

TIRZEPATIDE

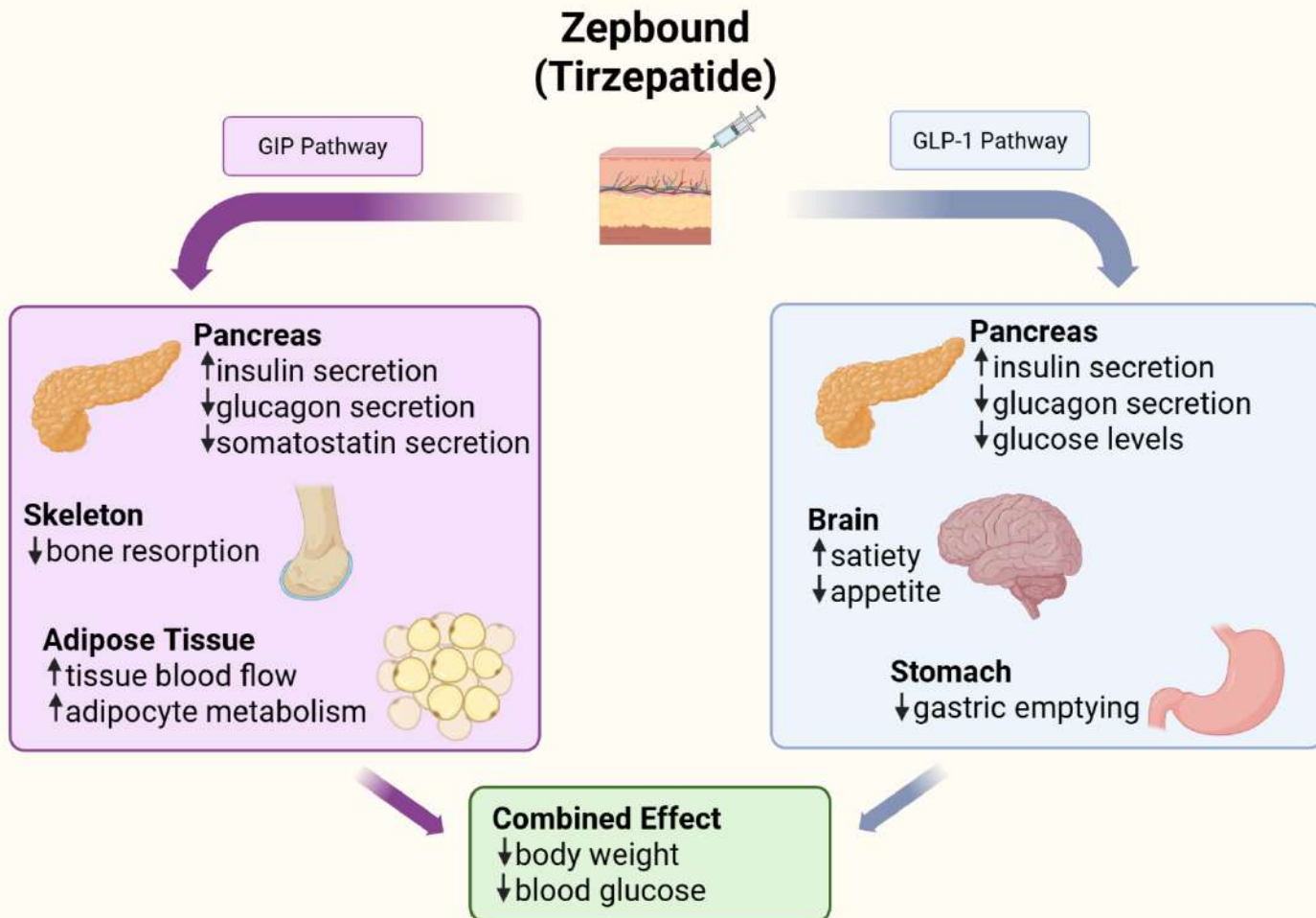
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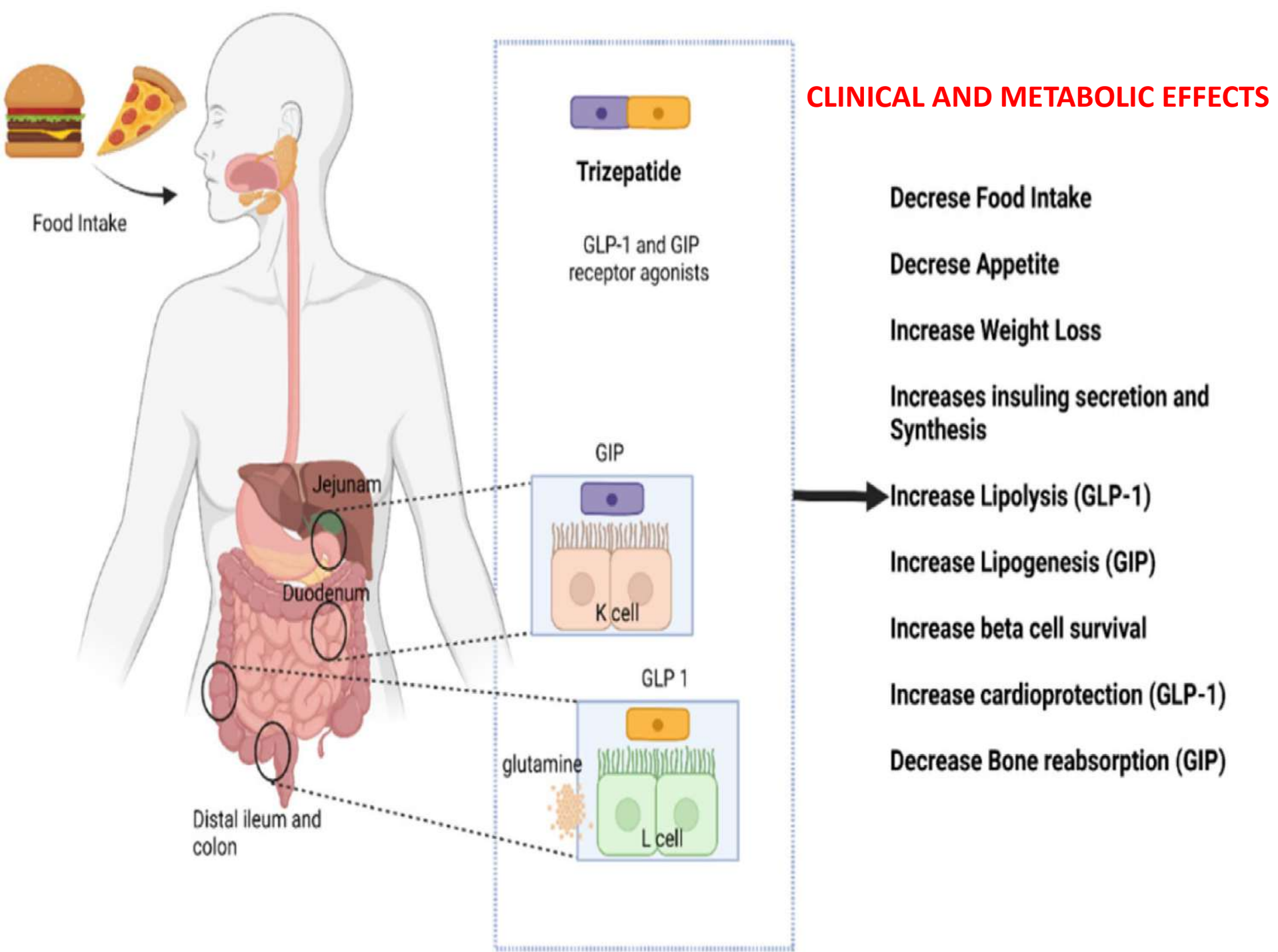
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INTRODUCTION

- Tirzepatide is a **dual agonist** for the glucagon-like peptide-1 (**GLP-1**) and glucose-dependent insulinotropic polypeptide (**GIP**) receptors.
- Administered **once weekly via subcutaneous** (SC) injection with incremental dosage adjustments.[2.5 /5/7.5/10/12.5/15 MG S.C]
- Tirzepatide is contraindicated in patients with **medullary thyroid cancer , MEN -2 [multiple endocrine neoplastic syndrome type-2] ,** pancreatitis and hypersensitivity reactions.
- The most common adverse events are **gastrointestinal**, including nausea, diarrhea, vomiting, constipation, abdominal pain, and decreased appetite. Other effects include fatigue, indigestion, and injection site reactions.


MECHANISM OF ACTION







Kidney Parameters with Tirzepatide in Obesity with or without Type 2 Diabetes

SURMOUNT-1 (N=2539)

 Overweight/ obese participants

 Without type 2 diabetes


 Tirzepatide 5 mg, 10 mg, and 15 mg or placebo

SURMOUNT-2 (N=938)

 Participants with type 2 diabetes

 Tirzepatide 10 mg and 15 mg or placebo

 **Change from baseline to week 72 for urine albumin-to-creatinine ratio (UACR)**

 **eGFR assessed using**
Creatinine-based eGFR (Cr-eGFR)
Cystatin-C-based-eGFR (Cys-C-eGFR)
Creatinine-cystatin-C-based-eGFR (Cr-Cys-C-eGFR)



Change in UACR from baseline to week 72

	SURMOUNT-1	SURMOUNT-2
Median baseline UACR (mg/g)	6.0 [4.0, 11.0]	13.0 [6.0, 35.1]
Estimated UACR difference at week 72 (vs. placebo)	-8.4% [-14.7 to -1.6]	-31.1% [-40.9 to -19.7]
UACR change among participants with baseline UACR ≥ 30 mg/g with placebo-corrected changes from baseline at week 72	-42.3% [-60.8 to -15.0]	-55.2% [-68.5 to -36.4]



eGFR assessment

	SURMOUNT-1	SURMOUNT-2
Mean difference in eGFR vs. placebo at week 72 (ml/min per 1.73 m ²)	+3.2 [2.1-4.3] Cys-C-eGFR +1.9 [0.9-2.0] Cr-Cys-C-eGFR	Increases seen in both groups for Cys-C or Cr-Cys-C-eGFR with no between-group differences

Conclusions: In participants with obesity/overweight with or without type 2 diabetes, tirzepatide was associated with reduced albuminuria without adverse changes in eGFR.

Hiddo J.L. Heerspink, Allon N. Friedman, Petter Bjornstad, et al. Kidney Parameters with Tirzepatide in Obesity with or without Type 2 Diabetes. JASN doi: 10.1681/ASN.0000000764. **Visual Abstract by Michelle Lim, MBChB, FRCPE**

Table 1. The SURPASS trials

	Comparator	Population	Duration	Outcome
SURPASS 1	Placebo	Inadequately controlled with diet and exercise alone and who were naive to injectable diabetes therapy. HbA1c 7-9%	40 weeks	HbA1c ↓ -1.87 to -2.07% Weight loss -7 to -9.5 kg and continuing
SURPASS 2	Semaglutide 1mg	Inadequately controlled on at least 1.5g metformin, HbA1c 7-10.5%	40 weeks	HbA1c ↓ -2.01 to -2.30% compared with semaglutide ↓ -1.86% Weight loss -7.6 to -11.2kg compared with semaglutide -5.7kg
SURPASS 3	Insulin degludec	Inadequately controlled on metformin +/- SGLT2i but insulin naive, HbA1c 7-10.5%	52 weeks	HbA1c ↓ -1.93 to -2.37% compared with insulin ↓ -1.86% Weight loss -7.5 to -12.9kg compared with insulin ↑+2.3kg
SURPASS 4	Insulin glargine	Inadequately controlled on metformin +/- SGLT2i +/- SU, HbA1c 7.5-10.5% Est CVD or high CV risk	52 weeks	HbA1c ↓ -1.93 to -2.37% compared with insulin ↓ -1.86% Weight loss -7.5 to -12.9kg compared with insulin ↑+2.3kg
SURPASS 5	Stable on insulin Add-on Tirzepatide vs placebo	Inadequately controlled with or without metformin and stable on insulin, HbA1c 7-10.5%	40 weeks	HbA1c ↓ -2.40% to -2.34% compared with placebo ↓ -0.86% Weight loss -5.4 to -8.8kg compared with placebo ↑+1.6kg

TIRZEPATIDE FOR WEIGHT LOSS - COMPARISONS WITH OTHER DRUGS

FEATURE	TIRZEPATIDE (MOUNJARO)	SEMAGLUTIDE (OZEMPIC/WEGOVY)	LIRAGLUTIDE (SAXENDA)
TYPE	Injectable	Injectable	Injectable
PRIMARY USE	Type 2 Diabetes & Weight Loss	Type 2 Diabetes & Weight Loss	Weight Loss
MECHANISM OF ACTION	GLP-1 and GIP receptor agonist	GLP-1 receptor agonist	GLP-1 receptor agonist
FDA APPROVAL FOR WEIGHT LOSS	Approved	Approved (Wegovy)	Approved
AVERAGE WEIGHT LOSS	Up to 15%	10-15%	5-10%
DOSING FREQUENCY	Once weekly	Once weekly	Once daily
ADMINISTRATION	Subcutaneous injection	Subcutaneous injection	Subcutaneous injection
COMMON SIDE EFFECTS	Nausea, vomiting, diarrhea, constipation	Nausea, vomiting, diarrhea	Nausea, vomiting, diarrhea
AVAILABILITY	Available	Available	Available
TYPICAL COST	High (around \$1,000+/month)	High (around \$1,000+/month)	High (around \$1,000+/month)
INSURANCE COVERAGE	Varies, typically with prior authorization	Varies, typically with prior authorization	Varies, typically with prior authorization