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Evaluation of Safety and Efficacy of Glaritus® versus Lantus® in Combination with Insulin Lispro among Adults with Type 1 Diabetes Mellitus-Phase IV Study

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Abstract

Objective: The present study assessed safety and efficacy of Glaritus® among adults with Type 1 Diabetes Mellitus (T1DM). **Methodology:** This prospective, randomized, multicenter, comparative, non-inferiority, open-label, parallel group, phase IV study was conducted in 14 study centers in India. Subjects were randomly allocated to receive either Glaritus® or Lantus® for 12 weeks. Each week, the dose of insulin was titrated to maintain target fasting blood glucose (FBG) level range of 80 - 120 mg/dL. **Results:** A total of 171 subjects were randomized (Glaritus® arm-86; Lantus® arm-85) and 161 subjects completed the study. The mean change in the glycosylated haemoglobin (HbA1c) levels from visit 3 (baseline) to visit 6 (end of trial) in Glaritus® arm was −0.69 ± 1.81 and in Lantus® arm was −0.53 ± 1.94. The mean change in glucose levels between week 1 and end of week 11 in Glaritus® arm was −8.81 ± 34.57 and in Lantus® arm was −5.28 ± 30. At least one hypoglycemic episode was experienced by 27.2% subjects of Glaritus® arm and 28.6% subjects of Lantus® arm. A total of 24 adverse events (AEs) such as pain, pyrexia, few infection related including urinary tract infections, metabolic related such as decreased appetite, musculoskeletal, neurological and skin related were reported in the study (Lantus® arm: 14 AEs; Glaritus® arm: 10 AEs). **Conclusion:** In this short term, 12-week study, biosimilar insulin glargine, Glaritus®, is comparable to the reference product, Lantus®, when combined with Insulin Lispro® in terms of glycemic control, risk of hypoglycemia and occurrence of adverse drug reactions among adults with T1DM.

Keywords

Diabetes Mellitus, Insulin Glargine, Insulin Lispro

1. Introduction

Diabetes is one of the biggest global health emergencies of the 21st century. Each year, more and more people live with this condition, which can result in life-changing complications. As per the International Diabetes Federation (IDF) atlas (2015), in addition to the 415 million adults who are estimated to currently have diabetes globally, there are 318 million adults with impaired glucose tolerance, which puts them at high risk of developing the disease in the future. India ranks second after China where 69.2 million people are living with diabetes; the figure shall be doubled by 2040 as per the forecasting reports of IDF [1].

Type 1 diabetes mellitus (T1DM) is an autoimmune disorder resulting from impaired function of β-cells leading to insulin deficiency [2]. Insulin supplementation is the mainstay of therapy for patients with T1DM for adequate glycemic control. Optimum glycemic control in patients with T1DM delays the onset and progression of microvascular and neuropathic complications as confirmed by the Diabetes Control and Complications Trial (DCCT) [3].

In the last few decades, significant contributions have been made in medical research for understanding and management of diabetes. Various new interventions have been proposed including insulin analogs that are similar to human insulin but have their amino acid sequences altered to provide desired chemical properties [4]. Biosimilar drugs differ from generic drugs which have simpler chemical structures and are considered to be identical to their reference medicines in terms of efficacy and safety [5]. The recent inclusion of insulin analogues for diabetes management has been designed more closely to mimic physiologic insulin profiles through improved pharmacokinetics (PK) characteristics that result in either more rapid or prolonged pharmacodynamics (PD) effects. The various subcutaneous insulin preparations available are primarily differentiated by the shape of their plasma time-concentration profiles, which depicts their duration of action (slow, rapid or prolonged) and their ultimate effect on glucose levels [6] [7].

Insulin glargine, one of the primary targets for biosimilars' producers, was the first long acting insulin analogue to become available and provide a more physiological and convenient method of basal insulin replacement than older long acting insulin formulations [8] [9]. It is a human insulin analogue produced from non-pathogenic strain of *Escherichia coli* [10]. Management of T1DM is thus aimed at mimicking endogenous insulin secretion precedent that is characterized by continuous basal insulin secretion using longer-acting insulin preparations and meal-related peaks using rapid acting insulin preparations. A combination therapy with rapid-acting insulin analogues like insulin aspart and

lispro and long acting insulin analogues (LAIA) such as insulin glargine and detemir have been shown to be effective for T1DM [11] [12] [13]. These LAIA achieve consistent glycemic control for a longer period of time ruling out the need for multiple dosing [10]. However, the development of even longer-acting insulins and improved insulin delivery techniques may lead to better glycemic control for patients in the future [14].

A systematic review by Wang *et al.* showed that insulin glargine is effective in the management of T1DM and provides consistent insulin delivery which ensures effective glycemic control for 24 hours making it suitable for once daily dosing [15].

The DCCT illustrated a 3-fold higher risk of severe hypoglycemia ($p < 0.001$) in the patients with intensive therapy, thereby, indicating a challenge in maintaining equilibrium between tight glycaemic control and hypoglycemia [16]. Also few studies in T1DM patients reported that intensification of treatment with insulin analogues can induce generalized edema [17] [18]. Treatment of diabetes mellitus with insulin glargine has demonstrated fewer hypoglycemic episodes and better patient acceptability. A review showed that nocturnal hypoglycemic episodes in patients with T1DM were significantly fewer among patients who received insulin glargine as compared with the patients who received Neutral Protamine Hagedorn (NPH) insulin. In addition, insulin glargine reduced glycosylated hemoglobin (HbA1c) levels to a greater extent as compared with NPH insulin [19]. Addition of bolus insulin to therapy with insulin glargine may further boost glycemic control [20]. A study comparing combination of insulin glargine and insulin lispro with insulin lispro mix (25% insulin lispro, 75% insulin lispro protamine suspension) combination demonstrated comparable results between the two treatment groups with respect to glycemic control in patients with type 2 diabetes mellitus (T2DM) [21].

Concerns are being raised as more and more biopharmaceutical products are becoming off-patent and many companies are bringing the biosimilars or follow-on biologics of these products. It is essential to affirm confidence in such copy biologics being as safe and effective to conventional products by generating evidence through clinical data [22]. Hence the present study was conducted to assess safety and efficacy of two brands of insulin glargine; Glaritus® in comparison with innovator, Lantus®, in combination with Lispro.

2. Methodology

2.1. Study Characteristics

This was a prospective, randomized, multicenter, comparative, non-inferiority, open-label, parallel group, phase IV study conducted between Mar. 2012 and Jul. 2013 at 14 study centres across India. The study (Protocol Number: GLA/WOC/CT/010/ 11 - 12 and CTRI reg. Number: CTRI/2011/11/002173) was approved by the Institutional Review Board (IRB)/Independent Ethics Committees (IEC) of all the 14 study centers. The study was conducted in accordance to the

ethical principles in the current Declaration of Helsinki [23] and good clinical practices (GCP). A written informed consent was obtained from all the subjects prior to enrolment in the study.

2.2. Inclusion and Exclusion Criteria

Men and women aged 18 to 55 yr diagnosed with T1DM more than one year prior to the study were included. Subjects with less than normal C-peptide levels and those who were on insulin regimen for at least a period of 12 months, with HbA1c levels ≥ 7 were included in the present study.

Subjects with impaired hepatic and renal function, borderline or positive serum anti-insulin antibody (AIA) result (>0.95 index value), hepatitis B or C, HIV positive, hyperthyroidism, hypothyroidism, severe proliferative retinopathy, nephropathy and/or neuropathy, cardiovascular disease, anemia (80 - 109 g/l), hemoglobinopathy, alcohol or drug abuse, receiving more than 1.4 units/kg total daily dose of insulin, history of allergy to insulin preparations, history of receiving insulin of animal origin in the past three years or receiving immunomodulatory medications or hypoglycaemic agents 4 weeks prior to screening were excluded from the study. Subjects who had undergone pancreatectomy or transplant of pancreas or islet cells were also excluded.

2.3. Study Medications

The study medications included Glaritus® (insulin glargine, Wockhardt), comparator drug Lantus® (insulin glargine, Sanofi Aventis), and meal time bolus of rapid acting insulin lispro.

2.4. Data Collection

The study initiated with a screening period (visit 1) followed by a run-in period (visit 2) of 4 weeks during which the subjects received only Lantus® for stabilization. After the completion of run-in period, the subjects were randomly allocated to receive either Glaritus® or Lantus® for a period of 12 weeks (**Figure 1**). All the subjects were advised diabetes diet. However, supervision of the diet condition of the subjects was not carried out during the study period. The subjects were required to have their respective glargine dose once daily at bedtime. All the subjects were instructed to have insulin lispro three times a day before meals. Subjects recorded time of glargine administration, and FBG levels on daily basis. All the subjects were required to use self-glucose monitoring device (Sugarcheck™, an amperometric Biosensor marketed by Wockhardt Ltd.) and self-administer insulin during the study period.

2.5. Initial Dose Calculation and Titration

The initial dose of insulin was based on total daily insulin being taken by the subject. The dose of insulin was reduced by 10% in subjects with HbA1c level of more than 9% and by 20% in subjects with HbA1c level of less than 9%. The total insulin dose was then divided into basal (50% of total insulin glargine [Glari-

tus®/Lantus®] subcutaneously once daily at bed time) and bolus (50% of total insulin lispro [Eli Lilly's insulin lispro-Humalog®] subcutaneously divided equally into three doses before meals) dosing.

Each week the dose of insulin was titrated based on three consecutive levels of fasting blood sugar (FBG) recorded by the subjects. Dose titration was done to maintain the target FBG level in the range of 80 - 120 mg/dL. The total daily insulin dose was reduced by 10% if the average of last three consecutive FBG levels was less than 80 mg/dL and was increased by 10% if the average of last three consecutive FBG was more than 120 mg/dL. The total titrated dose of insulin glargine was divided into basal (50% of total insulin glargine [Glaritus®/Lantus®] once daily subcutaneously) and bolus (50% of total insulin lispro three times daily before meals subcutaneously).

2.6. Efficacy and Safety Assessments

The efficacy assessments included HbA1c levels during visit 3 (week 1) and visit 6 (week 12), FBG at the end of each week from week 1 and week 12, and change in glargine dose at the end of each week between visit 3 and visit 6.

All the subjects were screened for safety assessments during screening (visit 1), at regular intervals of time during the entire study period (visit 2, visit 3, visit 4 and visit 5), and at end of the study (visit 6). Safety assessments included screening of adverse events (AEs), including hypoglycemia events.

Hypoglycemia is the most common side effect of this treatment regimen which was captured on a log both in the CRF and the source documents/subject diary, instead of capturing it on the adverse event form. However severe hypoglycemia which satisfies the serious adverse event (SAE) criteria was captured as an SAE and reported accordingly. The subject was considered as hypoglycemia case as per the guidelines of American Diabetes Association [24].

Other safety assessments recorded were; SAE, laboratory test results, ECG findings, vital signs, and physical examination findings. The change in serum anti-insulin antibodies (AIA) during visit 3 and visit 6 was evaluated as a long term safety parameter.

2.7. Statistical Analysis

Sample size and statistical power calculations were based on assumptions of 0% (*i.e.*, $\epsilon = 0$) mean difference, a standard deviation as 0.07, 134 subjects were required per arm to have a power of 90% and alpha 5%. Total estimated sample size was 268 (1:1) for all the treatment groups. Considering a drop-out rate of 20%, a total of 322 subjects were planned to be randomized for the study. Sample Size was calculated by using the power analysis of following test for non-inferiority by normal approximation [25]

$$n_1 = n_2 = \frac{2\left(z_\alpha + z_\beta\right)^2 \sigma^2}{\left(\epsilon - \delta\right)^2}$$

For comparison of efficacy variables over different age groups, Analysis of covariance (ANCOVA) test [95% Confidence Interval (CI), *p*-0.00] was used. An interim analysis of the data was planned once 50 subjects were randomized in each treatment arm *i.e.* 100 patients in study. Continuous variables were summarized using sample counts, mean, median, standard deviation, range, and 95% CI. Categorical variables were presented with number of exposed subjects, and number (N) with percentages. Change in HbA1c from baseline to end of trial was analyzed in per protocol (PP) population. PP population consisted of all the randomized subjects (N = 158) who came for all the visits within window period and had at least 80% compliance to protocol defined study drug administration and had not missed 4 consecutive doses of the study drug. The 95% CI were calculated for difference in HbA1c levels at baseline and at the end of trial between the two study arms. Mean with standard deviation and *p* value was calculated for change in FBG, variability in FBG from baseline to each visit and to end of trial. The primary and secondary efficacy analysis was performed at 5% level of significance and no adjustments were required for multiple comparisons.

Although a total of 322 subjects were planned for inclusion in the present study, the results of interim analysis were satisfying with more than 80% power. Therefore, the study was closed with 171 randomized subjects, out of which 161 subjects completed the study.

3. Results

3.1. Study Subjects Included

Of the total 433 subjects who were screened, 202 subjects entered the run-in period. A total of 171 subjects were randomized (Glaritus® arm-86 subjects; Lantus® arm-85 subjects) and 161 subjects completed the study (Figure 1). A total of 14 investigational sites recruited subjects for inclusion in the present study. The subject disposition is presented in Figure 2. The mean age of the subjects included in the present study was 28.1 yr and majority were men (113; 66.1%). The most common concomitant condition among the subjects was hypertension. The demographic parameters of all study subjects are tabulated in Table 1.

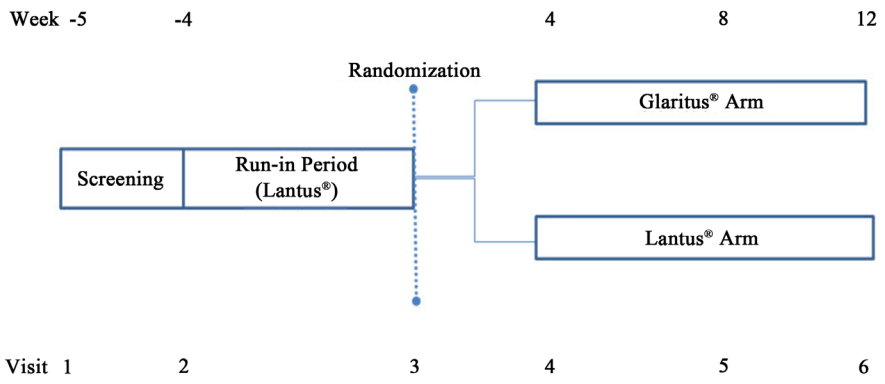
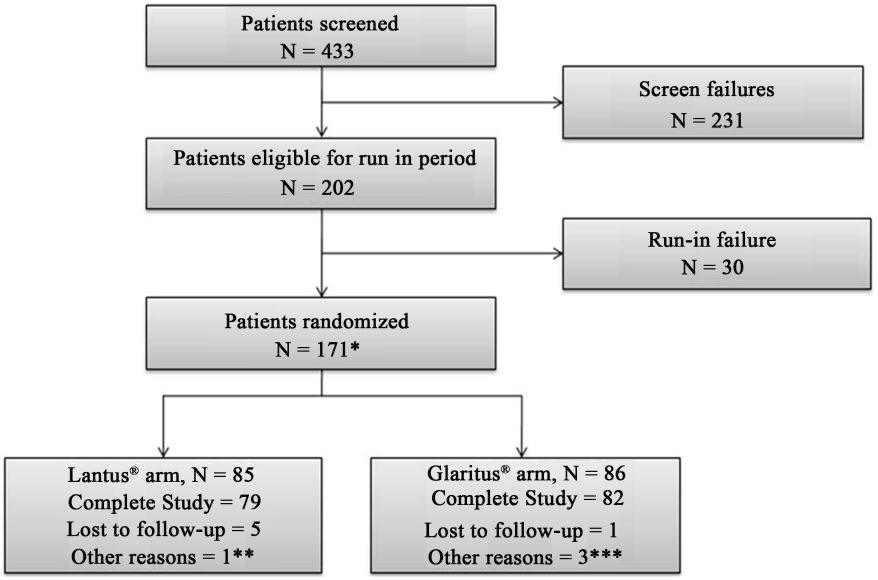


Figure 1. Study design.



*Subject no. G14002 completed the study, but not included in the analysis because the subject was randomized to receive Lantus® however could not continue the study as the site was closed. Other two subjects (G20072 and G20082) completed the study, but were not meeting the age criteria so were not considered for analysis.

**One subject (G16004) from Lantus® arm (was withdrawn from the study as treatment compliance was unsatisfactory.

***Three subjects (G20027, G11016 and G23016) from Glaritus® arm did not give consent to continue the study.

Figure 2. Disposition of study subjects.

Table 1. Demographics and baseline characteristics of study subjects.

Parameters	Glaritus® arm (N = 86*)	Lantus® arm (N = 85**)	Total (N = 171)
Age (yr)	28.19 ± 9.17	28.1 ± 9.58	28.1 ± 9.35
Height (cm)	162.61 ± 9.3	162.6 ± 7.5	162.6 ± 8.5
Weight (Kg)	58.28 ± 9.9	59.9 ± 10.4	59.1 ± 10.2
BMI (Kg/m^2)	22.12 ± 3.0	22.4 ± 3.0	22.3 ± 3.0
Male	56 (65.1)	57 (67.1)	113 (66.1)
	Ethnicity-n (%)		
Indian	82 (95.3)	80 (94.1)	162 (94.7)
Asian	4 (4.7)	5 (5.9)	9 (5.3)
	Education-n (%)		
Literate	86 (100)	84 (98.8)	170 (99.4)
Illiterate	0 (0)	1 (1.2)	1 (0.6)
Baseline characteristics			
HbA1c	9.71 ± 1.93	9.74 ± 2.30	9.71 ± 2.12
Fasting blood glucose	115.57 ± 30.40	112.10 ± 24.82	113.84 ± 27.61

*One Subject was not considered in the analysis as the subject was randomized under Glaritus® arm, as subject was not satisfying age criteria. **One Subject was not considered in the analysis as the subject was randomized under Lantus® arm, as subject was not satisfying age criteria.

3.2. Measurement of Efficacy Variables

HbA1c

The mean change in the HbA1c levels from visit 3 to visit 6 in Glaritus® arm was −0.69 ± 1.81 and in Lantus® arm was −0.53 ± 1.94. Although the decrease in HbA1c among subjects of both arms was significant ($p < 0.05$), the difference between the two treatment groups was not significant ($p = 0.454$). The difference of adjusted means of change in HbA1c was −0.20 with an upper limit of 95% CI of 0.32 (less than the USFDA specified non-inferiority margin of 0.4). These results demonstrate Glaritus® to be non-inferior to Lantus® in glycemic control.

Glucose Measurements and Change in Glargine Dose

The measurement of FBG was done at the end of each week throughout the study and the change in FBG was evaluated between week 1 and week 11. The mean change in glucose levels between week 1 and end of week 11 in Glaritus® arm was −8.81 ± 34.57 and in Lantus® arm was −5.28 ± 30 ($p = 0.792$).

The dose of glargine was titrated in the beginning of the study (randomization visit) and at the end of each week throughout the study as per the glucose reading on the self-monitoring device. The dose of glargine was not changed in 56 subjects (69.1%) of Glaritus® arm and in 49 subjects (63.6%) of Lantus® arm ($p = 0.5373$). The dose of glargine was increased by more than 10% in 19 subjects (23.5%) of Glaritus® arm and in 21 subjects (27.3%) of Lantus® arm. The dose of glargine was decreased by more than 10% in 6 subjects of Glaritus® arm (7.4%) and Lantus® arm (9.1%) each ($p = 0.5373$).

3.3. Reporting of Safety Variables

During the study, 21 subjects (12.3%) reported at least one AE. A total of 24 AEs (14%) were reported during the study of which 14 were reported by the subjects of Lantus® arm (2 AEs resolved with sequelae and 12 AEs resolved without sequelae) and 10 were reported by the subjects of Glaritus® arm (4 AEs resolved with sequelae and 6 resolved without sequelae). All AEs were mild to moderate in severity (Table 2). No deaths and SAEs were reported during the study period.

Table 2. Incidence of adverse events (AEs).

Adverse events; n (%)	Glaritus® (N = 86)	Lantus® (N = 85)
Total number of AEs	10 (11.6)	14 (16.4)
Number of subjects with at least one AE	9 (10.5)	12 (14.1)
General disorders	2 (2.3)	5 (5.9)
Urinary tract infections	3 (3.5)	1 (1.2)
Headache	3 (3.5)	2 (2.4)
Nasopharyngitis	1 (1.2)	3 (3.5)
Skin and subcutaneous tissue disorders	0 (0.0)	2 (2.4)
Decreased appetite	1 (1.2)	0 (0.0)

3.4. Immunogenic Response Evaluation

The immunogenic evaluation was done in all subjects at visit 1 and immunogenic response was assessed at visit 3, and visit 6. The change in serum AIA was assessed at baseline (visit 3; week 1 ± 1 day) and at the end of trial (visit 6; end of week 12 ± 3 days). The mean immunogenic response from baseline to the end of trial in Glaritus® arm and Lantus® arm was 0.25 ± 0.97 and 0.02 ± 0.68 respectively (p = 0.306). The immunogenic response was comparable between both arms of the study.

Hypoglycemic Episodes

A total of 22 subjects (27.2%) in Glaritus® arm and 22 subjects (28.6%) in Lantus® arm (p = 0.8432) experienced at least one hypoglycemic episode during the study.

4. Discussion

The long-acting basal insulins are the most commonly prescribed therapy for patients with T1DM and T2DM. Insulin glargine 100 units/mL and insulin detemir are the established long-acting basal insulins available in the United States and Europe, both of which exhibit similar glycemic control to that of the intermediate-acting NPH, but with a reduction in hypoglycaemia. Newer insulin products which are currently in development are; new insulin glargine 300 units/mL (United States and Europe) and the ultra-long-acting insulin degludec (Europe) with basal insulin peglispro. These new insulins have comparatively different pharmacokinetic/pharmacodynamic profiles and demonstrate longer durations of action (>24 h) compared with insulin glargine 100 units/mL, which may lead to potential benefits. Hence, the launch of biosimilar insulins may also widen the access to insulins by reducing treatment costs [14].

Insulin glargine is a LAIA which was first introduced in 1992 and was approved by the US FDA in April 2000 [18]. Insulin glargine regulates glucose metabolism by stimulating peripheral glucose uptake resulting in improved HbA1c levels and FBG levels [26]. The clinical benefits of insulin glargine over traditional basal insulin have been proven in various studies. The characteristic features of insulin glargine such as once daily regimen and absence of suspension problems, recommends it one of the best strategy in achieving tight glycemic control in many patients with diabetes [27] [28].

The results of the present study demonstrated comparable efficacy and safety of Glaritus® and Lantus®. The difference in mean HbA1c and FBG levels in subjects of both treatment arms was comparable. Several studies have been conducted in the past to evaluate the efficacy and safety of insulin glargine in patients with T1DM. Most studies comparing insulin glargine with other insulin analogs such as insulin detemir, insulin degludec, biphasic human insulin, and Neutral Protamine Hagedorn (NPH) insulin in patients with diabetes mellitus have shown comparable results with insulin glargine. Insulin glargine provides consistent plasma insulin concentration similar to the continuous subcutaneous

insulin infusion (CSII). This is achieved as a result of stable serum insulin concentration on administration of insulin glargine without significant fluctuations [29].

A study comparing the effects of insulin glargine with NPH insulin demonstrated that Insulin glargine was associated with significantly greater reductions in FBG than NPH ($p = 0.0001$) in T1DM patients [30]. Patients who switched from NPH insulin to insulin glargine showed significant improvement in HbA1c levels ($p < 0.05$) over a period of 3 months [31]. Studies by Bellia A *et al*.; to observe the effects of switching from NPH insulin to insulin glargine on glycaemic control in patients with T2DM have shown that HbA1c levels decreased after 4 - 8 months with glargine ($p < 0.001$) but not with NPH ($p = 0.20$) [32]. Lepore *et al.* showed that plasma insulin concentration with NPH insulin showed a peak within 4 h of administration (22.8 ± 2.2 μU/ml) and decreased below the baseline value within 13 h; however, insulin glargine achieved a plateau concentration of 18.9 ± 0.3 μU/ml between 3 and 24 h after its administration [33].

Some more comparative studies reported effect of insulin glargine with other insulin analogs where there was greater reduction in HbA1c levels in patients receiving insulin glargine [34] [35].

Besides NPH, there have been many studies conducted where better efficacy results with insulin glargine have been reported. Studies conducted by Abe S. *et al*., have demonstrated that insulin glargine leads to be more effective and more stable glycemic control than the same dose of insulin detemir (Mean blood glucose was significantly lower with insulin glargine compared with insulin detemir (9.6 ± 2.4 mmol/L versus 10.4 ± 2.8 mmol/L, $p = 0.038$) [36]).

Most patients with T1DM experience hyperglycemia early in the morning due to decreasing effect of short or intermediate acting insulin analogues. In a previous study, hyperglycemia was observed in 60% patients receiving NPH insulin and in very few patients receiving CSII and insulin glargine. In addition, patients receiving insulin glargine experienced fewer nocturnal hypoglycemic episodes [20].

Hypoglycemia is a known and common AE of anti-diabetic drugs. In the present study, 27.2% subjects of the Glaritus® arm and 28.6% subjects of the Lantus® arm experienced at least one hypoglycemic episode during the study period. A review of several studies reported fewer nocturnal hypoglycemic episodes in patients receiving insulin glargine as compared with isophane insulin; however the effect of glycemic control was comparable [37].

Kumar S. *et al*.; demonstrated the efficacy and safety of once-daily insulin degludec/insulin aspart compared with once-daily insulin glargine in participants with T2DM, insulin degludec/insulin aspart led to higher rates of overall hypoglycaemia than insulin glargine, with no significant difference in rates of nocturnal hypoglycaemia. The overall confirmed hypoglycaemia rate was higher with daily insulin degludec/insulin aspart once daily (estimated rate ratio 1.43; 95% CI 1.07, 1.92; $p < 0.05$) [38].

Another 24 weeks study conducted in Turkish population to evaluate the

safety and effectiveness of insulin initiation with once-daily insulin detemir or insulin glargine with T2DM have shown clinically significant glycaemic improvements. A lower risk of minor hypoglycaemia was observed with insulin detemir compared with insulin glargine [39].

Besides hypoglycemia, other AEs reported with insulin glargine are few and mild in severity. A recent study evaluating the effect of insulin glargine and insulin lispro in patients with diabetes mellitus reported no AEs in patients throughout the study period [40]. Heller *et al.* reported fewer AEs with insulin glargine (4.9%) as compared with insulin detemir (11.7%) among patients with T2DM [41]. Insulin glargine was associated with fewer gastrointestinal AEs such as nausea (insulin glargine-3%; exenatide-43%), vomiting (insulin glargine-0%; exenatide-10%), and upper abdominal pain (insulin glargine-0%; exenatide-8%) as compared with exenatide in patients with diabetes mellitus [42].

Biosimilar drugs may have a different source for biological materials and manufacturing processes than innovator. These differences between innovator and non-innovator or biosimilar products can be identified by analytical methods like, batch-to-batch consistency, product stability as well as by clinical methods with safety and efficacy studies [22]. The present study was, to some extent, able to address the concerns associated with the use of biosimilar insulin glargine in the treatment of diabetes mellitus patients. As biosimilar insulins are approved copies of insulins outside patent protection they can provide healthy market competition and potential cost reduction for the patients [43].

Limitations of this study

This was a non-inferiority trial and both Glaritus® and Lantus® demonstrated comparable efficacy and safety during the study period. However the study was crippled with certain limitations which make the confirmatory concluding remarks improbable.

The present study was of short duration and was not planned and conducted as per the clinical data requirements mentioned in the available guidelines for preparation and marketing of similar biological medicinal products [44] [45]. A cross-over study design would have been more appropriate for such kind of comparative studies.

Screening for antibodies specific for the 65 kDa isoform of glutamic acid decarboxylase (GAD65) for diagnosis of type 1 diabetes was not done in this study. The screen failure rate for the study was found to be high. Such a high screen failure rate may signify non-representative sample to the target population.

Also pre-screening insulin doses have not been extracted from source data while preparing the final clinical study report. Further, this was an open-label study and pre-approval assessment of safety is lacking. Therefore, well-designed studies for the evaluation of innovator comparable efficacy and long term safety are being planned.

5. Conclusion

In conclusion, both Glaritus® and Lantus® demonstrated comparable effects on

HbA1c, and FBG in patients with T1DM. Glycemic control observed in patients of both treatment arms was comparable. There were few hypoglycemia episodes observed in both the arms. There were no deaths and SAEs reported in the study. Overall, the results of the present study suggest that biosimilar insulin glargine, Glaritus, is comparable to the reference product, Lantus, providing a safe and effective option for patients with T1DM. Further adequately designed studies are required to be conducted in accordance to the guidelines for similar biologics.

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Conflict of Interest

The authors have no conflict of interest.

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