

News 2. Tirzepatide:
novità nel diabete e nell'obesità.

Dario Tuccinardi M.D. Ph.D.



Disclosure

Dr. Dario Tuccinardi has received funding from the following companies:

For providing educational sessions

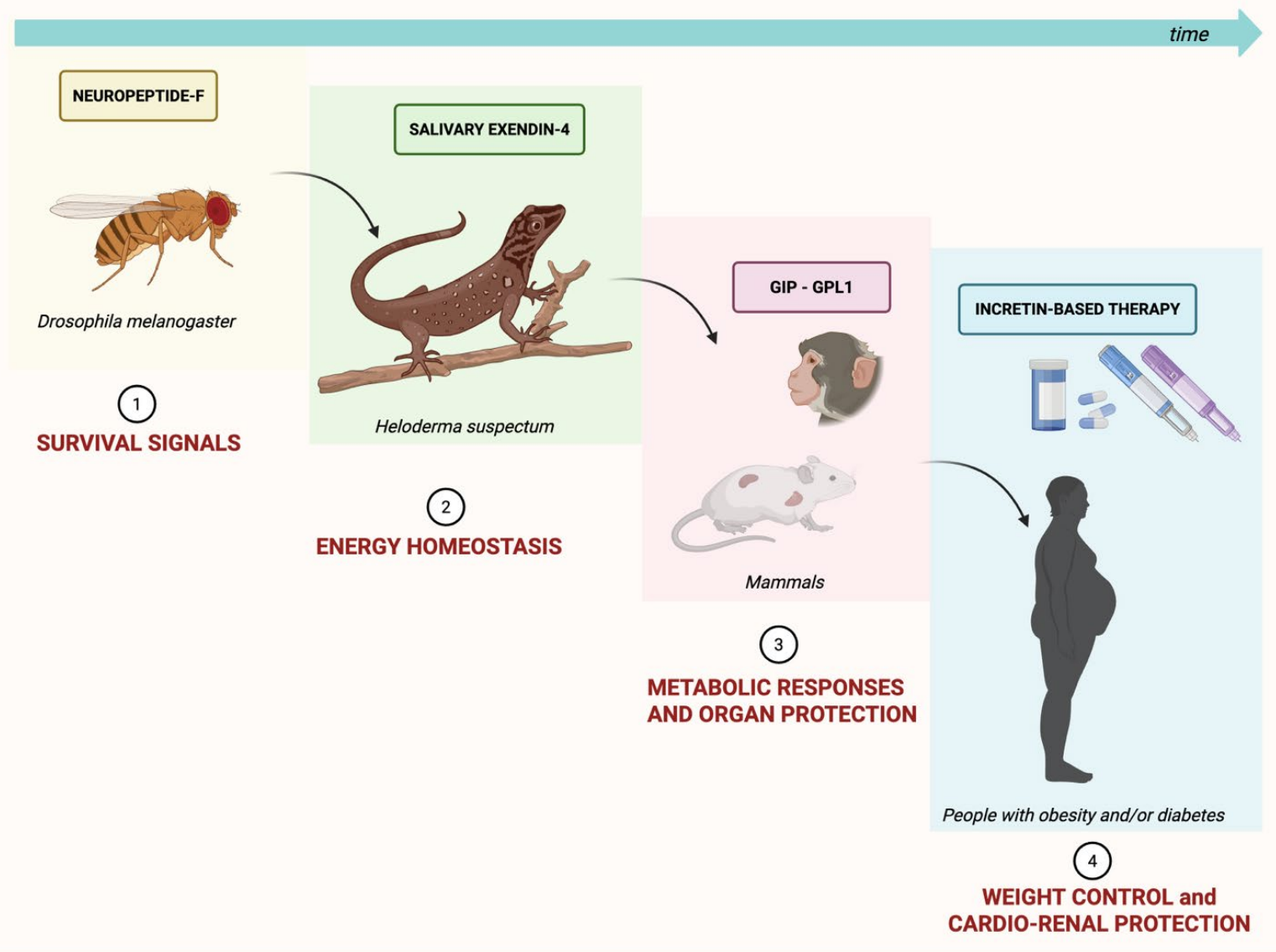
-Novo Nordisk, AstraZeneca, Eli Lilly, Mundipharma, boehringer Ingelheim

Institutional research grant support or funding for clinical trials

-Novo Nordisk, Abbott, LJ Pharma, Eisai, Eli Lilly and Boehringer Ingelheim

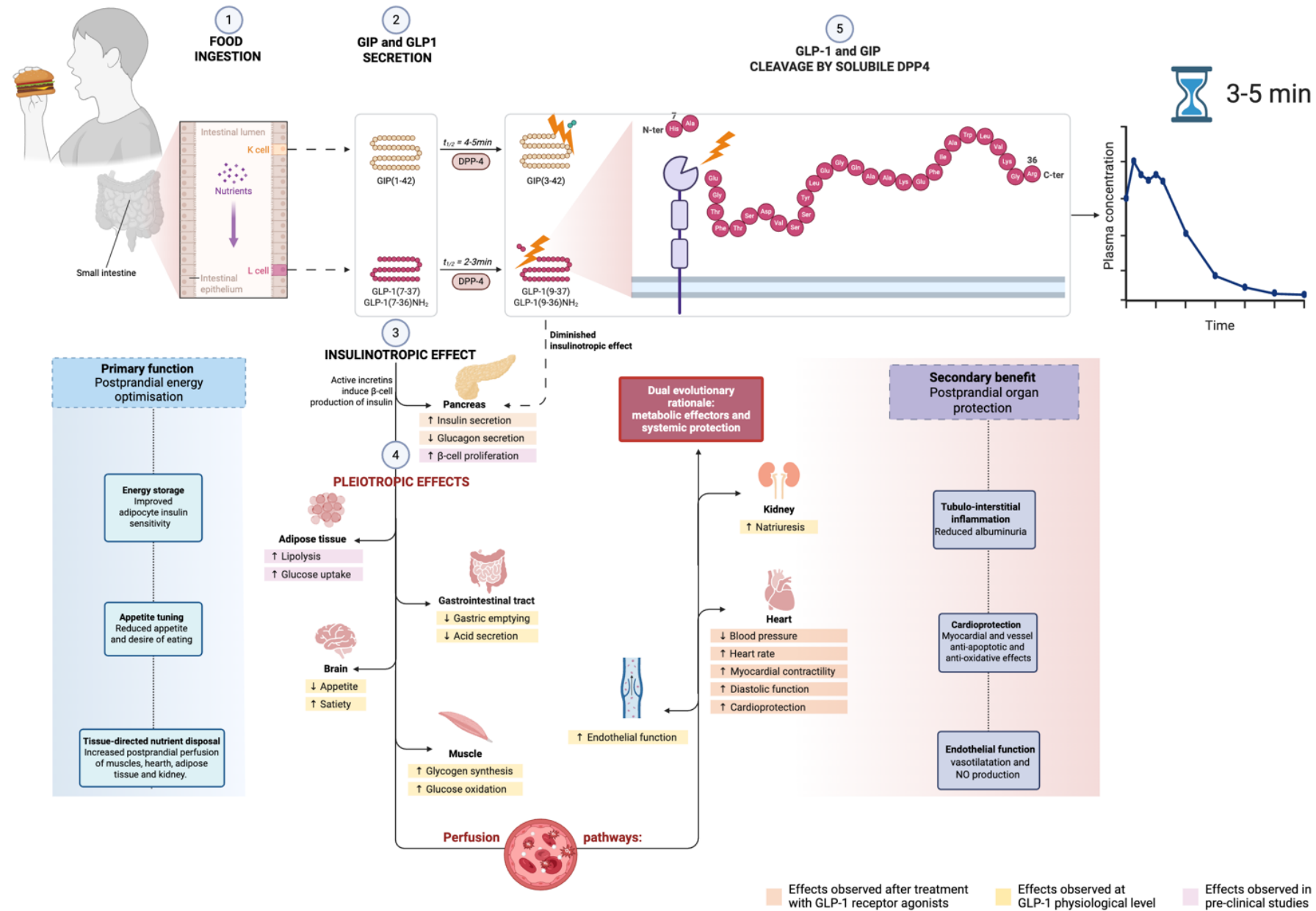
Institutional Scientific Board and/or consulting

- Novo Nordisk



L'origine evolutiva degli agonisti incretinici

Dai segnali di fame ancestrali alla protezione cardio-renale



Il doppio volto dell'incrétina: energia e protezione

Come GIP e GLP-1 orchestrano la risposta postprandiale

GLP-1 and GIP Beyond Glycaemia: Evolutionary Roles in Energy Optimisation and Organ Protection.

Tuccinardi D, Watanabe M, Masi D, Gianfrilli D, Manfrini S, Le Roux CW.

Diabetes Metab Res Rev. 2025; in press. doi:10.1002/dmrr.70108.

Ruoli proposti di GIP e GLP-1 nella regolazione del metabolismo^{1,2,*}

Attività del GIP

Sistema nervosa centrale

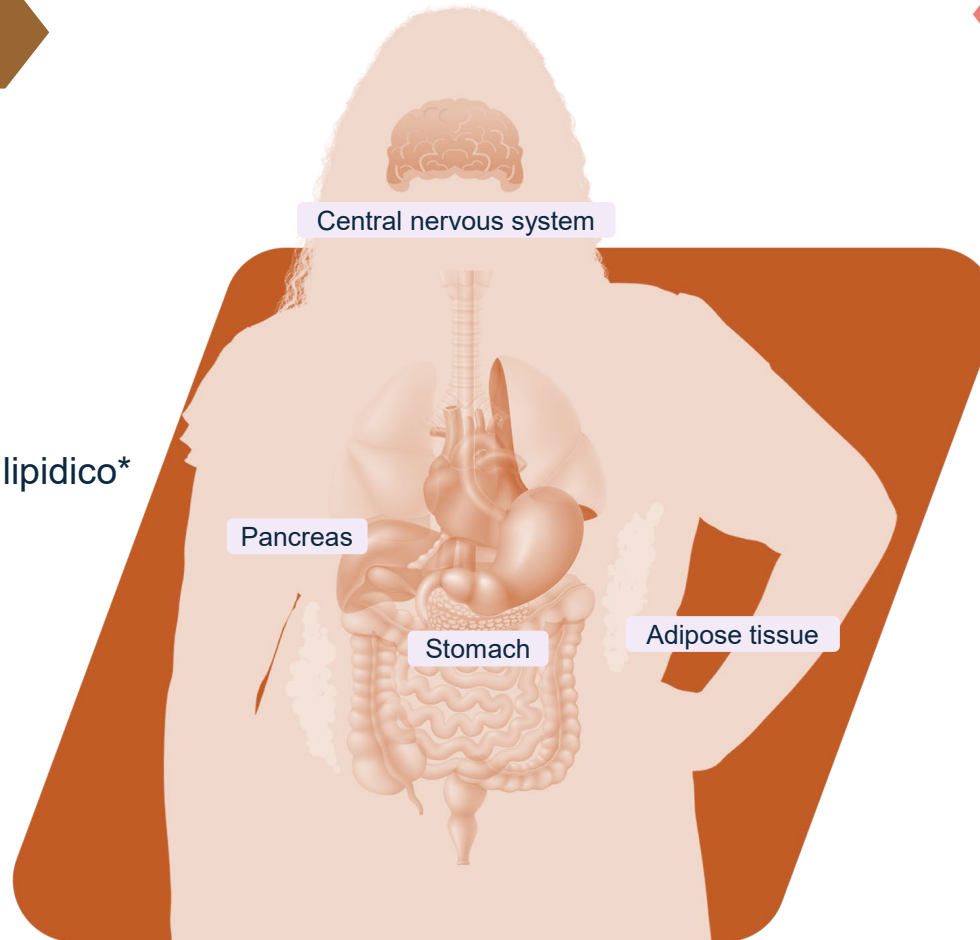
- ▼ Riduzione dell'assunzione di cibo*
- ▼ Diminuzione della nausea

Tessuto adiposo

- ▲ Aumento della sensibilità insulinica*
- ▲ Aumento capacità di tamponamento lipidico*
- ▲ Aumento del flusso sanguigno
- ▲ Aumento capacità di storage*
- ▼ Ridotta infiltrazione di cellule immunitarie pro-infiammatorie

Pancreas

- ▲ Aumento della secrezione di insulina
- ▲ Aumento del glucagone in modo glucosio-dipendente



Attività del GLP-1

Sistema nervosa centrale

- ▼ Riduzione dell'assunzione di cibo
- ▲ Aumento della sazietà
- ▲ Aumento della nausea

Pancreas

- ▲ Aumento della secrezione di insulina
- ▼ Riduzione del glucagone

Stomaco

- ▼ Ritardo svuotamento gastrico

*Demonstrated in preclinical research.

GIP=glucose-dependent insulintropic polypeptide; GLP-1=glucagon-like peptide-1.

1. Samms RJ, et al. Trends Endocrinol Metab. 2020;31(6):410–421. 2. Roh E, Choi KM. Int J Mol Sci. 2023;24(4):3384.

OBESEITY TREATMENT BASED ON PATIENT PHENOTYPING

FIRST-LINE THERAPY IS LIFESTYLE MODIFICATION (MEDICAL NUTRITIONAL APPROACH AND IMPLEMENTATION OF PHYSICAL ACTIVITY AND BEHAVIOURAL THERAPY)*

EXCLUDE ENDOCRINE FORMS OF OBESEITY, if suspected, investigate MONOGENIC FORMS

ASSESSMENT OF THE PRESENCE OF COMPLICATIONS AND PATIENT PHENOTYPING

OBESEITY TREATMENT BASED ON PATIENT COMPLICATIONS AND PHENOTYPING

METABOLIC CARDIO RENAL COMPLICATIONS						MECHANICAL COMPLICATIONS		WEIGHT LOSS TARGETS /OWCMC**	AGE	EATING BEHAVIOUR	SPECIAL POPULATIONS	COSTS /QALY
+ASCVD	Indicators of High CV Risk:	HF	CKD	GLYCEMIC CONTROL	MASH/MASLD	OSTEOARTRITIS	OSAS					
Cardiovascular disease was defined as a previous myocardial infarction, previous stroke, or symptomatic peripheral arterial disease in people who are ≥ 45 years of age, with a BMI ≥ 27 kg/m².	Definitions vary; most comprise ≥ 40 years of age, BMI ≥ 27 kg/m², male gender, high blood pressure, atherogenic dyslipidemia, smoking, prediabetes, ASCVD risks (ACC/AHA).	Clinical heart failure (NYHA II–IV) with LVEF ≥50% (tirzepatide) or ≥45% (semaglutide), BMI ≥30 kg/m², reduced functional capacity (KCCQ-CSS <80 or <90), 6-minute walk ≥100 m, and elevated filling pressures (NT-proBNP, echocardiographic criteria, or recent HF hospitalization). T2D was all in the tirzepatide trial.	eGFR < 60 ml/ min per 1.73 m² OR albuminuria (ACR ≥ 3.0 mg/mmol (30mg/g)	PREDIABETES (HbA1c ≥ 5.7% and < 6.5%, FPG > 100 ng/dl < 126 mg/dl, OGTT 120 min glucose ≥ 140 mg/dl < 200 mg/dl) Tirzepatide 15 mg Semaglutide 2.4 mg Liraglutide 3 mg ^{12,74} Orlistat 120 mg ¹⁴ Metformin: off-label; may reduce diabetes incidence ²⁴ .	Adults with biopsy-confirmed MASH, fibrosis stage (F2–F3) for semaglutide 2.4 and tirzepatide 15 mg, F0–F3 for liraglutide 3 mg, BMI ≥25 kg/m² for semaglutide 2.4 mg and liraglutide 3 mg, BMI ≥27 kg/m² for tirzepatide 15 mg; with or without type 2 diabetes but not for semaglutide 2.4.	Adults ≥18 years with BMI ≥30 kg/m², clinically and radiographically confirmed knee osteoarthritis (ACR criteria; Kellgren–Lawrence grade 2–3), and baseline knee pain ≥40/100 on the WOMAC pain scale.	Adults ≥18 years, BMI ≥30 kg/m², with moderate-to-severe obstructive sleep apnea (AHI ≥15 events/hour); CPAP use allowed (tirzepatide) or excluded (liraglutide); no diagnosis of T2D.	Set individualized weight management goals 5-10% WL Orlistat ¹⁴ Liraglutide 3 mg ⁷⁴ Naltrexone/ Bupropion ²⁷ Phentermine/Topiramate (low-mid doses) ⁶⁰	≥ 2 y.o. ¹⁰⁴ Setmelanotide (rare genetic obesity) Metreleptin (rare genetic obesity) 6-12 y.o. Liraglutide 3mg ¹⁰⁹ (EMA only) 12-18 y.o. Liraglutide 3mg ¹¹² Semaglutide 2.4mg ¹¹³ Phentermine/Topiramate ¹¹⁵ (FDA only) Orlistat 120 mg ¹¹⁴ (FDA only) 18-65 y.o. Phentermine/Topiramate ¹¹⁶ Tirzepatide 15 mg Semaglutide 2.4 mg Naltrexone/Bupropion ^{27,28} Phentermine/Topiramate ²⁶ Orlistat ¹⁴ >65 y.o. Naltrexone/Bupropion ²⁷ (Caution; limited data >75 yrs) Phentermine/Topiramate ²⁶ (Caution; monitor CNS/renal) Orlistat ¹⁴ (Usable; limited efficacy data) Sarcopenic obesity pervised Resistance Training + Protein Intake + 2.1–2.5 g/kg/day ¹¹⁸ Liraglutide 3 mg is preferred for gradual weight loss with lean mass preservation and proven cardiovascular safety ³³	EMOTIONAL EATING Bupropion / Tirzepatide 15 mg ¹³⁶ mg ¹²⁵ BINGE EATING Not AOMs approved explicitly for binge eating disorder. Liraglutide 3.0 mg ¹²³ Phentermine/Topiramate ¹²⁸ Naltrexone/Bupropion ²⁸ Orlistat 120 mg ¹²⁹ Semaglutide 2.4 mg ¹²⁵ Tirzepatide 15 mg ^{128,134}	CANCER safety No significant increase in thyroid cancer risk from Semaglutide 2.4 mg ¹⁴⁰ Tirzepatide 15 mg ¹⁴⁷ Evidence of increased thyroid cancer risk in mixed T2D populations. ¹⁴⁵ No evidence of increased cancer risk (for other AOMs: Orlistat, Phentermine/Topiramate, Bupropion/Naltrexone) Familial Partial Lipodystrophy 1-3 (FPLD1-3) Acquired Partial Lipodystrophy (Barraquer-Simons) HIV-Associated Lipodystrophy Semaglutide 2.4 mg ¹⁵² MONOGENIC OR SYNDROMIC OBESEITY Congenital leptin deficiency Metreleptin ¹⁵³ (biallelic POMC, PCSK1, or LEPR deficiency and for BBS) Setmelanotide 3 mg ¹⁵⁴ ACQUIRED HYPOTALAMIC OBESEITY Setmelanotide 3 mg ¹⁵⁴ Semaglutide 2.4 mg ¹⁵⁵ PREGNANCY/WILLINGNESS TO CONCEIVE AOMs are either contraindicated or advised against during pregnancy due to insufficient safety data and potential risks to the fetus Stop Liraglutide 3 mg/Semaglutide 2.4 mg at least 2 months before Stop Tirzepatide 15 mg at least 1 month before	BS 176,177
Semaglutide 2.4 mg ⁴	Tirzepatide 15 mg ^{2,10} Semaglutide 2.4 mg ^{3,4} Liraglutide 3 mg ¹²	Tirzepatide 15 mg ¹¹ Semaglutide 2.4 mg ⁵	Semaglutide 2.4 mg ^{3,11,19} Tirzepatide 15 mg ^{11,19} (use if eGFR>30 ml/min; If eGFR<30 use with caution due to limited data)	Tirzepatide 15 mg ¹¹ Semaglutide 2.4 mg ¹¹ Liraglutide 3 mg ³³	Semaglutide 2.4 mg ⁵⁴ Tirzepatide 15 mg ⁵ Liraglutide 3 mg ¹²	Semaglutide 2.4 mg ⁶³ Tirzepatide 15 mg ⁶⁸ Liraglutide 3 mg ⁶⁹ Orlistat 120 mg ¹⁴ Naltrexone/bupropione ⁶⁴ Phentermine/Topiramate ²⁶	Tirzepatide 15 mg ⁶⁸ Liraglutide 3 mg ⁶⁹ Phentermine/Topiramate ⁷⁰ Tirzepatide 15 mg ⁷⁷ Semaglutide 2.4 mg ⁷⁸ (not available yet) Cagrisema ⁷⁸ (not available yet)	10-20% WL Tirzepatide 5 mg ⁷ Semaglutide 2.4mg ³ Phentermine/Topiramate ¹⁴ >20% WL Tirzepatide 15mg ⁷ Semaglutide 2.4 mg ⁷⁷ (not available yet) Cagrisema ⁷⁸ (not available yet)				

If additional weight loss and reduction of weight-related complications are needed

Bariatric Surgery¹⁷⁷

If insufficient weight loss or weight regain after BS consider: Tirzepatide¹⁹⁷, Semaglutide¹⁹⁴, Liraglutide^{195,196}

*This framework promotes a phenotype-based, individualized approach to obesity care, prioritizing complications and patient preferences over rigid treatment hierarchies, with patient-HCP shared decision-making considering goals, tolerability, contraindications, and cost. **OWCMC, obesity without clinically manifest complications

Set
individualized
weight
management
goals

5-10% WL

Orlistat¹⁴

Liraglutide 3 mg⁷⁴

Naltrexone/
Bupropion²⁷

Phentermine/Topiramate (low-mid doses)⁶⁰

10-20% WL

Tirzepatide 5 mg²

Semaglutide 2.4mg³

Phentermine/Topiramate (low-mid doses)¹⁶

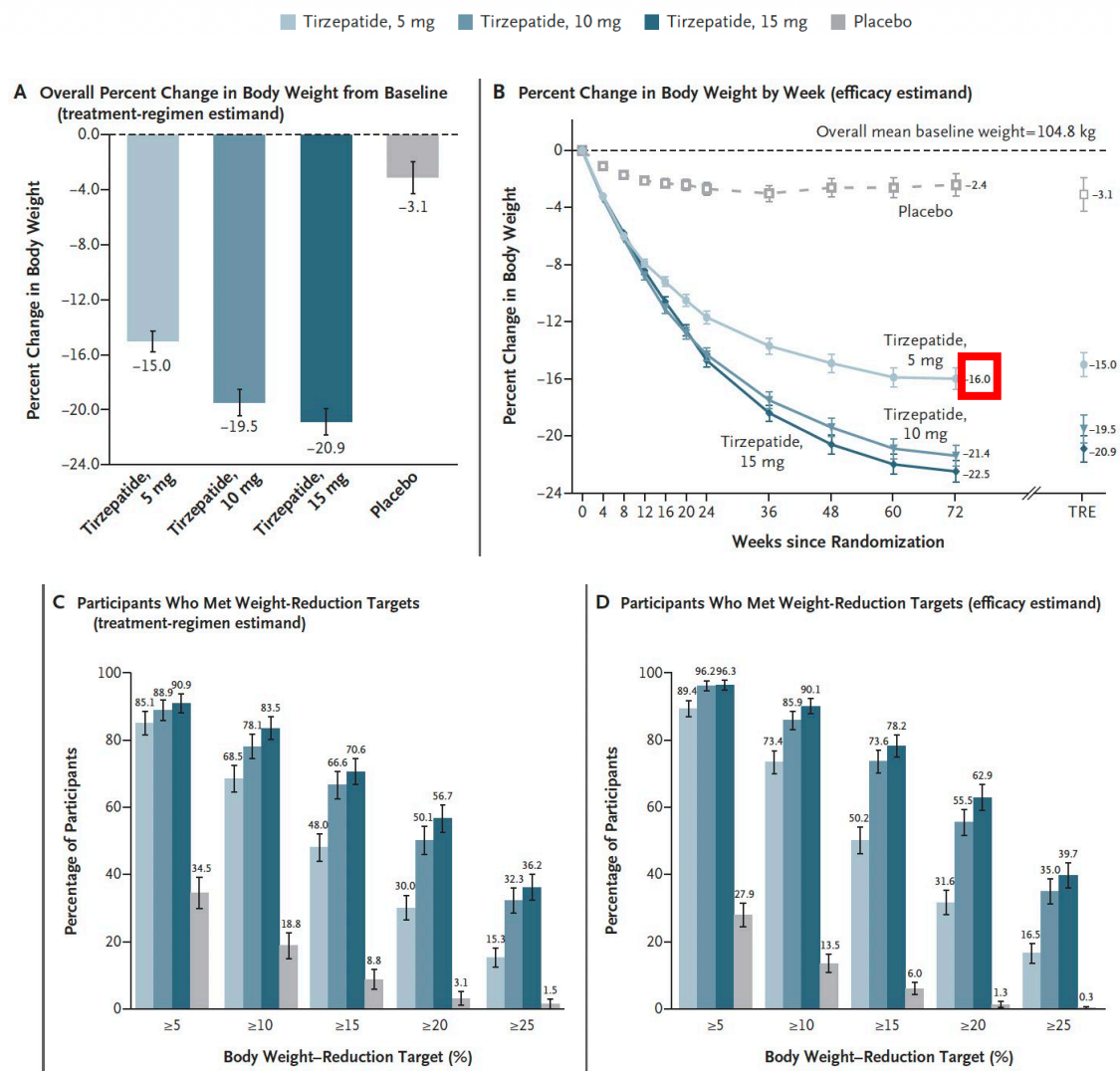
>20% WL

Tirzepatide 15mg²

Semaglutide 7.2 mg⁷⁷
(not available yet)

Cagrisema⁷⁸
(not available yet)

Efficacia e durabilità: la base del paradigma tirzepatide Studio cardine in adulti con obesità senza diabete



Nel SURMOUNT-1, i pazienti in trattamento con **tirzepatide** hanno ottenuto una perdita di peso media del 15–21% rispetto al 3% con placebo, oltre l'80% dei pazienti ha raggiunto $\geq 10\%$ e **oltre il 50% ha raggiunto il $\geq 20\%$** di calo ponderale. L'effetto è progressivo, stabile fino alla settimana 72 e mostra durabilità.

Già alla dose di 5mg ha dimostrato una perdita di peso maggiore rispetto al placebo **fino al 16% dopo 72 settimane**

WEIGHT LOSS
TARGETS /OWCMC**

Set
individualized
weight
management
goals

5-10% WL

Orlistat¹⁴
Liraglutide 3 mg⁷⁴
Naltrexone/
Bupropion²⁷
Phentermine/Topira
mate (low-mid
doses)⁶⁰

10-20% WL

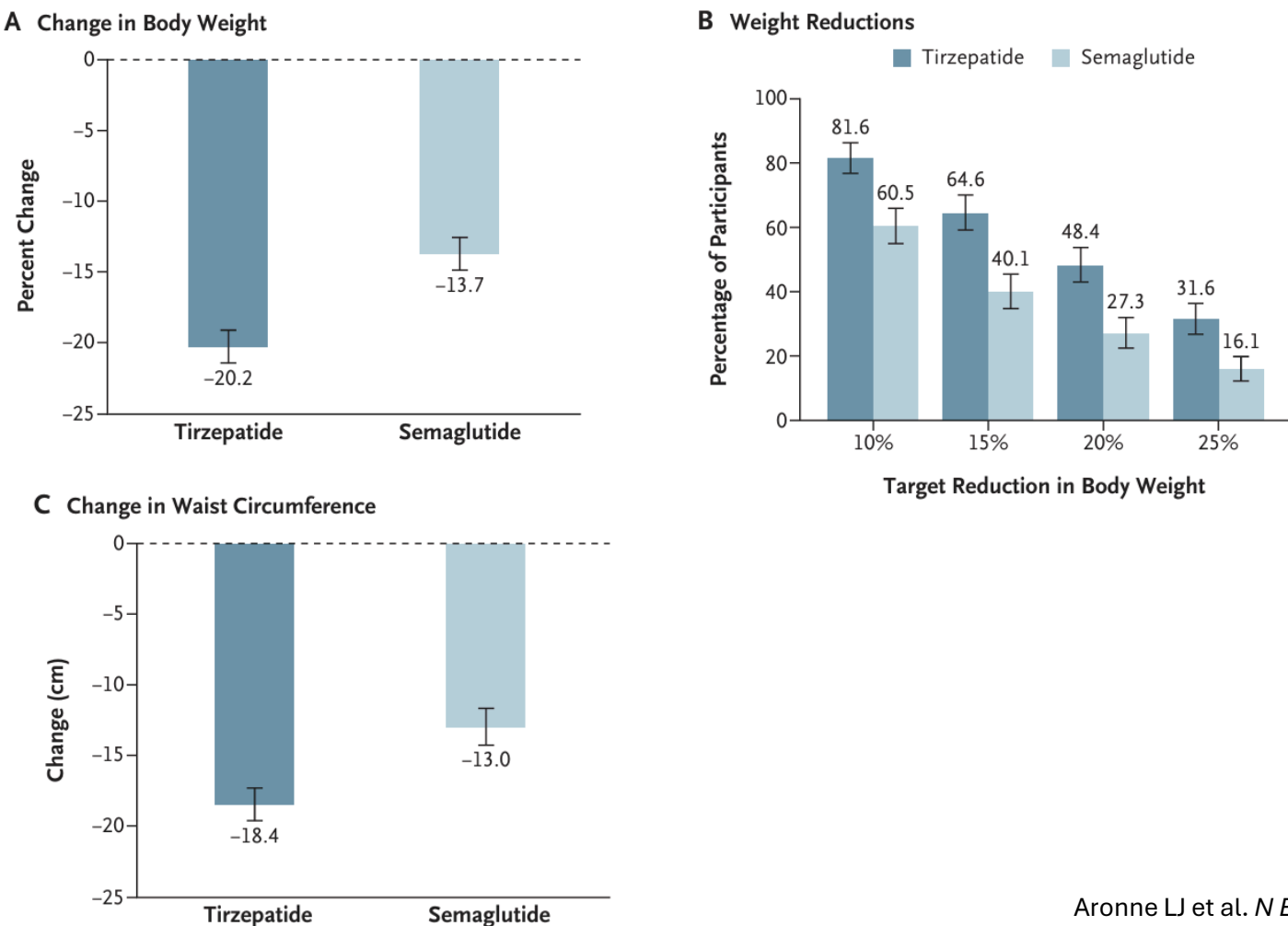
Tirzepatide 5 mg²
Semaglutide
2.4mg³
Phentermine/
Topiramate (low-
mid doses)¹⁶

>20% WL

Tirzepatide 15mg²
Semaglutide 7.2
mg⁷⁷
(not available yet)
Cagrisema⁷⁸
(not available yet)

Tirzepatide vs semaglutide: confronto diretto nell'obesità senza diabete (SURMOUNT-5)

Trial di fase 3b, 72 settimane, 751 adulti con obesità senza diabete, randomizzati 1:1 a tirzepatide o semaglutide massimo dosaggio tollerato



Nel SURMOUNT-5, tirzepatide ha ottenuto un calo ponderale medio del **-20,2 % rispetto al -13,7%** con semaglutide, -6,5 pp (P < 0,001), con quasi il 50% dei partecipanti che ha superato il 20 % di perdita di peso e **una maggiore riduzione della circonferenza della vita -5,4 cm (P < 0,001)**. Risultati coerenti in entrambi i sessi e nei sottogruppi di BMI e prediabete.

GLYCEMIC CONTROL

PREDIABETES

HbA1c 5.7–6.4%, fasting plasma glucose 100–125 mg/dL, or 2-hours OGTT glucose 140–199 mg/dL

- Tirzepatide 15 mg²
- Semaglutide 2.4 mg²²
- Liraglutide 3 mg^{12,74}
- Orlistat 120 mg¹⁴

Metformin: off-label use; may reduce the incidence of type 2 diabetes²⁴.

TYPE 2 DIABETES

HbA1c ≥ 6.5%, fasting plasma glucose ≥ 126 mg/dL, or 2-hours OGTT plasma glucose ≥ 200 mg/dL

- Tirzepatide 15 mg³¹
- Semaglutide 2.4 mg²⁹
- Liraglutide 3 mg³³

SGLT2 inhibitors support weight loss^{37,38,39,40,41}. If glycemic control allows, insulin^{44,45}, thiazolidinediones, and sulfonylureas should be avoided due to their propensity to induce weight gain.²⁰³

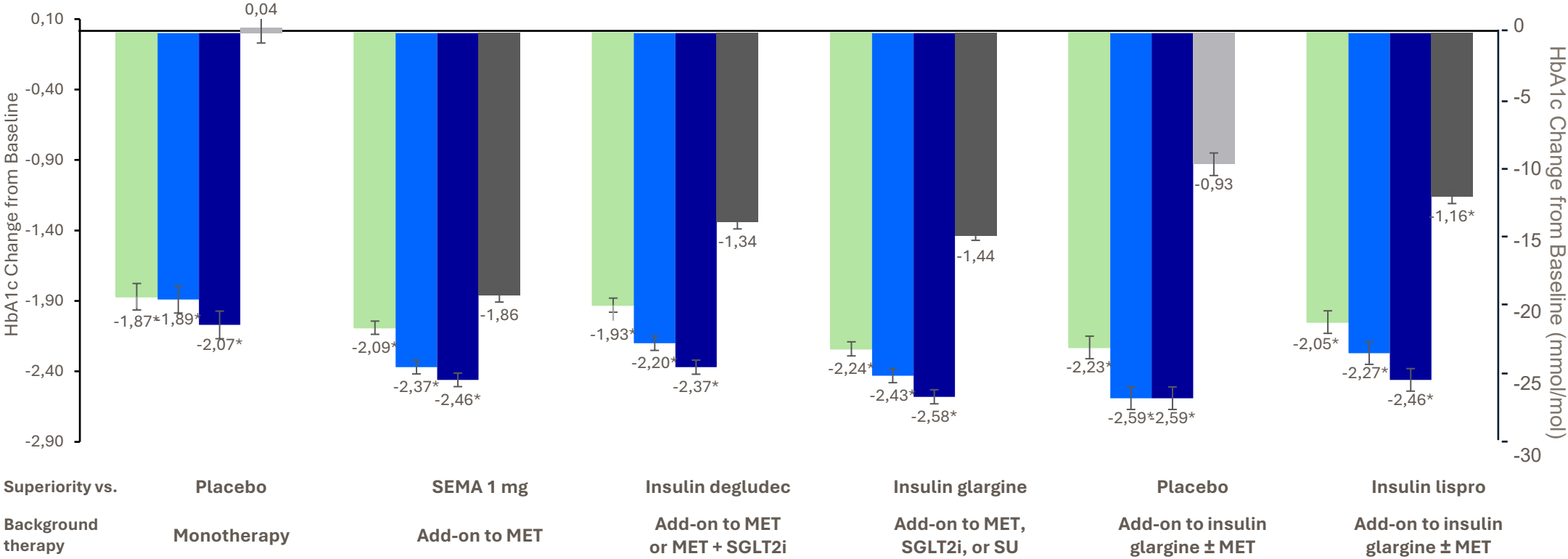
TYPE 1 DIABETES

(OFF-LABEL only for weight loss purposes)

- Tirzepatide 15 mg⁵²
- Semaglutide 2.4 mg⁵¹

SURPASS PROGRAM: tirzepatide provides superior reduction in HbA1c from baseline to primary endpoint vs all comparators

Study	SURPASS-1 ¹	SURPASS-2 ²	SURPASS-3 ³	SURPASS-4 ⁴	SURPASS-5 ⁵	SURPASS-6 ⁶
Duration	40 Weeks	40 Weeks	52 Weeks	52 Weeks	40 Weeks	52 Weeks
Baseline HbA1c	7.9%	8.3%	8.2%	8.5%	8.3%	8.8%
N	478	1879	1444	2002	475	1425



*p<0.001 vs. placebo or active comparator.

Data are LSM (SE). mITT population (efficacy analysis set). MMRM analysis. Data labels are % HbA1c. Number of participants (N) mentioned is randomized participants.

DPP4i= dipeptidyl peptidase-4 inhibitor; HbA1c = glycated hemoglobin; LSM = least squares mean; MET = metformin; mITT = modified intent-to-treat; MMRM = mixed model repeated measures; SE = standard error; SEMA = semaglutide; SGLT2i = sodium-glucose co-transporter-2 inhibitor; SU = sulfonylurea; TZP = tirzepatide.

1. Rosenstock J, et al. *Lancet*. 2021;398(10295):143-155. 2. Frias JP, et al. *N Eng J Med*. 2021;385(6):503-515. 3. Ludvik B, et al. *Lancet*. 2021;398(10300):583-598. 4. Del Prato S, et al. *Lancet*. 2021;398(10313):1811-1824. 5. Dahl D, et al. *JAMA*. 2022;327(6):534-545. 6. Rosenstock J, et al. Poster from ADA 2023 750P.

GLYCEMIC CONTROL

Prevenzione del diabete

PREDIABETES

HbA1c 5.7–6.4%, fasting plasma glucose 100–125 mg/dL, or 2-hours OGTT glucose 140–199 mg/dL

Tirzepatide 15 mg ²

Semaglutide 2.4 mg ²²

Liraglutide 3 mg ^{12,74}

Orlistat 120 mg ¹⁴

Metformin: off-label use; may reduce the incidence of type 2 diabetes²⁴.

TYPE 2 DIABETES

HbA1c ≥ 6.5%, fasting plasma glucose ≥ 126 mg/dL, or 2-hours OGTT plasma glucose ≥ 200 mg/dL

Tirzepatide 15 mg ³¹

Semaglutide 2.4 mg ²⁹

Liraglutide 3 mg ³³

SGLT2 inhibitors support weight loss ^{37,38,39,40,41}. If glycemic control allows, insulin^{44,45}, thiazolidinediones, and sulfonylureas should be avoided due to their propensity to induce weight gain.²⁰³

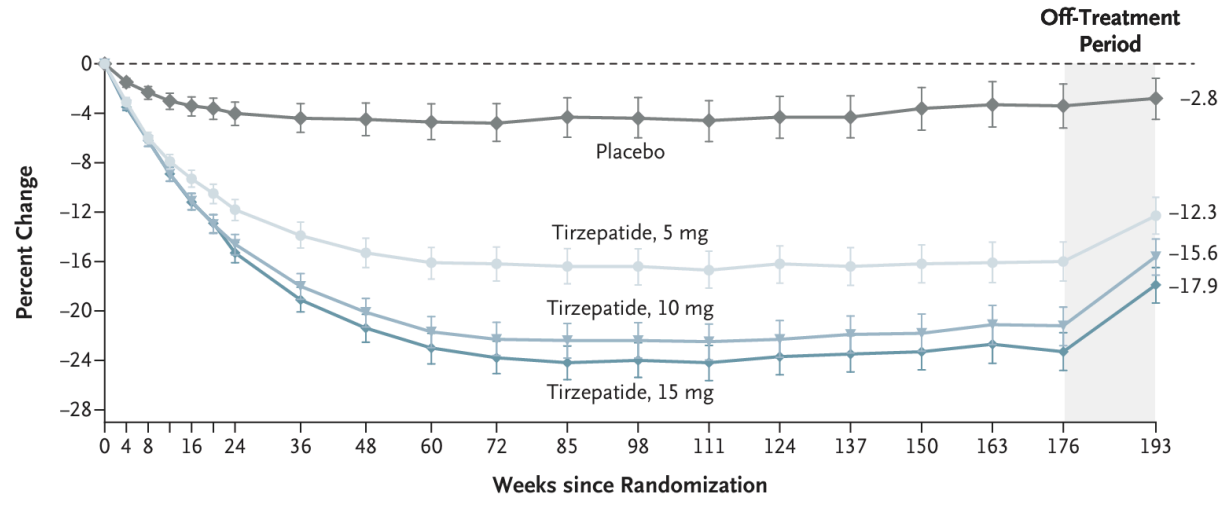
TYPE 1 DIABETES

(OFF-LABEL only for weight loss purposes)

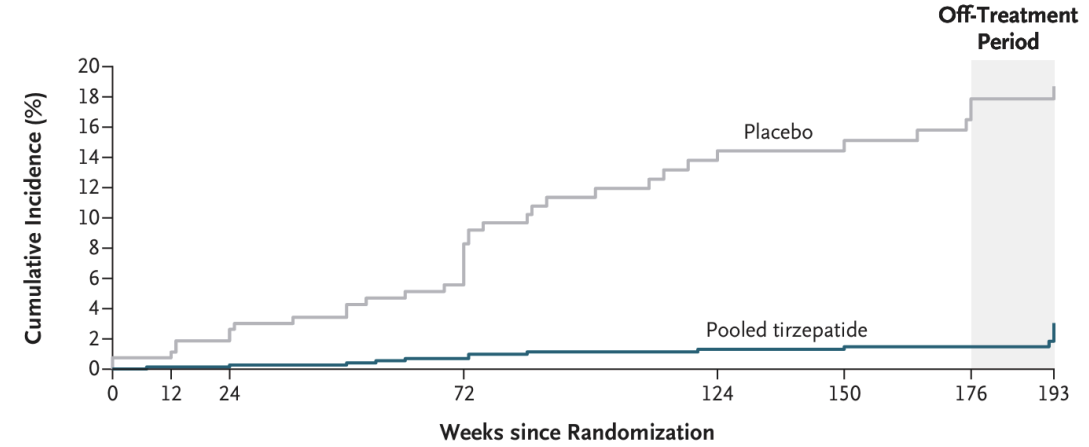
Tirzepatide 15 mg ⁵²

Semaglutide 2.4 mg ⁵¹

B Change in Body Weight



C Incidence of Type 2 Diabetes



No. at Risk										
Placebo	270	266	257		209		137	126	121	99
Pooled tirzepatide	762	751	742		700		581	570	557	494
No. of Participants with Diagnosis										
Placebo	2	3	7		20		31	32	36	37
Pooled tirzepatide	0	1	2		5		9	10	10	18

Tirzepatide ha ridotto del **90–93%** il rischio relativo e di circa **12 punti percentuali** il rischio assoluto di sviluppare il diabete tipo 2 nei soggetti con obesità e prediabete, con un **NNT di 9** per prevenire un caso di diabete in 3 anni.

GLYCEMIC CONTROL

PREDIABETES

HbA1c 5.7–6.4%, fasting plasma glucose 100–125 mg/dL, or 2-hours OGTT glucose 140–199 mg/dL

- Tirzepatide 15 mg²
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- Liraglutide 3 mg^{12,74}
- Orlistat 120 mg¹⁴

Metformin: off-label use; may reduce the incidence of type 2 diabetes²⁴.

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- Tirzepatide 15 mg³¹
- Semaglutide 2.4 mg²⁹
- Liraglutide 3 mg³³

SGLT2 inhibitors support weight loss^{37,38,39,40,41}. If glycemic control allows, insulin^{44,45}, thiazolidinediones, and sulfonylureas should be avoided due to their propensity to induce weight gain.²⁰³

TYPE 1 DIABETES

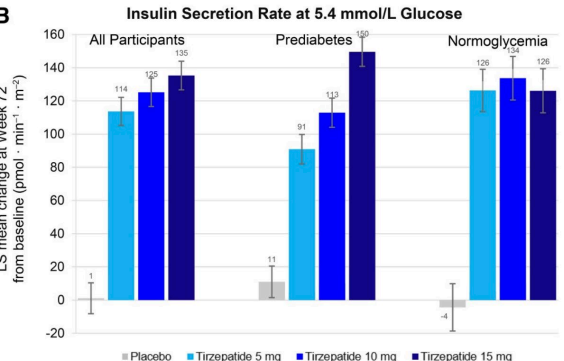
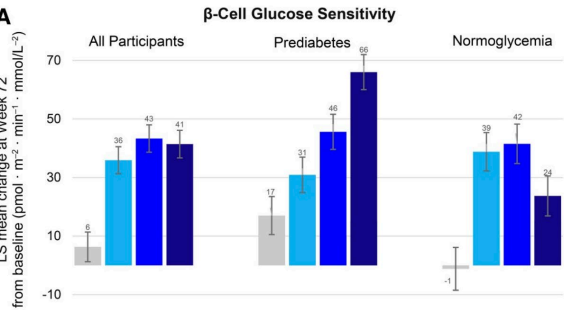
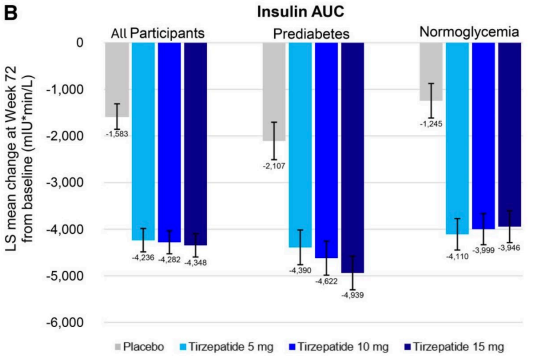
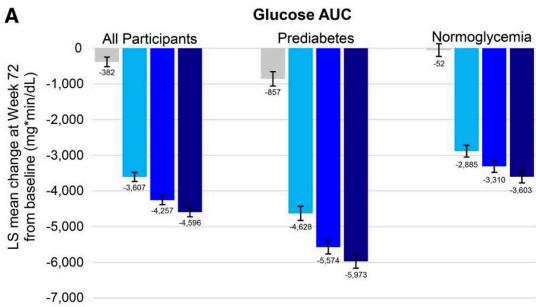
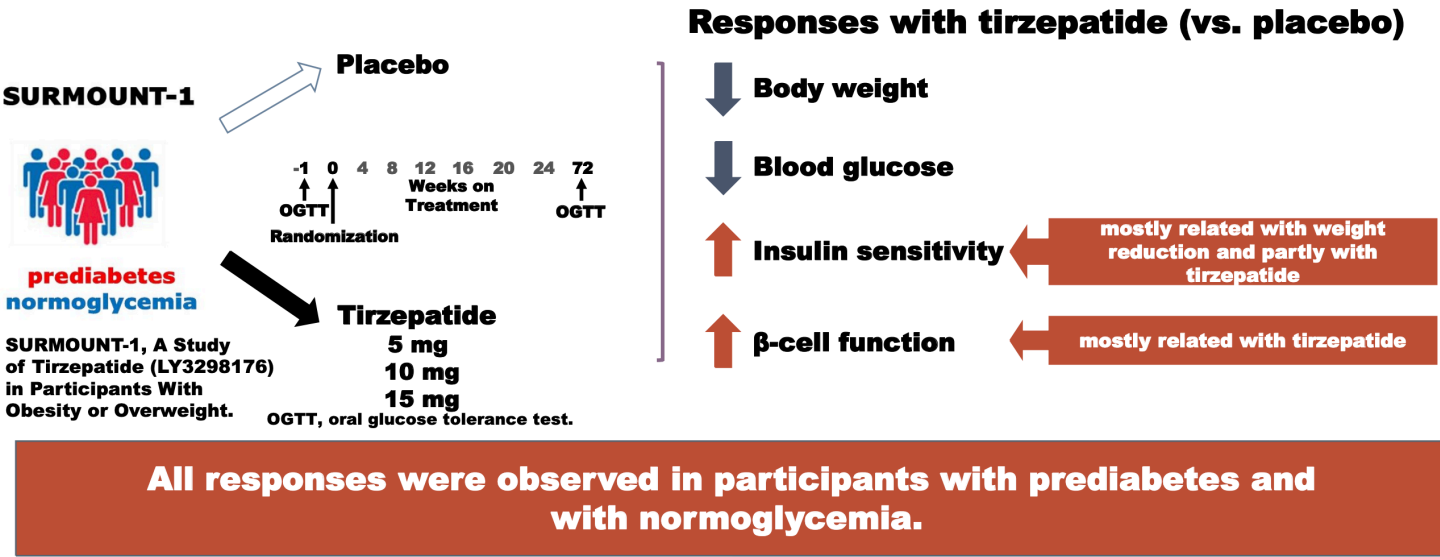
(OFF-LABEL only for weight loss purposes)

- Tirzepatide 15 mg⁵²
- Semaglutide 2.4 mg⁵¹

Tirzepatide Enhances β-Cell Function and Insulin Sensitivity in People with Obesity without Diabetes

SURMOUNT-1 post hoc analysis: insulin sensitivity improves with weight loss and direct GIP-mediated effects, while β-cell function enhancement is primarily driven by tirzepatide itself, independent of weight reduction

Objective: to assess insulin sensitivity and β-cell function in adults with obesity or overweight (BMI ≥ 27 kg/m²) and with either prediabetes or normoglycemia at baseline treated with tirzepatide for 72 weeks (post hoc analysis from SURMOUNT-1 trial)



GLYCEMIC CONTROL

PREDIABETES

HbA1c 5.7–6.4%, fasting plasma glucose 100–125 mg/dL, or 2-hours OGTT glucose 140–199 mg/dL

Tirzepatide 15 mg ²

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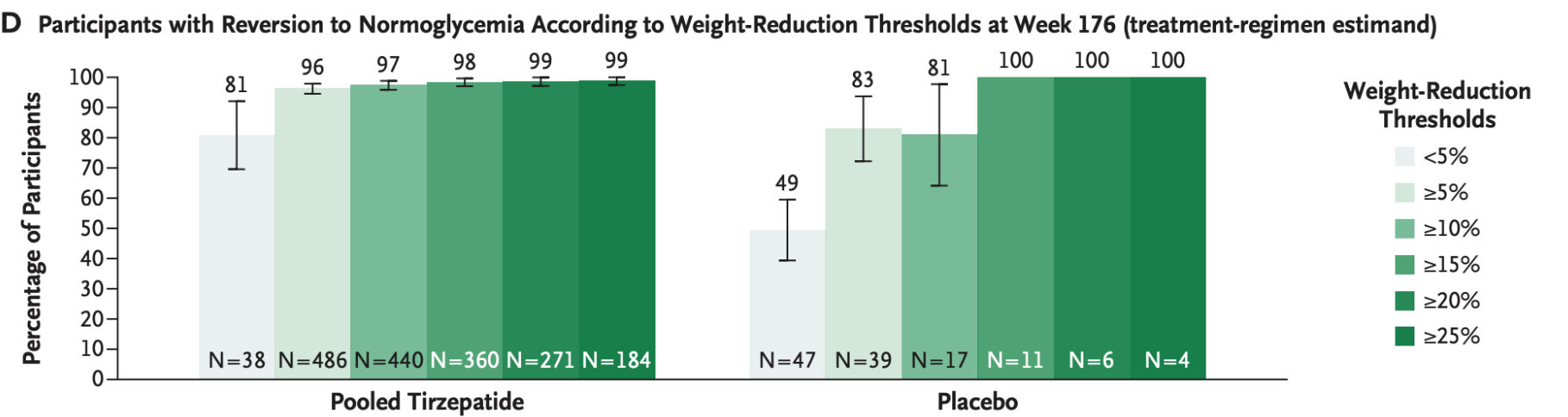
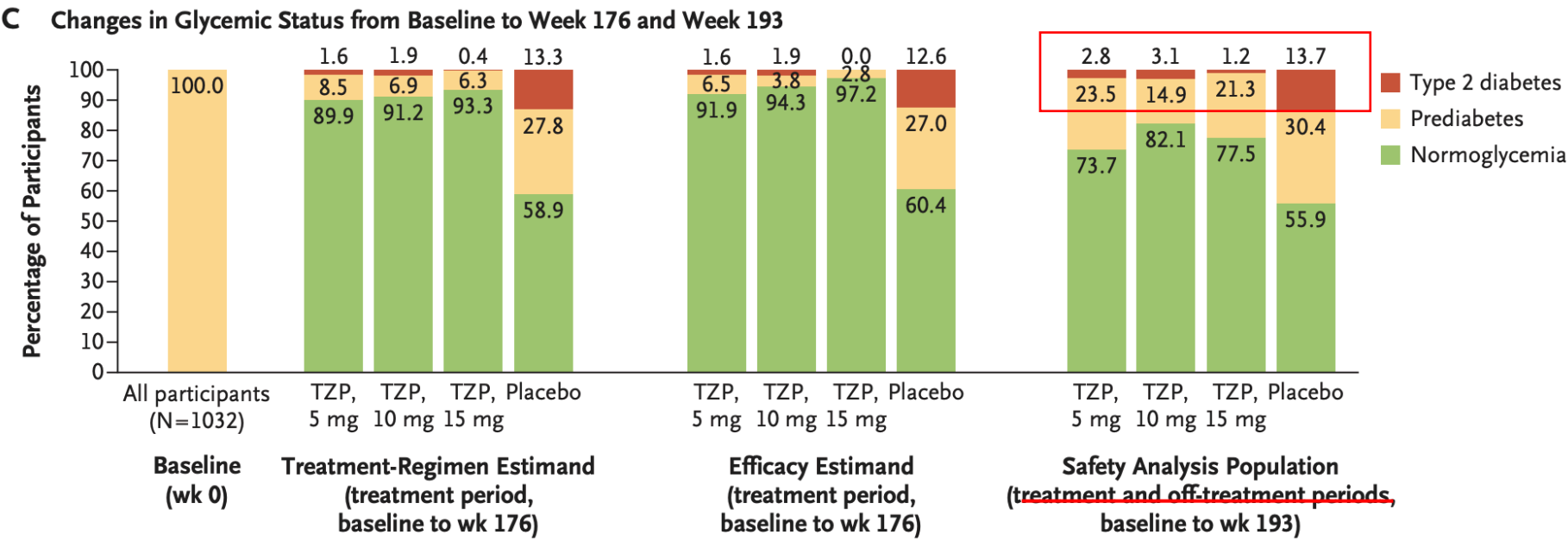
TYPE 1 DIABETES

(OFF-LABEL only for weight loss purposes)

Tirzepatide 15 mg ⁵²

Semaglutide 2.4 mg ⁵¹

Tirzepatide drives long-term reversion to normoglycemia — sustained only with continued therapy At 176 weeks, >90% achieved normoglycemia; rates declined after withdrawal, highlighting the link between weight maintenance and glycemic remission.



Not All Prediabetes Is the Same: Heterogeneity Explains Why Only Some Individuals Progress to Diabetes.

Distinct pathophysiological subtypes — from β -cell failure to hyperinsulinemic insulin resistance — determine who will and who will not progress despite treatment or weight loss.

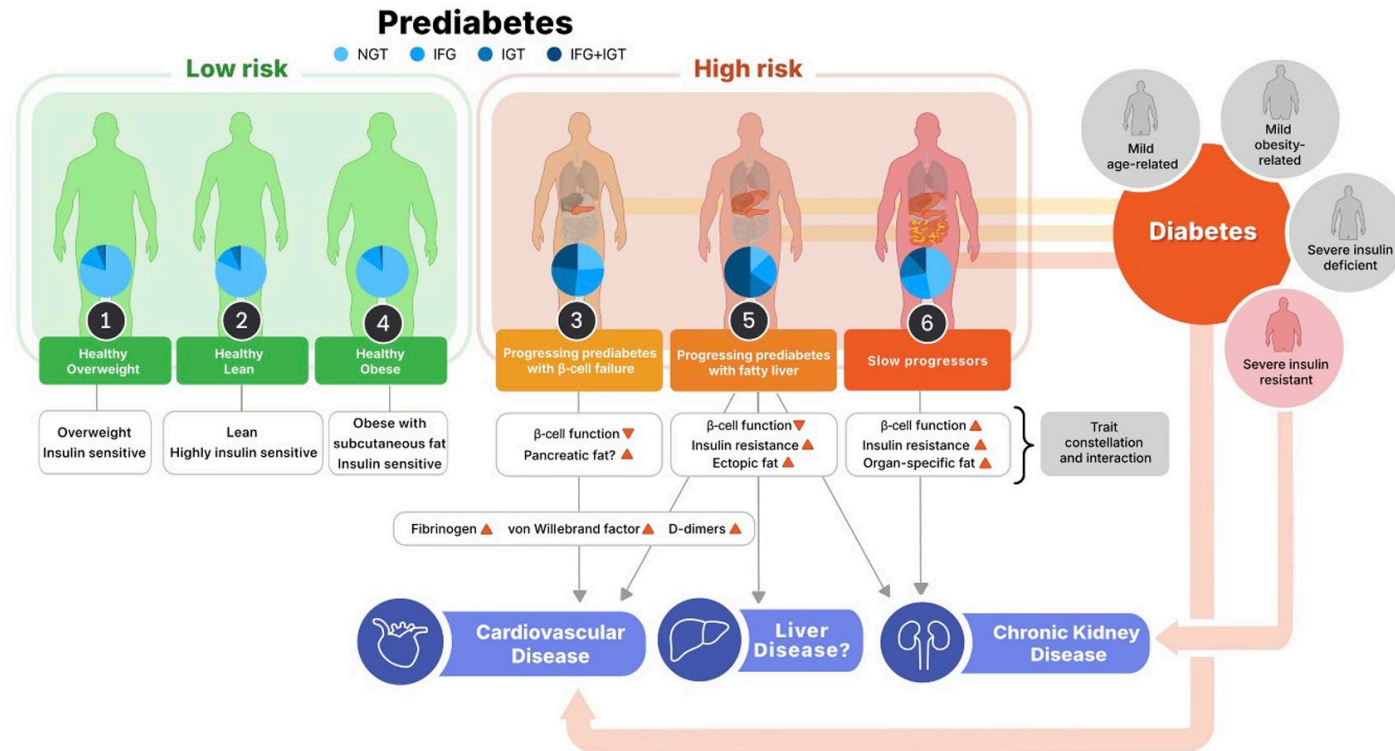
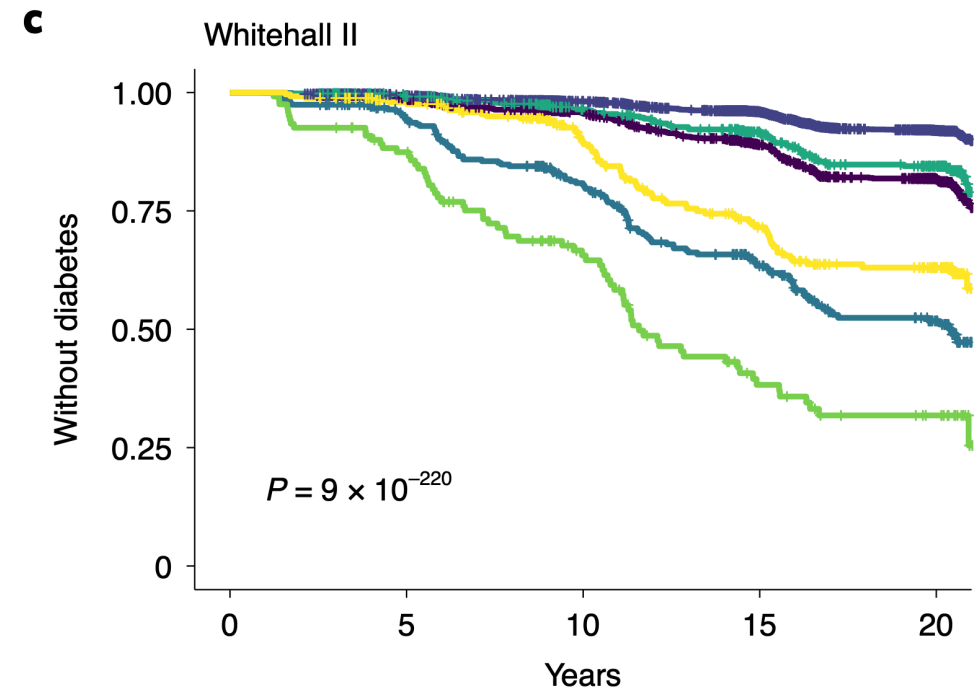


Figure 1—Distinct constellations of traits, including variations in insulin sensitivity, β -cell function, and organ-specific fat distribution, are seen among prediabetes subtypes. For these subtypes there are different trajectories toward diabetes, its subtypes, associated complications, and mortality. NGT, normal glucose tolerance.



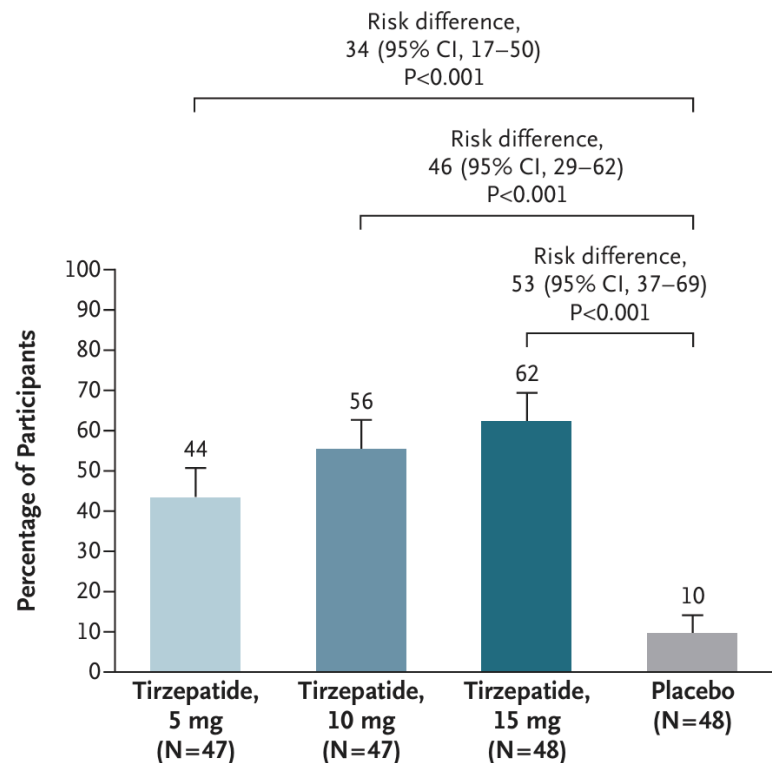
Tirzepatide e MASH: dal trattamento del metabolismo alla regressione istologica

Adults with biopsy-confirmed MASH, fibrosis stage F2–F3 for semaglutide 2.4 mg and tirzepatide 15 mg; F0–F3 for liraglutide 3 mg. BMI ≥ 25 kg/m² for semaglutide 2.4 mg and liraglutide 3 mg; BMI ≥ 27 kg/m² for tirzepatide 15 mg, with or without type 2 diabetes; BMI not restricted, and ,with or without type 2 diabetes, for semaglutide 2.4.

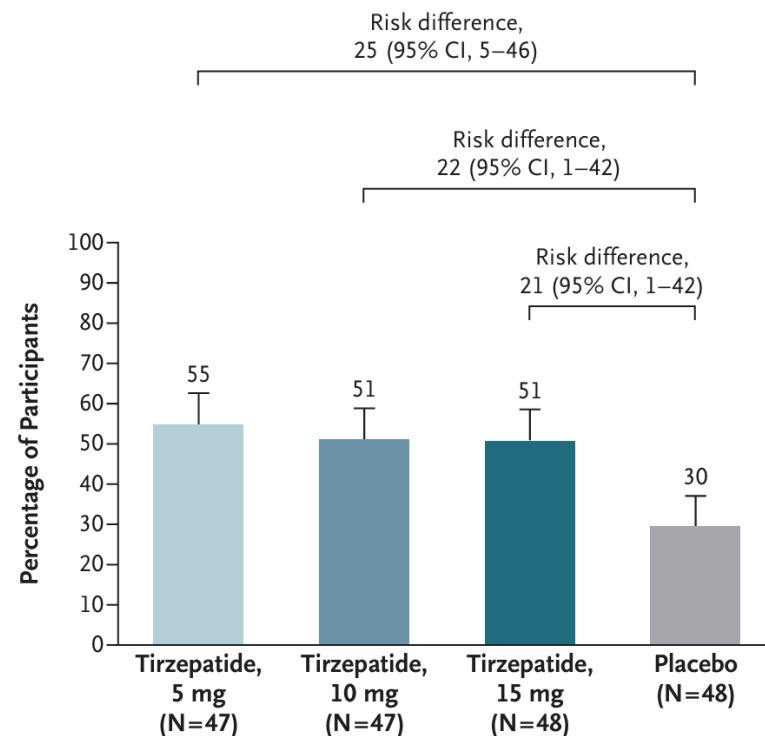


Semaglutide 2.4 mg⁵⁴
Tirzepatide 15 mg⁵⁶
Liraglutide 3 mg OD⁵⁷

A Resolution of MASH and No Worsening of Fibrosis



B Decrease of ≥ 1 Fibrosis Stage and No Worsening of MASH



Dopo 52 settimane, tirzepatide ha determinato la **risoluzione della MASH nel 54% dei pazienti**, rispetto al 10% con placebo, con una **riduzione assoluta del rischio del 44%** e un **NNT di 3**.

Anche la regressione fibrotica è stata significativamente superiore al placebo (52% vs 30%), con **ARR del 22%** e **NNT di 5**.

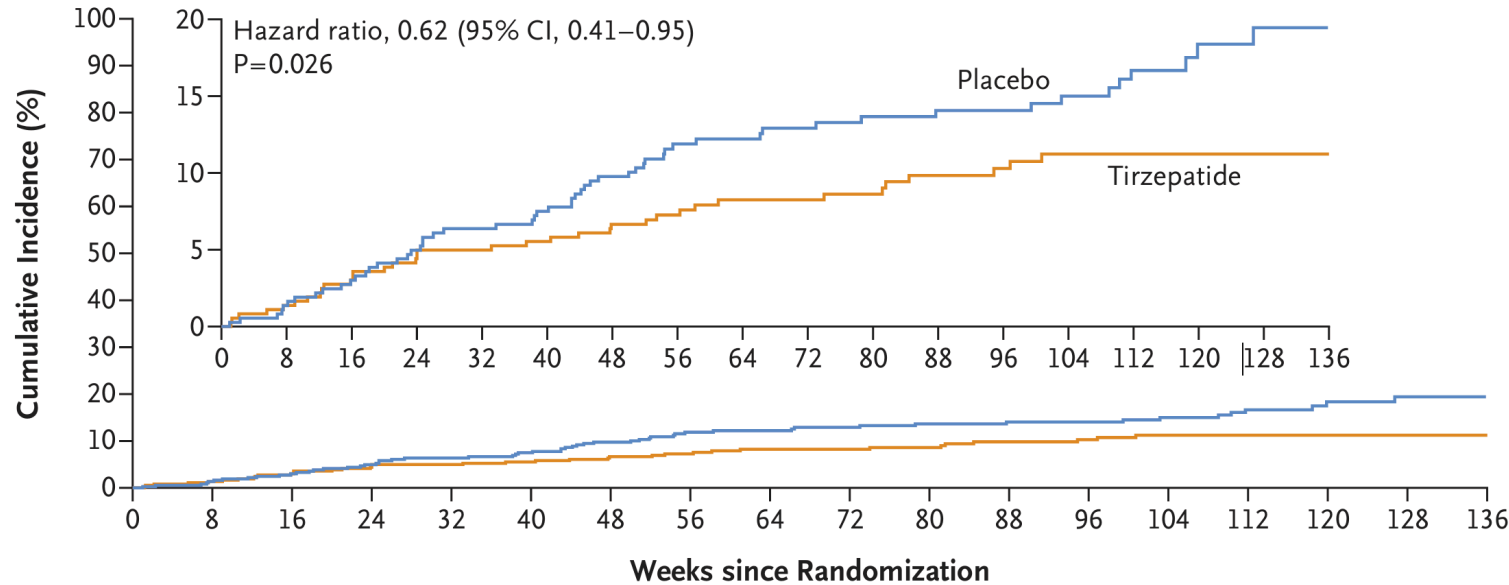
Tirzepatide nello scompenso con frazione di eiezione preservata e obesità

Clinical heart failure (NYHA II–IV) with preserved or mildly reduced ejection fraction (LVEF $\geq 50\%$ for tirzepatide, $\geq 45\%$ for semaglutide), BMI ≥ 30 kg/m², impaired functional capacity (KCCQ-CSS $< 80-90$), 6MWT distance ≥ 100 m, and elevated filling pressures (e.g., NT-proBNP, echocardiographic abnormalities, or recent HF hospitalization). Type 2 diabetes was an inclusion criterion in the tirzepatide trial.



**Tirzepatide
15 mg¹¹**

**Semaglutide
2.4 mg⁵**



No. at Risk

Placebo	367	361	349	339	332	328	318	268	259	240	219	215	195	165	145	94	73	45
Tirzepatide	364	359	349	344	340	338	333	284	275	251	228	220	196	167	146	105	82	46

Tirzepatide è indicato per il trattamento dei pazienti affetti da diabete tipo -2 e per la gestione del peso corporeo. Non sono autorizzate da FDA/EMA indicazioni al trattamento dello scompenso cardiaco con tirzepatide

Nel trial SUMMIT, tirzepatide ha ridotto del **38% il rischio relativo HR 0.62 (IC 95% 0.41–0.95; p=0.026)**, e di circa **5 % il rischio assoluto** di morte cardiovascolare o nuovo evento di scompenso rispetto al placebo, con un **NNT di 19** in due anni. L'effetto è stato guidato in larga parte dalla riduzione delle ospedalizzazioni per scompenso (HR 0.44; **NNT ≈ 26**)

**Naltrexone/
Bupropion
(not recommended)¹⁵**

Definitions vary; however, most include age ≥40 years, BMI ≥27 kg/m², male sex, hypertension, atherogenic dyslipidemia, smoking, prediabetes, and elevated ASCVD risk (per ACC/AHA criteria)



Tirzepatide 15 mg^{2,10}

Semaglutide 2.4 mg^{3,4}

Liraglutide 3 mg¹²

Naltrexone/
Bupropion
(not recommended)¹⁵

Oltre il peso: effetti sul rischio cardiovascolare nello studio SURMOUNT-5

Tertiary Endpoints – efficacy estimand

Endpoints	Semaglutide MTD	Tirzepatide MTD	Estimated treatment difference (95% CI)
Change in systolic blood pressure, mmHg	−7.7 (−8.9 to −6.4)	−10.2 (−11.4 to −8.9)	−2.5 (−4.2 to −0.7)
Change in diastolic blood pressure, mmHg	−3.2 (−4.0 to −2.3)	−4.6 (−5.5 to −3.8)	−1.5 (−2.7 to −0.3)
Change in HbA1c, %	−0.39 (−0.42 to −0.36)	−0.50 (−0.53 to −0.47)	−0.10 (−0.15 to −0.06)
Change in fasting serum glucose, mg/dL	−11.6 (−12.4 to −10.7)	−13.4 (−14.2 to −12.5)	−1.8 (−3.1 to −0.6)
Change in fasting insulin, pmol/L	−35.0 (−39.5 to −30.1)	−53.0 (−56.2 to −49.5)	−27.7 (−34.7 to −20.0)
Change in triglycerides, mg/dL	−27.5 (−30.9 to −24.1)	−34.9 (−38.0 to −31.8)	−7.4 (−12.0 to −2.8)
Change in VLDL cholesterol, mg/dL	−5.3 (−6.0 to −4.6)	−6.8 (−7.4 to −6.2)	−1.5 (−2.4 to −0.6)
Change in non-HDL cholesterol, mg/dL	−12.8 (−15.7 to −9.9)	−15.6 (−18.4 to −12.7)	−2.7 (−6.8 to 1.3)
Change in LDL cholesterol, mg/dL	−5.9 (−8.6 to −3.2)	−7.8 (−10.4 to −5.2)	−1.9 (−5.6 to 1.9)
Change in HDL cholesterol, mg/dL	2.9 (2.0 to 3.8)	5.7 (4.8 to 6.7)	2.8 (1.5 to 4.1)

• The CIs have not been adjusted for multiplicity and should not be used to make inferences. Data are LSM (95% CI).
• CI=Confidence Interval; HbA1c=Glycated Haemoglobin; HDL=High-Density Lipoprotein; LDL=Low-Density Lipoprotein; LSM=Least Squares Mean; MTD=Maximum Tolerated Dose; VLDL=Very-Low-Density Lipoprotein.

Tirzepatide migliora l'apnea ostruttiva del sonno nei soggetti con obesità, con o senza CPAP

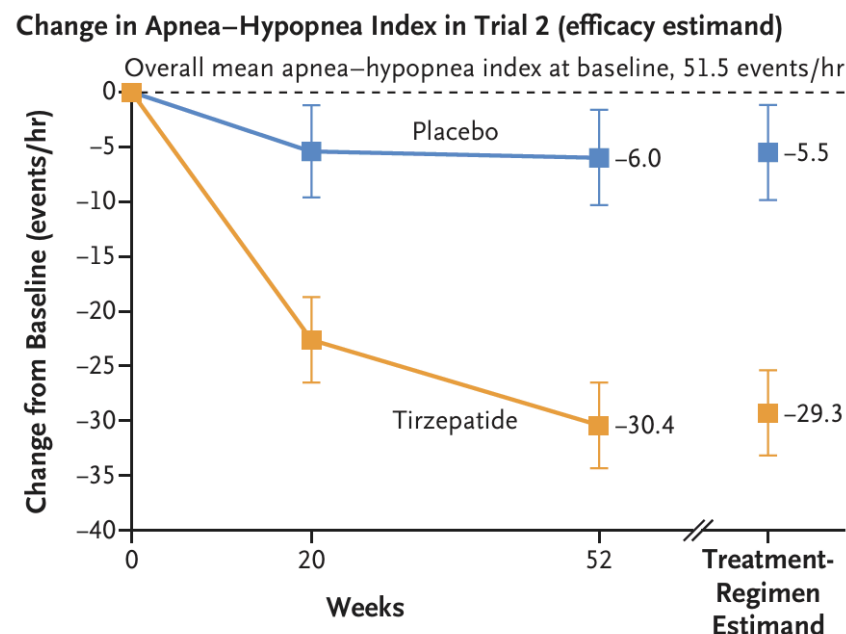
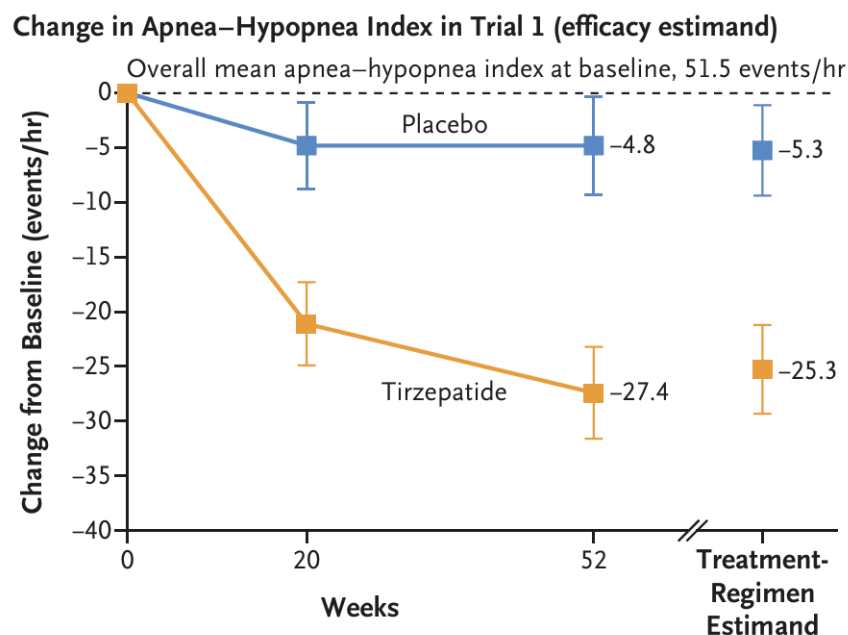
Adults ≥ 18 years, BMI ≥ 30 kg/m², with moderate-to-severe obstructive sleep apnea (AHI ≥ 15 events/h); CPAP use allowed (tirzepatide) or excluded (liraglutide); no diagnosis of T2D.



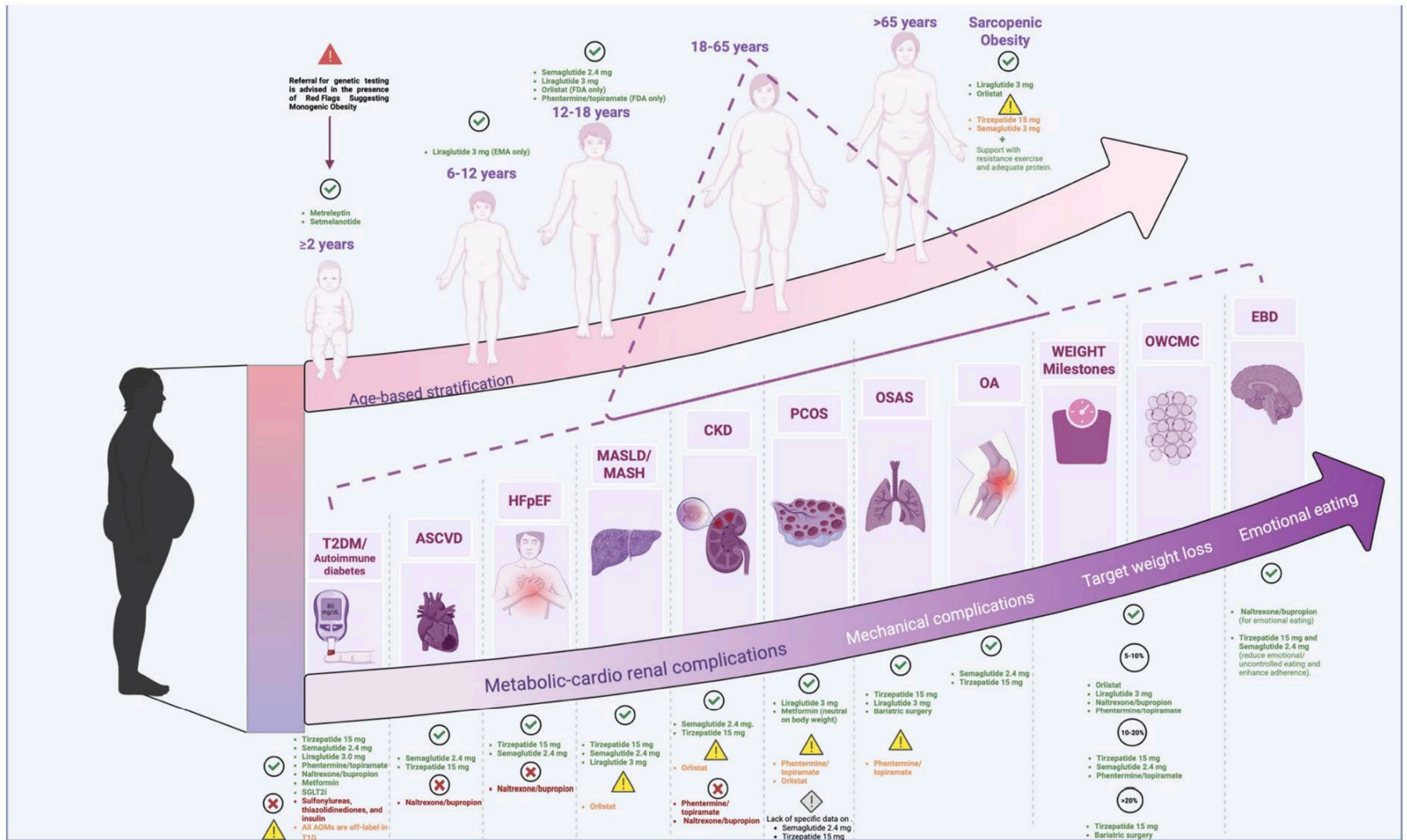
Tirzepatide 15 mg⁶⁸

Liraglutide 3 mg⁶⁹

Phentiramine/Topiramate⁷⁰



In entrambi i trial SURMOUNT-OSA, **tirzepatide ha ridotto l'indice apnea-ipopnea di circa 25–30 eventi/ora (–50%)** e il peso di ~20%, con miglioramento di sonnolenza, pressione arteriosa e infiammazione. Efficacia comparabile nei soggetti con e senza CPAP, con circa la metà dei pazienti che raggiunge la remissione clinica dell'OSA.



MESSAGGI CHIAVE

Dalle radici biologiche alla terapia moderna: l'evoluzione di GLP e GLP-1, da ormoni ancestrali del metabolismo a target chiave della medicina di precisione per l'obesità.

Dai trial alla rivoluzione terapeutica: tirzepatide riduce peso, rischio di diabete, danno cardio-renale, fegato grasso e apnea del sonno.

Dal singolo al doppio agonista: nello studio SURMOUNT-5 tirzepatide è risultato superiore a semaglutide nella riduzione del peso corporeo a 72 settimane e ha presentato un tasso di discontinuazione per EA gastrointestinali inferiore rispetto a semaglutide