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Effectiveness and Safety of iGlarLixi in People with Type 2 Diabetes (PwT2D), Not at Target on Basal Insulin (BI) and Oral Antidiabetic Therapy (BOT)—Results from the Observational, Prospective Study CHANCE

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INTRODUCTION

- In suboptimal controlled PwT2D on a BOT regimen, intensifying to the fixed-ratio combination (FRC) insulin glargine 100 U/mL plus lixisenatide 33 µg/mL (iGlarLixi 100/33) may provide a simple and effective treatment option to improve glycemic control vs BOT[1] or other intensification options like premix insulin[2] or basal-bolus[3] regimens.
- In current guidelines, use of FRCs is recommended.[4,5]
- Efficacy and safety of intensifying from a BOT setting to iGlarLixi was assessed in the phase 3 study LixiLan-L.[1] However, prospective data assessments on translation of these trial results into daily clinical practice are still rare.

OBJECTIVE

The CHANCE‡ study was conducted to assess efficacy and safety of intensifying antiglycemic treatment to iGlarLixi 100/33 in PwT2D, suboptimal controlled on BOT, in daily clinical practice in Germany.

METHODS

- Prospective observational multicenter trial in PwT2D in primary care (general practitioners, internists and diabetologists) all over Germany. PwT2D were enrolled after the physician had decided to intensify an existing BOT to iGlarLixi 100/33 due to suboptimal glycemic control (HbA_{1c} at baseline [BL] 7.5-10%), independent of inclusion of the patient into this study, after informed consent.
- **Primary endpoint:** absolute change in HbA_{1c} (%) from BL until approx. 12 and 24 weeks, respectively.
- **Secondary endpoints**: include changes from BL in FPG, 7-point blood glucose profiles, body weight, iGlarLixi dose and body mass index (BMI), proportion of patients at individualized, prespecified HbA_{1c} and FPG target ≤110 mg/dL, hypoglycemia incidence and rates, BL previous BI doses, and safety after approximately 12 and 24 weeks.
- In addition, a subgroup using flash glucose monitoring (FGM) was evaluated for time in range (TIR), time above range (TAR) and time below range (TBR), respectively.
- Patients with self-measured blood glucose (SMBG) were evaluated for derived TIR (dTIR), dTAR and dTBR.

Figure 1: Study design

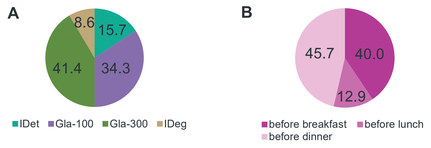
Demographics and baseline characteristics were documented at baseline only. Primary and secondary endpoints were documented at baseline, and after approximately 12 and approximately 24 weeks, respectively. In addition, self-measured fasting plasma glucose and current iGlarLixi dose were documented monthly.

Table 1: Demographics and baseline characteristics

	FAS n = 70	FGM n = 20	SMBG n = 50
Age, years	64.6 (9.5)	60.3 (7.9)	66.4 (9.6)
Male, [n (%)]	42 (60.0)	12 (60.0)	30 (60.0)
Weight, kg	104.3 (22.5)	107.0 (23.1)	103.1 (22.4)
BMI, kg/m²	35.1 (7.2)	35.8 (7.6)	34.8 (7.0)
Duration T2D, years	12.3 (6.7)	14.3 (8.3)	11.6 (6.1)
FPG*, mg/dL	174.3 (44.6)	159.3 (27.3)	180.6 (49.0)
HbA_{1c}, %**	8.5 (0.8)	8.4 (0.8)	8.6 (0.9)
Indiv. target HbA_{1c}, %	6.9 (0.4)	6.9 (0.5)	7.0 (0.3)

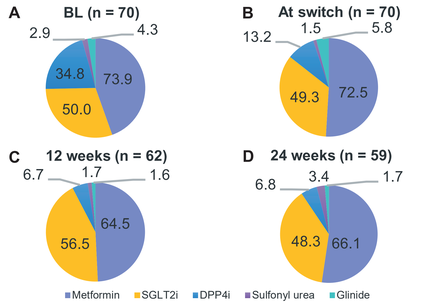
Data are mean (SD), unless otherwise specified. * Self-measured fasting plasma glucose; ** Last value within last 3 months. BMI, body mass index; FAS, full analysis set; FGM, flash glucose monitoring; FPG, fasting plasma glucose; HbA_{1c}, glycated hemoglobin A_{1c}; indiv., individual; SD, standard deviation; SMBG, self-measured blood glucose; T2D, type 2 diabetes.

Figure 2: Previous basal insulin therapy (A) and timepoint of iGlarLixi 100/33 administration (B)



Data are % of full analysis set population (n = 70); one value missing for (B). Gla-100, insulin glargine 100 U/mL; Gla-300, insulin glargine 300 U/mL; IDeg, insulin degludec; IDet, insulin detemir; iGlarLixi 100/33, insulin glargine 100 U/mL + lixisenatide 33 µg/mL.

Figure 3: Oral antidiabetic drug use at BL (A), at switch (B), after 12 weeks (C) and after 24 weeks (D)

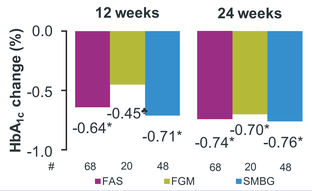


	BL	At switch	12 weeks	24 weeks
No OAD	4.3	14.3	19.4	20.3
1 OAD	41.4	38.6	37.1	40.7
2 OADs	40.0	40.0	37.1	32.2
≥3 OADs	14.3	7.1	6.5	6.8

Figure: percent sum up to > 100% due to ≥ 1 OAD in most patients. **Figure** + **Table**: Data are percent of full analysis set population with data available. BL, baseline; DPP4i, dipeptidyl peptidase 4 inhibitor; OAD, oral antidiabetic drug; SGLT2i, sodium-glucose cotransporter-2 inhibitor.

Figure 4: HbA_{1c} change from baseline

	FAS n = 70	FGM n = 20	SMBG n = 50
Baseline, %	8.5 (0.8)	8.4 (0.8)	8.6 (0.9)
After 12 weeks, %	7.9 (0.8)	8.0 (0.9)	7.9 (0.8)
After 24 weeks, %	7.7 (0.8)	7.8 (0.9)	7.7 (0.7)



Data are mean (SD). p-value calculated for paired t-test. * p < 0.001; ♣ p = 0.005. FAS, full analysis set; FGM, flash glucose monitoring; HbA_{1c}, glycated hemoglobin A_{1c}; SD, standard deviation; SMBG, self-measured blood glucose.

Table 2: Body weight change from baseline

	FAS n = 68	FGM n = 20	SMBG n = 48
After 24 weeks, kg	101.3 (21.6)	102.6 (22.8)	100.8 (21.2)
Weight change‖, kg	-3.0 (-4.8, -1.1)	-4.5 (-7.3, -1.6)	-2.3 (-4.7, -0.0)
p-value	0.002	0.004	0.049

Data are mean (SD), unless otherwise specified. ‖ Data are mean (95% CI). p-value calculated for paired t-test. CI, confidence interval; FAS, full analysis set; FGM, flash glucose monitoring; SD, standard deviation; SMBG, self-measured blood glucose.

Figure 5A: Derived time in range (dTIR) from 7-point blood glucose daily profiles‡

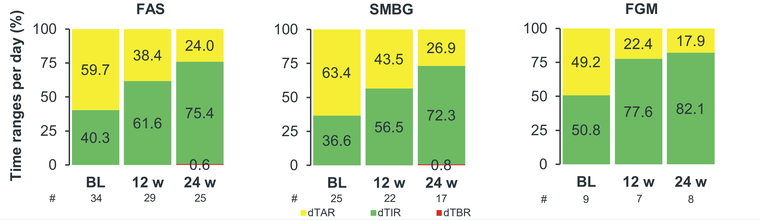
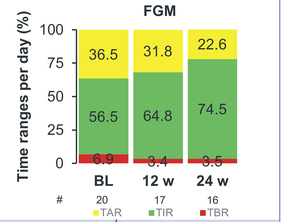


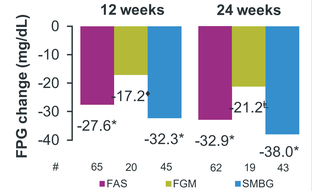
Figure 5B: Time in range‾ (TIR)



Percentage per day of dTIR / dTAR / dTBR = number of SMBGs within 70-180 mg/dL / above 180 mg/dL / below 70 mg/dL devided by number of all SMBGs times 100[6]. # Number of patients with data available. ‡ 7-point blood glucose daily profiles were self-measured; ‾ derived from FGM measurements. BL, baseline; 12 w, at week 12; 24 w, at week 24; d, derived; FAS, full analysis set; FGM, flash glucose monitoring; SMBG, self-measured blood glucose; TAR, time above range (> 180 mg/dL); TBR, time below range (< 70 mg/dL); TIR, time in range (70-180 mg/dL).

Figure 6: FPG change from baseline

	FAS n = 68	FGM n = 20	SMBG n = 48
Baseline, mg/dL	174.3 (44.6)	159.3 (27.3)	180.6 (49.0)
After 12 weeks, mg/dL	147.1 (36.5)	142.2 (30.5)	149.3 (39.0)
After 24 weeks, mg/dL	141.4 (34.1)	139.0 (26.3)	142.5 (37.2)



Data are mean (SD); values of 3 patients are missing after 12 weeks, values of 5 patients are missing after 24 weeks in groups FAS and SMBG. p-value calculated for paired t-test. * p < 0.001; ♦ p = 0.050; ♣ p = 0.010. FAS, full analysis set; FGM, flash glucose monitoring; FPG, fasting plasma glucose; SD, standard deviation; SMBG, self-measured blood glucose.

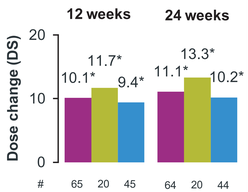
Table 3: Patients at individualized HbA_{1c} target (Tab. 1) and at FPG target ≤110 mg/dL

HbA_{1c} at indiv. target	FAS n = 70	FGM n = 20	SMBG n = 50
0-12 weeks	8 (11.4)	2 (10.0)	6 (12.0)
0-24 weeks	12 (17.1)	4 (20.0)	8 (16.0)
FPG at target ≤110 mg/dL	**FAS n = 70**	**FGM n = 20**	**SMBG n = 50**
0-12 weeks	15 (21.4)	5 (25.0)	10 (20.0)
0-24 weeks	21 (30.0)	5 (25.0)	16 (32.0)

Data are n (%). FAS, full analysis set; FGM, flash glucose monitoring; FPG, fasting plasma glucose; HbA_{1c}, glycated hemoglobin A_{1c}; SMBG, self-measured blood glucose.

Figure 7: iGlarLixi dose change from baseline

	FAS n = 70	FGM n = 20	SMBG n = 50
Baseline, DS	30.0 (0.0)	30.0 (0.0)	30.0 (0.0)
After 12 weeks, DS	40.1 (9.8)	41.7 (9.2)	39.4 (10.0)
After 24 weeks, DS	41.1 (9.5)	43.3 (9.8)	40.2 (9.4)



Data are mean (SD). p-value calculated for paired t-test. * p < 0.001. DS, dose steps: 1 DS = 1 U insulin glargine + 0.33 µg lixisenatide; FAS, full analysis set; FGM, flash glucose monitoring; SD, standard deviation; SMBG, self-measured blood glucose; U, unit.

Table 4: Hypoglycemia events (reported)

ADA level 1	FAS; n = 67	FGM; n = 19	SMBG; n = 48
BL incidence◊, %	4.5 (0.9, 12.5)	5.3 (0.1, 26.0)	4.2 (0.5, 14.3)
BL events PPY	0.58	0.92	0.45
24 w incidence◊, %	3.6 (0.4, 12.3)	-	5.1 (0.6, 17.3)
24 w events PPY	0.52	-	0.73
ADA level 2	**FAS; n = 67**	**FGM; n = 19**	**SMBG; n = 48**
BL incidence◊, %	-	-	-
BL events PPY	-	-	-
24 w incidence◊, %	3.6 (0.4, 12.3)	-	5.1 (0.6, 17.3)
24 w events PPY	0.37	-	0.52

ADA level 1: BG < 70 mg/dL and ≥ 54 mg/dL; ADA level 2: BG < 54 mg/dL. ◊ data are mean (95% CI). 24 w, after 24 weeks (reported for last 12 weeks before); BL, baseline (reported for last 12 weeks before). CI, confidence interval; FAS, full analysis set; FGM, flash glucose monitoring; PPY, per patient year; SMBG, self-measured blood glucose.

RESULTS

- Previous basal insulin dose was [mean (SD)] 38.7 (9.6) U/d (FAS), 40.8 (10.9) U/d (FGM) and 37.8 (8.9) U/d (SMBG). iGlarLixi was started as per European Medicines Agency label for the (30-60) pen at 30 dose steps (DS); dose increased significantly by 11.1 DS after 24 weeks (**Figure 7**)
- HbA_{1c} (**Figure 4**), FPG (**Figure 6**) and body weight (**Table 2**) decreased significantly after 12 and 24 weeks.
- dTIR increased and dTAR decreased, both significantly, after 24 weeks (all p < 0.05; **Figure 5A**). FGM data in a subgroup of patients showed similar patterns for TIR and TAR and a reduction in TBR (p = 0.007; **Figure 5B**).
- Hypoglycemia events did not change significantly and were low in number (**Table 3**). No severe hypoglycemia requiring outside assistance was reported.

DISCUSSION

- Treatment intensification from a BOT regimen to iGlarLixi significantly improved HbA_{1c} and FPG levels, leading to recommended[7] dTIR/TIR > 70% and dTBR/TBR < 4%, respectively, as well as dTAR/TAR around 25%.
- Hypoglycemia were seldom reported, probably due to underreporting, because more hypoglycemic events were seen from FGM readings.
- This is the first study reporting on real world use of iGlarLixi in Germany with 29% of PwT2D using FGM devices. Limitations are its non-randomized, single arm design, which might have led to bias from unknown con-founders and to selection bias.

CONCLUSION

Intensifying antiglycemic treatment from a BOT regimen to iGlarLixi 100/33 in suboptimal controlled PwT2D in daily clinical practice allowed patients to reach glycemic target ranges with no increased hypoglycemia and favorable body weight change.

‡ CHANCE: A prospective observational study to assess glycaemic **C**ontrol by intensifying therapy wit**H** iGlarLixi in the Suliqua® (30-60) pen in d**A**ily practice in patie**N**ts with type 2 diabetes whose blood sugar is not adequately **C**ontrolled on basal insulin and oral antidiabetic th**E**rapy (BOT)

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DISCLOSURES

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