

Evidence Tables

EXEN 1: Is exenatide effective in the control of blood glucose in people with type 2 diabetes either alone or in combination, compared to other antidiabetic regimes?

| Reference | Study type Evidence level | Number of patients | Patient characteristics | Intervention | Comparison | Length of follow-up | Outcome measures | Effect size | Source of funding |
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| Buse JB, Henry RR, Han J et al. Effects of exenatide (exendin-4) on glycemic control over 30 weeks in sulfonylurea-treated patients with type 2 diabetes. <i>Diabetes Care</i> . 2004; 27(11):2628-2635. Ref ID: 3367 | RCT, triple-blind, multi-centre 1++ | N=377, 101 sites, USA (ITT, N=377) | Inclusion criteria: 22-76yrs, T2D treated with at least the maximally effective dose of a sulphonylurea for at least 3 months prior to screening, fasting plasma glucose <240mg/dL, BMI 27-45kg/m ² , HbA1c 7.1-11.0%, stable weight ($\pm 10\%$) for 3 months. Exclusion criteria: used other oral anti diabetic agents or insulin or weight loss drugs in the previous 3 months, use of corticosteroids, drugs which affect GI motility, transplant medications, evidence of clinically significant co-morbidity. | N=125, 5 μ g exenatide s/c BD 15 mins before meals N=129, 10 μ g exenatide s/c BD ¹ 15 mins before meals NOTE: there was a 4-week acclimation period at a lower dose of 5 μ g before the | N=123, placebo injection (considered as 2 treatment arms) 15 mins before meals | 34 weeks 4 week single-blind placebo lead-in, 30 week triple-blind study period | Glycaemic control, primarily assessed by HbA1c and safety. The effects of exenatide on fasting plasma glucose, body weight, fasting concentrations of circulating insulin, pro-insulin and lipids. | *HbA1c At week 30, the HbA1c change from the baseline was $-0.86\pm 0.11\%$ for the 10 μ g group; $-0.46\pm 0.12\%$ for the 5 μ g group and $0.12\pm 0.09\%$ for the placebo group (adjusted $p\leq 0.0002$ for pairwise comparisons). For those with a baseline of >7% HbA1c (N=353) the proportions of N=41 in the 10 μ g group and N=31 in the 5 μ g group who reached an HbA1c of $\leq 7\%$ were significantly greater than the N=9 for the placebo groups ($p<0.0001$). Baseline HbA1c $\geq 9\%$ - the exenatide groups had significant decreases compared with increases with placebo; $-1.22\pm 0.19\%$ (10 μ g), $-0.58\pm 0.24\%$ (5 μ g), $0.13\pm 0.17\%$ (placebo), $p<0.05$, pairwise comparisons. Baseline HbA1c <9% - the exenatide groups had significant decreases | Amylin Pharmaceuticals and Eli Lilly |

¹ If required subjects had their sulfonylurea dose adjusted before the placebo lead-in period to the maximally effective dose

² For mild/moderate hypoglycaemia subjects reported symptoms consistent with hypoglycaemia that may have been documented by a plasma glucose concentration (60mg/dl)

³ To address the risk of hypoglycaemia the protocol recommended progressive 50% reductions in SU dose, eventual discontinuation in the event of a documented episode of hypoglycaemia (glucose <60 mg/dl), to two undocumented but suspected episodes of hypoglycaemia

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| | | | <p>The groups were similar at baseline, though the placebo group had a slightly higher average body weight than the exenatide groups.</p> | <p>fixed dose was either increased to 10µg or remained at 5µg</p> | | | <p>compared with increases with placebo; -0.65±0.12% (10 µg), -0.39±0.12% (5 µg), 0.11±0.12% (placebo), p<0.01, pairwise comparisons.</p> <p>*Fasting plasma glucose There was a significant decrease in fasting plasma glucose in the 10 µg group (-0.6±0.3mmol/l) compared with an increase with placebo (0.4±0.3mmol/l), p<0.05. The decrease with the 5 µg group was NS compared with placebo.</p> <p>*Body weight There was a significant decrease in body weight in the 10µg group (-1.6±0.3kg/m2) compared with placebo (-0.6±0.3kg/m2), p<0.05. The decrease with the 5 µg group was NS compared with placebo.</p> <p>*Insulin and Proinsulin There were no significant differences in fasting plasma insulin concentrations across treatment groups throughout the study.</p> <p>There was a significant reduction in fasting proinsulin concentrations in the 10µg group (-16 pmol/l, CI -26.1 to -6.0) compared with placebo (p<0.01).</p> <p>*Proinsulin to insulin ratio In the 10µg group the mean proinsulin-to-insulin ratio was reduced -0.13 compared with baseline, this was significantly lower than with placebo (p=0.001)</p> | |
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| | | | | | | | | <p>*Lipids There were small reduction in LDL (p<0.05) with exenatide compared with placebo.</p> <p>*Discontinuation Placebo, N=49 (39.8%), due to AEs N=4(3.3%) 5µg exenatide, N=30 (24.0%), due to AEs N=9(7.2%) 10µg exenatide, N=38 (29.5%), due to AEs N=13(10.1%)</p> <p>*Adverse Events One participant in the 10µg group and one experienced an MI and one in the placebo group experienced clinical manifestations of CAD.</p> <p>Nausea was the most frequent AE, placebo N=9 (7%), 5µg exenatide, N=49 (39%), 10µg exenatide, N=66 (51%). Withdrawals due to nausea were 0% with placebo, 2% with 5µg exenatide and 4% with 10µg exenatide.</p> <p>*Hypoglycaemia There were no cases of severe hypoglycaemia. The incidence of mild-to-moderate hypoglycaemia² was 3% with placebo, 14% with 5µg exenatide and 36% with 10µg exenatide. One subject withdrew due to hypoglycaemia (in the 5µg exenatide group).³ The incidence of treatment-emergent, dose-dependent hypoglycaemia peaked during the initial weeks, then decreased</p> | |
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| <p>DeFronzo RA, Ratner RE, Han J et al. Effects of exenatide (exendin-4) on glycemic control and weight over 30 weeks in metformin-treated patients with type 2 diabetes. <i>Diabetes Care</i>. 2005; 28(5):1092-1100. Ref ID: 3327</p> | <p>RCT, triple-blind, multi-centre 1++</p> | <p>N=336, 82 sites, USA (N=336. ITT)</p> | <p>Inclusion criteria: 19-78yrs, T2D treated with metformin monotherapy dose $\geq 1,500$mg/day for previous 3 months, fasting plasma glucose < 13.3mmol/l (240mg/dl), BMI 27-45kg/m², HbA1c 7.1-11.0%, stable weight ($\pm 10\%$) for 3 months, with no clinically significant abnormal lab tests.</p> <p>Exclusion criteria: used other oral anti diabetic agents or insulin or weight loss drugs in the previous 3 months, use of corticosteroids, drugs which affect GI motility, transplant medications, evidence of clinically significant co-morbidity.</p> <p>The groups were similar at baseline.</p> | <p>N=110, 5μg exenatide s/c BD 15 mins before meals</p> <p>N=113, 10μg exenatide s/c BD⁴ 15 mins before meals</p> <p>NOTE: there was a 4-week acclimation period at a lower dose of 5μg before the fixed dose was either increased to 10μg or remained at 5μg</p> | <p>N=113, placebo injection (considered as 2 treatment arms) 15 mins before meals</p> | <p>34 weeks 4 week single-blind placebo lead-in, 30 week triple-blind study period</p> | <p>Glycaemic control, primarily assessed by HbA1c and safety. The percentage of patients achieving HbA1c $\leq 7\%$, the effects of exenatide on fasting and postprandial plasma glucose, body weight, fasting and post prandial concentrations of circulating insulin, fasting pro-insulin and lipids.</p> | <p>over time.</p> <p>*HbA1c At week 30, there was a significant dose-dependent reduction in HbA1c compared with placebo ($p < 0.001$).</p> <p>For those with a baseline of $> 7\%$ HbA1c N=41 (40%) in the 10μg group and N=27 (27%) in the 5μg group reached an HbA1c of $\leq 7\%$, these were significantly greater than the N=11 (11%) for the placebo groups ($p < 0.01$ for pairwise comparisons).</p> <p>*Fasting plasma glucose The difference from the 10μg group and placebo at the end of the study averaged -1.4 mmol/l (-25mg/dl), $p = 0.0001$</p> <p>*Postprandial glucose⁵ At week 4 concentrations were reduced in both exenatide arms compared with placebo ($p = 0.006$), this was also found at week 30, ($p = 0.004$ for 10μg group, $p = 0.03$ for 5μg group). Geometric mean area under the curve 15-180 min values averaged 34% lower than baseline in each exenatide arm compared with 9% for placebo.</p> <p>*Body weight</p> | <p>Amylin Pharmaceuticals and Eli Lilly</p> |
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⁴ All subjects continued their current regimen of metformin treatment ($\geq 1,500$ mg/day)

⁵ A subset of participants underwent a standardised meal tolerance test on weeks 0,4 and 30. Baseline data (week 0) showed a similar rise in postprandial plasma glucose concentrations across treatment groups

⁶ For mild/moderate hypoglycaemia subjects reported symptoms consistent with hypoglycaemia that may have been documented by a plasma glucose concentration (60mg/dl)

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| | | | | | | | | <p>Decreases in body weight were significant for both 10µg group (-2.8±0.5kg, p≤0.001) and the 5µg group (-1.6±0.4kg, p≤0.05), compared with placebo (-0.3±0.3kg).</p> <p>For changes in body stratified by BMI the decreases in body weight were significant for the 10µg group for both a baseline BMI of <30 (p≤0.001) and a baseline BMI of ≥30 (p≤0.05) compared with placebo. For the 5µg group changes were significant for a baseline BMI of ≥30 (p≤0.05) compared with placebo.</p> <p>*Insulin and proinsulin There were no significant differences in fasting plasma insulin concentrations across treatment groups throughout the study. Changes for proinsulin from baseline were NS.</p> <p>*Proinsulin to insulin ratio In the 10µg group the mean proinsulin-to-insulin ratio was reduced significantly compared with placebo (p<0.001)</p> <p>*Discontinuation Placebo, N=24 (21.2%), due to AEs N=1(0.9%) 5µg exenatide, N=20 (18.2%), due to AEs N=4(3.6%) 10µg exenatide, N=20 (17.7%), due to AEs N=8(7.1%)</p> <p>*Adverse Events Nausea was the most frequent AE, placebo N=26 (23%), 5µg exenatide, N=40 (36%), 10µg exenatide, N=51</p> |
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| | | | | | | | | (45%). 4 of the 11 withdrawals due to nausea were in the exenatide groups. There was no correlation between change in body weight and duration of nausea. *Hypoglycaemia There were no cases of severe hypoglycaemia. The incidence of mild-to-moderate hypoglycaemia ⁶ was 5.3% with placebo, 4.5% with 5µg exenatide and 5.3% with 10µg exenatide. | |
| Kendall DM, Riddle MC, Rosenstock J et al. Effects of exenatide (exendin-4) on glycemic control over 30 weeks in patients with type 2 diabetes treated with metformin and a sulfonylurea. <i>Diabetes Care</i> . 2005; 28(5):1083-1091. Ref ID: 3331 | RCT, double-blind, multi-centre 1++ | N=733, 91 sites, USA N=733 ITT | Inclusion criteria: 19-78yrs, T2D treated with metformin (≥1,500mg/day) and a maximally effective dose of a sulfonylurea for the previous 3 mths, fasting plasma glucose <13.3mmol/l, BMI 27-45kg/m ² , HbA1c 7.5-11.0%, stable weight (±10%) for 3 months, with no clinically significant abnormal lab tests. Exclusion criteria: used other oral anti diabetic | N=245, 5µg exenatide s/c BD 15 mins before meals N=241, 10µg exenatide s/c BD ⁷ 15 mins before meals NOTE: there was a 4- | N=247, placebo injection s/c BD 15 mins before meals | 34 weeks 4 week single-blind placebo lead-in, 30 week double-blind study period | Glycaemic control, primarily assessed by A1c and safety. The effects of exenatide on fasting and postprandial plasma glucose, body weight, fasting and fasting plasma lipids. | *A1c Exenatide treatment arms had significant reductions, 10µg group (-0.77±0.08%) and 5µg group (-0.55±0.07%) compared an increase with placebo (0.23±0.07%), p<0.0001. Baseline A1c ≥9% - the exenatide groups had significant decreases compared with increases with placebo; p≤0.0002, pairwise comparisons. Baseline A1c <9% - the exenatide groups had significant decreases compared with an increase with placebo; p<0.0001, pairwise comparisons. | Amylin Pharmaceuticals and Eli Lilly |

⁷ All subjects continued their current regimen of metformin treatment (≥1,500mg/day) or were randomised to either a maximally effective SU dose or a minimally recommended SU dose.

⁸ A subset of participants underwent a standardised meal tolerance test on weeks 0,4 and 30. Baseline data (week 0) showed a similar rise in postprandial plasma glucose concentrations across treatment groups

⁹ For mild/moderate hypoglycaemia subjects reported symptoms consistent with hypoglycaemia that may have been documented by a plasma glucose concentration (60mg/dl)

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| | | | <p>agents or insulin or weight loss drugs in the previous 3 months, use of corticosteroids, drugs which affect GI motility, transplant medications, evidence of clinically significant co-morbidity.</p> <p>The groups were similar at baseline.</p> | <p>week acclimation period at a lower dose of 5µg before the fixed dose was either increased to 10µg or remained at 5µg</p> | | | <p>For those with a baseline of >7% A1c 30% in the 10µg group and 24% in the 5µg group reached an A1c of ≤7%, these were significantly greater than the 7% for the placebo groups (p<0.0001 for pairwise comparisons).</p> <p>*Fasting plasma glucose At week 30 the fasting plasma glucose were reduced in the 10µg group (-0.6±0.2mmol/l) and the 5µg group (-0.5±0.2mmol/l), compared with an increase with placebo (0.8±0.2mmol/l), p<0.0001 for pairwise comparison.</p> <p>*Postprandial glucose⁸ At week 4 concentrations were reduced in both exenatide arms compared with placebo (p<0.001), this was sustained at week 30, (p=0.001). Incremental AUC values were reduced by 87% (10µg group) and 59% (5µg group) compared with a <1% decrease in the placebo arm.</p> <p>*Body weight Decreases in body weight were significant for both groups of -1.6±0.2kg) compared with placebo (-0.9±0.2kg), p≤0.01.</p> <p>*Discontinuation Placebo, N=59 (23.9%), due to AEs N=11(4.5%) 5µg exenatide, N=39 (15.9%), due to AEs N=14(5.7%) 10µg exenatide, N=43 (17.8%), due to AEs N=22(9.1%)</p> | |
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| | | | | | | | | <p>*Adverse Events Nausea was the most frequent AE, placebo N=51 (20.6%), 5µg exenatide, N=96 (39.2%), 10µg exenatide, N=117 (48.5%). Withdrawals due to nausea were <1%, placebo; 2%, 5µg group; 4% 10µg group. There was no correlation between change in body weight and duration of nausea.</p> <p>*Hypoglycaemia The incidence of hypoglycaemia was 12.6% with placebo, 19.2% with 5µg exenatide and 27.8% with 10µg exenatide. There was one case of severe hypoglycaemia, which did not require medical intervention occurred in the 5µg exenatide group. All other hypoglycaemic events were mil-to-moderate hypoglycaemia⁹ and there were no withdrawals due to hypoglycaemia.</p> | |
| Heine RJ, Van Gaal LF, Johns D et al. Exenatide versus insulin glargine in patients with suboptimally controlled type 2 diabetes: a randomized trial.[see comment][summary for patients in Ann | RCT, phase III, open-label, multi centre 1+ | N=551, 82 sites, 13 countries ITT, N=549 | Inclusion criteria: 30-75 years, treated with stable and maximally effective metformin and a sulphonylurea for at least 3 months prior to screening, HbA1c from 7.0-10.0%, BMI from 25-45kg/m ² , a history of stable body weight (≤10% variation for ≥3 months before | N=282 exenatide 5µg BD for 6 weeks, 10µg BD for 20 weeks ¹⁰ | N=267 insulin glargine 10U/day, then using a fixed dose algorithm to adjust the dose, they self titrated the dose in 2u | 26 weeks | HbA1c, FPG, self-monitored blood glucose, adverse events | <p>*HbA1c HbA1c was reduced from baseline at week 26 by 1.11% in both treatment groups. The percentage of participants who achieved the target HbA1c of equal to 7% or less were similar; 46% for exenatide and 48% for insulin glargine.</p> <p>*Fasting plasma glucose The reduction in fasting plasma glucose was significantly greater for those</p> | Eli Lilly and Amylin Pharmaceuticals |

¹⁰ Metformin and sulphonylurea doses were fixed at prestudy levels unless patients experienced hypoglycaemia when a 50% reduction in sulphonylurea dose was recommended

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| <p>Intern Med. 2005 Oct 18;143(8):130; PMID: 16230718]. <i>Annals of Internal Medicine</i>. 2005; 143(8):559-569. Ref ID: 1124</p> | | | <p>screening)</p> <p>Exclusion criteria: had more than 3 episodes of severe hypoglycaemia within the previous 6 months, cardiac disease class III or IV (New York Heart Association criteria), serum creatinine greater than 135µmol/L for men and 110µmol/L for women, were receiving long-term systemic glucocorticoid therapy, had used prescription drugs for weight loss within the last 3 months, had been treated with other anti-diabetic treatments within the last 3 months (for thiazolidinediones 4 months)</p> <p>Groups were similar at baseline</p> | | <p>increments every 3 days to achieve a fasting blood glucose target level of less than 5.6mmol/L (<100mg/dL) on daily glucose monitoring. At week 26 the average dose of insulin glargine was 25.0 U/d</p> | | | <p>treated with insulin glargine (initially 10.4 mmol/L reduced by 2.9) compared with exenatide (initially 10.1mmol/L reduced by 1.4), p<0.001. 21.6% of those in the insulin glargine group compared with 8.6% in the exenatide group achieved a fasting glucose of less than 5.6mmol/L (p<0.001).</p> <p>*Body weight Mean change in body weight at week 26 was -2.3kg for exenatide and 1.8kg increase for insulin glargine.</p> <p>*Self-monitored blood glucose Glucose profiles were similar between the groups at baseline with inadequate postprandial glucose control observed after each meal. At week 26 mean daily self-monitored blood glucose levels were not difference between the groups. Those using insulin glargine had lower glucose levels at fasting (p<0.001), before meals (pre-unch p=0.023; pre-dinner p=0.006), at 3:00 a.m. (p<0.001) and evening (p<0.001) compared with exenatide.</p> <p>*Adverse events The most frequent adverse events were nausea and vomiting with 57.1% (N=161) and 17.4%(N=49) respectively in the exenatide group and 8.6% (N=23) and 3.7%(N=10) respectively in the insulin glargine group.</p> <p>Overall rates of hypoglycaemia was</p> | |
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| | | | | | | | | similar across treatment groups (7.3 events/patient year with exenatide vs. 6.3 in the insulin glargine group). | |
| | | | | | | | | *Discontinuation N=54 withdrew from the exenatide group (N=27 due to adverse events) and N=25 from the insulin glargine group (N=2 due to adverse events). | |
| Nauck MA, Duran S, Kim D, Johns D, Northrup J, Festa A et al. A comparison of twice-daily exenatide and biphasic insulin aspart in patients with type 2 diabetes who were suboptimally controlled with sulfonylurea and metformin: a non-inferiority study. Diabetologia 2007; 50(2):259-267. Ref ID: 4988 | RCT, open label. Non-inferiority trial 1+ | N= 501 13 countries | Inclusion criteria: Patients between 30 and 75 years of age with suboptimal glycaemic control despite receiving optimally effective metformin and sulfonylurea therapy for at least 3 months. Inclusion criteria included, at the time of screening, HbA1c levels ≥ 7.0 and $\leq 11.0\%$, a BMI ≥ 25 and ≤ 40 kg/m ² , and a history of stable body weight ($\leq 10\%$ variation for ≥ 3 months) Exclusion criteria: patients had had more than three episodes of severe hypoglycaemia within 6 months prior to screening. Patients had used any prescription | Exenatide 5ug bid for 4 weeks, 10ug thereafter N= 253 | Biphasic aspart bid. Dose titrated for optimal control ¹¹ N = 248 | 52 weeks | HbA1c FPG PPG Body weight Safety | *HbA1c Mean HbA1c change: <i>Exenatide:</i> $-1.04 \pm 0.07\%$ <i>Biphasic aspart:</i> $-0.89 \pm 0.06\%$ Difference -0.15 (95% CI -0.32 to 0.01%) *FPG <i>Exenatide:</i> -1.82 ± 0.2 mmol/l <i>Biphasic aspart:</i> -7 ± 0.2 mmol/l Difference -0.15 (95% CI -0.32 to 0.01%) *Body weight Exenatide-treated patients lost weight, while patients treated with biphasic insulin aspart gained weight. Between group difference -5.4 kg (95% CI -5.9 to -5.0 kg) *Withdrawal rate: Exenatide 21.3% (54/253) Aspart 10.1% (25/248) * Adverse events The incidence of GI adverse events was higher with exenatide than with aspart. | Eli Lilly |

¹¹ A forced titration schedule was not used on this trial. Investigators were instructed to adjust insulin doses to achieve an optimal balance between glycaemic control and risk of hypoglycaemia.

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| | | | <p>drug to promote weight loss within 3 months ; or patients had been treated with insulin, glitazones, alpha-glucosidase inhibitors or meglitinides for longer than 2 weeks within 3 months.</p> <p>Baseline characteristics: at baseline, participants were generally overweight (BMI 30.4±4.1 kg/m²) with a long history of diabetes (duration ±10.6 years) and suboptimal glycaemic control (HbA1c 8.6 ±1.0%).</p> | | | | | <p>Nausea (33% incidence, 3.5% discontinuation) observed with exenatide.</p> <p>Vomiting (15% incidence)</p> <p>The overall hypoglycaemia rates were similar across treatment groups at endpoint.</p> | |
| <p>Poon T, Nelson P, Shen L et al. Exenatide improves glycaemic control and reduces body weight in subjects with type 2 diabetes: a dose-ranging study. <i>Diabetes Technology & Therapeutics</i>. 2005; 7(3):467-477. Ref ID: 3364</p> | <p>RCT, phase 2, triple-blinded, multi centre</p> <p>1+</p> | <p>N=156, 32 sites, USA</p> <p>N=156 ITT</p> | <p>Inclusion criteria; 18-65yrs, T2D treated either with diet modification and exercise alone or a stable dose of metformin for at least the previous 3 months, ¹²HbA1c of 6.8-9.0%, FBG <240mg/dL, BMI of 27-45kg/m² and a stable body weight (not varying by >10% for at least the previous 3 months,, no clinically relevant abnormal lab</p> | <p>N=30, 2.5µg exenatide s/c BD, 15 mins before meals</p> <p>N=31, 5 µg exenatide s/c BD, 15 mins before meals</p> <p>N=31, 7.5 µg exenatide s/c BD, 15 mins before</p> | <p>N=33, placebo, s/c BD, 15 mins before meals</p> | <p>6 weeks</p> <p>2 week single-blind placebo lead-in</p> <p>4 week treatment study period</p> | <p>HbA1c, FPG, body weight, adverse events</p> | <p>*HbA1c Exenatide showed a significant decrease in HbA1c levels compared to an increase with placebo (0.1±0.1%), with all dose groups; 2.5µg (-0.3±0.1%), 5µg (-0.4±0.1%), 7.5µg (-0.5±0.1%), 10µg (-0.5±0.1%), p<0.01. Reductions were significantly greater than with placebo at each exenatide dose.</p> <p>*Fasting blood glucose Exenatide showed significant decrease in FBG compared with an increase found with placebo. (6.8±4.1mg/dL), with all dose groups; 2.5µg (-20.1±5.2mg/dL), 5µg (-21.2±3.9mg/dL),</p> | <p>Amalyin Pharmaceuticals</p> |

¹² For participants taking metformin the dose was fixed at pre-study levels

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| | | <p>test values.</p> <p>Exclusion criteria: having taken insulin therapy, other OADs, if they were taking lipid-lowering agents that had not been stable for a minimum of 6 wks, or taking anti-hypertensives that had not been stable for 4 wks, or were taking glucocorticoid</p> <p>Treatment groups were generally well balanced at baseline, though there were some differences between groups in the male:female ratios, body weight, duration of diabetes and BMI data.</p> | <p>meals</p> <p>N=31, 10 µg exenatide s/c BD, 15 mins before meals</p> | | | <p>7.5µg (-17.7±4.8mg/dL), 10µg (-17.3±4.4mg/dL), p<0.01. The magnitude of this decrease did not appear to be dose dependent. These reductions were similar for participants treated with diet/exercise and those treated with metformin.</p> <p>*Body weight Those taking exenatide showed dose-dependent reduction in body weight compared with the placebo group who remained essentially weight neutral. These reductions were significant for the 7.5µg (-1.4±0.3kg), 10µg (-1.8±0.3kg), p<0.01.</p> <p>*Subgroup analysis Data from the placebo group and from the 5µg and 10µg exenatide doses were used. This considered the participants that were treated with diet/exercise (N=24 for HbA1c and FPG, N=23 for body weight) versus metformin (N=70 for HbA1c and FPG, N=69 for body weight). Mean reductions in HbA1c, FPG and body weight were greater for exenatide treated participants compared with placebo for both subgroups (P<0.05). The effects of exenatide were similar in those treated with diet and exercise and for those taking metformin.</p> <p>*Discontinuation 97% of the placebo group and 89% of the exenatide groups completed treatment.</p> |
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| | | | | | | | | <p>*Adverse events The most frequent AE reported was nausea (40.7% with exenatide and 12.1% with placebo), and vomiting (9.8% with exenatide and 3.0% with placebo). Severe nausea was reported in 6.5% of exenatide cases and in 3.0% of placebo. Severe vomiting was reported in 1.6% of exenatide cases and no placebo cases. Nausea was greater in the 7.5µg (61.3%) and the 10µg (51.6%) groups than in the 2.5µg (23.3%) and 5µg (25.8%) groups, indicating a dose-dependent response.</p> | |
| Secnik BK, Matza LS, Oglesby A et al. Patient-reported outcomes in a trial of exenatide and insulin glargine for the treatment of type 2 diabetes. <i>Health & Quality of Life Outcomes</i> . 2006; 4:80, 2006.:80, 2006. Ref ID: 3356 | RCT, open label, multi-centre 1+ | N=549, 13 countries Analysis done per protocol, N=455 | Inclusion criteria: T2D inadequately controlled by sulfonylurea and metformin (i.e HbA1c between 7.0-10.0%) ¹³ . There were no statistical differences between the groups at baseline. | N=228 exenatide BD 15 mins before meals, fixed dose 5µg for the first 4 weeks and subsequently increased to 10µg BD. | N=227 insulin glargine once daily at bedtime, forced titration to FBS ≤5.5mmol/L | 26 weeks | Glycaemic control as measured by HbA1c. To compare the two treatment groups with respect to change in patient-reported health outcomes measures, Diabetes Symptom Checklist (DSC-R), Diabetes treatment | <p>*HbA1c Glycaemic control results not reported</p> <p>*Health outcomes measures Both treatment groups demonstrated significant baseline to endpoint changes on several of the health outcomes instruments. Comparison of change in health outcomes between the two treatment groups indicated NS differences.</p> <p>*Adverse events N=126 (55%) participants in the exenatide group reported nausea compared with N=22 (10%) in the insulin glargine group</p> | Eli Lilly |

¹³ Oral medications were maintained at pre-study dose levels unless participants experienced hypoglycaemia, in which case a 50% reduction in SU was recommended

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| | | | | | | | Flexibility Scale (TFS), Diabetes Treatment Satisfaction Questionnaire (DTSQ), EuroQol EQ-5D and vitality scale of SF-36. | | |
| Blonde L, Klein EJ, Han J et al. Interim analysis of the effects of exenatide treatment on A1C, weight and cardiovascular risk factors over 82 weeks in 314 overweight patients with type 2 diabetes. <i>Diabetes Obes Metab.</i> 2006; 8(4):436-447. Ref ID: 3333 | Open-label extension study of {Buse, 2004 3367 /id; DeFronzo, 2005 3327 /id; Kendall, 2005 3331 /id} | N=974 ¹⁴ of this N=668 were eligible to continue in the open-label phase as they had been originally randomised to exenatide N=551 ITT | See initial studies | N=551 exenatide s/c BD 15 mins before meals, fixed dose 5µg for the first 4 weeks and subsequently increased to 10µg BD ¹⁵ | N/A | 82 weeks (initial RCTs, 30 weeks, open-label 52 weeks) | HbA1c, fasting plasma glucose, body weight, adverse events, hypoglycaemia | *HbA1c The reduction in HbA1c identified at the end of the 30 week RCTs was maintained to week 82. The proportion of those with a baseline A1c >7% (N=289) who achieved an A1c ≤7% were 39 and 48% at weeks 30 and 82 respectively. The group with baseline A1c ≥9% showed similar reductions at week 82 as had been found at week 30. *FPG The reduction in FPG found at week 30 at the end of the RCT was maintained to week 82. *Body weight Reduction in body weight was progressive to week 82. The changes from baseline at week 30, for the RCTs, for the 10 µg BD dose were -1.6 to - | Amalyin Pharmaceuticals and Eli Lilly |

¹⁴ 87% of the N-1125 who completed the 30 week RCTs

¹⁵ Those taking metformin continued with the same dosage, the open-label extension did not contain guidelines regarding the adjustment of SU dosage, therefore any dosage changes were at the investigator's discretion

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| | | | | | | | | <p>2.8kg (vs. -0.3 to -0.9kg for placebo). At week 82 the change from baseline was -4.4 ± 0.3kg (95% CI: -3.8 to -5.1kg), or 4.4% of baseline body weight. At week 82, 81% of participants had lost weight. Baseline BMI affected the magnitude of the weight reduction, participants with baseline BMI <25 had a mean weight reduction of 2kg (2.9% of baseline body weight), those with a baseline BMI of ≥ 40 had a mean reduction of over 7kg (5.5% of baseline body weight).</p> | |
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