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.

Aroda VR1, Rosenstock J2, Wysham C3, Unger J4, Bellido D5, González-Gálvez G6, Takami A7, Guo H8, Niemoeller E9, Souhami E10, Bergenstal RM11; LixiLan-L Trial Investigators.

Abstract information

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/m²) 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 HbA1c levels at 30 weeks.

RESULTS:

HbA1c 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 HbA1c from baseline compared with iGlar (-1.1% vs. -0.6%, P < 0.0001), reaching a mean final HbA1c of 6.9% (52 mmol/mol) compared with 7.5% (58 mmol/mol) for iGlar. HbA1c <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.

© 2016 by the American Diabetes Association.

PMID: 27650977
DOI: 10.2337/dc16-1495
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.

Rosenstock J¹, Aronson R², Grunberger G³, Hanefeld M⁴, Piatti P⁵, Serusclat P⁶, Cheng X⁷, Zhou T⁸, Niemoeller E⁹, Souhami E¹⁰, Davies M¹¹; LixiLan-O Trial Investigators.

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/m²) 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 HbA₁c change at 30 weeks.

RESULTS:

Greater reductions in HbA₁c 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 HbA₁c 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 HbA₁c <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 HbA1c reductions, close to near normoglycemia without increases in either hypoglycemia or weight, compared with iGlar, and had low gastrointestinal adverse effects compared with Lixi.

© 2016 by the American Diabetes Association.

PMID: 27527848
DOI: [10.2337/dc16-0917](10.2337/dc16-0917) [PubMed - as supplied by publisher]