The future for glycemic control and weight loss in T2D and obesity: Incretin-based dual-agonists and optimizing patient education

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Phase III data for tirzepatide: A dual GIP/GLP-1 RA

- The SURPASS clinical trials enrolled adults with T2D inadequately controlled by antihyperglycemic medication[1–4]
- Eligibility: HbA1c 7.0–10.5%; BMI ≥25 kg/m^2; stable weight[1–3]

Trial	Tirzepatide dose (mg)	Comparator	Duration (weeks)	HbA1c %-point change from BL (tirzepatide vs comparator)	Weight change from BL (15 mg dose vs comparator)
SURPASS-2[1] N=1,879	5, 10, 15	Semaglutide	40	**-2.0 to -2.3%** vs -1.9% (ETD, p<0.001 [10, 15 mg])	**-12.4 kg (-13.1%)** vs -6.2 kg (-6.7%) (ETD, p<0.001)
SURPASS-3[2] N=1,444	5, 10, 15	Insulin degludec	52	**-1.9 to -2.4%** vs -1.3% (ETD, all p<0.0001)	**-12.9 kg (-13.9%)** vs +2.3 kg (ETD, p<0.0001)
SURPASS-4[3] N=2,002 (Pts with T2D & ↑CV risk)	5, 10, 15	Insulin glargine	52	**-2.2 to -2.6%** vs -1.4% (ETD, all p<0.0001)	**-11.7 kg (-13.0%)** vs +1.9 kg (+2.2%) (ETD, p<0.0001)
SURPASS-5[4] N=475	5, 10, 15	Placebo	40	**-2.2 to -2.6%** vs -0.9% (ETD, all p<0.001)	**-10.9 kg (-11.3%)** vs +1.7 kg (+1.8%) (ETD, p<0.001)
	Both as add-on to insulin glargine				

BL, baseline; BMI, body mass index; CV, cardiovascular; ETD, estimated treatment difference; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1; HbA1c, glycated hemoglobin; pts, patients; RA, receptor agonist; T2D, type 2 diabetes.

1. Frías JP, et al. *N Engl J Med.* 2021;385:503–15; 2. Ludvik B, et al. *Lancet.* 2021;398:583–98; 3. Del Prato S, et al. *Lancet.* 2021;398:1811–24; 4. Dahl D, et al. *Diabetes.* 2021;70(Suppl_1):80-LB.

Phase I and II trials for BI 456906: A dual GLP-1/glucagon RA

- **In a phase I dose-escalation trial** in adults with obesity, BI 456906 was generally well tolerated and resulted in clinically relevant **body weight reductions** of up to **14**% (vs up to **1%** with placebo) after 16 weeks[1]
- **A phase II trial** is underway to compare efficacy of BI 456906 vs placebo and semaglutide in ~410 patients with obesity and T2D[2]
  Primary outcome: Absolute change in HbA1c from baseline to 16 weeks[2]

GLP-1, glucagon-like peptide-1; HbA1c, glycated hemoglobin; RA, receptor agonist; T2D, type 2 diabetes.

1. Arrubla J, et al. *Obesity.* 2021;29(Suppl. 2):47–197; 2. Clinicaltrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT04153929 (accessed 10 February 2022).

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Phase IIb data for cotadutide: A dual GLP-1/glucagon RA

Trial	Cotadutide dose (µg)	Comparator	Duration (weeks)	Co-primary outcome Cotadutide 100, 200 & 300 µg vs placebo	
				%-point change in HbA1c from BL at week 14	% change in body weight from BL at week 14
Phase IIb double-blind study (N=834) Adults with T2D inadequately controlled with metformin; **HbA1c** 7.0–10.5%; **BMI** ≥25 kg/m^2	100, 200 or 300 (double-blind)	Placebo or liraglutide 1.8 mg (open-label)	54	**-1.1 to -1.3** vs -0.23 (all p<0.001)	**-3.0 to -5.0** vs -0.74 (all p<0.001)

- Cotadutide also significantly decreased HbA1c and body weight at week 54 vs placebo (all p<0.001)

BL, baseline; BMI, body mass index; GLP-1, glucagon-like peptide-1; HbA1c, glycated hemoglobin; RA, receptor agonist; T2D, type 2 diabetes.

Nahra R, et al. *Diabetes Care.* 2021;44:1433–42.

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