**Methods:** Patients from the modified intent-to-treat populations of 9 GetGoal trials were categorized by baseline estimated GFR (eGFR) according to ADA 2013 categories of renal function at randomization (normal function, eGFR ≥90 mL/min; mild RI [Stage II], eGFR 60–89 mL/min; moderate RI [stage III], eGFR 30–59 mL/min). Meta-analyses of placebo-adjusted mean differences between baseline renal categories were performed for efficacy and safety outcomes.
**Results:** Patient distribution across renal function categories was: normal renal function, lixisenatide n=2081, placebo n=1158; mild RI, lixisenatide n=592, placebo n=404; moderate RI, lixisenatide n=110, placebo n=62. A1C, 2h postprandial plasma glucose and fasting plasma glucose were reduced in lixisenatide-treated patients with normal and stage I, II and III renal function. Meta-analyses showed no significant difference between normal renal function and mild or moderate RI groups for clinical endpoints (Table 1, page S10). The most common adverse events in all groups were gastrointestinal, mainly nausea and vomiting. There was 10% higher risk of nausea and vomiting between patients with normal renal function and those with mild RI (placebo-adjusted rate difference p=0.003), but no significant difference between patients with mild and moderate RI (p=0.92).
**Conclusion:** This study shows that a difference in baseline renal status did not have an effect on efficacy outcomes in lixisenatide vs. placebo-treated patients and a uniform effect of lixisenatide was observed across renal categories.

## 22

### Efficacy and Safety of Once Weekly Dulaglutide vs. Once Daily Liraglutide in Type 2 Diabetes (AWARD 6)

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**Background and aims:** This phase 3, randomized, open-label, parallel-arm 26-week study compared the efficacy and safety of once weekly dulaglutide (DU) 1.5 mg, a long-acting GLP-1 receptor agonist, with once daily liraglutide (LIRA) 1.8 mg in metformin-treated (≥1500 mg/day) patients with type 2 diabetes.
**Materials and methods:** Patients (n=599; mean baseline age, 57 years; A1C, 8.1 %; weight 94.1 kg) were randomized to DU 1.5 mg or LIRA 1.8 mg in a 1:1 ratio. The primary objective was A1C change from baseline at 26 weeks tested for noninferiority (margin 0.4%); DU 1.5 mg vs. LIRA 1.8 mg.
**Results:** DU 1.5 mg was noninferior to LIRA 1.8 mg at 26 weeks as measured by A1C change from baseline (between-group A1C change −0.06; 95% CI [−0.19, 0.07]) (Table 1). While both groups experienced significant weight reduction, LIRA-treated patients demonstrated a 0.71 kg greater weight reduction than DU-treated patients (p=0.01). The most common treatment-emergent gastrointestinal adverse events for DU 1.5 mg and LIRA 1.8 mg, respectively, were nausea (20.4%, 18.0%), diarrhea (12.0%, 12.0%), dyspepsia (8.0%, 6.0%) and vomiting (7.0%, 8.3%). Patients who discontinued study and/or study drug due to gastrointestinal adverse events were similar (DU 1.5 mg [3.0%], LIRA 1.8 mg [4.3%]). Rates of hypoglycemia (≤3.9 mmol/L ± symptoms) were 0.34 events/pt/yr (DU 1.5 mg) and 0.52 (LIRA 1.8 mg) events/pt/yr. No severe hypoglycemia was reported.
**Conclusions:** Once weekly DU 1.5 mg demonstrated noninferior glycemic control compared to once daily LIRA 1.8 mg with a similar safety and tolerability profile.

**Table 1**

| Efficacy measures (26 weeks, ITT) | DU 1.5 mg (n=299) | LIRA 1.8 mg (n=300) |
|---|---|---|
| A1C change, %, least square mean (SE)[a] | −1.42 (0.05)[‡] | −1.36 (0.05) |
| % of patients with A1C <7.0% | 68.3 | 67.9 |
| Weight change, kg, least square mean (SE)[b] | −2.90 (0.22)[#] | −3.61 (0.22) |

[‡] 1-sided p<0.001 for non-inferiority vs. LIRA for A1C change. [#] p=0.01 vs. LIRA. [a]MMRM. [b]ANCOVA LOCF.

## 23

### Reductions in Post-Prandial Glucagon by the GLP-1 Receptor Agonist Lixisenatide Correlate to Reductions in PPG and A1C in Patients with Type 2 Diabetes Mellitus

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**Background:** Inhibition of glucagon secretion is a key function of glucagon-like peptide 1 (GLP-1), but its contribution to improved glycemic control has not been established. This study assessed the role of the once daily GLP-1 receptor agonist lixisenatide (LIXI) on 2 h post-prandial glucagon in patients with type 2 diabetes mellitus (T2DM), and its impact on post-prandial glucose (PPG) and glycated hemoglobin (A1C).
**Methods:** Baseline (BL) and Wk24 2 h post-prandial glucagon data from the modified intent-to-treat populations of 3 LIXI phase III trials – GetGoal-M (+ metformin vs. placebo), GetGoal-S (+sulfonylurea ± metformin vs. placebo) and EFC10780 (vs sitagliptin) – were assessed for changes in 2 h PPG and A1C. Meta-analysis was performed with combined least square mean estimates and z-transformed Pearson correlation values.
**Results:** LIXI treatment reduced 2 h glucagon, 2 h PPG and A1C at Wk24 (all p<0.001). There was a significant positive correlation between the BL-subtracted Wk24 2 h post-prandial glucagon and PPG with LIXI across all studies combined and individually (p≤0.0003; Figure 1). LIXI was associated with a similar effect between BL-subtracted 2 h glucagon and the resulting A1C level (combined GetGoal p<0.0001).

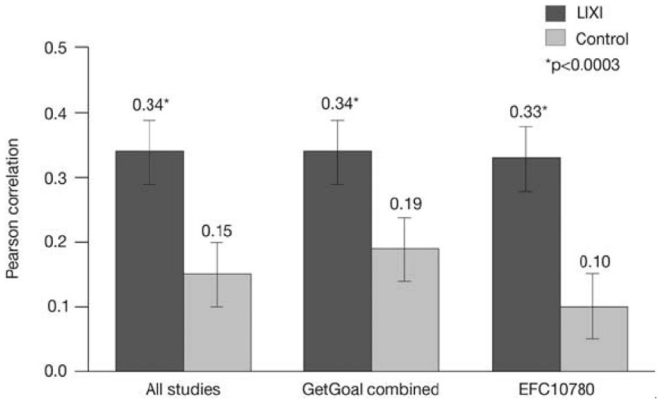


**Figure 1.** Correlation of Wk24 2 h glucagon and PPG (BL-subtracted)