NAPOLI, 6 - 7 MARZO 2025

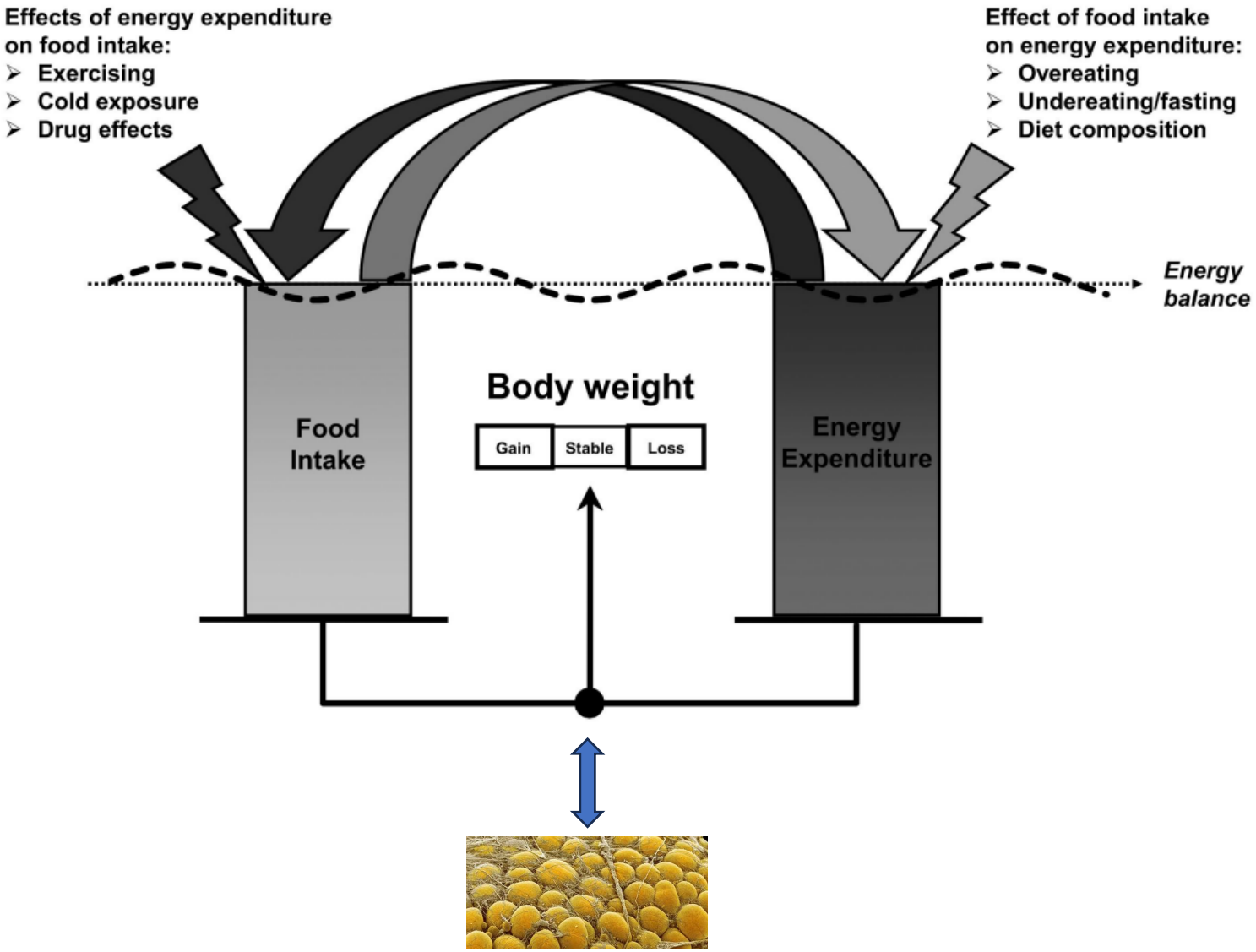
1° INTERNATIONAL BARIATRIC MEETING

Bariatric Surgery and Pharmacological approach to Morbid Obesity: An open debate

12.30 - 12.45 **KEY LECTURE 1**

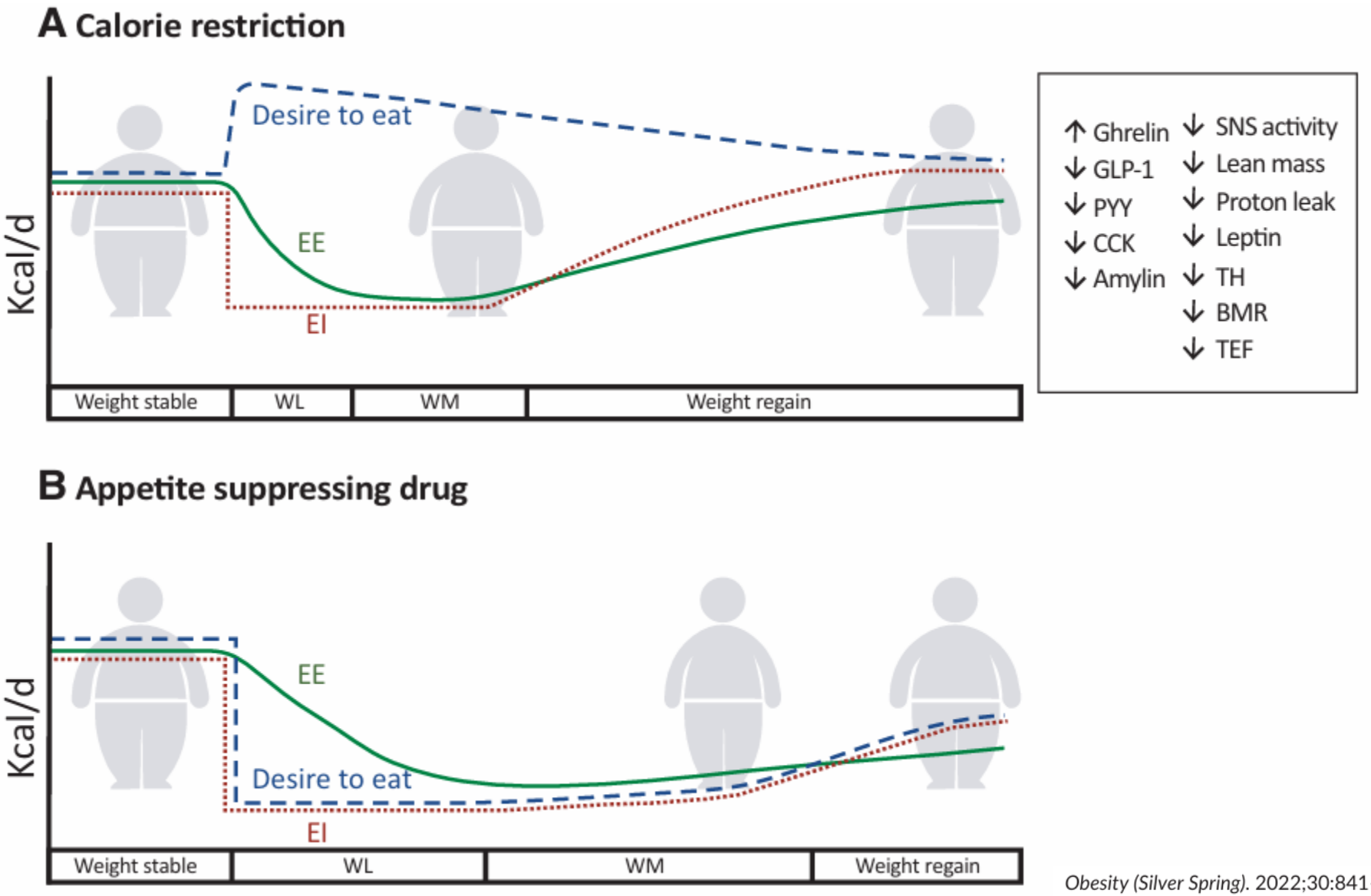
Stato attuale dell'approccio farmacologico all'obesità 2024.
F. Santini
Commenta G. Mingrone

Regolazione del bilancio energetico



Da: P. Piaggi[1,2] · K. L. Vinales[1] · A. Basolo[1,2] · F. Santini[2] · J. Krakoff[1] J Endocrinol Invest (2018) 41:83–89 (modificata)

Beyond appetite regulation: Targeting energy expenditure, fat oxidation, and lean mass preservation for sustainable weight loss Christoffersen BO et al.



Obesity (Silver Spring). 2022;30:841–857.

Sibutramine Produces Dose-Related Weight Loss

Sibutramine and Obesity, Bray et al.

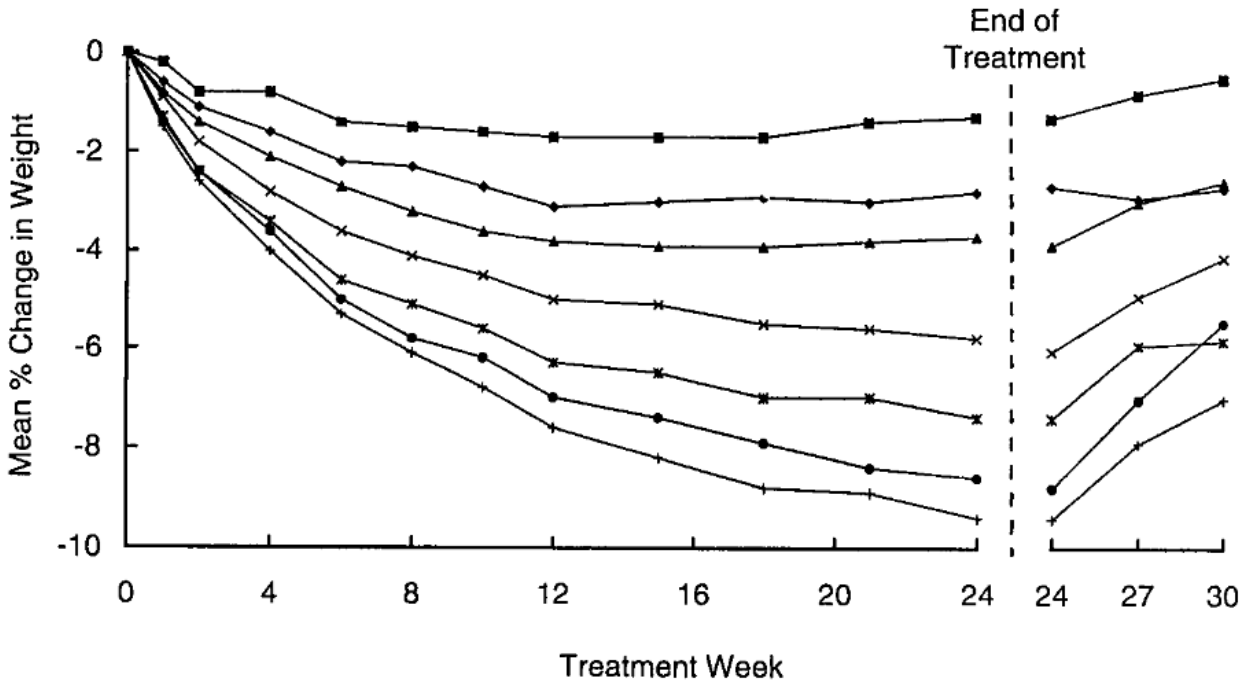
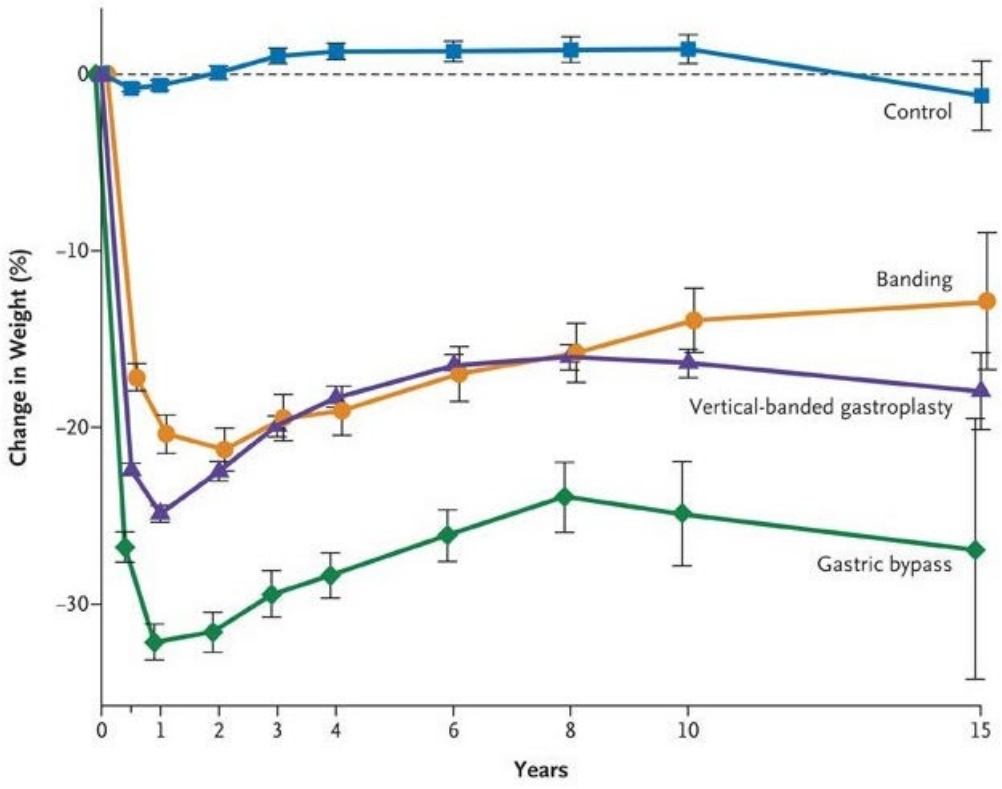


Figure 1: Weight loss in patients completing 24 weeks of treatment. ■, placebo; ♦, 1 mg sibutramine; ▲, 5 mg sibutramine; ×, 10 mg sibutramine; ✳, 15 mg sibutramine; ●, 20 mg sibutramine; +, 30 mg sibutramine; $p<0.05$ vs. placebo for all time-points for sibutramine doses 5 mg to 30 mg, nonparametric Williams' test. n = 87 to 107/group (Table 2). Posttreatment follow-up data are also shown for those patients in whom it was available (n = 50 to 61/group; Table 2).

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 23, 2007 VOL. 357 NO. 8

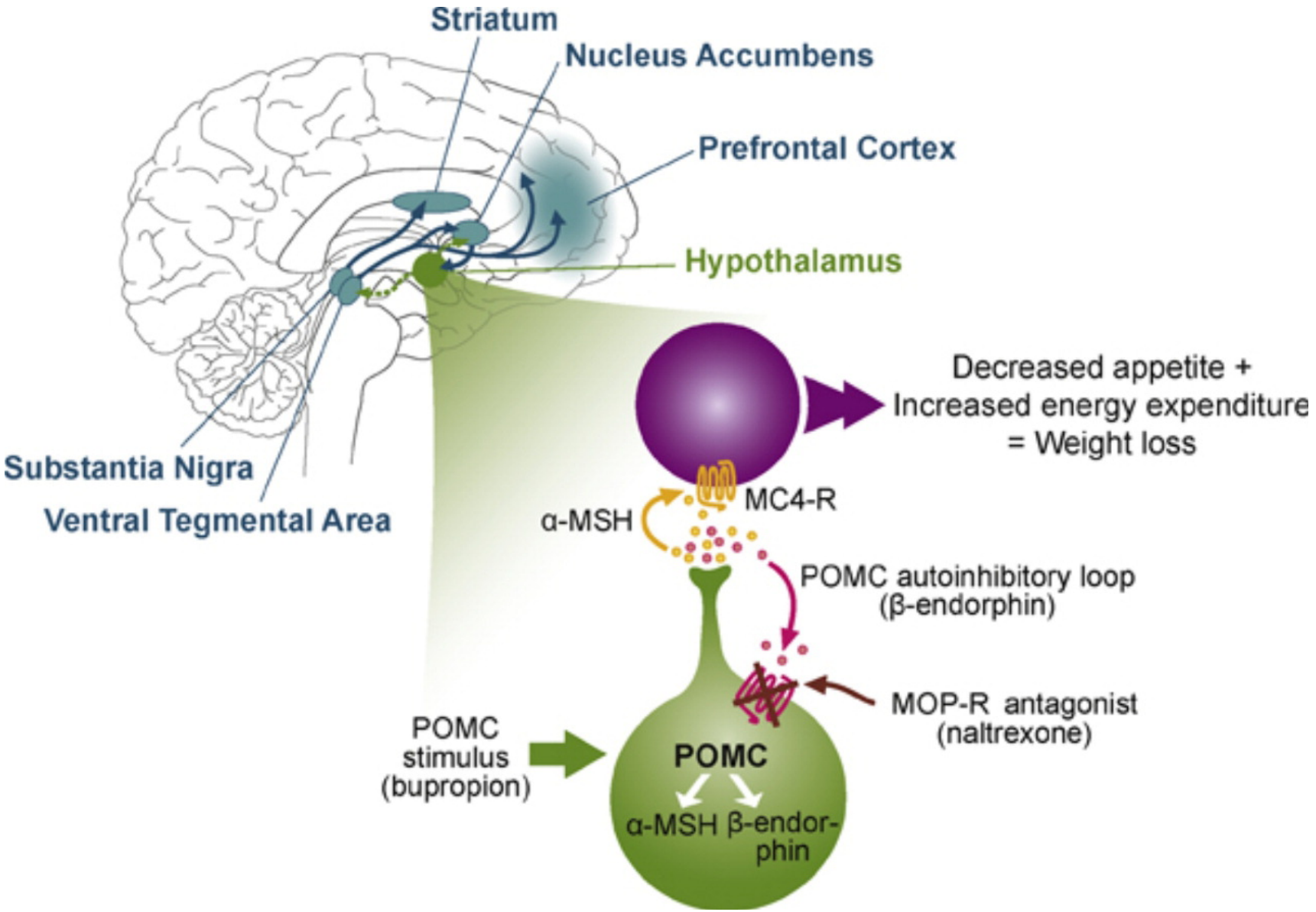
Effects of Bariatric Surgery on Mortality in Swedish Obese Subjects



No. Examined

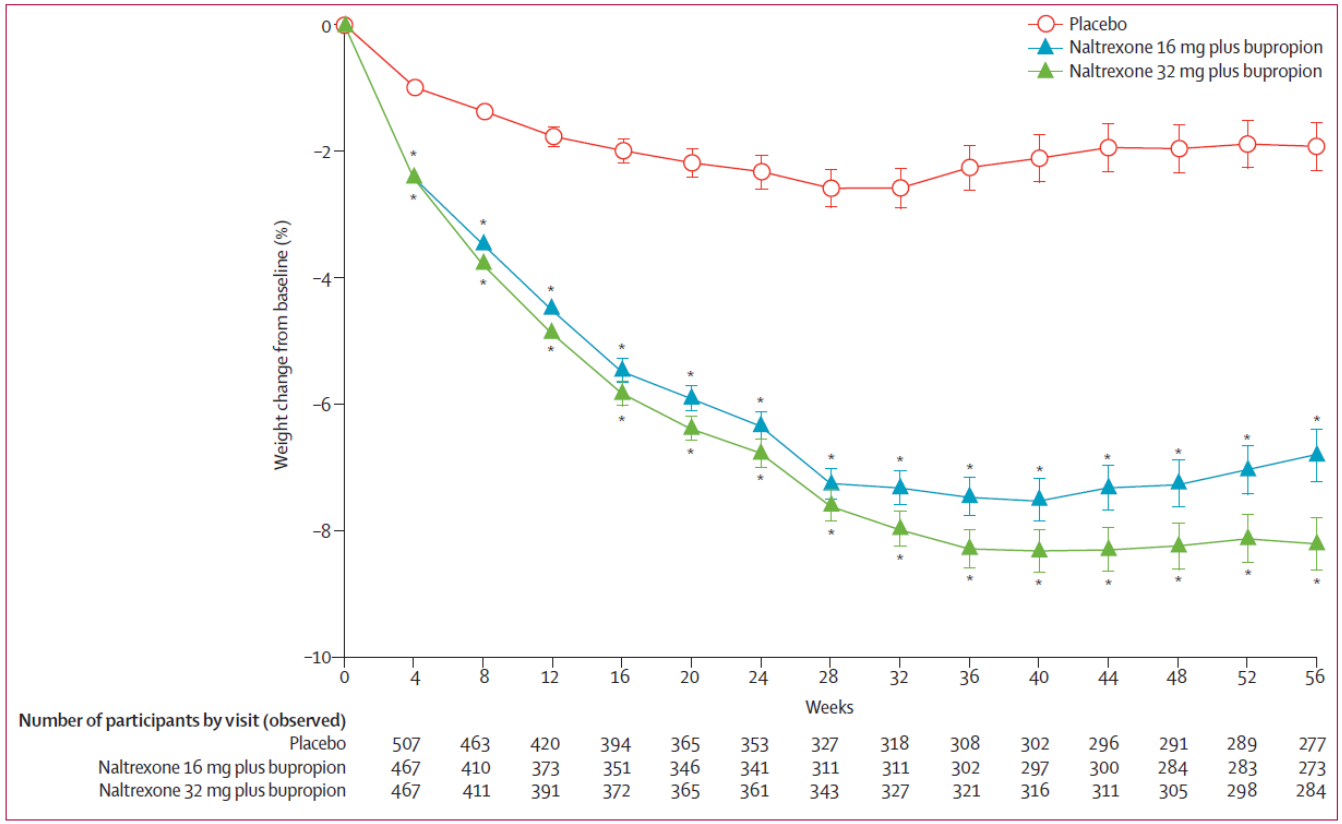
Control	2037	1768	1660	1553	1490	1281	982	886	190
Banding	376	363	357	328	333	298	267	237	52
Vertical-banded gastroplasty	1369	1298	1244	1121	1086	1004	899	746	108
Gastric bypass	265	245	245	211	209	166	92	58	10

Bupropione-Naltrexone: meccanismo d'azione



Effect of naltrexone plus bupropion on weight loss in overweight and obese adults (COR-I): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial

*Frank L Greenway, Ken Fujioka, Raymond A Plodkowski, Sunder Mudaliar, Maria Guttadauria, Janelle Erickson, Dennis D Kim, Eduardo Dunayevich, for the COR-I Study Group**



Number of participants by visit (observed)

Placebo	507	463	420	394	365	353	327	318	308	302	296	291	289	277
Naltrexone 16 mg plus bupropion	467	410	373	351	346	341	311	311	302	297	300	284	283	273
Naltrexone 32 mg plus bupropion	467	411	391	372	365	361	343	327	321	316	311	305	298	284

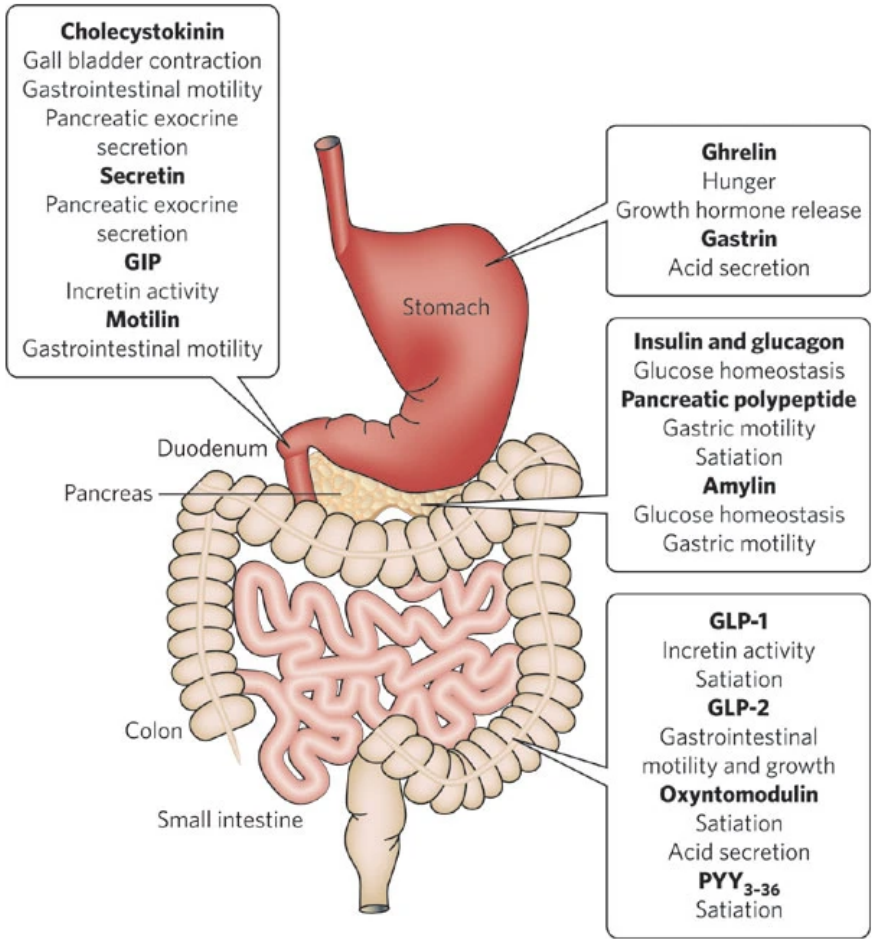
Figure 2: **Change in bodyweight**
Observed least squares mean (SE) percentage change from baseline in bodyweight and number of participants at each visit during 56 weeks. *p<0·0001 compared with placebo.

Lancet 2010; 376: 595–605

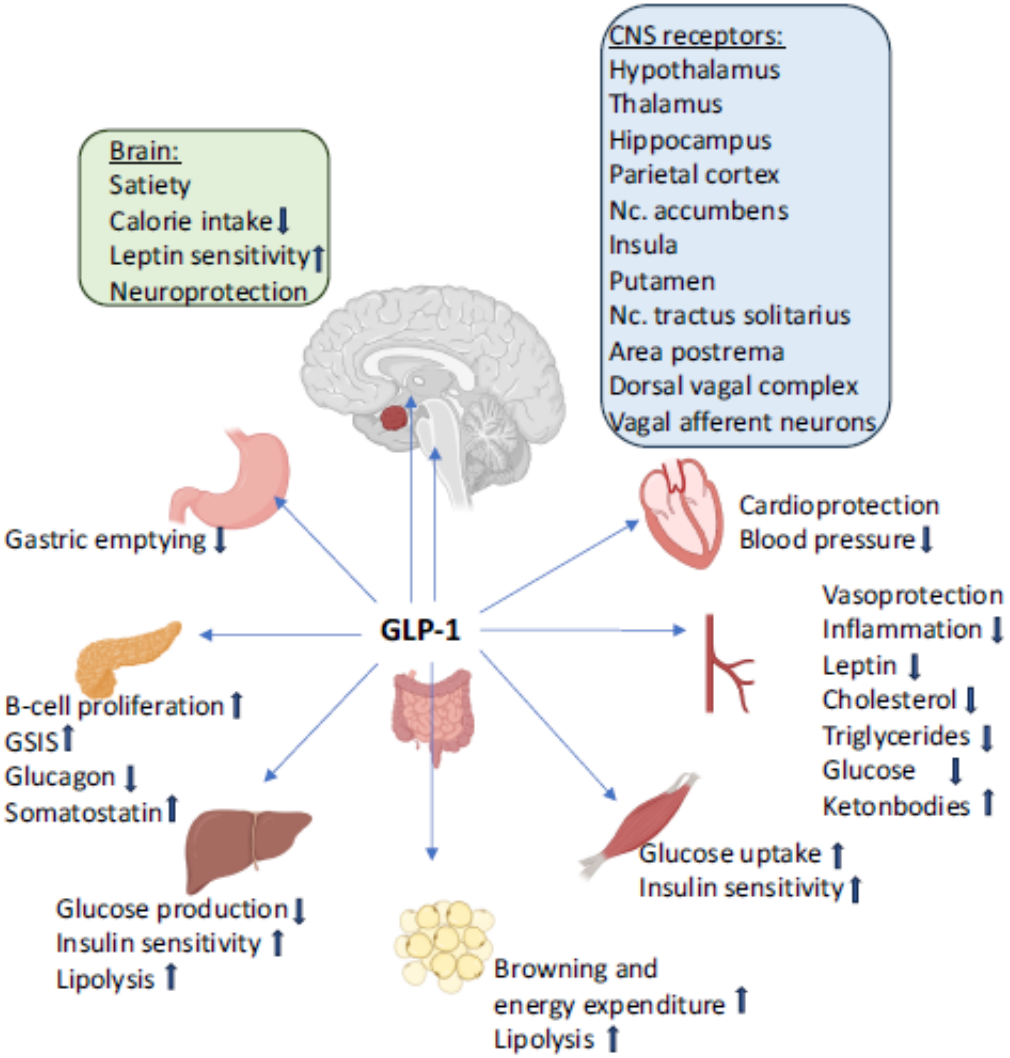
Figure 2: A schematic diagram of the gastrointestinal tract illustrating where particular gut hormones are concentrated and their major putative functions.

From: Gut hormones and the regulation of energy homeostasis

Murphy and Bloom, Nature 2006



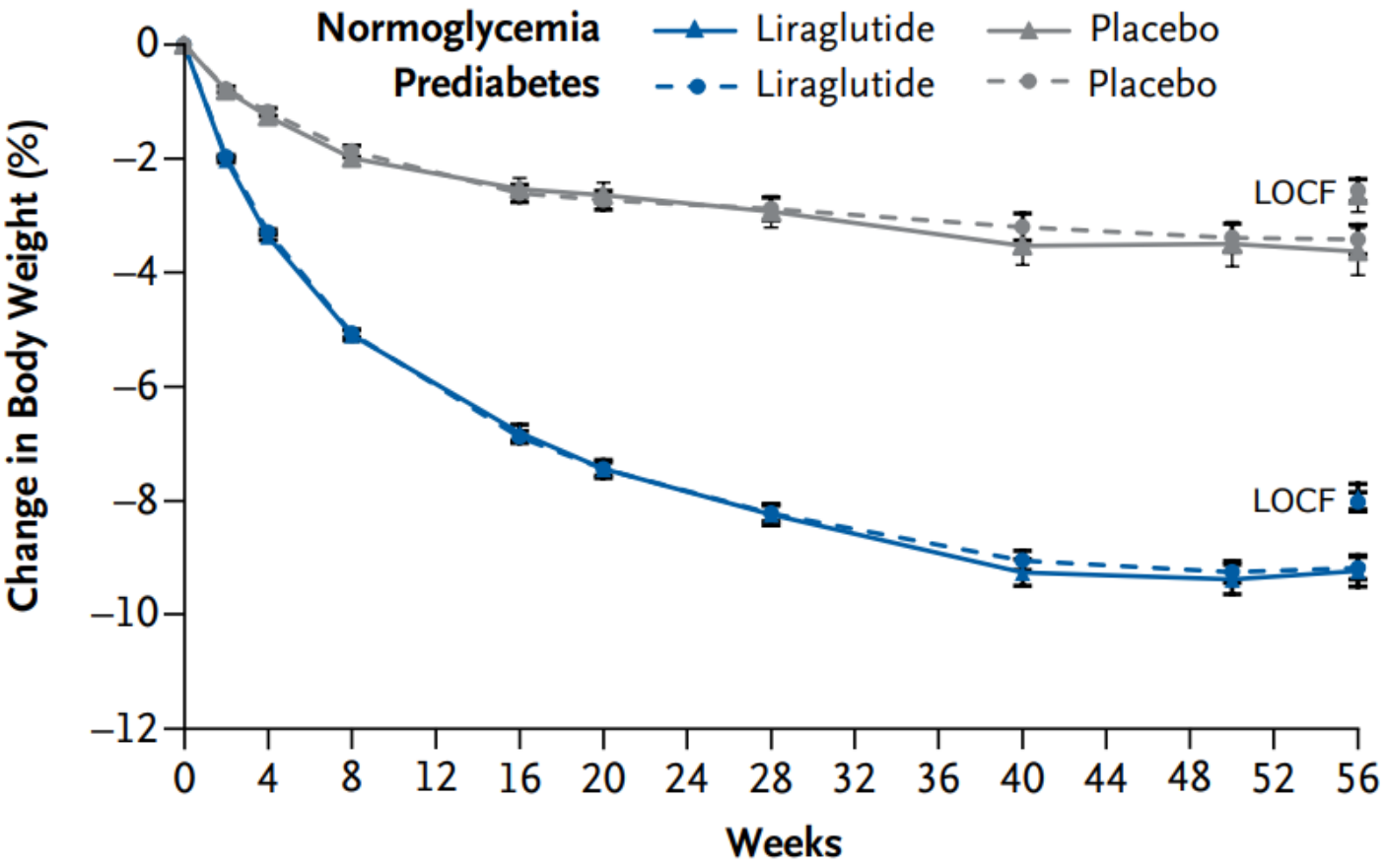
Physiological effects of GLP-1



Dimitri P et al. J. Endoc. Soc. 2025

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JULY 2, 2015 VOL. 373 NO. 1

A Randomized, Controlled Trial of 3.0 mg of Liraglutide in Weight Management



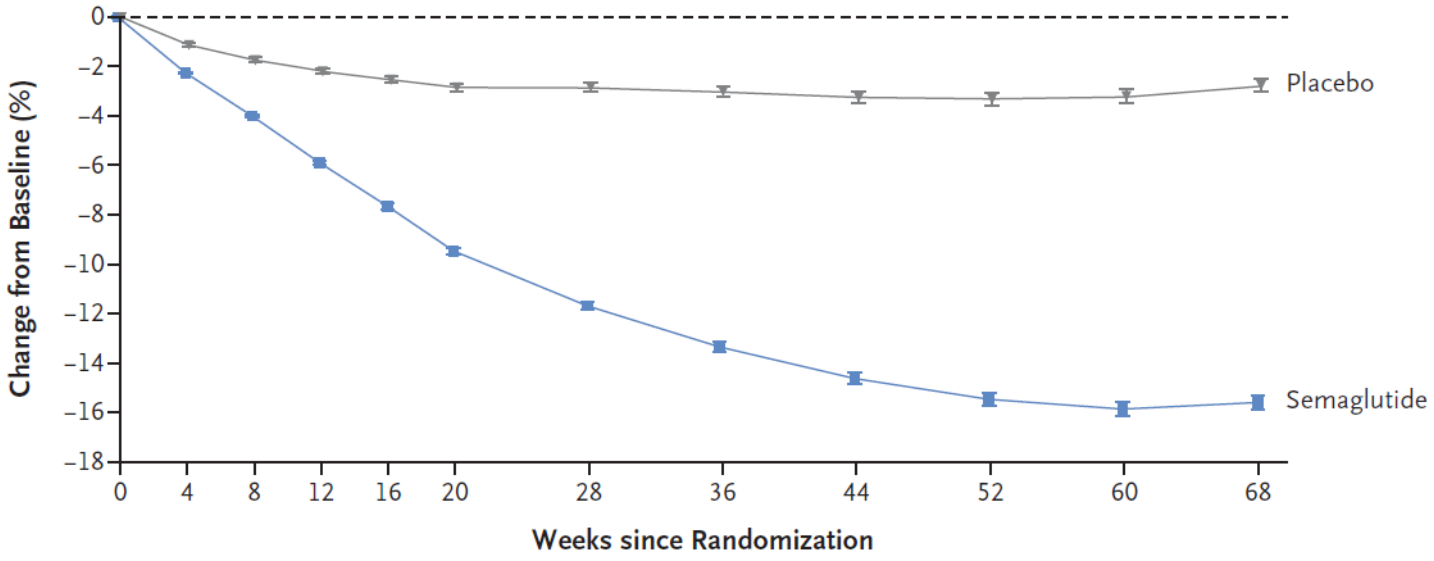
Pi-Sunyer X, et al.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 18, 2021 VOL. 384 NO. 11

Once-Weekly Semaglutide in Adults with Overweight or Obesity

A Body Weight Change from Baseline by Week, Observed In-Trial Data



No. at Risk												
Placebo	655	649	641	619	615	603	592	571	554	549	540	577
Semaglutide	1306	1290	1281	1262	1252	1248	1232	1228	1207	1203	1190	1212

GLP-1R and GIPR potential Mechanism of Action

GLP-1 Receptor Agonism

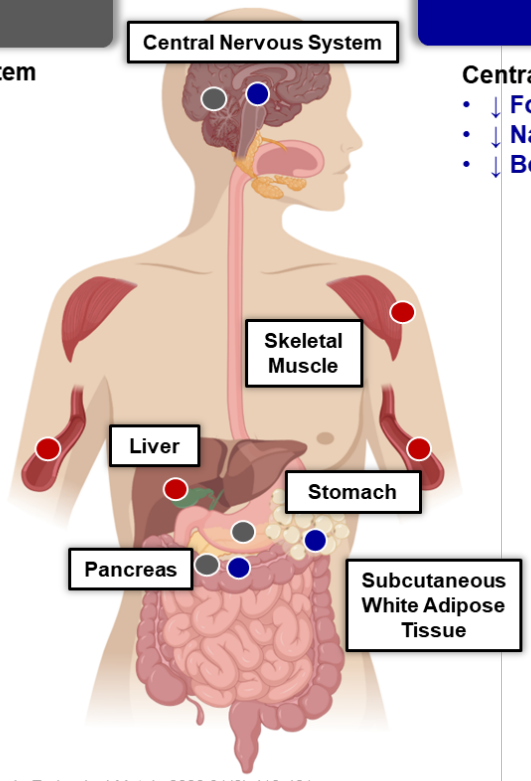
Central Nervous System
- ↑ Satiety
- ↓ Food Intake
- ↑ Nausea
- ↓ Body Weight

Pancreas
- ↑ Insulin
- ↓ Glucagon

Stomach
- ↓ Gastric Emptying

Systemic
- ↓ Hyperglycemia

Liver
- ↑ Insulin Sensitivity
- ↓ Hepatic Glucose Production
- ↓ Ectopic Lipid Accumulation



GIP Receptor Agonism

Central Nervous System
- ↓ Food intake
- ↓ Nausea
- ↓ Body weight

Pancreas
- ↑ Insulin
- ↑ Glucagon

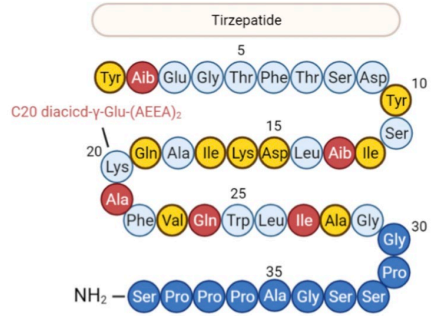
Systemic
- ↓ Hyperglycemia, Dietary Triglyceride

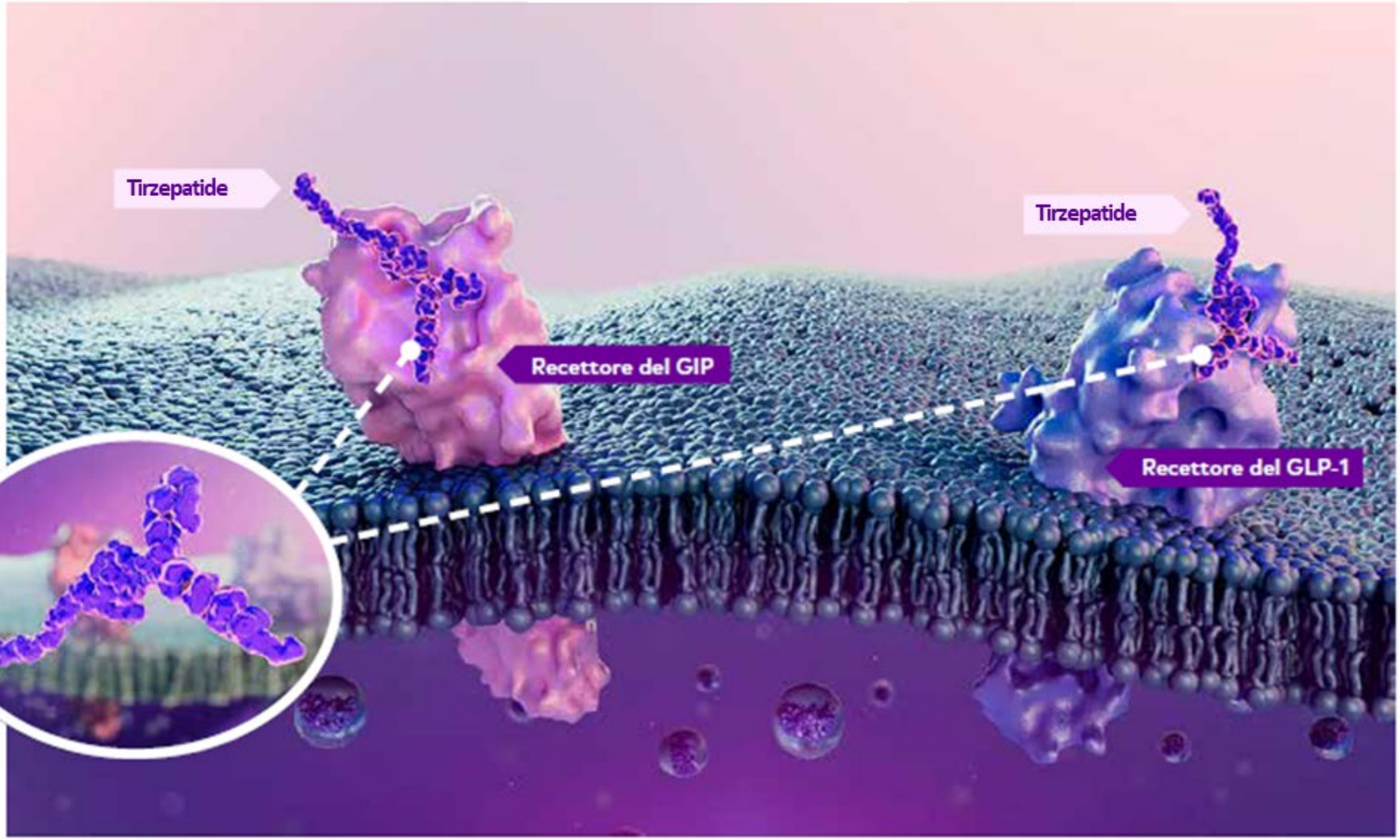
Skeletal Muscle
- ↑ Insulin Sensitivity
- ↑ Metabolic Flexibility
- ↓ Ectopic Lipid Accumulation

- GLP-1 Receptor Agonism
- GIP Receptor Agonism
- Indirect Action

Adapted from: Samms RJ, et al. *Trends Endocrinol Metab.* 2020;31(6):410-421

Tirzepatide non è ancora rimborsato/commercializzato in italia. Le informazioni riportate sono contenute nel Riassunto delle Caratteristiche del Prodotto- 29 Maggio 2024


Tirzepatide
5
Tyr Aib Glu Gly Thr Phe Thr Ser Asp
10
Tyr
C20 diacicd-γ-Glu-(AEEA)2
15
Ser
20
Lys
Gln Ala Ile Lys Asp Leu Aib Ile
Ala
25
Phe Val Gln Trp Leu Ile Ala Gly
30
Gly
Pro
35
NH2 — Ser Pro Pro Pro Ala Gly Ser Ser


Tirzepatide
Recettore del GIP
Tirzepatide
Recettore del GLP-1

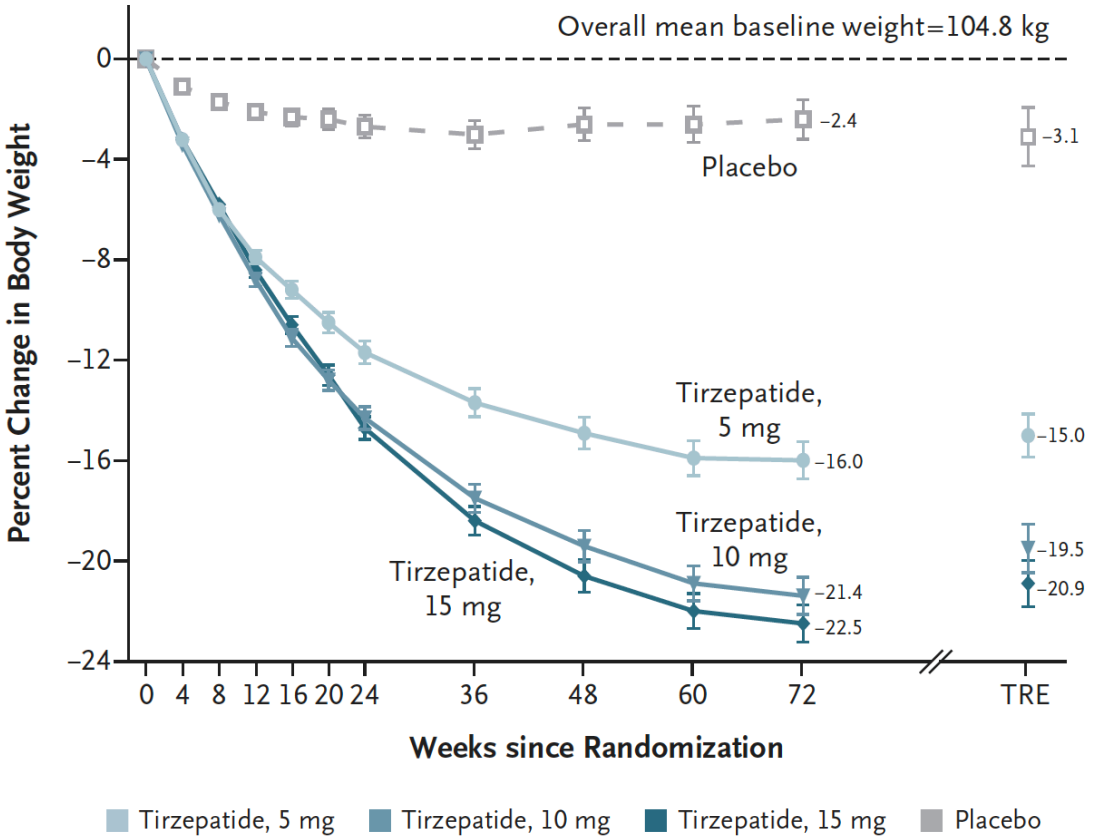
The NEW ENGLAND JOURNAL of MEDICINE

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*

B Percent Change in Body Weight by Week (efficacy estimand)



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]

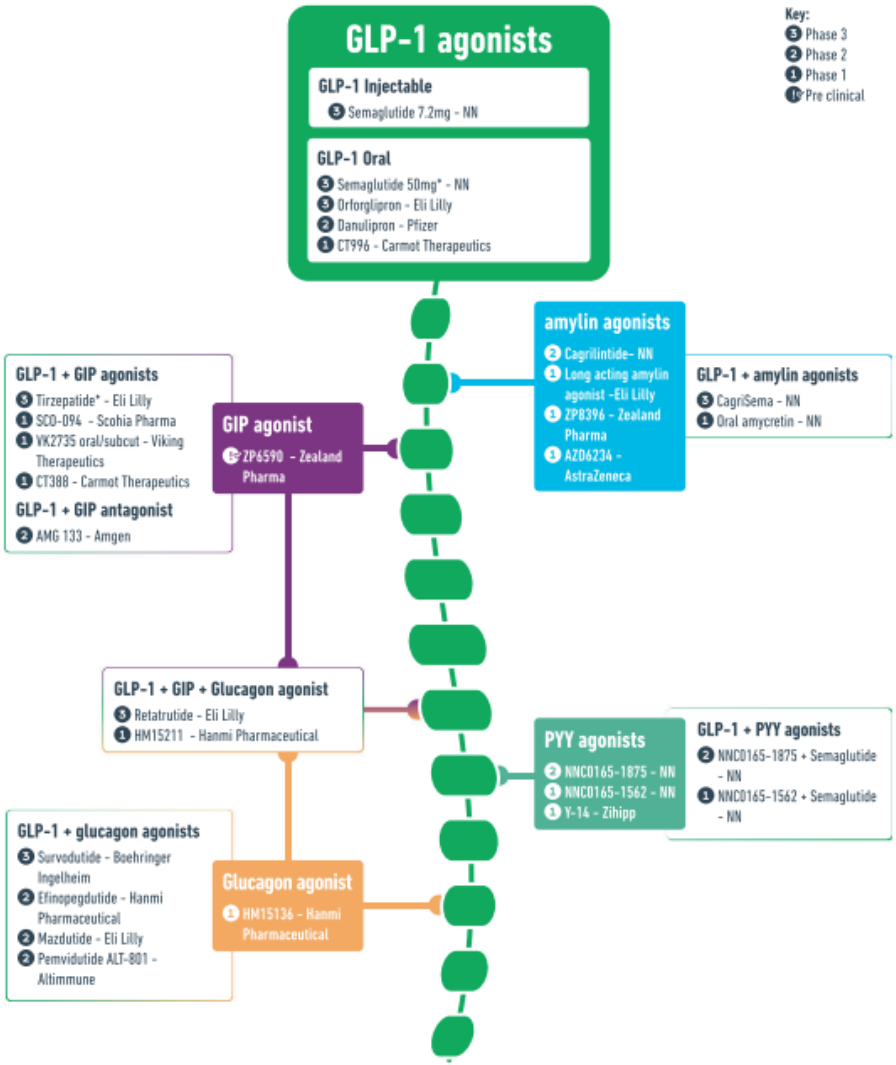
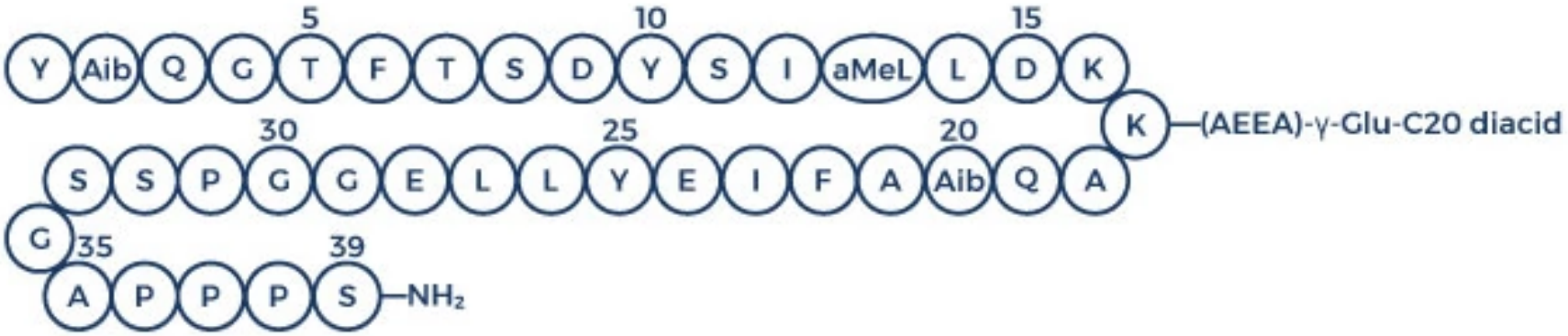


Fig. 2 Glucagon-like peptide-1 as the backbone of the pipeline for gut hormone-based obesity treatments. GLP-1 glucagon like peptide-1, GIP glucose-dependent insulinotropic polypeptide, PYY peptide YY, NN: novo nordisk, *completed phase 3 trials for obesity.

International Journal of Obesity
Published online: 01 February 2024

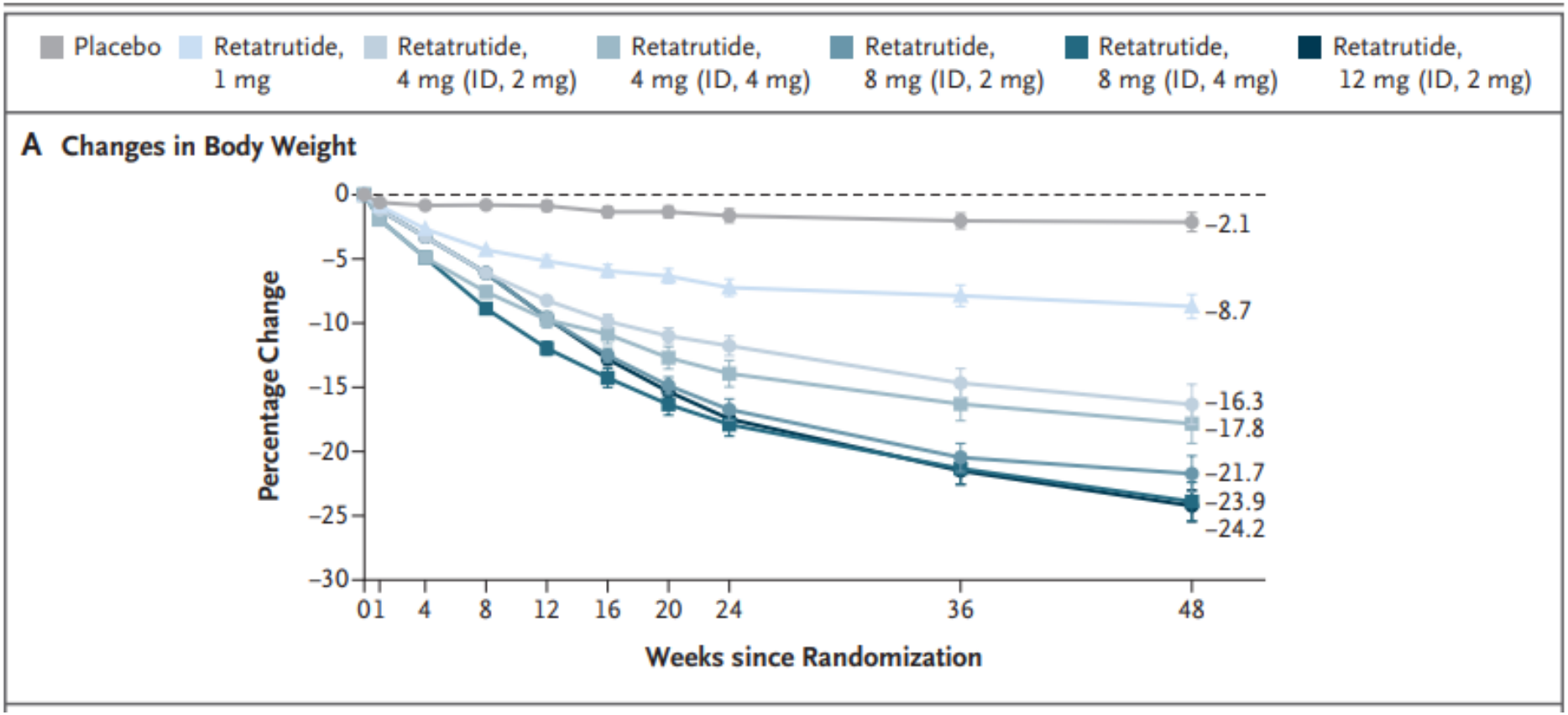
RETRATUTIDE

Retatrutide is a novel triple receptor agonist peptide that targets the glucagon receptor (GCGR), glucose-dependent insulinotropic polypeptide receptor (GIPR), and glucagon-like peptide-1 receptor (GLP-1R).



Triple–Hormone-Receptor Agonist Retatrutide for Obesity — A Phase 2 Trial

Ania M. Jastreboff, M.D., Ph.D., Lee M. Kaplan, M.D., Ph.D., Juan P. Frías, M.D., Qiwei Wu, Ph.D., Yu Du, Ph.D., Sirel Gurbuz, M.D., Tamer Coskun, M.D., Ph.D., Axel Haupt, M.D., Ph.D., Zvonko Milicevic, M.D., and Mark L. Hartman, M.D., for the Retatrutide Phase 2 Obesity Trial Investigators*



Triple–Hormone-Receptor Agonist Retatrutide for Obesity — A Phase 2 Trial

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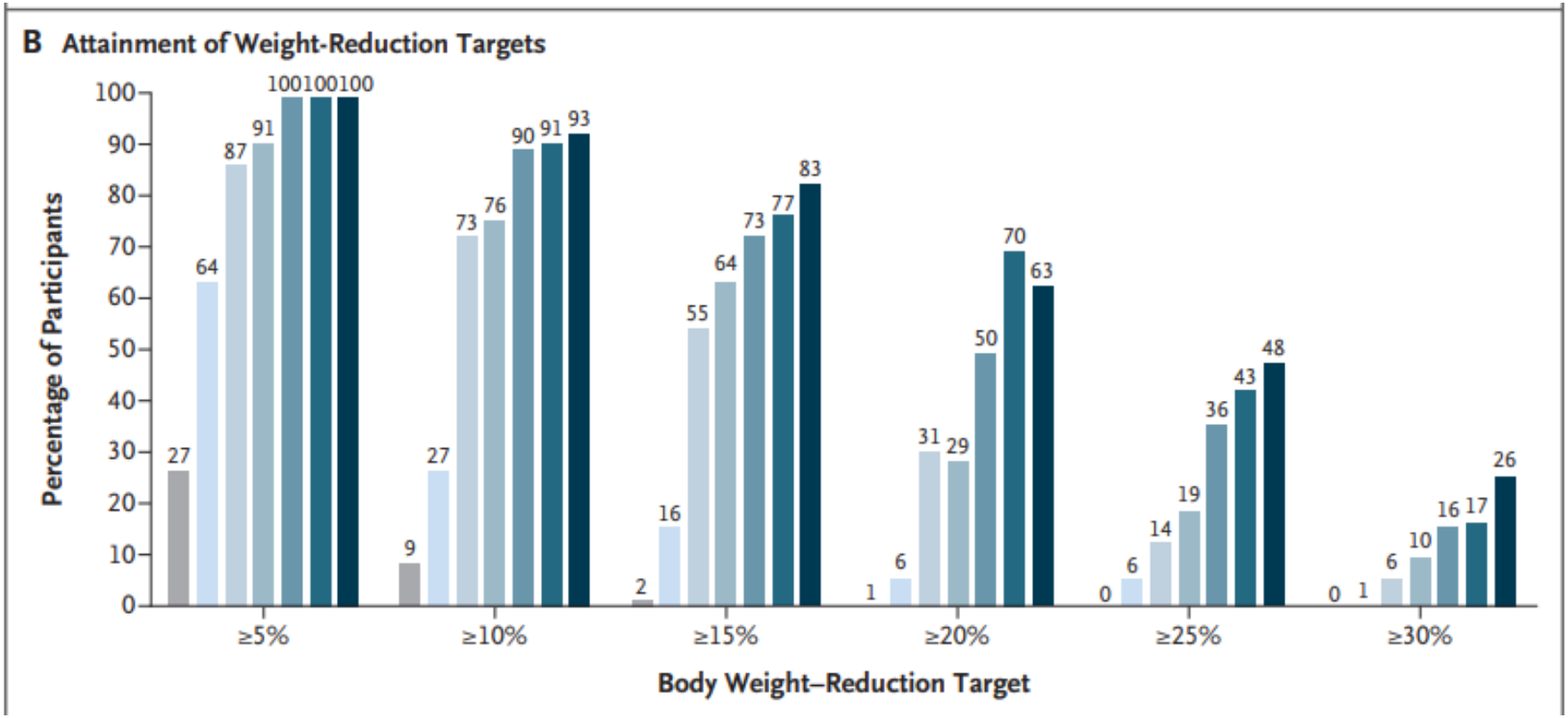


Development of Cagrilintide, a Long-Acting Amylin Analogue

Amylin[1] is a 37 amino acid peptide, produced in pancreatic beta cells and co-secreted with insulin. It has important effects on appetite, glucose management, and gastric emptying that warrant investigation for treatment of diabetes and obesity.

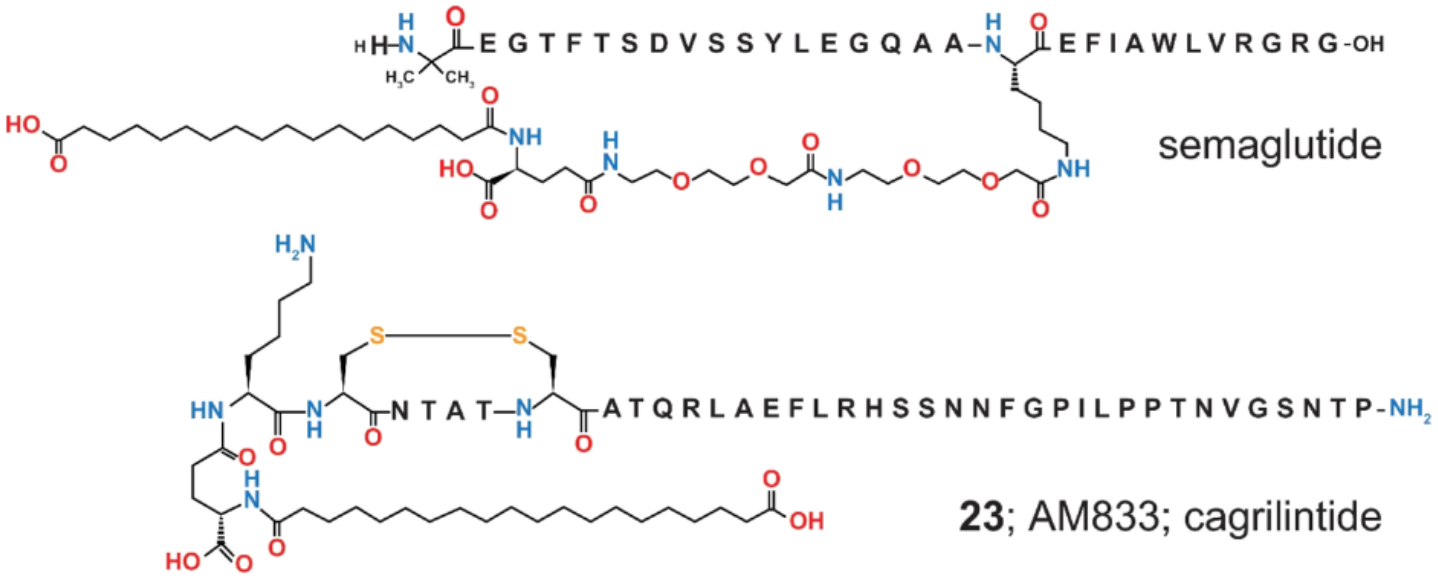
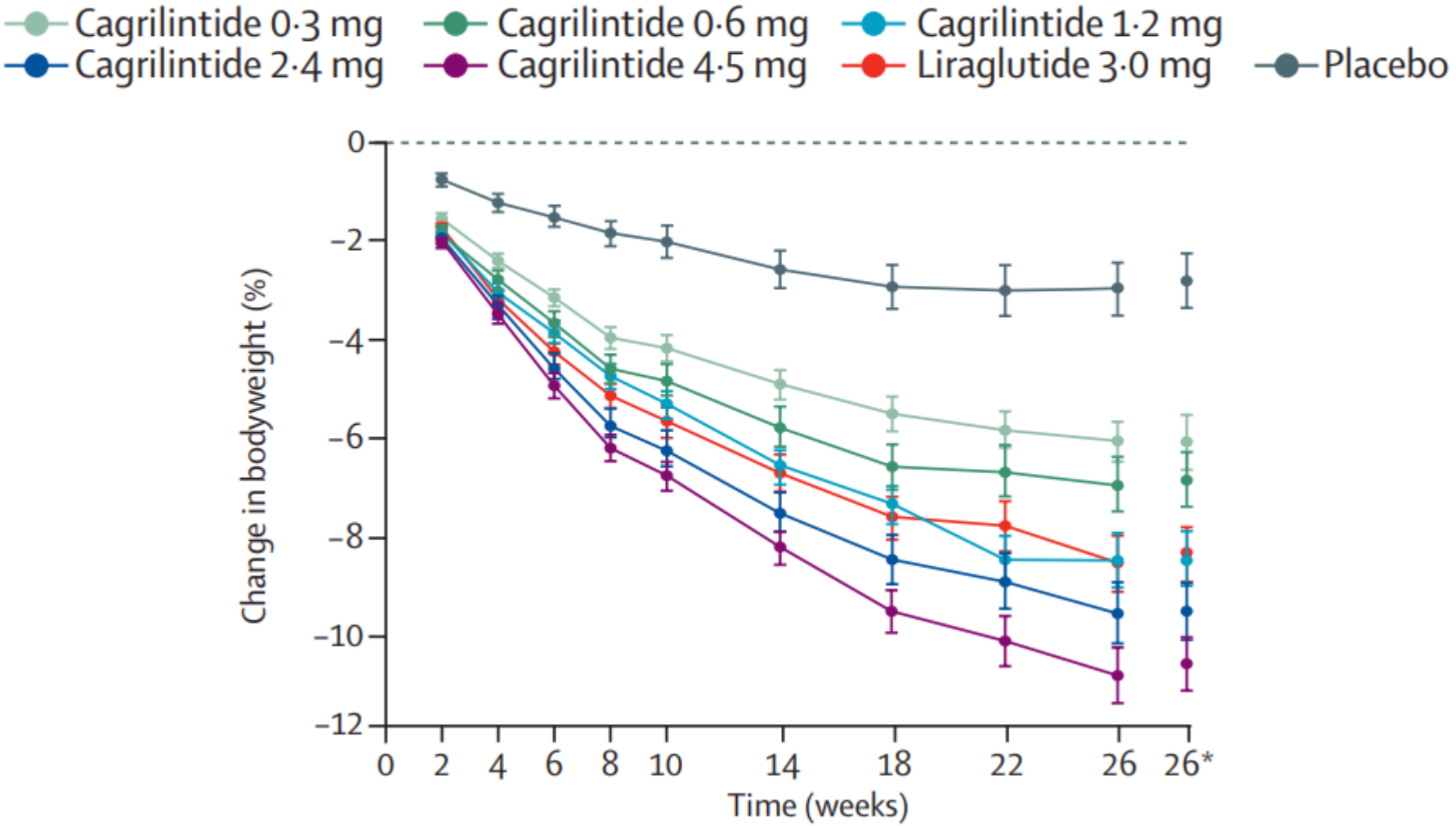


Figure 2. Chemical structures.

Kruse et al. *J. Med. Chem.* 2021, 64, 11183−11194

Once-weekly cagrilintide for weight management in people with overweight and obesity: a multicentre, randomised, double-blind, placebo-controlled and active-controlled, dose-finding phase 2 trial

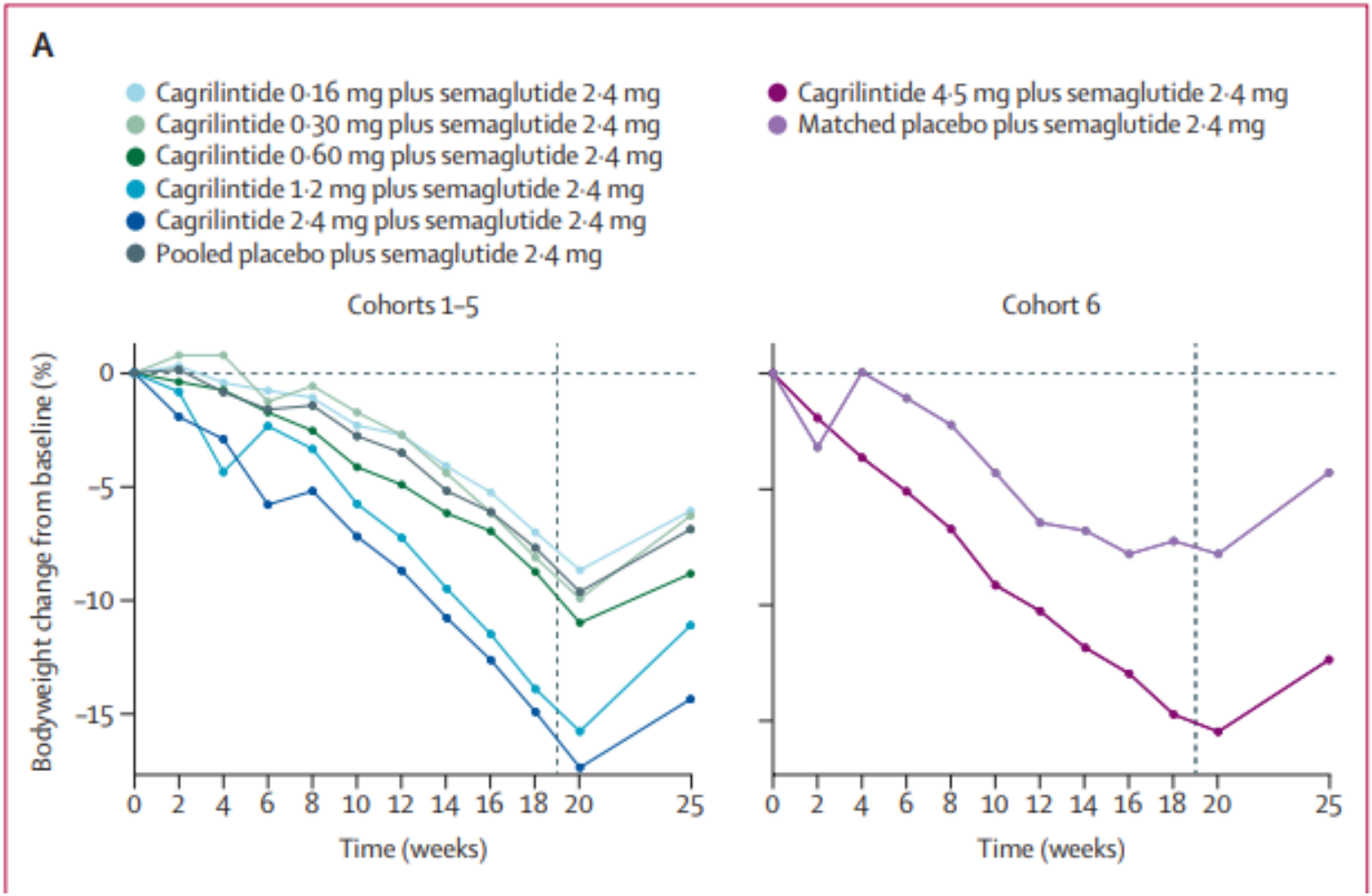
David C W Lau, Lars Erichsen, Ann Marie Francisco, Altynai Satylganova, Carel W le Roux, Barbara McGowan, Sue D Pedersen, Kirsi H Pietiläinen, Domenica Rubino, Rachel L Batterham



Lancet 2021; 398: 2160–72

Safety, tolerability, pharmacokinetics, and pharmacodynamics of concomitant administration of multiple doses of cagrilintide with semaglutide 2·4 mg for weight management: a randomised, controlled, phase 1b trial

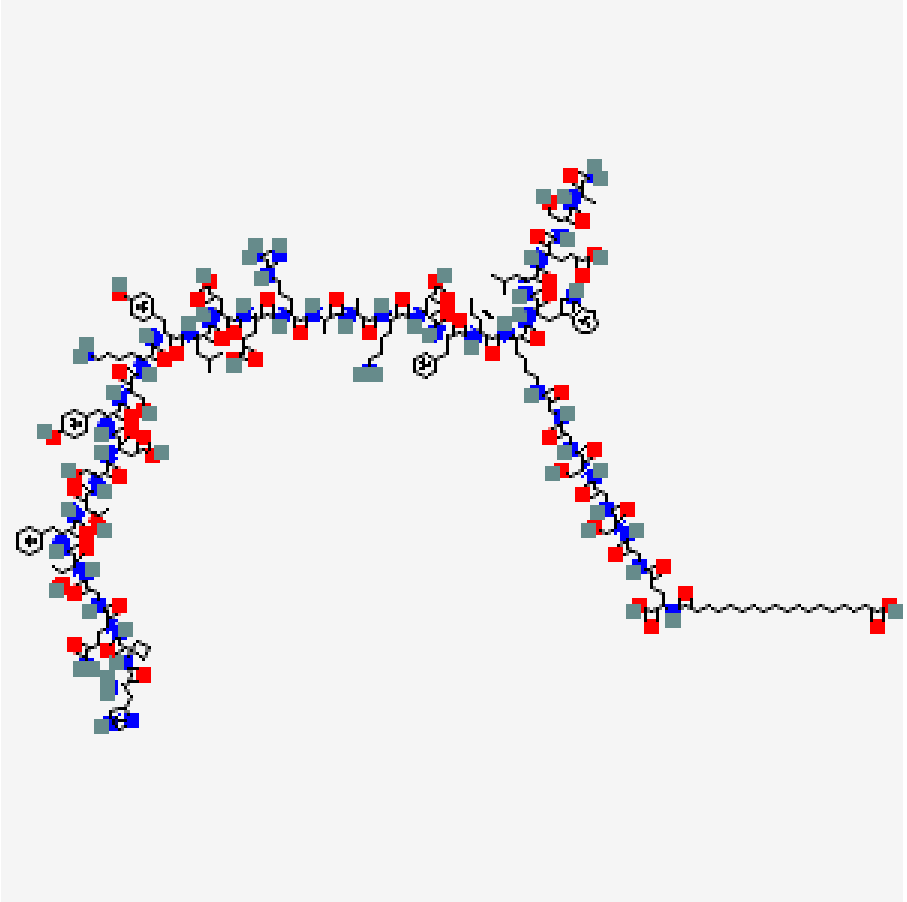
Lone B Enebo, Kasper K Berthelsen, Martin Kankam, Michael T Lund, Domenica M Rubino, Altynai Satylganova, David C W Lau



Lancet 2021; 397: 1736–48

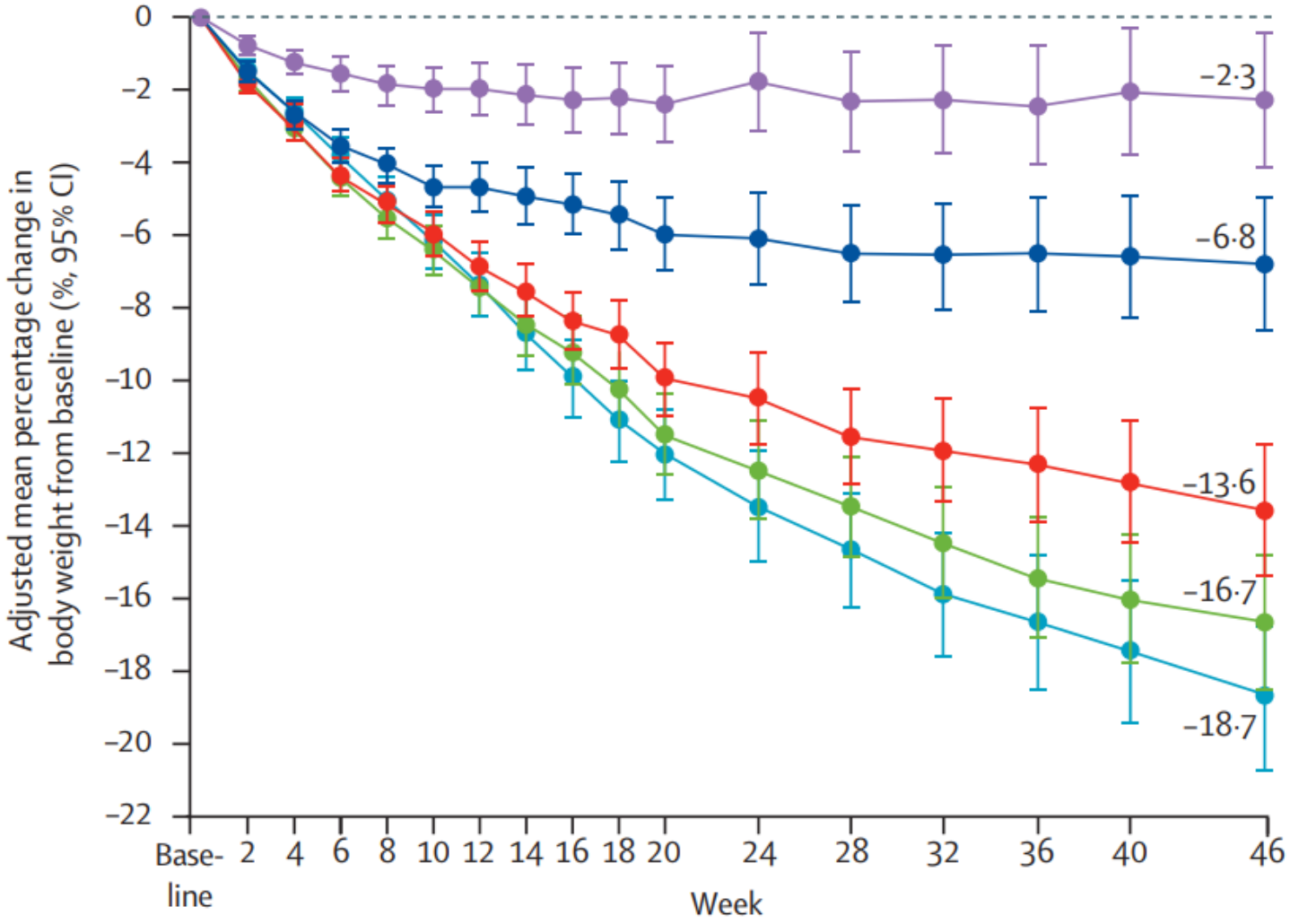
SURVODUTIDE

Survodutide is a dual glucagon-like peptide 1 receptor agonist (GLP-1RA) and glucagon receptor agonist



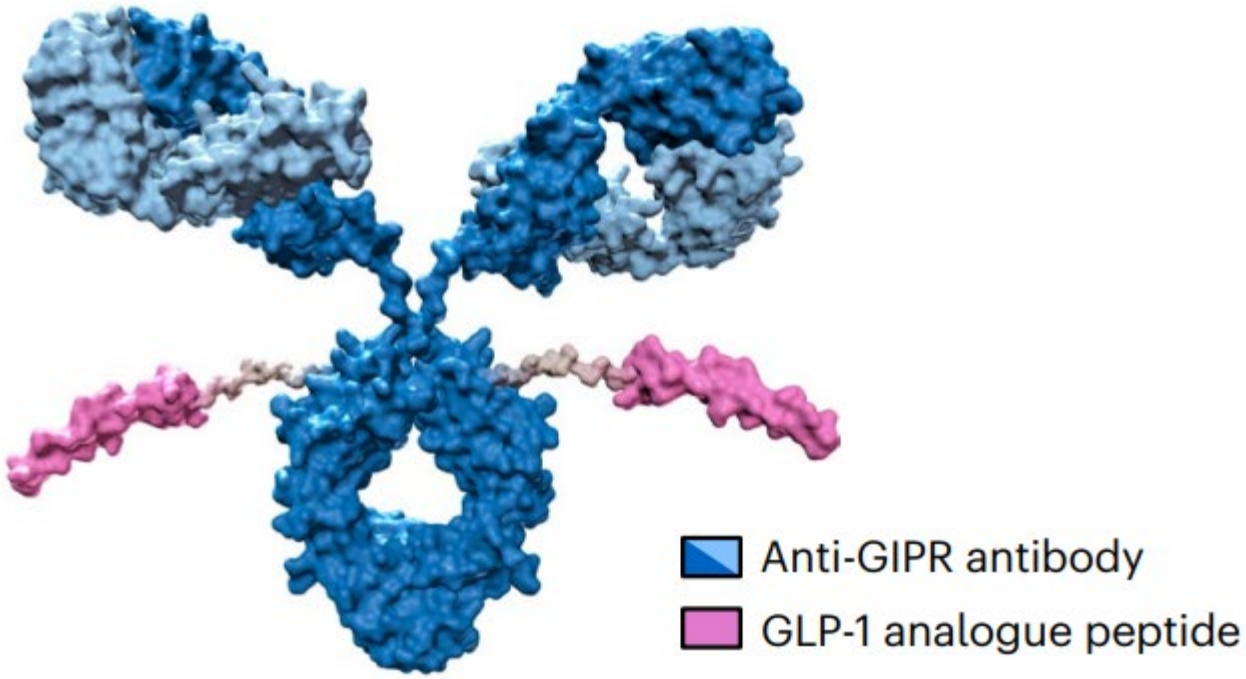
Glucagon and GLP-1 receptor dual agonist survodutide for obesity: a randomised, double-blind, placebo-controlled, dose-finding phase 2 trial

Carel W le Roux, Oren Steen, Kathryn J Lucas, Elena Startseva, Anna Unseld, Anita M Hennige

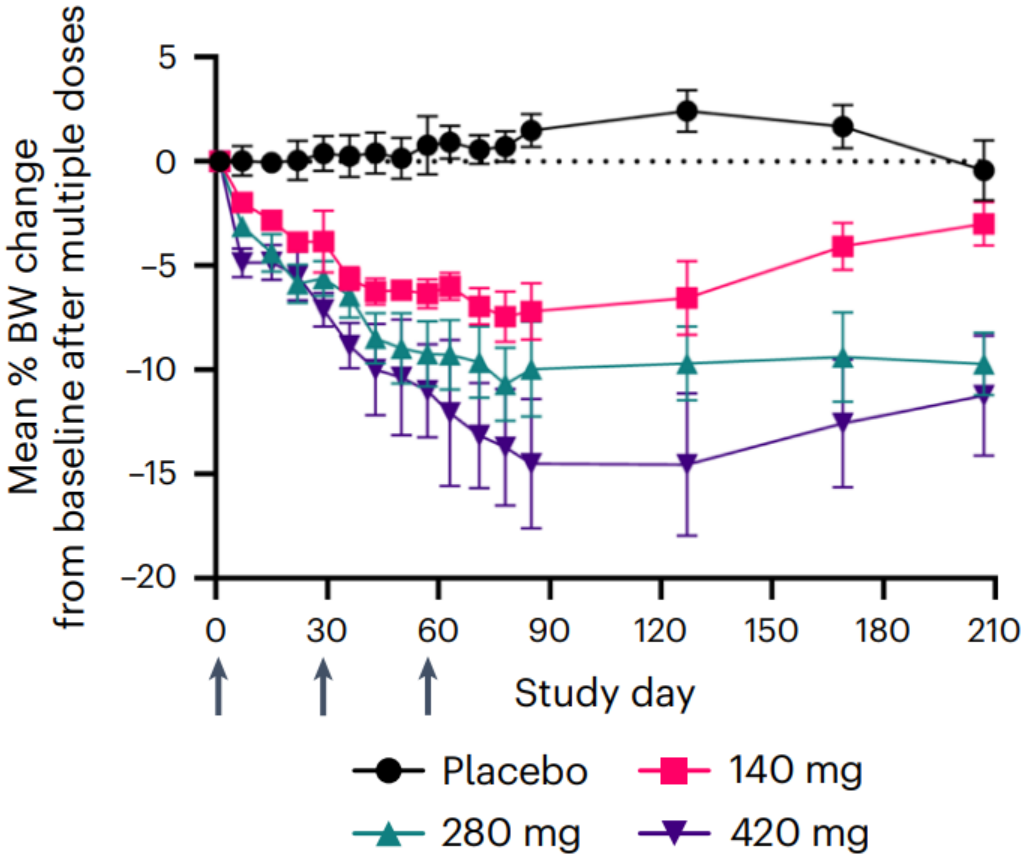


MARIDEBART CAFRAGLUTIDE (MARITIDE)

AMG 133 (now known as maridebart cafraglutide) is an optimized GIPR/GLP-1R bispecific molecule engineered by conjugating a fully human monoclonal anti-human GIPR-Ab with two GLP-1 analogue agonist peptides using amino acid linkers.



A GIPR antagonist conjugated to GLP-1 analogues promotes weight loss with improved metabolic parameters in preclinical and phase 1 settings



Veniant et al. Nature Metabolism | Volume 6 | February 2024 | 290–303

LE SFIDE CHE CI ATTENDONO

- Gestione degli effetti collaterali
- Velocità del calo ponderale
- Mantenimento degli effetti a lungo termine

PERSONALIZZAZIONE DELLA TERAPIA


thank
you