

**CONGRESSO SID-AMD UMBRIA
UMBRIA DIABETE 2024 RITORNO AL FUTURO
Sangallo Palace Hotel – Perugia
22-23 Novembre 2024**

Cosa ci aspetta...Farmaci iniettivi

Dr. Alessio Mazzieri
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Il sottoscritto Dr. Alessio Mazzieri dichiara di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

Novo-Nordisk
Eli-Lilly
Boehringer Ingelheim
Astrazeneca
MSD
Guidotti
Sanofi
Bruno Farmaceutici

Dichiara altresì il proprio impegno ad astenersi, nell'ambito dell'evento, dal nominare, in qualsivoglia modo o forma, aziende farmaceutiche e/o denominazione commerciale e di non fare pubblicità di qualsiasi tipo relativamente a specifici prodotti di interesse sanitario (farmaci, strumenti, dispositivi medico-chirurgici, ecc.).

Kai

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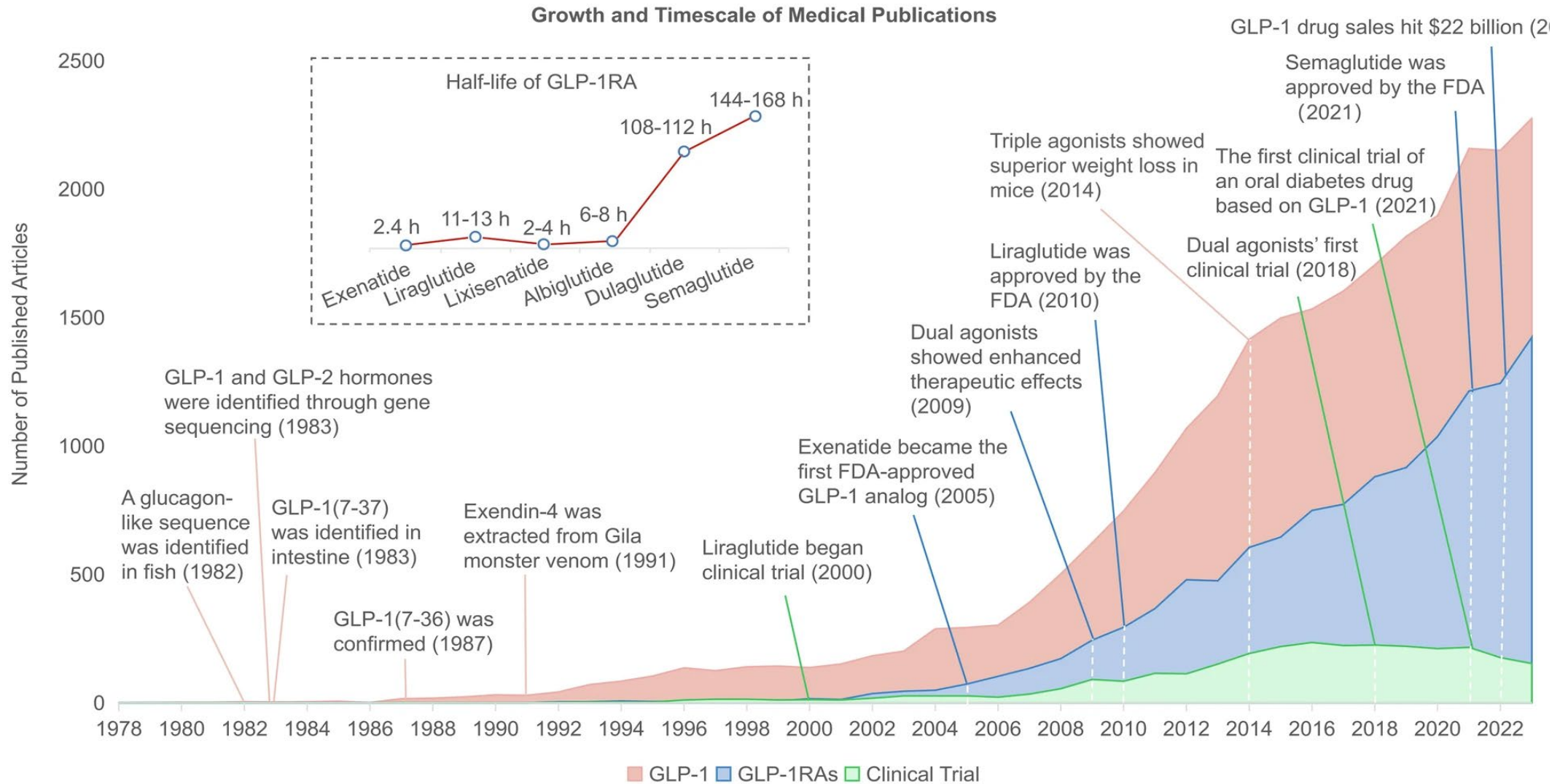
Cambiamento

Zen

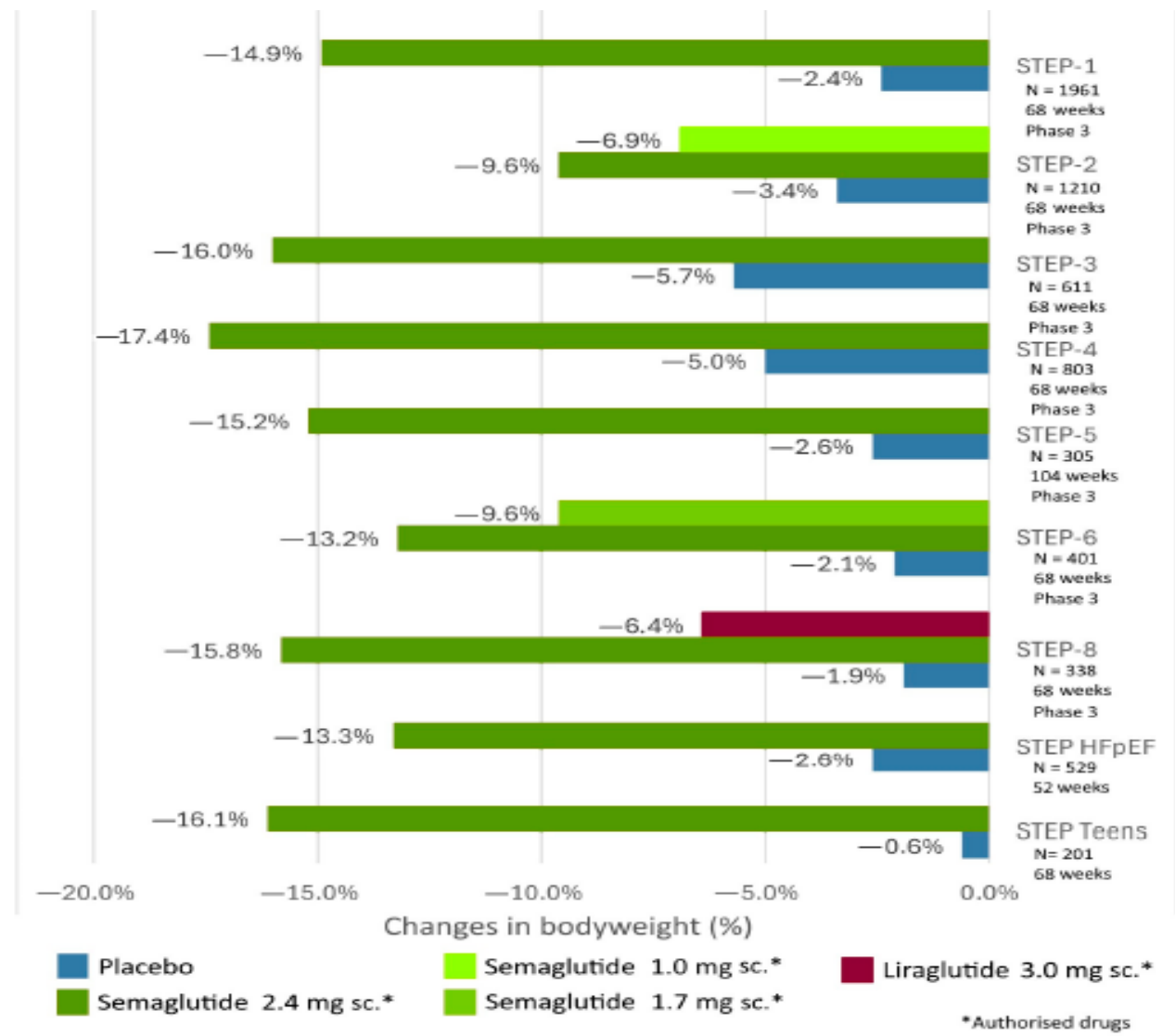
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Miglioramento

Timeline delle incretine

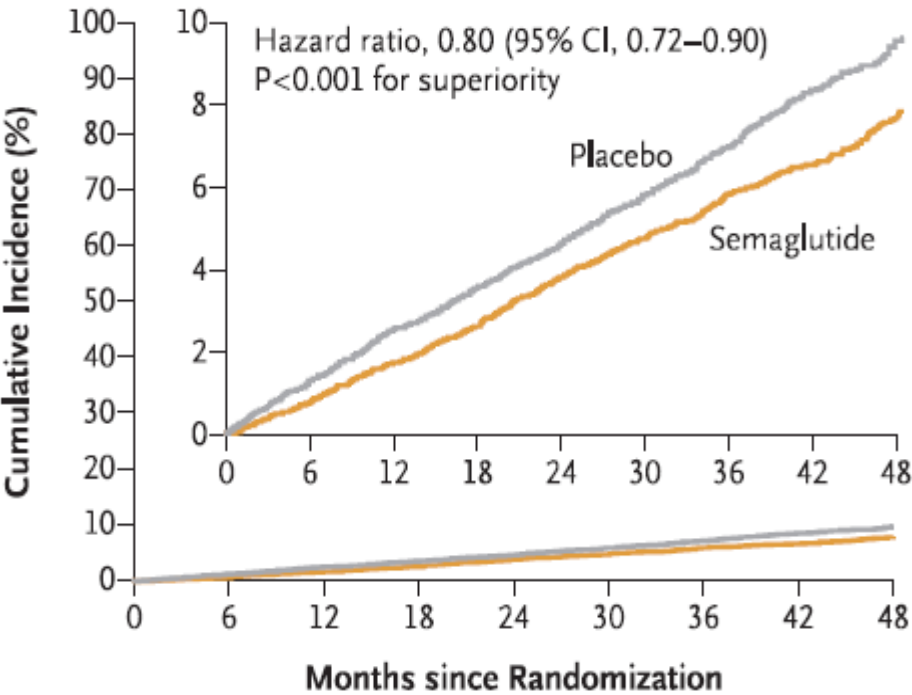


L'impatto sul peso corporeo di semaglutide 2.4 mg/settimana in pazienti con sovrappeso/obesità



La protezione cardiovascolare di semaglutide 2.4 mg/settimana in pazienti con sovrappeso/obesità

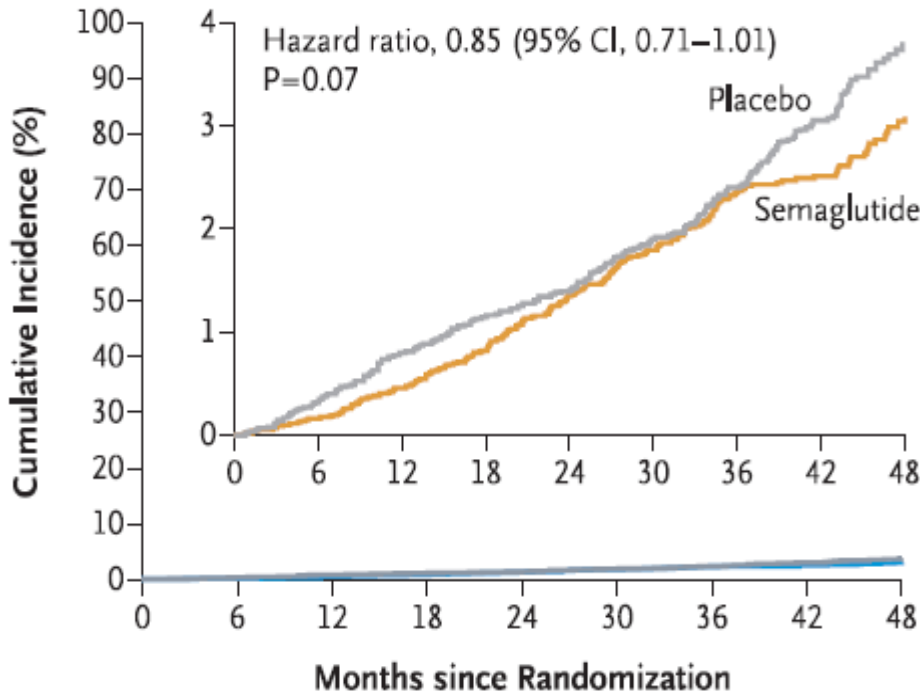
A Primary Cardiovascular Composite End Point



No. at Risk

Placebo	8801	8652	8487	8326	8164	7101	5660	4015	1672
Semaglutide	8803	8695	8561	8427	8254	7229	5777	4126	1734

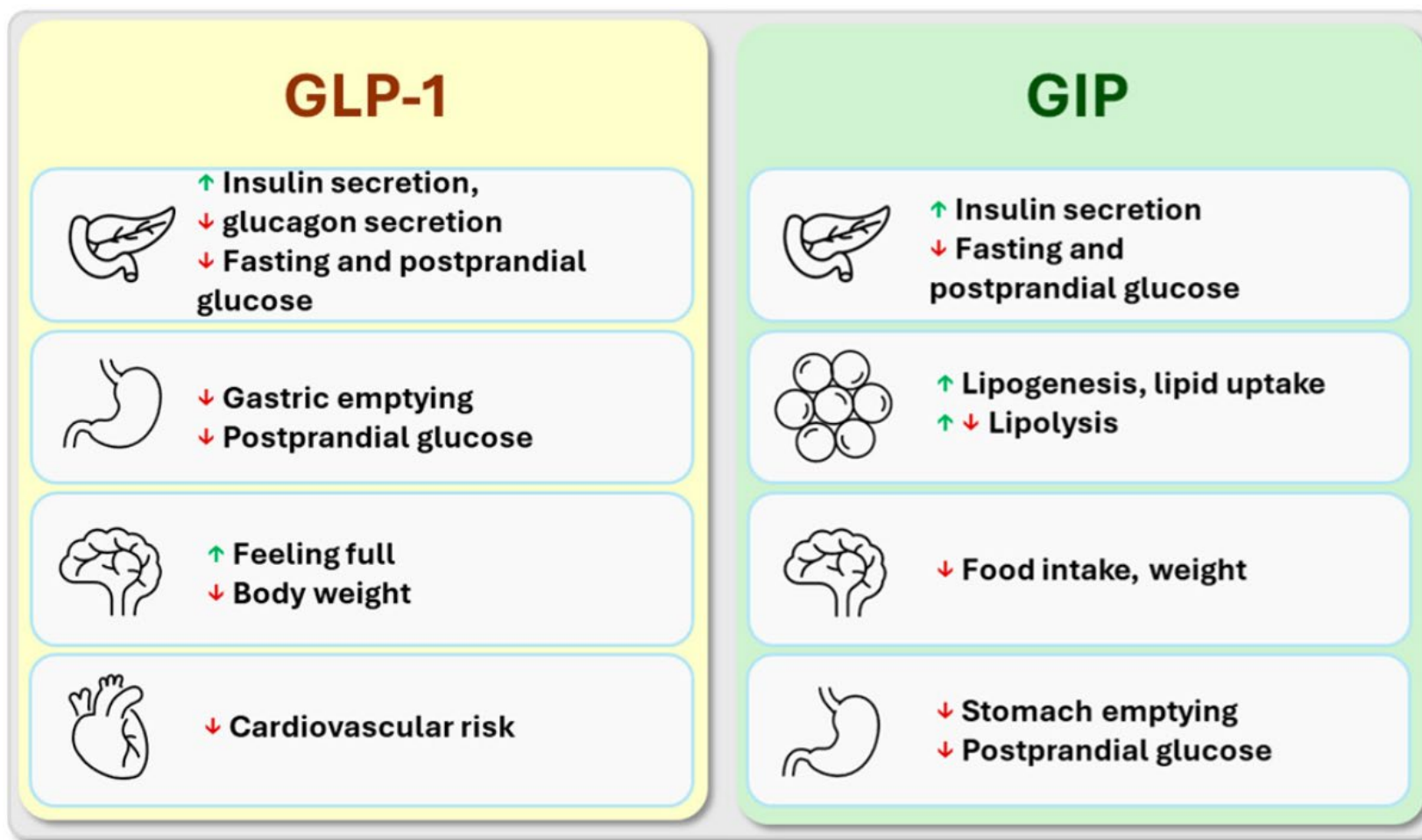
B Death from Cardiovascular Causes



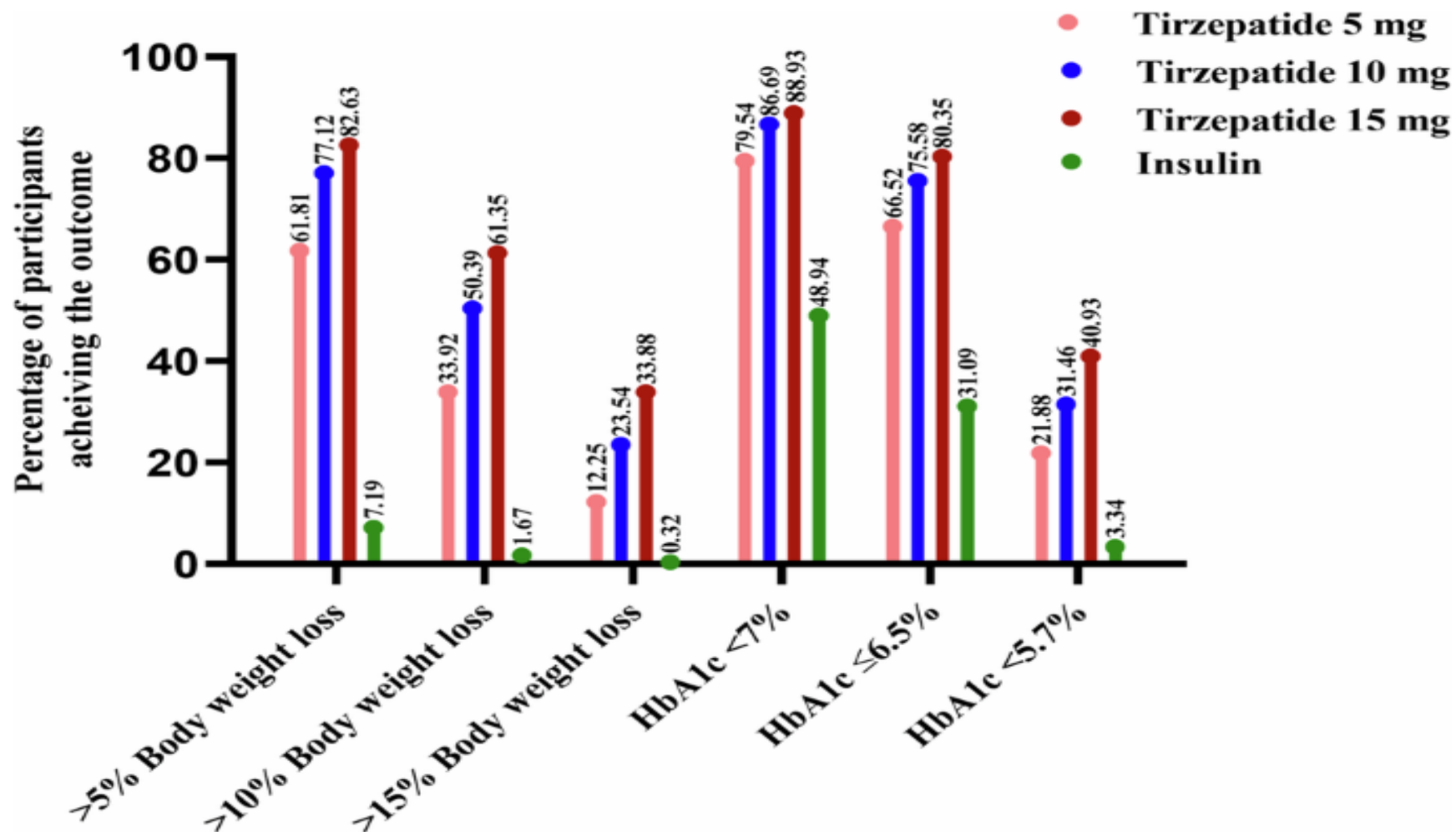
No. at Risk

Placebo	8801	8733	8634	8528	8430	7395	5938	4250	1793
Semaglutide	8803	8748	8673	8584	8465	7452	5988	4315	1832

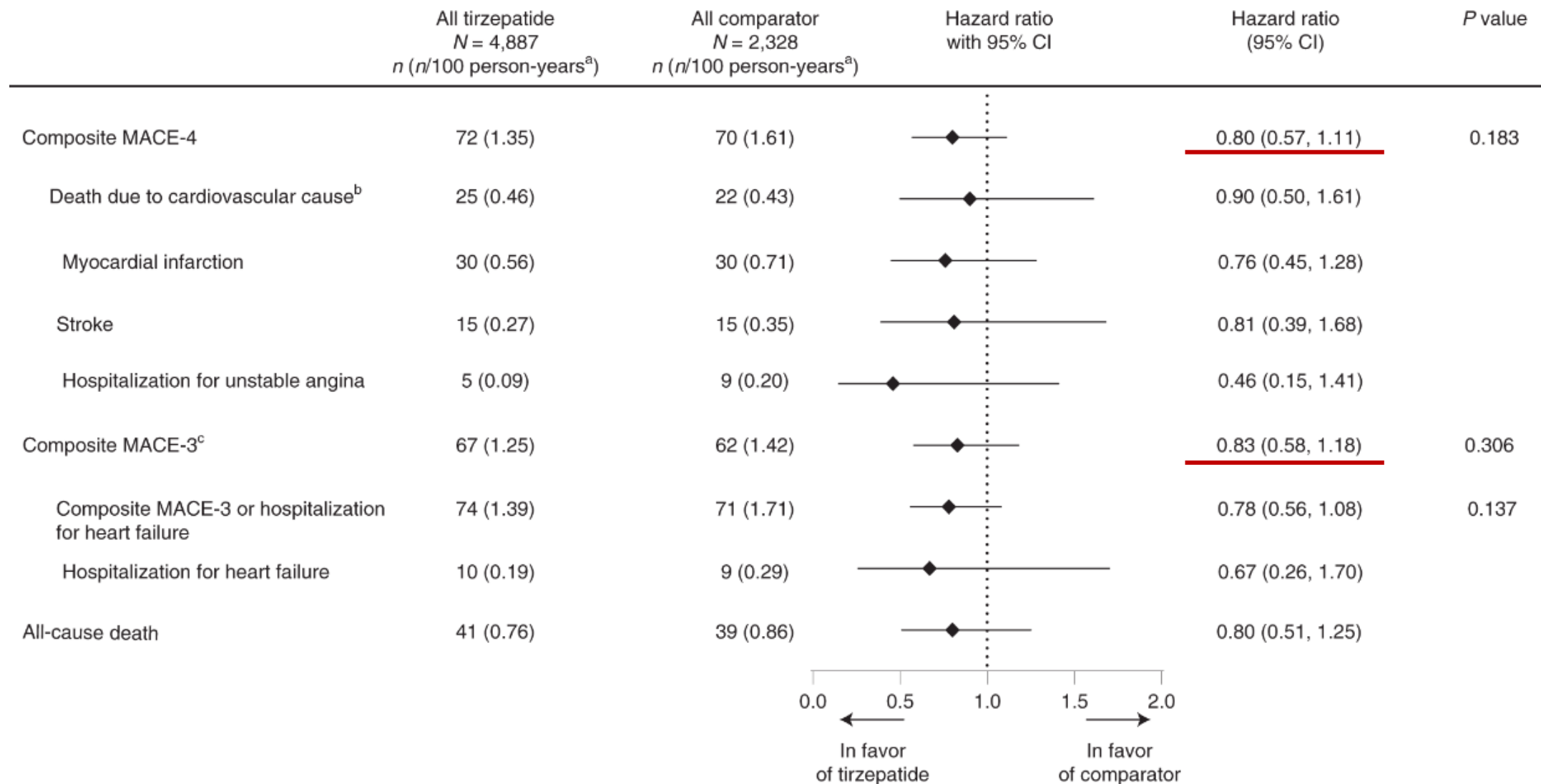
Il razionale del doppio agonista: GLP-1 e GIP



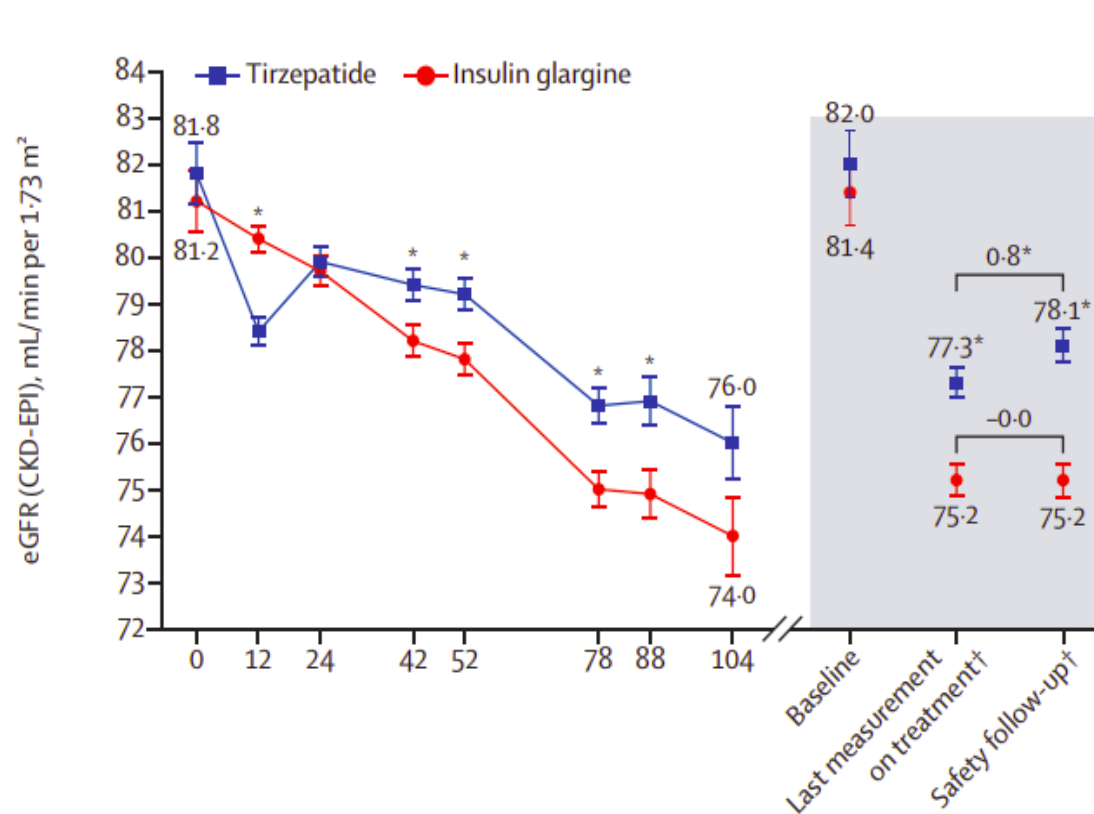
L'effetto di Tirzepatide su peso corporeo e glicata in pazienti con diabete di tipo 2



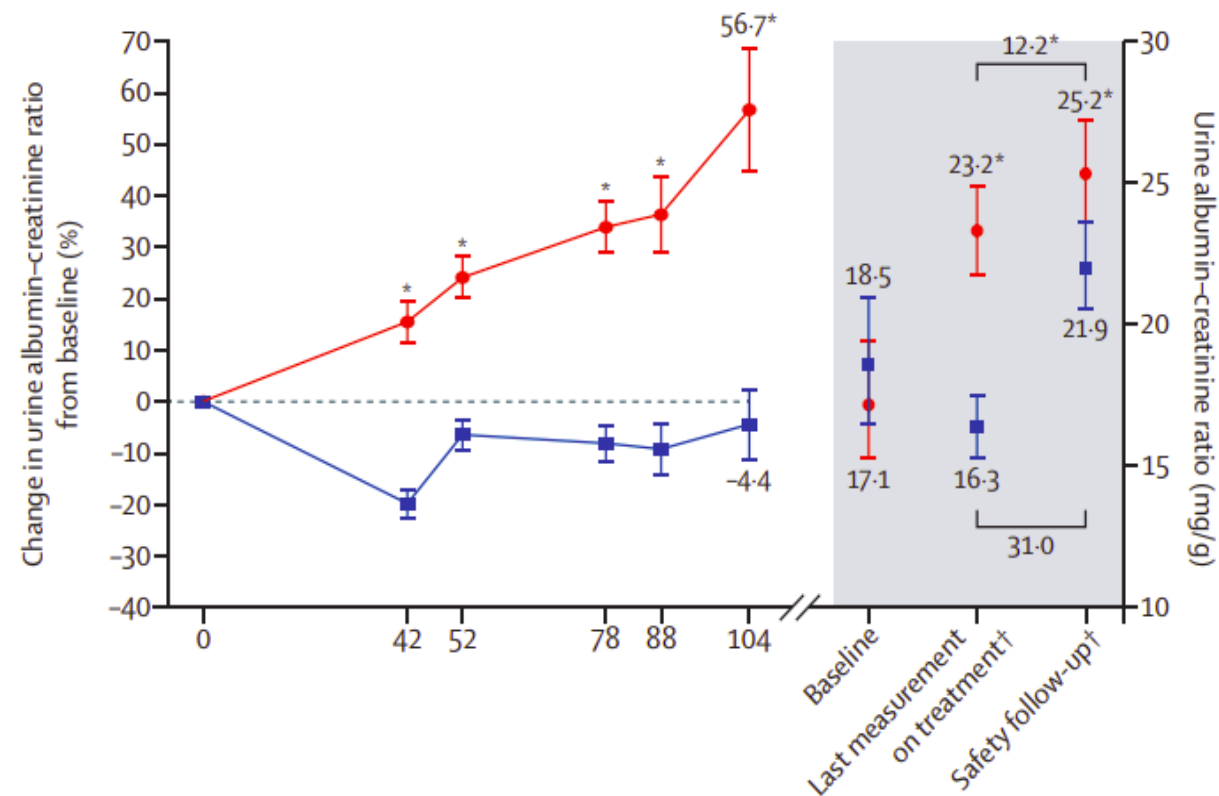
L'effetto cardioprotettivo di Tirzepatide



L'effetto nefroprotettivo di Tirzepatide

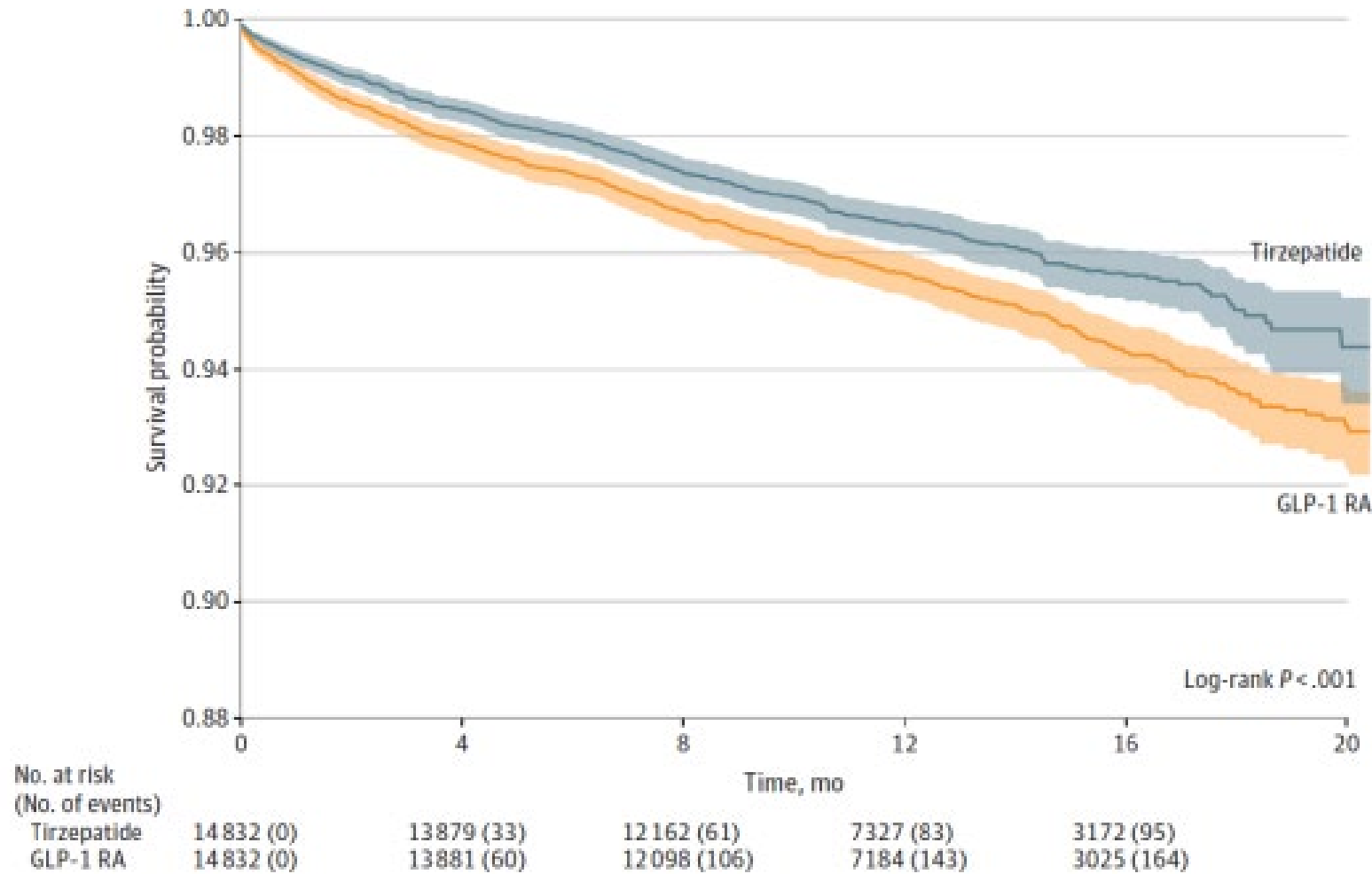


Number at risk											
Tirzepatide	949	934	852	866	857	581	286	106	866	866	866
Insulin glargine	969	957	864	870	886	590	291	95	847	847	847



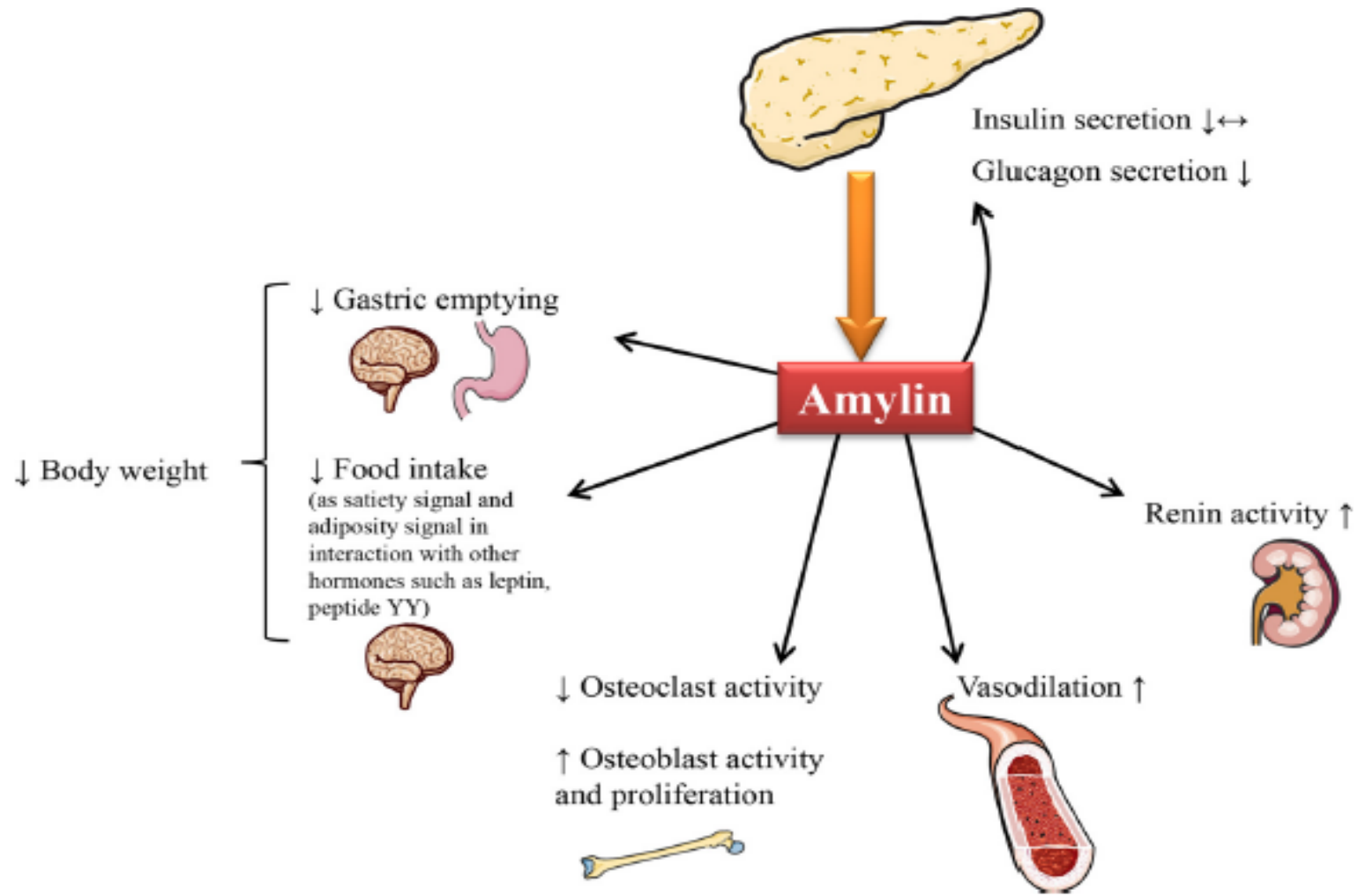
Number at risk											
Tirzepatide	870	838	833	567	279	102	816	816	816		
Insulin glargine	897	847	859	577	279	90	809	809	809		

La cardionefroprotezione di Tirzepatide da dati real-world

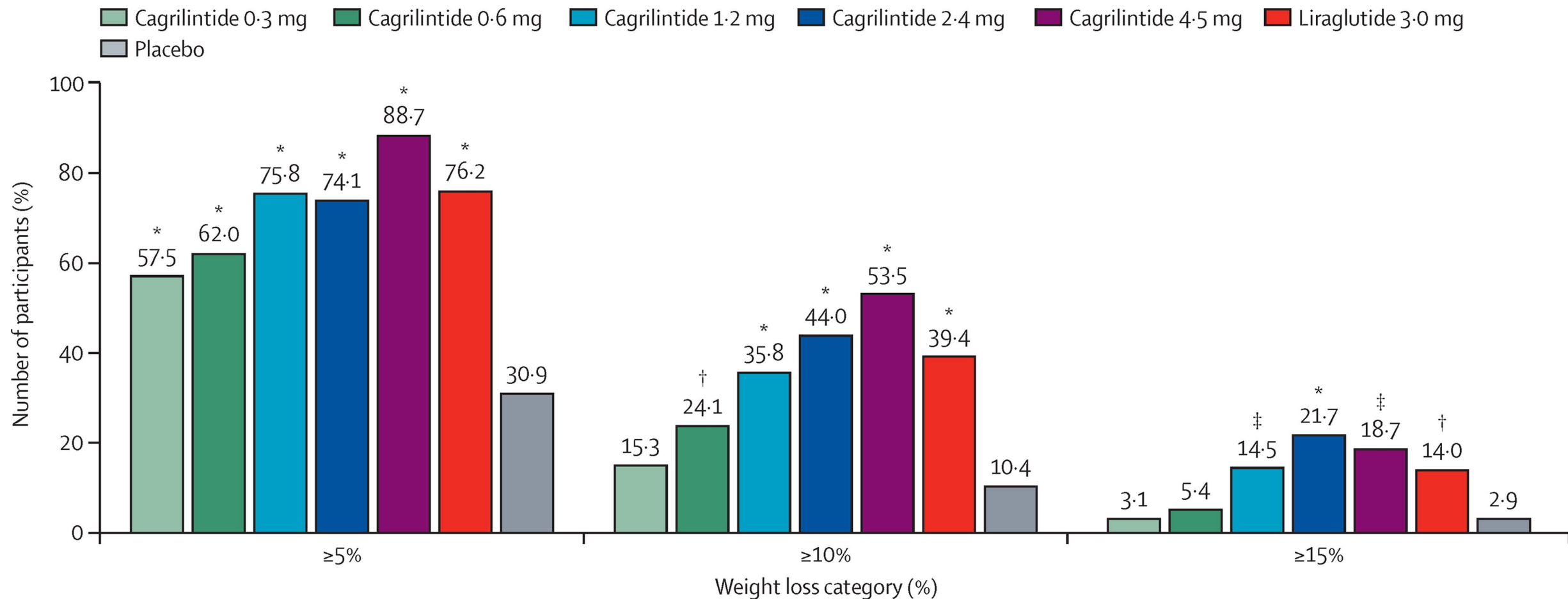


- mortalità per tutte le cause: -42%
- di MACE -20%
- di MACE e mortalità per tutte le cause -24%
- di eventi renali -48%

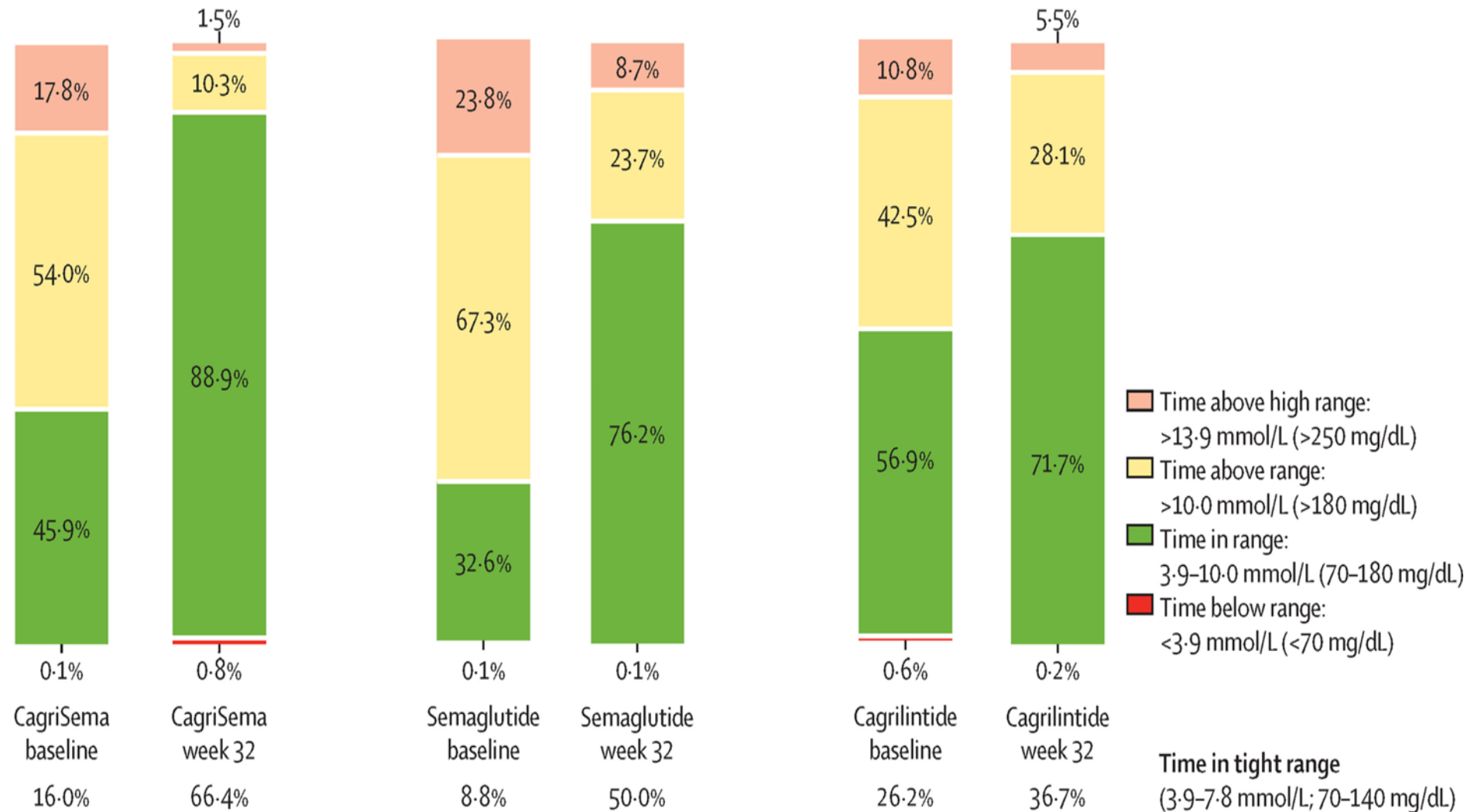
Il ruolo dell'amilina



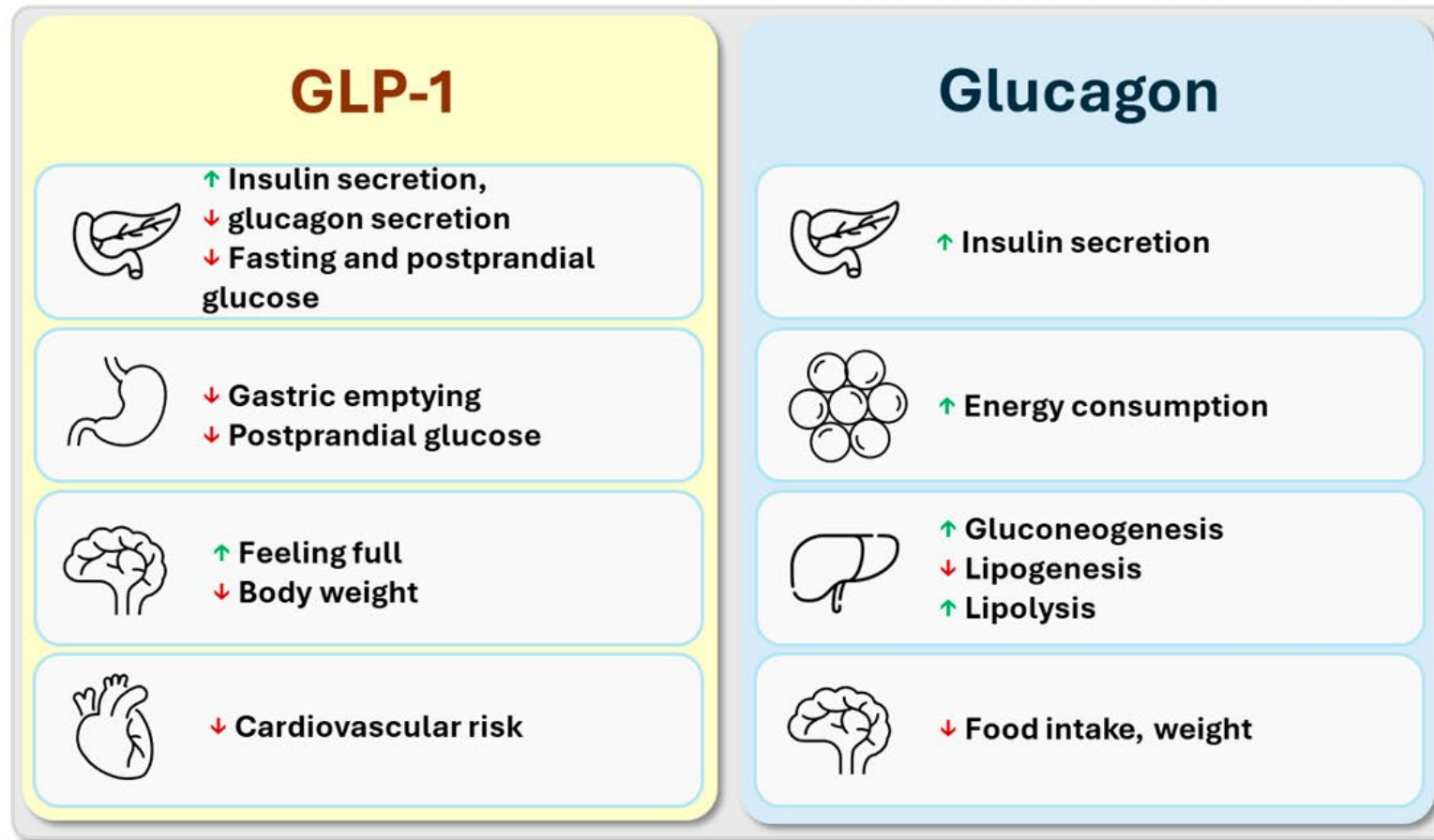
L'impatto di Cagrilintide in pazienti con sovrappeso/obesità



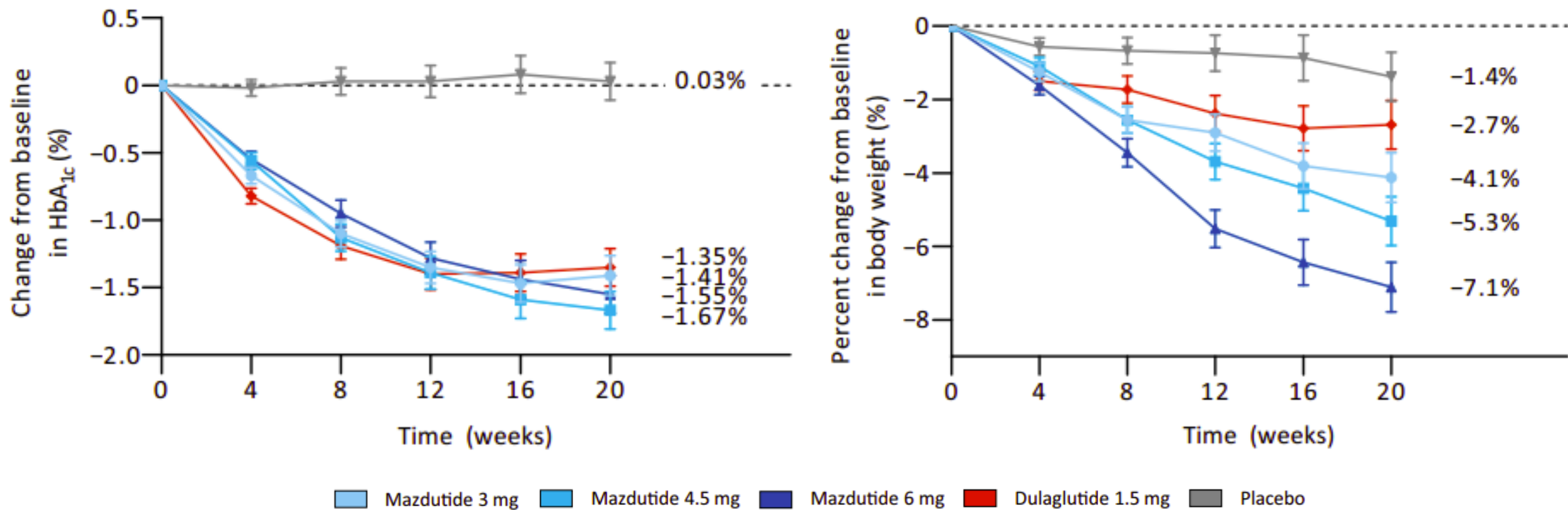
L'effetto di Cagrilintide-Semaglutide in pazienti con diabete di tipo 2



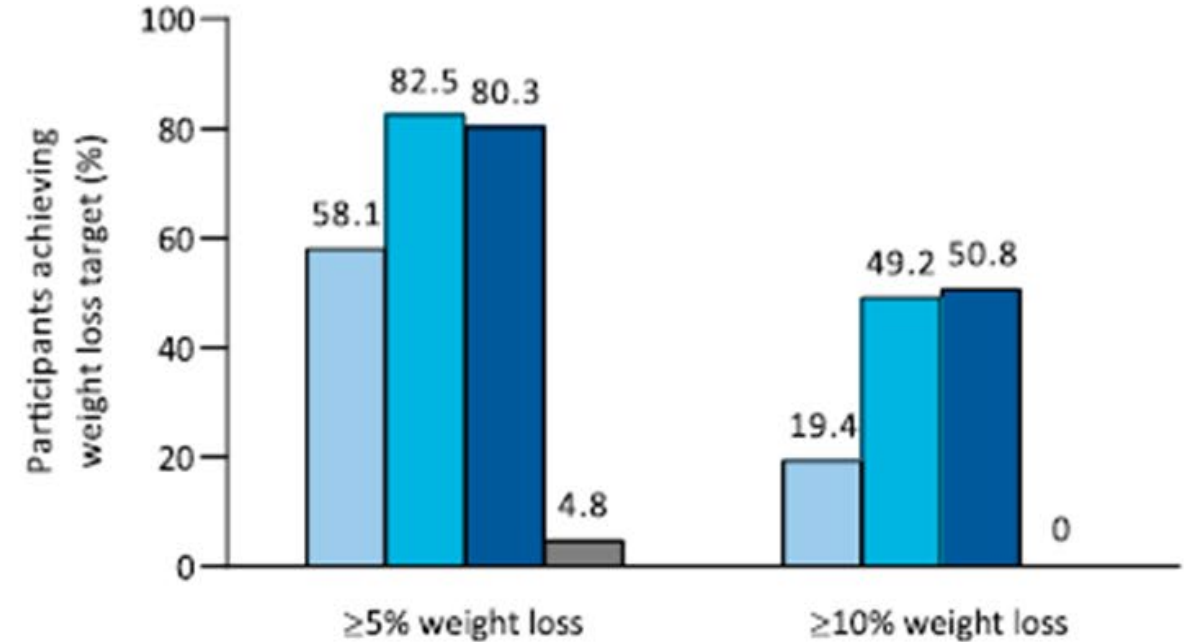
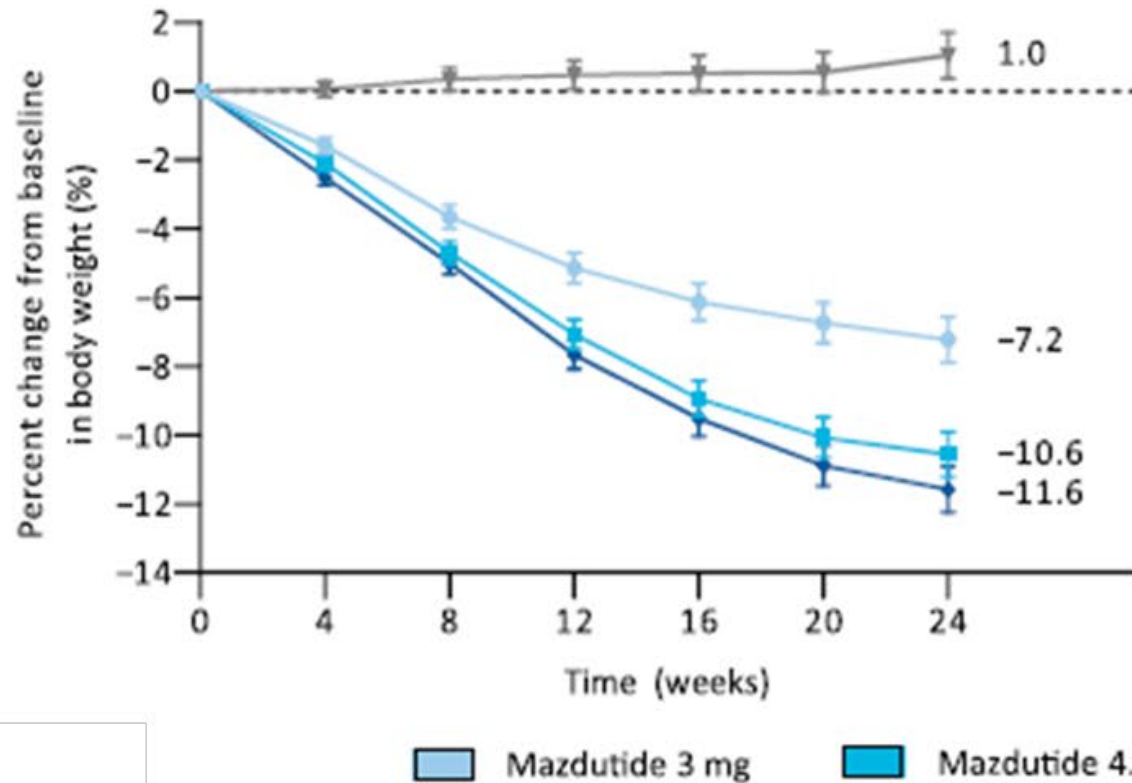
Il razionale del doppio agonista: GLP-1 e Glucagone



L'effetto di Mazdutide in pazienti con diabete di tipo 2

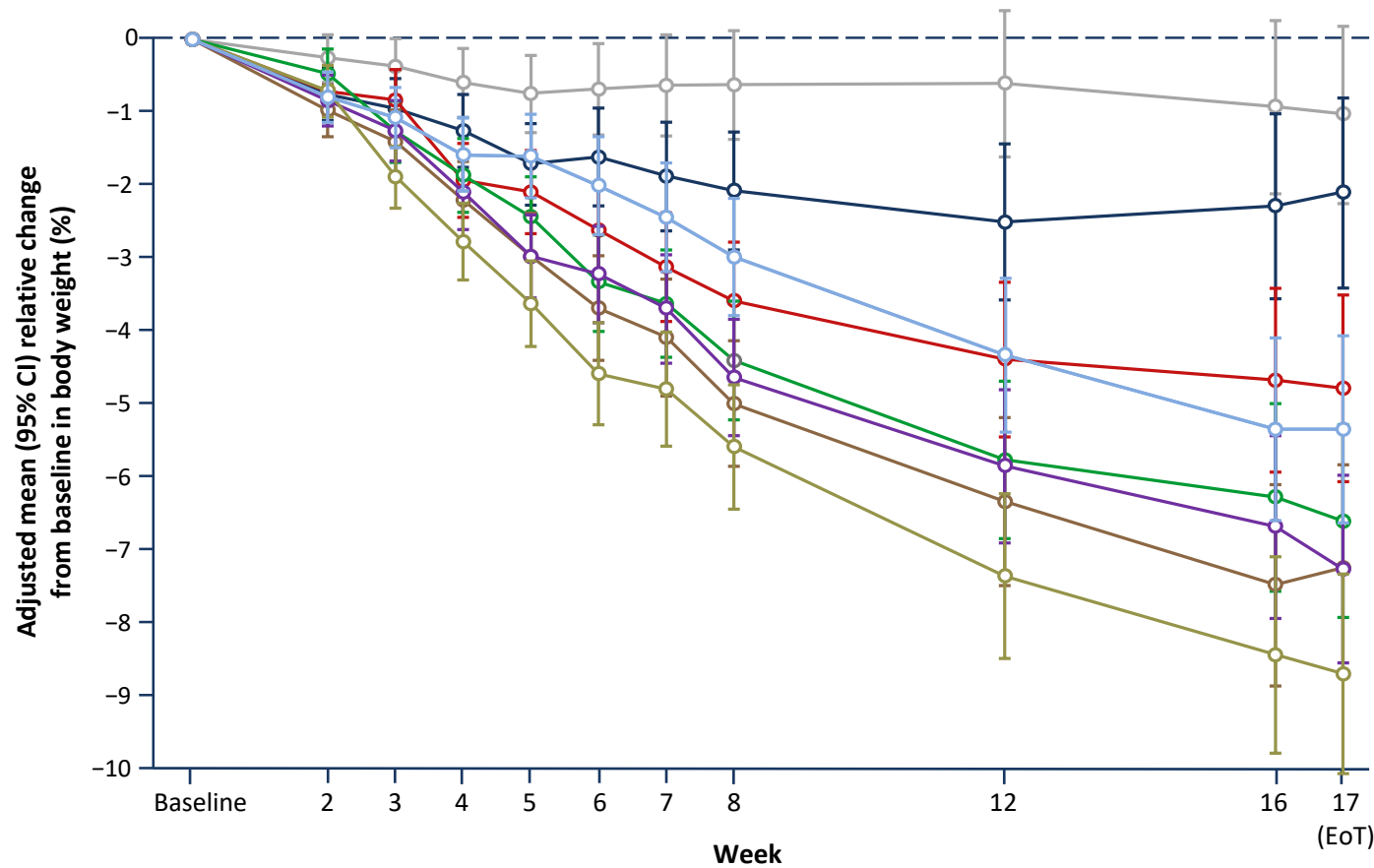


L'effetto di Mazdutide in pazienti con sovrappeso/obesità



L'effetto di Survodutide in pazienti con diabete di tipo 2

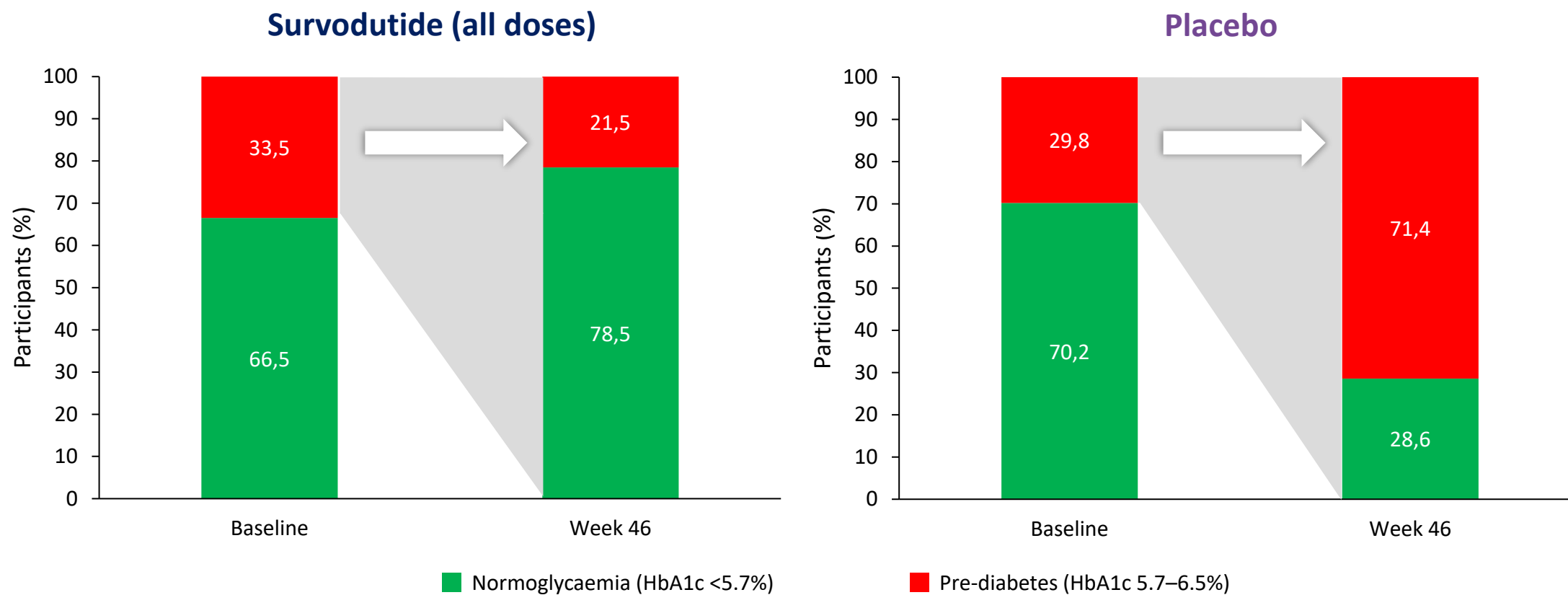
Mean baseline body weight ($\pm$ SD): 96.6 ± 21.6 kg



Adjusted mean relative change in body weight after 16 weeks of treatment (%)

Placebo	NR
Survodutide 0.3 mg QW (n=41)	NR
Survodutide 0.9 mg QW	NR
Survodutide 1.8 mg QW (n=36)	-6.6
Survodutide 2.7 mg QW	NR
Survodutide 1.2 mg BIW*	NR
Survodutide 1.8 mg BIW* (n=37)	-8.7
Semaglutide 1.0 mg QW† (n=45)	-5.3

L'effetto di Survodutide in pazienti con sovrappeso/obesità



Il razionale del triplo agonista: GLP-1, GIP, Glucagone

GLP-1



↑ Insulin secretion,
↓ glucagon secretion
↓ Fasting and postprandial
glucose



↓ Gastric emptying
↓ Postprandial glucose



↑ Feeling full
↓ Body weight



↓ Cardiovascular risk

GIP



↑ Insulin secretion
↓ Fasting and
postprandial glucose



↑ Lipogenesis, lipid uptake
↑ ↓ Lipolysis



↓ Food intake, weight



↓ Stomach emptying
↓ Postprandial glucose

Glucagon



↑ Insulin secretion



↑ Energy consumption

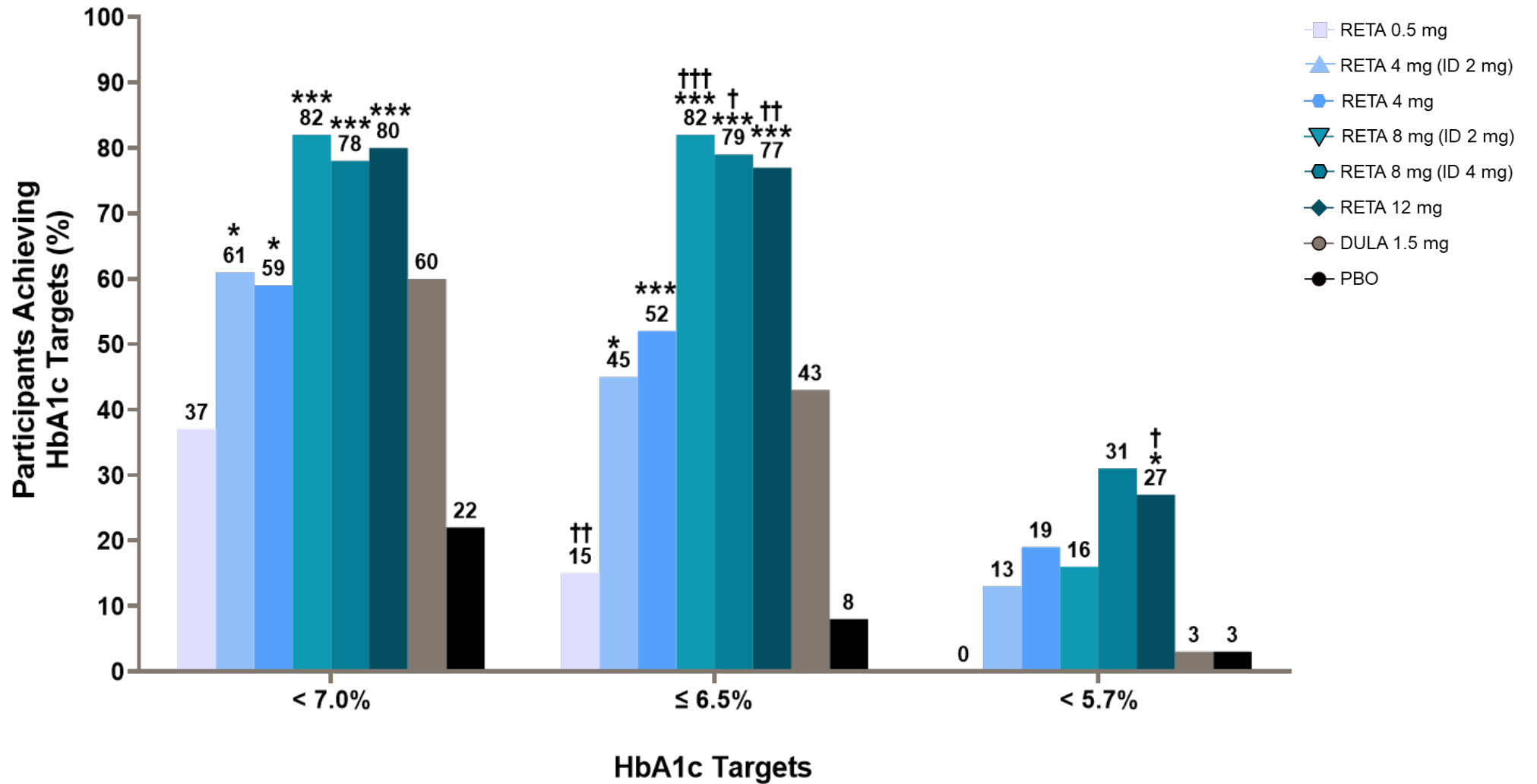


↑ Gluconeogenesis
↓ Lipogenesis
↑ Lipolysis



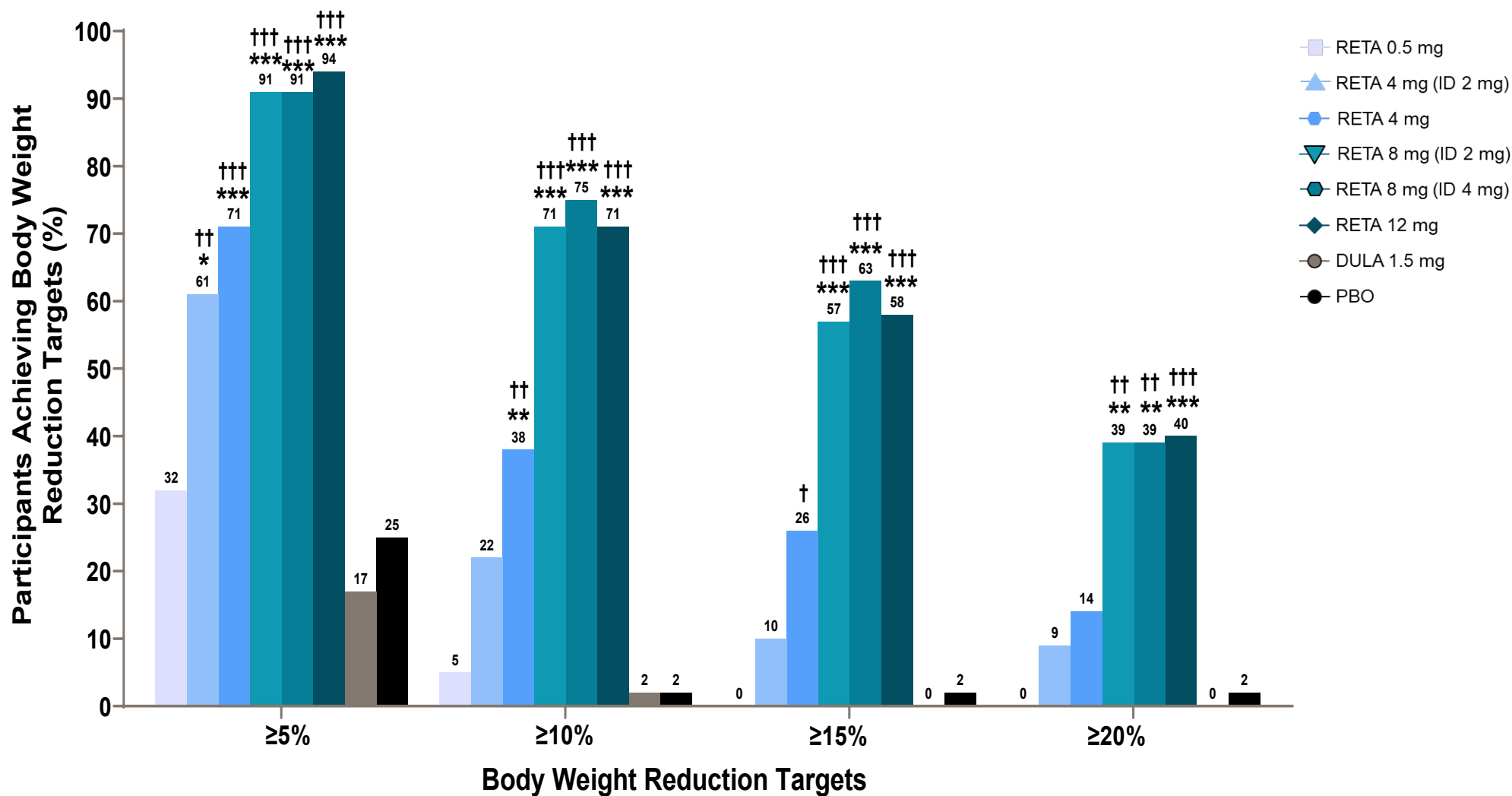
↓ Food intake, weight

L'impatto di Retatrutide sulla glicata in pazienti con diabete di tipo 2



Rosenstock, Julio et al. "Retatrutide, a GIP, GLP-1 and glucagon receptor agonist, for people with type 2 diabetes: a randomised, double-blind, placebo and active-controlled, parallel-group, phase 2 trial conducted in the USA." *Lancet (London, England)* vol. 402,10401 (2023): 529-544. doi:10.1016/S0140-6736(23)01053-X

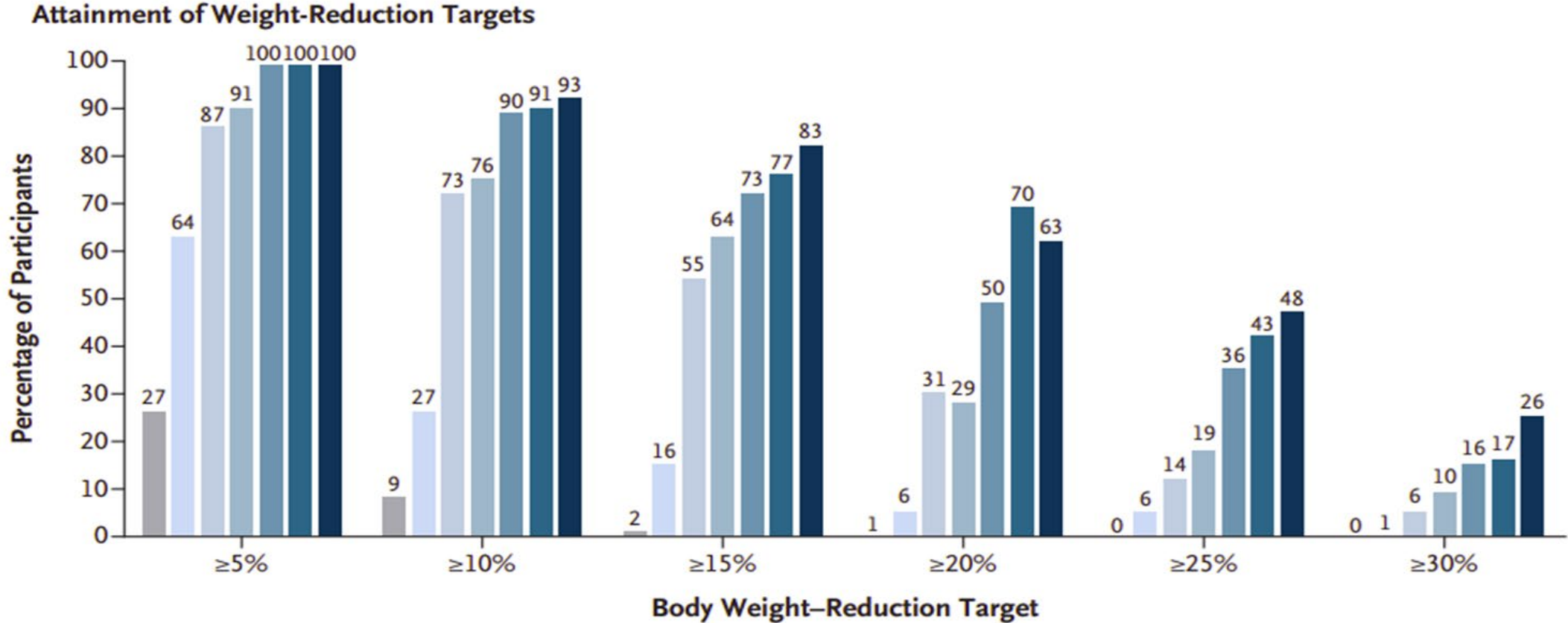
L'impatto di Retatrutide sul peso corporeo in pazienti con diabete di tipo 2



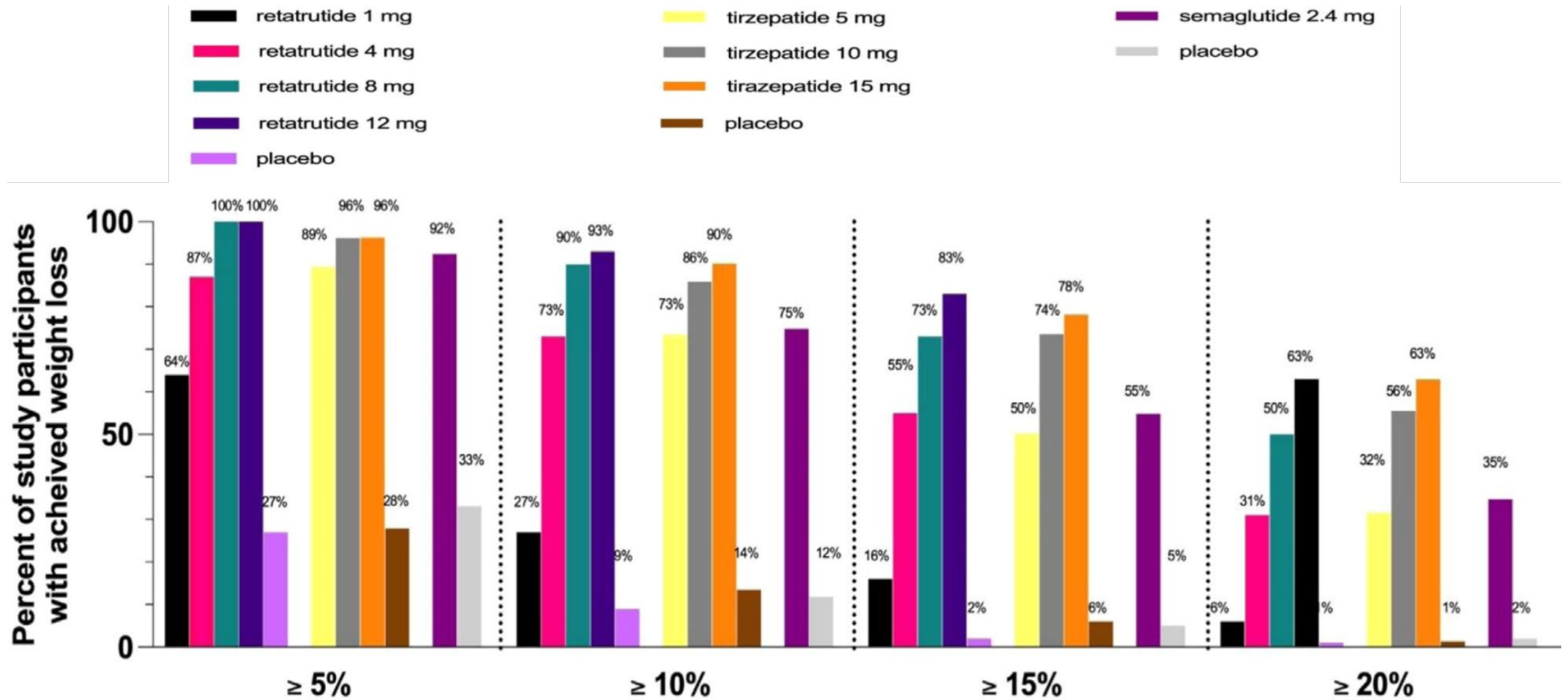
Rosenstock, Julio et al. "Retatrutide, a GIP, GLP-1 and glucagon receptor agonist, for people with type 2 diabetes: a randomised, double-blind, placebo and active-controlled, parallel-group, phase 2 trial conducted in the USA." *Lancet (London, England)* vol. 402,10401 (2023): 529-544. doi:10.1016/S0140-6736(23)01053-X

L'impatto di Retatrutide sul peso corporeo in pazienti con sovrappeso/obesità

■ Placebo ■ Retatrutide, 1 mg ■ Retatrutide, 4 mg (ID, 2 mg) ■ Retatrutide, 4 mg (ID, 4 mg) ■ Retatrutide, 8 mg (ID, 2 mg) ■ Retatrutide, 8 mg (ID, 4 mg) ■ Retatrutide, 12 mg (ID, 2 mg)



Le armi per la diabetità a confronto



Dolenti note...ma non troppo

Medication	Semaglutide [21] 50 mg ^A	Tirzepatide [46] 5, 10, 15 mg ^A	Orforglipron [25] 12, 24, 36, 45 mg ^A	Cagrilintide [87] 0.3, 0.6, 1.2, 2.4, 4.5 mg ^A	Survodutide* [68] 0.6, 2.4, 3.6, 4.8 mg ^{A,B}	Efinopegdutide [77] 5, 7.4, 10 mg ^B	Mazdutide [70] 3, 4.5, 6.0 mg ^B	Mazdutide* [71] 9 mg ^C	Pemvidutide (ALT-801)* [74] 1.2, 1.8, 2.4 mg ^A	Retatrutide [81] 1, 4, 8, 12 mg ^A	CagriSema [76] (0.16, 0.3, 0.6, 1.2, 2.4, 4.5 mg/ 2.4 mg) ^B
AE leading to medication discontinuation (%)	6% vs. 4%	4–7% vs. 3%	10–21% vs. 2%	1–6% vs. (i) 7% (ii) 3%	20–29% vs. 4%	20–34% vs. (i) 18% (ii) 3%	0–2% vs. 0%	0% vs. 0%	5–20% vs. 6%	6–16% vs. 8%	0–8% vs. 0%
Nausea (%)	52% vs. 15%	25–33% vs. 10%	37–58% vs. 10%	20–47% vs. (i) 39% (ii) 18%	34–65% vs. 20%	51–68% vs. (i) 40% (ii) 7%	21–41% vs. 5%	13–63% vs. 13%	26–60% vs. 11%	14–60% vs. 11%	50–83% vs. 33%
Vomiting (%)	24% vs. 4%	8–12% vs. 2%	14–32% vs. 6%	6–8% vs. (i) 20% (ii) 3%	9–35% vs. 5%	20–55% vs. (i) 17% (ii) 0%	13–28% vs. 3%	38% vs. 0%	6–28% vs. 3%	3–26% vs. 1%	0–75% vs. 13%
Diarrhoea (%)	27% vs. 17%	19–23% vs. 7%	3–36% vs. 10%	7–18% vs. (i) 18% (ii) 9%	18–28% vs. 10%	14–20% vs. (i) 23% (ii) 5%	19–31% vs. 15%	25–50% vs. 50%	8–19% vs. 5%	9–20% vs. 11%	0–17% vs. 38%
Constipation (%)	28% vs. 15%	12–17% vs. 6%	13–32% vs. 6%	8–21% vs. (i) 26% (ii) 7%	12–26% vs. 5%	12–18% vs. (i) 17% (ii) 5%	NA	NA	13–23% vs. 5%	6–16% vs. 3%	NA

