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EFFICACY AND SAFETY OF LIRAGLUTIDE VS PLACEBO WHEN ADDED TO BASAL INSULIN ANALOGUES IN SUBJECTS WITH TYPE 2 DIABETES (LIRA-ADD2BASAL): A RANDOMISED, PLACEBO-CONTROLLED TRIAL

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Background and aims:This trial aimed to establish the superior efficacy and acceptable safety of liraglutide (LIRA) vs. placebo (PLAC) added to pre-existing basal insulin analogue ± metformin in subjects with inadequately controlled type 2 diabetes (T2D).

Materials and methods: Subjects with T2D, age 18–80 years, BMI 20–45kg/m^2, HbA_{1c}7.0–10.0% and on stable insulin analogue dose ≥20U/day ± stable metformin ≥1500mg/day were eligible for participation. In a multi-centre, multi-national, double-blind, parallel-group design, subjects were randomised 1:1 to receive once-daily LIRA 1.8 mg or PLAC added to pre-existing treatment for 26W. Following randomisation, insulin adjustments above the pre-trial dose were not allowed. The primary endpoint was the change in HbA_{1c} from baseline to W26.

Results: A total of 451 subjects were randomised (226 LIRA; 225 PLAC). Mean baseline characteristics were similar between the two groups (LIRA;PLAC): HbA_{1c} 8.2;8.3%, BMI 32.3;32.2 kg/m^2, diabetes duration 12.1y. and insulin dose 48.3;45.9 U (geometric mean 40.5 U for both groups). After 26W of treatment, subjects on LIRA had a greater decrease in HbA_{1c} from baseline than PLAC, and more LIRA subjects reached HbA_{1c} <7.0% and HbA_{1c} ≤6.5% using a lower mean estimated daily dose of basal insulin analogue compared to PLAC (35.8 U vs. 40.0 U). Subjects on LIRA also achieved greater decreases from baseline in fasting plasma glucose (FPG), incremental post-prandial self-measured plasma glucose (SMPG), body weight, systolic blood pressure and lipids. Nausea and vomiting occurred more frequently with LIRA than PLAC (22.2% vs. 3.1% and 8.9% vs. 0.9%, respectively). Minor hypoglycaemia (plasma glucose <3.1 mmol/L) occurred in 18.2% and 12.4% of LIRA and PLAC subjects, respectively. No severe hypoglycaemic events were reported during this trial. **Conclusion**: The addition of LIRA to basal insulin analogues ± metformin significantly improved glycaemic control, which can be attributed to the effect of LIRA on both FPG and post-prandial glucose levels. Additionally, LIRA induced greater weight loss and a reduction in systolic blood pressure and selected lipids compared to PLAC. Typical gastrointestinal symptoms and minor hypoglycaemia were more frequent with LIRA than PLAC. No severe hypoglycaemic events were reported during this trial.