Advancing therapy in suboptimally controlled basal insulin-treated type 2 diabetes: Clinical outcomes with iGlarLixi versus premix BIAsp 30 in the SoliMix randomized controlled trial

iGlarLixi vs BIAsp 30

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Introduction

For people with T2D on basal insulin who fail to reach their recommended glycemic targets, options for treatment advancement include:
- Basal insulin + progressive addition of rapid-acting insulin
- Premix insulin
- Basal insulin + GLP-1 RA
- Fixed-ratio combination (FRC) of basal insulin + GLP-1 RA

All these treatment options have been shown to improve glycemic control when used to advance therapy from basal insulin, but are associated with specific side-effects:
- GLP-1 RA therapy can be associated with gastrointestinal AEs and resultant adherence issues
- Basal + rapid-acting insulin and premix insulin regimens can increase the risk of hypoglycemia and weight gain, require multiple daily injections and frequent glucose monitoring

Globally, premix insulins are widely used to advance insulin therapy from basal insulin

iGlarLixi is a once-daily titratable FRC of basal insulin glargine 100 U/mL (iGlar) and the GLP-1 RA, lixisenatide (Lixi), which offers an alternative option to premix insulin for treatment advancement

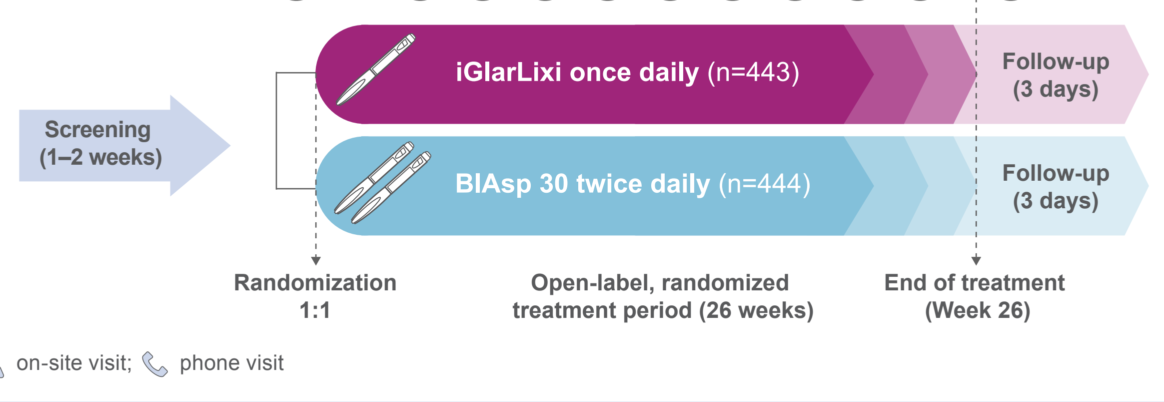
Objective

SoliMix is the first RCT to directly compare the efficacy and safety of an FRC of basal insulin and GLP-1 RA, **iGlarLixi**, with premix insulin analog, biphasic insulin aspart 30 (**BIAsp 30**), in people with T2D advancing from basal insulin plus one or two OADs

Methods

Population

- Adults (≥18 years)
- Suboptimally controlled by basal insulin combined with metformin ± SGLT2i
- HbA_{1c} of ≥7.5 % and ≤10.0 % (≥58.5–≤85.8 mmol/mol)



on-site visit; phone visit

Primary efficacy endpoints

26 weeks

- **Non-inferiority** of **iGlarLixi** to **BIAsp 30** in HbA_{1c} reduction from baseline to Week 26
- **Superiority** of **iGlarLixi** versus **BIAsp 30** in bodyweight change from baseline to Week 26

Detailed methods have been previously published[1]

Key baseline characteristics

Overall, baseline characteristics did not differ between the two treatment groups (randomized population)

	Mean ± SD age, years	Sex, % female	Mean ± SD BMI, kg/m²	Mean ± SD duration of T2D, years	Mean ± SD HbA_{1c}, %	Mean ± SD HbA_{1c}, mmol/mol
iGlarLixi (n=443)	59.8 ±10.3	49.4%	29.7 ±4.7	13.0 ±7.1	8.6 ±0.7	71 ±7
BIAsp 30 (n =444)	59.8 ±10.0	50.9%	30.0 ±5.1	13.0 ±7.4	8.6 ±0.7	70 ±7

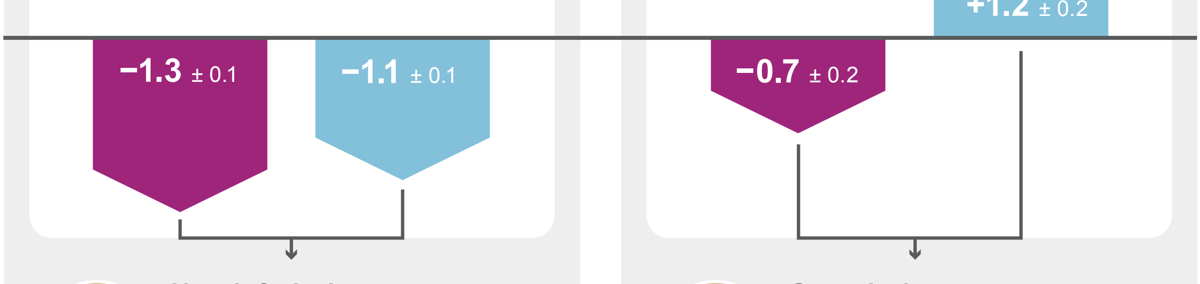
Further details on baseline characteristics have been previously published[1]

Key results: Efficacy

Both primary efficacy endpoints were met: **iGlarLixi** demonstrated non-inferiority in HbA_{1c} reduction and superiority in bodyweight change from baseline to Week 26 versus **BIAsp 30** (ITT population). Secondary analyses showed iGlarLixi was superior to **BIAsp 30** in HbA_{1c} reduction

iGlarLixi (n=443) vs BIAsp 30 (n=444)

LS mean ± SE change in HbA_{1c} from baseline to Week 26, % | LS mean ± SE change in bodyweight from baseline to Week 26, kg



Achieved — **Non-inferiority** (primary endpoint)
LS mean difference (97.5% CI): −0.2 (−0.4, −0.1); p<0.001

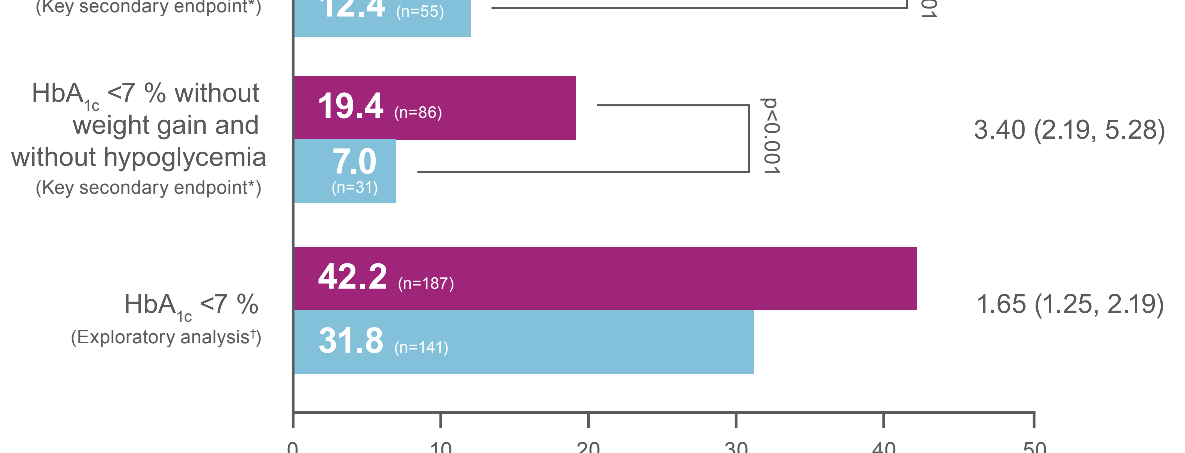
Achieved — **Superiority** (key secondary endpoint)
LS mean difference (95% CI): −0.2 (−0.4, −0.1); p<0.001

Achieved — **Superiority** (primary endpoint)
LS mean difference (95% CI): −1.9 (−2.3, −1.4); p<0.001

Secondary efficacy endpoints

Significantly greater proportion of participants reached HbA_{1c} <7 % (<53.0 mmol/mol) without weight gain at Week 26 or HbA_{1c} <7 % (<53.0 mmol/mol) without weight gain at Week 26 and without hypoglycemia (<70 mg/dL [<3.9 mmol/L]) during the treatment period in the **iGlarLixi** versus **BIAsp 30** group (key secondary endpoints*; ITT population)

The proportion of participants reaching HbA_{1c} <7 % was greater with **iGlarLixi** versus **BIAsp 30** (exploratory analysis†; ITT population)


iGlarLixi (n=443)
BIAsp 30 (n=444)
OR (95% CI)
HbA1c <7 % without weight gain (Key secondary endpoint*)
27.5 (n=122)
12.4 (n=55)
p<0.001
2.83 (1.98, 4.04)
HbA1c <7 % without weight gain and without hypoglycemia (Key secondary endpoint*)
19.4 (n=86)
7.0 (n=31)
p<0.001
3.40 (2.19, 5.28)
HbA1c <7 % (Exploratory analysis†)
42.2 (n=187)
31.8 (n=141)
1.65 (1.25, 2.19)
0
10
20
30
40
50
Percentage of participants reaching target

*hierarchical analysis adjusted for multiplicity; †not included in the multiple testing process

Key results: Safety

iGlarLixi demonstrated lower incidence and rates of ADA Level 1 and Level 2 hypoglycemia compared with **BIAsp 30** (safety population)

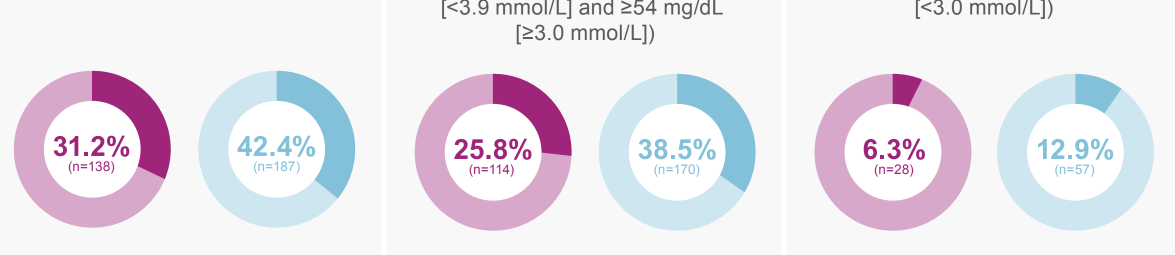
iGlarLixi also demonstrated lower incidence and rates of ADA Level 2 hypoglycemia compared with **BIAsp 30** between bedtime and waking, or between midnight and 6am

ADA Level 3 hypoglycemia (severe hypoglycemia; any event with severe cognitive impairment requiring assistance for recovery) was low with one event in the **iGlarLixi** group and two events in the **BIAsp 30** group

iGlarLixi (n=442; 223.15 PY) vs BIAsp 30 (n=441; 217.85 PY)

Incidence of anytime hypoglycemia, % (n)

Any hypoglycemic event | Level 1 hypoglycemia (ADA definition: <70 mg/dL [<3.9 mmol/L] and ≥54 mg/dL [≥3.0 mmol/L]) | Level 2 hypoglycemia (ADA definition: <54 mg/dL [<3.0 mmol/L])

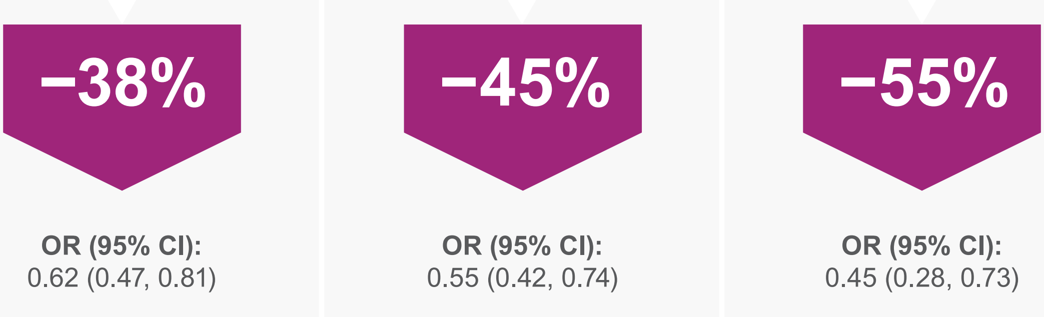


Relative odds reduction with iGlarLixi versus BIAsp 30

Any hypoglycemic event	Level 1 hypoglycemia	Level 2 hypoglycemia
−38%	−45%	−55%
OR (95% CI): 0.62 (0.47, 0.81)	OR (95% CI): 0.55 (0.42, 0.74)	OR (95% CI): 0.45 (0.28, 0.73)

Rates of anytime hypoglycemia, PPY (events)

Any hypoglycemic event | Level 1 hypoglycemia (ADA definition: <70 mg/dL [<3.9 mmol/L] and ≥54 mg/dL [≥3.0 mmol/L]) | Level 2 hypoglycemia (ADA definition: <54 mg/dL [<3.0 mmol/L])



Relative rate reduction with iGlarLixi versus BIAsp 30

Any hypoglycemic event	Level 1 hypoglycemia	Level 2 hypoglycemia
−33%	−29%	−60%
RR (95% CI): 0.67 (0.49, 0.91)	RR (95% CI): 0.71 (0.52, 0.99)	RR (95% CI): 0.40 (0.23, 0.71)

The most commonly reported treatment-emergent AE in the **iGlarLixi** group was nausea (7.7% vs 0% for **BIAsp 30**), while nasopharyngitis was the most commonly reported treatment-emergent AE in the **BIAsp 30** group (2.7% vs 3.2% for **iGlarLixi**) (safety population)

n (%)	iGlarLixi (n=442)	BIAsp 30 (n=441)
Any treatment-emergent AE	144 (32.6)	122 (27.7)
Any serious AE	12 (2.7)	13 (2.9)
Any AE leading to treatment discontinuation	4 (0.9)	4 (0.9)
Any AE leading to death	0 (0)	2 (0.5)

Conclusions

Compared with twice-daily **premix BIAsp 30**, once-daily FRC **iGlarLixi** demonstrated better glycemic control and weight benefit with less hypoglycemia

iGlarLixi is a more efficacious, simpler, and well-tolerated alternative to **premix BIAsp 30** for advancing therapy in people with T2D previously suboptimally controlled with basal insulin plus OADs

Abbreviations
ADA, American Diabetes Association; AE, adverse event; BIAsp 30, biphasic insulin aspart 30 (30% insulin aspart + 70% insulin aspart protamine); BMI, body mass index; CI, confidence interval; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA_{1c}, glycated hemoglobin; iGlarLixi, a fixed-ratio combination of insulin glargine 100 U/mL and the GLP-1 RA, lixisenatide; ITT, intent-to-treat; LS, least squares; OAD, oral antihyperglycemic drug; OR, odds ratio; PPY, per participant-year; PY, participant-year; RCT, randomized controlled trial; RR, rate ratio; SD, standard deviation; SE, standard error; SGLT2i, sodium glucose co-transporter 2 inhibitor; T2D, type 2 diabetes

References
[1]McCrimmon et al. *Diabetes, Obes Metab*. 2021;23(6):1221–31

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Julio Rosenstock, MD, and Pascaline Picard, MSc, are the guarantors of this work and, as such, have full access to all the data in this study and take responsibility for the integrity of the data and accuracy of the data analysis.

Disclosures
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