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

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Meredith Hoog[1*], Carlos Vallarino[1], Juan M. Maldonado[1], Michael Grabner[2], Chia-Chen Teng[2], Kendra Terrell[1], Emma Richard[2]

[1]Eli Lilly and Company, Indianapolis, USA, [2]Carelon Research, Wilmington, USA

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OBJECTIVE

- To describe and compare baseline characteristics, treatment patterns, and change in glycated hemoglobin (HbA1c) and weight among glucagon-like peptide-1 (GLP-1) receptor agonists (RAs)-experienced individuals with type 2 diabetes (T2D) initiating tirzepatide or injectable semaglutide.

CONCLUSIONS

- In this real-world study, GLP-1 RA-experienced individuals with T2D starting tirzepatide had greater reductions in HbA1c and weight compared to those starting injectable semaglutide over a 12-month follow-up.
- These results are consistent with the findings from both the SURPASS-2 phase 3 clinical trial and the SWITCH-2 phase 4 clinical trial, reinforcing the efficacy and tolerability of tirzepatide in managing T2D.
- This study offers insights for clinicians regarding clinical decision-making in managing T2D for individuals who have previously used GLP-1RA treatment.

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BACKGROUND

- Glucagon-like peptide-1 (GLP-1) receptor agonists (RAs) are effective treatment options for individuals with type 2 diabetes (T2D) that promote glycemic control and weight reduction.[1]
- The SURPASS-2 phase 3 clinical trial showed tirzepatide, a dual glucose-dependent insulinotropic polypeptide/GLP-1 RA, is superior to semaglutide, a GLP-1 RA, in reducing glycated hemoglobin (HbA1c) and weight in individuals with T2D.[2]
- To our knowledge, the current study represents the first real-world comparison evaluating HbA1c and weight changes in GLP-1 RA-experienced individuals with T2D initiating tirzepatide or semaglutide.

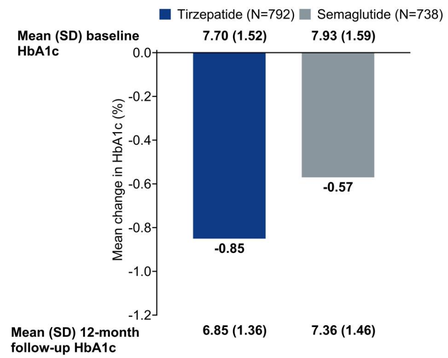
RESULTS

Demographics, clinical characteristics, and treatment patterns over 6-month pre-index period after PS matching

Characteristics	Tirzepatide initiators (N= 5,577)	Semaglutide initiators (N= 5,577)	SMD
Age, years, mean (SD)	54.9 (9.2)	55.0 (9.5)	-0.013
Sex, n (%)			
Male	3,069 (55)	3,014 (54)	0.020
Race, n (%)			
White	4,100 (74)	4,061 (73)	0.032
Black/African American	492 (9)	506 (9)	
Asian	166 (3)	169 (3)	
Others*	818 (15)	840 (15)	
Ethnicity, n (%)			
Non-Hispanic	4,595 (82)	4,592 (82)	0.000
Hispanic	403 (7)	400 (7)	
Unknown	579 (10)	585 (10)	
Payor, n (%)			
Commercial (vs. Medicare Advantage	5,060 (91)	5,038 (90)	0.013
aDCSI score, mean (SD)	1.1 (1.5)	1.1 (1.6)	-0.027
Comorbidities of interest[#], n (%)			
Dyslipidemia	4,141 (74)	4,019 (72)	-0.049
Hypertension	4,073 (73)	4,033 (72)	-0.016
Obesity^	3,013 (54)	2,872 (51)	-0.051
OSA	1,237 (22)	1,164 (21)	-0.032
Antihyperglycemic medication Use, n (%)			
Insulin	1,854 (33)	1,860 (33)	0.002
Metformin	3,542 (64)	3,713 (67)	0.064
Thizolidinedione	423 (8)	369 (7)	-0.038
Sulfonylurea	1,103 (20)	1,333 (24)	0.100
DPP-4 inhibitor	368 (7)	372 (7)	0.003
SGLT2 inhibitor	2,328 (42)	2,180 (39)	-0.054

Semaglutide refers to injectable semaglutide.
SMD >0.1 denotes imbalance after matching.
*Others included American Indian or Alaska Native, Other, and Unknown. Data included Multi Racial (tirzepatide initiators: <5; semaglutide initiators:0) and Native Hawaiian or Other Pacific Islander (tirzepatide initiators: 0; semaglutide initiators:<5).
[#]Individuals with ≥1 medical claims with diagnosis for condition of interest during the six-month pre-index period.
^Includes individuals with ≥1 medical claims with diagnosis for obesity and among individuals with BMI ≥30 kg/m^2 among subset with available clinical data.

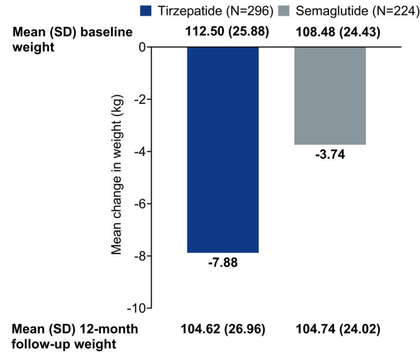
At the 12-month follow-up, greater mean change in HbA1c from baseline was reported for individuals starting tirzepatide than injectable semaglutide (p=0.0001)



Note: Semaglutide refers to injectable semaglutide

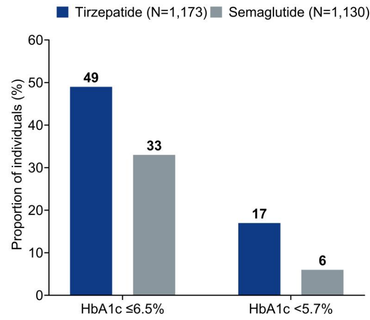
- Most individuals (72% tirzepatide initiators and 82% injectable semaglutide initiators) were on dulaglutide therapy during the 6-month pre-index period.
- Tirzepatide was most frequently initiated at 2.5 mg (37%) or 5.0 mg (44%), while injectable semaglutide was most frequently initiated at 0.5 mg (57%) or 1.0 mg (31%).
- Over half of the individuals increased their dosage during the 12-month follow-up (81% tirzepatide; 55% injectable semaglutide).
- At 12-month follow-up, numerically higher proportion of individuals on tirzepatide (66%) showed greater adherence (≥80% PDC) than injectable semaglutide (48%).

At the 12-month follow-up, greater mean change in weight from baseline was reported for individuals starting tirzepatide than injectable semaglutide (p<0.0001)



Note: Semaglutide refers to injectable semaglutide

Numerically higher proportion of individuals on tirzepatide treatment achieved glycemic targets HbA1c (≤6.5% and <5.7%) than injectable semaglutide at 12-month follow-up



Note: Semaglutide refers to injectable semaglutide

Limitations

- The present study is limited to a 12-month follow-up, possibly missing the longer-term T2D impacts.
- The study relied on administrative claims data that may have diagnostic or treatment inaccuracies.
- The study focused primarily on commercially insured individuals, which could have limited the generalizability of the results.
- Certain results may be impacted by selection bias from the exclusion of individuals with fewer than two measures of HbA1c/weight and <12 months of post-index health plan enrollment.

METHODOLOGY

Study design: Retrospective, observational study

Data source: Healthcare Integrated Research Database (HIRD®) containing US-based administrative claims linked to clinical data

Intake period: May 13, 2022 – May 29, 2023

Study variables:
- Demographics, 6-month baseline clinical characteristics and 12-month follow-up treatment patterns
- Changes in HbA1c and weight from baseline to follow-up (Co-primary endpoints)

Study population:
- Adults with T2D having ≥1 pharmacy claim for any dose of index medication: tirzepatide (Mounjaro®) or injectable semaglutide (Ozempic®).
- Continuous enrollment for ≥6 months prior to and 12 months following GLP-1 RA initiation (index date is the first claim of GLP-1 RA).
- Individuals with 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 were excluded.
- Individuals with ≥1 fill for a non-index GLP-1 RA during the 6-month baseline were categorized as GLP-1 RA experienced.
- Individuals were stratified based on their index medication (tirzepatide or injectable semaglutide) during the 6-month pre-index period.

Statistical analyses:
- A propensity score (PS) adjustment was used to balance individuals' baseline characteristics across cohorts and reduce bias from observed confounders.
- Baseline variable balance was assessed with standardized mean differences (SMD >0.1 denotes imbalance after matching).
- The co-primary and secondary endpoints (follow-up HbA1c ≤6.5% and <5.7%) were measured from baseline (90 days before to 14 days after index) to follow-up (index date to 12 months ± 45 days). Only individuals with data for both time points were analyzed.
- Unpaired t-tests were used for comparisons. Ordinary least squares regression analyses were conducted to address potential residual confounding after PS matching.
- Missing values were not imputed.
- Primary and secondary endpoints comparisons were adjusted for multiplicity using the Holm method.[3]

Abbreviations: aDCSI, adapted diabetes complication severity index score; BMI, body mass index; DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; HbA1c, glycated hemoglobin; N, total number of individuals; n, number of individuals in the specified category, PDC, proportion of days covered; PS, propensity scores; RA, receptor agonist; SD, standard deviation; SGLT2; sodium-glucose cotransporter-2; SMD, standardized mean difference; T2D, type 2 diabetes US, United States.

Disclosures: Meredith Hoog, Carlos Vallarino, Juan M. Maldonado and Kendra Terrell: Employees and shareholders of Eli Lilly and Company. Michael Grabner, Chia-Chen Teng, Emma Richard: Employees of Carelon Research (which received funding from Eli Lilly and Company for the conduct of this study) and shareholders of Elevance Health.

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