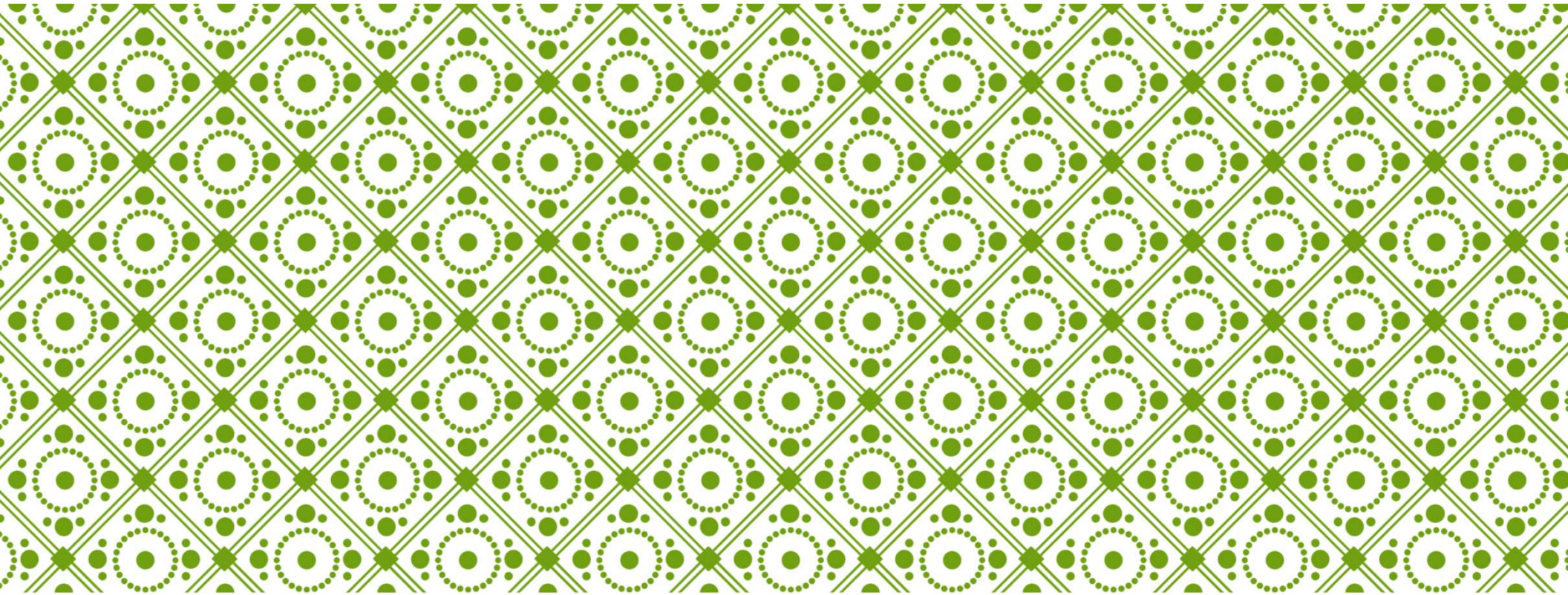
ADRENAL LESIONS AND REFERRAL TO ENDOCRINOLOGY

- All functional lesions
- Including those with MACS
- All lesions in the size 2-4cm
- Bilateral adenomas
-Adenomas associated with Tumour syndromes
-PET avid adenomas

- All lesions> 10 HU (suspicious)



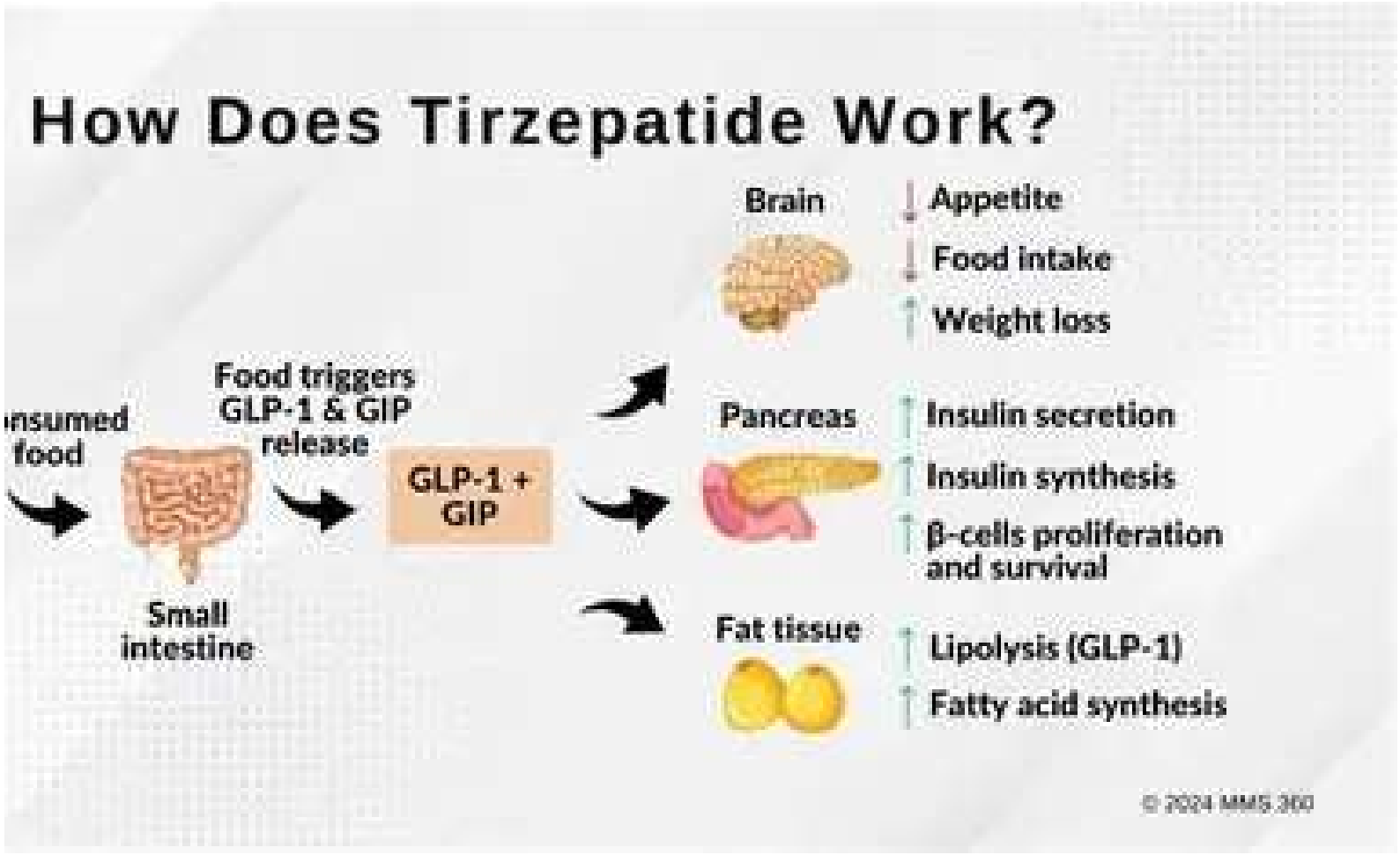
TIRZEPATIDE

The Twin incretin approach

BACKGROUND

- Tirzepatide, a novel, once weekly, GIP and GLP-1 receptor agonist -> approved by US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for treating adults with T2D
- The combination of GLP-1 and GIP (the "twincretin" concept), appeared as one of the most attractive strategies for treating T2DM,

- Considering that both these hormones have glucose-lowering actions
- The most frequent adverse events with tirzepatide were mild to moderate gastrointestinal events, similar to other incretin-based therapies, namely nausea, diarrhea, and vomiting


How Does Tirzepatide Work?
Brain
Appetite
Food intake
Weight loss
Food triggers GLP-1 & GIP release
nsumed food
GLP-1 + GIP
Pancreas
Insulin secretion
Insulin synthesis
β-cells proliferation and survival
Small intestine
Fat tissue
Lipolysis (GLP-1)
Fatty acid synthesis
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TIRZEPATIDE FOR DIABETES

SURPASS trials- 7 trials – Phase 3 for licencing Tirzepatide

Individuals recruited to SURPASS covered a large part of the T2DM continuum, ranging from those with less than 5 years since diagnosis to those with advanced disease (>10 years)

- Participants were given subcutaneous tirzepatide 5, 10, or 15 mg once weekly either as monotherapy, or in combination with other glucose-lowering medications, including insulin
- Tirzepatide initiation dose was 2.5 mg once weekly and increased by 2.5 mg every 4 weeks until reaching the target dose

TRIAL	Design	Change in HbA1C	Glycaemic Targets	CHANGE IN WEIGHT
SURPASS-1 Tirzepatide 5/10/15mg Vs placebo	HbA1c 7%–9.5%, BMI ≥ 23 kg/m^2, treated with diet and exercise	-1.87% vs. -2.07%	82% reached <7% 75% reached 6.5% 31% reached 5.7%	5mg -6.3kg 10mg-7.0kg 15mg-7.8kg
SURPASS -2 Tirzepatide 5/10/15mg Vs Semaglutide 1mg	HbA1c 7%–10.5%, BMI ≥ 25 kg/m^2, treated with metformin	-2.09 to-2.46%	86% reached<7% 80% reached <6.5% 46% reached <5.7%	5mg-6.9 10mg-9.6 15mg-9.9
SURPASS-3 Tirzepatide 5/10/15mg Vs insulin degludec	HbA1c 7%–10.5%, BMI ≥ 25 kg/m^2, treated with metformin ± SGLT2 inhibitor	-1.9 to -2.5%	93% reached <7% 85% reached <6.5% 48% reached,5.7%	5mg -7.1 10mg-9.4 15mg-10.9
SURPASS-4 Increased cardiovascular risk,Tirzepatide 5/10/15 vs glargine	HbA1c 7.5%–10.5%, BMI ≥ 25 kg/m^2, treated with metformin, SGLT2 inhibitor, sulfonylurea	-2.24 to-2.58%	91 Reached <7% 81 Reached 6.5% 43% Reached 5.7%	5mg-7.5 10mg-9.5 15mg-11.7
SURPASS-5 Tirzepatide 5/10/15 vs placebo	HbA1c 7%–10.5%, BMI ≥ 23 kg/m^2, receiving once-daily	-2.23 to -2.59%	93 Reached <7% 94 Reached 6.5% 62 Reached 5.7%	5mg -6.2 10mg-8.2 15mg -10.9

TIRZEPATIDE FOR OBESITY-SURMOUNT

- 2539 participants with obesity or overweight were randomised to Tirz 5/10/15mg
- At 72 weeks
- Weight loss 16% to 22.5%
- 31.6% to 62.9% achieved >20% weight loss
- 95% with prediabetes converted to normoglycemia vs 62% with lifestyle alone
- Various cardiometablic risk factors, Inflammatory markers and the physical function all improved with tirzepatide vs placebo

- Garvey WT, Frias JP, Jastreboff AM, le Roux CW, Sattar N, Aizenberg D, Mao H, Zhang S, Ahmad NN, Bunck MC, Benabbad I. Tirzepatide once weekly for the treatment of obesity in people with type 2 diabetes (SURMOUNT-2): a double-blind, randomized, multicenter, placebo-controlled, phase 3 trial. The Lancet. 2023 Aug 19;402(10402):613-26.

TIRZEPATIDE AND SLEEP APNOEA-SURMOUNT OSA

Two trials of 469 individuals not receiving CPAP

Moderate to severe OSA randomised to 10/15mg of Tirzepatide or Placebo

In both intervention groups the number of Apnoea Hyponex Index(ahi 25.3 vs 5.3, $p<0.001$)

Mild GI side effects did occur

Reduced BP and CRP

Malhotra A, Bednarik J, Chakladar S, Dunn JP, Weaver T, Grunstein R, Fietzes I, Redline S, Azar Barzin A, Sands SA, Schwab RJ. Tirzepatide for the treatment of obstructive sleep apnea: rationale, design, and sample baseline characteristics of the SURMOUNT-OSA phase 3 trial. Contemporary clinical trials. 2024 Jun 1;141:107516.

TIRZEPATIDE FOR HEART FAILURE -SUMMIT

- Obesity increases the risk of Heart failure with preserved EF
- 731 patients randomised (1:1) up to 15mg vs placebo
- Worsening heart-failure events occurred in 29 patients (8.0%) in the tirzepatide group and in 52 patients (14.2%) in the placebo group
- Death from CVS causes occurred 9.9% vs. 15.3%(p=0.026)
- 52 weeks, the mean (±SD) change in the KCCQ-CSS was 19.5±1.2 in the tirzepatide group as compared with 12.7±1.3 in the placebo group (between-group difference, 6.9; 95% CI, 3.3 to 10.6; P<0.001).
- Treatment with tirzepatide led to a lower risk of a composite of death from cardiovascular causes or worsening heart failure than placebo and improved health status in patients with heart failure with preserved ejection fraction and obesity.

Borlaug BA, Zile MR, Kramer CM, Ye W, Ou Y, Hurt K, Murakami M, Packer M, SUMMIT Trial Study Group. Impact of body mass index, central adiposity, and weight loss on the benefits of tirzepatide in HFpEF: the SUMMIT trial. Journal of the American College of Cardiology. 2025 Jul 29;86(4):242-55.

TIRZEPATIDE FOR LIVER DISEASE

190 Patients

Biopsy proven MASH

Randomly assigned 5/10/15mg of Tirzepatide or Placebo

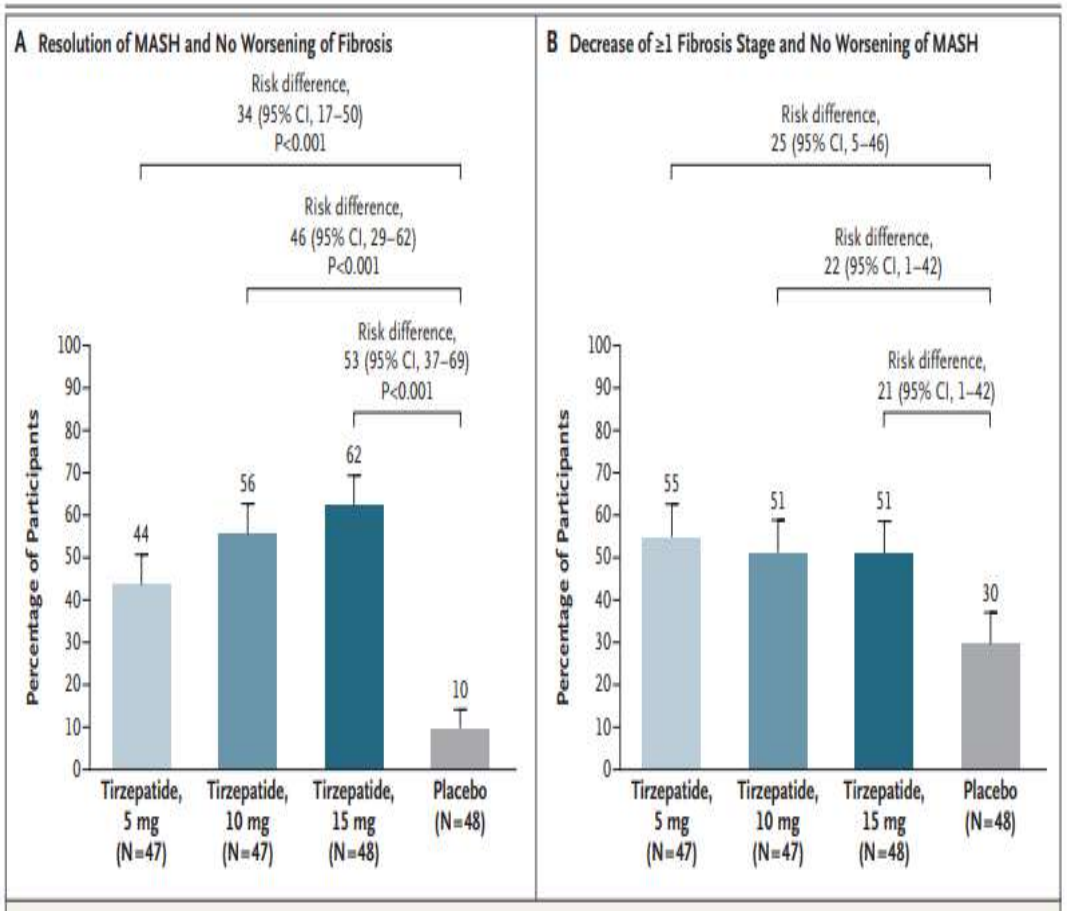
Results

- 44% resolution of Fibrosis in 5mg Group

-56% in 10mg group

-62% in 15mg group

Loomba R, Hartman ML, Lawitz EJ, Vuppalanchi R, Boursier J, Bugianesi E, Yoneda M, Behling C, Cummings OW, Tang Y, Brouwers B. Tirzepatide for metabolic dysfunction–associated steatohepatitis with liver fibrosis. New England Journal of Medicine. 2024 Jul 25;391(4):299-310.



CONCLUSIONS

- Tirzepatide is a novel GLP/GIP Agonist
- Indicated for the management of weight loss and T2DM
- Fewer side effects than GLP-1
- Improves both weight loss and glycaemic control
- Reduces total insulin dose and hypoglycaemia in insulin treated T2DM
- Reduces AHI in sleep Apnoea
- Reduces MASH and fibrosis
- Reduces Symptoms and Progression in HF-REF.