Switching exenatide or gliptins to liraglutide in the Association of British Clinical Diabetologists (ABCD) nationwide liraglutide audit

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Introduction

- Results from LEAD-6 and an extension study provide efficacy data comparing patients started on liraglutide 1.8 mg *vs.* exenatide twice daily (BD), as well as the effects of switching exenatide BD to liraglutide 1.8 mg after 26 weeks.
- National guidelines in the UK discourage the use of liraglutide 1.8 mg dose.
- In clinical practice, some patients persist with exenatide BD despite gastrointestinal (GI) side-effects or have problems of compliance with two injections.
- Dipeptidyl peptidase-4 (DPP-4) inhibitors, which share a similar mechanism of action with glucagon-like peptide-1 (GLP-1) receptor agonists (GLP-1RA), are mostly stopped when GLP-1RAs are started.

Aims

- To identify whether additional HbA_{1c} and weight benefits are obtained when exenatide BD or DPP-4 inhibitors are switched to liraglutide 1.2 mg (rather than the 1.8 mg dose).
  - Comparison with control group of patients adding liraglutide to non-incretin diabetes treatment.
- To identify whether rates of GI side-effects and liraglutide discontinuation are higher among patients switching from exenatide BD.

Methods

- The ABCD nationwide liraglutide audit:
  - invited diabetes centres across the UK to contribute data on patients started on liraglutide in clinical practice;
  - called for data in 2010 and 2011;
  - had 77 centres participating, registering 4129 patients: currently, 2995 patients have follow-up data.
- Patients were divided into those on exenatide BD, on DPP-4 inhibitor, or not on any incretin-based therapy at the time of liraglutide initiation.
- HbA_{1c} and weight changes, rates of any GI side-effects (nausea, vomiting, diarrhoea) and liraglutide discontinuation were compared between groups at 3 months (taken as ± 6 weeks for HbA_{1c} and weight data).
- For HbA_{1c} and weight comparisons, we excluded patients who:
  - were on liraglutide 1.8 mg dose;
  - lacked paired baseline and 3-month HbA_{1c} or weight data;
  - started or stopped insulin;
  - increased or reduced number of oral hypoglycaemic agents (OHAs).

Results

- 2995 audit patients with follow-up data:
  - 640 (21.4%) on exenatide;
  - 323 (10.8%) on DPP-4 inhibitor;
  - 2032 (67.8%) on non-incretin-based diabetes treatment.

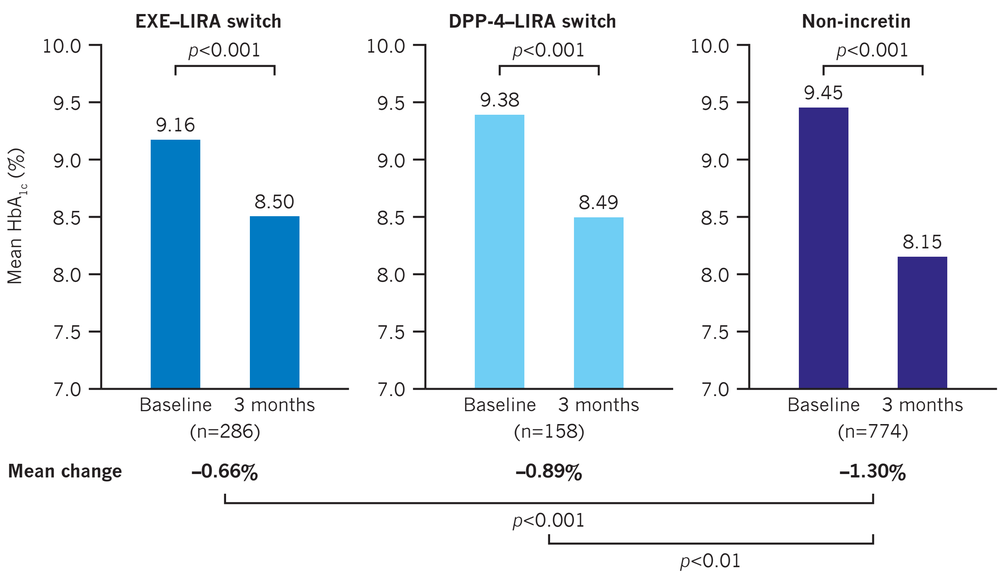
Baseline characteristics of patients starting on liraglutide in the ABCD nationwide liraglutide audit

	On exenatide (n=640)	On DPP-4 inhibitors (n=323)	Not on incretin medications (n=2032)	*p*-value
Gender (% male)	53.0	55.1	54.4	0.768
Ethnic (% Caucasian)	87.5	90.5	91.0	0.057
Age (years)	55.2 (11.1)	57.2 (11.7)	55.5 (10.9)	0.022
Diabetes duration (years)	10 (7–13)	8 (5–11)	9 (5–13)	<0.001
HbA_{1c} (%)	9.12 (1.77)	9.41 (1.61)	9.38 (1.73)	0.004
Weight (kg)	107.3 (22.7)	107.4 (20.8)	111.9 (23.1)	<0.001
BMI (kg/m^2)	37.9 (7.0)	37.7 (6.5)	39.4 (7.7)	<0.001
On insulin treatment (%)	38.8	13.3	46.7	<0.001

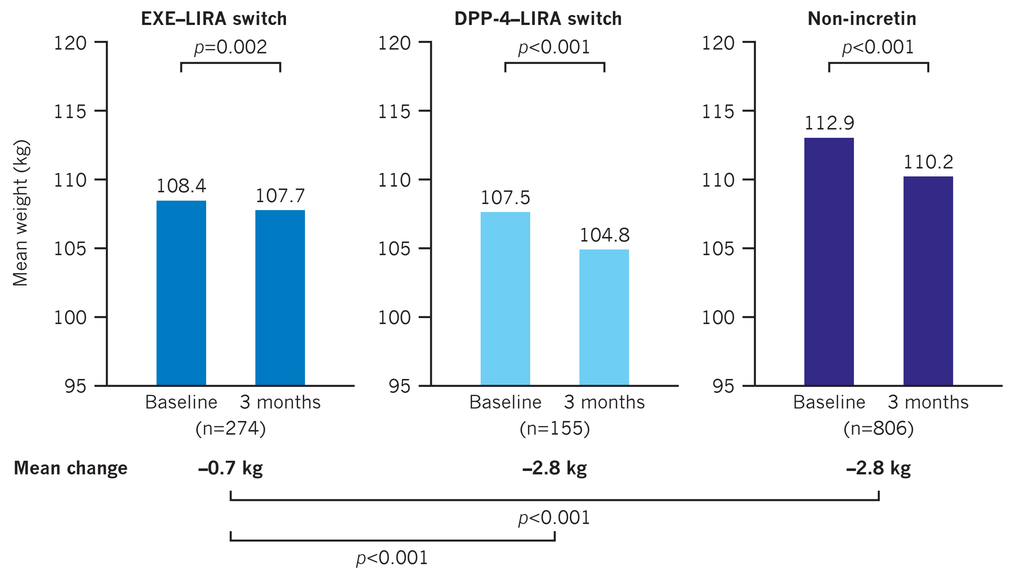
Results for age, HbA_{1c}, weight and BMI quoted as mean (SD) and diabetes duration as median (interquartile range). BMI, body mass index.

- After exclusions, 1218 HbA_{1c} and 1235 weight data available for comparisons at 3 months.

3 month HbA_{1c} changes of patients switching exenatide BD or DPP-4 inhibitors to liraglutide 1.2 mg in comparison with liraglutide add-on therapy



3-month weight changes of patients switching exenatide BD or DPP-4 inhibitors to liraglutide 1.2 mg in comparison with liraglutide add-on therapy



Rates of GI side effects and liraglutide discontinuation among patients on exenatide BD, DPP-4 inhibitors or non-incretin therapies

	On exenatide (n=640)	On DPP-4 inhibitors (n=323)	Not on incretin medications (n=2032)	*p*-value
GI side-effects	10.2%	14.2%	14.1%	0.033
Discontinuation	9.4%	10.2%	7.7%	0.184
GI side-effects	3.3%	3.1%	2.9%	
Lack of efficacy	1.7%	2.8%	1.4%	
Patient choice	1.4%	0.9%	0.2%	
Other reason	3.0%	3.4%	3.2%	

- 135 of 640 patients on exenatide BD provided a reason for switching to liraglutide:
  - 64 were due to persistent GI side-effects;
  - 22 were due to lack of HbA_{1c} or weight efficacy of exenatide BD;
  - 45 preferred one injection or had problems with complying with two injections;
  - 4 had non-GI side-effects to exenatide.
- 76 of 135 and 73 of 135 had HbA_{1c} and weight data available at 3 months.

3-month HbA_{1c} and weight changes, rates of GI side-effects and liraglutide discontinuation among patients switching exenatide to liraglutide

	GI side-effects (n=64)	Lack of efficacy (n=22)	Preference/ compliance (n=45)
n	36	13	27
HbA_{1c} change (%)	–0.51 (0.23)	–0.47 (0.39)	–0.96 (0.26)
p-value	0.034	0.249	0.001
n	36	13	24
Weight change (kg)	–1.6 (0.4)	–0.4 (0.8)	–0.5 (0.8)
p-value	0.001	0.638	0.564
GI side-effects	8/64 (12.5%)	1/22 (4.5%)	6/45 (13.3%)
Liraglutide discontinuation	5/64 (7.8%)	2/22 (9.1%)	0/45 (0%)

Conclusions

- We provide data on the effects of switching exenatide BD or DPP-4 inhibitors to liraglutide 1.2 mg.
- While HbA_{1c} and weight reductions are clearly superior when liraglutide is used as add-on therapy, patients with problems with exenatide BD are able to obtain further HbA_{1c} and weight reductions when switched to liraglutide 1.2 mg.
  - Patients with GI side-effects with exenatide BD, who had preference for one injection or had compliance issues obtained benefit.
- GI side-effects were lower and rates of discontinuation similar among patients switching from exenatide BD to liraglutide in comparison with other groups of patients.

Acknowledgement

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Disclosure

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