Tirzepatide; a new promise in the management of Diabetes and Obesity

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INTRODUCTION

- Diabetes and obesity are major 21st-century health problems often seen as "twin epidemics" affecting millions worldwide (5).
- Incretins, natural hormones produced in the gut, play a significant role in controlling blood sugar and reducing weight.
- GLP-1 (Glucagon-like peptide-1) and GIP (Glucose-dependent insulinotropic polypeptide) are two naturally occurring incretin hormones (2).
- Tirzepatide, the first dual GLP-1/GIP receptor co-agonist, has recently been approved to treat type 2 diabetes mellitus (T2DM) based on findings from the SURPASS program. It garners attention as it addresses the inextricable link between obesity and diabetes (5).
- This poster intends to analyze the effects of Tirzepatide on glycaemic control and weight reduction.

MECHANISM OF ACTION OF TIRZEPATIDE

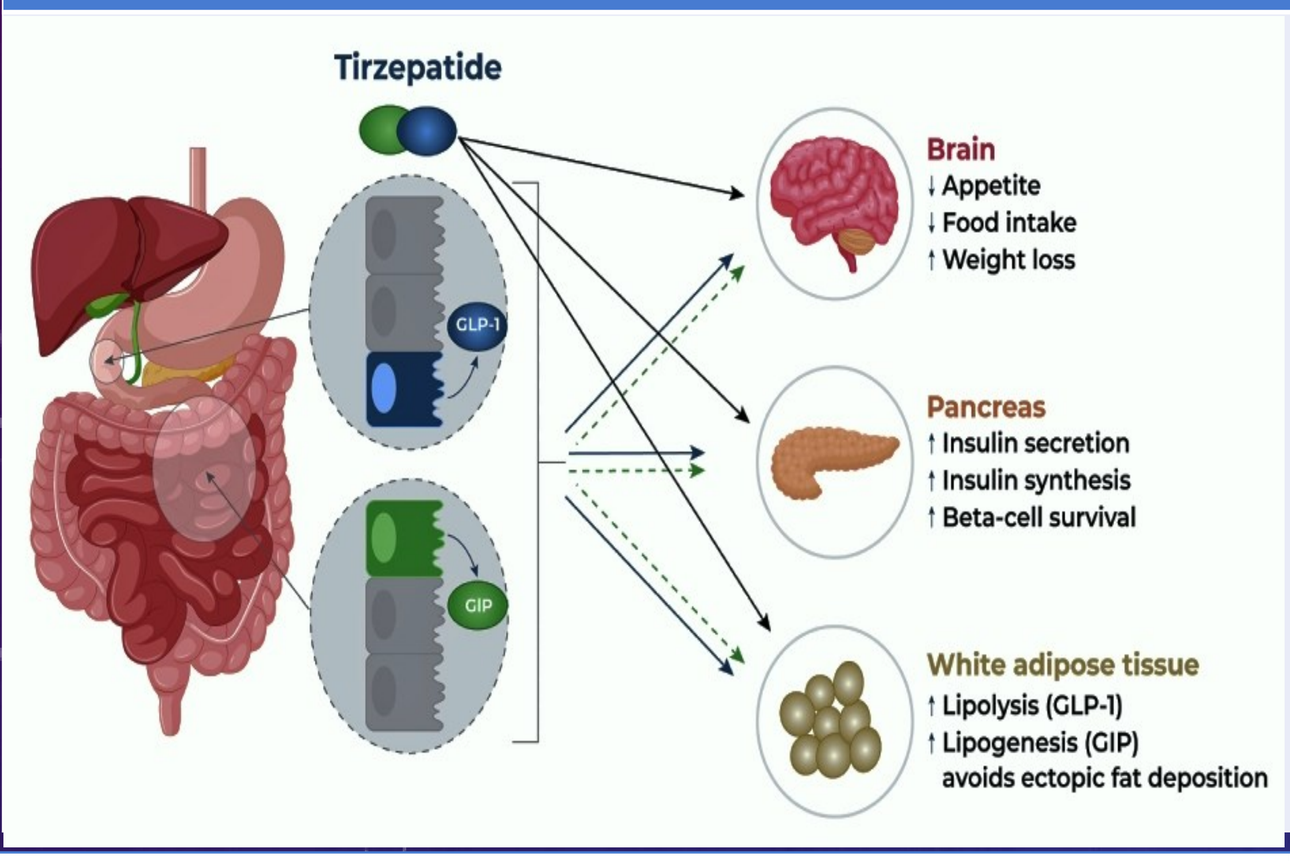

Figure 1 Mechanism action of Tirzepatide (5)

METHODS

- SURPASS Clinical trials (1-5) are the phase 3 Randomised Controlled Trials (RCT) which has Studied the effects of Tirzepatide in T2DM over its comparators.
- Trial Design : RCT, Multicentre and Multinational active-comparator trials

Table 1. Base line characteristics of the SURPASS Trials

Trial and setting	SURPASS 1 Vs placebo	SUPPAS 2 Semaglutide	SURPASS 3 Insulin degludec	SURPASS 4 Insulin glargine	SURPASS 5 placebo
Background Regimen	Diet & Exercise	Metformin (Met)	Met + SGLT-2i	Met + SGLT-2i + SU	Insulin +Met
Duration of Diabetes (years)	4.7 (early)	8.6 (established)	8.4 (established)	11.8 (advanced)	13.3 (advanced)
Duration of Study	40 weeks	40 weeks	52 weeks	52 weeks	40 weeks

Table.2 Summary of the results

TRIAL	Tirzepatide dose:	Mean difference in HbA_1C over control	Mean difference in body weight over control
SURPASS-1 (n: 478)	5mg (n: 121)	-1·91%	-7.0 Kg
	10mg (n: 121)	-1·93 %	-7.8 Kg
	15 mg (n: 121)	-2·11% (all p<0·0001)	-9.5 Kg (all p <0·001)
SURPASS-2 (n: 1879)	5mg (n: 470)	-0.15% (p<0.02)	-1.9 Kg
	10mg (n: 469)	-0.39% (p<0.001)	-3.6 Kg
	15mg (n: 470)	-0.45% (p <0.001)	-5.5 Kg (all, p <0·001)
SURPASS-3 (n: 1444)	5mg (n: 358)	-0·59%	-9.8 Kg
	10mg (n: 360)	-1.01%	-12.8 Kg
	15mg (n: 359)	-1·04%	-15.2 kg (p <0·0001) for all
SURPASS-4 (n:2002)	10mg (n: 328)	-0·99%	-8.5 Kg
	15mg (n: 338)	-1·14%	-9.3 Kg p <0·0001)
SURPASS-5 (n: 475)	5mg (n: 116)	-1.24% (p <0·0001)	-7.1 kg (p <0·0001)
	10mg (n: 119)	-1.53%	-9.1 kg
	15mg (n: 120)	-1.47% (all p <0·01)	-10.5 kg (all p <0·01)

SAFETY OUTCOMES

Tirzepatide 5-15mg doses were found to be well tolerated in all trials.

The commonly observed adverse events were gastro-intestinal side effects of mild-moderate severity.

DISCUSSION AND CONCLUSION

- The SURPASS trials provide strong evidence that Tirzepatide, the once-a-week oral incretin-based peptide, improves glycaemic control and leads to more significant weight reduction compared to GLP-1 RAs (e.g., Semaglutide) and basal insulin. All Tirzepatide doses were well tolerated with similar side-effect profile to the GLP-1 receptor analogues.
- This breakthrough offers promising prospects for managing both diabetes and obesity.
- Future research: Studies focussing on long-term cardiovascular safety and including diverse populations beyond Europe and America are required.

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