**The effect of lixisenatide on post-prandial blood glucose and glucagon in type 1 diabetes**

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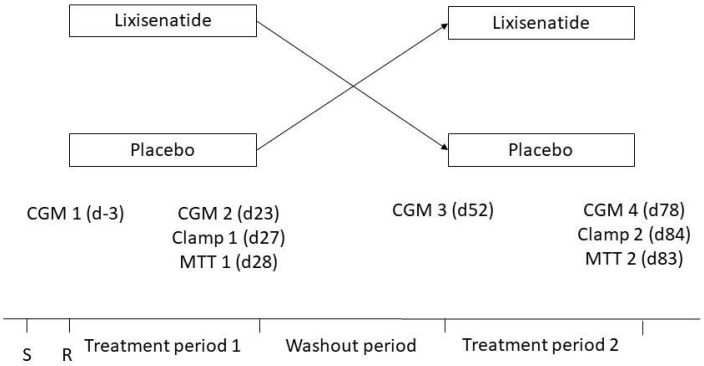
**Background and aims:** The glucagon-like peptide-1 receptor agonist, Lixisenatide (Lix), suppresses glucagon and reduces hyperglycaemia in type 2 diabetes. We studied the effect of Lix on post-prandial blood glucose (PPBG) and glucagon in type 1 diabetes (T1D).
**Materials and methods:** In a double-blinded, placebo-controlled, crossover study, 25 patients with T1D (13 females, mean±SE $HbA_{1C}$ 65.6±8.1 mmol/mol, BMI 27.0±3.6 Kg/$m^2$) received treatment in random order with Lix and placebo (Plac) in addition to their usual insulin therapy for four weeks, with a four week washout period in between. Participants had continuous glucose monitoring (CGM) for at least 3 days before and at the end of each treatment period, as well as post treatment standard mixed meal tests (MMT; Fortisip 360 Kcal) and hyperinsulinaemic hypoglycaemic clamps (target glucose 2.5 mmol/L). (See Figure). The primary outcome was defined as the proportion of CGM readings in the range 4 to 10 mmol/L during the 3-hour post-prandial period.
**Results:** The mean±SE percentage of PPBG CGM readings in range was similar before and after treatment and for each meal for Lix compared with Plac (breakfast 45.4±6.0 vs. 44.3±6.0, p=0.9, lunch 45.5±5.8 *vs.* 50.6±5.3, p=0.6, and dinner 43.0±6.7 *vs.* 47.7±5.6, p=0.6). Mean HbA1c did not change during treatment periods and was similar between Lix and Plac (64.7±1.6 *vs.* 64.1±1.6 mmol/mol, p=0.3). The overall daily prandial insulin dose post-treatment was significantly less after Lix compared with Plac (-0.7±0.6 *vs.* +2.4±0.7 units/day, p=0.004), but the total insulin dose was not different between treatments. The post MMT mean±SE 120 minute glucose area under the curve (AUC) was lower with Lix compared with Plac (392.0±167.7 *vs.* 628.1±132.5 mmol/L x min, p< 0.001), as was the corresponding glucagon AUC (140.0 ±110.0 *vs.* 304.2±148.2 nmol/L x min, p<0.001). Glucagon values at a blood glucose level of 2.4 mmol/L during the hypoglycaemic clamp, were similar for Lix compared with Plac (3.1±3.7 *vs.* 2.6±1.7 nmol/L, p=0.7). Mean adrenaline, noradrenaline, cortisol and pancreatic polypeptide values did not differ during the clamp between Lix and Plac.
**Conclusion:** Lixisenatide suppresses glucagon and may reduce post prandial glycaemia without compromising counter-regulatory responses during hypoglycaemia in T1D.

**Figure 1. Trial design (S: screening, R: Randomisation, d: day)**




*Clinical Trial Registration Number: ISRCTN no. 00290196*
*Supported by: Funding for this Investigator Sponsored research was provided by Sanofi*
*Disclosure:* **C. Ballav:** None.