

New Medications for Obesity – The Future is NOW!

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1

Disclosure

Advisory Board: AbbVie; Addition; Altimune; Amgen; AstraZeneca; Autonomy Bio; Biohaven; Boehringer Ingelheim; Carmot/Roche/Regeneron; CinRx; Currax; Eli Lilly; Epitomee Medical; Fractyl Health; i2o Therapeutics; ICON; Kailera; Nestle Healthcare Nutrition; Novo Nordisk; Pfizer; Protagonist Therapeutics; Regor; Souffle; Source Bio; Structure Therapeutics; Tenvie; Viking Therapeutics; Wondr Health; Zealand Pharma

Consultant: Calibrate; PPD; Rhythm; Weight Watchers

Data Monitoring Committee: CinRx; Eli Lilly; Rhythm

Speaker's Bureau: Boehringer Ingelheim; Eli Lilly; Novo Nordisk

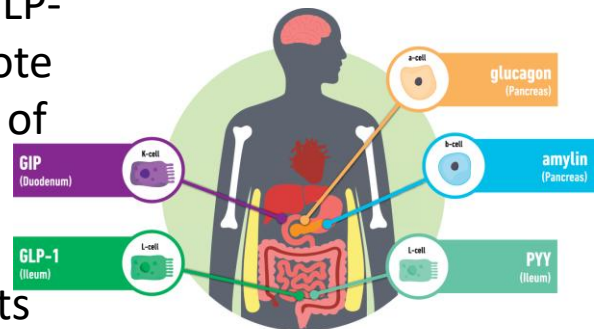
Stock Options: Calibrate; Epitomee Medical; Ro

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The Lexicon

- **Incretin** medication: GIP & GLP-1 targeted medication promote insulin secretion in presence of increased blood glucose
- **NuSH** medication: Nutrient Stimulated Hormone – targets GIP, GLP-1, Glucagon, Amylin $\pm$ calcitonin



Melson E., et al. *Int J Obes* 49, 433–451 (2025).

3

ARS Question #1

Where Do You Stand?

- I don't want to incorporate obesity management medications in my practice; they are too much trouble, and it doesn't really fit in my practice.
- I have a primary care practice and use GLP-1 medications for weight management sparingly.
- I write prescriptions for GLP-1 obesity management medications but mostly for OSA, secondary prevention of CV events, and MASH.
- I have a practice that has a large obesity management population, and I prescribe all available obesity management medications.
- Something else

4

The Future Is Now for Obesity Medications. Why You Should Care

- 2026 - 8 OMMs (obesity management medications) - 4 target GLP-1 or GLP-1/GIP; 4 “legacy” medications
- 2027 - 2 new formulations; 1 oral small molecule GLP-1 RA
- 2028 - 11 more medications targeting NuSHs
- 2026 – 18 million US adults are taking a GLP-1 medication
- 2030 - XX million US adults taking NUSHs.
- The focus is shifting from OM to chronic disease modifications
- Patients want to take these medications.
- There is potential for a profound impact on public health, if we have informed health care providers skilled in the use of these medications.

5

Learning Objectives

At the end of the presentation, learners will be able to

- describe the medications for weight management, including those currently available and those arriving in 2026 and 2027;
- relate the principles and standards of care in prescribing these medications, with focus on NuSH* –based therapies; and
- discuss how NuSH*-based therapies have actions beyond weight loss and glycemic management.

*NuSH = Nutrient Stimulated Hormone

6

Obesity Medications 2025 Use Patterns

Sympathomimetics
Phentermine

Orlistat

Phentermine/
Topiramate

Liraglutide

Bardet Biedl
POMC
PCSK1
LEPR

Naltrexone/
Bupropion

Setmelanotide

Semaglutide

Tirzepatide

7

Obesity Medications 2025 Use Patterns

Sympathomimetics
Phentermine

Orlistat

Phentermine/
Topiramate

Liraglutide

BARRIERS TO
SEMA AND TZP

Naltrexone/
Bupropion

Setmelanotide

Semaglutide

Tirzepatide

8

Obesity Medications 2025 Use Patterns

Sympathomimetics
Phentermine

Orlistat

Phentermine/
Topiramate

Liraglutide

OVER THE
COUNTER

Naltrexone/
Bupropion

Setmelanotide

Semaglutide

Tirzepatide

9

Obesity Medications 2025 Use Patterns

Sympathomimetics
Phentermine

Orlistat

Phentermine/
Topiramate

Liraglutide

???

Naltrexone/
Bupropion

Setmelanotide

Semaglutide

Tirzepatide

10

Obesity Medications 2025 Use Patterns

Sympathomimetics
Phentermine

Orlistat

Phentermine/
Topiramate

Liraglutide

OVERWEIGHT &
OBESITY WITH
REIMBURSEMENT
OR OUT-OF-
POCKET

Naltrexone/
Bupropion

Setmelanotide

Semaglutide

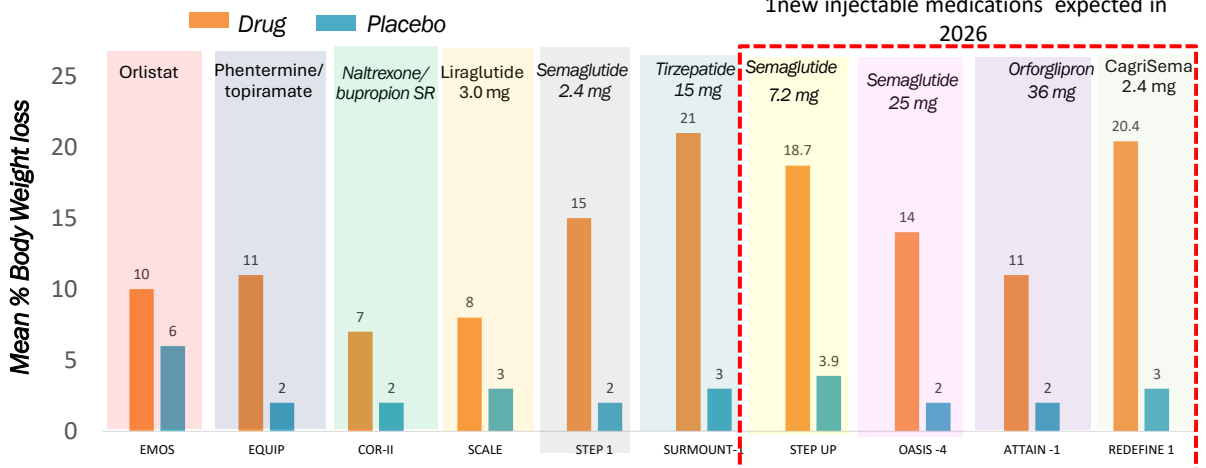
Tirzepatide

11

Mean Percentage Weight Loss for FDA-Approved Medications Percent Weight Loss (Drug vs Placebo) in Patients Without Diabetes

4 new formulations this year!

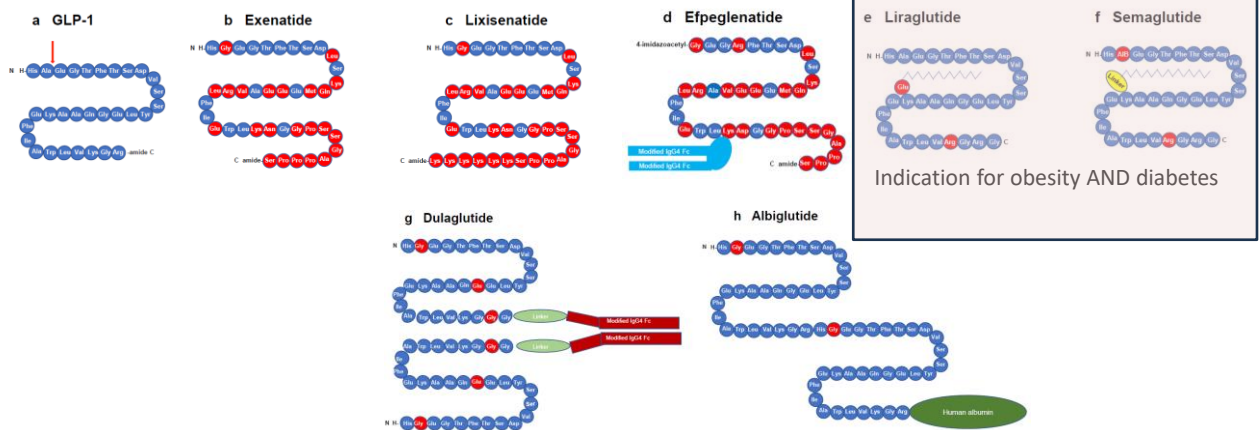
1↑ dose injectable, 2 oral &
1 new injectable medications expected in
2026



Sjöström L, et al. Lancet. 1998;352(9123):167-172; Allison DB, et al. Obesity (Silver Spring). 2012;20(2):330-342; Gadde KM, et al. Lancet. 2011;377(9774):1341-1352; Greenway FL, et al. Lancet. 2010;376(9741):595-605; Apovian CM, et al. Obesity (Silver Spring). 2013;21(5):935-943; Pi-Sunyer X, et al. N Engl J Med. 2015;373:11-22; Wilding JPH, et al. N Engl J Med. 2021;384(11):989-1002; Jastreboff AM, et al. N Engl J Med. 2022;387(3):205-216; Wadden TA, et al. Nat Med. 2023;29(11):2909-2918. Wharton S, et al. N Engl J Med 2025;393:1077-1087. Wharton S, et al. DOI: 10.1056/NEJMoa251177. Garvey TM, et al. N Engl J Med 2025;393:635-647

12

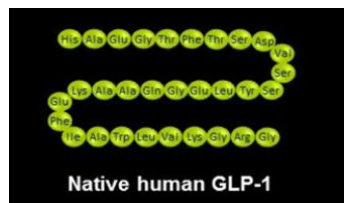
How Did We Get Here? GLP-1 Receptor Agonists Initially Developed for Diabetes, Then Obesity



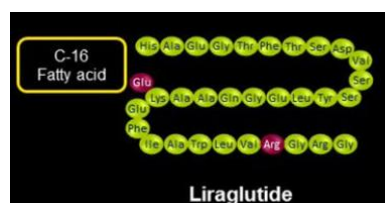
Tschöp et al (2023) Diabetologia DOI 10.1007/s00125-023-05929-0

13

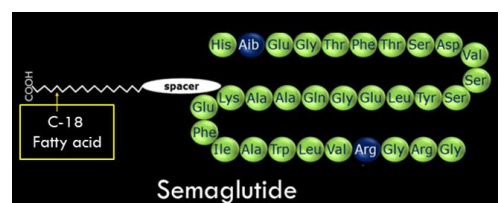
GLP 1 Physiology to Pharmacology



- Half life 1-2 minutes
- Deactivated by DPP-4



- 97% homology
- Arginine replaces lysine @ 28
- Lysine at 20 is conjugated to c-16 palmitic acid via gamma glutamic acid spacer (albumen binding)
- Forms heptamers
- Reduced degradation and clearance
- Half Life 13 hours

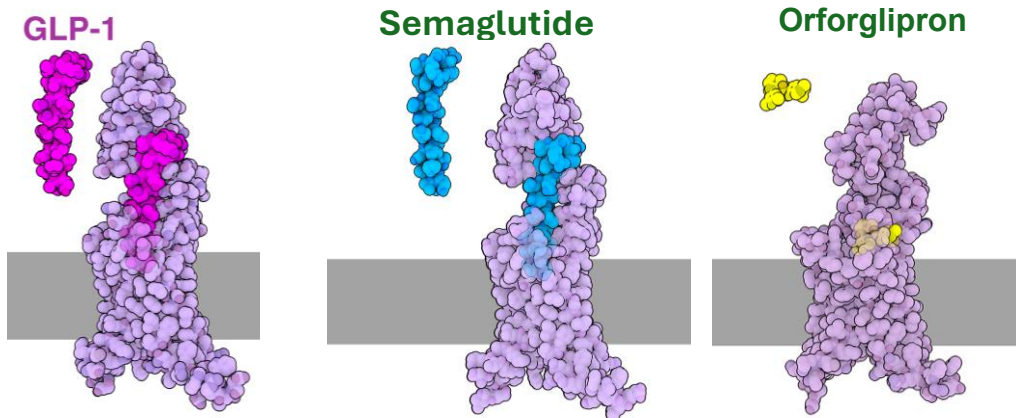


- 94% homology
- Arginine replaces lysine @ 28
- Aminoisobutyric acid replaces glycine at position 2 (resists degradation)
- C-18 fatty acid and lengthier spacer attached to Lysine (albumen binding)
- Reduced degradation and clearance
- Half Life 165 hours

Brandt SJ, et al. Journal Internal Medicine 2018. 284: 581-602.

14

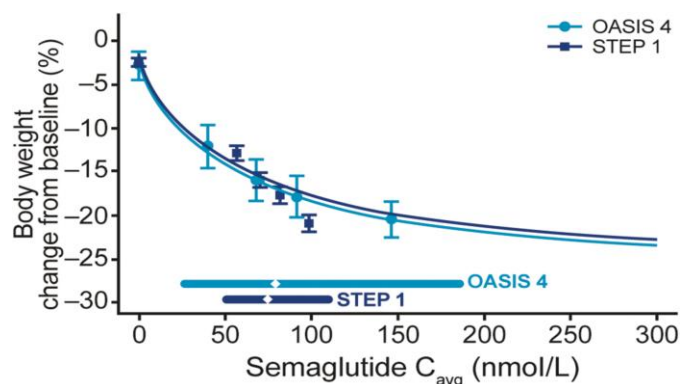
2026: Two Oral GLP-1 Receptor Agonists Approved for Obesity Management



<https://pdb101.rcsb.org/motm/311>

15

Pharmacokinetic Modeling: Semaglutide 25 mg Oral (OASIS 4) and STEP 1.
82.2% of Participants Receiving 25 mg Oral Semaglutide Achieved
Exposure Levels in Same Range as Semaglutide 2.4 mg Sc



Overgaard RV, et al. Diabetes Obes Metab. 2026 Apr 23. doi: 10.1111/dom.70769. Epub ahead of print. PMID: 42023428.

16

Absorption and Metabolism Properties of Oral Semaglutide and Orforglipron

Semaglutide

- **Label advice:** take on an **empty stomach** with **≤120 mL of water**, then **wait at least 30 minutes** before eating, drinking, or taking other oral medications
- Coformulated with **SNAC** (sodium N-[8-(2-hydroxybenzoyl) aminocaprylate])
- Absorption predominantly occurs in the stomach, not the intestine.
- **T_{max}** is approximately **1 hour** after oral administration.
- **Steady-state exposure** is achieved after **4–5 weeks** of daily dosing.
- Semaglutide is **>99% bound to plasma albumin**, with an elimination half-life of approximately one week and **persistence in circulation for about 5 weeks after the last tablet dose**.
- Metabolized by proteolysis

Orforglipron

- **77% absolute bioavailability at the 0.8 mg dose**
- **T_{max}** is reached **4 to 8 hours** post-dose.
- Exposure increases in a dose-proportional manner.
- Plasma **protein binding is >99%**.
- **Metabolized by CYP3A4 enzymes**
- **Strong CYP3A4 inhibitors:** Maximum orforglipron dose is 9 mg once daily.
- If the strong CYP3A4 inhibitor also inhibits OATP1B (e.g., ritonavir), concomitant use should be avoided entirely.
- **Strong CYP3A4 inducers** (e.g., carbamazepine, phenytoin, rifampin): Avoid concomitant use.
- **Moderate CYP3A4 inducers** (e.g., efavirenz): Monitor effectiveness and escalate orforglipron dose as needed.
- **Simvastatin:** Do not exceed simvastatin 20 mg once daily when used concomitantly with orforglipron

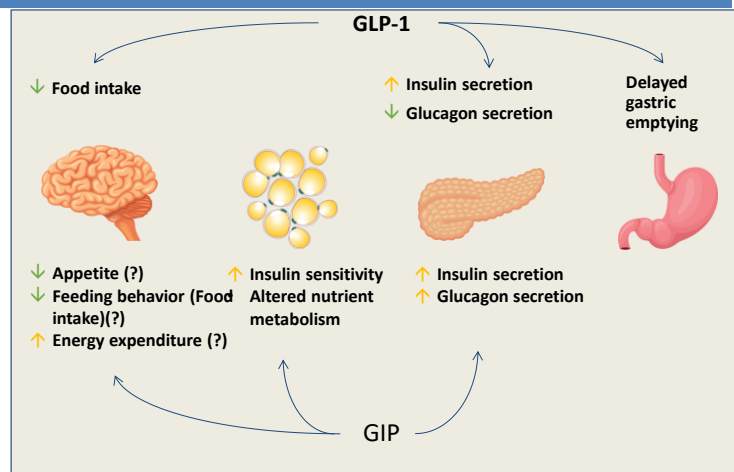
Information from US FDA Labels

17

GLP-1 and GIP Dual Agonism May Have Synergistic Effects

- GLP-1 has suggested direct actions in CNS, islets, and stomach^{1,2}
- GIP has shown potential actions in current research in CNS, adipose, and islets^{2,3,4}
- A single molecule GIP/GLP-1 receptor dual agonist may enable improved physiology over the sum of its individual agonist components^{5,6}

CNS = central nervous system



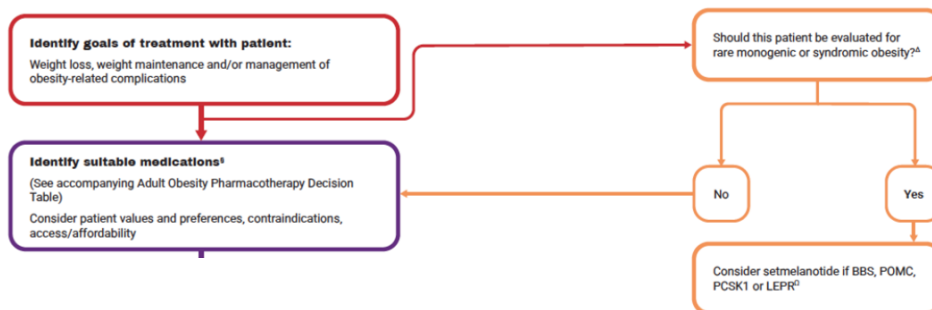
1. Müller TD et al. *Mol Metab.* 2019;30:72-130. 2. Seino Y et al. *J Diabetes Investig.* 2010;1(1-2):8-23. 3. Fukuda M. *Diabetes.* 2021;70(8):dbi210001. 4. Nauck MA et al. *Diabetes Obes Metab.* 2021 (ahead of print). doi:10.1111/dom.14496. 5. Samms RJ et al. *Trends Endocrinol Metab.* 2020;31(6):410-421. 6. Bastin M et al. *Diabetes Metab Syndro Obes.* 2019;12:1973-1985.

18

Let's Discuss How We Go About Selecting an Obesity Management Medication ...

19

Adult Obesity Pharmacotherapy Decision Tool



^Δ Consider genetic testing if early onset obesity with hyperphagia, features of monogenic obesity (see text)

^Ω BBS - Bardet-Biedl Syndrome ; POMC - pro-opiomelanocortin deficiency; PCSK1 - proprotein convertase subtilisin/kexin type 1 deficiency; LEPR - leptin receptor deficiency

[§] Medications approved in Canada: Liraglutide 3 mg daily, Naltrexone/Bupropion 16/180 mg bid, Orlistat 120 mg tid, Semaglutide 2.4 mg weekly, tirzepatide 5/10/15 mg weekly. All are recommended in conjunction with health behavior changes.

^Ψ The weight that a person can achieve and maintain while living their healthiest and happiest life

see <https://obesitycanada.ca/wp-content/uploads/2020/10/191707-guide-2-at.pdf>

Pedersen SD, Manjoo P, Dash S et al. Pharmacotherapy for Obesity Medicine in Adults. <https://obesitycanada.ca/guidelines>

20

Adult Obesity Pharmacotherapy Decision Table

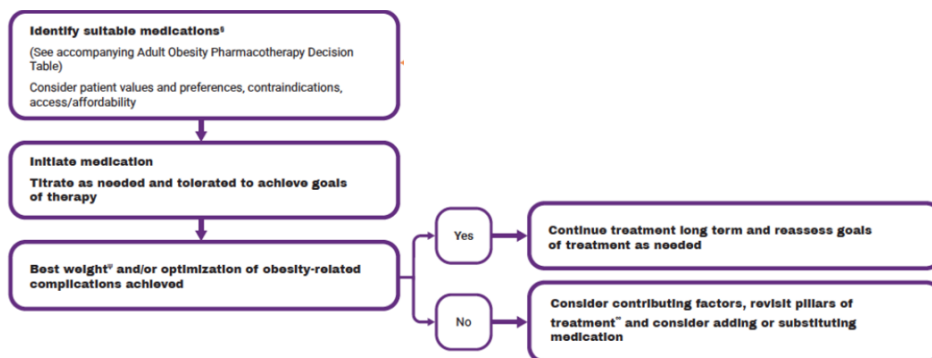
		Liraglutide 3 mg daily	Naltrexone/ Bupropion 16/180 mg BID	Orlistat 120 mg TID	Semaglutide 2.4 mg weekly	Tirzepatide 5/10/15 mg weekly
Cardio-Metabolic Complications	Prediabetes	✓		✓	✓	✓
	T2D	✓	✓	✓	✓	✓**
	MASH	✓		∅	✓	✓
	ASCVD		Q		✓	Q
	HFpEF				✓	✓*
Mechanical Complications	OSA	✓				✓**
	OA	∅			✓	Q
Patient Reported Outcome Measures (PROMS)	QoL	+	+		+	+
	Physical Function	+	+		+	+
	Cravings		+		+	
Average weight loss (placebo subtracted)		5.4%	4.6%	2.9%	12.4%	11.9/16.4/17.8%
✓ Level 1a Very High Certainty		✓ Level 2a Moderate Certainty	✓ Level 3 Low Certainty	∅ No Benefit	⊕ Benefit	Q In study as identified on www.clinicaltrials.gov

*15 mg, **10 mg or 15 mg. T2D - type 2 diabetes, MASH - metabolic dysfunction-associated steatohepatitis, ASCVD - atherosclerotic cardiovascular disease, HFpEF - heart failure with preserved ejection fraction, OSA - obstructive sleep apnoea, OA - osteoarthritis, QoL - quality of life

Pedersen SD, Manjoo P, Dash S et al. Pharmacotherapy for Obesity Medicine in Adults.
<https://obesitycanada.ca/guidelines>

21

Adult Obesity Pharmacotherapy Decision Tool



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Pedersen SD, Manjoo P, Dash S et al. Pharmacotherapy for Obesity Medicine in Adults.
<https://obesitycanada.ca/guidelines>

22

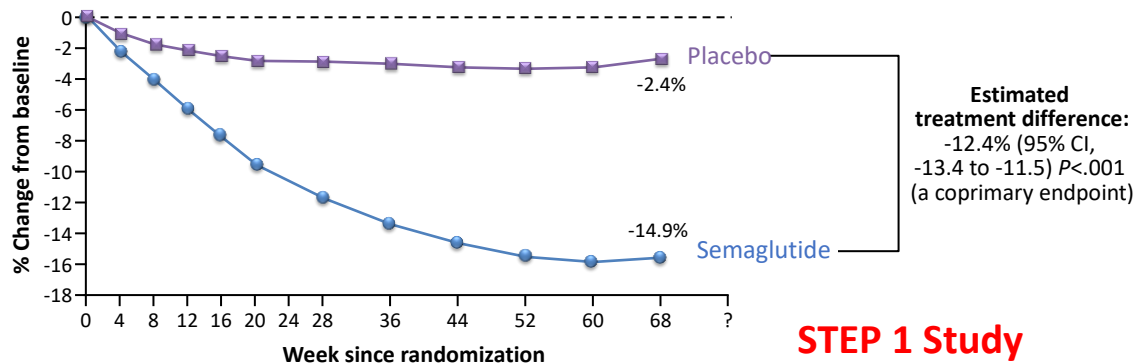
Let's Discuss Weight Loss Efficacy...

23

Semaglutide 2.4 mg

GLP-1 Receptor Agonist:

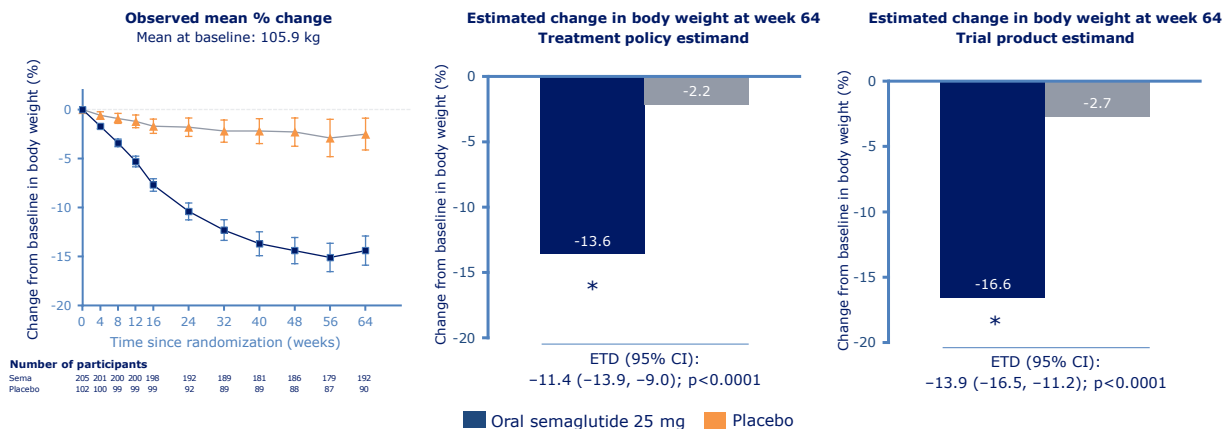
- Common SE: GI – nausea, vomiting, diarrhea, constipation.
- Avg. weight loss of 34 lbs = 14.9% weight loss in the total trial population.
- 16.9% weight loss compared to 2.4% in subjects who completed the trial and stayed on medication



Wilding JM, et al. *N Engl J Med*. Feb 2021.

24

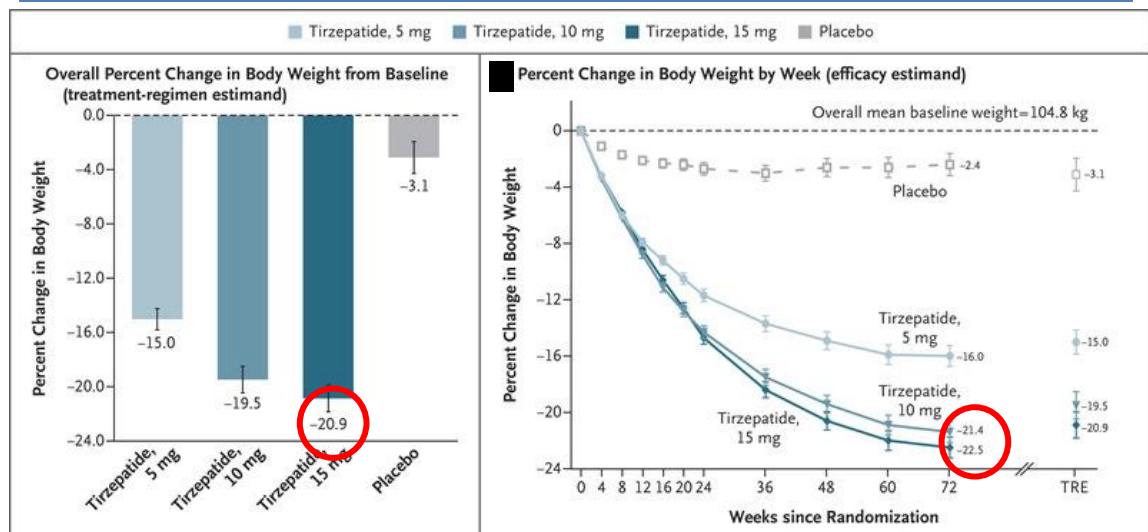
OASIS 4 Oral Semaglutide 25 mg: Change in Body Weight (%) at 64 Weeks (Co-Primary Endpoint)



Wharton S. et al. N Engl J Med 2025;393:1077-1087

25

Tirzepatide 5 mg, 10 mg, 15 mg

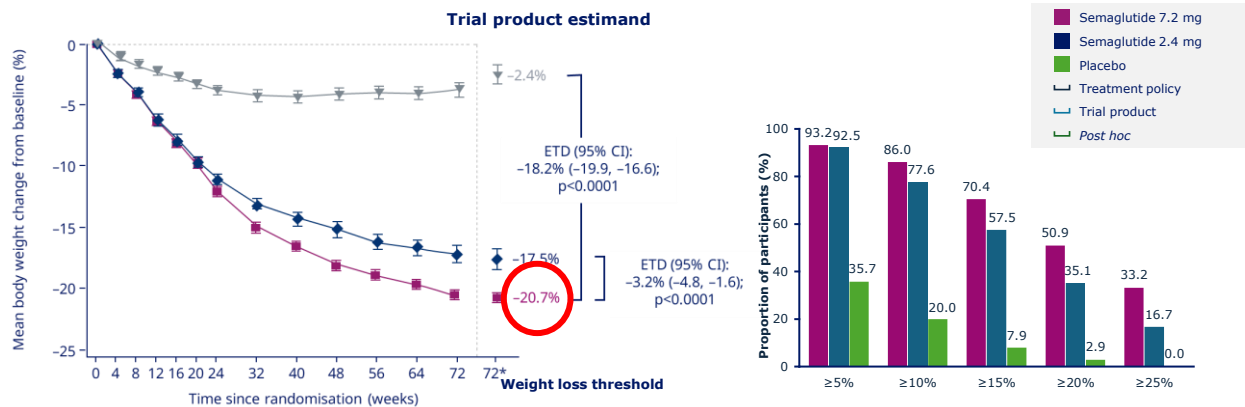


Jastreboff et al. NEJM Jun 2022

26

STEP UP Study: Semaglutide 7.2 mg vs. 2.4 mg vs Placebo

STEP UP

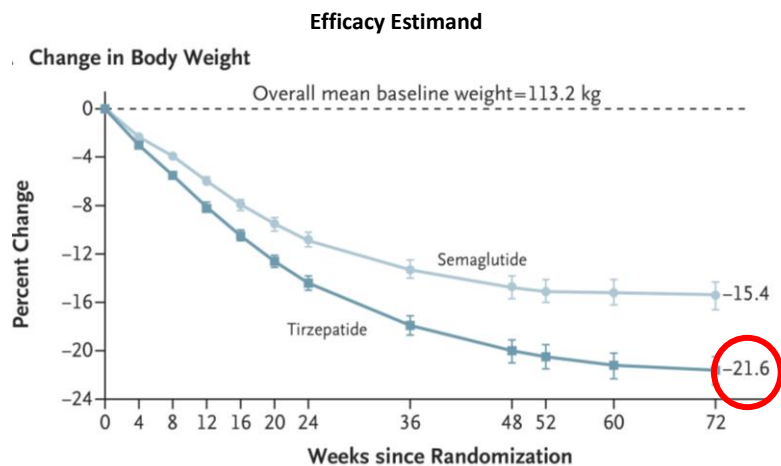


Wharton S et al. Lancet Diabetes Endocrinol 2025;13:949-963.

27

Randomized Comparison of Semaglutide (1.7 or 2.4 mg) vs. Tirzepatide (5 or 10 mg)

- 751 randomized adults with overweight and obesity without diabetes
- 85% completed trial in each arm
- Mean age 45
- 65% women
- 76% white
- Mean BMI 30.4 kg/m²

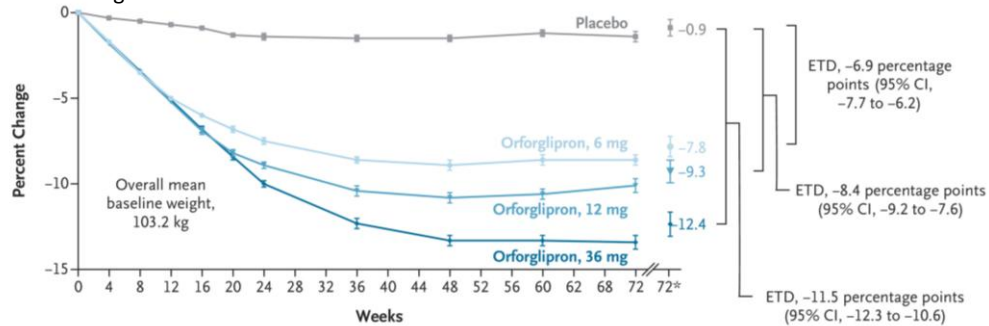


Aronne LJ et al. N Engl J Med 2025;393:26-36.

28

ATTAIN 1: Orforglipron Trajectory of Change in Body Weight to Week 72

Treatment Regimen Estimand



No. of Patients

Placebo	949	937	923	910	875	847	817	766	716	688	654	949
Orforglipron, 6 mg	723	713	702	690	675	664	652	630	601	578	559	723
Orforglipron, 12 mg	725	719	695	687	672	652	648	624	602	582	559	725
Orforglipron, 36 mg	730	715	704	689	670	662	644	617	583	573	549	730

5.5 mg

9 mg

17.2 mg

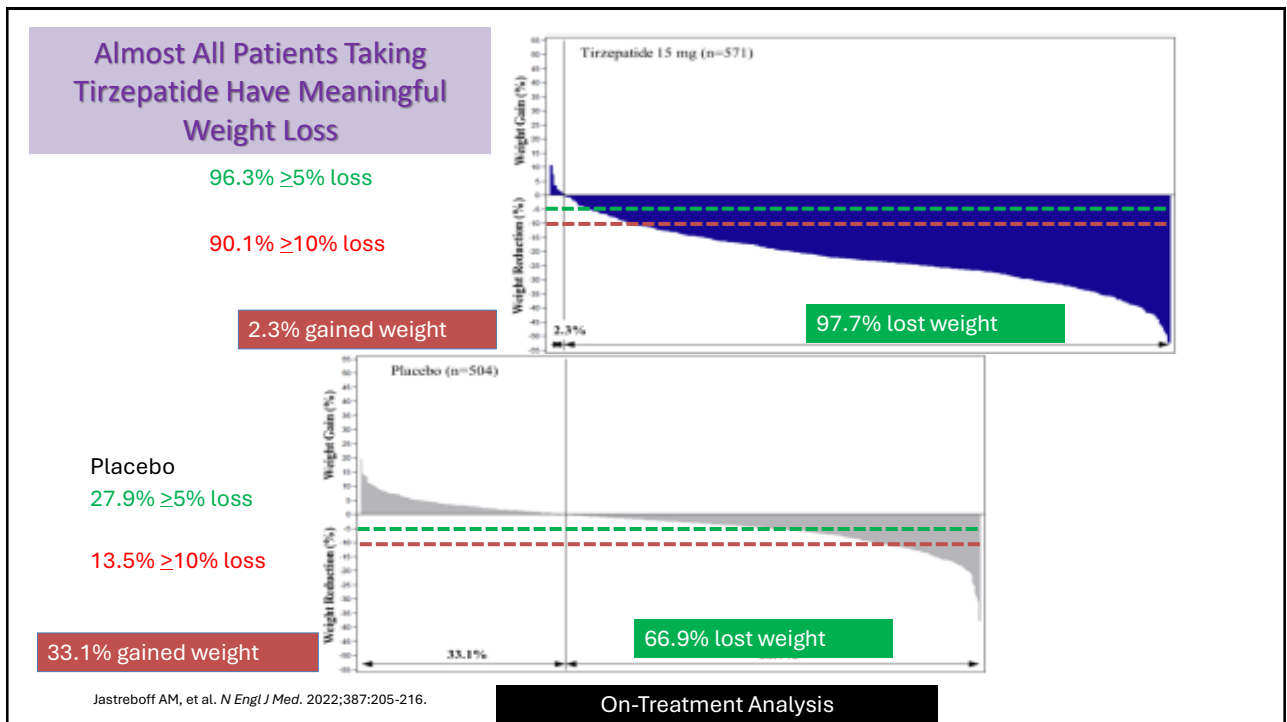
NOTE: Bioequivalence studies confirm the marketed doses are the same as the formulations in the clinical trials.

Wharton S, et al. N Engl J Med 2025;393:1796-1806

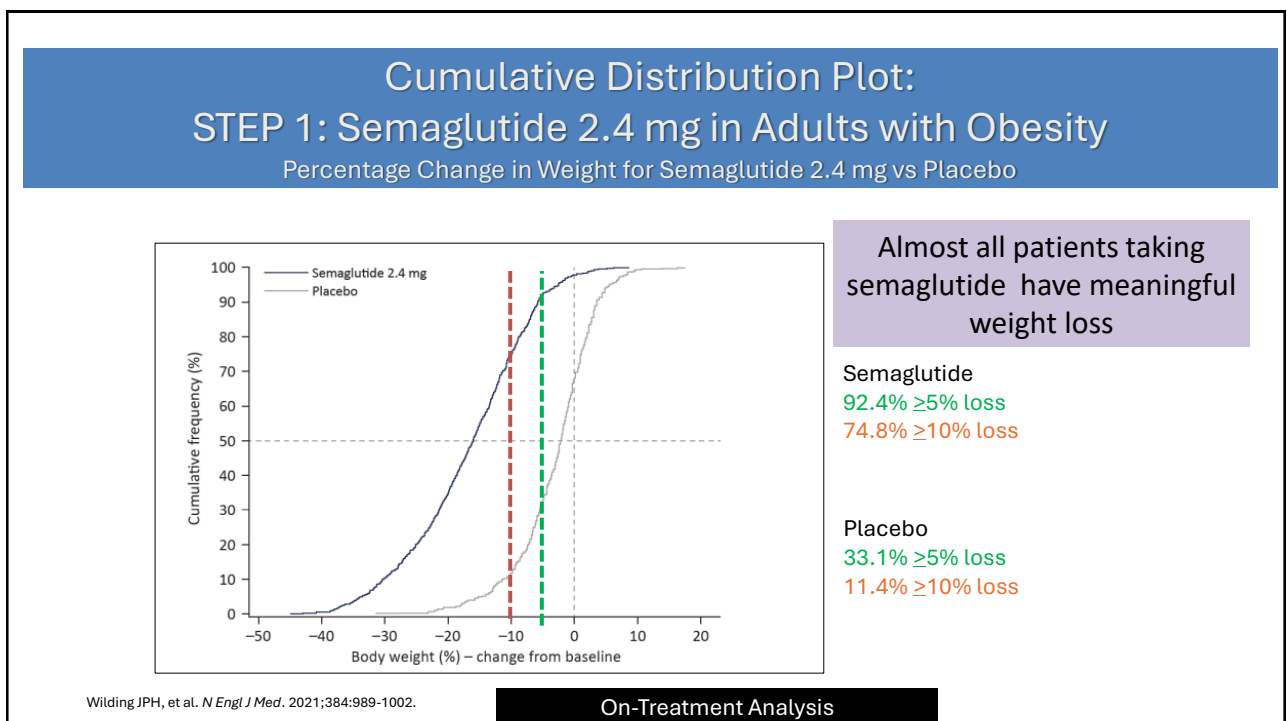
29

Let's Discuss What Mean Percent Weight Loss Means in the Context of Variability of Patient Response...

30



31



32

Let's Discuss Safety and Tolerability with GLP-1 Targeted Therapies in the Presentation That Follows. We Will Also Learn How to Manage Them to Limit Risk and Improve Adherence...

33

ARS Question #2**The Mechanism of Actions of Medications Targeting the GLP-1 Receptor Include**

- A. Incretin effect via beta cell stimulation to promote insulin secretion in the presence of elevated blood glucose and better glycemic control mediates improvements in cardiometabolic diseases.
- B. Reduction in food intake as a result of targeting multiple appetite areas of the brain causes weight loss which mediates improvements in cardiometabolic diseases.
- C. GLP-1 RA medications have incretin effects, appetite effects which drive weight loss, powerful anti-inflammatory effects, are cardioprotective, renoprotective, modulate the immune system and reduce inflammation and steatosis in the liver.



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34

Let's Discuss the Effects of the Medications Beyond Glycemia and Weight Loss...

35

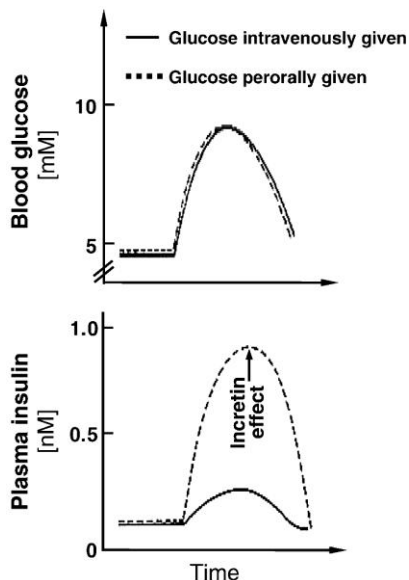
The Message: Multiple Mechanisms for Health Benefits of GLP-1s

Weight Loss Produces Health Benefits
Glycemic Improvement produces Health Benefits



Organ Protection Produces Health Benefits

36



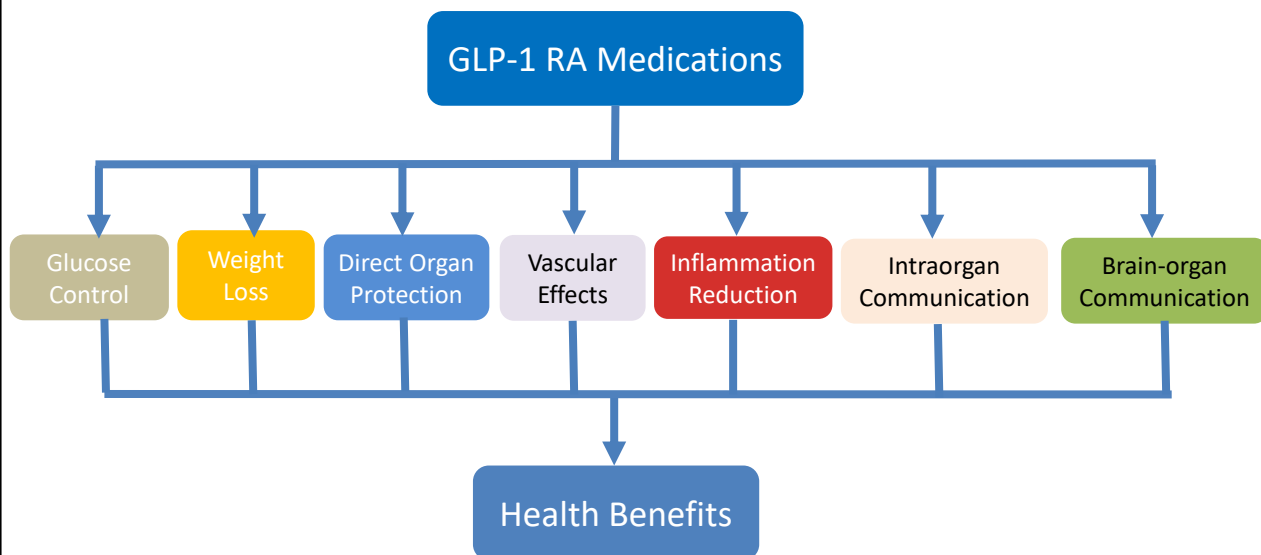
The Incretin Effect: Increased Insulin Secretion Associated with Oral Glucose Load vs. IV Glucose Load

(Glp-1 and GIP)

Verspohl EJ. Pharmacology And Therapeutics. 2009. 124:113-138.

37

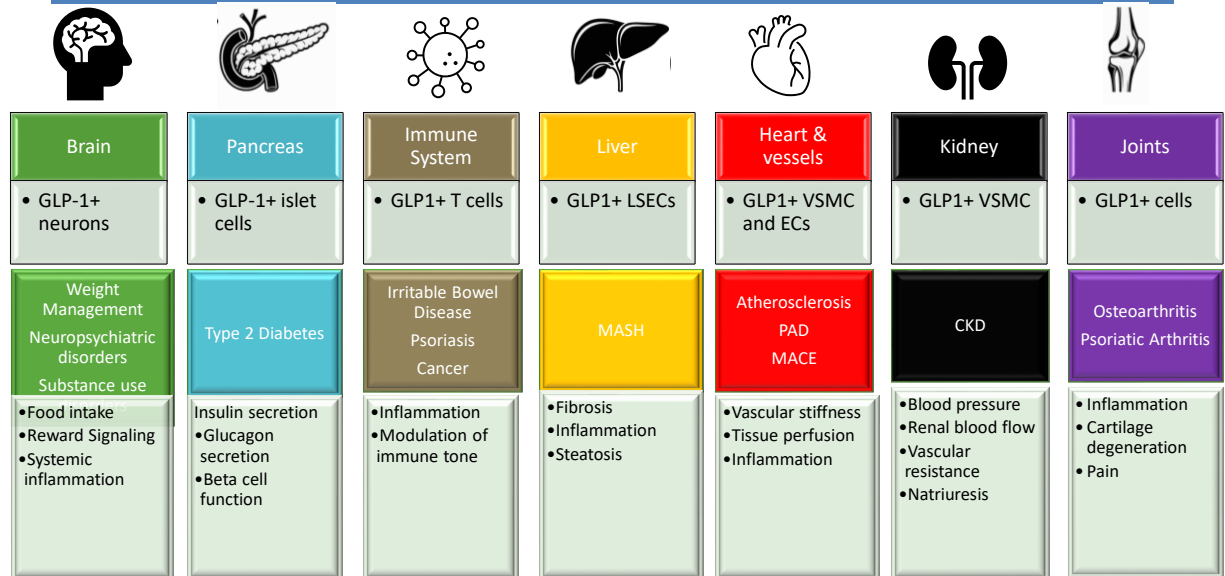
Emerging Paradigm of GLP-1 Mechanisms of Action



Adapted from: Gonzalez-Rellan M, Drucker D. Cell Metabolism, 38, 1535-1539

38

Emerging Paradigm of GLP-1 Mechanisms of Action



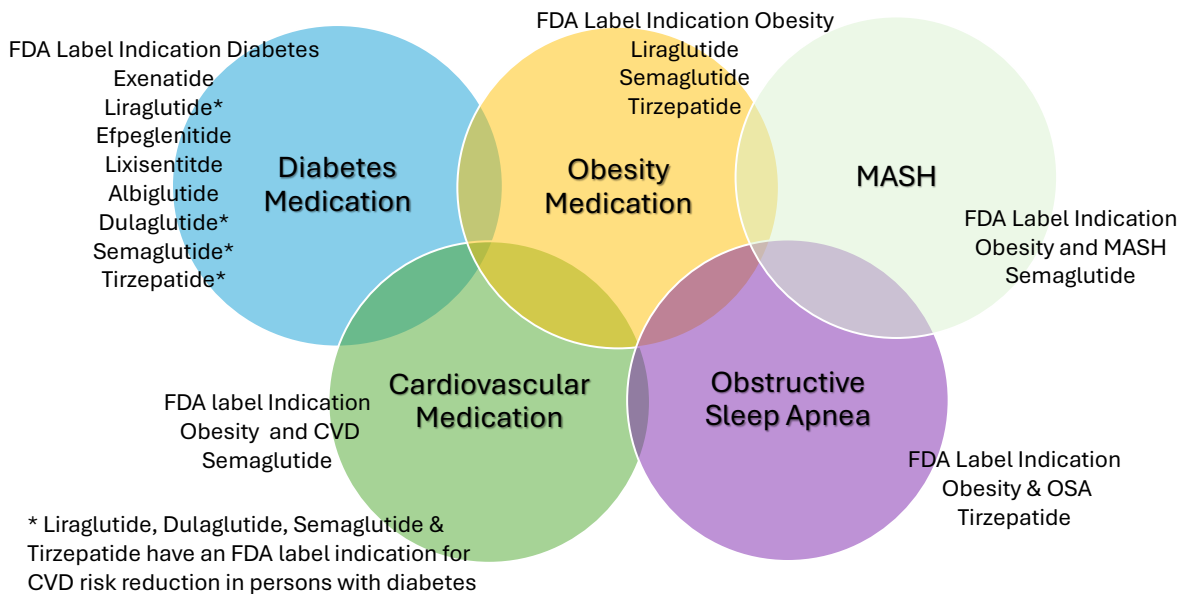
Adapted from: Gonzalez-Rellan M, Drucker D. Cell Metabolism, 38, 1535-1539

39

For Now, All Medications Target the GLP-1 Receptor Alone or in Combination with Another NuSH Target. However, DACRA (Dual Amylin Calcitonin RAs) and SARA (Single Amylin RAs) Are in Development.

40

Current Label Indications for Obesity Management Medications



41

Let's Look at the Evidence for Benefits Beyond Weight Loss ...

42

ARS Question #3

In Your Clinical Judgment, for a Patient With BMI 40 kg/m² Without Type 2 Diabetes and an Acute MI, in Addition to Standard Therapies for CV Risk Reduction, the Best GLP-1 RA to Prescribe Would Be:

- A. Semaglutide
- B. Tirzepatide
- C. Liraglutide

To date the only proven agent for secondary prevention of CVD in persons without obesity is semaglutide. If the patient had diabetes, both semaglutide and tirzepatide have been shown in CVOT to reduce CV events



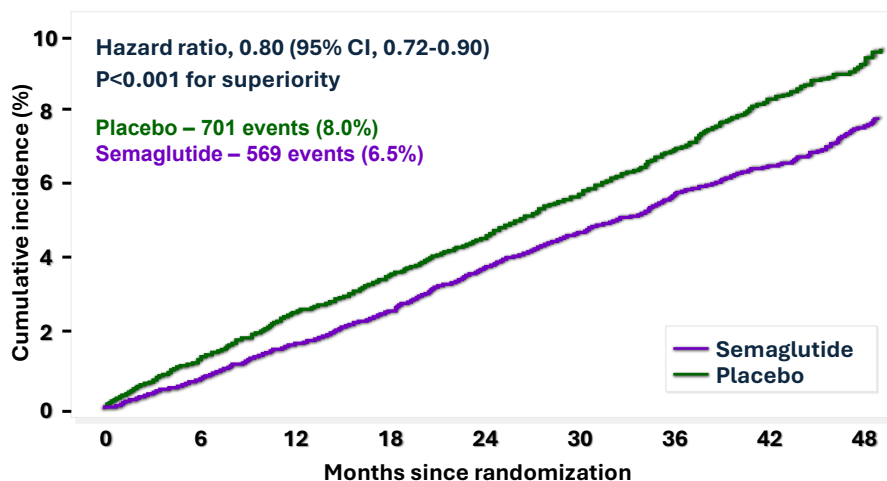
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43

SELECT Trial – Cardiovascular Efficacy

CV Death, Nonfatal MI, or Nonfatal Stroke

Primary Cardiovascular Composite Endpoint



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

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

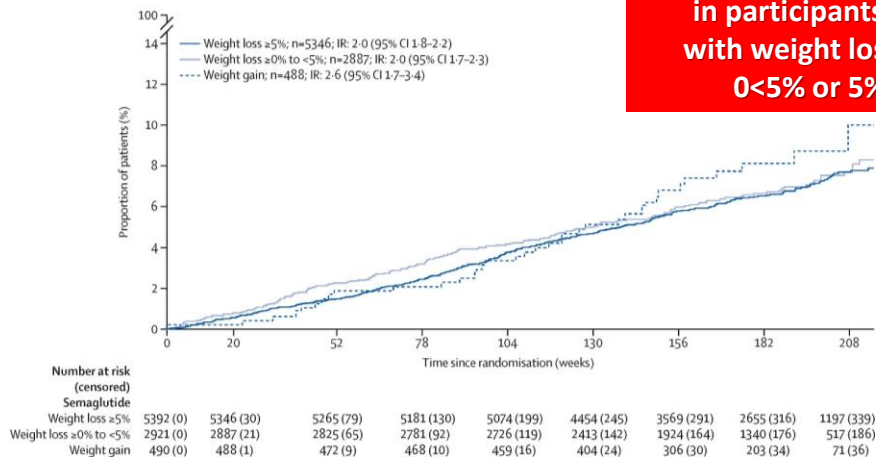
Mean follow-up time was 39.8 months

Lincoff AM, et al. *N Engl J Med*. 2023;389:2221-2232.

44

MACE Reduction by Semaglutide in SELECT Is Independent of Weight Loss

No effect on MACE event reduction in participants on Semaglutide with weight loss, weight change 0<5% or 5%+weight gain



Deanfield J. The Lancet. 2025;406: 2257-2268

45

GLP-1RA A1c Improvement and Weight Loss Are Not Interdependent.

Diabetologia (2025) 68:1666–1673
<https://doi.org/10.1007/s00125-025-06448-w>

SHORT COMMUNICATION

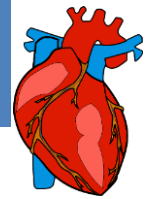
Heterogeneity in response to GLP-1 receptor agonists in type 2 diabetes in real-world clinical practice: insights from the DPV register – an IMI-SOPHIA study

Martin Heni^{1,2} · Lisa Frühwald³ · Wolfram Karges⁴ · Michael Naudorf⁵ · Kathrin Niemöller⁶ · Frank Pagnia⁷ · Jörg Reindel⁸ · Jochen Seufert⁹ · Gisa Ufer¹ · Christian Wagner¹⁰ · Reinhard W. Holl^{11,12} · Nicole Prinz^{11,12}

Weight loss and Glycemia not linked

46

Semaglutide and Tirzepatide Effects on Heart Failure with Preserved Ejection Fraction STEP HFpEF, STEP HpEF DM and SUMMIT



Improved
feeling and
function



Reduced
hospitalization

Kosiborod MN, et al. *N Engl J Med*. 2023;389:1069-1084.
Kosiborod MN, et al. *N Engl J Med*. 2024;390:1394-1407.
Packer M, et al. *N Engl J Med* 2025;392:427-37.

47

SELECT and FLOW: Semaglutide Effects on Chronic Kidney Disease

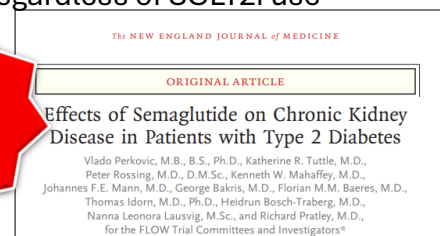


22% kidney
endpoint
reduction

FLOW: Semaglutide in patients with T2D

- In patients with CKD and T2D, semaglutide reduced the risk of the primary outcome* by 24% compared to placebo
- Benefits occurred regardless of SGLT2i use

24% risk
reduction

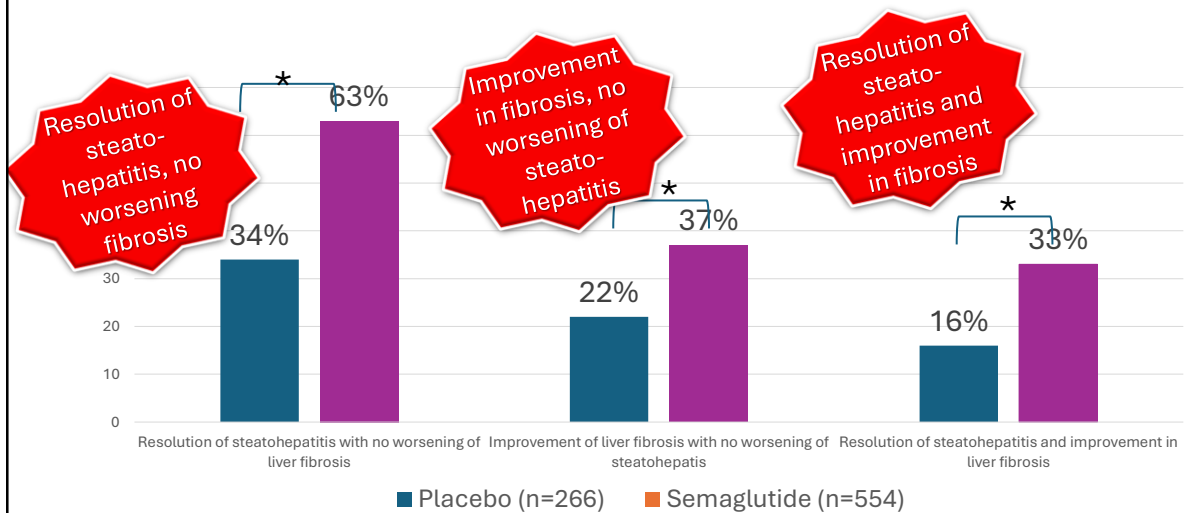


CKD, chronic kidney disease; T2D type 2 diabetes; SGLT2i, sodium-glucose cotransporter-2 inhibitor; T2D, type 2 diabetes.

Calhoun HM, et al. *Nature Medicine*
Perkovic V, et al. *N Engl J Med* 2024;91(2):109-21; Mann JFE, et al. *Nat Med* 2024;30(10):2849-56

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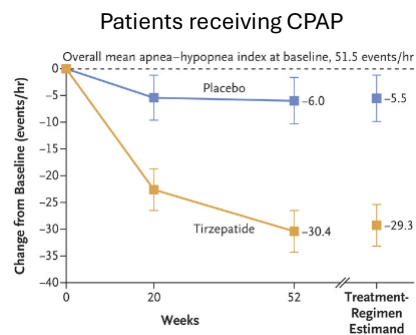
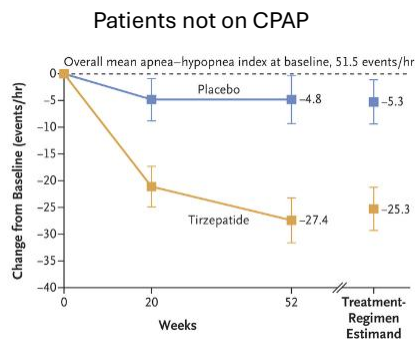
ESSENCE Trial: Semaglutide 2.4 mg vs. Placebo in MASH Biopsy Confirmed MASH + Fibrosis, Stage 2 or 3; Efficacy Results Week 72



Sanyal AJ, et al. N Engl J Med 2025;392:2089-2099

49

Obstructive Sleep Apnea: SURMOUNT OSA - Tirzepatide



Semaglutide also reduced body weight, hypoxic burden, hsCRP concentration, and systolic blood pressure and improved sleep-related patient-reported outcomes.

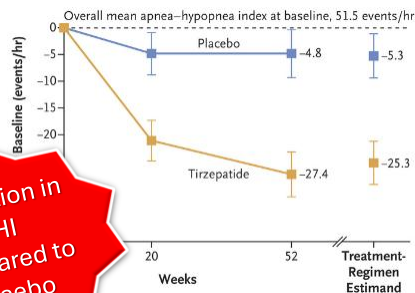
Malhotra A, et al. N Engl J Med 2024;391:1193-1205

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Obstructive Sleep Apnea: SURMOUNT OSA - Tirzepatide

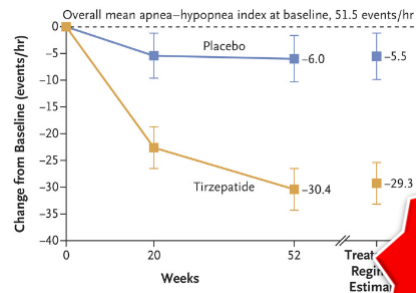


Patients not on CPAP



Reduction in AHI compared to placebo

Patients receiving CPAP



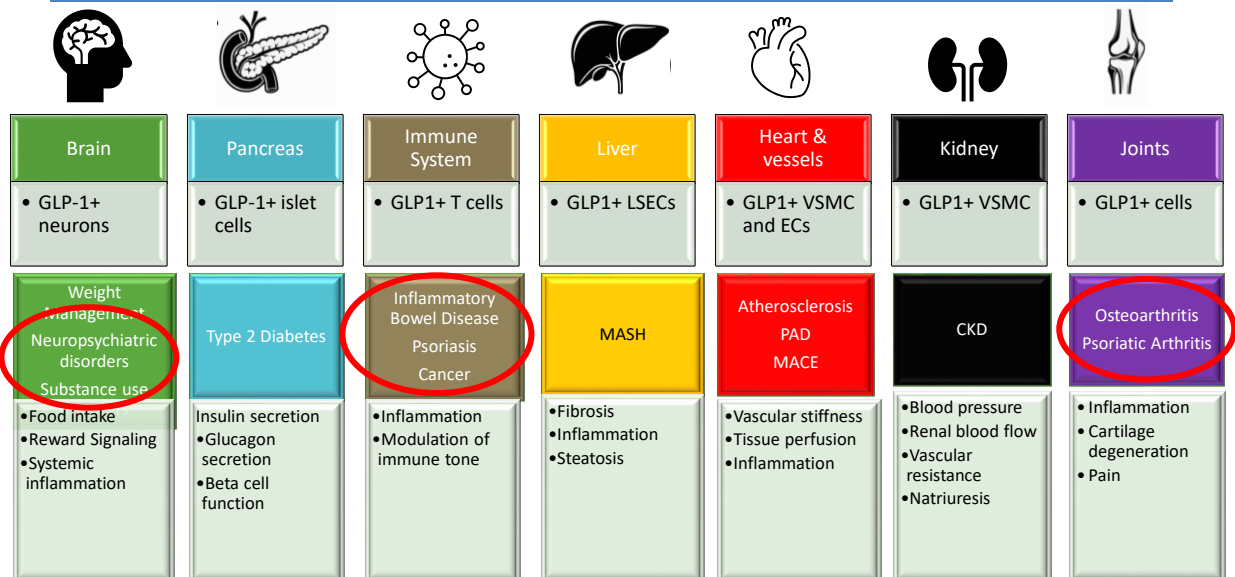
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Tirzepatide also reduced body weight, hypoxic burden, hsCRP concentration, and systolic blood pressure and improved sleep-related patient-reported outcomes.

Malhotra A, et al. N Engl J Med 2024;391:1193-1205

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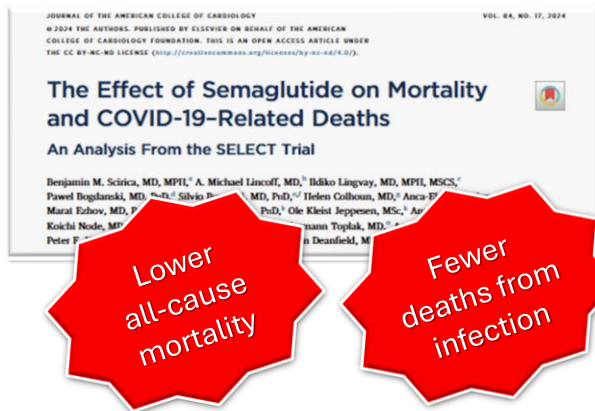
Emerging Paradigm of GLP-1 Mechanisms of Action



Adapted from: Gonzalez-Rellan M, Drucker D. Cell Metabolism, 38, 1535-1539

52

SELECT: Semaglutide Effects on Mortality and COVID



- **4,258 patients (24.2%) reported COVID-19**
 - No difference in reported cases of COVID between arms (2108 vs 2150 events; $P=0.46$)
- Fewer COVID SAEs with semaglutide (232) vs. placebo (277)
- Fewer COVID deaths with semaglutide (19 vs. 65)
- Fewer infection deaths with semaglutide (62 vs. 87)

SAE, serious adverse event.

Scirica BM, et al. J Am Coll Cardiol 2024;84(17):1632-42.

53

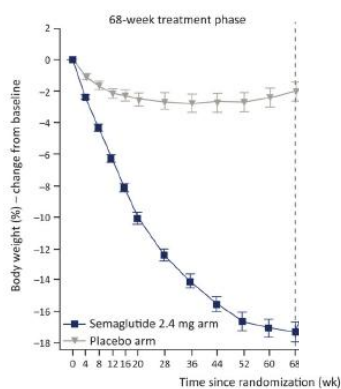
The Clinical Effects of the GLP-1 RAs Are Much More than Weight Loss and Glycemic Improvement. These Are Chronic Disease Medications.

54

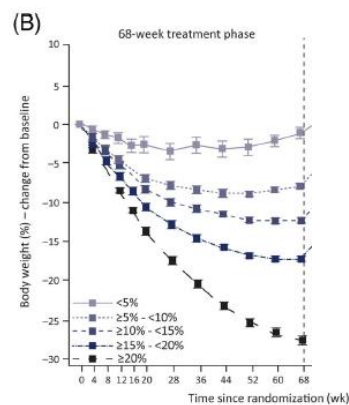
Let's Discuss Stopping the Obesity Medications ...

55

The STEP 1 Trial Extension of Semaglutide 2.4 mg



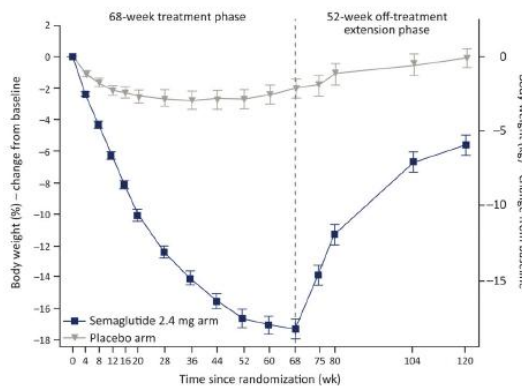
N=327 subject



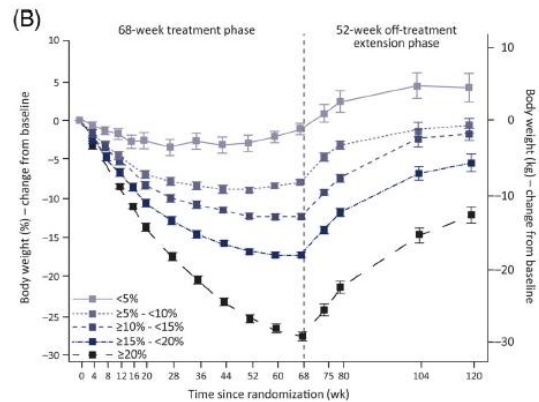
Wilding JPH et al. Diab Obes Metab 2022;1-12

56

The STEP 1 Trial Extension of Semaglutide 2.4 mg



N=327 subject



Wilding JPH et al. Diab Obes Metab 2022;1-12

57

We Don't Discuss Stopping Blood Pressure Medicines, or Lipid Medicines, or Diabetes Medicines. Still, This Issue Is Not Going Away.

58

Managing Stopping Issues

- Change from injectable to oral
- Reduce dose and see what happens
- Spread dosing and see what happens
- To work, medicines must be taken
- If patients stop, you should restart when needed

59

Potential Strategies to Address Weight Regain

- Restoring sensitivity to leptin - Leptin signaling restoration via amylin
- Medications targeting hypothalamic inflammation

60

December 1, 2025 WHO Issues Global Guidance

JAMA | Special Communication | CURRENT TOPICS IN OBESITY

World Health Organization Guideline on the Use and Indications of Glucagon-Like Peptide-1 Therapies for the Treatment of Obesity in Adults

Francesca Celletti, MD, PhD; Jeremy Farrar, MD, PhD; Luz De Regil, PhD

CME at jamacmelookup.com

IMPORTANCE Obesity is a chronic, relapsing disease affecting over 1 billion people worldwide, driving substantial morbidity, mortality, and economic burden. Glucagon-like peptide-1 therapies (GLP-1 therapies) provide clinically meaningful weight loss and broad metabolic benefits. In response to Member State requests, the World Health Organization (WHO) has issued guidelines for adults living with obesity.

OBSERVATIONS The guidelines recognize obesity as a chronic, relapsing disease requiring lifelong care and emphasize early diagnosis and integrated, person-centered approaches combining behavioral, medical, surgical, and other interventions alongside prevention and management of comorbidities. WHO recommends long-term GLP-1 therapies combined with intensive behavioral therapy to maximize and sustain benefits. Both recommendations were graded conditional, reflecting that GLP-1 therapies—with or without behavioral therapy—are effective, but limited long-term data, cost, system readiness, equity, variability in patient priorities, and context-specific feasibility remain considerations. Implementation of these guidelines depends on equitable access to affordable therapies, health system preparedness, and most importantly assurance that care is person-centered, nondiscriminatory, and universally accessible. Given the time required to implement these measures, a priority is a transparent, equitable, evidence-based framework to identify those at highest need while allowing incremental expansion of eligibility as access, capacity, and readiness evolve; this will be the next focus of the WHO guideline.

CONCLUSIONS AND RELEVANCE Medication alone cannot solve the global obesity burden. The availability of GLP-1 therapies should galvanize the global community to build a fair, integrated, and sustainable obesity ecosystem. Countries must ensure equitable access not only to comprehensive disease management, but also to health promotion and prevention policies and interventions targeting the general population and those at high risk.

Author Affiliations: Senior Advisor, Obesity, Department of Nutrition and Food Safety, World Health Organization, Geneva, Switzerland (Celletti); Assistant Director General, Health Promotion, Prevention, and Care, World Health Organization, Geneva, Switzerland (Farrar); Director, Department of Nutrition and Food Safety, World Health Organization, Geneva, Switzerland (De Regil).

Corresponding Author: Francesca Celletti, MD, PhD, Senior Advisor, Obesity, Department of Nutrition and

Celletti F, et al. World Health Organization Guideline on the Use and Indications of Glucagon-Like Peptide-1 Therapies for the Treatment of Obesity in Adults. *JAMA*. Published online December 01, 2025. doi:10.1001/jama.2025.24288

61

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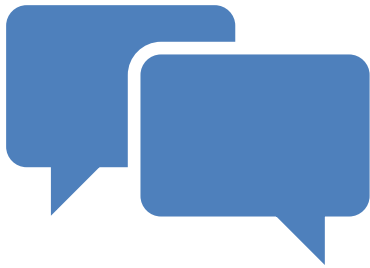
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62

Donna Ryan, MD
New Medications for Obesity – The Future is NOW!



Talking to Patients:
“These New GLP-1
Medications Do More than
Reduce Appetite. They Have
Many Effects Throughout the
Body. They Are Serious
Medications and We Need
to Take Them Seriously.”

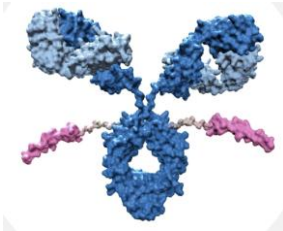
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and Finally, a Look at What the Future Holds for Obesity Medications

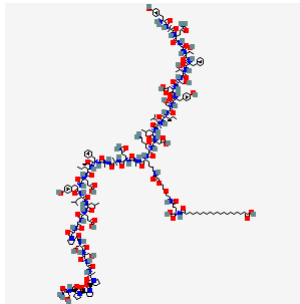


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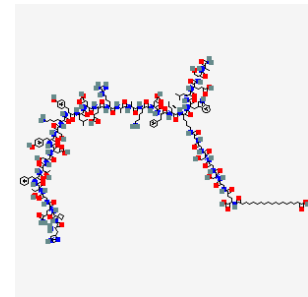
Other Nush-Targeted Candidates Projected for 2027 in USA



MariTide
Antibody to GIP receptor
2 GLP-1 molecules



Retatrutide
Unimolecular GGG* agonist



Survodutide
Unimolecular GLP-1 and
Glucagon agonist

Structures vis PubChem

65

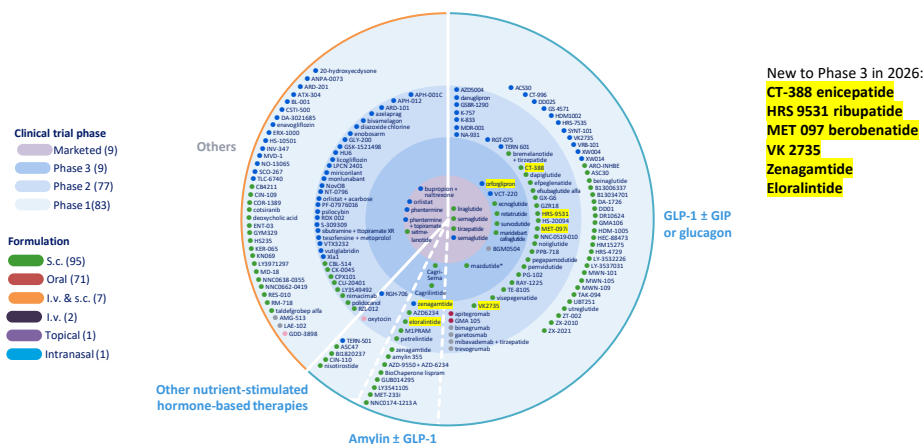
Amylin Receptor Targeted Medications in Phase 3

- Eloralintide
 - Cagrilintide
 - Zenagamtide (amylin + semaglutide) — single molecule, dual agonist
- These are being developed as single agents and in combination with a GLP-1 RA

Rationale:

- New target –
 - Additive weight loss
 - Weight loss in non-responders
- New disease modifying properties?
 - Better Bone/body composition?
 - Better glycemic management?
 - Better long-term weight loss?
 - Other?

66



Many More Tools to Come!

67

Let's Sum Up with What You Should Take Away ...

68

These are
serious
medications.
Take them
seriously

Start low
and go slow
to improve
tolerability

Basic Principles

Consider
dual
benefits

Recognize
variability in
response

Know weight loss
trajectory and
what happens
when you stop