Real-World Effectiveness of Once-Weekly Glucagon-Like Peptide-1 Receptor Agonists (OW GLP-1 RAs) on Glycemic Control and Weight Outcomes in Type 2 Diabetes

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https://sciencehub.novonordisk.com/adces2023/Tan.html?cid=qr-1yv8ll7kyo

Aims

- Evaluate the association of OW GLP-1 RAs and change in glycated hemoglobin (HbA_{1c}) and weight.
- Compare the changes in HbA_{1c} and weight associated with initiating OW GLP-1 RA vs dipeptidyl peptidase-4 inhibitors (DPP-4i).

Introduction

- OW GLP-1 RAs have been shown in clinical trials to improve glycemic control and promote weight loss to differing degrees in patients with type 2 diabetes (T2D).[1]
- Little is known about the real-world association between OW GLP-1 RAs and changes in HbA_{1c} and weight. Also, there are few real-world comparisons of OW GLP-1 RA and DPP-4i in terms of changes in HbA_{1c} and weight.

Methods

- This observational cohort database study evaluated patients during the selection window (01 Jan 2018 to 30 Apr 2021). IQVIA's PharMetrics® Plus and Ambulatory Electronic Medical Records (AEMR) were utilized.
- Eligible patients were adults with 2 or more filled prescription claims for the same OW GLP-1 RA (date of first claim was the index date) who were continuously enrolled in PharMetrics® Plus during the 12-month pre- and post-index periods, and had a T2D diagnosis in the pre-index period, available HbA_{1c} and weight values during the pre- and post-index periods, and an HbA_{1c} of ≥7.0% at baseline.

Pre- and post-index analyses

- Changes in HbA_{1c} and weight were evaluated descriptively from the 12-month pre-index period (baseline) to the end of the 12-month post-index period (follow-up) for OW GLP-1 RA.
- The paired t-test, Wilcoxon signed-rank test, and McNemar's test were used in pre- and post-index comparisons.

Inverse probability of treatment weighting (IPTW) analyses

- Patients initiating OW GLP-1 RA without baseline DPP-4i use were compared with patients initiating DPP-4i with no prior baseline GLP-1 RA use.
- To adjust for imbalances in baseline characteristics between the cohorts, IPTW was applied. Standardized mean differences (SMDs) ≥0.1 (absolute) indicated imbalance between baseline characteristics.
- Post-IPTW pairwise dependent comparisons of HbA_{1c} and weight were conducted between the two cohorts by using weighted t-tests, Wilcoxon rank-sum test, and weighted chi-square tests. Logistic regression was also used to adjust for any remaining imbalanced variables.

Results

Results of pre- and post-index analyses

- A total of 921 patients in the OW GLP-1 RA cohort were assessed in the pre- and post-index analyses.
- The mean (SD) age was 54.5 years (8.6), 53.5% of patients were male, and nearly all patients were commercially insured (55.3%) or self-insured (41.2%).
- For the OW GLP-1 RA cohort, the mean (SD) HbA_{1c} declined significantly from 8.9% (1.5%) in the pre-index period to 7.5% (1.4%) in the post-index period (Table 1). An HbA_{1c} <6.5% was achieved by 24.3% of the cohort in the post-index period (Table 1).

Table 1. HbA_{1c} changes from the pre-index to the post-index periods for the OW GLP-1 RA cohort

HbA_{1c}	OW GLP-1 RA (N=921)		p-value
	12 months pre-index (baseline)	12 months post-index	
Baseline/post-index HbA_{1c} (continuous) (%)			
Mean (SD)	8.9% (1.5%)	7.5% (1.4%)	<0.0001
Median	8.5%	7.2%	<0.0001
Baseline/post-index HbA_{1c} (categorical) (n, %)			
HbA_{1c} <6.5%	0 0%	224 24.3%	<0.0001
HbA_{1c} ≥6.5% to <7.0%	0 0%	157 17.1%	
HbA_{1c} ≥7.0% to <8.0%	294 31.9%	273 29.6%	
HbA_{1c} ≥8.0% to <9.0%	267 29.0%	123 13.4%	
HbA_{1c} ≥9.0%	360 39.1%	144 15.6%	
Baseline/post-index HbA_{1c} (binary) (n, %)			
HbA_{1c} <7.0%	0 0%	381 41.4%	<0.0001
HbA_{1c} ≥7.0%	921 100%	540 58.6%	

Post-index values measured at 12 months post-index (360 days post-index ± 90 days, taking the value closest [absolute] to day 360).

- In the OW GLP-1 RA cohort, most patients (71.4%) experienced a decrease in weight, and 27.7% of patients experienced ≥5.0% reduction in weight (Table 2).

Table 2. Weight changes from the pre-index to the post-index period for the OW GLP-1 RA cohort

Weight	OW GLP-1 RA cohort (N=921)		p-value
	12 months pre-index (baseline)	12 months post-index	
Baseline/post-index weight (continuous) (kg)			
Mean (SD)	107.1 (24.5)	103.7 (24.4)	<0.0001
Median	104.0	100.3	0.002
Difference between baseline and post-index weight (kg)			
Mean (SD)		−3.3 (6.4)	
Median		−2.27	
Patients with decrease in weight (n, %)		658 71.4%	
≥5.0% decrease in weight (n, %)		255 27.7%	
≥10.0% decrease in weight (n, %)		91 9.9%	
≥15.0% decrease in weight (n, %)		32 3.5%	

Results of the IPTW analyses

- The pre-IPTW OW GLP-1 RA cohort consisted of 662 patients, and the pre-IPTW DPP-4i cohort consisted of 431 patients. Post-IPTW, a total of 651 and 431 patients made up the cohorts, respectively (Table 3).
- Post-IPTW, mean (SD) age was 54.4 years (8.7) in the OW GLP-1 RA cohort and 54.6 years (9.5) in the DPP-4i cohort, and 55.0% and 55.7% of patients were male, respectively (Table 3).
- Post-IPTW, characteristics of the OW GLP-1 RA and DPP-4i cohorts were well balanced (Table 3).

Table 3. Pre-IPTW and post-IPTW characteristics of the OW GLP-1 RA cohort and the DPP-4i cohort

Characteristic	Pre-IPTW					Post-IPTW				
	OW GLP-1 RA cohort N=662		DPP-4i cohort N=431		SMD	OW GLP-1 RA cohort N=651		DPP-4i cohort N=431		SMD
	n	%	n	%		n	%	n	%	
Age (years)										
Mean (SD)	54.1 (8.7)	—	55.5 (9.9)	—	0.152	54.4 (8.7)	—	54.6 (9.5)	—	0.021
Age group (years) (n,%)										
18–44	94	14.2	56	13.0	−0.035	89.3	13.7	62.4	14.5	0.022
45–54	241	36.4	132	30.6	−0.123	227.2	34.9	143.2	33.2	−0.036
55–64	274	41.4	185	42.9	0.031	271.7	41.7	183.5	42.5	0.016
65+	53	8.0	58	13.5	0.177	62.8	9.6	42.2	9.8	0.005
Gender (n,%)										
Male	352	53.2	242	56.1	0.060	358.0	55.0	240.2	55.7	0.014
Geographic region (n, %)										
Northeast	132	19.9	111	25.8	0.139	141.5	21.7	95.4	22.1	0.009
Midwest	134	20.2	77	17.9	−0.061	124.7	19.2	83.6	19.4	0.006
South	355	53.6	227	52.7	−0.019	349.0	53.6	224.6	52.1	−0.030
West	41	6.2	16	3.7	−0.115	35.8	5.5	27.7	6.4	0.039
Payer type (n,%)										
Commercial	372	56.2	239	55.5	−0.015	359.3	55.2	250.0	58.0	0.056
All other	290	43.8	192	44.5	0.015	291.7	44.8	181.2	42.0	−0.056
CCI										
Mean (SD)	0.8 (1.7)	—	0.7 (1.5)	—	−0.055	0.8 (1.6)	—	0.8 (1.6)	—	0.007
DCSI										
Mean (SD)	0.89 (1.3)	—	0.82 (1.3)	—	−0.050	0.82 (1.2)	—	0.83 (1.3)	—	0.007
Pre-index ADM classes[a] (n, %) (not mutually exclusive)										
Biguanides	513	77.5	364	84.5	0.178	519.9	79.9	351.5	81.5	0.042
Sulfonylurea	214	32.3	148	34.3	0.043	213.7	32.8	153.5	35.6	0.058
Thiazolidinedione	56	8.5	32	7.4	−0.038	52.4	8.0	35.6	8.3	0.008
SGLT-2	220	33.2	93	21.6	−0.264	189.9	29.2	129.9	30.1	0.021
Insulin	181	27.3	44	10.2	−0.450	140.2	21.5	95.4	22.1	0.014

ADM, antidiabetic medication; CCI, Charlson Comorbidity Index; DCSI, Diabetes Complications Severity Index; SGLT-2, sodium-glucose co-transporter-2.

[a]Only classes that were used by at least 5% of the cohorts pre- and post-IPTW are shown.

- Mean and median decreases in HbA_{1c} were significantly greater for the OW GLP-1 RA cohort vs the DPP-4i cohort (Figure 1A).
- HbA_{1c} goals of <7.0% and <6.5% were achieved by significantly greater proportions of the OW GLP-1 RA cohort than the DPP-4i cohort (Figure 1B).
- Compared with the DPP-4i cohort, the OW GLP-1 RA cohort had significantly greater mean and median weight reductions, and significantly higher proportions of patients with weight reductions ≥5.0% and ≥10.0% (Figure 2).

Figure 1. HbA_{1c} results for OW GLP-1 RA vs DPP-4i cohorts. (A) Post-index mean and median decrease in HbA_{1c}. (B) Proportions that achieved HbA_{1c} goals of <7.0% and <6.5%
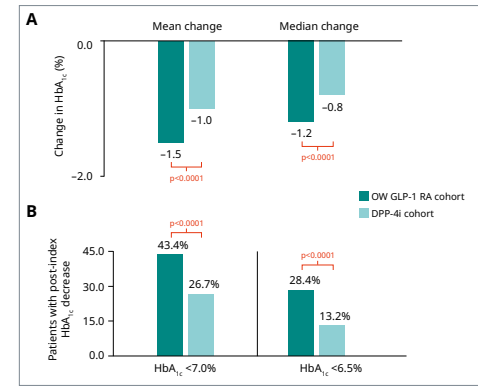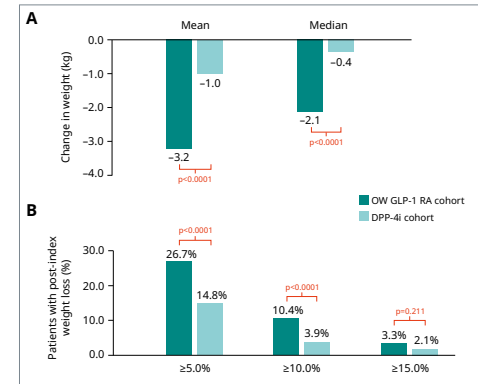

Figure 2. Weight results for OW GLP-1 RA vs DPP-4i cohorts. (A) Post-index mean and median weight changes. (B) Proportions with post-index weight reductions


- Composite goals of ≥5.0% and ≥10.0% reduction in weight in combination with a post-index HbA_{1c} <7.0% were achieved by a significantly greater proportion of patients in the OW GLP-1 RA cohort than in the DPP-4i cohort (Figure 3).

Figure 3. Composite changes in HbA_{1c} and weight in the OW GLP-1 RA and DPP-4i cohorts

- Logistic regression revealed that patients initiating OW GLP-1 RA had higher odds of achieving post-index HbA_{1c} goals and weight loss compared with DPP-4i patients after adjusting for remaining imbalance (Figure 4).

Figure 4. Odds ratios from multivariate logistic regression models for HbA_{1c} and weight outcomes
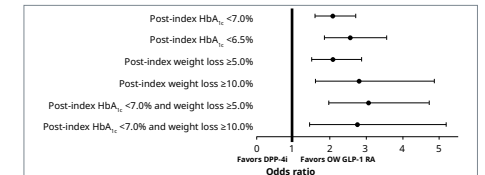
Limitations

- These descriptive study findings establish associations and not cause-and-effect relationships.
- Miscoding or misclassification in claims data is possible.
- PharMetrics® Plus included only commercially insured patients.
- The study sample may not be representative of the overall US T2D population initiating OW GLP-1 RA therapy and may be biased towards capturing patients who more frequently touch the healthcare system and have available values for HbA_{1c} and weight.

Conclusions

- These findings show the real-world effectiveness of OW GLP-1 RA in glycemic and weight control in the T2D population.
- After adjustment for imbalanced covariates, patients initiating OW GLP-1 RA had more than two-times higher odds of achieving HbA_{1c} and weight-loss goals than did patients initiating DPP-4i.
- These findings may provide clinicians and diabetes educators with additional evidence to better incorporate OW GLP-1 RAs in overall T2D management.

Reference
(1) Holst JJ, et al. *Ann N Y Acad Sci.* 1996;805:729–36.