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Efficacy and Safety of LixiLan, a Titratable Fixed-Ratio Combination of Insulin Glargine Plus Lixisenatide in Type 2 Diabetes Inadequately Controlled on Basal Insulin and Metformin: The LixiLan-L Randomized Trial.

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Abstract

OBJECTIVE:

This study was conducted to demonstrate the efficacy and safety of LixiLan (iGlarLixi), a novel, titratable, fixed-ratio combination of insulin glargine (iGlar) (100 units) and lixisenatide, compared with iGlar in patients with type 2 diabetes inadequately controlled on basal insulin with or without up to two oral glucose-lowering agents.

RESEARCH DESIGN AND METHODS:

After a 6-week run-in when iGlar was introduced and/or further titrated, and oral antidiabetic drugs other than metformin were stopped, 736 basal insulin-treated patients (mean diabetes duration 12 years, BMI 31 kg/m^2) were randomized 1:1 to open-label, once-daily iGlarLixi or iGlar, both titrated to fasting plasma glucose <100 mg/dL (<5.6 mmol/mol) up to a maximum dose of 60 units/day. The primary outcome was change in HbA_{1c} levels at 30 weeks.

RESULTS:

HbA_{1c} decreased from 8.5% (69 mmol/mol) to 8.1% (65 mmol/mol) during the run-in period. After randomization, iGlarLixi showed greater reductions in HbA_{1c} from baseline compared with iGlar (-1.1% vs. -0.6%, P < 0.0001), reaching a mean final HbA_{1c} of 6.9% (52 mmol/mol) compared with 7.5% (58 mmol/mol) for iGlar. HbA_{1c} <7.0% (53 mmol/mol) was achieved in 55% of iGlarLixi patients compared with 30% on iGlar. Mean body weight decreased by 0.7 kg with iGlarLixi and increased by 0.7 kg with iGlar (1.4 kg difference, P < 0.0001). Documented

symptomatic hypoglycemia (≤70 mg/dL) was comparable between groups. Mild gastrointestinal adverse effects were very low but more frequent with iGlarLixi.

CONCLUSIONS:

Compared with iGlar, a substantially higher proportion of iGlarLixi-treated patients achieved glycemic targets with a beneficial effect on body weight, no additional risk of hypoglycemia, and low levels of gastrointestinal adverse effects in inadequately controlled, basal insulin-treated, long-standing type 2 diabetes.

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Benefits of LixiLan, a Titratable Fixed-Ratio Combination of Insulin Glargine Plus Lixisenatide, Versus Insulin Glargine and Lixisenatide Monocomponents in Type 2 Diabetes Inadequately Controlled With Oral Agents: The LixiLan-O Randomized Trial.

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Abstract

OBJECTIVE:

To evaluate efficacy and safety of LixiLan (iGlarLixi), a novel titratable fixed-ratio combination of insulin glargine (iGlar) and lixisenatide (Lixi), compared with both components, iGlar and Lixi, given separately in type 2 diabetes inadequately controlled on metformin with or without a second oral glucose-lowering drug.

RESEARCH DESIGN AND METHODS:

After a 4-week run-in to optimize metformin and stop other oral antidiabetic drugs, participants (N = 1,170, mean diabetes duration ~8.8 years, BMI ~31.7 kg/m^2) were randomly assigned to open-label once-daily iGlarLixi or iGlar, both titrated to fasting plasma glucose <100 mg/dL (<5.6 mmol/mol) up to a maximum insulin dose of 60 units/day, or to once-daily Lixi (20 µg/day) while continuing with metformin. The primary outcome was HbA_{1c} change at 30 weeks.

RESULTS:

Greater reductions in HbA_{1c} from baseline (8.1% [65 mmol/mol]) were achieved with iGlarLixi compared with iGlar and Lixi (-1.6%, -1.3%, -0.9%, respectively), reaching mean final HbA_{1c} levels of 6.5% (48 mmol/mol) for iGlarLixi versus 6.8% (51 mmol/mol) and 7.3% (56 mmol/mol) for iGlar and Lixi, respectively (both P < 0.0001). More subjects reached target HbA_{1c} <7% with iGlarLixi (74%) versus iGlar (59%) or Lixi (33%) (P < 0.0001 for all). Mean

body weight decreased with iGlarLixi (-0.3 kg) and Lixi (-2.3 kg) and increased with iGlar (+1.1 kg, difference 1.4 kg, $P < 0.0001$). Documented symptomatic hypoglycemia (≤70 mg/dL) was similar with iGlarLixi and iGlar (1.4 and 1.2 events/patient-year) and lower with Lixi (0.3 events/patient-year). iGlarLixi improved postprandial glycemic control versus iGlar and demonstrated considerably fewer nausea (9.6%) and vomiting (3.2%) events than Lixi (24% and 6.4%, respectively).

CONCLUSIONS:

iGlarLixi complemented iGlar and Lixi effects to achieve meaningful HbA_{1c} reductions, close to near normoglycemia without increases in either hypoglycemia or weight, compared with iGlar, and had low gastrointestinal adverse effects compared with Lixi.

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