Nov/Dec 2022 Winning E-Journal Club Submission by Dr Jayleigh Lim

Training Programme: GIM BST

Title: Efficacy of once-weekly tirzepatide versus once-daily insulin degludec on glycaemic control measured by continuous glucose monitoring in adults with type 2 diabetes (SURPASS-3 CGM): a substudy of the randomised, open-label, parallel-group, phase 3 SURPASS-3 trial

Author(s): Tadej Battelino, MD Richard M Bergenstal, MD Angel Rodríguez, MD Laura Fernández Landó, MD Ross Bray, PhD Zhentao Tong, PhD Katelyn Brown, PharmD

Introduction/Aim

Tirzepatide is a synthetic dual GIP and GLP-1 receptor agonist peptide developed for the treatment of T2DM. This study sought to evaluate and compare the glucose profile and associated glucose metrics measured with CGM in patients with T2DM, with the hypothesis that patients given tirzepatide would spend more time in tight target range (TITR; 71-140mg/dL) than patients given insulin degludec at 52 weeks.

Design & Methods

Design:

- Substudy of the SURPASS-3 trial - a 52 week, active-controlled, open-label, parallel-group, phase 3 trial.
- Study countries: Hungary, Poland, Romania, Spain, Ukraine, USA.

Inclusion criteria:

- Adults (≥18 years)
- Insulin-naive
- Inadequately controlled T2DM (HbA1c 53-91 mmol/mol) on stable treatment with metformin alone or metformin and SGLT2 inhibitor for at least 3 months before screening
- BMI ≥25 kg/m2
- Stable weight in the previous 3 months

<u>Primary endpoint</u>: Proportion of time CGM glucose values were in tight target range (71-140mg/dL) at 52 weeks in the tirzepatide groups vs insulin degludec group

Results & Conclusions

Once-weekly tirzepatide resulted in superior glycaemic control and decreased glycaemic variability measured by CGM with lower risk of hypoglycaemia compared to insulin degludec in adults with T2DM given metformin with or without a SGLT2 inhibitor.

Strengths & Limitations

<u>Strengths</u>:

- First to evaluate the effect of tirzepatide using CGM data.
- First to evaluate a tighter glycaemic control.
- Prospective, randomised, active-controlled design, with a long treatment duration and an adequate sample size to assess TITR.
- Population in the substudy had similar baseline characteristics, efficacy, and safety outcomes to those in the overall SURPASS-3 study.
- Used the DexCom G6 - one of the most accurate sensors.

<u>Limitations</u>:

- Sensor was worn for 7–10 days. 10–14 days is recommended for most accurate assessment and comparison of CGM metrics
- Open-label design. However, this is more of an issue when considering subjective endpoints, whereas those used in this study were objective and collected in a masked way.
- Although the CGM device values were masked to participants, there could have been behavioural changes when wearing versus not wearing the device.
- Majority of the study population were White.

Applicability & Future Direction

These positive findings brings optimism that tirzepatide would revolutionise the management of poorly-controlled T2DM. It has received FDA approval for use in T2DM, and fast-track designation for use in Obesity. The European Commission has also approved its use in T2DM. Future research to establish if these positive results apply to other racial and ethnic groups are underway. -