSSIBILI SVILUPPI FUTURI

Le donne in **prevenzione primaria** mostrano un migliore controllo glicemico e una maggiore perdita di peso rispetto agli uomini in corso di GLP-1 RA

In **prevenzione secondaria**, le donne beneficiano meno del trattamento con GLP-1 RA rispetto agli uomini

Le donne in **prevenzione secondaria** potrebbero trarre maggior beneficio da un inizio precoce del trattamento

Journal of Diabetes and Its Complications 38 (2024) 108779

Contents lists available at ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: www.elsevier.com/locate/jdiacomp

Tirzepatide ameliorates eating behaviors regardless of prior exposure to glucagon-like peptide receptor agonists in Japanese patients with type 2 diabetes mellitus

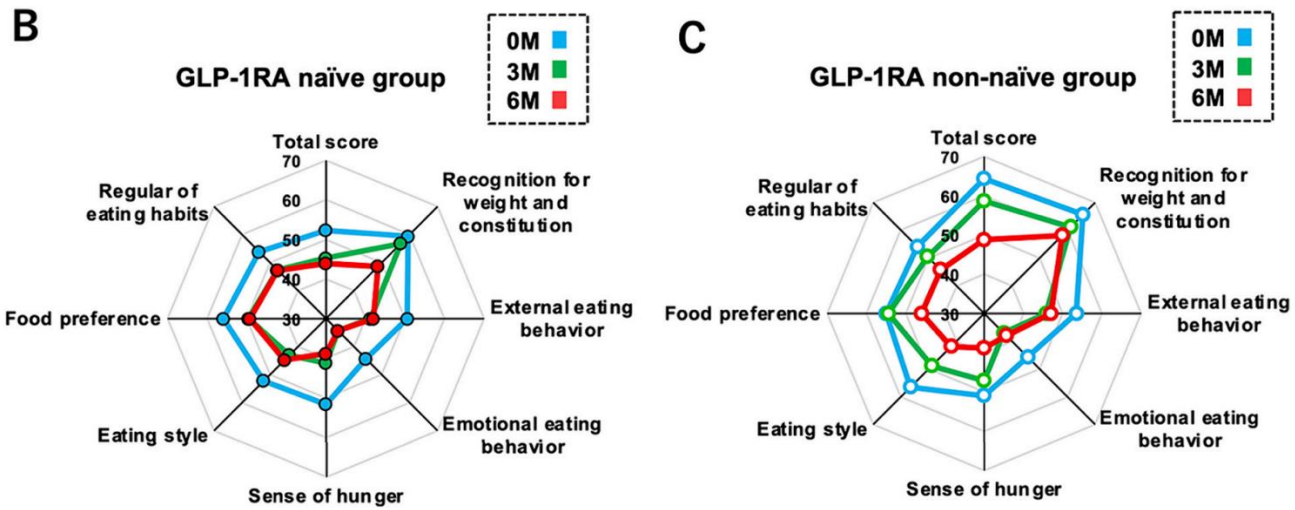
Toru Suzuki [a,b,1], Tatsuya Sato [c,1], Marenao Tanaka [a,d], Keisuke Endo [a], Kei Nakata [a], Toshifumi Ogawa [a,c], Itaru Hosaka [e], Yukinori Akiyama [f], Araya Umetsu [g], Masato Furuhashi [a,*]

GLP-1 RA E GLP-1RA/GIP

TERAPIA SEQUENZIALE O MUTUAMENTE ESCLUSIVA?

Nel **gruppo naïve a GLP-1RA** (n = 20, uomini/donne: 13/7) le modificazioni del comportamento alimentare sono state osservate principalmente nei primi 3 M

Nel **gruppo non naïve al GLP-1RA** (n = 13, uomini/donne: 8/5) le modificazioni del comportamento alimentare sono state osservate fino a 6 M



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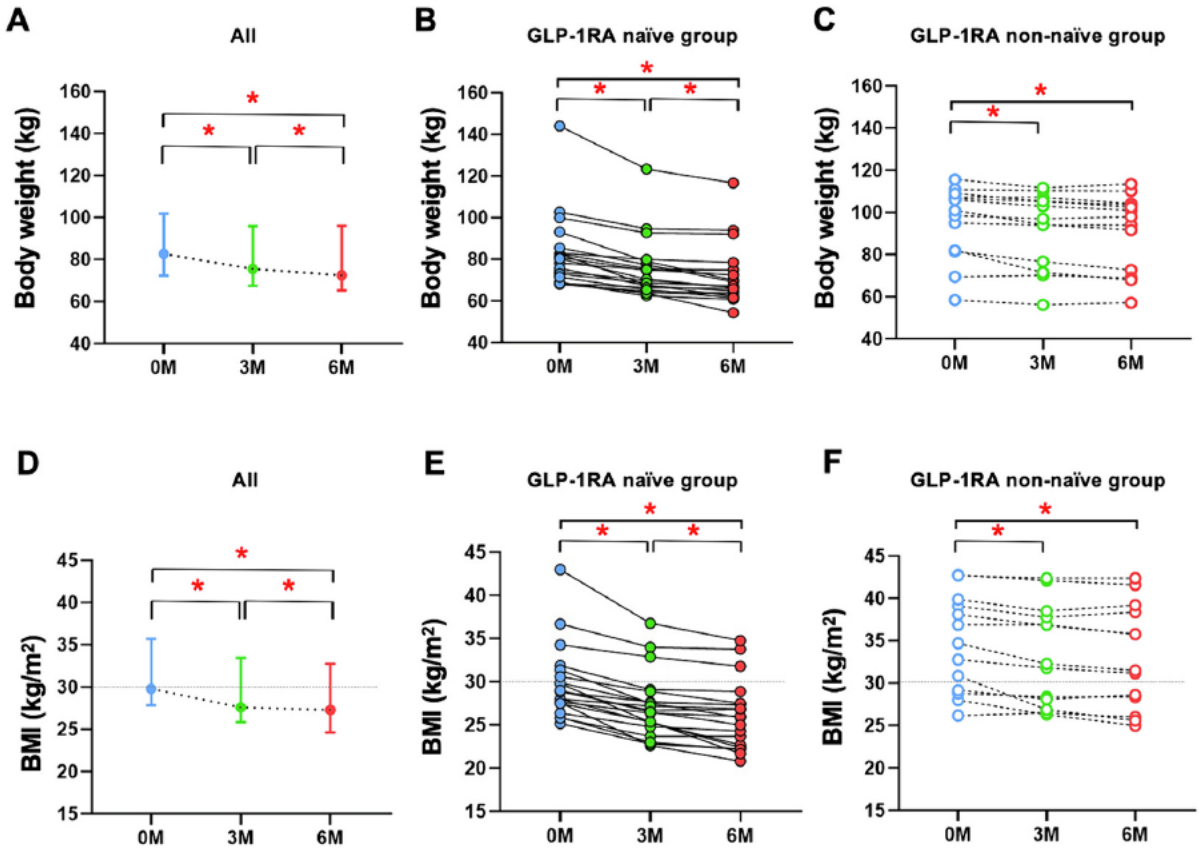
GLP-1 RA E GLP-1RA/GIP

TERAPIA SEQUENZIALE O MUTUAMENTE ESCLUSIVA?

Nel **gruppo naïve a GLP-1RA** (n = 20, uomini/donne: 13/7) il peso corporeo è diminuito in modo continuo fino a 6 M

Nel **gruppo non naïve al GLP-1RA** (n = 13, uomini/donne: 8/5) la riduzione del peso corporeo è stata predominante nei primi 3 M



GAZZETTA UFFICIALE

DELLA REPUBBLICA ITALIANA

Atto Completo | Avviso di rettifica Errata corrige | Lavori Preparatori | Direttive UE recepite

AGENZIA ITALIANA DEL FARMACO

DETERMINA 13 febbraio 2025

Riclassificazione del medicinale per uso umano «Mounjaro», ai sensi dell'articolo 8, comma 10, della legge 24 dicembre 1993, n. 537. (Determina n. 223/2025). (25A01127) (GU Serie Generale n.44 del 22-02-2025)

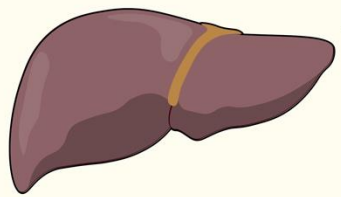
Classificazione ai fini della rimborsabilità

«Mounjaro» è indicato per il trattamento di adulti affetti da diabete mellito di tipo 2 non adeguatamente controllato, in aggiunta alla dieta e all'esercizio fisico:

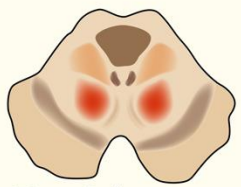
- come monoterapia quando l'uso di metformina è considerato inappropriato a causa di intolleranza o controindicazioni
- in aggiunta ad altri medicinali per il trattamento del diabete
- **nota AIFA: 100**

GLP-1 medicines

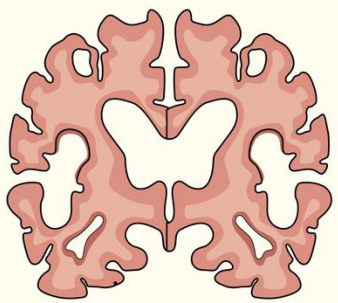
Investigational



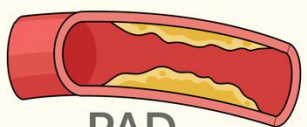
Metabolic Liver Disease



Parkinson



Alzheimer



PAD

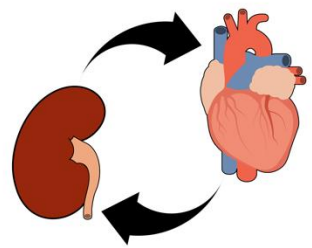
Evidence-based medicine

Type 2 Diabetes

⬇HbA_{1c}

Cardiorenal disorders

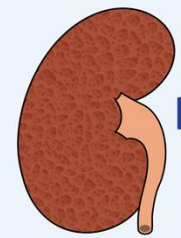
⬇MACE
⬇HFpEF
⬇DKD
⬇CV death



Obesity

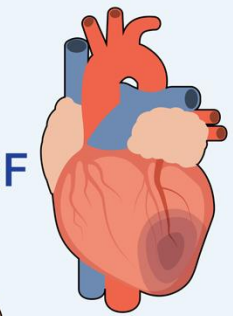
Weight loss

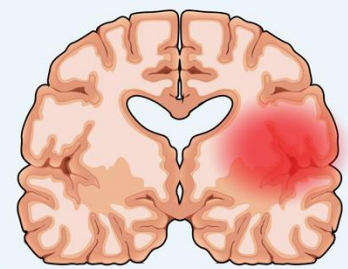
Established benefit



DKD

MI
HFpEF





Stroke

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