Impact of type 2 diabetes duration on response to iGlarLixi vs iGlar: a subanalysis of LixiLan-L

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Background and aims: Glucagon-like peptide-1 receptor agonists such as lixisenatide have insulin-independent effects, which may allow benefit for patients with a longer duration of type 2 diabetes (T2D) and greater loss of β-cell function.

Materials and methods: We assessed the effects of insulin glargine U100 (iGlar) vs fixed-ratio iGlar plus lixisenatide (iGlarLixi) by T2D duration in the LixiLan-L trial (N=736). Changes in glycated haemoglobin (HbA1c), weight, and insulin dose from baseline to Week 30, as well as hypoglycaemia rates, were analysed in patients divided into quartiles by recorded baseline T2D duration (<7.3, 7.3-<10.7, 10.7-15.7, and >15.7 yrs). Patients were also grouped by both duration and baseline insulin dose, both of which may relate inversely to β-cell function.

Results: Baseline HbA1c was higher in longer-duration quartiles but similar with iGlarLixi vs iGlar. iGlarLixi reduced HbA1c more vs iGlar across all duration quartiles (Figure). The difference was greatest in patients in the longest duration quartile (least squares mean difference [standard error], -0.62 [0.13]; p<0.0001). Mean (SD) weight change across quartiles ranged from -0.95 (3.50) to -0.11 (3.65) with iGlarLixi and from 0.43 (2.81) to 1.13 (2.83) with iGlar (p<0.0001, 0.0053, <0.0001, and 0.3281 for between-group differences, in lowest to highest duration quartiles). In both treatment groups, patients in the shortest duration quartile had the greatest mean insulin dose change from baseline to Week 30 (11.91 and 14.36 U for iGlarLixi and iGlar, respectively, versus 8.84 and 8.90, respectively, in the longest duration quartile). The difference in hypoglycaemia (iGlarLixi vs iGlar) was greatest in patients in the longest duration quartile (3.3 vs 6.9 events/patient-yr; p<0.0001). In patients grouped by T2D duration and insulin dose, those with both long duration (≥15.7 yrs) and high dose (≥42 U) showed the greatest difference in HbA1c lowering with iGlarLixi vs iGlar.

Conclusion: In LixiLan-L, iGlarLixi lowered HbA1c more vs iGlar regardless of T2D duration, with the greatest difference in those with the longest duration.

Figure. HbA1c at baseline and Week 30 by baseline T2D duration

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