

# Evaluation of Patient Reported Satisfaction and Clinical Efficacy of Insulin Glargine 300 U/mL Versus 100 U/mL in Patients With Type 1 Diabetes Using Flash Glucose Monitoring System

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## ABSTRACT

**BACKGROUND AND AIMS:** To analyze patient-reported satisfaction and clinical effectiveness of concentrated insulin glargine 300 U/mL (Gla-300) among patients with type 1 diabetes (T1D) using a flash glucose monitoring (FGM) system.

**METHODS:** This comparative study was conducted among 86 patients with T1D (aged 14–40 years), who were treated with Glargine 100 U/mL (Gla-100) and switched to Gla-300 at day 1 (baseline). The following data were collected from each patient: demographic information, clinical parameters, and glycemic control markers. All patients completed the Diabetes Treatment Satisfaction Questionnaire (Arabic version), first at baseline and then after 12 weeks. A comparison was done for all the data recorded at baseline (on Gla-100) and after 12 weeks (on Gla-300) and subjected to analysis.

**RESULTS:** Compared to patients treated with Gla-100, significant improvements were observed in the Gla-300 group, in terms of the ambulatory glucose profile (AGP) markers, such as percentage of time spent within the target range of the glucose levels (70–180 mg/dL) ( $P = .037$ ), percentage which fell below the target ( $<70$  mg/dL) ( $P = .027$ ), and percentage of time spent ( $<54$  mg/dL) ( $P = .043$ ). Compared to Gla-100, patients treated with Gla-300 experienced significant improvements in the current treatment satisfactions ( $P = .047$ ), convenient finding treatment recently ( $P = .034$ ), and flexible finding treatment recently ( $P = .041$ ), recommend the current treatment ( $P = .042$ ) and satisfied to continue the current treatment ( $P = .035$ ).

**CONCLUSION:** Compared to the patients on Gla-100, patients treated with Gla-300 exhibited significant improvements in the AGP markers and degree of treatment satisfaction.

**KEYWORDS:** Type 1 diabetes, glargine 300 U/mL, glargine 100 U/mL, patient satisfaction

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## Introduction

The treatment of type 1 diabetes (T1D) remains one of the critical healthcare challenges for physicians and care providers.<sup>1,2</sup> In a recent report, the International Diabetes Federation (IDF), estimated that 10% of the global population with diabetes have T1D. Most often, this condition is diagnosed during childhood or adolescence.<sup>3,4</sup> Patients with T1D need insulin injections, every day to ensure blood glucose control, and in the absence of access to insulin, they face a higher risk of death.<sup>4</sup> From many studies, it was concluded that even developed countries found that, in comparison to healthy children (without diabetes), children with T1D had double the death rate.<sup>5</sup> However, over recent time, a broad spectrum of treatment choices have been advanced for T1D patients, facilitating individualized care, enhancing clinical outcomes, and lowering the mortality rate.<sup>6,7</sup>

For T1D patients, the typical regimen they need includes Multiple Daily Injections (MDI) of insulin, which are

composed of a basal component (long-acting) and a bolus component (short-acting) at mealtimes.<sup>8</sup> Over time, this basal insulin therapy has advanced from first-generation analogs (glargine U-100) to second-generation analogs (glargine U-300) and also to ultra-long-acting formulations. It is hoped that these features may provide more constant glycemic control, with sustained effect, through a treating interval of 24 hours.<sup>9,10</sup> Such developments have boosted the treatment options for patients, hopefully offering better glycemic control and thereby improving the choices for optimal insulin therapy, especially to suit adolescents and children with diabetes. They should also be able to bestow adequate glycemic control and reduce the risks of hypoglycemia and hyperglycemia. If the T1D treatment is interrupted (interruption of insulin therapy), it induces rapid Diabetic Ketoacidosis (DKA), a serious condition that can prove life-threatening.<sup>11,12</sup>

Since 2006, a number of developing countries have approved Insulin glargine 100 U/mL (Gla-100; Lantus®) and Insulin



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glargine U300 (Gla-100; Toujeo®), while by early 2015, the European Medicines Agency and United States Food and Drug Administration sanctioned the use of Glar-300.<sup>9,13</sup> Although both brands are similar in composition<sup>14,15</sup> they exhibit different actions.<sup>16</sup> For the Gla-100, using the euglycemic clamp, the mean duration of action was found to be 25.5 hours after a single-dose of 0.3 U/kg.<sup>17</sup> However, the Gla-300, when compared to Gla-100, shows a flatter and extra-long time-action, which may possibly ensure that the glycemic control is more stable and constant over the 24-hour inter-dosing interval<sup>9</sup> and thus establish a higher degree of constancy in the glucose-lowering action.<sup>18</sup> Until the present, only a limited number of studies, besides anecdotal reports, on the new generation of a basal insulin analog, are in existence in the Arab region (none among the FGM users), specifically in Saudi Arabia, which from the perspective of the rate of diabetes, is ranked the second-highest in the Middle East, and seventh in the world.<sup>1,19</sup> Therefore, the aim of the present study was to analyze the clinical efficacy and patient-reported satisfaction and of concentrated insulin glargine 300U/mL (Gla-300) in T1D patients using the FGM system.

## Methods

### *Study design, setting, and sampling*

A 12-weeks comparative study involving a convenience sample of 86 T1D (aged 14-40 years) with the previous receipt of basal insulin using Gla-100 insulin plus fast-acting insulin therapy (MDI). The patients were then taken off Gla-100 and placed on Gla-300, according to the discretion of the treating physician, as part of their usual clinical practice were collected for this study.

The study was conducted at Diabetes Treatment Center, Prince Sultan Military Medical City (PSMMC), Riyadh, Saudi Arabia, between March 2021 and August 2021. Both retrospective data extraction and prospective data collection were done to determine the efficacy and patient satisfaction of Gla-300 versus Gla-100 units/mL, in T1D patients utilizing the FGM system. The study adhered to the norms of the Declaration of Helsinki and received approval from the PSMMC, Research and Ethics Committee, Riyadh, Saudi Arabia.

### *Inclusion and exclusion criteria*

The participants included in this study were patients who had T1D for  $\geq 1$  year and had been on basal insulin treatment, using Gla-100 insulin plus the fast-acting insulin therapy of MDI, and who used the continuous FreeStyle Libre® (Abbott Diabetes Care, Alameda, CA, USA) for self-glucose monitoring, for a minimum period of the last 12 months.

The following constraints were specified as the exclusion criteria (1) Patients had been on treatment for  $< 1$ -year with basal plus mealtime insulin, utilizing any type of basal insulin,

except the long-acting insulin analogs (ie, Levemir and Tresiba) for 3 months prior to screening, (2) insulin pump usage for 6 months prior to the screening visit or plans to opt for the pump treatment within 6 months post the screening, (3) any use of other types of glucose-lowering agents in the 3 months prior to the screening, (4) any use of systemic glucocorticoids for  $\geq 1$  week in the 3 months prior to screening, (5) a history of severe hypoglycemia followed by seizures, hospitalization for diabetic ketoacidosis or unconsciousness in the past 3 months (6) severe or unstable, clinical-related nondiabetic disorder or mental issues that could likely be a hindrance to the protocol of the present study or interfere with the execution of assessing the medications used and (7) improper employment of the FGM system during the screening period, indicated by at least 70% of time sensor is active.

All participants in the research were given unconditional or absolute “right to withdraw” at any time, without citing any reason or offering prior notice. All the participants or their caregivers/parents were informed regarding the part they would play in the current study, and were required to provide signed informed consent prior to enrollment.

### *Data collection*

At the baseline visit, the patient-related data were drawn from the standardized case record, which included their demographic data, clinical characteristics, and treatment history. Besides, at the baseline, as well as at the end of the study, the HbA1c was recorded from the laboratory of PSMMC, utilizing the COBAS INTEGRA 400 plus/800 analyzer.

### *Glucometric data*

With help from the LibreView website, data were collected on the Ambulatory Glucose Profile (AGP) glucometric parameters (14 days) prior to treatment transition, which included the mean glucose (mg/dL), TIR (% of the time between 70 and 180 mg/dL), TAR (% of time above 180 mg/dL), and glycemic variability (GV) expressed as the percent coefficient of variation (% CV). These were compared with data drawn from the earlier 14 days after 12 weeks of the Gla-300 treatment were completed. Patients who were excluded from the cohort were those who showed insufficient use of the FGM system (% time sensor active below 70%).

### *Outcomes*

The main objective was to compare the effects that the patients experienced after treatment with the Gla-100 and Gla-300, in terms of the changes identified in the mean glucose values (mg/dL), TIR (% of the time from 70 to 180 mg/dL), TAR (% of time exceeding 180 mg/dL), time-below-range (TBR)  $< 70$  mg/dL or  $< 54$  mg/dL, glucose variability (GV) defined as the glucose coefficient of variation (%CV),<sup>20</sup> as well as the

difference in patient-reported satisfaction on their present diabetes treatment. The secondary endpoint included the change experienced from baseline to week 12, with regards to the calculated total daily dose of insulin-IU (TDD), and changes in the Glucose Monitoring Indicator (GMI %).

#### Diabetes treatment satisfaction questionnaire (DTSQ)

All the participants completed the Arabic version of the Diabetes Treatment Satisfaction Questionnaire (DTSQ) at baseline and the end of the study. Also, the total treatment satisfaction score in the DTSQ was calculated.<sup>21</sup>

Treatment satisfaction in patients with T1D was assessed using the DTSQ, which is a very useful tool.<sup>22</sup> In the DTSQ, 8 health concepts are included: 6 questions deal with general satisfaction, with a scoring from 0 (very dissatisfied) to 6 (very satisfied). The total score is calculated as the sum of all the 6 individual item scores. Obviously, the higher the final score, the higher the level of patient satisfaction with the diabetes treatment.<sup>22</sup> Two questions were linked to the incidence of hypoglycemic and hyperglycemic events and separately assessed. The scoring for both questions is from 0 (never experienced) to 6 (most of the time).<sup>22</sup>

#### Statistical analysis

The Data were analyzed using Excel 2019 (Microsoft Corporation, Seattle, WA, USA) and SPSS version 22 (SPSS Inc., Chicago, IL, USA). Besides the descriptive analysis, the paired “*t*-test differences were employed to identify the differences in effectiveness between the Gla-100 and Gla-300.” The *P*-value of <.05 was accepted as statistically significant.

#### Results

The clinical and demographic aspects of the study population are revealed in Table 1. In the study population, the mean age was  $23.4 \pm 7.4$  years; and 54.7% of the total sample were males. A higher percentage of the study population came under the age group of  $\geq 20$  (69.8%) years, 62 (72.1%) had been affected with diabetes for  $\leq 10$  years, and 52 (60.5%) showed BMI of  $\geq 25$  kg/m<sup>2</sup>.

The results prior to and post 12 weeks of the analysis of the AGP after the initiation of the Gla-300 treatment are given in Table 2. For the Gla-100 users, the HbA1c level shown was  $7.93 \pm 2.54$ , while for the Gla-300 users, after 12 weeks, a slight decline of  $7.76 \pm 2.53$  was noted. Likewise, at 12 weeks, after the patients were put on the Gla-300, the calculated total daily dose of insulin was observed to reduce. At 12 weeks after the patients were switched to the Gla-300, the improvement in the hypoglycemic episodes showed a significant difference ( $P = .048$ ). Compared to the use of Gla-100, the patients treated with Gla-300, displayed remarkable improvement in the AGP markers, that is, glucose variability, percentage of time spent

**Table 1.** Baseline demographic and clinical characteristics of the study population (Gla-100 treated patients).

VARIABLE(S)	FREQUENCY	%
Gender		
Male	47	54.7
Female	39	45.3
Age		
<20y	26	30.2
$\geq 20$ y	60	69.8
BMI		
<25kg/m <sup>2</sup>	34	39.5
$\geq 25$ kg/m <sup>2</sup>	52	60.5
Duration of type 1 diabetes		
$\leq 10$ y	62	72.1
>10y	24	27.9

within the target range of glucose levels (70-180 mg/dL) ( $P = .037$ ), percentage in below target (<70 mg/dL) ( $P = 0.027$ ), percentage of time spent <54 mg/dL ( $P = .043$ ) when they were switched to the Gla-300.

The comparative study of the T1D patients' reported treatment satisfaction with the use of Gla-300 versus Gla-100 is displayed in Table 3. In comparison to the use of Gla-100, patients after 12 weeks of Gla-300 treatment revealed a striking upswing in the current treatment satisfaction values ( $P = .047$ ). Patients given the Gla-300 treatment for 12 weeks likewise reported significant enhancement for the variables of current treatment satisfaction values, convenient finding treatment recently ( $P = .034$ ), and flexible finding treatment recently ( $P = .041$ ), recommend the current treatment ( $P = .042$ ) and satisfied to continue the current treatment ( $P = .035$ ) compared those on the Gla-100.

A comparison of Gla-300 versus Gla-100 in terms of hyperglycemia, hypoglycemia and total satisfaction is listed, as given in Figure 1. Patients receiving the Gla-300 treatment displayed a decrease in hypoglycemia (2.57 vs 2.13;  $P = .048$ ) and a significantly higher degree of total satisfaction (16.8 vs 21.4;  $P = .037$ ).

#### Discussion

Insulin glargine Gla-100 (HOE901), is recombinant human insulin, which after a single-dose subcutaneous injection, ensures a 24-hour supply of basal insulin.<sup>23</sup> From the extensive broad data collected from over 100 000 patients in clinical studies, randomized and controlled clinical trials, it is evident that its safety profile and efficiency are widely acknowledged; also, the results drawn include post-marketing surveillance

**Table 2.** Ambulatory glucose profile before (IGlar U100) and after the introduction of IGlar U300.

VARIABLE(S)	IGLAR U100	IGLAR U300	P VALUE
HbA1c % (Lab measured)	7.93 ± 2.54	7.76 ± 2.53	.642
Calculated total daily dose of insulin (IU/kg )	1.12 ± 0.19	1.01 ± 0.13	.534
Hypoglycemia (episodes/2 weeks)	6.0 ± 1.39	4 ± 1.06	.048
Mean FGM scanning frequency	7.73 ± 1.36	8.12 ± 2.14	.072
Percentage time sensor active (%)	83.8 ± 12.5	91.1 ± 14.65	.214
Average Glucose (mg/dL)	191 ± 21.4	187 ± 14.6	.083
Glucose Management Indicator % (GMI)	7.91 ± 2.21	7.75 ± 2.24	.076
Glucose variability %	42.9 ± 12.7	36.53 ± 10.7	.026
Percentage of time spent within the target range of glucose levels (70-180mg/dL) (%)	46.1 ± 10.7	49.38 ± 12.8	.037
Percentage in below target (<70mg/dL) (%)	5.58 ± 2.41	4.65 ± 1.23	.027
Percentage of time spent < 54 mg/dL (%)	1.42 ± 0.72	0.87 ± 0.32	.043
Percentage of time spent (181-250 mg/dL) (%)	42.4 ± 16.3	39.1 ± 13.2	.054
Percentage of time spent above 250 mg/dL (%)	18.5 ± 7.3	14.6 ± 6.5	.064

Glucose variability (GV) defined as percent coefficient of variation (% CV); target ≤36%.

**Table 3.** Comparisons of treatment satisfaction outcomes of IGlar U100 versus IGlar U300 in patients with type 1 diabetes.

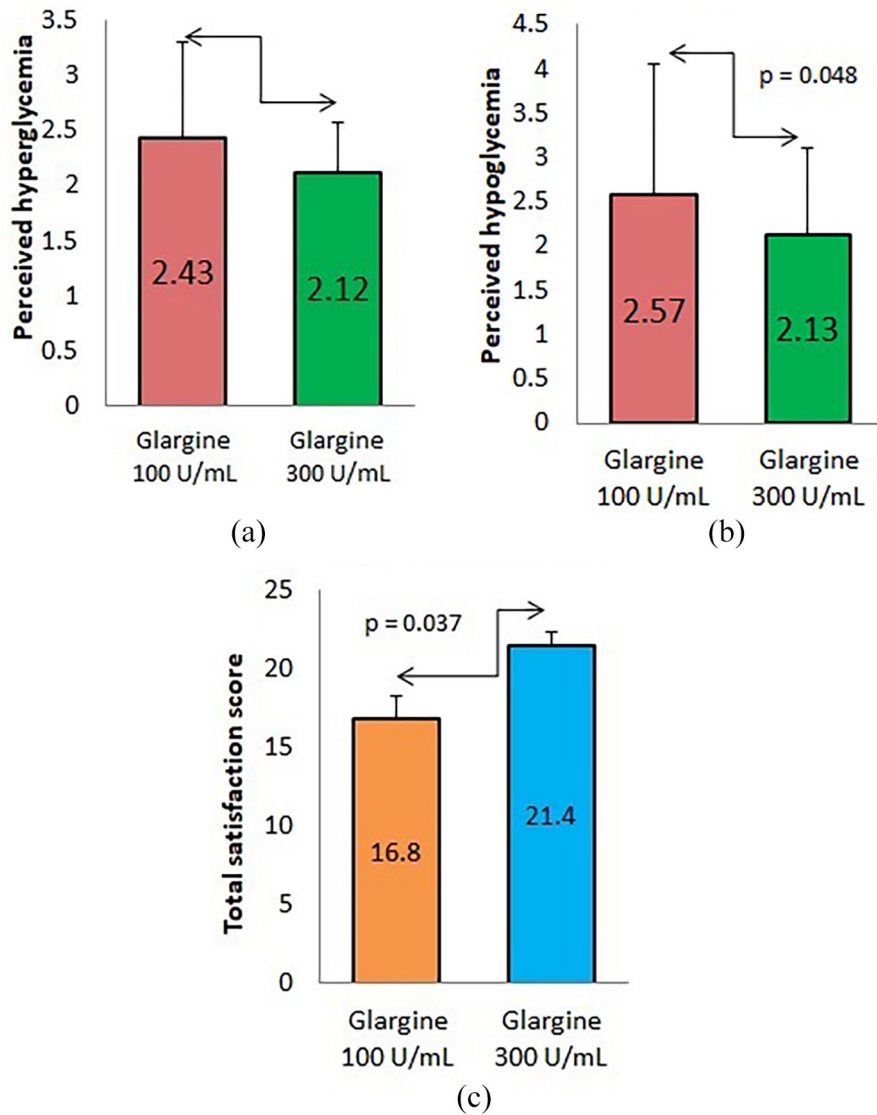
VARIABLE(S)	IGLAR U100 (MAXIMUM SCORE 6)	IGLAR U300 (MAXIMUM SCORE 6)	P VALUE
Satisfied with current treatment	3.24 ± 1.21	3.92 ± 1.21	.047
How convenient finding treatment recently	2.32 ± 1.26	2.61 ± 0.83	.034
How flexible finding treatment recently	3.23 ± 1.47	3.94 ± 1.34	.041
How satisfied with understanding diabetes	3.56 ± 1.28	3.81 ± 1.97	.064
Would you recommend the current treatment	3.12 ± 1.56	3.97 ± 1.34	.042
How satisfied to continue the current treatment	3.41 ± 1.56	4.12 ± 1.78	.035

Scoring in the range of 0 (very dissatisfied) to 6 (very satisfied). The higher score represent higher level of patient satisfaction with the diabetes treatment.

from the clinical experience of around 30 million patient-years. The HOE901-U300 is comparable in composition to the current Gla-100; however, it has been modified, using thrice the quantity of the active pharmaceutical ingredient (insulin glargine) and matching zinc content.<sup>24</sup> In this study, an analysis is done of the effectiveness and satisfaction of the T1D patients with concentrated insulin glargine and use of the FGM system.

In the current study, the T1D patients, post the initiation of Gla-300 revealed results for the 12 weeks ambulatory glucose profile that indicated a statistically negligible reduction in the HbA1c level (7.93 ± 2.54; 7.76 ± 2.53) compared to patients

on the Gla-100 treatment. Similarly, 12 weeks after the patients were placed on the Gla-300, the value of the calculated total daily dose of insulin dropped. However, concerning hypoglycemic episodes, a marked difference was observed at 12 weeks post switching these patients to the Gla-300. From prior studies, it was clearly evident that the change in the regimen of basal insulin from Gla-100 to Gla-300 caused the hypoglycemic episodes in patients with diabetes to sharply decrease.<sup>15,25,26</sup> Also, a study indicated that the Gla-300 provides almost similar glyce-mic control to that resulting from the Gla-100 treatment in East Asian patients; although they had a broad clinical spectrum of T2D, they showed consistently lowered hypoglycemia,



**Figure 1.** Comparisons of (a) hyperglycemia, (b) hypoglycemia and (c) total treatment satisfaction of Gla-100 versus Gla-300 in patients with type 1 diabetes.

at any part of day or night.<sup>27</sup> Further, from various studies done globally, reports of comparable glycemic control of Gla-300 versus Gla-100 is evident in several populations.<sup>28,29</sup> One study reported, that although the dose of Gla-300 was higher than that of the Gla-100, the glycemic control achieved by the patients was almost similar; however, lower hypoglycemia levels were noted.<sup>29</sup> While the Gla-300 and Gla-300 are similar in composition, the principal focus of the education given to the patients was that, in the change-over phase, an initial 10% reduction will be noticeable in the long-acting insulin, with upward titration, to achieve the levels of fasting blood glucose within 5 to 7 mmol/L. It is this which induces a reduction in the risk of hypoglycemia during the transition, as identified in the current study.<sup>15</sup> In comparison to the Gla-100, the AGP markers of this present study, that is, glucose variability, % of time used up within the target range of glucose levels

(70-180 mg/dL), percentage in below target (< 70 mg/dL), percentage of time spent <54 mg/dL demonstrated significant improvements in the patients receiving the Gla-300 treatment; hypoglycemia also was under control.

Although many attempts were made to individualize diabetes care and identify effective patient communication methods, several patients reported experiences with clinical encounters that left them disappointed and dissatisfied. Such experiences/encounters included aspects that could threaten the perception of their own selves and their identity; however, the aspects of satisfying encounters are the ones that denote good patient-centered care.<sup>30</sup> In the current study, the comparison between patients on Gla-100 treatment with those on the Gla-300 revealed improvement in response to current treatment satisfaction. Further, patients on Gla-300 treatment for 12 weeks reported marked improvement in the variables of treatment

satisfaction, convenient finding treatment recently, and flexible finding treatment recently, recommend the current treatment and satisfied to continue the current treatment when compared to their responses with the Gla-100 treatment.

The results from a recent study on among the T2D patients recorded a reduction in the HbA1c in response to the commencement of the Gla-300 treatment (89.7% of participants) and a decline in the frequency of hypoglycemic events (35.6% of participants). The study also reported remarkable improvements in the categories of treatment satisfaction and perceived hyperglycemia/hypoglycemia.<sup>31</sup> Yet another study stated that when the patients with diabetes were switched on to Gla-300, with other basal insulin, enhancement of the glycemic control was observed and the risk of hypoglycemia was reduced, with no accompanying weight gain, and patient satisfaction with treatment escalated.<sup>32</sup> Further, in a recent study conducted on Japanese individuals having T2D, less hypoglycemia was experienced when on the Gla-300 treatment than when taking the Gla-100 treatment, although no changes were evident in the glycemic control.<sup>25</sup> One more study done on adult Japanese T1D subjects, using basal plus mealtime insulin, showed less hypoglycemia detected in those on the Gla-300 treatment than when on the Gla-100 treatment, particularly in the night; however, no changes were noted in the glycemic control.<sup>33</sup> The present study revealed statistically negligible improvements in the variables of HbA1c and glucose level, and less hyperglycemia. But it must be understood here that this study was done only for a 12-week period, and the improvements could be much more significant with the Gla-300 treatment over a longer duration of time.

A few limitations were identified in this study, including the small sample size, short study duration, limited demographic variables analyzed, and performance of the study at a single center. These can be avoided by conducting the research on a larger scale. However, in the face of these limitations, the present study provides valuable data on the responses of the patients with T1D through patient self-reported satisfaction and clinical efficacy values for both the Gla-300 and Gla-100 treatments. In conclusion, compared to the patients on Gla-100, patients treated with Gla-300 exhibited remarkable improvements in the AGP markers and degree of treatment satisfaction. However, some variations appear in the results of the trials from different studies conducted across the globe. Therefore, more data collected over longer time durations are necessary to authenticate the efficacy of the Gla-300 in patients with T1D compared to that of the Gla-100.

### Author contribution(s)

All authors contributed equally to this work.

### Data Sharing Statement

No data sharing as this manuscript and the data were not published elsewhere.

### Ethical Approval

The study protocol was approved by the Research and Ethics committee of Prince Sultan Military Medical City, Riyadh, Saudi Arabia (Approval #: 1196)

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