Comparing Adherence in Patients with Type 2 Diabetes Initiating Glucagon-like Peptide-1 Receptor Agonists or Sodium-Glucose Cotransporter-2 Inhibitors

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Objectives

- Non-adherence to antidiabetics is associated with worse clinical outcomes.
- Both sodium-glucose cotransporter 2 (SGLT2I) inhibitors and glucagon-like peptide 1 (GLP-1) receptor agonists demonstrate clinical benefits in patients with type 2 diabetes (T2DM) and increased cardiovascular disease risk.
- However, evidence suggests the route of administration and the common gastrointestinal effects associated with GLP-1 may affect medication adherence.
- Therefore, the objective of this study is to evaluate and compare medication adherence among adult new users of SGLT2I and GLP-1

Methods

Study design: Retrospective, cohort study.

Data source: This study utilized a 10% random sample of enrollees within IQVIA PharMetrics® Plus for Academics data.

Study sample

- New users of GLP-1 (i.e., dulaglutide, exenatide, liraglutide, semaglutide) or SGLT2I (i.e., canagliflozin, dapagliflozin, ertugliflozin or empagliflozin) naive to the index classes in the prior 6 months were identified from January 1, 2013, to December 31, 2019
- Individuals were required to have ≥6 months pre-index (baseline) and ≥9 months post-index (follow-up) continuous enrollment; and at least one T2DM International Classification of Diseases (ICD) diagnosis claim in the baseline period.
- Individuals were excluded if they had claims for both GLP-1 agonists and SGLT2 inhibitors on the index date; if they were indexed to the discontinued product albiglutide, or if they had at least one medical claim with a diagnosis of type 1 diabetes, neoplasms, human immunodeficiency virus (HIV), or pregnancy in the baseline period.

Study Outcome

- Medication adherence was measured using the proportion of days covered (PDC).[1]
- The PDC was calculated by dividing the number of days the patient was "covered" by the medication during the follow-up period (numerator) by 270 days (denominator).
- The PDC was dichotomized at the threshold of <80% (non-adherent) versus ≥80%(adherent).

Statistical analysis

- Baseline characteristics were compared across the treatment groups using chi-square tests and t-tests/ Wilcoxon rank-sum tests.
- Covariates were balanced across index treatment groups using 1:1 propensity score matching and a standardized difference of <10% was used to assess balance.

Methods (continued)

- Variables that remained unbalanced were included as covariates in the outcome model.
- A logistic regression model was used to compare the odds of achieving the PDC ≥80% threshold between the matched GLP-1 agonists and SGLT2I groups
- The University of Maryland, Baltimore Institutional Review Board determined that the study was exempt.

Results

- 10,307 patients met study eligibility criteria **(Table 1).**
- The GLP-1 cohort had a significantly higher proportion of females, individuals with >3 Charlson Comorbidity index (CCI), and individuals with more than 5 chronic medications at baseline.
- The matched treatment groups included 7694 patients.
- A greater proportion of patients receiving an SGLT2I were adherent to therapy as compared to patients receiving a GLP-1 (49.7% vs 41.8%, P < 0.05) during the follow-up period (**Table 2**).
- The estimated adjusted odds ratio of adherence was 1.36; 95% confidence interval [CI], 1.24–1.49; P <.01), (**Table 3)**.

TTable 1: Baseline characteristics of patients newly initiating SGLT2I compared to GLP-1s between 2013-2019

Characteristics	Total N=10307	SGLT2I N=5218	GLP-1 Agonists N=5089	P-value
Age Categories, n (%)				
18-34 years	568	244 (4.7)	324 (6.4)	<0.01
35-44 years	1758	846 (16.2)	912 (17.9)	
45-54 years	3627	1933 (37.0)	1694 (33.3)	
55-64 years	3027	1577 (30.2)	1450 (28.5)	
65-74 years	1229	576 (11.0)	653 (12.8)	
75-84 years	98	42 (0.8)	56 (1.1)	
Gender, n (%)				
Female	6360	1631 (42.9)	4729 (53.3)	<0.01
Male	6315	2173 (57.1)	4142 (46.7)	
Health plan type				<0.01
HMO	2727	1218 (23.6)	1509 (29.9)	
PPO	6782	3638 (70.4)	3144 (62.3)	
CDHP	343	174 (3.4)	169 (3.4)	
Others	365	140 (2.7)	225 (4.5)	
Charlson Comorbidity index n, (%)				<0.01
0	2027	998 (19.1)	1029 (20.2)	
1-2	5973	3189 (61.1)	2784 (54.7)	
3-4	1739	813 (15.6)	926 (18.2)	
>=5	568	218 (4.2)	350 (6.9)	
Cardiovascular risk factors				
Hypertension	5544	2786 (53.4)	2758 (54.2)	0.41
Hyperlipidemia	5329	2789 (53.5)	2540 (49.9)	<0.01
Obesity	1741	696 (13.3)	1045 (20.5)	<0.01
Baseline medications count, n (%)				<0.01
< 5	7669	4029 (77.2)	3640 (71.5)	
>=5	2638	1189 (22.8)	1449 (28.5)	
Baseline AHA medications				
DPP4	2738	1622 (31.1)	1116 (21.9)	<0.01
Insulin	3081	1095 (21.0)	1986 (39.0)	<0.01

N=frequencies for each characteristic, *=p-values (<.05) indicate statistical significance, SGLT2I= Sodium-glucose co-transporter 2 inhibitors; GLP-1= Glucagon-like peptide-1 receptor agonists; AHA: Antihyperglycemic agents; CDHP, consumer-driven health plan (health reimbursement account, health savings account); MO, health maintenance organization; PPO, preferred provider organization
Region : 206 missing values

Results

Table 2: The proportion of days covered for the matched patients newly initiating SGLT2I compared to GLP-1s during a 9-month follow-up period

	GLP-1 Agonists N=3847	SGLT2I N=3847	p-value
PDC, mean (SD)	0.75 (0.26)	0.80 (0.24)	-
PDC, median (IQR)	0.86 (0.41)	0.88 (0.33)	<0.01
PDC≥80%, %	508 (57.7)	576 (65.5)	<0.01

PDC: proportion of days covered; SD, standard deviation; SGLT2I= Sodium-glucose co-transporter 2 inhibitors; GLP-1= Glucagon-like peptide-1 receptor agonists
The proportion of days covered: calculated as the number of days with index medication class "on-hand" divided by 180 days
Statistical significance: *p-value < 0.05

Table 3. The adjusted odds ratio for adherence as defined by the PDC ≥80% for the matched patients newly initiating SGLT2I compared to GLP-1s during a 9-month follow-up period

Drug exposure N=7694	Odds Ratio	95% CI	p-value
Treatment group			
GLP-1	Ref	Ref	
SGLT2 I	1.36	1.24-1.49	<0.01
Baseline AHA			
Baseline Insulin use	0.91	0.83-1.02	0.10
Baseline DPP4 use	1.51	1.36-1.68	<0.01

SGLT2I= Sodium-glucose co-transporter 2 inhibitors; GLP-1= Glucagon-like peptide-1 receptor agonists
PDC =Proportion of days covered; 95% CI= 95% Confidence Interval., AHA=antihyperglycemic agents
Statistical significance: *p-value < 0.05

Conclusions

- Individuals newly initiating SGLT2I were more likely to adhere to treatment compared to GLP-1 users during the 9-month follow-up period.
- Further research is needed to determine if the better adherence associated with taking an SGLT2I translates into better glycemic control and fewer complications in patients with T2DM.

References

1. "Adherence Measures." https://www.pqaalliance.org/adherence-measures (accessed May 16, 2022).
2. B. Zhao, "167-2013: Estimating Patient Adherence to Medication with Electronic Health Records Data and Pharmacy Claims Combined," p. 7, 2013.

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