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ORIGINAL RESEARCH

LIVE INDIA: Effectiveness of Gla-100 in a Post hoc Pooled Analysis of FINE ASIA and GOAL Registries

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ABSTRACT

Introduction: Real-world evidence on insulin glargine 100 U/ml (Gla-100) initiation in Indian type 2 diabetes mellitus (T2DM) individuals is limited. The present study aimed to evaluate the effectiveness of Gla-100 in insulin-naïve T2DM participants from India.

Methods: This post hoc analysis includes real-world data of insulin-naïve Indian participants with T2DM who started Gla-100 treatment in two Asian registries: FINE ASIA and GOAL. Changes in glycated hemoglobin (HbA1c), fasting plasma glucose (FPG), body weight, insulin dose, and incidence of hypoglycemia from baseline to 6 months were assessed.

Prior Publication: This study is based on the pooled analysis of data from two registries FINE ASIA and GOAL that has been previously published in the Diabetes Therapy (2015) and BMJ Open Diabetes Research & Care journals (2018). The publication details are as follows: [20, 21].

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Results: A total of 955 participants with T2DM were identified and analyzed. The mean [standard deviation (SD)] age and duration of diabetes were 54.7 (9.8) years and 9.8 (6.3) years, respectively. Mean HbA1c and FPG were significantly reduced after 6 months of Gla-100 treatment [− 2.07 (1.4) %; − 94.4 (65.2) mg/dl, respectively]. HbA1c targets of < 7.0% and < 7.5% were achieved by 292 (30.6%) and 589 (61.7%) study participants, respectively. The overall incidence of hypoglycemia was low (n = 52; 5.4%); only two participants (0.2%) reported severe hypoglycemia. Insulin was titrated with a mean (SD) increment of 2.5 (5.6) U/day after 6 months, leading to a mean Gla-100 dose of 18.2 (8.9) U/day. Mean body weight remained unchanged from baseline to 6 months (− 0.1 kg).

Conclusion: In routine clinical practice, Gla-100 significantly improved glycemic parameters after 6 months of treatment with a low risk of hypoglycemia and no weight change in participants with T2DM.

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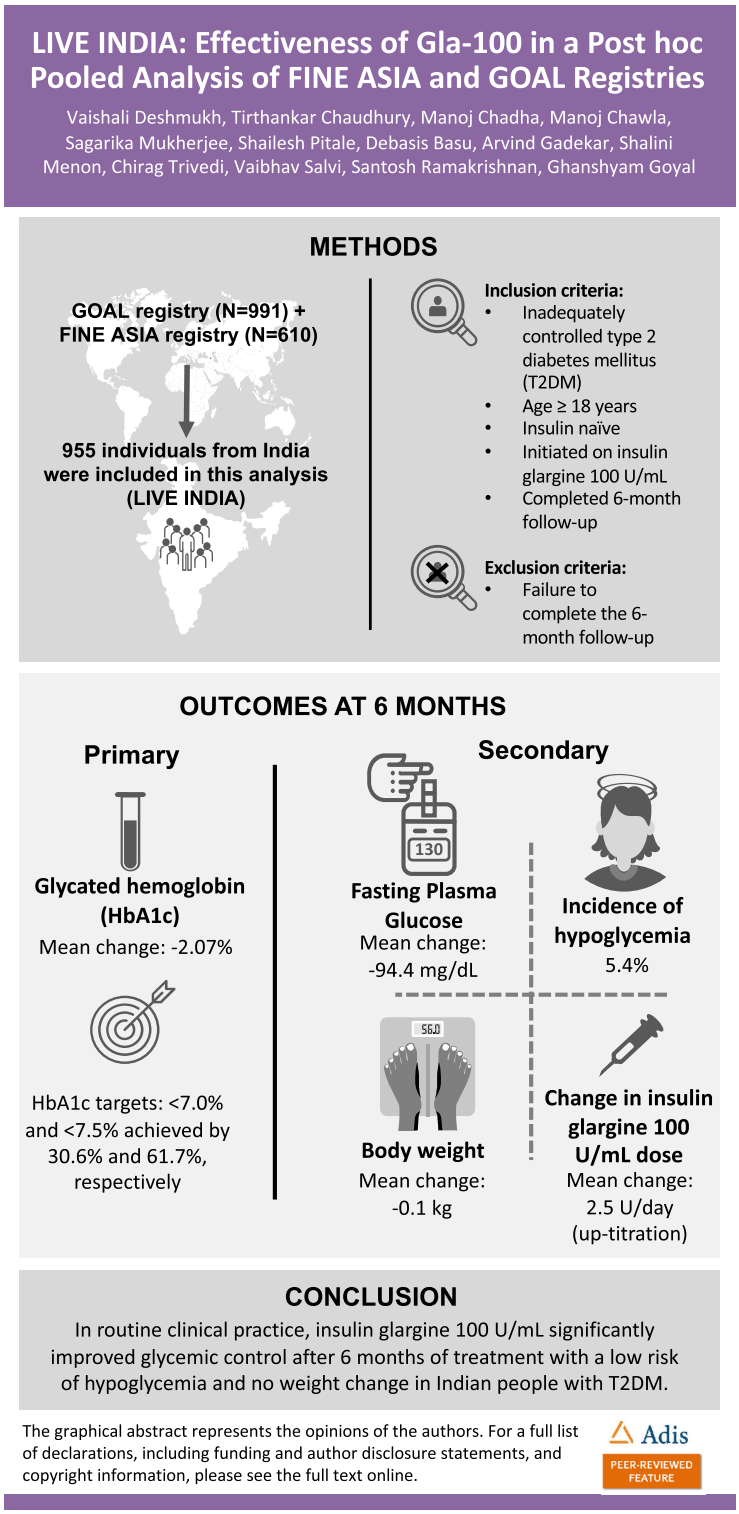
Graphical Abstract:



Keywords: Type 2 diabetes; Basal insulin; Glargine; Post hoc analysis; Pooled analysis

Key Summary Points
Real-world evidence on insulin glargine 100 U/ml (Gla-100) initiation in Indian participants with type 2 diabetes mellitus (T2DM) is limited
The present study is the first pooled post hoc analysis of two large population-based observational studies (FINE ASIA and GOAL registries) wherein we evaluated the real-world effectiveness of Gla-100 in insulin-naïve T2DM participants from India
In routine clinical practice, Gla-100 significantly improved glycemic parameters after 6 months of treatment with a low risk of hypoglycemia and no weight change in participants with T2DM
Therefore, this study highlights real-world data on the initiation of Gla-100 in the Indian context and demonstrates the real-world effectiveness and safety of Gla-100 in insulin-naïve T2DM population

DIGITAL FEATURES

This article is published with digital features, including a graphical abstract to facilitate understanding of the article. To view digital features for this article, go to https://doi.org/10.6084/m9.figshare.24064605.

INTRODUCTION

Diabetes and its complications are a significant cause of morbidity and mortality worldwide [1]. In India, type 2 diabetes mellitus (T2DM) is a major public health burden, with an estimated prevalence of 9.6% in the age group of 20 to 79 years, accounting for almost 74.2 million people [2]. Type 2 diabetes mellitus is a progressive disease that results in suboptimal glycemic control even after the usage of new-generation oral antidiabetic drugs (OADs). Suboptimal glycemic control in people with T2DM on conventional OADs can result in the risk of both microvascular (e.g., retinopathy, nephropathy) and macrovascular complications (e.g., myocardial infarction, amputations) [3].

Clinical inertia, non-compliance, and adverse events often result in a prolonged glycemic burden for individuals with T2DM receiving OADs. Several clinical studies support the early initiation and intensification of therapy to reduce the risk of de novo or worsening of diabetes complications. The landmark UK Prospective Diabetes Study (UKPDS) showed that an intensive glucose-lowering therapy decreases the risk of T2DM complications [4]. This finding is also supported by other studies including Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE) and Veterans Affairs Diabetes Trial (VADT). In both studies, people on intensive treatment attained lower glycated hemoglobin (HbA1c) values and had lower risk of developing both micro- and macro-vascular complications [5, 6].

One of the important aspects related to the difficulty of achieving and maintaining optimal glycemic control is clinical inertia, which is defined as the failure to start therapy or its intensification/de-intensification when appropriate [7–10]. Clinical inertia may contribute to inadequate glycemic control for many years, with a significant impact on outcomes in terms of quality of life, morbidity and mortality, and public health due to the huge costs associated with uncontrolled T2DM [11].

The current guidelines recommend a stepwise treatment intensification approach [12–14], and while resistance to intensification is evident at each stage, it seems more prominent when initiating insulin [15, 16]. Clinical inertia in insulin initiation is a global challenge in clinical practice [16]. Type 2 diabetes mellitus begins half a decade earlier and progresses more rapidly in the Indian population than in the Western population [17]. Yet, the window of opportunity to effectively intervene is missed

because of over-reliance on OADs and/or clinical inertia to insulin initiation [8, 16].

The American Diabetes Association (ADA) recommends initiation of basal insulin in people with uncontrolled HbA1c even after > 3 months of combination therapy or symptomatic hyperglycemia [13]. According to the most recent position statement by the ADA and the European Association for the Study of Diabetes (EASD), basal insulin should be considered an essential component of the treatment strategy in any individual with diabetes who is unable to achieve the HbA1c target despite intensive oral therapy [12]. Over the last decade, many people with diabetes worldwide have used the basal insulin analog glargine 100 U/ml (Gla-100). Insulin glargine 100 U/ml has been proven to be effective and shows less risk of hypoglycemia and weight gain compared to other insulin analogs. It also provides a near-24-h glucose-lowering effect with low variability [18, 19].

To substantiate real-world data on effectiveness of basal insulin treatment in the Indian population, in this post hoc analysis, we evaluated the insulin-naïve T2DM subgroups from India treated with Gla-100 in the First Basal Insulin Evaluation (FINE) ASIA and GOAL studies [20, 21].

METHODS

Objective

The primary objective of this post hoc analysis was to assess the change in HbA1c from baseline to 6 months in insulin-naive participants with T2DM treated with Gla-100 in the Indian subgroups of FINE ASIA and GOAL studies. The secondary objectives were to evaluate the changes in fasting plasma glucose (FPG), body weight, and insulin dose and to assess the incidence of hypoglycemia (from baseline to the end of 6 months). A snapshot of the FINE ASIA and GOAL study is provided in Supplementary Fig. 1. Hypoglycemia was considered according to the definitions in the individual registries [20–22].

The analysis of hypoglycemia events included symptomatic or documented events according to the individual registries [20, 21].

Study Design

This post hoc analysis pooled data from the multinational observational studies, FINE ASIA and GOAL, which included insulin-naïve participants from India who were started on Gla-100 as part of routine clinical practice.

Study Site Details of FINE ASIA and GOAL

FINE ASIA: This observational study was carried out from 2005 to 2010 in 132 centers/sites across 11 different Asian countries (Bangladesh, China, Hong Kong, India, Indonesia, Korea, Pakistan, Singapore, Taiwan, Thailand, and Vietnam). The Indian data subset and sites were considered for the current study [20]. (Supplementary Fig. 1).
GOAL: This observational study was carried out from October 2012 to January 2015 in ten developing countries from Africa (Egypt, South Africa), the Middle East (Israel, Saudi Arabia, United Arab Emirates, Iran, and Lebanon), and South Asia (Bangladesh, India, and Pakistan). For the current analyses, only the Indian data subset and sites were considered [21]. (Supplementary Fig. 1).

Study Population

India subset from FINE ASIA and GOAL registries meeting the eligibility criteria (diagnosed with inadequately controlled T2DM, aged ≥ 18 years, insulin-naïve, initiated on Gla-100 treatment, and received consistent treatment with Gla-100 from baseline to 6 months) was considered for the study. The India subset from FINE ASIA and GOAL registries who failed to complete the 6-month follow-up were excluded.

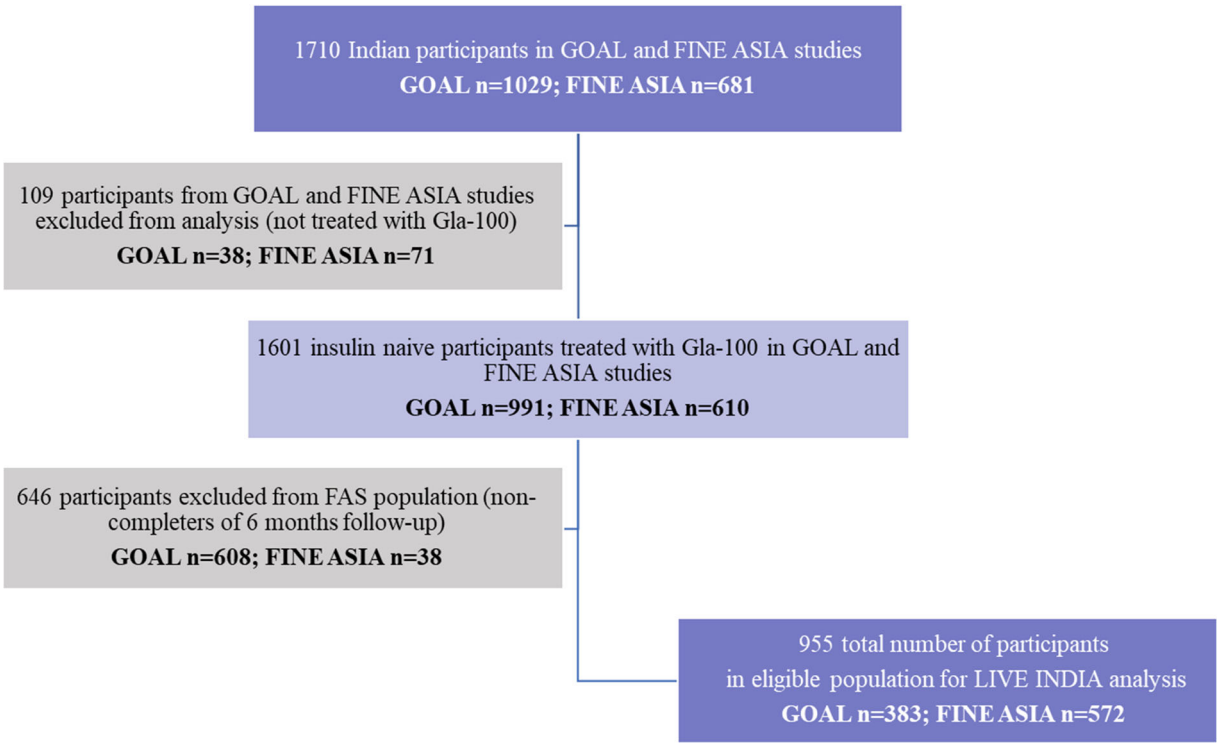


Fig. 1 Flow chart of study participants' disposition. Abbreviations: FAS = full analysis set, FINE = First Basal Insulin Evaluation, Gla-100 = insulin glargine 100 U/ml; *n* number of participants in a specified category

Data Sources and Collection

Since this is an analysis of a pre-existing database (FINE ASIA and GOAL), no case report form was used. Statistical analysis software [SAS version 9.4 (SAS Institute, USA)] along with Analysis Data Model (ADaM) format was used. ADaM format defines the standards used for the creation of analysis datasets and associated metadata. It is used for data derivation and analysis. The pooling of two datasets was performed by SAS.

Statistical Analysis

The data were analyzed using descriptive statistics. Quantitative data were presented as mean and median with standard deviation (SD) and ranges, respectively. Qualitative data were presented by frequency and proportions. Study participant characteristics and treatment patterns were analyzed. Mean change from baseline to 6 months was analyzed using paired *t*-test. A p value < 0.05 was considered statistically significant.

Compliance with Ethics Guidelines

Being a retrospective analysis, as per the applicable local regulations, approval of the study protocol, protocol amendments, and other relevant documents from an independent ethics committee registered with the National Ethics Committee Registry for Biomedical and Health Research, Department of Health Research (NECRBHR, DHR) were obtained prior to the study initiation. The primary studies were conducted in accordance with the ethical principles laid down by the Helsinki Declaration of 1964, and its later amendments, all international applicable guidelines, and national laws and regulations of each country. Written informed consent was provided by study participants for both studies. Appropriate measures were taken to ensure the confidentiality of the data [20, 21].

Table 1 Baseline and demographic characteristics of the study population

Characteristics	Gla-100 (*N* = 955)
Gender	
Female, *n* (%)	408 (42.7)
Male, *n* (%)	547 (57.3)
Age (years)	
Mean (SD)	54.7 (9.8)
Age groups	
18–29 years, *n* (%)	7 (0.7)
30–39 years, *n* (%)	45 (4.7)
40–64 years, *n* (%)	750 (78.5)
≥ 65 years, *n* (%)	153 (16.0)
Vital statistics	
Weight (kg), *N*	954
Mean (SD)	72.0 (12.5)
Height (cm), *N*	942
Mean (SD)	162.5 (9.4)
BMI, *N*	941
Mean (SD)	27.4 (5.1)
Waist (cm), *N*	856
Mean (SD)	92.8 (15.6)
Systolic blood pressure (mmHg), *N*	955
Mean (SD)	136.9 (16.2)
Diastolic blood pressure (mmHg), *N*	955
Mean (SD)	84.4 (8.4)
Duration of diabetes (years), *N*	951
Mean (SD)	9.8 (6.3)
Duration of diabetes, *N*	951
≤ 1 year, *n* (%)	33 (3.5)
> 1–5 years, *n* (%)	193 (20.2)
> 5–10 years, *n* (%)	331 (34.7)
> 10 years, *n* (%)	394 (41.3)
Education, *N*	939
Illiterate, *n* (%)	25 (2.6)
Reads and writes, *n* (%)	105 (11.0)
Primary, *n* (%)	140 (14.7)
Secondary, *n* (%)	256 (26.8)
Preparatory, *n* (%)	60 (6.3)
University/higher education, *n* (%)	353 (37.0)

Percentages are based on the number of study participants in the specified category

BMI body mass index, *Gla-100* insulin glargine 100 U/ml, *N* number of Indian participants on Gla-100 throughout the study, *n* number of study participants in a specified category, *SD* standard deviation

RESULTS

The eligible population comprised of 955 participants (GOAL: *n* = 383 and FINE ASIA: *n* = 572). Study participant disposition is summarized in Fig. 1.

Demographic and Baseline Characteristics

The demographic characteristics of the eligible population are presented in Table 1. More than half of the study participants were men (*n* = 547, 57.3%). The mean (SD) age was 54.7 years (9.8), and 37% (*n* = 353) of the participants had completed university or higher education.

The mean (SD) duration of diabetes was 9.8 years (6.3), and 394 (41.3%) participants had diabetes for > 10 years. Diabetes-related complications were noted in a total of 477 individuals; the majority (*n* = 314, 65.8%) had neuropathy. The most common diabetes-related comorbidities were hypertension (87.4%, *n* = 674) and dyslipidemia (73.5%, *n* = 567). Diabetes-related complications and comorbidities are summarized in Table 2.

Table 2 Diabetes-related complications and comorbidities

Characteristics	Gla-100 (N = 955)
Diabetes-related complications, *N*	477
Neuropathy, *n* (%)	314 (65.8)
Foot ulcer, *n* (%)	3 (0.6)
Amputation, *n* (%)	1 (0.2)
Retinopathy, *n* (%)	136 (28.5)
Microalbuminuria, *n* (%)	29 (6.1)
Proteinuria, *n* (%)	5 (1.0)
Renal insufficiency, *n* (%)	22 (4.6)
Nephropathy, *n* (%)	70 (14.7)
Dialysis, *n* (%)	1 (0.2)
Peripheral vascular disease, *n* (%)	4 (0.8)
Angina, *n* (%)	14 (2.9)
Myocardial infraction, *n* (%)	14 (2.9)
Coronary artery disease, *n* (%)	87 (18.2)
Stroke, *n* (%)	10 (2.1)
History of revascularization, *n* (%)	15 (3.1)
Other diabetic vascular disorder, *n* (%)	10 (2.1)
Other complications, *n* (%)	24 (5.0)
Comorbidities of diabetes, *N*	771
Hypertension, *n* (%)	674 (87.4)
Dyslipidemia, *n* (%)	567 (73.5)
Other, *n* (%)	34 (4.4)

Percentages of complications and comorbidities are based on the number of study participants in the specified category

N number of Indian participants on Gla-100 throughout the study, *n* number of study participants in a specified category

Change in HbA1c Levels

Glycated hemoglobin improved significantly ($p < 0.05$) over 3- and 6-month periods from baseline. An absolute change in HbA1c of − 1.3% (SD 1.3; 95% CI − 1.4 to − 1.3) and − 2.1% (SD 1.4; 95% CI − 2.2 to − 2.0) was observed from baseline to 3 and 6 months of treatment, respectively. HbA1c targets of < 7.0% and < 7.5% were achieved by 292 (30.6%) and 589 (61.7%) participants, respectively. A summary of HbA1c changes is presented in Table 3.

Change in FPG Levels

Significant ($p < 0.05$) reductions in FPG levels were observed after Gla-100 initiation. A mean change in FPG of − 66.9 mg/dl (SD 60.6; 95% CI − 71.1 to − 62.6) and − 94.4 mg/dl (SD 65.2; 95% CI − 98.9 to − 89.9) was observed from baseline to 3 and 6 months of treatment, respectively. Mean changes in FPG levels from baseline to 3 and 6 months are presented in Table 3.

Incidence of Hypoglycemia

A total of 52 (5.4%) study participants experienced a hypoglycemic event after initiation of Gla-100, out of which only 34 (3.6%) participants reported a hypoglycemic event in the first 3 months, and 19 (2%) participants reported a hypoglycemic event between 3 and 6 months. One person each at 3 and 6 months reported a severe hypoglycemic event (Table 3).

Change in Body Weight

The mean changes in body weight from baseline to 3 and 6 months were − 0.1 kg (SD 3.4; 95% CI − 0.3 to 0.1) and − 0.1 kg (SD 3.8; 95% CI − 0.3 to 0.2), respectively. However, the difference between body weight at baseline and at the end of the study was not statistically significant (Table 3).

Change in Gla-100 Dose

The mean insulin dose was significantly ($p < 0.05$) up-titrated over 3- and 6-month periods from baseline. The absolute change in

Table 3 Change in glycemic status, insulin dose, body weight, and incidence of hypoglycemia after 3 and 6 months of Gla-100 treatment

N = 955	HbA1c (%)	< 7.0% HbA1c	< 7.5% HbA1c	FPG (mg/dl)	Body weight (kg)	Gla-100 dose (U/day)	Hypoglycemia	Severe hypoglycemia
Baseline								
n	939	–	–	945	954	954	–	–
Mean (SD)	9.54 (1.5)	–	–	215.5 (68.8)	72.0 (12.5)	15.7 (7.3)	–	–
3 months								
n	882	52 (5.4%)	188 (19.7%)	772	955	953	34 (3.6%)	1 (0.1%)
Mean (SD)	8.2 (1.1)	–	–	147.7 (40.1)	71.9 (12.2)	17.3 (8.0)	–	–
Change from baseline to 3 months								
n	871	–	–	766	954	952	–	–
Mean (SD)	− 1.33 (1.2)*	–	–	− 66.9 (60.6)*	− 0.1 (3.4)**	1.6 (4.2)*	–	–
95% CI	− 1.4; − 1.3	–	–	− 71.1; − 62.6	− 0.3; 0.1	1.3; 1.8	–	–
6 months								
n	948	292 (30.6%)	589 (61.7%)	813	953	955	19 (2.0%)	1 (0.1%)
Mean (SD)	7.5 (1.0)	–	–	122.7 (33.4)	71.9 (11.7)	18.2 (8.9)	–	–
Change from baseline to 6 months								
n	932	–	–	806	952	954	–	–
Mean (SD)	− 2.1 (1.4)*	–	–	− 94.4 (65.2)*	− 0.1 (3.8)**	2.5 (5.6)*	–	–
95% CI	− 2.2; − 2.0	–	–	− 98.9; − 89.9	− 0.3; 0.2	2.1; 2.8	–	–

CI confidence interval, *FPG* fasting plasma glucose, *Gla-100* insulin glargine 100 U/ml, *HbA1c* glycated hemoglobin, *N* number of Indian participants initiated on Gla-100 who completed the 6 months treatment period, *n* number of study participants in a specific category (non-missing data), *SD* standard deviation

*p value < 0.05. p values are presented for comparison between baseline and 3 months and between baseline and 6 months. p values are calculated using paired t-test

**p value > 0.05

Gla-100 dose from baseline to 3 and 6 months was 1.6 U/day (SD 4.2; 95% CI 1.3 to 1.8) and 2.5 U/day (SD 5.6; 95% CI 2.1 to 2.8), respectively. The mean dose at 6 months was 18.2 U/day (8.9) (Table 3).

Vital Signs

No significant changes were observed regarding body mass index, systolic blood pressure, diastolic blood pressure, and waist circumference from baseline to the end of the study.

OADs at Baseline to Month 6

Biguanides (68.2% and 67.2%) and sulfonylureas (63.4% and 61.8%) were the most prescribed OAD classes at baseline and at 6 months, respectively (Table 4).

DISCUSSION

To our knowledge, this is the first pooled post hoc analysis of two large population-based studies conducted in India that highlight real-world data on the initiation of Gla-100 in

Table 4 OADs at baseline to month 6

N = 955	Biguanides	Sulfonylureas	Meglitinide	Thiazolidinediones	Alpha-glucosidase Inhibitor	DPP-4 Inhibitor	Other medications	Not specified
At baseline, *n* (%)	651 (68.2)	605 (63.4)	3 (0.3)	161 (16.9)	55 (5.8)	25 (2.6)	207 (21.7)	36 (3.8)
At month 3, *n* (%)	662 (69.3)	599 (62.7)	3 (0.3)	157 (16.4)	62 (6.5)	35 (3.7)	194 (20.3)	28 (2.9)
At month 6, *n* (%)	642 (67.2)	590 (61.8)	3 (0.3)	149 (15.6)	59 (6.2)	35 (3.7)	201 (21.0)	37 (3.9)

Percentages are based on the number of study participants in the specified category

DPP Dipeptidyl peptidase, *N* number of Indian participants on Gla-100 throughout the study, *n* number of study participants in a specified category, *OADs* oral antidiabetics drugs

insulin-naïve participants with T2DM. Our analysis indicates that participants with T2DM received Gla-100 at a mean age of 55 years even after being diagnosed with diabetes for about 10 years. As a result, individuals who have been taking OADs for a long duration (around 10 years) may eventually require insulin therapy, possibly because of disease progression or uncontrolled glycemia [12, 23]. The addition of insulin to existing antihyperglycemic agents helps restore glycemic control but may slightly increase the risk of hypoglycemia in some people with T2DM [24]. The post hoc analysis showed that Gla-100 initiation results in significant improvement in glycemic parameters (HbA1c and FPG). No marked changes were observed regarding body weight and BMI from baseline to 6 months, which indicated that weight gain in participants starting Gla-100 might not be a major concern. Few symptomatic hypoglycemia events were observed at 6 months with only one being severe. These real-world findings are comparable to those from the Asian Treat to Target Lantus Study (ATLAS): the 24 weeks of treatment with Gla-100 with ongoing OADs showed a substantial decline in HbA1c and FPG among participants with T2DM from India [25]. Another pooled analysis from 15 randomized controlled trials reported early and sustained glycemic benefits (HbA1c reduced by 1.4% at week 12 and 0.2% at week 24) after initiation of insulin glargine. The incidence of hypoglycemia is markedly lower for participants taking insulin glargine plus metformin compared to other combinations (Gla-100 plus sulfonylurea and Gla-100 plus metformin plus sulfonylurea) [26]. A similar prospective observational trial from a tertiary care hospital in India states that insulin glargine significantly decreases HbA1c and FPG ($p < 0.05$) in uncontrolled T2DM participants receiving one or more OAD regimens [27]. Significant reductions in HbA1c and FPG from baseline to 6 months suggest that diabetes individuals who show inadequate glycemic control with OADs may gain benefit from basal insulin. The benefit of insulin is more if started as early as possible [28–30]. Most diabetes societies, including the ADA, the American Association of Clinical Endocrinologists, and the EASD recommend insulin therapy if glycemic targets are not achieved despite lifestyle measures and oral antidiabetics [12, 13]. Early initiation of insulin has been recommended in the recent decade if HbA1c levels are high despite multiple OADs [31]. Therefore, the traditional view of insulin as the last resort is not relevant anymore [3].

This post hoc analysis indicates that although there was a marked increase in the proportion of individuals achieving glycemic control from 3 to 6 months follow-up post Gla-100 initiation, in total only around 30% of study population achieved control (HbA1c < 7%). These observations comprehensively portray a real-world picture of low glycemic control among participants with T2DM from India. These observations are in concordance with the previous evidence from India wherein uncontrolled glycemia was highlighted as a key feature of people with T2DM in India [32–34]. These results are further substantiated by a real-

world cross-sectional study by Ramachandran et al. wherein only 25.2% of participants with T2DM achieved glycemic control (HbA1c < 7%). The study highlighted that a greater number of participants treated with insulin alone were able to achieve glycemic targets than those treated with OADs alone. Authors acknowledged the lack of insulin titration and inability to self-manage the insulin dosing as the attributable reasons for poor glycemic control in people from India [32]. Appropriate dose titration is a key approach for optimizing glycemic control with insulin. Nonetheless, suboptimal titration is usually noted in routine clinical practice. This could be attributed to a conservative rather than an aggressive approach in insulin therapy contrary to clinical trials that involve the use of intensive insulin therapy with a high risk of adverse events. The findings from LIVE INDIA indicate that HbA1c and FPG targets were not achieved in the majority of participants. Expert opinion from an Indian panel using Delphi consensus also pointed out that basal insulin is initiated late in India and, once initiated, the dose is up-titrated to an average of 18 units [35]. Country-specific evidence on the effectiveness and safety of Gla-100 in people with T2DM has been limited.

Strengths and Limitations

The strength of this post hoc analysis from two multinational observational studies is that it provides valuable real-world data on the effectiveness and hypoglycemia risk associated with Gla-100 in participants with T2DM from India. This analysis captures real-world clinical practice for diabetes outside of rigid, protocol-driven controlled clinical trial settings. Another strength of this analysis is its large subset of adults (> 18 years) with inadequately controlled T2DM. The commonality of interest and uniformity of subgroups from FINE ASIA and GOAL studies ensured robustness in analysis.

The limitations of the individual studies (FINE ASIA and GOAL) are also applicable to this subgroup analysis, which include lack of randomization, predefined visits, or protocol-driven care that could potentially result in variations between participants regarding individual diabetes management [20, 21]. Additionally, lack of available information regarding the time of insulin administration, self-monitored blood glucose levels, concomitant medications, and HbA1c target selection as per physician's discretion may also influence glycemic control outcomes [20, 21]. Even though these are potential limitations of the analysis, they are reflective of real-world clinical practice, which was a key aim of the post hoc analysis. Additionally, this pooled analysis represents a point-in-time snapshot of the Gla-100 treatment approach for T2DM that could be helpful to understand past practices and provide valuable insights needed to carve future considerations in India.

CONCLUSION

This post hoc sub-analysis of two large-scale registries indicates the real-world effectiveness and safety of Gla-100 in the insulin-naïve T2DM population in India. In routine clinical practice, Gla-100 significantly improved HbA1c and FPG levels after 6 months of treatment with a low risk of hypoglycemia and no weight change in participants with T2DM. The results of the LIVE INDIA pooled analysis data have the potential to be valuable input for future reviews and research. Future research should highlight similarities with current knowledge about insulin glargine in T2DM participants, regardless of their country of origin.

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Salvi, and Chirag Trivedi were involved in drafting the manuscript or revising it critically for important intellectual content. All authors have given final approval to the version to be published and each author had participated sufficiently in the work to take public responsibility of the content and agreed to be accountable for all aspects of work in ensuring that questions related to accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Data Availability. Qualified researchers may request access to person-level data and related study documents, including the clinical study report, the study protocol with any amendments, the blank case report form, statistical analysis plan, and dataset specifications. Participant level data will be anonymized, and study documents will be redacted to protect the privacy of trial participants. Further details on Sanofi's data sharing criteria, eligible studies, and process for requesting access can be found at: https://www.vivli.org.

Declarations

Conflict of Interest. Manoj Chadha has received speaker fees from Eli Lilly and Company, Novo Nordisk and Sanofi. Manoj Chawla is on the advisory board for/has a speaker contract with/has a consultancy agreement with Sanofi India, Novo Nordisk India Pvt. Ltd., Eli Lilly India, Boehringer Ingelheim, MSD, AstraZeneca Pharma India Ltd., Novartis, Eris Lifesciences, and USV. Vaishali Deshmukh, Tirthankar Chaudhury, Sagarika Mukherjee, Shailesh Pitale, Debasis Basu, Santosh Ramakrishnan, Ghanshyam Goyal have nothing to disclose. Arvind Gadekar, Shalini Menon, Chirag Trivedi, and Vaibhav Salvi are employees of Sanofi and may hold stock options. The authors individually and collectively are responsible for all content and editorial decisions and did not receive any payment from Sanofi directly or indirectly (through a third party) related to the development or presentation of this study.

Ethical Approval. Being a retrospective analysis, as per the applicable local regulations, approval of the study protocol, protocol amendments, and other relevant documents from an independent ethics committee registered with the National Ethics Committee Registry for Biomedical and Health Research, Department of Health Research (NECRBHR, DHR) were obtained prior to the study initiation. The primary studies were conducted in accordance with the ethical principles laid down by the Helsinki Declaration of 1964, and its later amendments, all international applicable guidelines, and national laws and regulations of each country. A written informed consent was provided by participants for both the studies. Appropriate measures were taken to ensure the confidentiality of the data.

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