

# Safety and efficacy of using exenatide in combination with insulin in the Association of British Clinical Diabetologists (ABCD) nationwide exenatide audit

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## Background

Exenatide is not licensed for use with insulin in the UK. However many clinicians use the combination in suitable patients

## Aims

- ABCD began a nationwide audit in December 2008, to learn from experience of exenatide in real clinical use in the UK.
- The extent, safety and efficacy of off-license usage of exenatide with insulin was assessed from analysis of the audit data.

## Materials and methods

- An on-line questionnaire hosted on the password-protected ABCD website server was used for collection of anonymised patient data.
- Paired t-tests compared baseline and latest weight and HbA1c
- Hypoglycaemia reports were quantified to assess safety of the combination

## Results

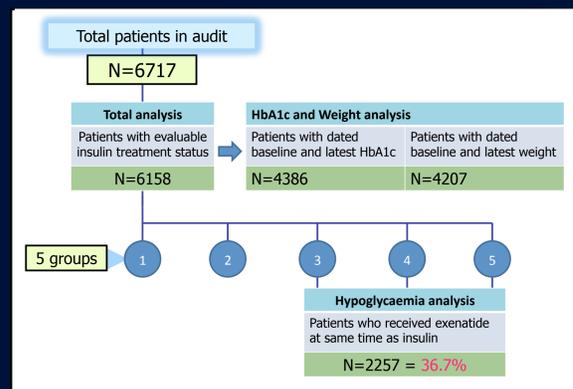
- 315 contributors from 126 centres submitted data on 6717 patients.
- Mean baseline values are as follows:
  - 55.5% male
  - Age 54.9 years
  - HbA1c 9.47%
  - Body weight 113.8 kg
  - BMI 38.9 kg/m<sup>2</sup>
- Of the 6717 patients, 6158 had data with assessable insulin treatment status at baseline and at analysis
- For an intention to treat analysis, 4386 patients had HbA1c data at baseline and at close of audit data collection; 4207 had similar weight data.

These 6158 patients were divided into 5 groups (Fig.1).

1. Not on insulin (n=3576)
2. Insulin stopped at start (n=325)
3. Insulin stopped at start but restarted (n=152)
4. Insulin continued at start (n=1584)
5. Not on insulin at start but added later (n=521)

Groups 3, 4, and 5 n=2257 patients had insulin and exenatide co-administered at some point during audit.

Fig. 1: Data break-down showing the numbers in each analysis arms

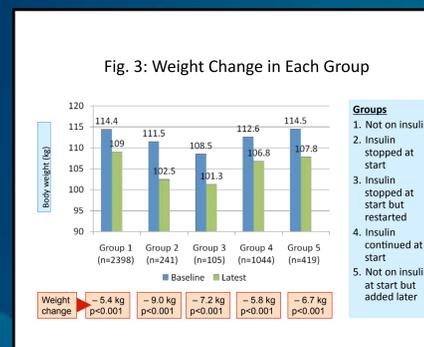
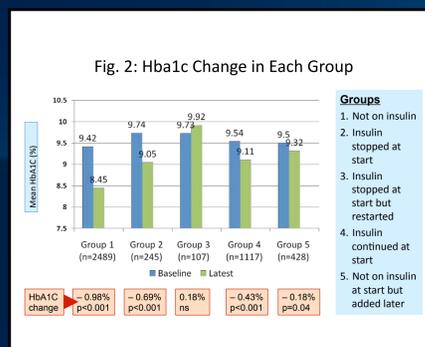


## Efficacy analysis

- Patients with HbA1c and weight data at baseline and at audit-end were identified for further analysis of efficacy.
- These were also divided into 5 groups, as for the total analysis
- Latest HbA1c and weight were at a median (range) of 26.3 (6.6-164.1) and 26.1 (6.6-159.0) weeks respectively after exenatide start.
- The difference in HbA1c and weight from baseline to the latest available in each of the five groups is shown in the figures 2 and 3.

## Change in HbA1C

The HbA1c change from baseline to the latest showed a statistically significant drop in all 5 groups except group 3 (insulin stopped, but restarted) See fig. 2

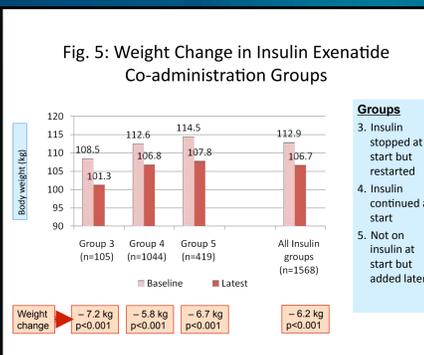
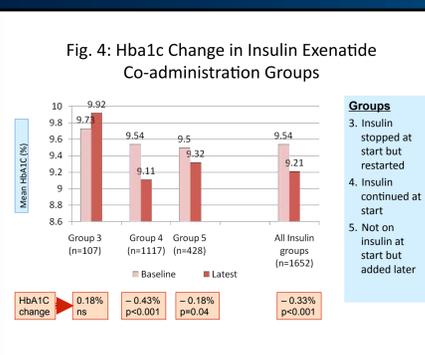


## Change in Weight

The change in body weight from baseline to the latest showed a statistically significant reduction across all 5 groups, including the group who remained on insulin from the start (group 4) See fig. 3

## Insulin-Exenatide Combination

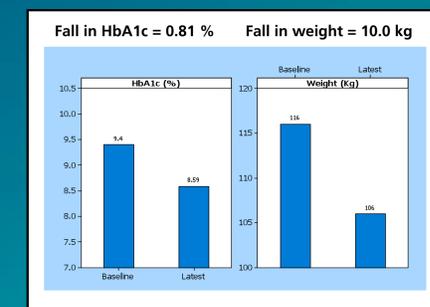
- The efficacy of the combination was analysed collectively using the data from groups 3, 4, and 5.
- The total reduction in HbA1c and body weight remained statistically significant (Fig. 4 and 5)
- The total HbA1c reduction was modest in real clinical terms (-0.33%; p<0.001)
- However, the total weight reduction was remarkable (-6.2 kg; p<0.001)



## Patients who managed to stop insulin

- From the 6158 evaluable patients, 1584 continued insulin at the time of exenatide start (group 4)
- Of these 201/1584 (12.7%) came off insulin during exenatide treatment
- This group did particularly well
  - There was a significant reduction in both HbA1c and bodyweight (fig. 6).

Fig.6: Baseline versus latest HbA1c and Weight in patients who stopped insulin during exenatide treatment



## Hypoglycaemia

- Hypoglycaemia was more frequent among those who had combination therapy (see fig.7)
- However severe hypoglycaemia was rare
  - Only two cases were reported - 2/2257 (Both unlikely to have been related to exenatide)

Fig. 7: Hypoglycaemia in insulin-users before and after exenatide start

HYPOGLYCAEMIA in insulin-users	Groups 3, 4, 5 (N = 2257)	
Before exenatide	133/2257	5.9%
After exenatide	193/2257	8.6%

\*The difference in rate of hypoglycaemia was significant, p = 0.001

## Conclusions

- The combination of exenatide and insulin was commonly used by contributors in the ABCD nationwide exenatide audit
  - 36.7% (2257/6158) patients in the audit
- Exenatide with insulin in real clinical use in the UK has been moderately effective, demonstrated by
  - Statistically significant reductions in weight and HbA1c
- Exenatide allowed some patients to be weaned off insulin
  - This group experienced a considerable improvement in glycaemic control and weight
- Although hypoglycaemia was more frequent when used in combination, it appears to be generally safe
  - Only two cases of severe hypoglycaemia was reported

## Acknowledgements

We would like to thank Eli Lilly Ltd. for an unrestricted grant to ABCD to support this audit.

## Disclaimer

This audit was independently initiated by ABCD. ABCD remained independent in the analysis of the data and the writing of this report. The above analysis was intention to treat. A subsequent analysis has since been performed excluding patients who came off exenatide. Whilst the numbers in this analysis are different the overall results and conclusions remain the same.