Randomized comparison of initiating insulin glargine or iGlarLixi in South Asian participants with Type 2 Diabetes: VARIATION 2 SA trial

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Harpreet S. Bajaj, Lisa Chu, Ruth Brown, Gagandeep Dhillon, Rishabh Gupta, Jatminderpal S. Bhela, Nandini Bansal, Saudia Khan, Jagjit Padda, Hasnain Khandwala, Karri Venn, Ronnie Aronson

LMC Diabetes and Endocrinology, Ontario, Canada

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Background

- South Asians represent ~25% of the world's population, and form the largest minority population in Canada

- Together with a higher consumption of carbohydrates and fats in traditional South Asian diets, a high fat and high energy diet may lead to more severe metabolic affects, including greater insulin resistance, in South Asians compared to in Europeans [1,2]

- We have demonstrated that a combination of basal insulin with GLP-1 RA resulted in the least glucose variability, hypoglycemia and greatest time-in-range (TIR) on continuous glucose monitoring (CGM) among four commonly prescribed insulin regimens in patients with type 2 diabetes (T2D) of various ethnicities [3]

- The VARIATION 2 SA Trial is the first trial to compare a titratable fixed-ratio combination of glargine-GLP-1 RA (iGlarLixi) to a biosimilar basal insulin analog in Canadians of South Asian origin with T2D

Study Objective

- To compare iGlarLixi regimen to the traditional approach of initiating insulin glargine with a sulfonylurea, both added to metformin in people with T2D of South Asian origin

Methods

- Participants of South Asian origin who were not meeting glycemic targets (HbA1c: 7.1-11%) with oral hypoglycemic agents were enrolled from LMC Diabetes and Endocrinology centers

- The study was a 16-week randomized, pragmatic, multi-center trial (ClinicalTrials.gov Identifier: NCT03819790)

- Participants were randomized 1:1 to insulin glargine + gliclazide MR 60 mg OD vs. iGlarLixi regimen

- <u>Co-primary outcomes</u>: average % TIR for glucose (4.0-10.0 mmol/L) within 24-h and 12-hr (6AM-6PM) on 7-day CGM at the end of the trial

- <u>Secondary outcomes</u>: measures of glucose variability and hypoglycemia
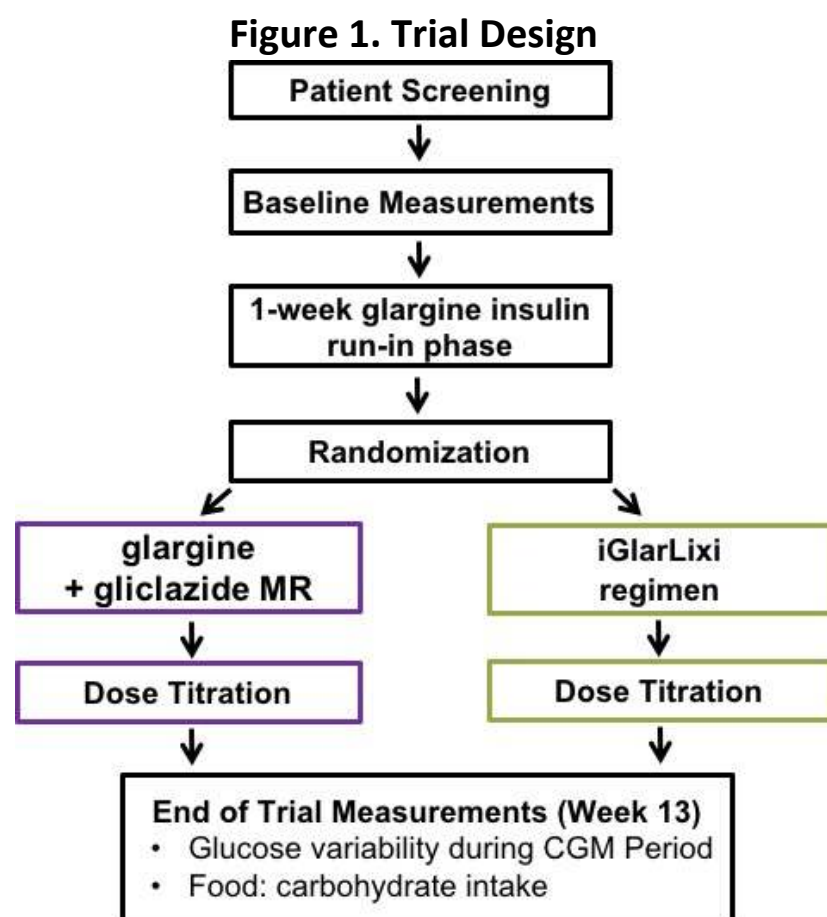
Figure 1. Trial Design

Patient Screening → Baseline Measurements → 1-week glargine insulin run-in phase → Randomization → glargine + gliclazide MR / iGlarLixi regimen → Dose Titration → Dose Titration → End of Trial Measurements (Week 13)
- Glucose variability during CGM Period
- Food: carbohydrate intake

Results

- 104 insulin-naïve participants were randomized from November 2018 to August 2019, with 94 of them completing the trial (Table 1)

Table 1. Baseline characteristics

	glargine + gliclazide MR (n=49)	iGlarLixi (n=45)
Age (years)	57.4 ± 11.1	61.2 ± 9.0
Female sex, N (%)	20 (41)	23 (49)
Diabetes duration (years)	13.6 ± 7.5	14.3 ± 6.9
Body mass index (kg/m^2)	27.8 ± 5.1	28.6 ± 5.3
HbA$_{1c}$ (%)	8.6 ± 1.1	8.4 ± 1.4
Fasting glucose (mmol/L)	9.0 ± 2.0 (n=46)	8.8 ± 1.7 (n=40)
Insulin glargine dose (units)	12.6 ± 1.5 (n=46)	12.5 ± 1.2 (n=40)

Results

Table 2. Ethnic Origin

	glargine + gliclazide MR (n=49)	iGlarLixi (n=45)
Ethnic origin, N (%):		
Afghanistan	0 (0)	1 (2)
Bangladesh	1 (2)	0 (0)
Indian	43 (88)	34 (76)
Pakistan	5 (10)	7 (15)
Sri Lanka	0 (0)	3 (7)

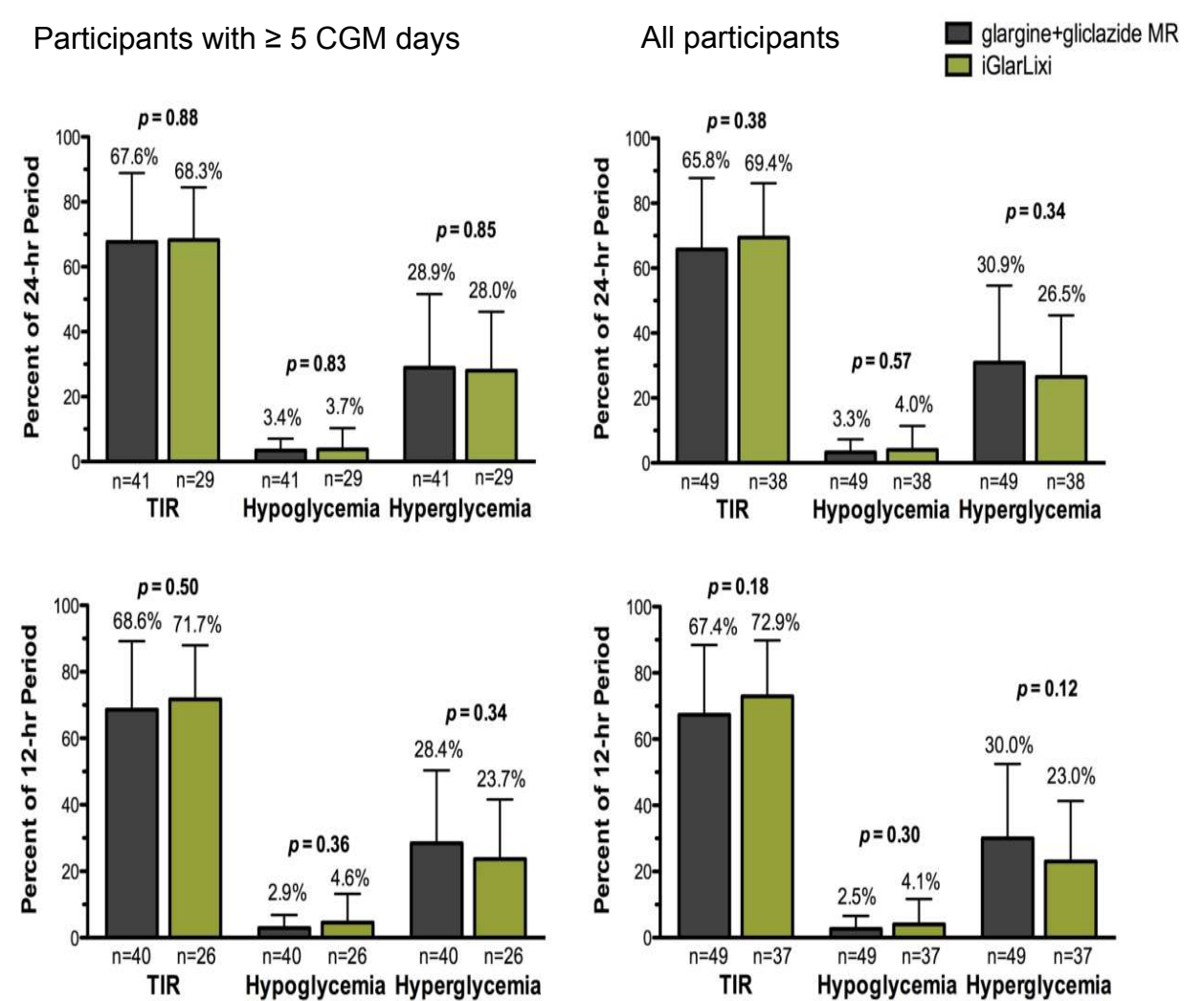**Figure 2. CGM outcomes at the end of the trial (Co-primary Outcomes)**

Table 3. Clinical outcomes at end of trial (week 13)

	glargine + gliclazide MR	iGlarLixi
Body mass index (kg/m^2)	29.1 ± 4.9 (n=48)	28.9 ± 4.6 (n=44)
HbA$_{1c}$ (%)	7.7 ± 1.3 (n=48)	7.5 ± 0.9 (N=42)
Insulin glargine dose (units)	34.4 ± 18.9 (n=41)	36.1 ± 13.2 (N=37)

- No significant differences were found for for body mass index (p=0.85), HbA1c (p=0.47) and insulin dose (p=0.64) at week 13 between groups

Conclusions

- The primary outcome of percent of time-in-range for glucose as well as time in hypoglycemia and hyperglycemia on CGM were not significantly different between insulin glargine + gliclazide MR vs. iGlarLixi regimen among insulin-naïve South Asian patients with T2D

- BMI, HbA1c and insulin dose were not significantly different between the two arms at the end of the trial

References

1. Bajaj H. S., et al. *Journal of Obesity*, 2014;2014:461956
2. Bajaj, H. S. et al. *Diab care* 40, 194-200 (2017)
3. Chiu, M., et al. *CMAJ* 182, E301-310 (2010)

Corresponding Author: Harpreet S. Bajaj, MD, MPH, 2979 Bovaird Drive E, Brampton, ON L6S 0C6, Canada. Email: harpreet.bajaj@lmc.ca ~ Tel: +1 (905) 595-0560 ~ Fax: +1 (905) 595-0562