North Carolina Society of Gastroenterology
2024 Annual Meeting

GLP-1 receptor agonists: Panacea and/or Problem?

John B. Buse, MD, PhD
Verne S. Caviness Distinguished Professor
Director, Diabetes Center
Co-Director, NC Translational and Clinical Sciences Institute
University of North Carolina School of Medicine

Joint Providership

Disclosures:

Contracted consulting fees and travel support for contracted activities are paid to the University of North Carolina by Novo Nordisk as well as grant support from Bayer, Boehringer-Ingelheim, Carmot, Corcept, Dexcom, Eli Lilly, Insulet, MannKind, Novo Nordisk, and vTv Therapeutics.

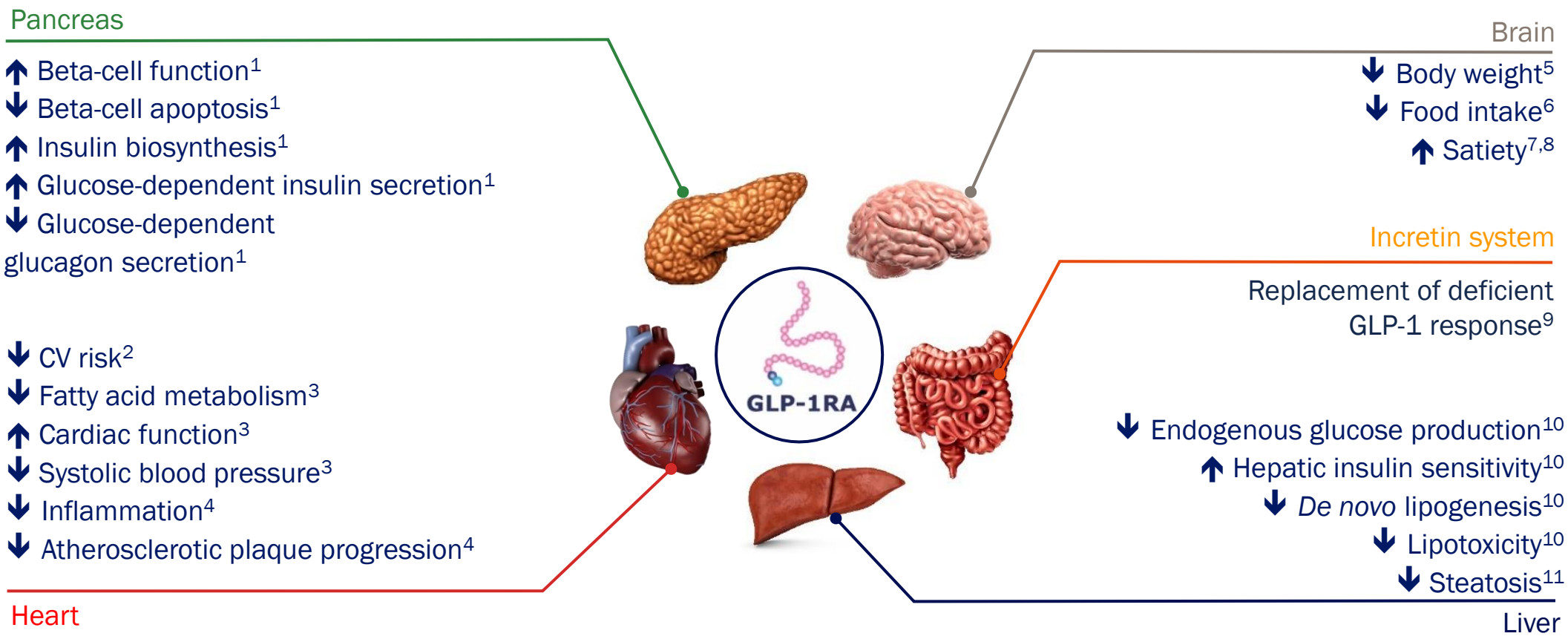
I am a consultant or contractor to Alkahest, Altimmune, Anji, Aqua Medical Inc, AstraZeneca, Bayer, Biomea Fusion Inc, Boehringer-Ingelheim, CeQur, Corcept Therapeutics, Dasman Diabetes Center (Kuwait), Eli Lilly, embecta, Fortress Biotech, GentiBio, Glycadia, Glyscend, Janssen, MannKind, Mediflix, Medscape, Mellitus Health, Metsera, Moderna, Pendulum Therapeutics, Praetego, ReachMD, Sanofi, Stability Health, Tandem, Terns Inc, Valo, and Zealand Pharma.

I have received payment for services as an expert witness from Medtronic MiniMed.

In lieu of payment, I have stock/options in Glyscend, Mellitus Health, Pendulum Therapeutics, PhaseBio, Praetego, and Stability Health.

I receive salary support from grants from the National Institutes of Health (UM1TR004406, U01DK098246, UC4DK108612, U54DK118612, P30DK124723, R33HL142680, R44DK096803, R01DK119913, R01DK112939, R01DK125831, R01DK127365) and PCORI (D1-2018C1-10853).

GLP-1RAs: multifactorial effects beyond glycemic control



CV, cardiovascular; GLP-1, glucagon-like peptide-1; GLP-1RA, glucagon-like peptide-1 receptor agonist.

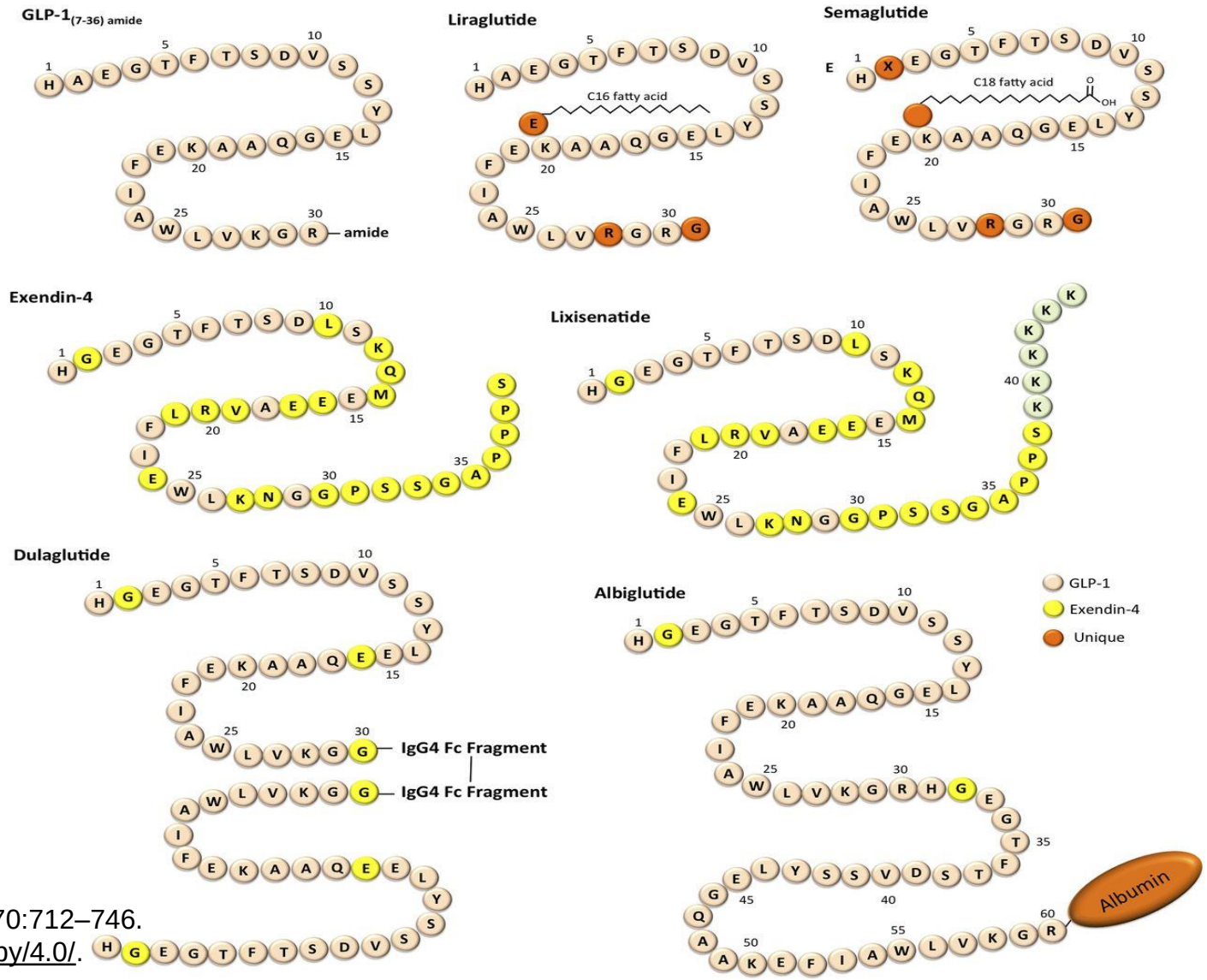
1. Campbell JE, DJ Drucker. *Cell Metab* 2013;17:819–37; 2. Marso SP, et al. *N Engl J Med* 2016;375:311–22; 3. Ryan D, Acosta A. *Obesity* 2015;23:1119–29;
4. Hogan AE, et al. *Diabetologia* 2014;57:781–84; 5. Baggio LL, Drucker DJ. *J Clin Invest* 2014;124:4223–26; 6. Bagger JI, et al. *Clin Endocrinol Metab* 2015;100:4541–52;
7. Flint A, et al. *J Clin Invest* 1998;101:515–20; 8. Blundell J, et al. Oral Presentation 23-OR. ADA 76th Annual Scientific Sessions. June 10–14, 2016;
9. Tong J, D'Alessio D. *Diabetes* 2014;63:407–9; 10. Armstrong MJ, et al. *J Hepatol* 2016;64:399–408; 11. Armstrong MJ, et al. *Lancet* 2016;387:679–90.

Overview: GLP-1 receptor agonists

UNC SCHOOL OF MEDICINE

- Excellent improvement in A1C
  - Head-to-head studies versus other classes suggest similar or greater efficacy of GLP-1 receptor agonists, even as compared to insulin
- Moderate to excellent weight loss
  - ~5-20% over 6-12 months (generally less in people with diabetes)
- Modest improvement in blood pressure
- No intrinsic increased risk of hypoglycemia
- Adverse events largely gastrointestinal
- Labelled safety considerations (pancreatitis, diabetic retinopathy complications, hypoglycemia [with concomitant use of secretagogues or insulin], acute kidney injury, hypersensitivity reaction, acute gallbladder disease)
- Labelled contraindications (personal of family history of medullary thyroid cancer or multiple endocrine neoplasia; serious hypersensitivity reaction to GLP-1RA or excipients)

GLP-1 Receptor Agonists (GLP-1 RA)



Albiglutide not available.
GLP-1, glucagon-like peptide 1;
IgG, immunoglobulin G;
RA, receptor agonist.
Müller TD et al. *Pharmacol Rev* 2018;70:712–746.

The GLP-1 receptor agonist landscape

GLP-1 RAs

- Exenatide BID (Byetta)
- Liraglutide (Victoza and Saxenda*)
- Exenatide QW (Bydureon)
- Lixisenatide (Adlyxin)
- Dulaglutide (Trulicity)
- Albiglutide (Tanzeum)
- Semaglutide (Ozempic and Wegovy*)
- Oral semaglutide (Rybelsus)

Fixed-ratio combination

- + insulin degludec (Xultophy)
- + insulin glargine (Soliqua)

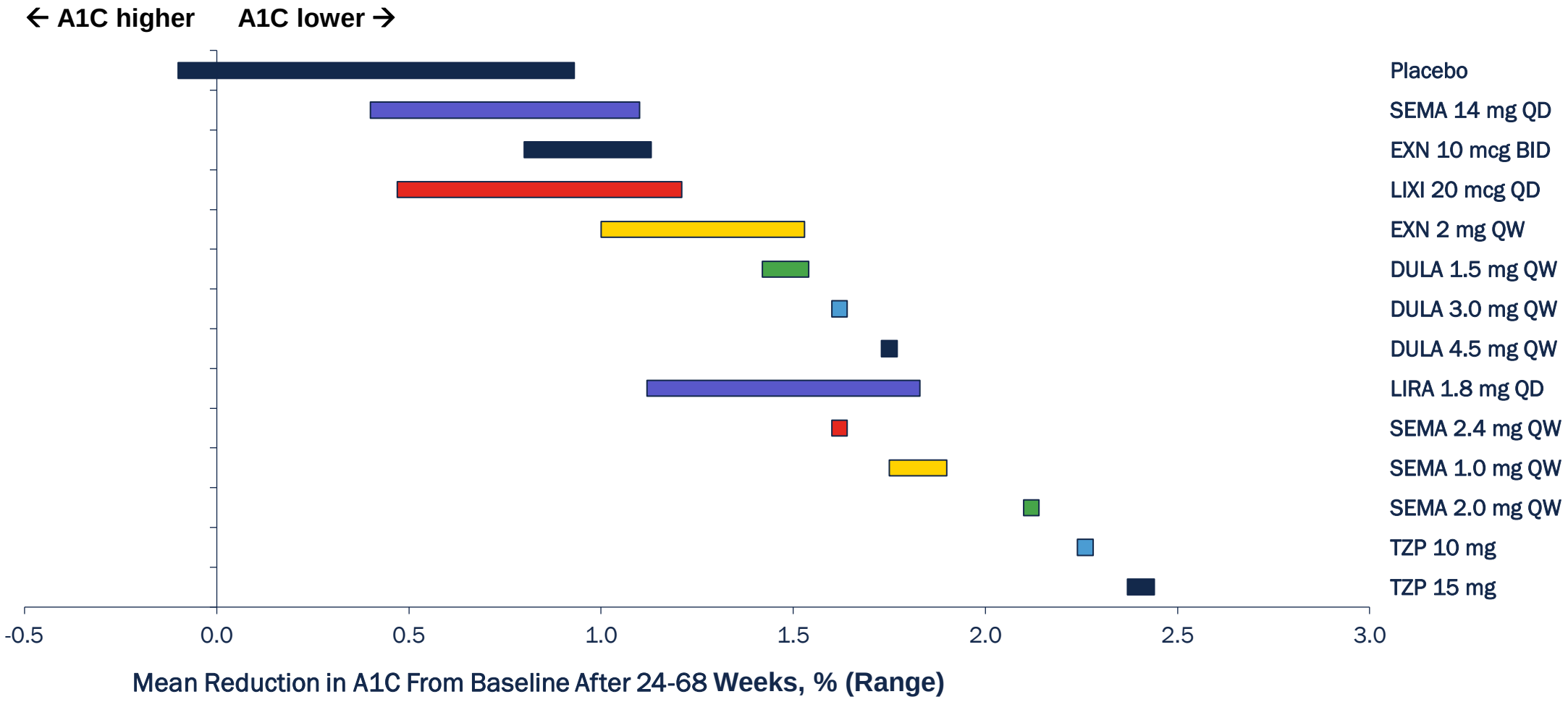
GIP+GLP-1 RA

- Tirzepatide (Mounjaro and Zepbound*)

GLP-1 RA, glucagon-like peptide-1 receptor agonist

*Indicated as an adjunct to a reduced calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of 30 kg/m^2 or greater (obesity) or 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia).

GLP-1 RAs At High Doses: A1C Reduction When Added to One or Two Oral Agents

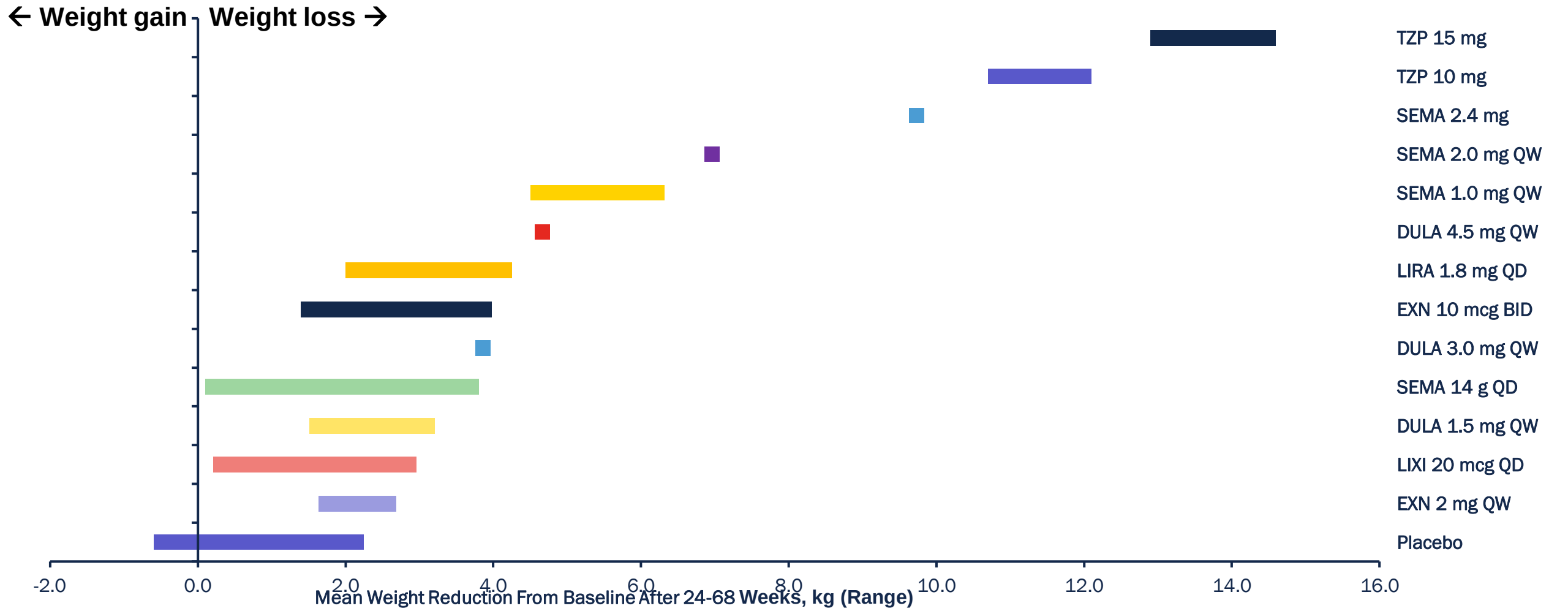


[a] Systematic review of 41 randomized controlled clinical trials; [b] Data for dulaglutide reported at 36 weeks; data for semaglutide 1.0-2.0 mg reported at up to 40 weeks and for semaglutide 2.4 mg at 68 weeks; data for tirzepatide reported at up to 52 weeks. Treatment policy estimands are reported .

1. Witkowski M et al. *Diabetes Ther*. 2018;9:1149-1167. 2. Morales J et al. *Postgrad Med*. 2020;132:687-696. 3. Frías JP et al. *Diabetes Care*. 2021;44:765-773.
4. Frías JP et al. *Lancet Diabetes Endocrinol*. 2021;9:563-574. 5. Frías JP et al. *N Engl J Med*. 2021;385:503-515. 6. Ludvik B et al. *Lancet*. 2021;398:583-598.
7. Davies M et al. *Lancet.* 2021;397:971-984.

GLP-1 RAs at High Doses: Weight Effects When Added to One or Two Oral Agents

UNC SCHOOL OF MEDICINE



[a] Systematic review of 41 RCTs of injectable agents; DULA 1.5 mg and SEMA 1.0 mg were the maximum doses available at the time this analysis. was performed.
[b] Systematic review of seven RCTs of oral SEMA. [c] Data for DULA 3.0 and 4.5 mg reported at 36 weeks; data for SEMA 2.0 mg reported at up to 40 weeks; data for TZP reported at up to 52 weeks. Treatment policy estimands are reported.

1. Witkowski M et al. *Diabetes Ther*. 2018;9:1149-1167. 2. Morales J et al. *Postgrad Med*. 2020;132:687-696. 3. Frías JP et al. *Diabetes Care*. 2021;44:765-773. 4. Frías JP et al. *Lancet Diabetes Endocrinol*. 2021;9:563-574. 5. Frías JP et al. *N Engl J Med*. 2021;385:503-515. 6. Ludvik B et al. *Lancet*. 2021;398:583-598. 7. Davies M et al. *Lancet.* 2021;397:971-984.

GLP-1 RAs are not exactly alike...

Pharmacokinetics		Structure		Size	
Short-acting	**Long-acting**	**Exendin-4-based**	**GLP-1-based**	**Small**	**Large**
Exenatide BID	Exenatide QW	Exenatide BID	Liraglutide	Exenatide BID	Albiglutide
Lixisenatide	Liraglutide	Exenatide QW	Albiglutide	Exenatide QW	Dulaglutide
	Albiglutide	Lixisenatide	Semaglutide	Liraglutide	
	Semaglutide		Dulaglutide	Lixisenatide	
	Dulaglutide			Semaglutide	
Short-acting GLP-1 RAs retain their effect on gastric emptying (and PPG), while long-acting GLP-1 RAs seem to have more pronounced effects on FPG and HbA_{1c}		Exendin-based GLP-1 RAs seem to give rise to the formation of antibodies to a higher degree than the GLP-1-based ones; clinical implication uncertain		The large GLP-1 RAs may not be able to penetrate into the brain to the same extent as the smaller ones, possibly affecting appetite signaling differently	

Oral formulation		
Product	**Molecule**	**Route**
Oral semaglutide	Semaglutide	Oral with carrier molecule

BID, twice daily; FPG, fasting plasma glucose; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA_{1c}, glycated haemoglobin; PPG, postprandial glucose; QW, once weekly

GLP-1 RA: summary

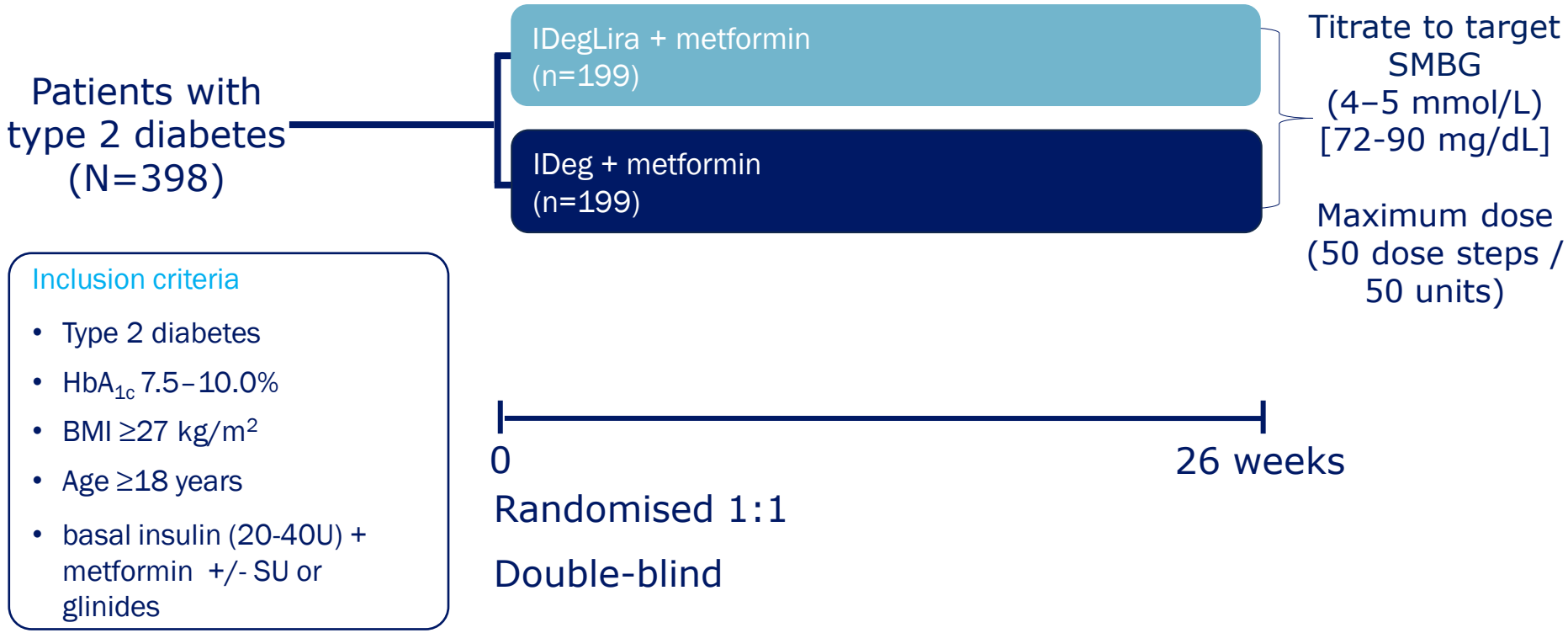
Drug	Within class comparability of A1C lowering efficacy	Within class comparability of effect on weight	Within class comparability of GI adverse effects
Exenatide (twice daily)	Low	Low	Highest
Lixisenatide	Low	Low	Intermediate
Liraglutide	High	High	Intermediate
Exenatide XR	Intermediate	Low	Low
Dulaglutide	High	Intermediate	Intermediate/high
Semaglutide	Highest	Highest	High
Semaglutide (oral)	High/highest	Highest	Intermediate/high

A1C, hemoglobin A1C; GI, gastrointestinal; GLP-1 RA, glucagon-like peptide-1 receptor agonists.

BID, twice daily; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA_{1c}, glycated haemoglobin; QW, once weekly

Trujillo JM, et al. *Ther Adv Endocrinol Metab* 2021 Mar 9;12:2042018821997320.

DUAL 2: study design

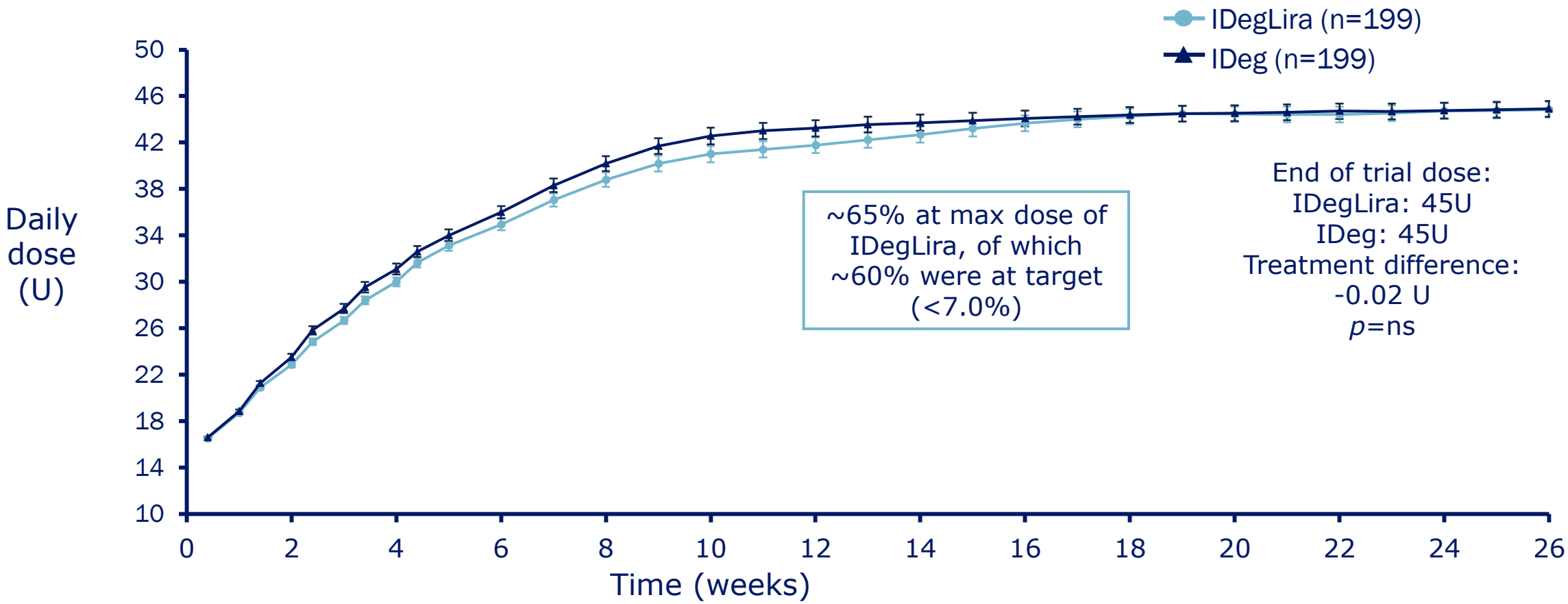


N: number of randomised subjects, excluding subjects from Site 105 (8 subjects for IDegLira and 7 subjects for IDeg); SMBG, self-monitoring blood glucose; SMBG measured using a glucometer which was calibrated to convert blood glucose measurements to plasma glucose values

NN9068-3912; IDegLira vs IDeg in T2DM

Buse JB, et al. *Diabetes Care*. 2014; 37:2926-33.

DUAL 2: daily dose of IDeg component

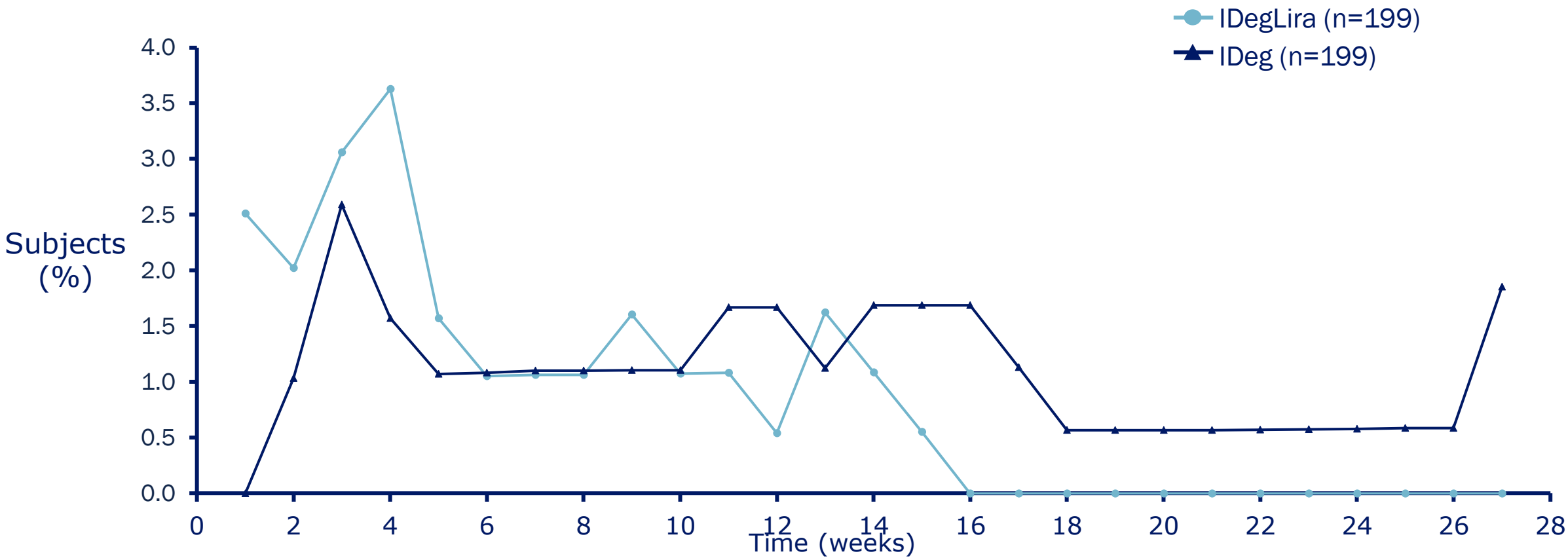


Mean values with error bars (standard error mean) based on safety population and LOCF imputed data
Estimated treatment differences are from an ANCOVA analysis

NN9068-3912; IDegLira vs IDeg in T2DM

Buse JB, et al. *Diabetes Care.* 2014; 37:2926-33.

DUAL 2: percentage of subjects with nausea



Data are from SAS
NN9068-3912; IDegLira vs IDeg in T2DM

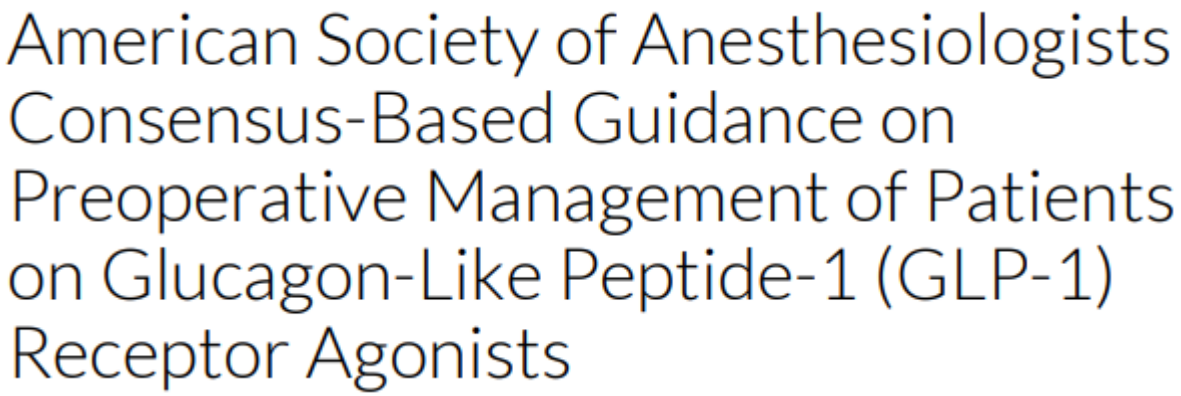
Buse JB, et al. *Diabetes Care.* 2014; 37:2926-33.

GLP-1 RA safety updates

- CVOT Meta-analyses: “The incidence of severe hypoglycemia, retinopathy, pancreatitis, and pancreatic cancer did not differ between GLP-1 receptor agonist treatment and placebo.” (Sattar N et al; *Lancet Diabetes Endocrinol* 2021)
- Retinopathy complications – attributable to magnitude and rapidity of HbA1c reduction in individuals with pre-existing diabetic retinopathy and poor glycemic control (similar to insulin) (Vilsbøll T et al; *Diabetes Obes Metab* 2018; 20: 889-897)
- Increased risk of gallbladder or biliary diseases, higher risk in trials for weight loss, higher doses compared with lower doses, and with longer duration of use (He L et al; *JAMA Intern Med* 2022; 182:513-519)
- SCALE studies: “Liraglutide resulted in dose-independent, reversible increases in amylase/lipase activity, unrelated to baseline characteristics, not predicting acute pancreatitis onset. . . . Data provide no basis for amylase/lipase level monitoring in liraglutide treatment except in suspected pancreatitis. Steinberg WM, et al; *Diabetes Care.* 2017; 40:839-848)
- Labels include risk of thyroid C-cell tumors in rodents; human relevance not determined. However contraindicated in those with a personal or family history of MTC or MEN.

GLP-1 RA safety updates, continued

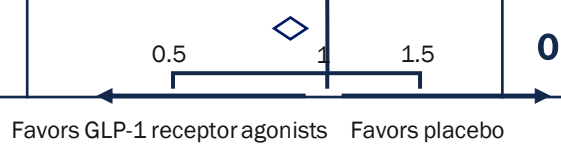
- Thyroid cancer: “Although the results are far from conclusive, . . . the estimated NNH, as calculated using data from clinical trials, is well above 1000 patients for 5 years. (Silverii, et al. **https://doi.org/10.1111/dom.15382**)
- GI disorders in obesity management: “Use of GLP-1 agonists compared with bupropion/naltrexone was associated with increased risk of pancreatitis (adjusted HR, 9.09 [95% CI, 1.25-66.00]), bowel obstruction (HR, 4.22 [95% CI, 1.02-17.40]), and gastroparesis (HR, 3.67 [95% CI, 1.15-11.90) but not biliary disease (HR, 1.50 [95% CI, 0.89-2.53]). (Sohi, et al. JAMA 2023; 330:1795-1797)
- Sarcopenia
- Aspiration risk: https://www.swa10.com/uploads/6/1/4/3/61438899/glp-1.asa.2023.pdf



Meta-analysis of GLP-1RA CVOTs in type 2 diabetes at high risk for CVD: MACE-3

UNC SCHOOL OF MEDICINE

	GLP-1 Receptor Agonist, n/N (%)	Placebo n/N (%)		Hazard Ratio (95% CI)	NNT (95% CI)	*P* Value
3-point MACE						
ELIXA (lixisenatide)	400/3034 (13%)	392/3034 (13%)		1.02 (0.89, 1.17)		.78
LEADER (liraglutide)	608/4668 (13%)	694/4672 (15%)		0.87 (0.78, 0.97)		.01
SUSTAIN-6 (semaglutide SQ)	108/1648 (7%)	146/1649 (9%)		0.74 (0.58, 0.95)		.016
EXSCEL (exenatide OW)	839/7356 (11%)	905/7396 (12%)		0.91 (0.83, 1.00)		.061
Harmony Outcomes (albi – NA)	338/4731 (7%)	428/4732 (9%)		0.78 (0.68, 0.90)		.0006
REWIND (dulaglutide)	594/4949 (12%)	663/4952 (13%)		0.88 (0.79, 0.99)		.026
PIONEER 6 (oral semaglutide)	61/1591 (4%)	76/1592 (5%)		0.79 (0.57, 1.11)		.17
AMPLITUDE-O (investigational)	189/2717 (7%)	125/1359 (9%)		0.73 (0.58, 0.92)		.0069
Subtotal (I^2 = 44.5%, *P* = .082)				**0.86 (0.80, 0.93)**	**65 (45, 130)**	**< .0001**



Weights are from random effect analysis. In addition to primary cardiovascular outcome results papers, data were extracted from additional sources. AMPLITUDE-O data were provided by the authors. Three-point MACE consisted of cardiovascular death, myocardial infarction, and stroke. NNTs were calculated over a weighted average median follow-up of 3.0 years. P values are for superiority

Efpeglenatide not FDA-approved. Not all agents and formulations are indicated for cardiovascular risk reduction.

CVOT, cardiovascular outcomes trial; MACE, major adverse cardiovascular event; NNT, number needed to treat.

Sattar N, et al. *Lancet Diabetes Endocrinol*. 2021;9:653-662.

Meta-analysis of GLP-1RA CVOTs in type 2 diabetes at high risk for CVD

UNC SCHOOL OF MEDICINE

Outcome	HR (95% CI)	NNT	*P* value	Heterogeneity
MACE-3	0.86 (0.80, 0.93)	65 (45, 130)	< .0001	Marginal
CV death	0.87 (0.80, 0.94)	163 (103, 353)	0.001	No
Fatal and non-fatal MI	0.90 (0.83, 0.98)	175 (103, 878)	0.02	No
Fatal and non-fatal stroke	0.83 (0.76, 0.92)	198 (140, 421)	0.0002	No
All-cause mortality	0.88 (0.82, 0.94)	114 (76, 228)	0.0001	No
Hospital admission for HF	0.89 (0.82, 0.98)	258 (158, 1422)	0.013	No
Composite kidney outcome, including macroalbuminuria	0.79 (0.73, 0.87)	47 (37, 77)	< .0001	Marginal
Worsening of Kidney Function	0.86 (0.72, 1.02)	241 (120 to 1694)	0.089	No

Efpeglenatide not FDA-approved. Not all agents and formulations are indicated for cardiovascular risk reduction.
CVOT, cardiovascular outcomes trial; MACE, major adverse cardiovascular event; NNT, number needed to treat.
Sattar N, et al. *Lancet Diabetes Endocrinol*. 2021;9:653-662.

Semaglutide 2.4 mg weekly (68 wks)

	Obesity		Type 2 diabetes	
ITT population	Plac (655)	Sema (1306)	Plac (403)	Sema (404)
Wt (kg)	105	105	100	100
% change	-2.4	-15	-3.4	-9.6
% difference	-12.4 (13.3; 11.6)		-6.2 (7.3; 5.2)	
% of patients losing 15%	5	48	4	25
% difference	43.1 (39.8; 46.3)		20.7 (15.7; 25.8)	

Generally less weight loss seen in people with type 2 diabetes

Semaglutide injection 2.4 mg prescribing information, revised June 2021. https://www.novo-pi.com/wegovy.pdf, accessed Jan 30, 2022

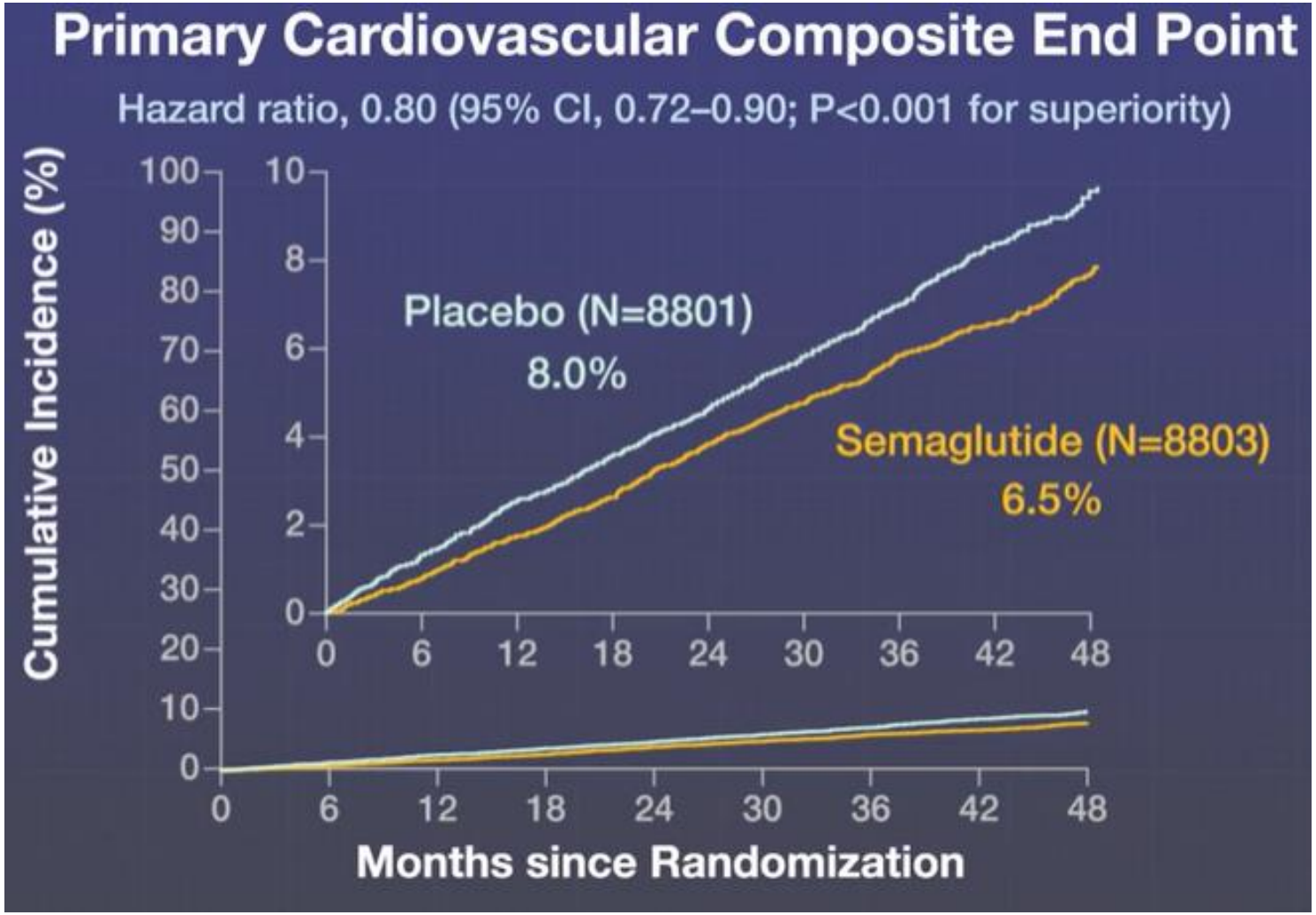
Semaglutide 2.4 mg weekly (68 wks)

	Obesity		Obesity with intensive lifestyle	
ITT population	Plac (655)	Sema (1306)	Plac (204)	Sema (407)
Wt (kg)	105	105	104	107
% change	-2.4	-15	-5.7	-16
% difference	-12.4 (13.3; 11.6)		-10.3 (11.8; 8.7)	
% of patients losing 15%	5	48	13	53
% difference	43.1 (39.8; 46.3)		40.2 (33.1; 47.3)	

Intensive behavioral weight-loss therapy does not add much to high dose/efficacy GLP-1RA

Semaglutide injection 2.4 mg prescribing information, revised June 2021. https://www.novo-pi.com/wegovy.pdf, accessed Jan 30, 2022

Semaglutide 2.4 mg: Obesity CVOT (SELECT)



Lincoff, et al. N Engl J Med 2023; 389:2221-2232 . Available at https://www.nejm.org/doi/full/10.1056/NEJMoa2307563, accessed Dec 21, 2023.

Semaglutide 2.4 mg for CV risk reduction in obesity is not an approved indication.

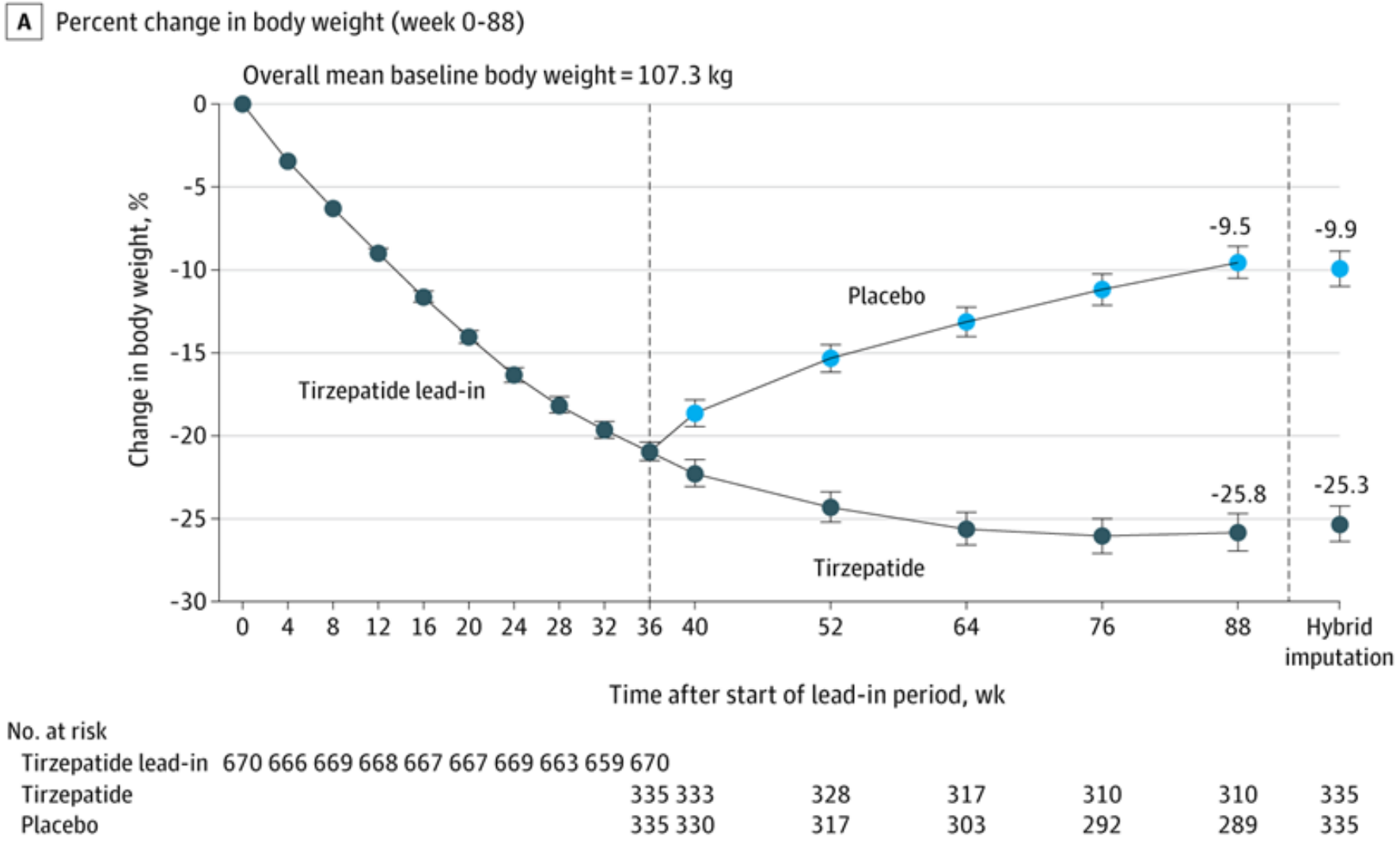
Tirzepatide vs semaglutide 1 mg (40 wk)
SURPASS-2 (type 2 diabetes)

UNC SCHOOL OF MEDICINE

	Tir 15 mg	Sema 1 mg	p
Change in A1C (%); baseline 8.3%	-2.3	-1.9	p<0.001
Change in weight (kg); baseline 93.8	-11	-5.7	p<0.001
% change in weight	13	6.7	
% with AE	69	64	
% with SAE	5.7	2.8	
% Death	0.9	0.2	
% AE leading to Discontinuation	8.5	4.1	

Frias JP, et al. N Engl J Med 2021; 385:503-515. DOI: 10.1056/NEJMoa2107519

Tirzepatide 1 mg (obesity)



Aronne LJ, et al. JAMA. 2023 Dec 11:e2324945. doi: 10.1001/jama.2023.24945. Epub ahead of print. PMID: 38078870; PMCID: PMC10714284.

Successful prescribing for GLP-1RA

UNC SCHOOL OF MEDICINE

- Discuss advantages – great efficacy, weight loss, blood pressure reduction
- Discuss compelling indications – prevalent CVD and high risk for CVD (indications for CVD reduction with liraglutide, dulaglutide, semaglutide only)
- Discuss adverse events
  - Nausea, other GI adverse events; generally, resolve over time; consider in the context of satiety
- Discuss important safety issues
  - Gall bladder events, acute kidney injury, pancreatitis (not increased vs placebo in CVOT's)
  - In the setting of persistent nausea and vomiting, hold the drug and seek medical attention if it does not resolve over hours or if other worrisome symptoms are present
- Do not use in those with medullary thyroid cancer, multiple endocrine neoplasia (MEN)-2, or fam hx
- Start with lowest dose, titrate slowly, back off for GI adverse events
- Consider specific attributes of specific products: exenatide twice daily (best postprandial efficacy), exenatide once weekly (lowest GI AE rate), liraglutide (most titratable), dulaglutide (easiest injection), semaglutide SQ (highest efficacy, particularly for weight), oral semaglutide (oral).
- Tirzepatide (GIP/GLP-1RA) is highest efficacy, greater than semaglutide and others
- Liraglutide maybe available at "generic" prices in the next 6 months

Adapted from Romera I, et al. *Diabetes Ther*. 2019;10:5-19.

Successful prescribing for GLP-1RA (2)

UNC SCHOOL OF MEDICINE

- Small servings, eat slowly, stop eating when no longer hungry
- Drink sips of cold water with nausea
- Caution with alcohol, high fat, spicy foods
- Exercise to minimize muscle mass loss
- Adverse effects of weight loss, independent of therapy: loss of muscle mass, fluid and electrolyte deficits, cold intolerance, constipation, gallbladder events[1]
  - >1 g/kg/d of high-quality protein intake, drink plenty of water, consider higher sodium intake (tomato juice, soups), eat vegetables and other sources of fiber
  - Exercise, preferably at least 5 days per week, particularly strength training
  - Take a jacket or sweater everywhere
  - Stool engineering is often necessary (Mg citrate 10 fl oz q1-4 wks, glycerin supp)
- Sense of well-being and the enjoyment of food improves once rapid weight loss resolves

1. Pi-Sunyer FX. *Ann Int Med.* 1993;119(7 part 2):722-726

What's next?

- Current indications for semaglutide and tirzepatide:
  - Type 2 diabetes and weight loss
  - MACE reduction for semaglutide and dulaglutide in high-risk patients with diabetes
- Areas of evolving studies:
  - Alcohol use disorders
  - Polycystic ovarian syndrome (PCOS) or ovarian hyperandrogenism
  - NAFLD/MAFLD
  - Cardiovascular disease
  - Sleep apnea
  - Kidney disease
  - Cognitive dysfunction/Alzheimer's disease

https://www.nytimes.com/interactive/2023/12/20/well/live/ozempic-weight-loss-drugs-diseases.html?searchResultPosition=1
Accessed Dec 21, 2023

Trick of the trade

- Semaglutide 4 mg and 8 mg pens are designed to administer 1 mg and 2 mg respectively for 4 weekly doses.
  - They cost the same
  - Each has 72 clicks to get to the maximum dose
  - Some patients may benefit from slower titration

CME/MOC question

- GLP-1 receptor agonist associated GI adverse effects
  A. Are generally mild to moderate in intensity and generally resolve over time.
  B. Can be reduced with slow titration or dose reduction and managed with standard approaches
  C. Include increased frequency of acute gallbladder complications
  D. All of the above

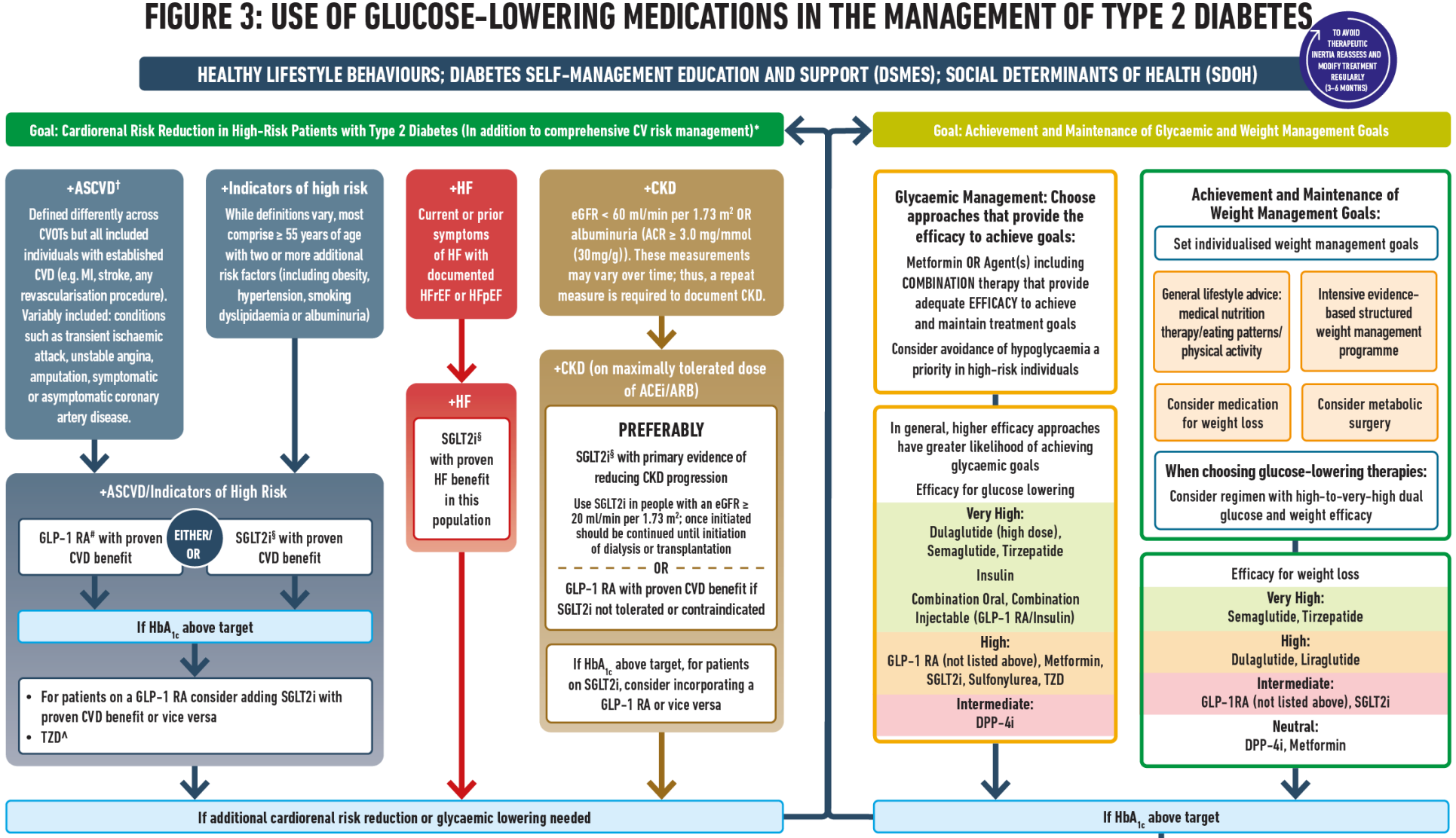
CME/MOC answer

- GLP-1 receptor agonist associated GI adverse effects
  A. Are generally mild to moderate in intensity and generally resolve over time.
  B. Can be reduced with slow titration or dose reduction and managed with standard approaches
  C. Include increased frequency of acute gallbladder complications
  D. All of the above

Thank you for listening!

Questions?

FIGURE 3: USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES



ACEi, Angiotensin-Converting Enzyme Inhibitor; ACR, Albumin/Creatinine Ratio; ARB, Angiotensin Receptor Blocker; ASCVD, Atherosclerotic Cardiovascular Disease; CGM, Continuous Glucose Monitoring; CKD, Chronic Kidney Disease; CV, Cardiovascular; CVD, Cardiovascular Disease; CVOT, Cardiovascular Outcomes Trial; DPP-4i, Dipeptidyl Peptidase-4 Inhibitor; eGFR, Estimated Glomerular Filtration Rate; GLP-1 RA, Glucagon-Like Peptide-1 Receptor Agonist; HF, Heart Failure; HFpEF, Heart Failure with preserved Ejection Fraction; HFrEF, Heart Failure with reduced Ejection Fraction; HHF, Hospitalisation for Heart Failure; MACE, Major Adverse Cardiovascular Events; MI, Myocardial Infarction; SDOH, Social Determinants of Health; SGLT2i, Sodium-Glucose Cotransporter-2 Inhibitor; T2D, Type 2 Diabetes; TZD, Thiazolidinedione.

* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke and renal endpoints in individuals with T2D with established/high risk of CVD.

Diabetes Care 2022; 45(11):2753-2786.
https://doi.org/10.2337/dci22-0034
Slides: https://professional.diabetes.org/2022ADA/EASDconsensus

American Diabetes Association. EASD European Association for the Study of Diabetes