Treatment effectiveness of exenatide once weekly compared with basal insulin for up to 2 years among type 2 diabetes patients naïve to injectable therapy in UK primary care

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Introduction

- Exenatide is a member of the glucagon-like peptide 1 receptor (GLP-1R) agonist class.
- In a formulation with microsphere technology, exenatide QW (EQW) (Bydureon) only has to be administered once weekly.
- Randomised control trial data has shown superiority in glucose control for patients treated with EQW compared with basal insulin (BI) and significant weight reduction[1,2].
- In this study we compared the effectiveness of weight and HbA1c control for patients treated with EQW versus BI in a real world setting.

Methods

- Patients were selected from the Clinical Practice Research Datalink (CPRD); a longitudinal, anonymized research database derived from nearly 700 primary-care practices in the UK
- Patients naïve to injectable therapy prescribed EQW or BI (as monotherapy or in combination with other glucose-lowering therapies) were compared.
- Patients were matched for each outcome by propensity score on age, gender, BMI, T2DM duration, year of index exposure, HbA1c, smoking status, systolic blood pressure, total cholesterol, serum creatinine and Charlson co-morbidity score. Date of first prescription of either EQW or BI was defined as the index date.

Outcomes

- The outcomes were change in HbA1c and weight.
- Baseline measures were defined as any measurement between -180 days and index date. Change in each outcome was measured from baseline to the nearest value recorded at a) 6 months, and b) between 12-24 months (± 90 days) for those patients remaining on their index regimen.
- Two composite end points were considered based on the proportion of patients reaching a target of HbA1c ≤7.0%
  i. with weight reduction
  ii. with weight reduction ≥5%

Results

Identified patients

- 485 patients initiated EQW and 13,503 initiated basal insulin. There were significant differences in baseline characteristics between the unmatched EQW and BI patients (table 1) but these were equalised in the propensity matched cohorts.
- Patient numbers included in each propensity matched analysis are shown in table 2.

HbA1c change

- In the propensity matched analysis, mean HbA1c fell for both EQW and BI with respective changes of -1.3% and -1.2% observed at 6 months and -1.2% and -1.2% at 12—24 months.
- There was no difference in the change in HbA1c between the two treatments (see figure 1, table 2).

Table 1 Baseline characteristics for patients treated with exenatide QW versus basal insulin

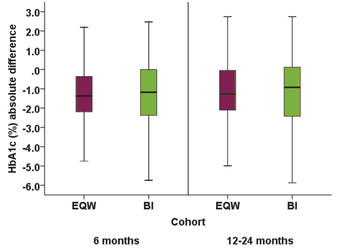
	Exenatide QW		Basal insulin		P-value
Number of patients	485		13,503		
Females (%)	206	(42.5%)	5913	(43.8%)	0.576
Age, years*	57	(11.3)	64.6	(15.2)	<0.001
T2DM duration, years*	8.5	(5.2)	10.2	(8.0)	<0.001
BMI *	37.5	(6.7)	29.9	(6.3)	<0.001
HbA1c DCCT, % *	9.4	(1.7)	9.8	(2.0)	<0.001
HbA1c IFCC *	79.3	(18.6)	83.2	(22.1)	<0.001
Serum creatinine umoll *	76.6	(21.2)	97.8	(49.4)	<0.001
Systolic BP mmHg *	133.6	(14.6)	132.5	(17.2)	0.124
Diastolic BP mmHg *	78.2	(9.3)	75.3	(10.4)	<0.001
Total cholesterol, mmol/l *	4.4	(1.1)	4.4	(1.4)	0.516
Charlson Index *	2.3	(1.3)	3.3	(2.1)	<0.001
Primary care contacts *	11.2	(11.2)	11.1	(11.4)	0.897
Prior MACE (%)	44	(9.1%)	2402	(17.8%)	<0.001
Prior cancer (%)	23	(4.7%)	1754	(13.0%)	<0.001
Smoking History					
Never smoked	209	(43.1%)	5741	(42.5%)	0.218
Ex-smoker	202	(41.6%)	5234	(38.8%)	
Current smoker	71	(14.6%)	2339	(17.3%)	
Monotherapy	55	(11.3%)	3306	(24.5%)	<0.001

* Mean (standard deviation)

Weight change

- In the propensity matched cohorts, mean weight change at six months was -3.7 kg for patients treated with exenatide QW compared with +1.2 kg for those treated with basal insulin (p<0.001).
- At 12—24 months, respective weight change was -3.2 kg and +2.4 kg (p<0.001; Figure 2, table 2).

Figure 1. Change in HbA1c from baseline for patients initiating therapy with either Exenatide QW or basal insulin.



Combined endpoint

- The proportion of patients achieving the target of HbA1c ≤7.0% and any weight loss (EQW versus BI) at 6 months was 22.4% vs 9.3% (p=0.002) and 18.2% vs 8.0% (p=0.007) at 12-24 months.
- For the target of HbA1c ≤7.0% and minimum 5% weight loss the proportions were 11.8% vs 3.7% (p=0.044), and 8.0% vs 0.0% (p=0.007)

Figure 2. Change in weight from baseline patients initiating therapy with either Exenatide QW or basal insulin.

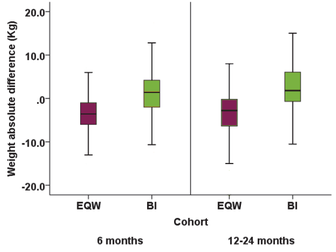


Table 2. Change in HbA1c and weight from baseline for patients initiating therapy with either Exenatide QW or basal insulin.

Time	Cohort	N	Change			
			Median	Mean	Mean difference	p-value
HbA1c						
6 months	EQW	206	-1.37	-1.33	-0.09	0.583
	BI	206	-1.18	-1.24		
12-24 months	EQW	111	-1.28	-1.19	-0.02	0.923
	BI	111	-0.92	-1.17		
Weight (kg)						
6 months	EQW	201	-3.59	-3.7	-4.9	<0.001
	BI	201	1.40	1.20		
12-24 months	EQW	100	-2.80	-3.25	-5.73	<0.001
	BI	100	1.80	2.48		

Conclusions

- Patients prescribed EQW had equivalent HbA1c reduction to those prescribed BI.
- EQW was associated with significant weight reduction compared to those prescribed BI.
- These findings based on a small real-world cohort found similar weight differences to those observed in clinical trials.

References

1. Davies M, Heller S, Sreenan S, Sapin H, Adetunji O, Tahbaz A, Vora J. Once-weekly exenatide versus once- or twice-daily insulin detemir: randomized, open-label, clinical trial of efficacy and safety in patients with type 2 diabetes treated with metformin alone or in combination with sulfonylureas. *Diabetes Care.* 2013;36:1368-76.
2. Diamant M, Van Gaal L, Guerci B, Stranks S, Han J, Malloy J, Boardman MK, Trautmann ME. Exenatide once weekly versus insulin glargine for type 2 diabetes (DURATION-3): 3-year results of an open-label randomised trial. *Lancet Diabetes Endocrinol.* 201;42:464-73.

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Treatment Effectiveness up to 24 Months following Initiation of Exenatide Twice Daily vs. Basal Insulin among Type 2 Diabetes Patients in UK Primary Care

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Introduction

- Exenatide is a member of the glucagon-like peptide 1 receptor (GLP-1R) agonist class.
- Randomized controlled trial data has shown at least equivalence in glucose control for patients treated with exenatide BID (EBID) compared with basal insulin (BI) and significant weight reduction[1].
- In this study we compared the effectiveness of weight and HbA1c control for patients treated with EBID versus BI in a real world setting.

Methods

Data source and patients

- Patients were selected from the Clinical Practice Research Datalink (CPRD); a longitudinal, anonymized research database derived from nearly 700 primary-care practices in the UK.
- Patients naïve to injectable therapy prescribed EBID or BI (as monotherapy or in combination with other glucose-lowering therapies) were compared.
- Patients were matched for each outcome by propensity score on age, gender, BMI, T2DM duration, year of index exposure, HbA1c, smoking status, systolic blood pressure, total cholesterol, serum creatinine and Charlson co-morbidity score.
- Date of first prescription of either EBID or BI was defined as the index date.

Outcomes

- The outcomes were change in HbA1c and weight.
- Baseline measures were defined as any measurement between -180 days and index date. Change in each outcome was measured from baseline to the nearest value recorded at a) 6 months, and b) between 12-24 months (± 90 days) for those patients remaining on their index regimen.
- Two composite end points were considered based on the proportion of patients reaching a target of HbA1c ≤7.0%
  a. with weight reduction
  b. with weight reduction ≥5% of baseline

Results

Identified patients

- 3,573 patients initiated EBID and 13,503 initiated basal insulin. There were significant differences in baseline characteristics between the unmatched EBID and BI patients (table 1) but these were equalised in the propensity matched cohorts.
- Patient numbers included in each propensity matched analysis are shown in table 2.

HbA1c change

- In the propensity matched analysis, mean HbA1c was reduced in both treatment groups with changes of -0.99% for EBID and -1.04% for BI at six months and -1.03% and -0.93% at 12—24 months. There was no difference in the change in HbA1c between the two treatments (see figure 1, table 2).

Table 1 Baseline characteristics for patients treated with exenatide BID versus basal insulin

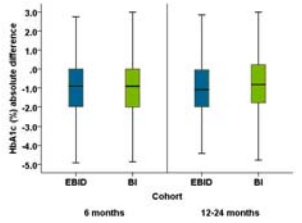
	Exenatide BID		Basal insulin		P-value
Number of patients	3,573		13,503		
Females (%)	1,627	(45.5%)	5,913	(43.8%)	0.063
Age, years*	56.6	(10.6)	64.6	(15.2)	<0.001
T2DM duration, years*	7.9	(4.8)	10.2	(8.0)	<0.001
BMI *	38.7	(6.7)	29.9	(6.3)	<0.001
HbA1c DCCT, % *	9.2	(1.6)	9.8	(2.0)	<0.001
HbA1c IFCC *	77	(17.8)	83.2	(22.1)	<0.001
Serum creatinine umoll *	79.3	(22.5)	97.8	(49.4)	<0.001
Systolic BP mmHg *	134.5	(14.8)	132.5	(17.2)	<0.001
Diastolic BP mmHg *	79.2	(9.3)	75.3	(10.4)	<0.001
Total cholesterol, mmol/l *	4.3	(1.1)	4.4	(1.4)	<0.001
Charlson Index *	2.3	(1.4)	3.3	(2.1)	<0.001
Primary care contacts *	10.8	(9.1)	11.1	(11.4)	0.145
Prior MACE (%)	312	(8.7%)	2,402	(17.8%)	<0.001
Prior cancer (%)	188	(5.3%)	1,754	(13.0%)	<0.001
Smoking History					
Never smoked	1,438	(40.2%)	5,741	(42.5%)	<0.001
Ex-smoker	1,574	(44.1%)	5,234	(38.8%)	
Current smoker	545	(15.3%)	2,339	(17.3%)	
Monotherapy	480	(13.4%)	3,306	(24.5%)	<0.001

* Mean (standard deviation)

Weight change

- In the propensity matched cohorts, mean weight change at 6 months was -3.5 kg for patients treated with EBID compared with +0.8 kg for those treated with BI (p<0.001).
- At 12—24 months, respective weight change was -4.7 kg and +1.7 kg (p<0.001; Figure 2).

Figure 1. Change in HbA1c from baseline for patients initiating therapy with either Exenatide BID or basal insulin.



Combined endpoint

- The proportion of patients achieving the target of HbA1c ≤7.0% and any weight loss (EBID versus BI) was 15.2% vs 6.2% (p<0.001) at 6 months and 18.4% vs 8.1% (p<0.001) at 12—24 months.
- For the target of HbA1c ≤7.0% and minimum 5% weight loss the proportions were 10.0% vs 2.6% (p<0.001), and 13.9% vs 2.4 % (p<0.001)

Figure 2. Change in weight from baseline patients initiating therapy with either Exenatide BID or basal insulin.

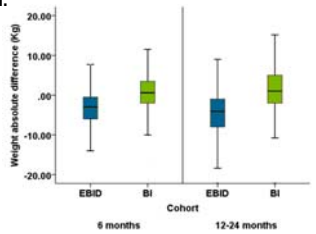


Table 2. Change in HbA1c and weight from baseline for patients initiating therapy with either Exenatide BID or basal insulin.

Time	Cohort	N	Change			
			Median	Mean	Mean difference	p-value
HbA1c						
6 months	EBID	960	-0.90	-0.99	-0.05	0.505
	BI	960	-0.91	-1.04		
12-24 months	EBID	411	-1.09	-1.03	-0.10	0.425
	BI	411	-0.82	-0.93		
Weight (kg)						
6 months	EBID	808	-3.00	-3.46	-4.28	<0.001
	BI	808	0.59	0.82		
12-24 months	EBID	458	-4.11	-4.65	-6.36	<0.001
	BI	458	1.00	1.71		

Conclusions

- Patients prescribed exenatide BID had equivalent HbA1c reduction to those prescribed BI.
- Exenatide BID was associated with significant weight reduction compared to those prescribed BI.
- These findings based on a real-world observational database are similar to those observed in clinical trials

References

[1]Blevins T, Han J, Nicewarner D, Chen S, Oliveira JH, Aronoff S. Exenatide is non-inferior to insulin in reducing HbA1c: an integrated analysis of 1423 patients with type 2 diabetes. Postgrad Med. 2010; 122:118-28.

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