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Response at 3 months to insulin dose decisions made at exenatide initiation in the Association of British Clinical Diabetologists (ABCD) nationwide exenatide audit

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Background and aims: To learn from experience of exenatide in real clinical use in the UK, ABCD began a nationwide audit in December 2008. Though exenatide is not licensed for use with insulin many contributors to the audit used the combination. There is uncertainty about what should be done with insulin dose when exenatide is added. We therefore studied the response at 3 months after exenatide initiation in relation to insulin dose decisions made when exenatide was started.
Materials and methods: Patients were analysed according to three groups at initiation: non-insulin users (Group 1), insulin users in whom insulin was stopped (Group 2), and insulin users with insulin continued (Group 3). Group 3 was divided further into groups who had insulin doses unchanged, reduced by 1-40% (mean dose reduction 25.3%), 41-60% (mean 49.7%) and 61-99% (mean 67.4%) for further analyses. HbA1c and weight changes were compared within and across groups at baseline and 3 months. Correlation between insulin dose reduction and HbA1c and weight changes were assessed. Differences in group characteristics were examined.
Results: Amongst 6717 patients in the audit, exact data on diabetes treatment at baseline and initiation as well as suitable HbA1c and weight data were available for 2575 and 2454 patients respectively. The distribution in each group (HbA1c data, weight data) was: Group 1 (1626, 1545), Group 2 (275, 271) and Group 3 (674, 638). Mean age (54.1, 54.8, 55.0yrs), BMI (40.0, 39.3, 40.3kg/m^2), and initial HbA1c (9.5, 9.7, 9.6%) were not statistically different between groups. Group 2 had lower baseline weight than Group 1 (110.8 v 114.6kg, p=0.009). Group 2 had longer diabetes duration than Group 1 (10.8 v 8.3yrs, p<0.001), but lesser duration (10.8 v 12.3yrs, p<0.001) and total insulin dose (92 v 121U, p<0.001) compared with Group 3. Group 1 and 3 achieved significant HbA1c reductions (-0.95%, -0.53%, both p<0.001), but not Group 2 (-0.01%, p=0.948). 48% in Group 2 had HbA1c increases, with 15% ≥ 2.0%. All 3 groups achieved weight reductions (-3.7, -6.6 and -4.3kg, all p<0.001). Across groups, Group 2 achieved no HbA1c benefit compared with Group 1 and 3 (both p<0.001) but the most weight benefit (both p<0.001). Group 3 had intermediate results showing less HbA1c reduction but more weight loss than Group 1 (p<0.001, p=0.007 respectively). Among Group 3, weight reduction, but not HbA1c change, correlated with total insulin dose reduction (p=0.003, p=0.158 respectively). Subgroup analyses revealed the group with average insulin dose reduction of around half, and two-thirds, achieved more weight loss than the group with no dose changes (p=0.010, and p=0.037) or average dose reduction of a quarter (p=0.018, and p=0.035 respectively). Analyses on HbA1c changes among different insulin dose reduction groups did not reveal any significant differences. No severe hypoglycaemia was recorded in Group 3.
Conclusion: Our analysis shows that continuing insulin at exenatide initiation was safe and yielded HbA1c and weight reductions. Progressive insulin dose reductions yielded increasing weight loss but at the expense of HbA1c reduction, although there was no clear threshold when glycaemic reduction was negatively affected. When insulin was substituted, rather than combined with exenatide, almost half of patients had worsened glycaemic control.
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Superior glycaemic control with taspoglutide, a once-weekly human GLP-1 analogue, compared with twice daily exenatide in type 2 diabetes: the T-emerge 2 Trial

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Background and aims: Taspoglutide is a once-weekly (QW) human GLP-1 analog in Phase 3 development. T-emerge 2 compared the safety and efficacy of QW taspoglutide (Taspo) with twice-daily (BID) exenatide (Exe) in adult patients with type 2 diabetes (T2DM) inadequately controlled with metformin+/-thiazolidinedione.
Materials and methods: In this multinational, open-label study, 1149 subjects were randomized (1:1:1) to subcutaneous Taspo 10 mg QW (Taspo10), Taspo 10 mg QW for 4 wks titrated to 20 mg QW (Taspo20), or Exe 5 mcg BID for 4 wks titrated to 10 mcg BID. Primary outcome was HbA1c change at wk 24, testing for non-inferiority (NI) vs Exe (using 2-sided 95% CI for HbA1c difference and noninferiority margin of 0.4%) in the intent-to-treat (ITT) population. If NI was demonstrated, then statistical superiority was tested under closed test procedure.
Results: Baseline characteristics (56 yrs, 6.5 yrs T2DM, HbA1c 8.1%, BMI 33 kg/m^2) were similar across groups. At 24 wks in the ITT population, reductions in HbA1c and FPG with Taspo10 and Taspo20 were superior to Exe (Table). More patients on Taspo10 or Taspo20 achieved target HbA1c ≤7% than Exe: 64.8% (95% confidence interval [CI], 59.8-69.6), 67.9% (95% CI, 63.0-72.5), and 51.5% (95% CI, 46.3-56.7); respectively. Dose-dependent weight loss was seen with Taspo and weight loss with Taspo20 was similar to Exe (Table). Gastrointestinal (GI) complaints were the most frequently reported adverse events across all arms. Although they occurred with a higher incidence in the Taspo groups, discontinuation rate due to GI events was similar in the 3 arms.
Conclusion: Once-weekly Taspo provided superior glycemic control to Exe, with similar body weight reduction at the higher dose and comparable tolerability. (NCT00717457)

LSMean ± SE	Taspo10 (n=384)	Taspo20 (n=392)	Exe (n=373)
Baseline HbA1c (%)	8.08±0.05	8.08±0.05	8.05±0.05
Change from baseline HbA1c (95% CI)	-1.24±0.09 (-1.41, -1.08)	-1.31±0.08 (-1.48, -1.15)	-0.98±0.08 (-1.14, -0.82)
Diff from Exe	-0.26±0.06**	-0.33±0.06**	_
24 Week HbA1c%	6.91±0.05	6.84±0.04	7.15±0.05
Baseline FPG (mmol/l)	9.91±0.13	9.83±0.13	9.87±0.13
Change from baseline FPG (95% CI)	-2.18±0.20 (-2.57, -1.79)	-2.48±0.20 (-2.87, -2.10)	-1.81±0.19 (-2.19, -1.43)
Diff from Exe	-0.37±0.14	-0.67±0.13	_
Baseline body weight (kg)	95.46±0.98	93.18±0.97	94.48±0.99
Change from baseline body weight (95% CI)	-1.60±0.37 (-2.33, -0.88)	-2.33±0.37 (-3.05, -1.60)	-2.27±0.36 (-2.98, -1.56)
Diff from Exe	0.67±0.25*	-0.05±0.25	_

*P<0.05; **P<0.0001

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Retrospective cohort studies of the risk of acute pancreatitis: initiators of exenatide compared to other antidiabetic drugs in two commercial US health insurance claims databases

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Background and aims: Cases of acute pancreatitis (AP) in patients treated with exenatide BID (Ex BID) have been reported.
Objective: To estimate the risk of AP in Ex BID initiators compared to initiators of other antidiabetic drugs (AD).
Materials and methods: Two retrospective studies were conducted to compare the rates of AP between patients without prior claims for pancreatic disease who initiated Ex BID or other AD (from 6/2005 to 12/2008) within 2 US commercial healthcare claims databases (Normative Health Information Database [NHI], Lifelink). The study protocols were similar to evaluate reproducibility of results. Both studies compared the risk of AP during periods of current, recent, or past exposure to Ex BID relative to other AD. AP cases were defined as patients with medical chart-confirmed acute pancreatitis (NHI) or claims for a hospitalisation associated with a primary diagnosis of AP (Lifelink). The NHI study used a multivariable Poisson regression model to estimate the AP propensity score adjusted rate ratios (RRs), and 95% confidence intervals (CIs) for current, recent, or past exposure. It included a blinded-medical record adjudication of claims-identified AP cases and a nested case-control study (NCCS) that involved conditional logistic regression modeling to obtain odds ratios (ORs) and 95% CIs adjusted for differences in the prevalence of risk factors between patients who persisted or discontinued the study drugs. The LifeLink study