Real-World Utilization Differences Between SGLT2 Inhibitors and GLP-1 Receptor Agonists Post Metformin Monotherapy

A.M. Wilson, PharmD; B.D. Hunter, MS; K. Brown-Gentry, MS; K. Lockhart, MS; J. Scripture, PhD, MS Magellan Rx Management, a Prime Therapeutics company

BACKGROUND

- Diabetes is a chronic condition that is associated with significant macrovascular and microvascular complications that may lead to significant comorbidity, decreased quality of life and death.[1] In 2022, the estimated total cost of diabetes in the U.S. was $413 billion.[1]
- An estimated 38.4 million Americans were living with diabetes in 2021, and nearly 38% of the adult U.S. population was diagnosed with prediabetes.[1] Although diabetes prevalence in the U.S. remained staggering, the diabetes guidelines remained largely unchanged for several decades.[2]
- In 2022, the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) released a report recommending the use of GLP-1 receptor agonists (GLP-1s) or SGLT2 inhibitors (SGLT2s) as first-line therapy for certain patients with type 2 diabetes mellitus (T2DM).[3,4]
- Prior to these updates, metformin was the first-line therapy drug of choice due to its favorable efficacy and safety profile and low cost.[2] More expensive therapeutic classes, such as SGLT2s and GLP-1s, were typically used in second line treatment after metformin.[2] Although the cardiorenal and weight loss benefits of SGLT2s and GLP-1s had been well-established in prior literature, the decision between drug class based on comparative efficacy and safety data was unclear due to a lack of head-to-head trials.[5] However, recent studies have shown that SGLT2 and GLP-1 efficacy and safety differences are narrowing.[6]
- The ADA and EASD have also highlighted the importance of a holistic, patient-centered approach to providing effective T2DM care. Therefore, the decision between a GLP-1 and SGLT2 for most comorbidities and risk categories should be individualized based on patient preference, characteristics and tolerability rather than a strict glycemic control treatment algorithm.[3,4]
- Drug formulation, price, side effect profile and perceived benefit may drive patients and prescribers to one therapy versus the other. Understanding the real-world utilization differences between these drug classes will be pivotal to informing formulary decisions and patient and prescriber preference.

OBJECTIVE

To examine the relationship between proportion of days covered (PDC), adherence, persistence and time to add or switch therapies over 18 months post SGLT2 vs. GLP-1 initiation.

4085-U © 2024 Prime Therapeutics LLC | Magellan Rx Management, LLC, a Prime Therapeutics LLC company 04/24
2900 Ames Crossing Road, Eagan, MN 55121

Academy of Managed Care Pharmacy (AMCP) Annual Meeting, April 15 – 18, 2024, New Orleans, LA

Kristin Brown-Gentry
kristin.browngentry@primetherapeutics.com

Sponsorship: Prime Therapeutics LLC

All brand names are the property of their respective owners.

METHODOLOGY

Factors Considered in the Medication Nonadherence Social Determinants of Health Risk Score Model

Sample Identification Window:
- Commercial health plan; continuously enrolled members during entire measurement period

Exclusion Window:
- Under age 18 or over 65; used other diabetic drugs or insulin prior to SGLT2/GLP-1; used Rybelsus as initial GLP-1; initiated an SGLT2/GLP-1 in combination with another anti-glycemic agent other than metformin

Inclusion Window:
- ≥ 1 metformin claim during 6-month baseline period; new start to SGLT2/GLP-1 post-metformin monotherapy

Baseline Characteristics Assessed:
- Age, gender, chronic disease score: measures the level of comorbid burden at a patient level

Primary Outcomes:
Regression models were used to assess the relationship between drug class and outcomes while controlling for demographic differences (α=.05).
- Proportion of days covered (PDC): calculated as an all-class rate consistent with URAC/PQA guidance, adherence (PDC ≥80%), persistence: time from initiation to discontinuation using a 30-day gap

Secondary Outcomes:
- Time to add or switch therapies after SGLT2/GLP-1 initiation; proportion of patients who switched or added additional therapies

Measurement Period: 01/01/20 – 12/31/21

Baseline Period – 6 Months → ← Evaluation Period – 18 Months →

6 Months – Confirm Metformin Monotherapy	18 Months – Patient Initiates SGLT2 or GLP-1 With or Without Metformin
Jan 1, 2020–Jun 30, 2020	Jul 1, 2020–Dec 31, 2021

METHODS

Inclusion & Exclusion Criteria

- Continuously enrolled members aged 18+ years with commercial drug coverage were included if they were classified as a new-start to SGLT2/GLP-1 after using metformin monotherapy in the 6-month baseline period (01/01/2020–06/30/2020).
- Members were excluded if they used other diabetic drugs or insulin prior to SGLT2/GLP-1, used Rybelsus as an initial GLP-1, initiated either study drug in combination with another anti-glycemic agent other than metformin, or added or switched therapies 14 days after starting either study drug.
- Patients were excluded if they used Rybelsus as their initial GLP-1 therapy because it is the only oral GLP-1 formulation. If patients added or switched to Rybelsus after the 14-day window, they were not excluded.

Analytical Methods

- An 18-month evaluation period (07/01/2020–12/31/2021) was used to analyze the following: all-class rate PDC for diabetic drugs (consistent with PQA/URAC), adherence (PDC≥80%) and persistence (time from initiation to discontinuation using a 30-day gap).
- Regression models were used to assess the relationship between drug class and outcomes while controlling for demographic differences (age, sex, comorbidities; α=.05).

TABLE 1

Baseline Demographic Characteristics

	SGLT2 Cohort (n=443)		GLP-1 Cohort (n=489)		Total (N=932)	
	Mean/%	SD/Count	Mean/%	SD/Count	Mean/%	SD/Count
Age	53.44	9.10	49.54	10.26	51.39	9.91
% Female	40.00%	177	60.94%	298	50.97%	475
Chronic Disease Score	3.58	1.57	3.66	1.68	3.62	1.63

TABLE 2

Initial SGLT2/GLP-1 Medication

SGLT2 Brands	SGLT2 Cohort (n=443)	GLP-1 Brands	GLP-1 Drugs (n=489)
Farxiga	130	Bydureon	12
Invokana	9	Ozempic	245
Jardiance	261	Trulicity	180
Steglatro	1	Victoza	52
Synjardy	21		
Xigduo XR	21		

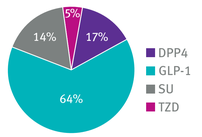
TABLE 3

Outcomes (Reference Group: SGLT2 Cohort)

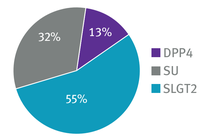
Outcomes	Parameter Estimate	Test Statistic	p-Value	Odds Ratio	95% CI
Proportion of Days Covered (PDC)	0.01 (SE: 0.01)	1.13	0.26		
Adherence (PDC≥80%)		1.51	0.22	0.83	0.61-1.12
Persistence	22.05 (SE: 10.35)	2.13	0.03		
Time to Add or Switch Therapy	20.81 (SE: 31.31)	0.66	0.51		
Switched or Added Therapy		24.11	<0.0001	0.31	0.19-0.50

FIGURE 3

Proportion of Patients Who Added or Switched Therapies



SGLT2 Cohort (N=81)	
Drug Name	Member Count
Bydureon	1
Ozempic	23
Rybelsus	10
Trulicity	15
Victoza	4
Glimepiride	4
Glipizide Ir/Er	7
Janumet Xr	3
Januvia	9
Tradjenta	1
Pioglitazone	4
Total Add/Switches	**81**



GLP-1 Cohort (N=31)	
Drug Name	Member Count
Farxiga	11
Jardiance	5
Synjardy	1
Glimepiride	2
Glipizide Ir/Er	8
Janumet Xr	1
Januvia	3
Total Add/Switches	**31**

DISCUSSION

- Persistence was significantly longer in the SGLT2 cohort; however, the effect size was small suggesting marginal clinical significance. This slight advantage of SGLT2 drugs may indicate preference for oral formulations with long-term use.
- Patients initiated on an SGLT2 post-metformin monotherapy were more likely to switch therapies or add additional agents. Furthermore, several patients who added or switched therapies in the SGLT2 cohort added or switched more than once, while those who added or switched therapies in the GLP-1 cohort only added or switched once. This clinical difference may indicate that drug formulation does not impact patient or provider preferences. For patients eligible for either an SGLT2 or GLP-1 at initial diabetes diagnosis, it may be more long-term cost-effective to initiate T2DM therapy with a GLP-1 given the significant number of switches and additions observed in the SGLT2 cohort.
- Future studies should incorporate medical claims data to determine if the statistically and clinically significant differences between the proportion of patients adding or switching therapies is due to adverse events, T2DM-related hospitalizations, disease progression and/or patient preference. Patient out-of-pocket costs should also be assessed to determine if there is a correlation between high out-of-pocket costs and the number of switches or additions.

RESULTS

- For members in the GLP-1 cohort, 50.10% and 36.80% of patients were initiated on Ozempic and Trulicity at the start of the evaluation period, respectively.
- For members in the SGLT2 cohort, 58.92% and 29.35% of patients were initiated on Jardiance and Farxiga at the start of the evaluation period, respectively.
- Linear regression models: PDC, Time to Add or Switch Therapy
- Logistic regression models: Adherence (PDC ≥80%), Switched or Added Therapy

Adherence & Proportion of Days Covered

- PDC and adherence were nonsignificant between cohorts.
- Patients in the SGLT2 and GLP-1 cohorts were 74.94% and 69.25% adherent, respectively (P=.220; Cohen's d=.13). The SGLT2 and GLP-1 cohorts had an average PDC of 85.92% (SD=.18) and 83.12% (SD=.20; P=.258; Cohen's d=.15), respectively.

Persistence

- The SGLT2 cohort had longer persistence than the GLP-1 cohort (β=22.1; P=.03; Cohen's d=.18).
- Patients in the SGLT2 cohort remained on therapy for an average of 203.16 days (SD=157.14), while the GLP-1 cohort remained on therapy for an average of 176.35 days (SD=145.43).

Time to Add/Switch

- The time to add or switch therapy was nonsignificant between cohorts.
- The SGLT2 cohort had significantly more switches or additions to their diabetes regimen than the GLP-1 cohort (θ=0.31; P=<.0001; Cohen's d=.26; 95% CI: 0.19-0.50).
- 11.27% of patients in the SGLT2 cohort who added or switched therapies also switched or added therapies more than once (n=8).

CONCLUSIONS

- Our results align with the 2023 ADA and EASD guidelines by indicating that first-line therapy should be guided by patient preference and attributes, rather than a strict glycemic control treatment algorithm.

LIMITATIONS

- Findings are generalizable to commercially insured members only and may not represent members enrolled in government programs.
- Data is limited to adjudicated prescription claims and, thus, does not include prescriptions paid in cash.
- Medical claims and lab data were not available and may provide further insight into why patients switched or added medications.
- The sample size may hinder study outcomes statistical and clinical significance.

REFERENCES

1. *National Diabetes Statistics Report:* Estimates of Diabetes and Its Burden in the United States. (2022, Jun 2). Centers for Disease Control and Prevention. https://www.cdc.gov/diabetes/data/statistics-report/index.html
2. Draznin B, Aroda VR, Bakris G, Benson G, et al. Glycemic Targets: *Standards of Care in Diabetes* – 2021. 2021; Jan;44 (Suppl 1):S73-S84. doi: 10.2337/dc21-S006
3. Samson SL, Vellanki P, Blonde L, et al. American Association of Clinical Endocrinology consensus statement: comprehensive type 2 diabetes management algorithm – 2023 update. *Endocr Pract.* 2023;29(5): 305-340. doi: 10.1016/j.eprac.2023.02.001
4. ElSayed NA, Aleppo G, Aroda VR, et al. Glycemic targets: Standards of Care in Diabetes - 2023. *Diabetes Care.* 2023; 46 (Suppl 1):S97-S110. doi: 10.2337/dc23-S006
5. Gurgle HE, White K, McAdam-Marx C. SGLT2 inhibitors or GLP-1 receptor agonists as second-line therapy in type 2 diabetes: patient selection and perspectives. *Vasc Health Risk Manag.* 2016 Jun 4;12:239-249. doi: 10.2147/VHRM.S83088
6. Giugliano, D, Scappaticcio, L, Longo, M et al. GLP-1 receptor agonists vs. SGLT-2 inhibitors: the gap seems to be leveling off. *Cardiovasc Diabetol* 20, 205 (2021). doi: 10.1186/s12933-021-01400-9