

RICCIONE, SABATO 12 APRILE 2025

CHIRURGIA DELL'OBESITA: DAL TRATTAMENTO INTEGRATO AL WELLNESS



Resp. Scientifico
Andrea Lucchi

iscriviti all'evento sicobriccione.cloud

POLICLINICO DI **SANT'ORSOLA**



SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Bologna
IRCCS Istituto di Ricovero e Cura a Carattere Scientifico



ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

L'endocrinologo: i nuovi farmaci soppianteranno la chirurgia?

SILVIA GARELLI

*UOC DI ENDOCRINOLOGIA E PREVENZIONE E CURA DEL DIABETE
IRCCS AZ. OSPEDALIERO-UNIVERSITARIA DI BOLOGNA
POLICLINICO DI SANT'ORSOLA*

*CENTRO INTERAZIENDALE DI CHIRURGIA DELL'OBESITÀ –
AUSL-AOU BOLOGNA*



SOMEONE SAYS «YES, OF COURSE!»

SEMAGLUTIDE ORFORGLIPRON

TIRZEPATIDE

RETATRUTIDE

SORVODUTIDE COTADUTIDE



GLP-1 agonists

GLP-1 Injectable

- 3 Semaglutide 7.2mg - NN

GLP-1 Oral

- 3 Semaglutide 50mg* - NN
- 3 Orforglipron - Eli Lilly
- 2 Danulipron - Pfizer
- 1 CT996 - Carmot Therapeutics

Key:
3 Phase 3
2 Phase 2
1 Phase 1
1 Pre clinical

CAGRISEMA

GLP-1 + GIP agonists

- 3 Tirzepatide* - Eli Lilly
- 1 SCO-094 - Scobia Pharma
- 1 VK2735 oral/subcut - Viking Therapeutics
- 1 CT388 - Carmot Therapeutics

GLP-1 + GIP antagonist

- 2 AMG 133 - Amgen

GIP agonist

- 1 ZP6590 - Zealand Pharma

amylin agonists

- 2 Cagrilintide - NN
- 1 Long acting amylin agonist -Eli Lilly
- 1 ZP8396 - Zealand Pharma
- 1 AZD6234 - AstraZeneca

GLP-1 + amylin agonists

- 3 CagriSema - NN
- 1 Oral amycretin - NN

GLP-1 + GIP + Glucagon agonist

- 3 Retatrutide - Eli Lilly
- 1 HM15211 - Hanmi Pharmaceutical

PYY agonists

- 2 NNC0145-1875 - NN
- 1 NNC0145-1562 - NN
- 1 Y-14 - Zhipp

GLP-1 + PYY agonists

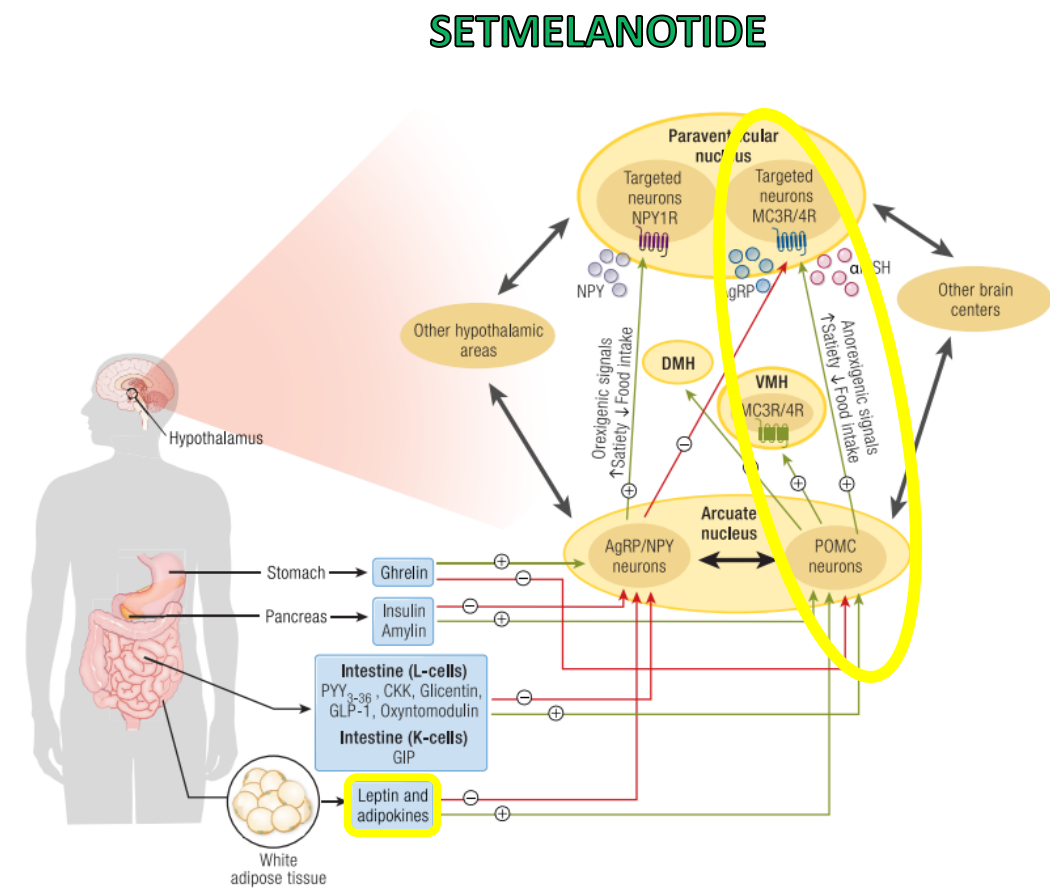
- 2 NNC0165-1875 + Semaglutide - NN
- 1 NNC0165-1562 + Semaglutide - NN

GLP-1 + glucagon agonists

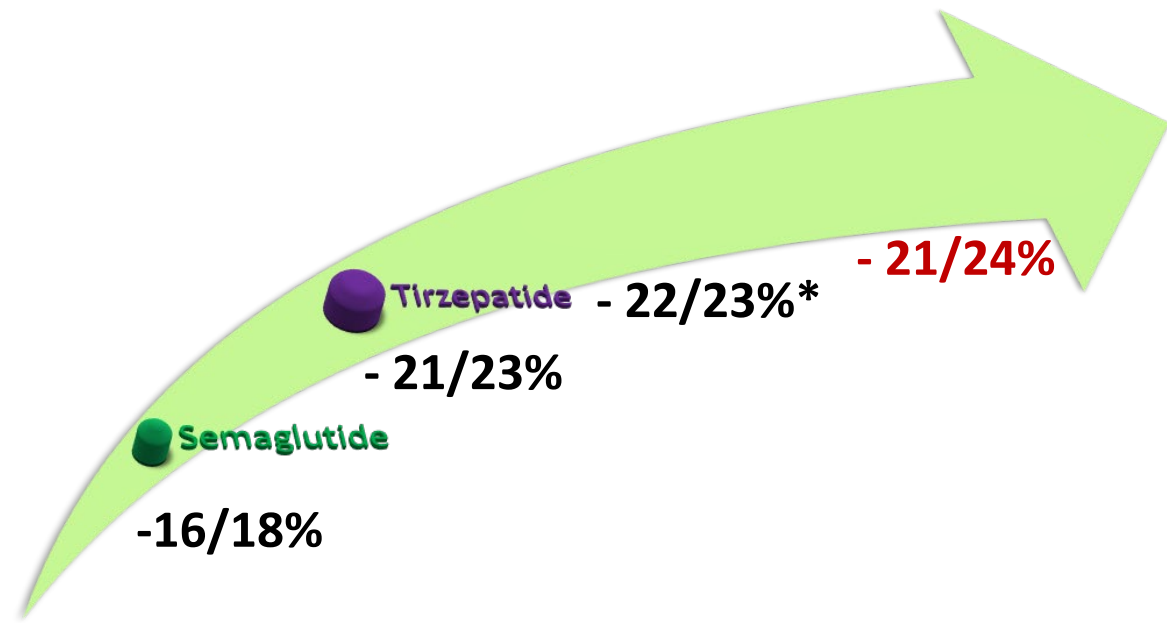
- 3 Survodutide - Boehringer Ingelheim
- 2 Efinopegdutide - Hanmi Pharmaceutical
- 2 Mazdutide - Eli Lilly
- 2 Pemvidutide ALT-801 - Altimmune

Glucagon agonist

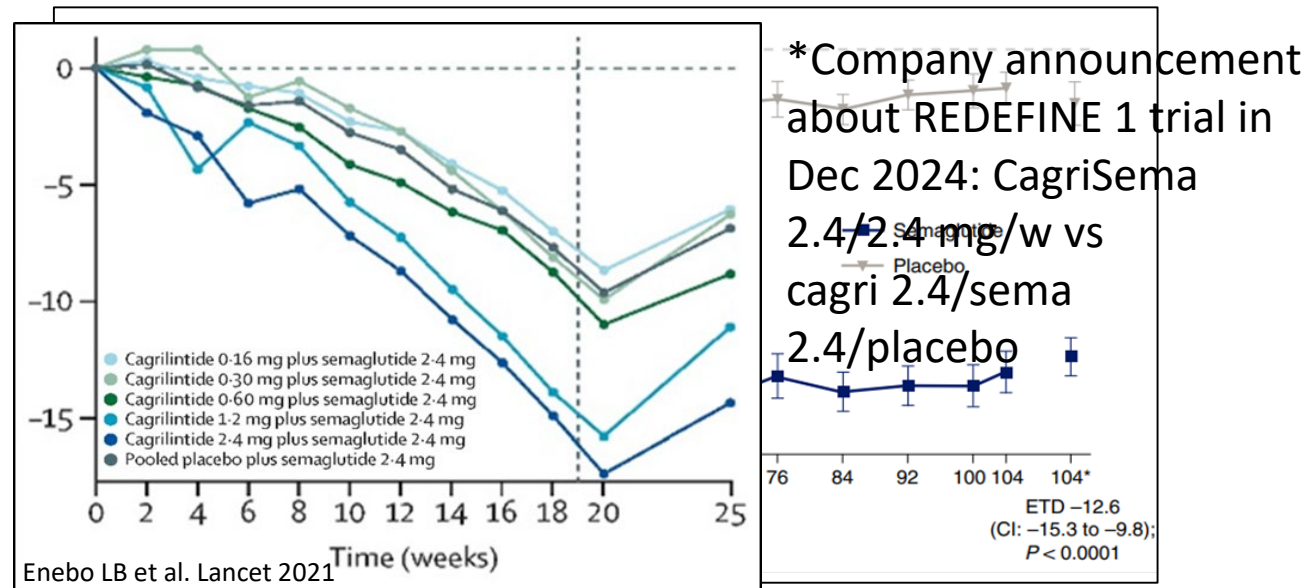
- 1 HM15136 - Hanmi Pharmaceutical



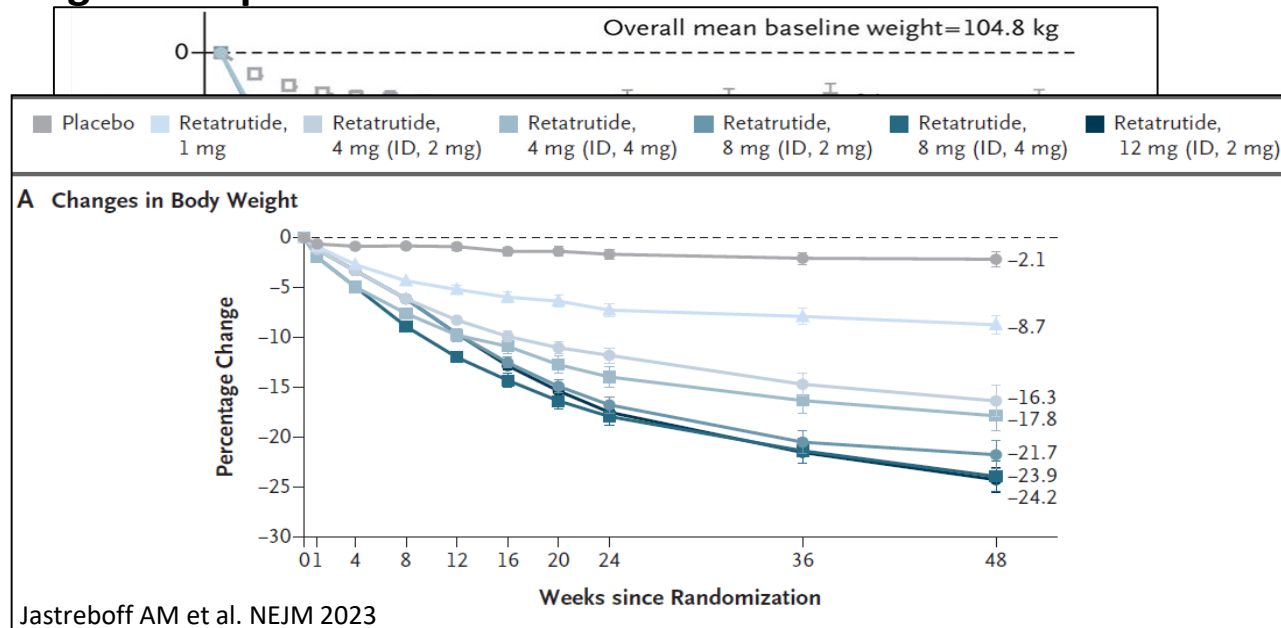
For genetic obesity disorders	Approved age categories
Biallelic POMC, LEPR, PCSK1 deficiency Bardet Biedl syndrome	FDA and EMA: adults, children ≥6 years



~ 75% of sbj lost $\geq 10\%$ of bw
 >50% of sbj lost $\geq 15\%$ of bw
 >30% of sbj lost $\geq 20\%$ of bw



STEP 5 trial
 CagriSema phase 1b trial

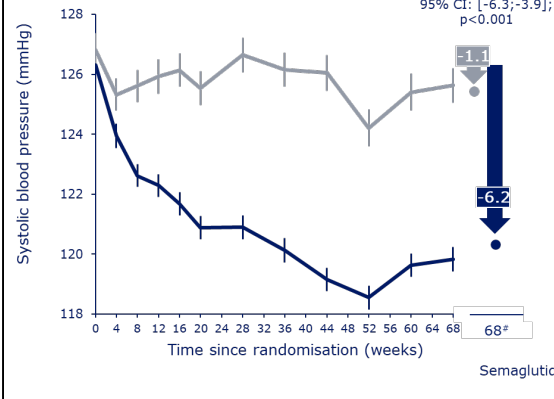


RETA phase 2 trial
 SURMOUNT-1 trial

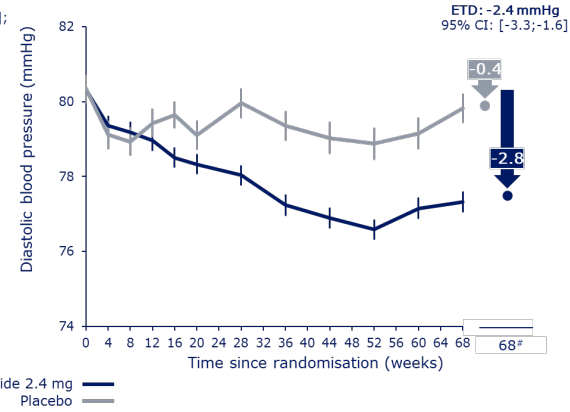
Change in blood pressure

STEP 1

Systolic blood pressure[§]



Diastolic blood pressure[§]

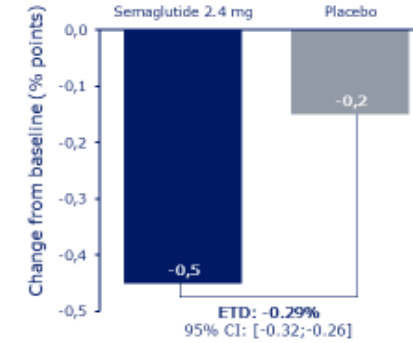


[§] Means are based on observed data from the in-trial period and the ETD is for the treatment policy estimand. [#] Estimated values at week 68. Error bars are +/- standard error of the mean. CI, confidence interval; ETD, estimated treatment difference. Widding et al. *N Engl J Med* 2021;384:989-1002.

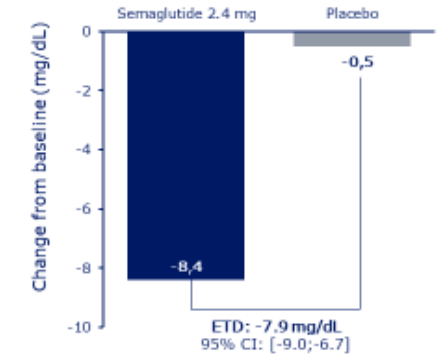
Change in glycaemic parameters

STEP 1

HbA_{1c}[#] Mean at baseline: 5.7%



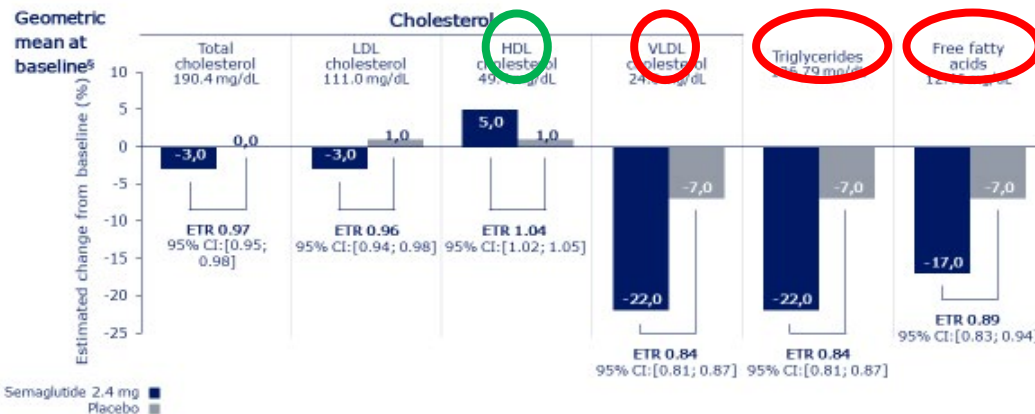
Fasting plasma glucose[#] Mean at baseline (95.2 mg/dL)



[#] Estimated change from baseline for treatment policy estimand. Error bars are +/- standard error of the mean. ETD, estimated treatment difference. Widding et al. *N Engl J Med* 2021;384:989-1002.

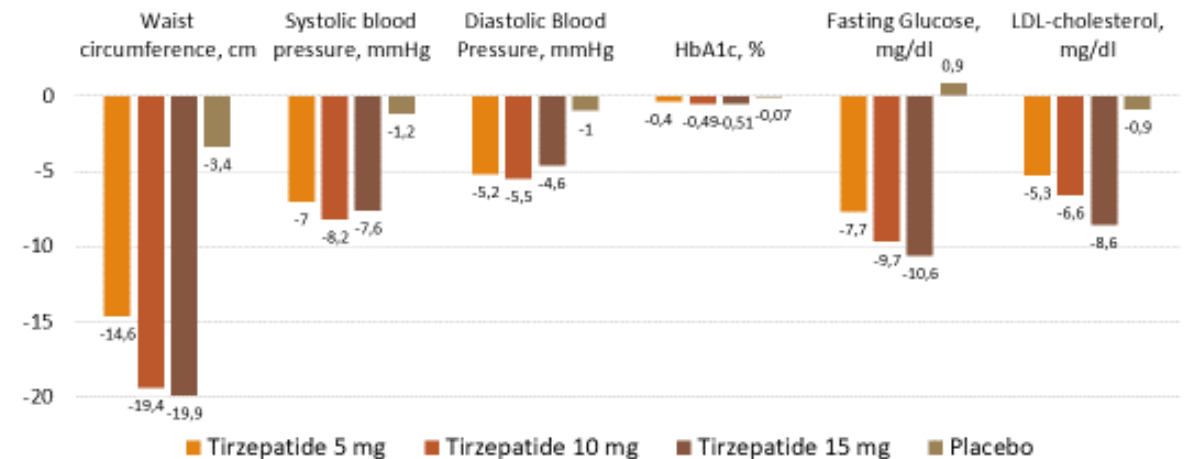
Change in fasting lipids

STEP 1



[§] Estimated change from baseline for treatment policy estimand. [§] Geometric mean at baseline for both treatment groups. CI, confidence interval; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ETR, estimated treatment ratio; VLDL, very low-density lipoprotein. Widding et al. *N Engl J Med* 2021;384:989-1002.

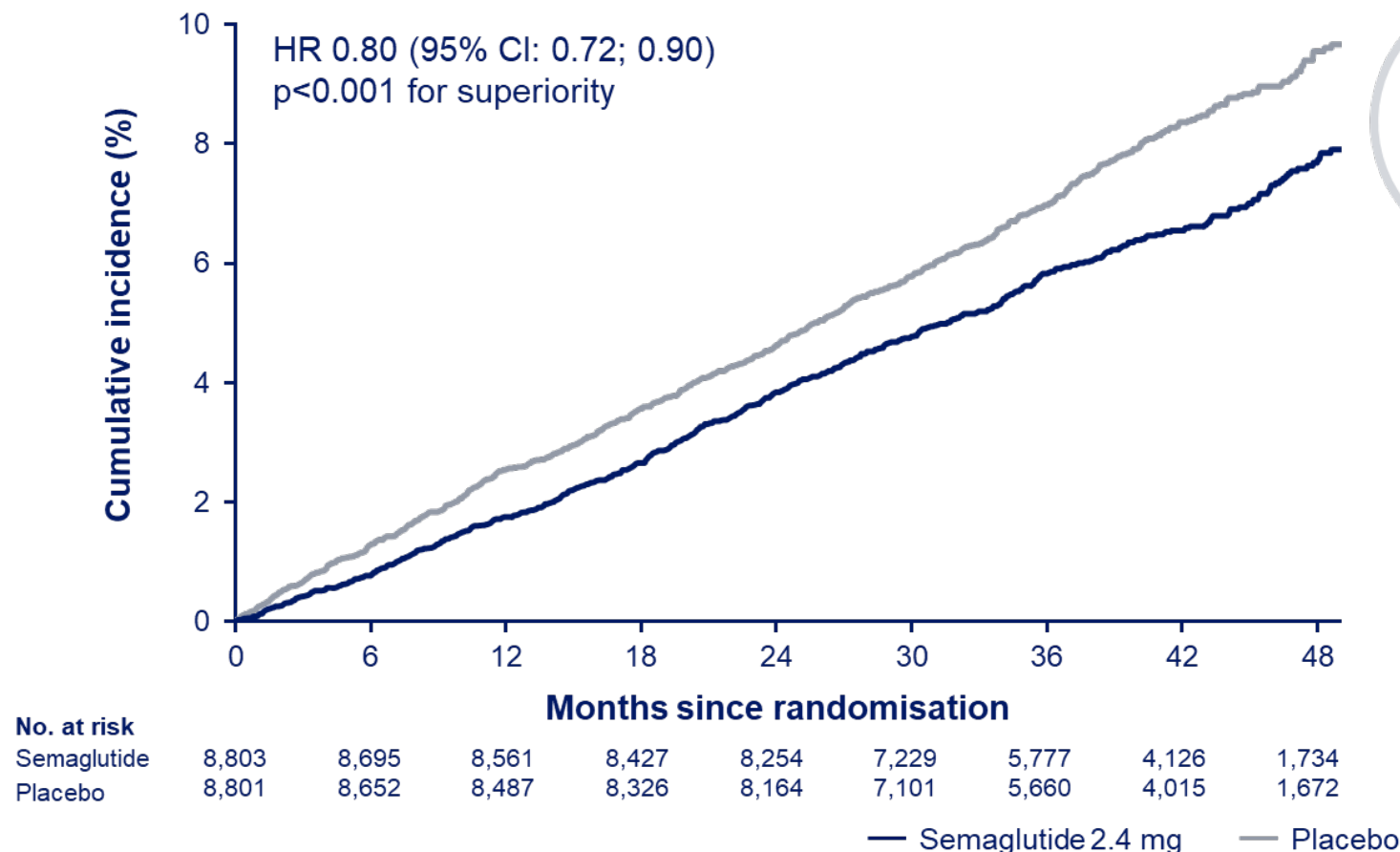
Surmount-1 trial: change in anthropometric and metabolic parameters



Cumulative incidence of MACE

SELECT: Primary cardiovascular composite endpoint

N=17,604



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.

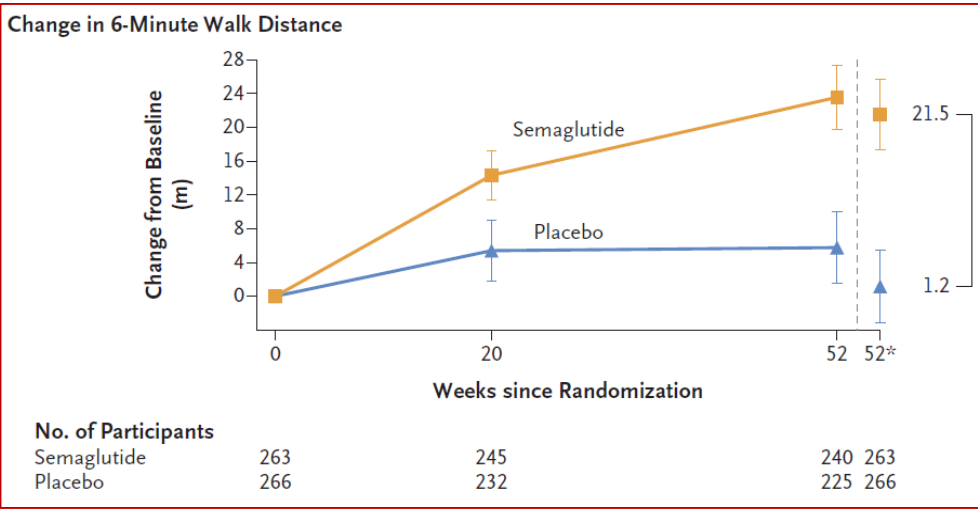
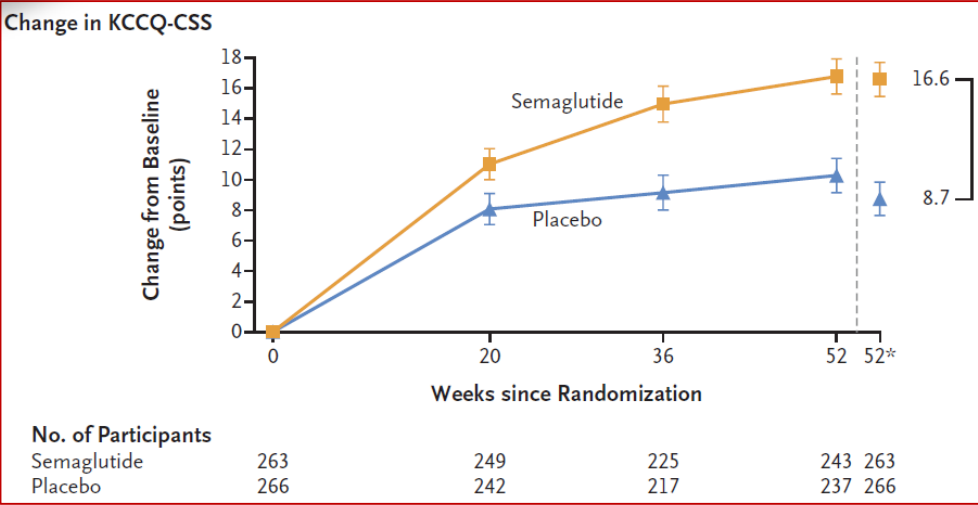
CI, confidence interval; HR, hazard ratio; MACE, major adverse cardiovascular events; MI, myocardial infarction.

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>

Sema in HFpEF: the STEP HFpEF TRIAL

Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity

M.N. Kosiborod, S.Z. Abildström, B.A. Borlaug, J. Butler, S. Rasmussen, M. Davies, G.K. Hovingh, D.W. Kitzman, M.L. Lindegaard, D.V. Møller, S.J. Shah, M.B. Treppendahl, S. Verma, W. Abhayaratna, F.Z. Ahmed, V. Chopra, J. Ezekowitz, M. Fu, H. Ito, M. Lelonek, V. Melenovsky, B. Merkely, J. Núñez, E. Perna, M. Schou, M. Senni, K. Sharma, P. Van der Meer, D. von Lewinski, D. Wolf, and M.C. Petrie, for the STEP-HFpEF Trial Committees and Investigators*



Tirzepatide for Heart Failure with Preserved Ejection Fraction and Obesity

Milton Packer, M.D., Michael R. Zile, M.D., Christopher M. Kramer, M.D., Seth J. Baum, M.D., Sheldon E. Litwin, M.D., Venu Menon, M.D., Junbo Ge, M.D., Govinda J. Weerakkody, Ph.D., Yang Ou, Ph.D., Mathijs C. Bunck, M.D., Karla C. Hurt, B.S.N., Masahiro Murakami, M.D., and Barry A. Borlaug, M.D., for the SUMMIT Trial Study Group*

ABSTRACT

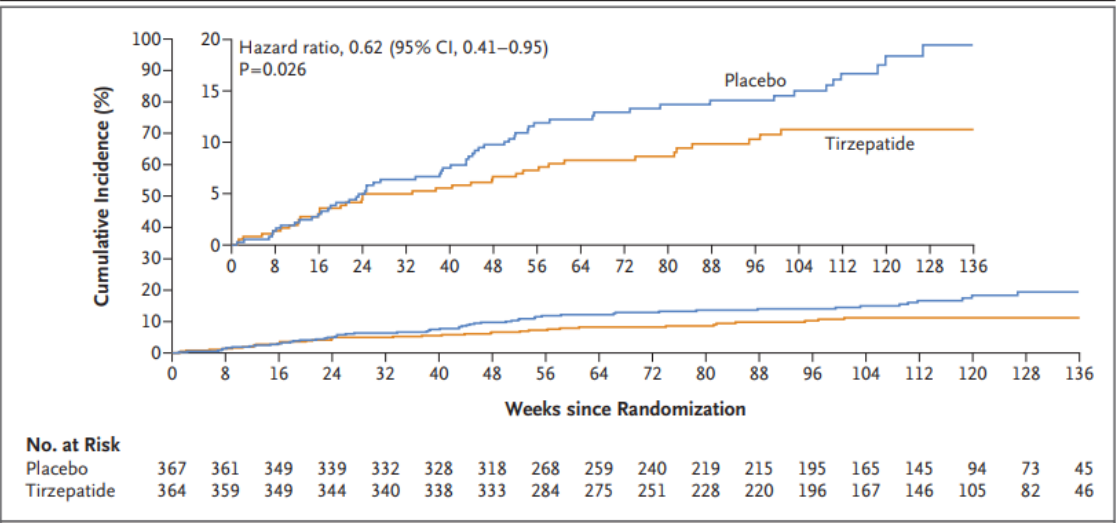


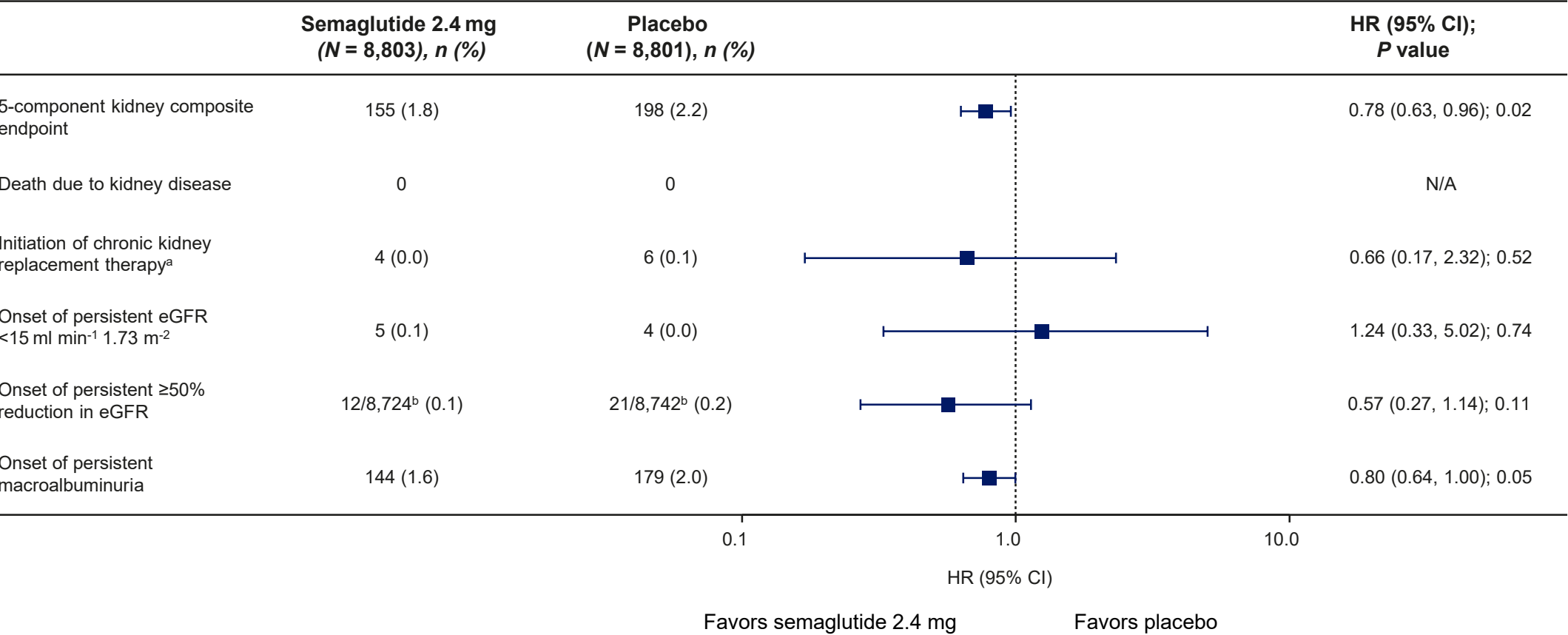
Figure 1. Composite of Death from Cardiovascular Causes or a Worsening Heart-Failure Event.

Shown is the cumulative incidence of death from cardiovascular causes or a worsening heart-failure event (the composite primary end point), assessed in a time-to-first-event analysis, among 364 patients who received tirzepatide and 367 patients who received placebo. The inset shows the same data on an expanded y axis.

Tirze in HFpEF: the SUMMIT TRIAL

Effect of semaglutide on the main kidney endpoint

Effect of semaglutide 2.4 mg on the main 5-component kidney composite endpoint



Data are the observed (that is, or measured) n (%) of patients experiencing the first event that contributed to the main 5-component kidney composite endpoint from the in-trial observation period and the HR, and 95% CI was estimated using a Cox regression model. The symbols are the HRs and error bars are 95% CIs. P values are two-sided and were not adjusted for multiplicity.

^aDialysis or kidney transplantation.

^bPercent reduction is defined from baseline; the denominator is therefore reduced because of patients missing baseline score.

CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; N/A, not applicable.

Adapted from Figure 2. Effect of semaglutide 2.4 mg on the main 5-component kidney composite endpoint.

INCRETIN-BASED AOM SIDE EFFECTS



Nausea and Vomiting



Diarrhea



Constipation



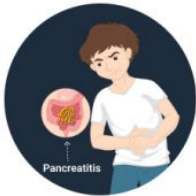
Stomach Pain



Gas and Bloating



Hair Loss



Pancreatitis



Gallbladder disease



Allergic reactions



Headaches

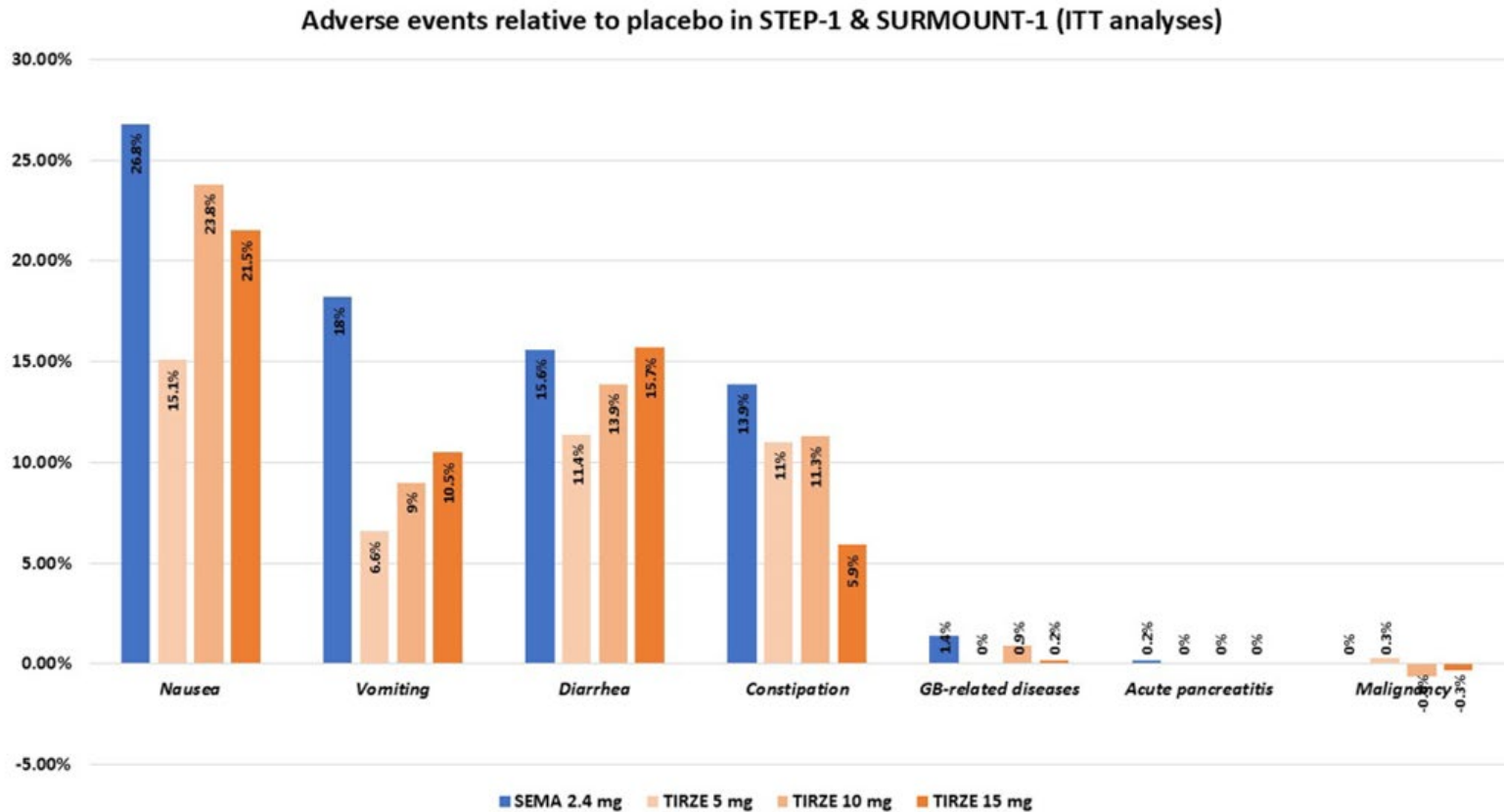


Fig. 4. Key side effects of semaglutide 2.4 mg and tirzepatide 5, 10, and 15 mg in people with obesity or overweight without type 2 diabetes (SEMA: Semaglutide, TIRZE: Tirzepatide, GB: Gall bladder).

Singh A et al. Diabetes Metab Syndr. 2025 Mar

MILD>>MODERATE>>>SEVERE

SI... PUÒ...

FARE'!!!



TERAPIA FARMACOLOGICA E CHIRURGICA PER L'OBESITA' SONO VERAMENTE PARAGONABILI?

	CHIRURGIA	FARMACI
EFFICACIA SU PESO E FATTORI DI RISCHIO CARDIOMETABOLICI	POCHI RCT, PERLOPIU' REAL LIFE DATA, STUDI OSSERVAZIONALI RETROSPETTIVI/PROSPETTICI	RIGOROSI RCT, CON PROTOCOLLI E RACCOLTA DATI STANDARDIZZATI + REAL LIFE DATA con breve osservazione
CARATTERISTICHE DELLA POPOLAZIONE STUDIATA	• PAZIENTI CON BMI > 30 KG/M2 + DM, • PAZIENTI CON BMI >35 MG/M2 + COMORBIDITA', • BMI >40 KG/M2 Coorti di pazienti con insufficienza d'organo in attesa di trapianto	• BMI > 27 KG/M2 +COMORBIDITA' BMI > 30 KG/M2 ANCHE IN ASSENZA DI COMORBIDITA', SPESSO NON DIABETICI NEI TRIAL FARMACOLOGICI CON INCLUSIONE DI PAZIENTI CON DM IL CALO PONDERALE E' LIMITATO • PAZIENTI AD ELEVATA COMPLESSITA': CON PREGRESSO MACE +/- DANNO RENALE +/- DM, DI ETA' SUPERIORE AI 45-50 ANNI, IN PREVENZIONE SECONDARIA QUESTI PAZIENTI TIPICAMENTE ACCEDONO CON DIFFICOLTA' ALLA SALA OPERATORIA
ACCESSIBILITA'	ACCESSIBILE A TUTTI	ACCESSIBILI SOLO AD UNA FETTA DELLA POPOLAZIONE (BIAS DI SELEZIONE)

A Real-World Study of the Effectiveness and Safety of Semaglutide for Weight Loss

Ploutarchos Tzoulis¹, Michael Batavanis², Stephanie Baldeweg³



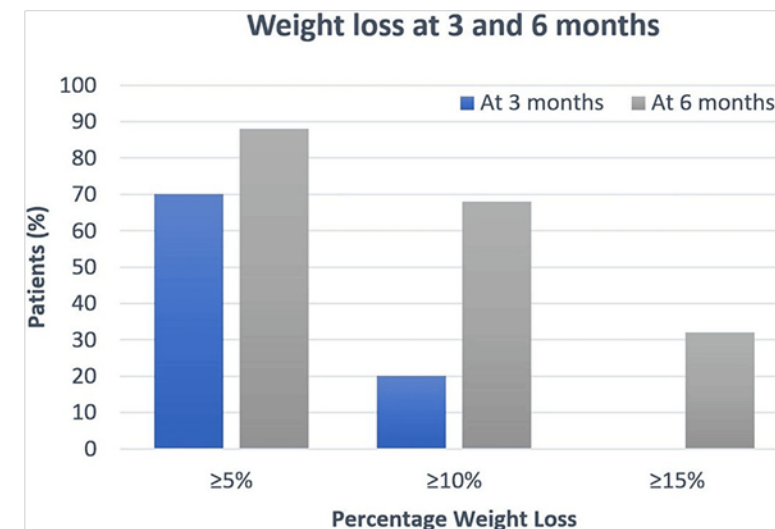
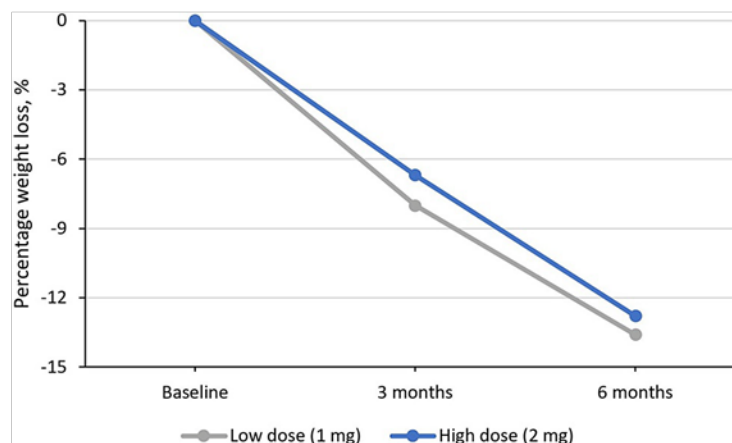
43 soggetti inclusi nello studio:
OW/OB non DM trattati con
semaglutide fino al 1 mg per 12
settimane, poi a dosaggi variabili



40 soggetti arruolati nello studio (3
non hanno raggiunto 12 settimane
di trattamento)



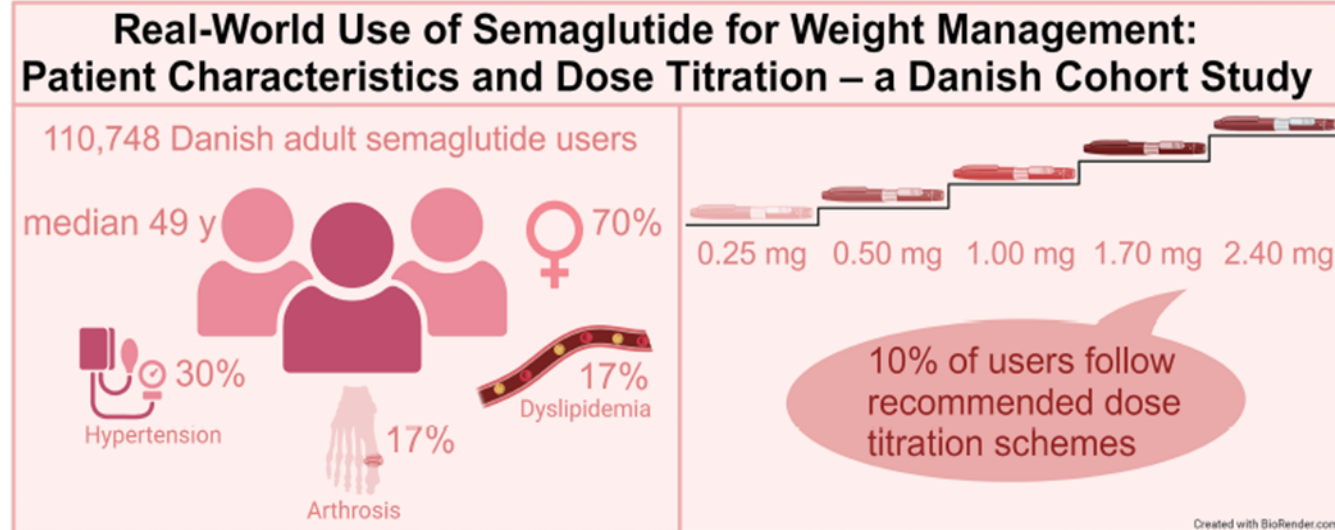
25 soggetti (62,5%) hanno
completato 6 mesi di FUP



**DOPO LE PRIME 12 SETTIMANE, OLTRE IL 50% DEI SOGGETTI HA
MANTENUTO UN DOSAGGIO DI 1 MG A SETTIMANA**

Real-World Use of Semaglutide for Weight Management: Patient Characteristics and Dose Titration—A Danish Cohort Study

Louise Ladebo, Martin T. Ernst, Aurélie Mailhac, Carsten Dirksen, Kirstine N. Bojsen-Møller, and Anton Pottegård



Only 13% reached the maximum dose of 2.4 mg by their fifth prescription, while 5.7% stopped after the first prescription. Few users (10%) followed recommended dose increases every 4 weeks.

Overall, 25% filled at least one prescription of 2.4 mg, while 33–48% continued with the 1.0-mg dosage from the fourth prescription onward.

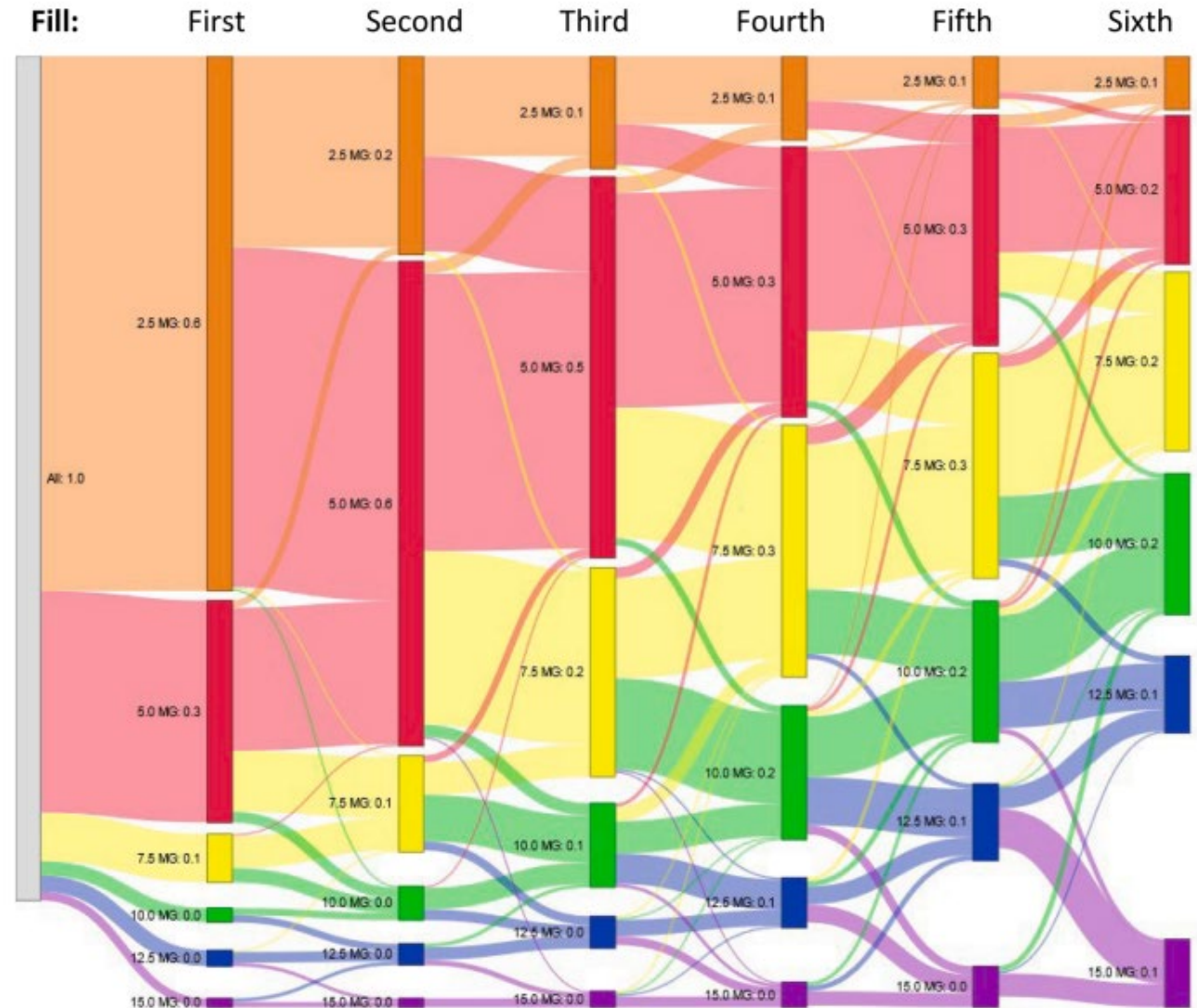
Original article

Real-world use and effectiveness of tirzepatide among people without evidence of type 2 diabetes in the United States

Emily R. Hankosky^a, Karishma Desai^b, Chanadda Chinthammit^a, Michael Grabner^b,
Grace Stockbower^b, Xuanyao He^a, Donna Mojdami^a, Cachet Wenziger^b,
Theresa Hunter Gible^a

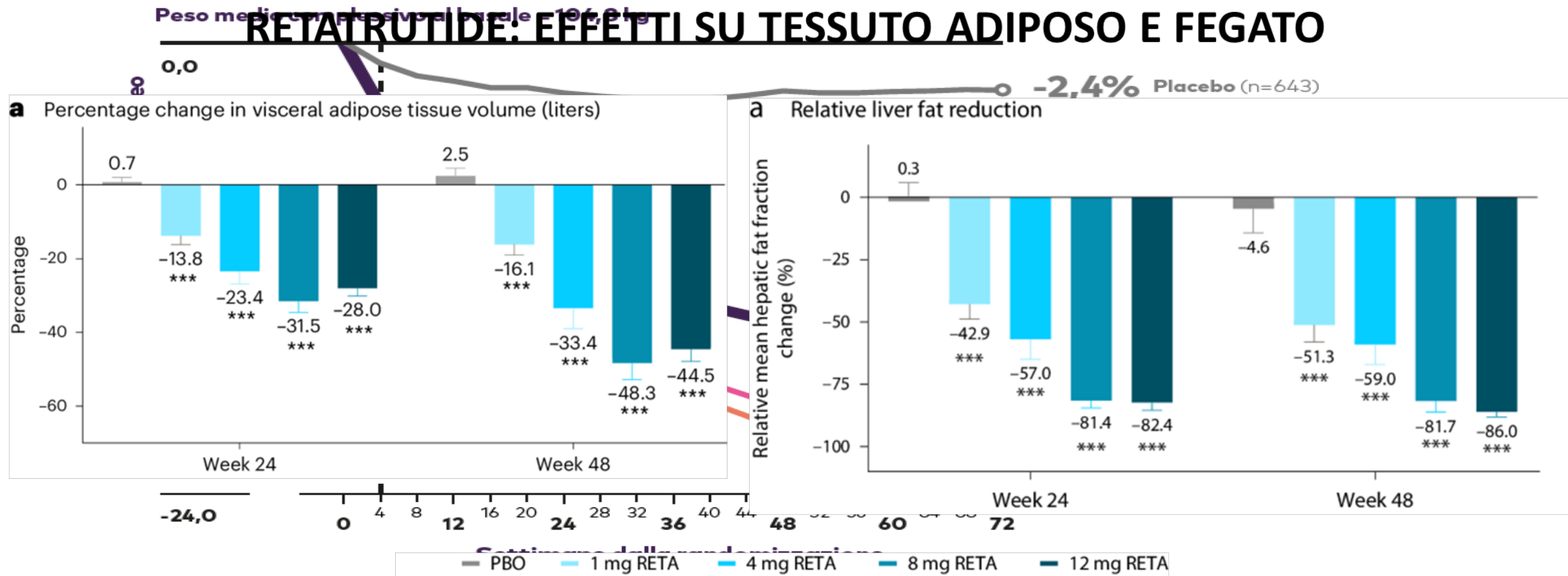
Almost three-quarters (73.8 %) of the OMM-eligible cohort was persistent on tirzepatide for ≥ 6 months

Among those with a sixth prescription fill, more than half of the OMM-eligible cohort was still receiving lower doses of tirzepatide (< 10 mg), indicating some inertia amongst providers, or preference for prescribing lower doses, supply constraints with the higher doses, or adverse effects



UTILIZZO DEI FARMACI PER OBESITA' COME TRATTAMENTO NEOADIUVANTE ALLA CB o IN ADDOME DIFFICILE

RETATRUTIDE: EFFETTI SU TESSUTO ADIPOSO E FEGATO



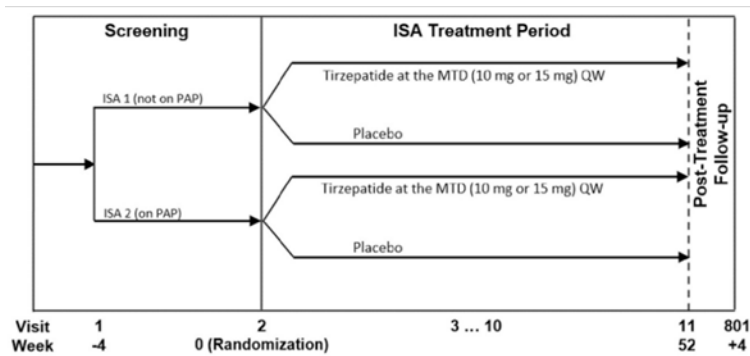
Trattamento dell'OSAS grave in preparazione ad intervento chirurgico

ORIGINAL ARTICLE

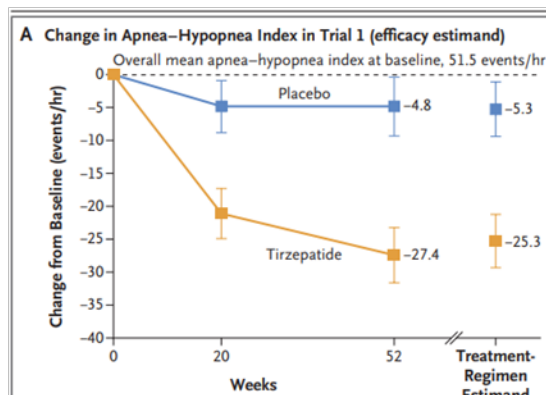
Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity

Atul Malhotra, M.D., Ronald R. Grunstein, M.D., Ph.D., Ingo Fietze, M.D., Terri E. Weaver, Ph.D., Susan Redline, M.D., M.P.H., Ali Azarbarzin, Ph.D., Scott A. Sands, Ph.D., Richard J. Schwab, M.D., Julia P. Dunn, M.D., Sujatro Chakladar, Ph.D., Mathijs C. Bunck, M.D., Ph.D., and Josef Bednarik, M.D., for the SURMOUNT-OSA Investigators*

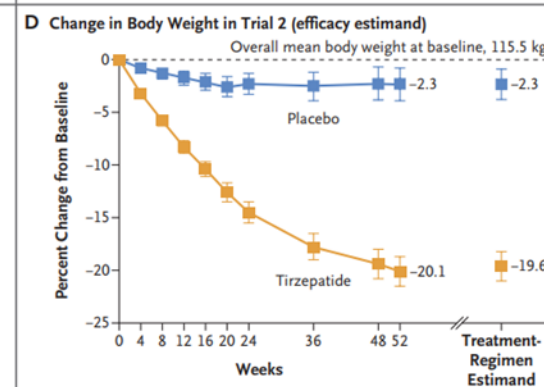
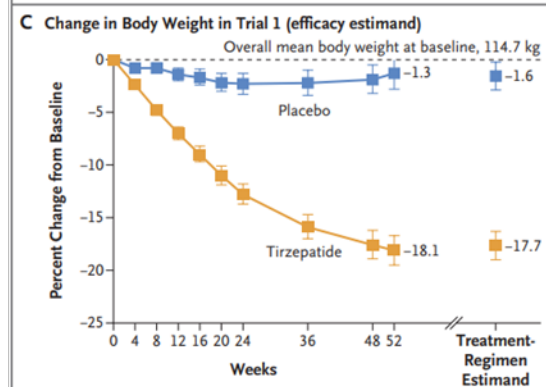
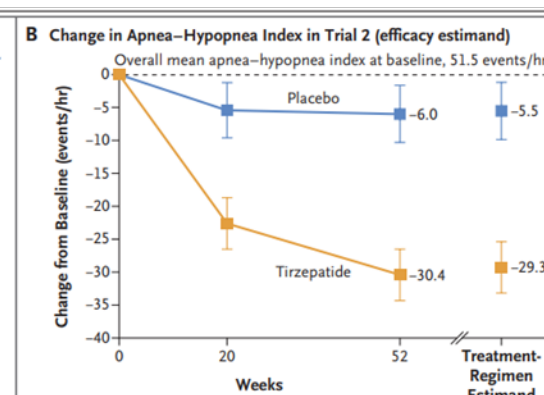
NEJM 2024



TIRZEPATIDE/pl



TIRZEPATIDE/pl + PAP



Up to 50.2% of patients in both SURMOUNT-OSA trials met the combined key secondary end-point criteria of fewer than 5 AHI events per hour or 5 to 14 AHI events per hour and an ESS of 10 or less

INSUFFICIENT WEIGHT LOSS E WEIGHT REGAIN



Tackling suboptimal clinical response after metabolic bariatric surgery:
Impact of tirzepatide on weight loss and body composition

Fabian Stoll^{a,*}, Tobias Kantowski^a, Jonas Laaser^a, Ulrike Kloiber^a, Gabriel Plitzko^b,
Oliver Mann^b, Jens Aberle^a, Anne Lautenbach^a

^a III Department of Medicine, University Medical Center Hamburg-Eppendorf, Hamburg 20246, Germany

^b Department of General, Visceral and Thoracic Surgery, University Medical Center Hamburg-Eppendorf, Hamburg 20246, Germany

Obes Res Clin Pract. 2025

Table 2

Anthropometric and biochemical characteristics at baseline and follow-up.

	Baseline (N = 21)	1M-FU (N = 21)	p-value	3M-FU (N = 21)	p-value	6M-FU (N = 17)	p-value
Body weight [kg]	122.1 ± 24.8	119.1 ± 23.6	< 0.001	113.5 ± 23.5	< 0.001	110.8 ± 24.3	< 0.001
Total weight loss [%]		− 2.4 ± 1.9	< 0.001	− 7.1 ± 3.3	< 0.001	− 12.0 ± 3.4	< 0.001
BMI [kg/m ²]	40.2 ± 6.4	39.2 ± 6.1	< 0.001	37.4 ± 6.1	< 0.001	36.0 ± 6.7	< 0.001
Total BMI change [%]		− 1.0 ± 0.8	< 0.001	− 2.8 ± 1.3	< 0.001	− 4.8 ± 1.4	< 0.001
Waist circumference [cm]	121.4 ± 17.4	118.6 ± 18.5	0.060	112.9 ± 16.0	< 0.001	111.3 ± 16.12	< 0.001
Body fat [%]	42.6 ± 7.7	41.3 ± 6.9	0.123	41.0 ± 8.2	0.266	39.2 ± 7.5	< 0.001
Fat mass change [kg]		− 1.8 ± 2.2	0.006	− 4.8 ± 4.0	< 0.001	− 9.5 ± 4.3	< 0.001
Fat-free mass [%]	57.4 ± 7.7	58.7 ± 6.9	0.123	59.0 ± 8.2	0.266	60.8 ± 7.5	< 0.001
Fat-free mass change [kg]		− 1.0 ± 1.9	0.103	− 4.4 ± 3.9	< 0.001	− 5.5 ± 4.3	< 0.001
Total body water [%]	42.8 ± 5.5	43.0 ± 5.0	0.638	43.5 ± 5.6	0.620	44.53 ± 5.5	0.010
Basal metabolism [kcal]	2211.4 ± 489.8	2161.9 ± 473.3	0.005	2065.4 ± 463.4	< 0.001	2045.8 ± 446.9	< 0.001
Hb [g/dl]	13.4 ± 1.4	13.7 ± 1.5	0.094	13.9 ± 1.6	0.106	14.0 ± 1.4	0.334
Platelets [10 ³ /μl]	254.1 ± 88.9	249.8 ± 81.5	0.918	273.7 ± 74.3	0.715	255.3 ± 69.4	0.870
HbA1c [%]	5.4 ± 0.3	5.2 ± 0.3	< 0.001	5.1 ± 0.3	< 0.001	5.1 ± 0.3	< 0.001

What Does the Rise of GLP-1 Drugs Mean for Bariatric Surgery?

Kate Schweitzer¹

» Author Affiliations

JAMA. 2025;333(9):743-745. doi:10.1001/jama.2024.25968



In US there was a 25% to 30% decrease in case volume that started in 2023, with the advent of new AOM **BUT** The ASMBS reports that in 2022 nearly **280,000** metabolic and bariatric procedures were performed in the U.S., which represents only about 1% of those who meet eligibility requirements based on BMI.

If weight-loss treatments, not just lifestyle modifications, gain traction, pervasive stigmas could be lessened and surgeons could begin to serve more than just the 1%. If this is an opportunity to bring more people in so they can learn about the benefits of bariatric surgery and not be afraid of it, that can increase those numbers.

“There’s enough room for all of us.”

Quando si considera la migliore opzione terapeutica è necessario considerare alcuni fattori:

- **gravità dell'obesità e delle comorbidità**
- **rapporto rischio/beneficio**
- **età del paziente e aspettativa di vita (mantenimento del peso)**
- **preferenza del paziente**

Choices (BMS/AOM) are being framed as «either-or» or «one-size-fits-all», but combination therapies are common in medicine, so why not consider them here?

Schweitzer K. *JAMA*. 2025



Nov 2023:

a 49-year-old male presented to the bariatric clinic seeking bariatric surgery. The patient had an initial weight of 272 kg (BMI 106.25 kg/m²) and a history of type 2 diabetes mellitus (T2DM), obstructive sleep apnea (OSA) requiring nocturnal BiPAP, bilateral lipedema, and had been bedbound for 2 years

The MDT collectively determined that the patient required preoperative optimization before considering laparoscopic sleeve gastrectomy (LSG)

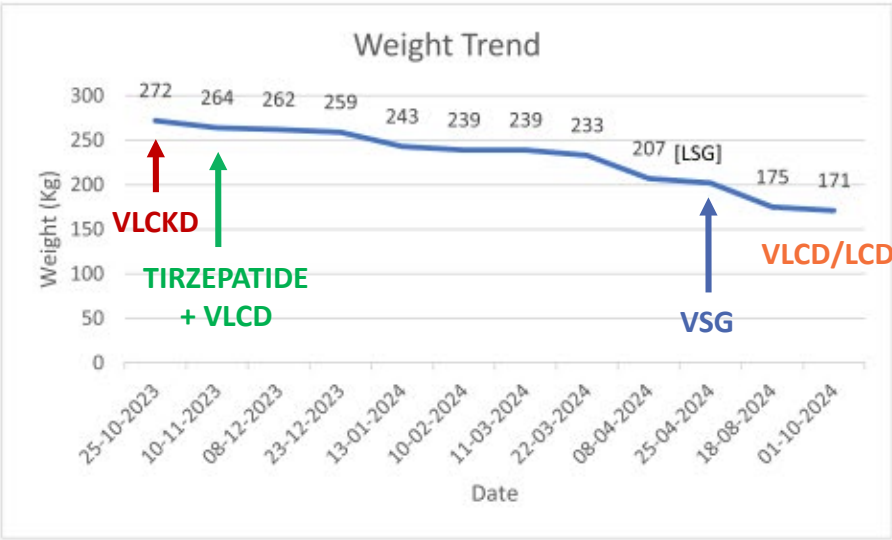


Figure 1. Weight trend since admission until October 2024, pre and post-op.

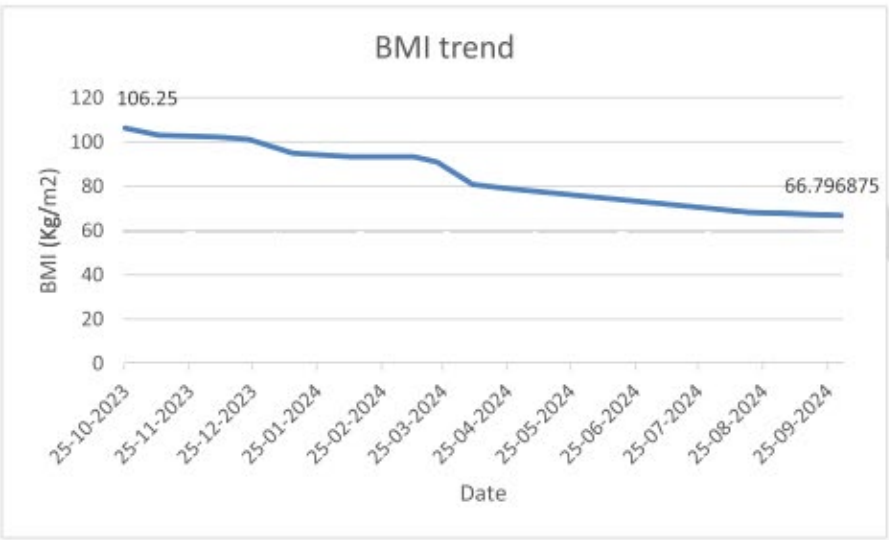


Figure 2. BMI trend since admission until October 2024, pre and post-op.

UOC Endocrinologia e Prevenzione e Cura del Diabete
IRCCS Az. Ospedaliero-Universitaria di Bologna

Prof. U. Pagotto



Thank You!

Gruppo Obesità

Prof.ssa M.L. Petroni
Dott. Emmanuele Capobianco
Dott. Ercole Franco
Dott.ssa Federica Pippa
Dott.ssa Valentina Pasquali
Dott.ssa Federica Delfini
Dott.ssa Beatrice Baldini
Dott.ssa Ida Sicilia

Dietiste/Nutrizioniste

Dott.ssa Vania Campanella,
Dott.ssa Roberta Fazzeri,
Dott.ssa Ilaria Improta

Case Manager

Lucia Falcone

