약물 치료

개인 맞춤형의 적절한 약제 선택을 위한 고려사항 - 누구에게 무엇을 쓸 것인가?

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2022 비만대사증후군연구회 추계학술대회 전공의 연수강좌

Currently available anti-obesity drugs in Korea

Drug	Short / long	Mechanism	Controlled substance	Note
Phentermine	Short-term	Sympathomimetic amine	IV	
Phendimetrazine	Short-term	Sympathomimetic amine	IV	
Diethylpropion	Short-term	Sympathomimetic amine	IV	
Mazindol	Short-term	Sympathomimetic amine	IV	
Orlistat	Long-term	gastric/pacreatic lipase inhibitor	NA	small weight reduction; fat stool
Phentermine/ topiramate	Long-term	Sympathomimetic amine/antiepileptic drug	IV	considerable weight reduction; AEs
Naltrexone/ bupropion	Long-term	Opioid antagonist/anti-depressant	NA	AEs (esp. nausea)
Liraglutide	Long-term	GLP-1 analogue	NA	high price

Screening and diagnosis of several obesity related comorbidities in ambulatory care clinic setting

Comoribity	Screening tool	Suggested additional test when needed
Type 2 diabetes	Fasting glucose, Hb A1c	Insulin, OGTT
Hypertension	Sitting blood pressure	Home blood pressure, ambulatory blood pressure monitoring
Dyslipidemia	Total cholesterol, triglycerides, HDL cholesterol	LDL cholesterol, non-HDL cholesterol, LDL particle size, apolipoprotein B-100, lipoprotein (a)
Cardiovascular disease	Electrocardiography	Ankle-brachial index, pulse wave velocity, carotid artery intima-media thickness
Non-alcoholic fatty liver disease	Liver function test	Ultrasonography, ultrasound-based elastography
Obstructive sleep apnea	Neck circumference, physical examination of oropharyngeal airway	Polysomnography
Osteoarthritis	X-ray	
Polycystic ovarian syndrome	Total testosterone, sex hormone-binding globulin	Human chorionic gonadotropin, prolactin, thyroid-stimulating hormone, and follicle-stimulating hormone (to rule out other causes of oligomenorrhea)
Targeted review of system and physical examination are essential for all comorbidities.		
Abbreviations: OGTT = oral glucose tolerance test		

Cho SH, Kim KK. Korean J Fam Pract. 2020;10(2):77-86

약제 선택을 위해 무슨 정보가 필요한가?

- 환자의 경제적 상황
- 환자의 합병증 - 심혈관 질환, 당뇨병, 정신과적 질환, 폐쇄성 수면무호흡증, 암
- 환자의 나이
- 치료자의 생활 습관 교육 능력 혹은 시간적 여유
- 환자의 생활 습관 변화 의지
- 환자의 수면 상태
- 환자의 변비 유무

환자의 경제적 상황

- 사업가, 형편이 좋은 자영업자, 고액 연봉자
- 몸매가 수입과 연결되는 직업

  ➡ 리라글루티드

- 일반적인 경제 상황

  ➡ 날트렉손/부프로피온

Variable	Author (year)					
	Bohula et al.[58] (2018)*		Nissen et al.[59] (2016)*		Marso et al.[60] (2016)†	
Noninferiority margin of HR	1.4		1.4		1.3	
Follow-up duration	3.3 y (3.0–3.5 y)		121 wk (114–128 wk) with 2-week crossover run-in		3.8 y with 2-week placebo run-in	
Group	Lorcaserin 20 mg	Placebo	NB	Placebo	Liraglutide 1.8 mg	Placebo
No.	6,000	6,000	4,455	4,450	4,668	4,672
No. of AEs leading to discontinuation of study drug	433 (7.22)	220 (3.67)	1,253 (28.1)	388 (8.7)	444 (9.5)	339 (7.3)
Age (y)	64 (58–69)	64 (58–69)	61.1±7.27	60.9±7.38	64.2±7.2	64.4±7.2
Initial bodyweight (kg)	102 (90–116)	102 (90–116)	105.6±19.1	106.3±19.2	91.9±21.2	91.6±20.8
Initial body mass index (kg/m^2)	35 (32–39)	35 (32–39)	36.6 (33.1–40.8)	36.7 (33.1–41.1)	32.5±6.3	32.5±6.3
Male	3,888 (64.8)	3,814 (63.6)	2,018 (55.3)	2,031 (55.6)	3,011 (64.5)	2,992 (64.0)
Baseline condition						
Diabetes	3,385 (56.4)	3,431 (57.2)	3,784 (84.9)	3,803 (85.5)	4,668 (100.0)	4,672 (100.0)
Glycated hemoglobin (%)	6.1 (5.7–7.0)	6.1 (5.6–7.0)	7.0 (6.1–8.1)‡	7.1 (6.4–8.2)‡	8.7±1.6	8.7±1.5
Cardiovascular disease	4,488 (74.8)	4,470 (74.5)	1,415 (31.8)	1,447 (32.5)	3,831 (82.1)	3,767 (80.6)
Mean weight loss	-4.2 kg at 1 y	-1.4 kg at 1 y	-3.6%	-1.1%	Difference between group was 2.3 kg	
MACE at trial completion	364	369	124	119	608	694
MACE at interim analysis	242	241	90	102	NA	NA
All cause death	212	202	43	51	381	447
HR (95% CI) for MACE	0.99 (0.85–1.14)		0.95 (0.65–1.38)§		0.87 (0.78–0.97)	

End Point	Change From Baseline to Week 56 or Percentage At Week 56			Estimate (95% CI)				
	Liraglutide				Liraglutide			
	3.0 mg (n = 411)	1.8 mg (n = 204)	Placebo (n = 211)	Estimate Type	3.0 mg vs Placebo	*P* Value	1.8 mg vs Placebo	*P* Value
Waist circumference, mean (SD), cm[b]	-6.1 (6.5)	-4.8 (5.6)	-2.7 (5.4)	Treatment difference	-3.22 (-4.20 to -2.23)	<.001	-2.06 (-3.20 to -0.92)	<.001
Body mass index, mean (SD)[b,c]	-2.2 (2.1)	-1.7 (2.1)	-0.8 (1.7)	Treatment difference	-1.50 (-1.83 to -1.18)	<.001	-0.95 (-1.33 to -0.57)	<.001
HbA_{1c}, mean (SD), % change[b]	-1.3 (0.9)	-1.1 (1.0)	-0.3 (0.9)	Treatment difference	-0.93 (-1.08 to -0.78)	<.001	-0.74 (-0.91 to -0.57)	<.001
No. of individuals achieving HbA_{1c} target, No. %[d]								
<7.0 %	278 (69.2)	130 (66.7)	56 (27.2)	Odds ratio	8.79 (5.74 to 13.44)	<.001	7.71 (4.76 to 12.51)	<.001
≤6.5 %	227 (56.5)	89 (45.6)	31 (15.0)	Odds ratio	9.61 (6.05 to 15.26)	<.001	5.98 (3.59 to 9.97)	<.001
Fasting plasma glucose, mean (SD), mg/dL[b]	-34.3 (38.5)	-26.8 (50.3)	-0.2 (37.0)	Treatment difference	-31.89 (-38.02 to-25.59)	<.001	-23.06 (-30.27 to -15.86)	<.001
PPG increment, mean (SD), mg/dL[b]	-16.2 (37.8)	-12.6 (37.8)	-5.4 (36.0)	Treatment difference	-9.91 (-15.14 to -4.68)	<.001	-7.93 (-13.87 to -1.98)	.009

Davies MJ, et al. The SCALE Diabetes Randomized Clinical Trial. JAMA. 2015 Aug 18;314(7):687.

End Point	Change From Baseline to Week 56 or Percentage At Week 56			Estimate (95% CI)				
	Liraglutide				Liraglutide			
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Fasting values, geometric mean (CV), %[e]								
Glucagon	-10.4 (34.7)	-7.9 (30.8)	0.6 (33.0)	Ratio	0.87 (0.83 to 0.92)	<.001	0.91 (0.86 to 0.96)	<.001
Insulin	6.87 (67.3)	10.65 (48.7)	1.94 (47.0)	Ratio	1.03 (0.94 to 1.12)	.50	1.07 (0.96 to 1.18)	.21
C-peptide	3.3 (53.4)	2.4 (34.0)	-2.4 (28.5)	Ratio	1.04 (0.98 to 1.10)	.17	1.03 (0.97 to 1.10)	.29
Proinsulin	-34.4 (78.9)	-23.6 (85.2)	-0.5 (61.6)	Ratio	0.65 (0.58 to 0.73)	<.001	0.77 (0.68 to 0.88)	<.001
Proinsulin to insulin ratio	-38.4 (64.4)	-31.6 (87.1)	-2.2 (176.0)	Ratio	0.63 (0.58 to 0.69)	<.001	0.72 (0.64 to 0.79)	<.001
HOMA-B, geometric mean (CV), %[e]	94.3 (419.0)	72.3 (55.1)	9.1 (57.0)	Ratio	1.71 (1.52 to 1.92)	<.001	1.53 (1.34 to 1.74)	<.001
HOMA-IR, geometric mean (CV), %[e]	-20.0 (76.7)	-10.5 (79.4)	-3.3 (79.5)	Ratio	0.84 (0.75 to 0.94)	.003	0.93 (0.82 to 1.07)	.32

Davies MJ, et al. The SCALE Diabetes Randomized Clinical Trial. JAMA. 2015 Aug 18;314(7):687.

End Point	Change From Baseline to Week 56 or Percentage At Week 56			Estimate (95% CI)				
	Liraglutide				Liraglutide			
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Waist circumference, mean (SD), cm[b]	-6.1 (6.5)	-4.8 (5.6)	-2.7 (5.4)	Treatment difference	-3.22 (-4.20 to -2.23)	<.001	-2.06 (-3.20 to -0.92)	<.001
Blood pressure, mean (SD), mm Hg[b]								
Systolic	-2.8 (13.5)	-3.5 (12.7)	-0.4 (13.4)	Treatment difference	-2.59 (-4.56 to -0.62)	.01	-2.68 (-4.98 to -0.38)	.02
Diastolic	-0.9 (8.7)	-1.1 (9.4)	-0.5 (9.1)	Treatment difference	-0.36 (-1.69 to 0.96)	.59	-0.19 (-1.74 to 1.36)	.81
Lipid profile[e]								
Cholesterol, geometric mean (CV), %								
Total	-1.46 (16.9)	-2.20 (20.2)	3.80 (16.2)	Ratio	0.96 (0.94to 0.99)	.01	0.97 (0.94 to 1.00)	.06
HDL	4.70 (16.1)	4.45 (14.2)	1.93 (14.3)	Ratio	1.03 (1.00 to 1.05)	.03	1.02 (0.99 to 1.05)	.16
LDL	0.58 (38.8)	-3.07 (30.5)	5.02 (27.3)	Ratio	0.98 (0.93 to 1.03)	.36	0.95 (0.90 to 1.01)	.10
VLDL	-14.10 (43.0)	-8.14 (41.7)	0.53 (35.5)	Ratio	0.87 (0.81 to 0.93)	<.001	0.94 (0.87 to 1.01)	.09

Davies MJ, et al. The SCALE Diabetes Randomized Clinical Trial. JAMA. 2015 Aug 18;314(7):687.

날트렉손/부프로피온 복용 방법

	Week 1	Week 2	Week 3	Week 4 and Beyond
AM Tip: Take with breakfast	1 pill in AM	1 pill in AM	2 pills in AM	2 pills in AM
PM Tip: Take before dinner		1 pill in PM	1 pill in PM	2 pills in PM

환자의 합병증

- 심혈관 질환, 당뇨병, 정신과적 질환

  ➡ 리라글루티드

- 우울증

  ➡ 날트렉손/부프로피온

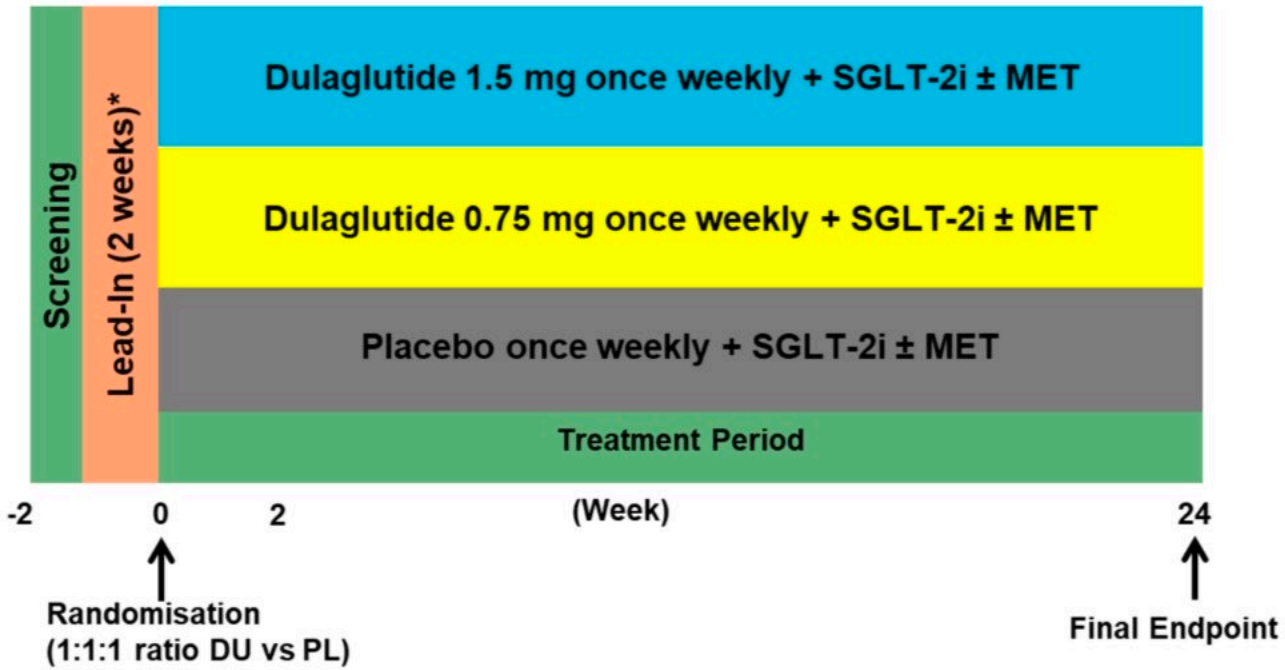
- 폐쇄성 수면무호흡증

- 유방암

  ➡ 펜터민/토피라메이트

Dulaglutide + SGLT-2i (AWARD-10)

STUDY DESIGN

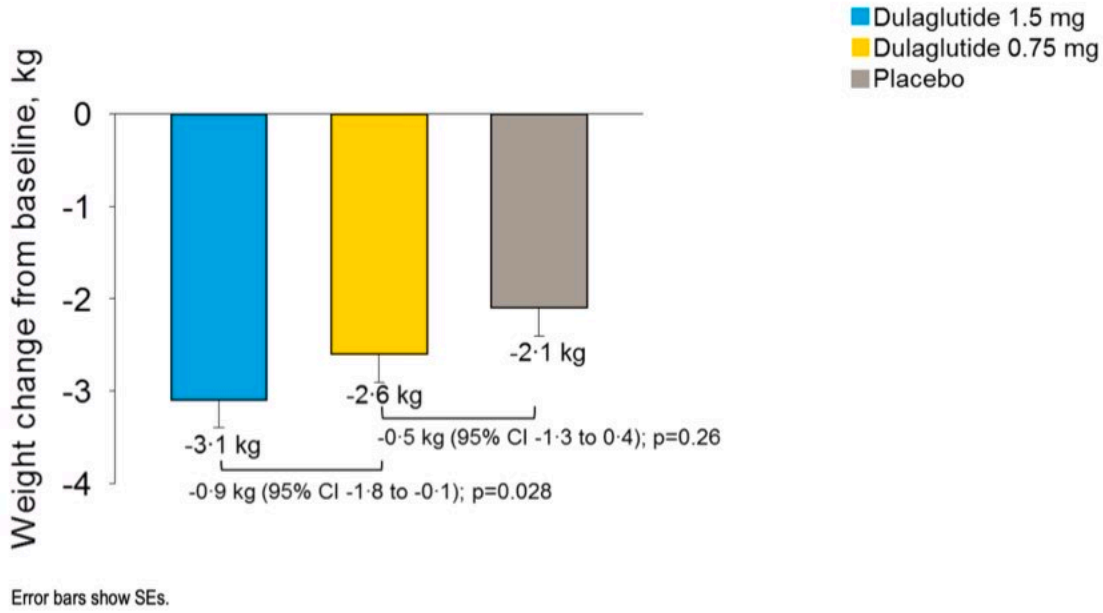


- **Key inclusion criteria**
  - T2D
  - HbA1c ≥7.0% and ≤9.5%
  - BMI ≤45 kg/m^2
  - SGLT-2i at locally approved doses ± metformin ≥1500 mg/day

- **Key exclusion criteria**
  - T1D
  - History of pancreatitis
  - Ketoacidosis or hyperosmolar state/coma
  - Recent CV event or active cancer

*Patients requiring adjustment (metformin <1500 mg/day; eGFR 45-59 ml/min/1.73 m^2) completed 12-week lead-in

Weight, change to 24 weeks



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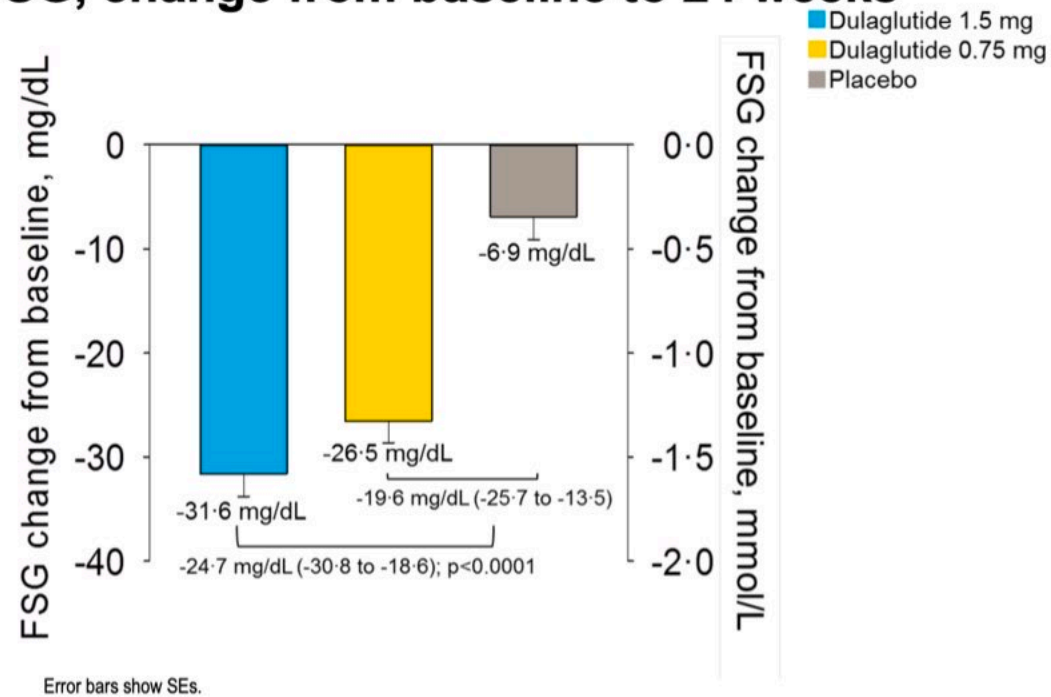
FSG, change from baseline to 24 weeks



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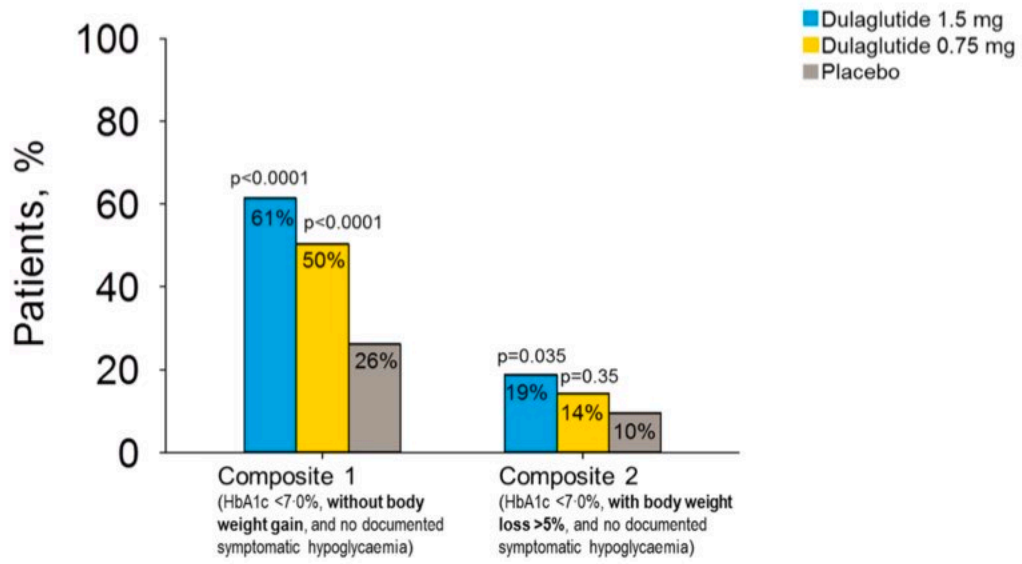
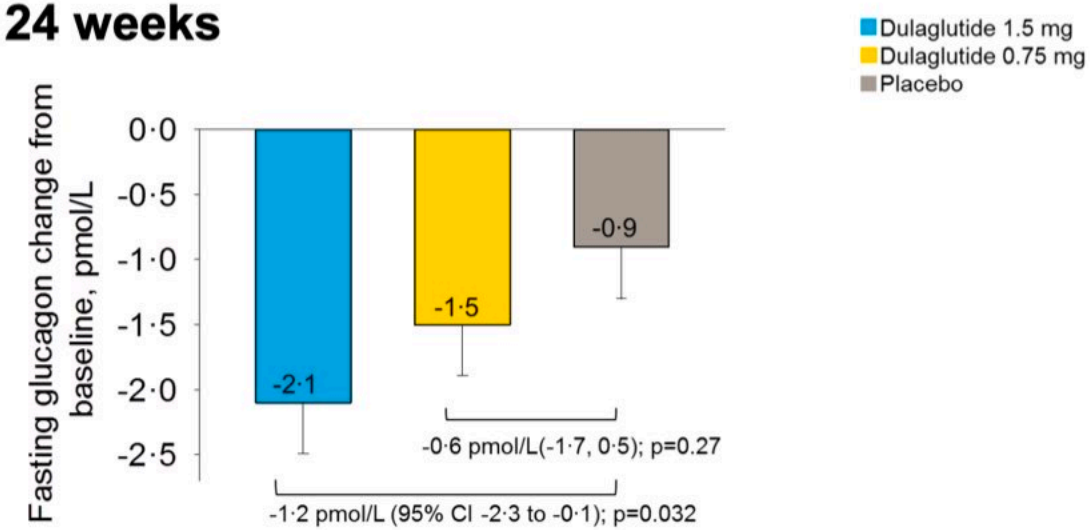
Composite endpoints at 24 weeks



Fasting glucagon, change from baseline to 24 weeks



Liraglutide Treatment on Prediabetes and Overweight/Obesity in Clozapine- or Olanzapine-Treated Patients With Schizophrenia Spectrum Disorder

- Design: Randomized clinical double-blind trial at 2 clinical sites in Denmark

- Participants: 103 eligible participants with a schizophrenia spectrum disorder, were randomized. Participants received stable treatment with clozapine or olanzapine, were overweight or obese, and had prediabetes. Data were collected from 2013-05-01, through 2016-02-25.

- Interventions: For 16 weeks with once daily subcutaneous injection of liraglutide or placebo. The participants followed a fixed uptitration schedule of 0.6 mg per week to a daily dose of 1.8 mg.

Larsen JR, et al. JAMA Psychiatry. 2017 Jul 1;74(7):719–28.

Characteristic	Liraglutide Treatment Group (n = 47)	Placebo Treatment Group (n = 50)	Estimated Treatment Difference, Liraglutide vs Placebo (95% CI)[b]	*P* Value[c]
Clinical, mean (SE)				
Body weight, kg	−4.7 (0.5)	0.5 (0.7)	−5.3 (−7.0 to −3.7)	<.001[d]
Waist circumference, cm	−4.0 (0.6)	0.5 (0.7)	−4.1 (−6.0 to −2.3)	<.001[d]
BMI	−1.6 (1.2)	0.08 (0.2)	−1.8 (−2.4 to −1.3)	<.001[d]
Systolic blood pressure, mm Hg	−1.4 (2.0)	1.1 (1.8)	−4.9 (−9.5 to −0.3)	.04
Diastolic blood pressure, mm Hg	0.5 (1.5)	2.4 (1.1)	−3.0 (−6.8 to 0.9)	.13
Prediabetes status, No. (%)[e]	−30 (63.8)	−8 (16.0)	9.2 (2.6 to 32.7)	<.001[d]
Elevated fasting plasma glucose level	−13 (85.7)	−6 (40.0)	2.1 (0.9 to 3.3)	<.001[d]
Elevated glycated hemoglobin level	−5 (83.3)	0 (0.0)	NA (too few events)	NA (too few events)
Impaired glucose tolerance	−28 (37.8)	−6 (12.5)	2.1 (0.8 to 3.5)	.002[d]
Glucose metabolism				
Glycated hemoglobin level, %	−0.2 (0.04)	0.06 (0.04)	−0.2 (−0.3 to −0.1)	<.001[d]
Fasting plasma glucose level, relative change	0.90	0.99	0.90 (0.88 to 0.95)	<.001[d]
Fasting C-peptide level, mean (SE), ng/mL	0.26 (0.15)	−0.20 (0.16)	0.46 (−0.02 to 0.94)	.06
Fasting glucagon level, mean (SE), pg/mL	−4.6 (2.4)	2.0 (2.8)	−4.7 (−8.6 to −0.05)	.02
Insulin resistance[f]	1.02	0.96	1.08 (0.96 to 1.22)	.21
Beta cell function[f]	1.28	0.99	1.29 (1.18 to 1.42)	<.001[d]
Insulin sensitivity[f]	0.99	1.04	0.93 (0.82 to 1.06)	.26
2-h, 75-g OGTT value	0.47	0.95	0.77 (0.70 to 0.85)	<.001[d]
Body composition				
Visceral fat, mean (SE), g	−315.8 (75.3)	−24.0 (41.7)	−250.19 (−459.9 to −40.5)	.02
Android to gynoid fat ratio	0.99	1.01	0.98 (0.94 to 1.01)	.23
Total body fat	0.91	0.99	0.96 (0.94 to 0.99)	.01

Adverse events

	Liraglutide (n=52)	Placebo (n=51)	*P* value
Admission to hospital for worsening of schizophrenia	3 / 50 (6%)	9 / 51 (17.7%)	0.08
Hypoglycemia	13 / 50 (26.0%)	7 / 50 (14.0%)	0.22
Nausea	31 / 50 (62.0%)	16 / 50 (32.0%)	0.008
Orthostatic hypotension	4 / 49 (8.2%)	0	0.04

Larsen JR, et al. JAMA Psychiatry. 2017 Jul 1;74(7):719–28.

Lancet. 2010; 376: 595–605.

Bupr/Nalt: Adverse Events

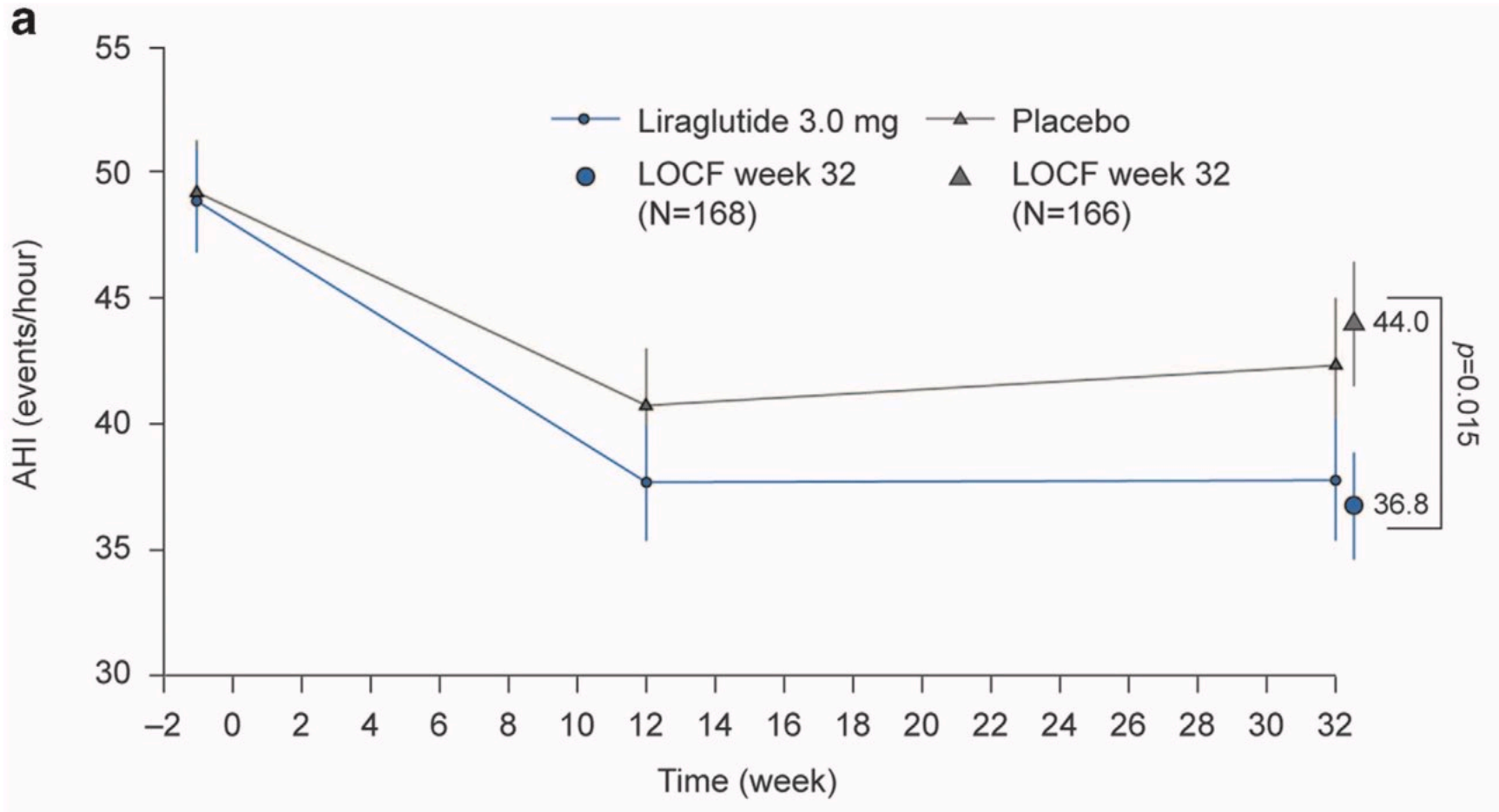
Lancet. 2010; 376: 595–605.

Bupr…vents

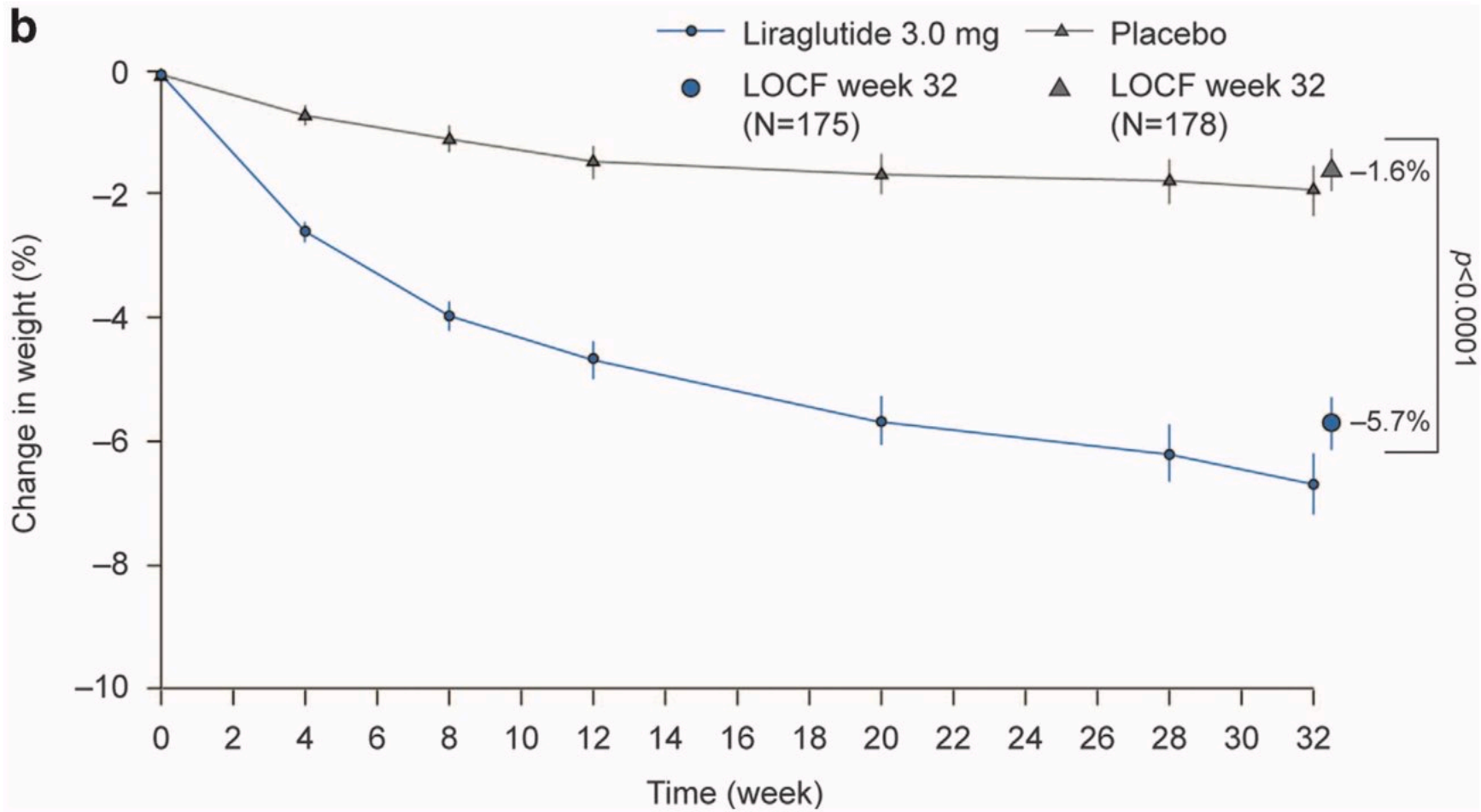
	P	NB16	NB32
Participants reporting any adverse event	390 (68·5%)	455 (80·0%)†	476 (83·1%)†
Nausea	30 (5·3%)	155 (27·2%)†	171 (29·8%)†
Headache	53 (9·3%)	91 (16·0%)†	79 (13·8%)†
Constipation	32 (5·6%)	90 (15·8%)†	90 (15·7%)†
Upper respiratory tract infection	64 (11·2%)	49 (8·6%)	57 (9·9%)
Dizziness	15 (2·6%)	44 (7·7%)†	54 (9·4%)†
Insomnia	29 (5·1%)	36 (6·3%)	43 (7·5%)
Vomiting	14 (2·5%)	36 (6·3%)†	56 (9·8%)†
Sinusitis	34 (6·0%)	34 (6·0%)	30 (5·2%)
Dry mouth	11 (1·9%)	42 (7·4%)†	43 (7·5%)†
Nasopharyngitis	31 (5·4%)	32 (5·6%)	29 (5·1%)
Diarrhoea	28 (4·9%)	31 (5·4%)	26 (4·5%)
Hot flush	7 (1·2%)	13 (2·3%)	30 (5·2%)†
Participants reporting any psychiatric adverse event	62 (10·9%)	76 (13·4%)	85 (14·8%)
Insomnia	29 (5·1%)	36 (6·3%)	43 (7·5%)
Anxiety	12 (2·1%)	12 (2·1%)	9 (1·6%)
Depression	6 (1·1%)	9 (1·6%)	3 (0·5%)

Phen/Topi: Adverse Events

	Placebo (*n* = 513)	PHEN/TPM CR 15/92 (*n* = 511)	
Adverse event	***n* (%)**	***n* (%)**	***P* value**
Cough	18 (3.5)	26 (5.1)	0.2218
Influenza	24 (4.7)	26 (5.1)	0.7740
Depression	6 (1.2)	24 (4.7)	0.0007
Diarrhea	23 (4.5)	24 (4.7)	0.8825
Fatigue	17 (3.3)	23 (4.5)	0.3385
Irritability	3 (0.6)	23 (4.5)	<0.0001
Vision blurred	16 (3.1)	23 (4.5)	0.2582
Alopecia	5 (1.0)	22 (4.3)	0.0008
Anxiety	6 (1.2)	19 (3.7)	0.0084
Disturbance in attention	3 (0.6)	18 (3.5)	0.0007
Hypoesthesia	4 (0.8)	17 (3.3)	0.0039
Dry eye	4 (0.8)	12 (2.3)	0.0470
Paresthesia oral	2 (0.4)	11 (2.2)	0.0123
Dry skin	1 (0.2)	8 (1.6)	0.0208



Int J Obes (Lond). 2016 Aug; 40(8): 1310–1319.



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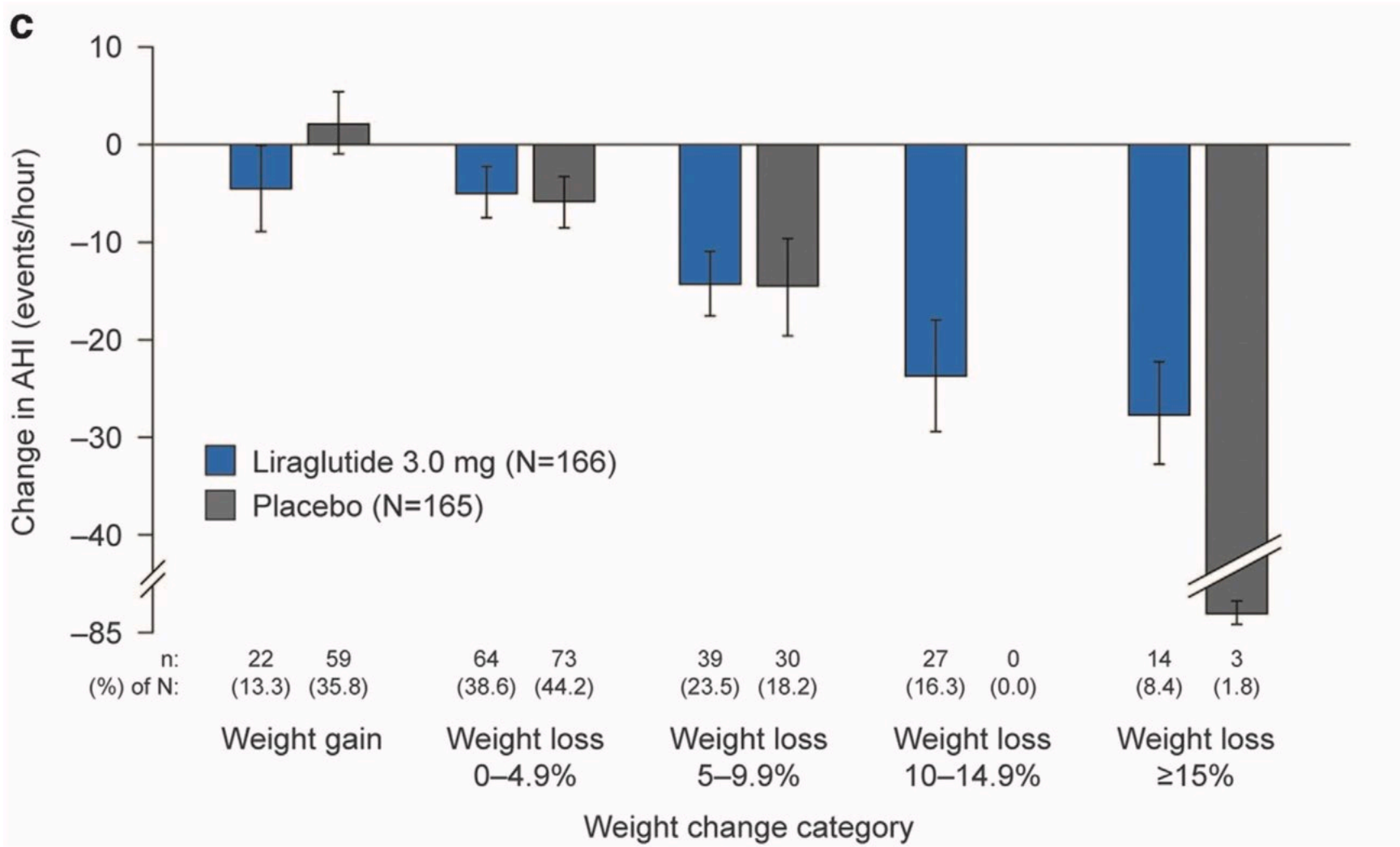

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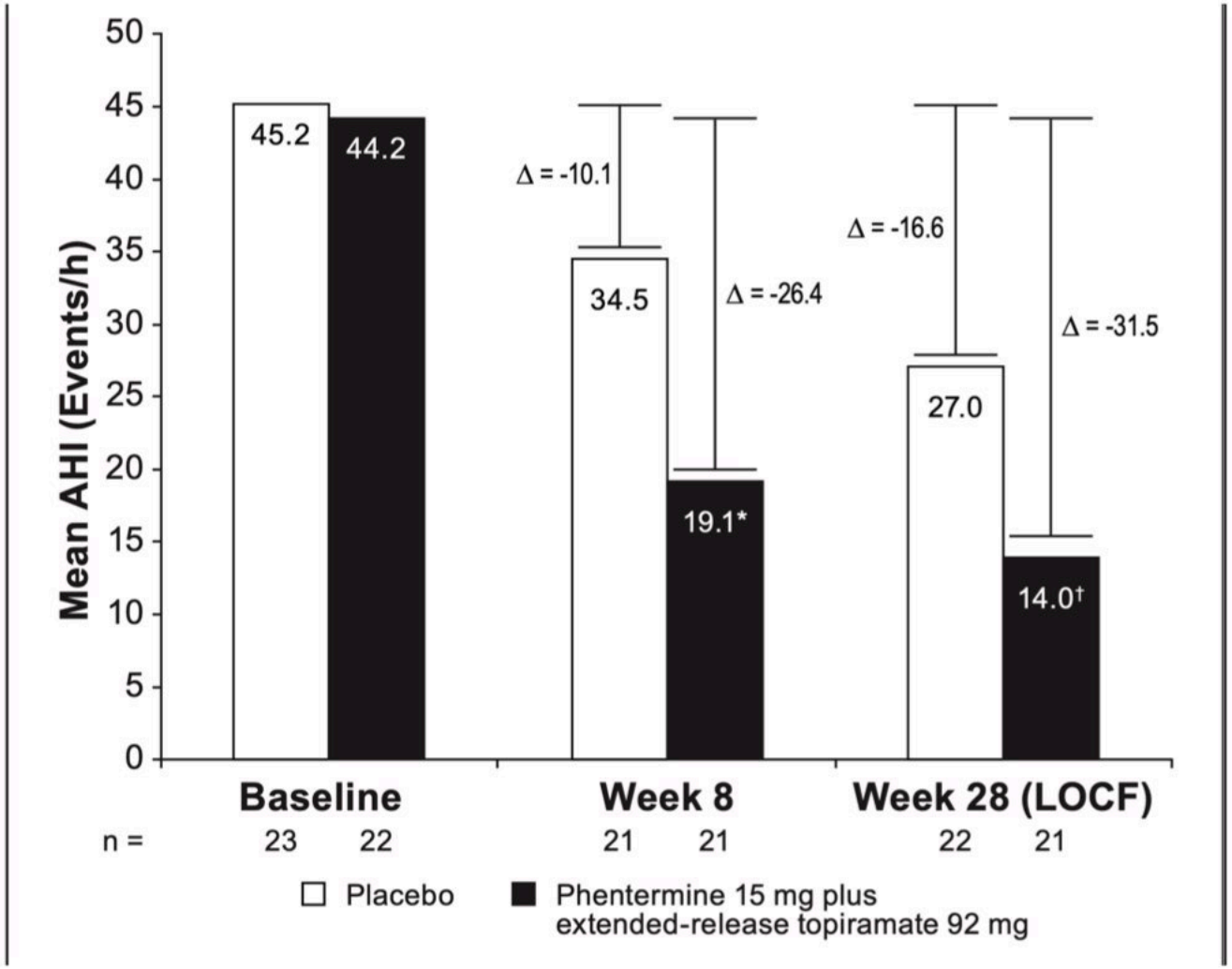
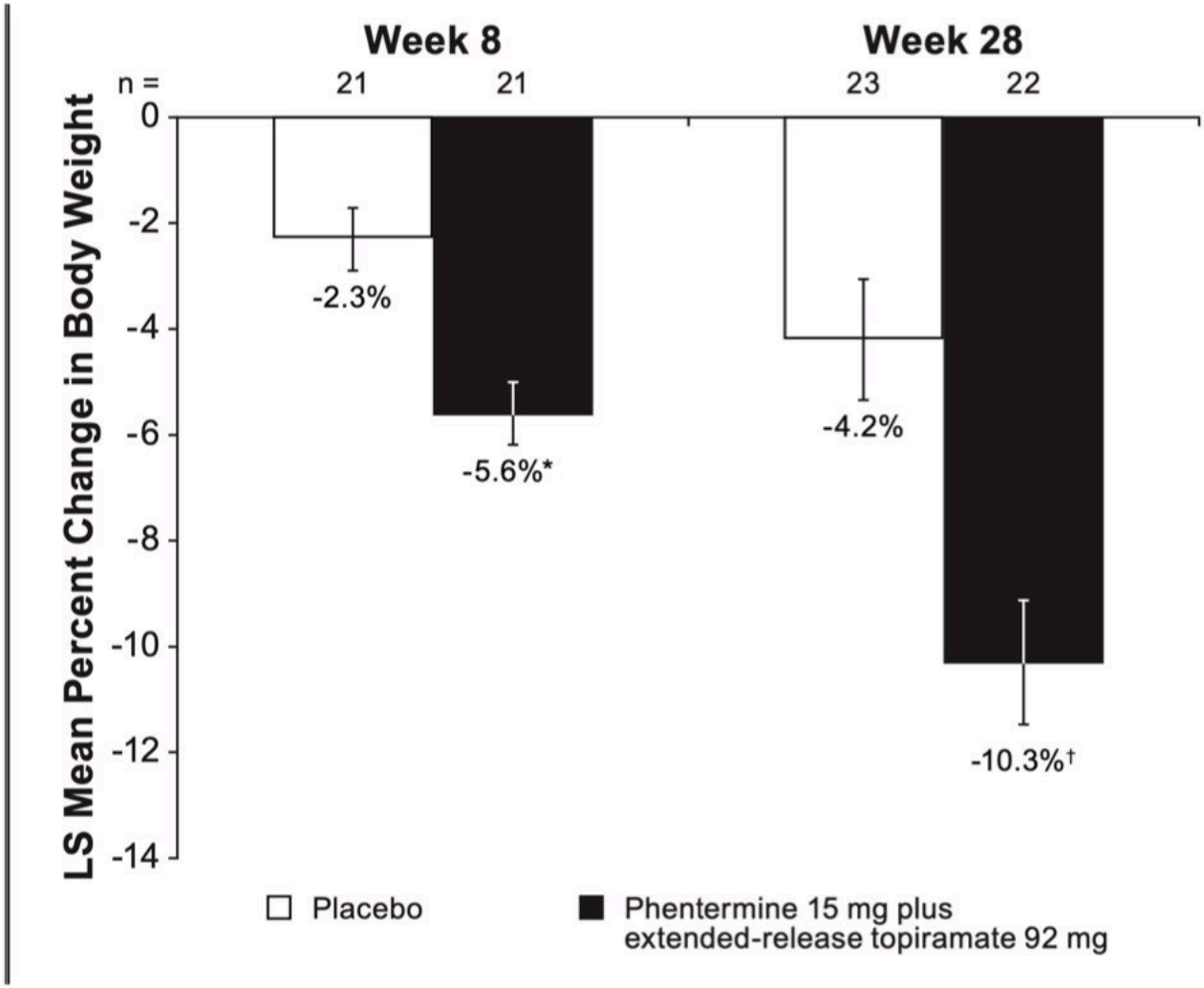
Change of AHI and % body weight



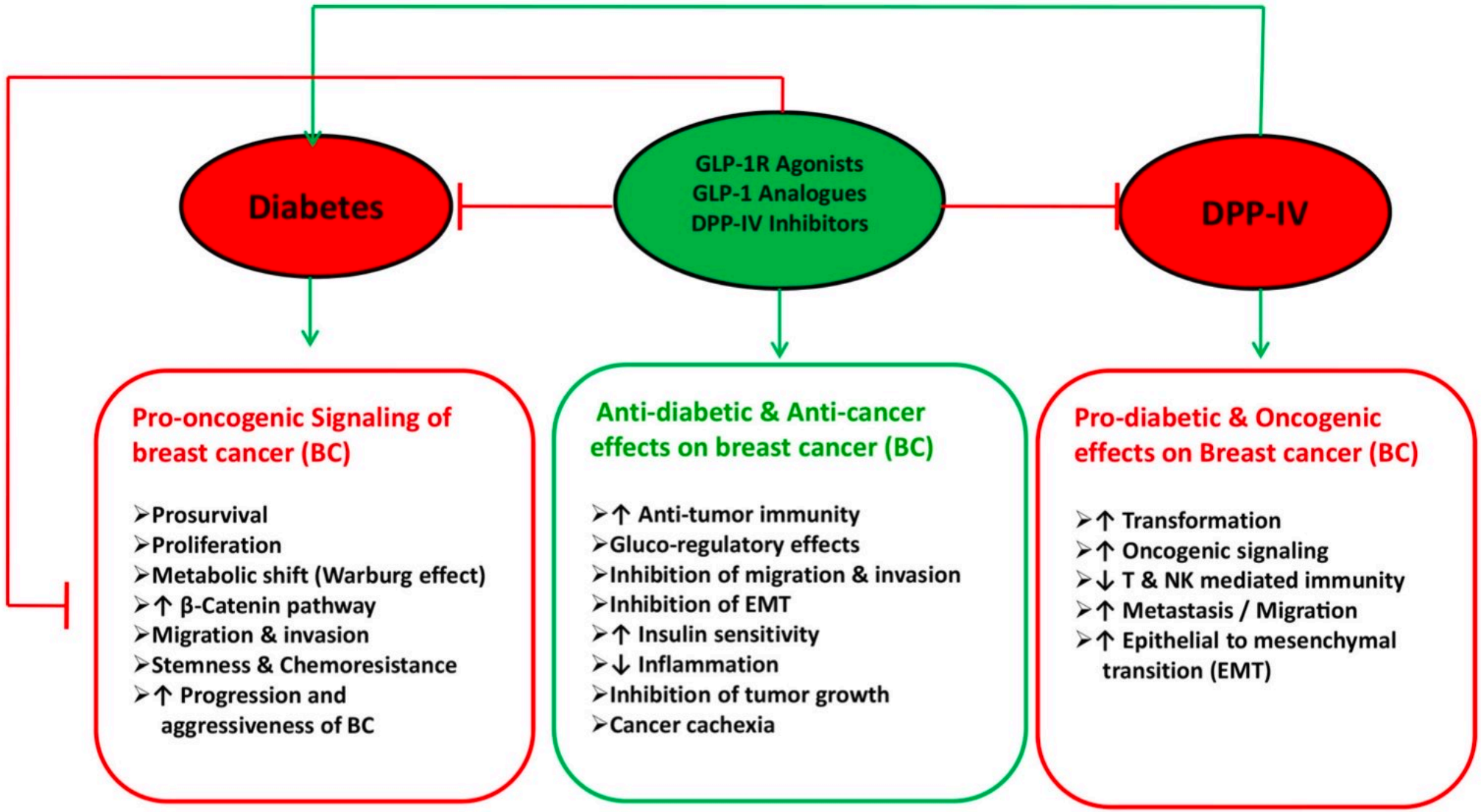


AHI, apnea-hypopnea index;

SLEEP, Vol. 35, No. 11, 2012

Jaiswal P, Tripathi V, Nayak A, et al. Curr Cancer Drug Targets 2021;21(10):829-848.

유방암과 인크레틴 1



A molecular linkbetween diabetes and breast cancer.

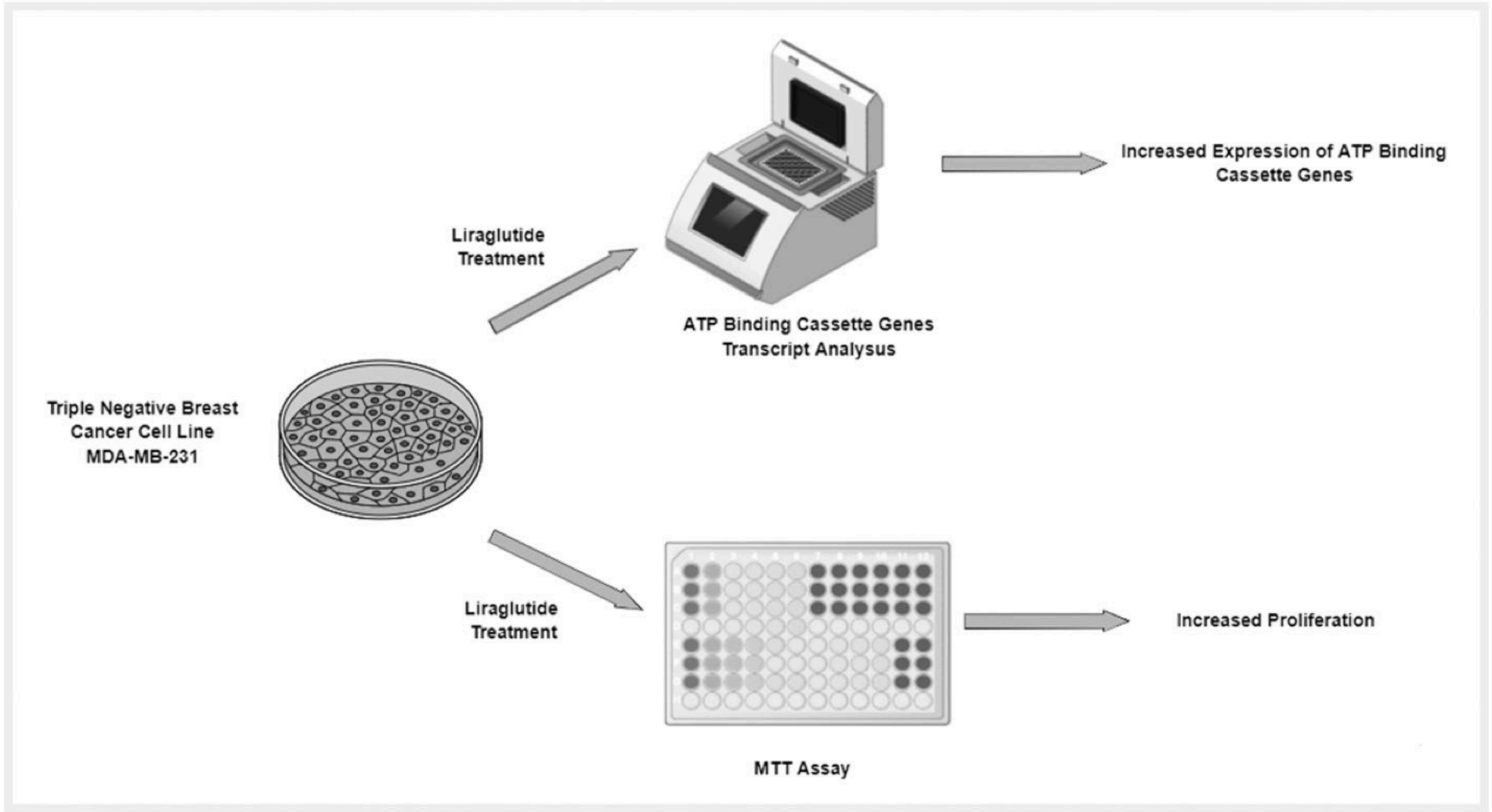
Caparrotta TM, Templeton JB, Clay TA, et al. Diabetes Therapy 2021;12(4):969-989.

유방암과 인크레틴 2

Exposure	Study synopsis
GLP1RA class	
8.1	A small 2016 British cohort study compared those taking GLP1RA class agents vs. DPP4Is on the risk of incident breast cancer [29]. Detection bias was handled in sensitivity analysis by varying lag time windows, censoring in situ breast cancer, performing an IPTW analysis and stratifying by mammography screening. Overall, there was a neutral association of GLP1RA class on breast cancer (and also for exenatide and liraglutide alone, when analysed separately). The dose–response analysis was associated with a transient increase in the breast cancer risk of those in the > 3 to ≤ 4-year exposure window, which attenuated in longer exposure (Table S12.1). Sensitivity analyses yielded similar results to the primary analysis, except that those with no mammography screening had an association with increased breast cancer risk (DNS). All of the CIs were wide
Liraglutide	
8.2	A large 2018 American cohort study compared individuals taking liraglutide vs. OADs on the risk of developing adjudicated incident breast cancer [17]. ITT and cumulative TOD analyses were performed. Detection bias was handled comparing mammography frequency between the groups. Liraglutide exposure was associated with a neutral risk of breast cancer in both the ITT (for all comparator agents) and also in the cumulative TOD analyses (Table S12.2). The CIs were narrow, except the recent TOD which was wide

유방암과 인크레틴 3

Shadboorestan A, Tarighi P, Koosha M, et al. Drug Res (Stuttg) 2021;71(6):307-311.



Situation		Orlistat	Naltrexone ER/ bupropion ER	Phentermine/ topiramate ER	Liraglutide
Type 2 diabetes					Preferred
Uncontrolled hypertension					
Old age (y)	65–75	Unknown	Caution	Unknown	Unknown
	≥75	Unknown			
Insomnia				Caution	
Obstructive sleep apnea				Preferred	Preferred
Constipation		Preferred			
Coronary heart disease			Caution		Preferred up to 1.8 mg qd
Renal impairment	30–50		Not exceed 2 T/day	Not exceed 7.5 mg/46 mg qd	
Creatinine clearance	<30	Caution			
	End stage renal disease	Caution			
Hepatic impairment	5–6	Monitor		Not exceed 7.5 mg/46 mg qd	Caution
Child-Pugh score	7–9	Monitor		Not exceed 7.5 mg/46 mg qd	Caution
	≥10				
Renal stone		Caution		Caution	
Depression			Caution	Caution	
Anxiety			Caution	Caution	
Glaucoma			Caution		
Chronic opioid usage					
Thyroid disease				Contraindicated to hyperthyroidism	Caution
Pancreatitis		Monitor			
Seizure				Caution	

Kim, KK. Korean J Fam Pract. 2020;10(2).

Figure 3. Comparison of Weight Loss and Adverse Events With Pharmacological Weight Loss Agents in Network Meta-analysis

Odds ratio (95% CrI) for discontinuation due to adverse events	Odds ratio (95% CrI) for achieving at least 5% weight loss					
	Phentermine-topiramate	**1.67 (1.03-2.56)**	**2.33 (1.54-3.59)**	**2.98 (1.95-4.54)**	**3.42 (2.40-4.91)**	**9.22 (6.63-12.85)**
	0.78 (0.48-1.20)	**Liraglutide**	1.4 (0.96-2.18)	**1.78 (1.22-2.78)**	**2.06 (1.51-2.96)**	**5.54 (4.16-7.78)**
	0.87 (0.59-1.25)	1.11 (0.74-1.72)	**Naltrexone-bupropion**	1.28 (0.87-1.84)	**1.47 (1.09-1.96)**	**3.96 (3.03-5.11)**
	1.71 (1.14-2.49)	**2.2 (1.43-3.39)**	**1.97 (1.38-2.76)**	**Lorcaserin**	1.15 (0.86-1.55)	**3.1 (2.38-4.05)**
	1.25 (0.88-1.76)	**1.6 (1.10-2.40)**	**1.44 (1.07-1.95)**	0.73 (0.54-1.02)	**Orlistat**	**2.7 (2.34-3.09)**
	2.29 (1.71-3.06)	**2.95 (2.11-4.23)**	**2.64 (2.1-3.35)**	**1.34 (1.05-1.76)**	**1.84 (1.53-2.21)**	**Placebo**

Summary estimate represents odds ratio of achieving at least 5% weight loss (light gray background) and discontinuation due to adverse events (light blue background). Agents are ordered by rankings for the 5% weight loss outcome. Odds ratio for comparisons are in the cell in common between the column-defining and row-defining treatment. For weight loss outcome, row treatment is compared with column treatment (ie, column treatment is reference). For adverse event outcome, column treatment is compared with row treatment (ie, row treatment is reference). Numbers in parentheses indicate 95% credible intervals (95% CrIs). Numbers in bold represent statistically significant results.

Khera R, Murad MH, Chandar AK, et al. JAMA 2016;315(22):2424-34.

수면 장애

	Insomnia	비고
Orlistat		임상 연구에서 조사하지 않는 부작용 관계 없는 것으로 간주할 수 있다
Liraglutide	2.0% vs 5.4%	1.2mg ?%; 1.8mg ?%; 2.4mg 2.2%; 3.0mg 5.4%
Bupr/Nalt	5.1% vs 7.5%	360/16mg 6.3%; 360/32mg 7.5% 수면 장애 역시 bupropion 때문으로 추정함
Phen/Topi	5% vs 10%	7.5/46mg 6%; 15/92mg 10% 용량 의존적

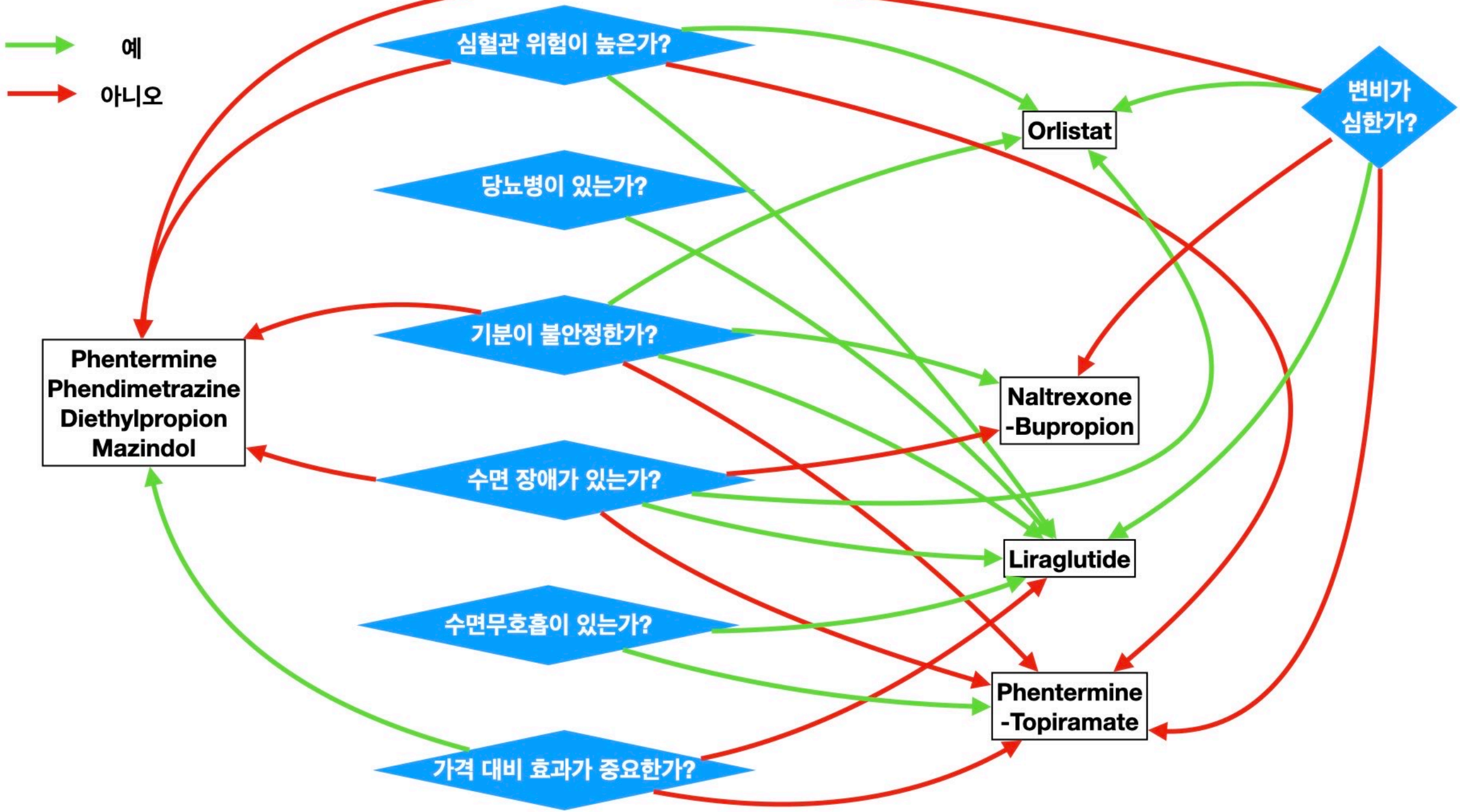
변비

	Constipation	비고
Orlistat	12.2% vs 7.4%	Increased defecation - 7% vs 20% Soft stool - 9% vs 15%
Liraglutide	12.2% vs 18.3%	1.2mg 15.8%; 1.8mg 12.2%; 2.4mg 22.6%; 3.0mg 18.3% diarrhoea도 종종 발생한다
Bupr/Nalt	5.6% vs 15.7%	저용량, 고용량 모두 발현률이 유사함 Bupropion 때문 (naltrexone 용량만 다름)
Phen/Topi	6% vs 17%	용량 의존적이기는 하지만 저용량과 고용량에서의 차이가 심하지는 않다

식욕 억제제 투여에 따른 변비가 심한 경우 → orlistat 병용을 시도할 수 있다

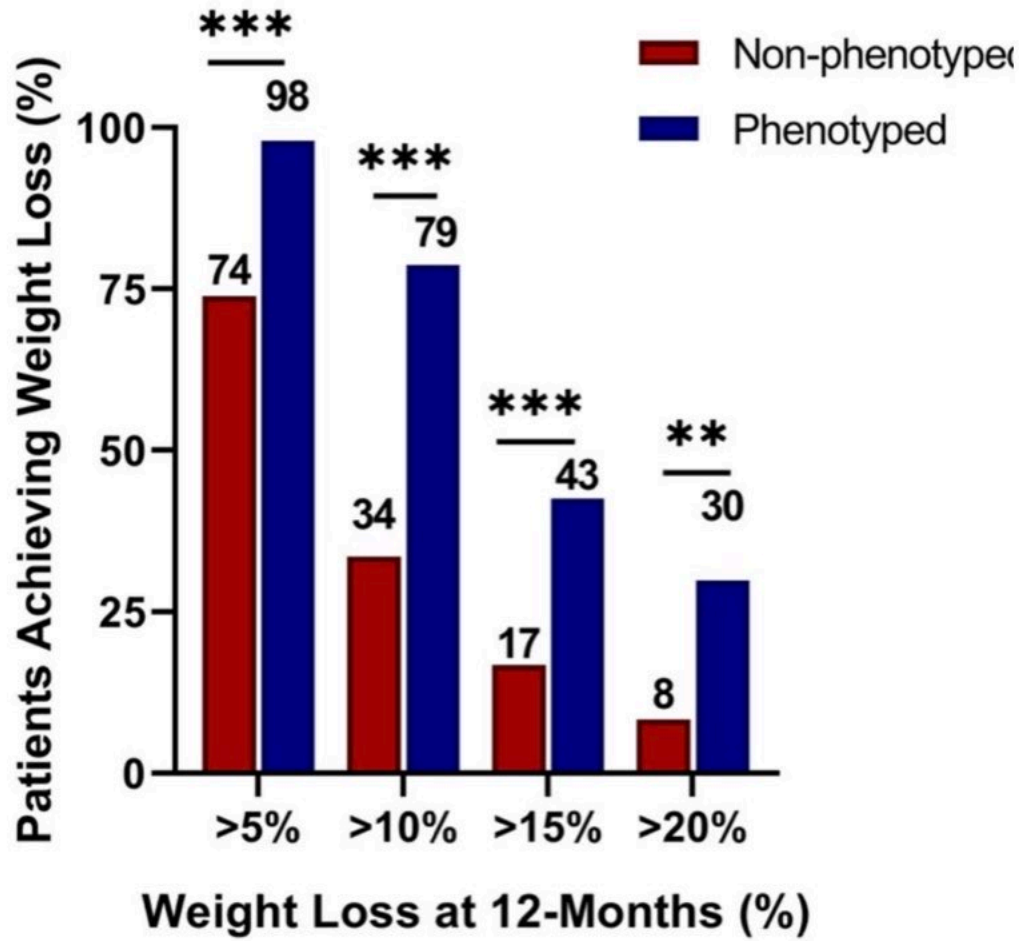
Summary of safety: SCALE Diabetes

	Liraglutide								
	3.0 mg (n = 422)			1.8 mg (n = 210)			Placebo (n = 212)		
	No. (%)	Events, No.	Rate[b]	No. (%)	Events, No.	Rate[b]	No. (%)	Events, No.	Rate[b]
Most common (≥5%) gastrointestinal adverse events									
Gastrointestinal disorders	275 (65.2)	851	224	118 (56.2)	280	148	83 (39.2)	150	83
Gastrointestinal signs and symptoms									
Abdominal distension	26 (6.2)	32	8	10 (4.8)	11	6	3 (1.4)	3	2
Abdominal pain	26 (6.2)	34	9	4 (1.9)	4	2	9 (4.2)	9	5
Abdominal pain, upper	15 (3.6)	21	6	14 (6.7)	17	9	2 (0.9)	2	1
Dyspepsia	47 (11.1)	59	16	14 (6.7)	16	8	5 (2.4)	5	3
Flatulence	22 (5.2)	26	7	8 (3.8)	8	4	4 (1.9)	4	2
Nausea	138 (32.7)	208	55	66 (31.4)	84	44	29 (13.7)	34	19
Vomiting	66 (15.6)	113	30	21 (10.0)	27	14	12 (5.7)	14	8
Gastrointestinal motility and defecation conditions									
Constipation	68 (16.1)	78	21	20 (9.5)	24	13	13 (6.1)	14	8
Diarrhea	108 (25.6)	173	46	37 (17.6)	50	26	27 (12.7)	35	19


예
아니오
심혈관 위험이 높은가?
당뇨병이 있는가?
기분이 불안정한가?
수면 장애가 있는가?
수면무호흡이 있는가?
가격 대비 효과가 중요한가?
변비가 심한가?
Orlistat
Naltrexone -Bupropion
Liraglutide
Phentermine -Topiramate
Phentermine
Phendimetrazine
Diethylpropion
Mazindol

Obesity Phenotypes Enhance Weight loss

- Hungry brain - 먹어도 쉽게 배부르지 않음 - 한번에 많이 먹게 된다 - 펜/토
- Hungry gut - 먹고 나서 빨리 배가 꺼진다 - 자꾸 먹게 된다 - 리라
- 감정적 식사 - 불안감이 높다, 맛 자체를 탐닉하는 경향, 단 것을 찾는다 - 날/부
- 대사 저하 - 기초대사량이 낮다 - 펜터민 + 저항성 운동

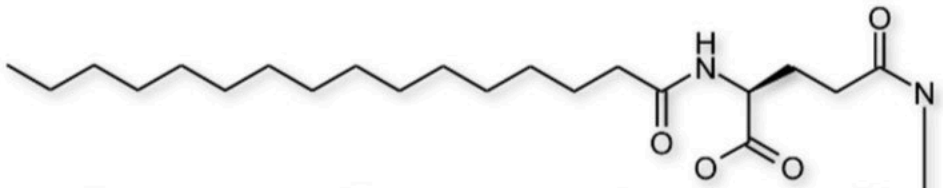


Obesity, Vol. 29, No. 4, 2021

Liraglutide

C16 fatty acid with LγGlu linker to obtain albumin binding and oligomerization

C16 LγGlu



7 10 15 20 25 30 35

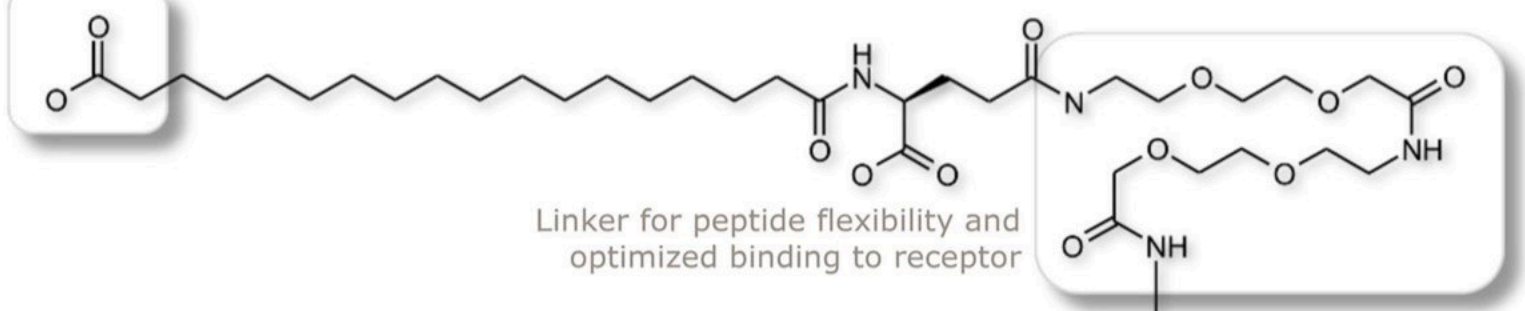
H_2N-HAEGTFTSDVSSYLEGQAAKEFIAWLVRGRG-COOH

Peptide chain based on human GLP-1

Semaglutide

Fatty acid optimization for strong albumin binding

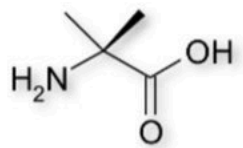
C18diacid LγGlu bis-aminodiethoxyacetyl



Linker for peptide flexibility and optimized binding to receptor

Aib is an unnatural amino acid for preventing peptidase degradation

X = Aib



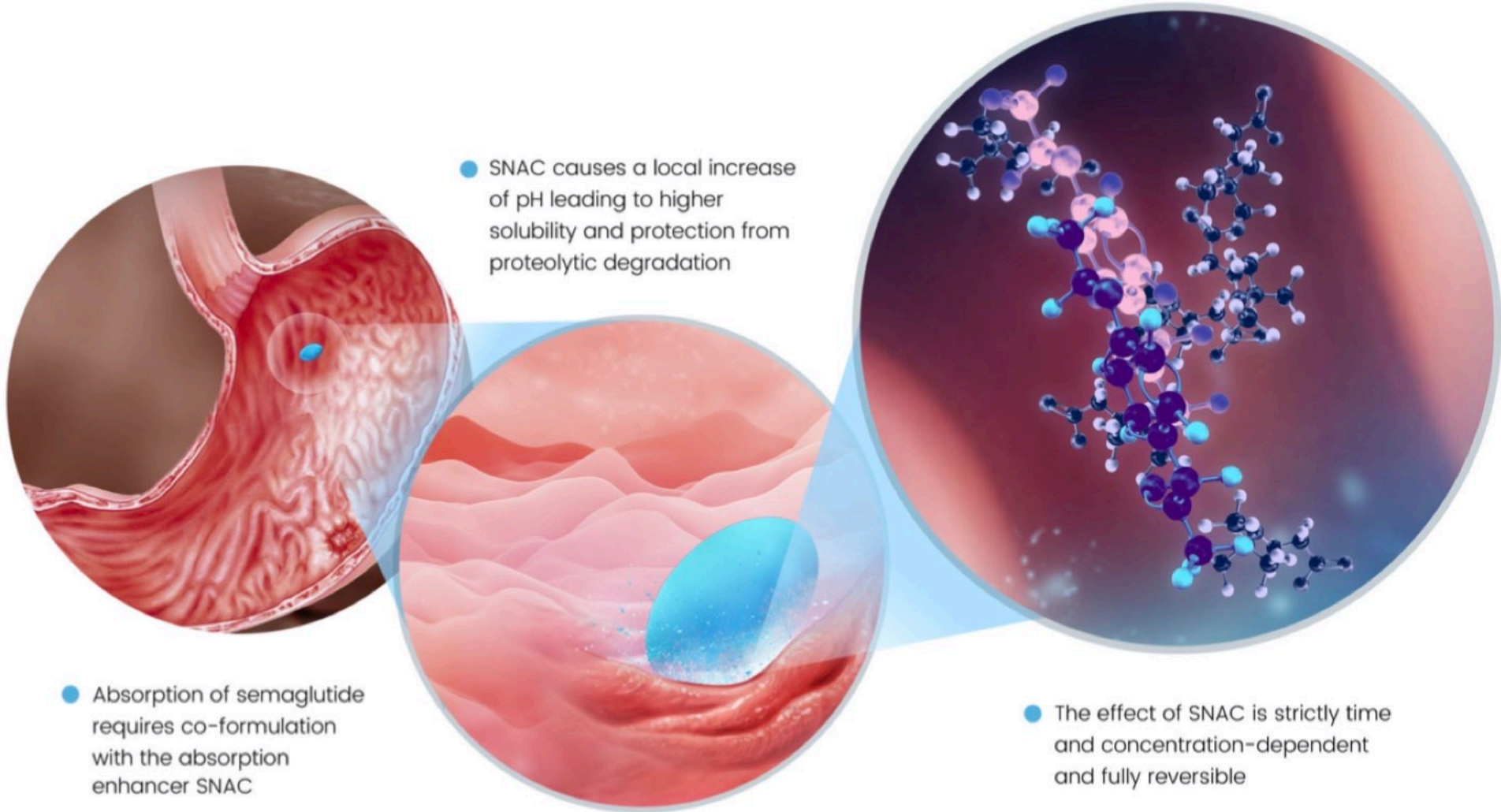
7 10 15 20 25 30 35

H_2N-HXEGTFTSDVSSYLEGQAAKEFIAWLVRGRG-COOH

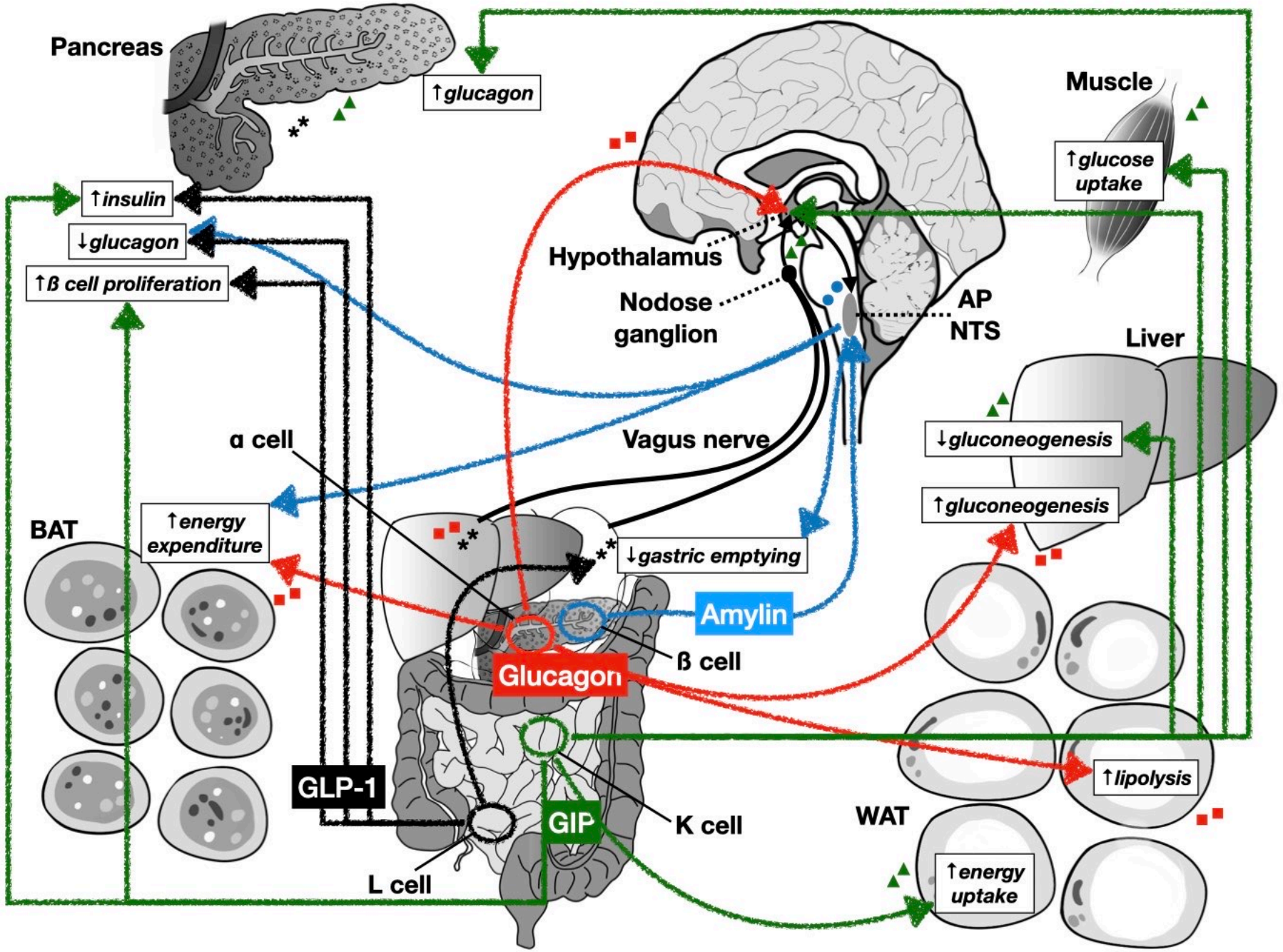
Peptide chain based on liraglutide discovery (human GLP-1)

Knudsen LB, Lau J. Front Endocrinol (Lausanne) 2019;10:155.

Mechanism of absorption of oral semaglutide



Diabetes, Obesity and Metabolism. 2020.


Pancreas
↑glucagon
↑insulin
↓glucagon
↑ß cell proliferation
Hypothalamus
Nodose ganglion
AP
NTS
Vagus nerve
Muscle
↑glucose uptake
Liver
↓gluconeogenesis
↑gluconeogenesis
α cell
BAT
↑energy expenditure
↓gastric emptying
Amylin
ß cell
Glucagon
GLP-1
GIP
K cell
L cell
↑lipolysis
WAT
↑energy uptake