CO23

Real-World Effectiveness of Tirzepatide vs. Injectable Semaglutide on HbA1c and Weight in GLP-1 RA Naïve Patients with T2D

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OBJECTIVE

To conduct one of the first real-world evidence studies comparing hemoglobin A1c (HbA1c) and weight changes in glucagon-like peptide-1 (GLP-1) receptor agonist (RA) naïve patients with type 2 diabetes (T2D) initiating either tirzepatide or injectable semaglutide.

CONCLUSION

Consistent with SURPASS-2 clinical trial findings, this real-world data shows GLP-1 RA-naïve patients with T2D starting tirzepatide experienced greater reduction in HbA1c and weight compared to those starting injectable semaglutide at 12-months of follow-up.

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BACKGROUND

- Effective management of T2D focuses on glycemic control and weight management to reduce burden of illness.
- GLP-1 RAs are effective at lowering HbA1c and promoting weight loss.[1] Semaglutide is an established GLP-1 RA while tirzepatide is a dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 RA.[2]
- The SURPASS-2 clinical trial compared tirzepatide (5mg, 10mg, 15mg) to semaglutide (1mg) in patients with T2D and found tirzepatide more effective in reducing HbA1c and weight compared to semaglutide over 10-months follow-up.[3]

STUDY DESIGN

Retrospective observational cohort study

DATA SOURCE

Healthcare Integrated Research Database (HIRD®), containing US-based administrative claims linked to clinical data[4]

INTAKE PERIOD

May 13,2022 – May 29, 2023

STUDY POPULATION

- Adults with T2D who initiated tirzepatide (Mounjaro®) or injectable semaglutide (Ozempic®) during the intake period (first claim = index date).
- Participants were required to have continuous health plan enrollment for at least 6 months prior to and 12 months following GLP-1 RA initiation
- Exclusions included prior GLP-1 RA use, gestational diabetes, or type 1 diabetes in the 6-month pre-index period, bariatric surgery or obesity procedures from January 1, 2016, to 12 months post-index, and pregnancy-related claims during 6-month pre-index or 12-month post-index periods.

CO-PRIMARY ENDPOINTS

Changes in HbA1c and weight were measured from baseline (90 days before to 14 days after index) to follow-up (14 days before or after index + 12 months). Only patients with data for both time points were analyzed. Missing data was not imputed.

STATISTICAL ANALYSIS

- Patients were stratified based on their index medication (tirzepatide or semaglutide) and matched 1:1 using propensity scores (PS) to reduce bias from observed confounders. Baseline variable balance was assessed with standardized mean differences (SMDs <0.1 in absolute value represent balance).
- Unpaired t-tests were used for comparisons of coprimary outcomes, using the Holm method to adjust for multiplicity. Ordinary least squares regression analyses were conducted to address potential residual baseline imbalances in observed confounders after PS matching.

BASELINE RESULTS

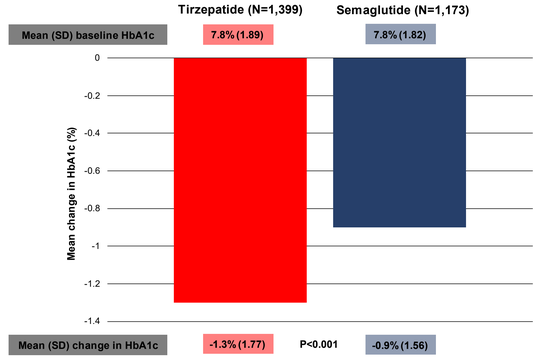
We identified 10,702 GLP-1 RA naïve matched tirzepatide and injectable semaglutide initiators. Adequate balance was achieved across baseline characteristics.

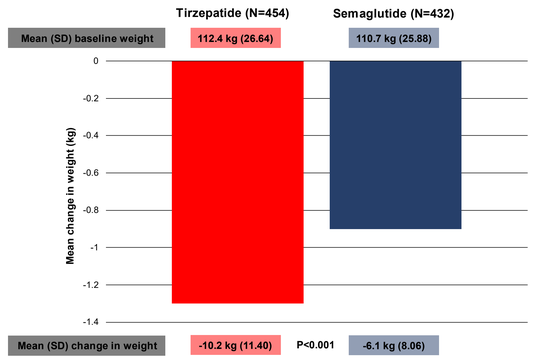
	Tirzepatide	Semaglutide	SMD
N	10,702	10,702	---
Age in years			
Mean (SD)	53.2 (9.94)	53.2 (9.92)	0.006
Sex, %			
Female	44	45	0.029
Race, %			
Asian	3	3	
Black	9	9	
White	71	71	0.060
Other	4	3	
Unknown	13	14	
Ethnicity, %			
Hispanic or Latino	8	8	
Non-Hispanic	81	80	0.032
Unknown	12	12	
Payer, %			
Commercial	92	92	0.006
aDCSI Score			
Mean (SD)	0.8 (1.35)	0.8 (1.36)	0.018
Comorbidities, %			
Dyslipidemia	66	64	0.044
Hypertension	68	66	0.045
Obesity	49	46	0.078
Obstructive Sleep Apnea	21	20	0.030
Antihyperglycemic Medication Use, %			
Insulin	19	18	0.026
Metformin	59	60	0.009
Thiazolidinediones	5	4	0.035
Sulfonylurea	15	16	0.032
DPP-4 inhibitor	10	11	0.032
SGLT2 inhibitor	24	21	0.071

Abbreviations: aDCSI (adapted Diabetes Complications Severity Index), DPP-4 (dipeptidyl peptidase-4), SD (standard deviation), SGLT2 (sodium-glucose cotransporter 2), SMD (standardized mean difference)

FOLLOW-UP RESULTS

At 12-months follow-up tirzepatide initiators had greater mean reduction in HbA1c (p<0.001) and weight (p<0.001) from baseline compared to patients initiating injectable semaglutide.





- In the six months prior to starting treatment, 76% of patients initiating tirzepatide or injectable semaglutide had ≥1 fill for a non-GLP-1 RA antihyperglycemic medication. Most patients (62% in both groups) were on monotherapy, with metformin being the most common regimen (27% tirzepatide; 28% semaglutide).
- Tirzepatide was most frequently initiated at 2.5 mg (59%) or 5.0 mg (31%), while injectable semaglutide was most frequently initiated at 0.25/0.5 mg (87%) or 1.0 mg (12%). Most patients in both cohorts increased their dose over the 12-month post-index period (78% tirzepatide; 54% semaglutide).
- More patients who initiated tirzepatide were adherent to index medication (≥0.80 proportion of days covered) over the 12-month post-index period than those who initiated semaglutide (60% tirzepatide; 45% semaglutide).

STRENGTHS AND LIMITATIONS

- Strengths: Provides real-world insights into treatment performance beyond controlled trials; Includes a diverse patient cohort with multiple comorbidities and varied GLP-1 RA dosages, enhancing generalizability; Large sample sizes to allow precise estimates; The HIRD is representative of the US population in terms of age, sex, and geographical distribution.[5]
- Limitations: Limited to a 12-month follow-up, possibly missing longer-term T2D impacts; Reliance on administrative claims data may result in diagnostic or treatment inaccuracies; Focus primarily on commercially insured patients could limit generalizability; Possible immortal time bias (in the form of selection bias) from exclusion of patients with <12 months of health plan enrollment; Inability to capture certain safety parameters; Possible selection bias from exclusion of patients with less than two measures of HbA1c/weight.

REFERENCES

1) Dhirani D, Shahid A, Mumtaz H. A new kind of diabetes medication approved by the FDA: is there hope for obesity? Int J Surg. 2023;109(2):81-82. 2) FDA NEWS RELEASE: FDA Approves New Medication for Chronic Weight Management [press release]. U.S. Food & Drug Administration, November 08 2023.3) Frías JP, Davies MJ, Rosenstock J, et al.: SURPASS-2 Investigators. Tirzepatide versus Semaglutide Once Weekly in Patients with Type 2 Diabetes. N Engl J Med. 2021 Aug 5;385(6):503-515. doi: 10.1056/NEJMoa2107519. 4) Barron JJ., Willey, VJ., Doherty BT., et al.: (2025), The Healthcare Integrated Research Database (HIRD) as a Real-World Data Source for Pharmacoepidemiologic Research. Pharmacoepidemiol Drug Saf, 34: e70110. https://doi.org/10.1002/pds.70110. 5) Stephenson JJ, Teng CC, Harris KM. Assessing the Representativeness of Real-World Claims Databases. Poster presentation at the 2024 ISPOR Annual Meeting, May 5-8, 2024, Atlanta, GA. https://www.ispor.org/heor-resources/presentations-database/presentation/intl2024-3897/139401 [Accessed 10 March 2025]

DISCLOSURES

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