

Clinical Experience with BIAsp 30: Results from the Philippine Cohort of the Global A₁chieve Study

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Abstract

Objective: To evaluate the safety, effectiveness and health-related quality of life (HRQoL) parameters of A₁chieve study participants in the Philippine cohort, who were treated with BIAsp 30.

Methodology: A₁chieve is a non-interventional, six-month, observational study of 66,726 people with type 2 diabetes mellitus (T2DM), including both insulin users and non-insulin users, started on insulin detemir, insulin aspart, or BIAsp 30 in 28 countries across four continents. The present study evaluates the safety, effectiveness and HRQoL in 1,252 subjects from the Philippine cohort of the A₁chieve study who were treated with BIAsp 30.

Results: At baseline, the mean age, duration of diabetes and mean BMI were found to be 55.5 ± 11.7 years, 7.2 ± 5.6 years and 25.4 ± 5.3 kg/m², respectively. Seventy-eight percent (78%) of subjects were insulin naïve and 22% were prior insulin users.

At baseline, glycemic control was poor (HbA_{1c} = 9.9%) in the entire cohort. Overall there was a 2.7% reduction in mean HbA_{1c} and 44.2% subjects achieved the HbA_{1c} target of <7.0%, after 24 weeks of therapy with BIAsp 30. There were significant reductions in total cholesterol, LDL-cholesterol, triglycerides and systolic blood pressure after 24 weeks of therapy with BIAsp 30. There was no increase in the incidence of hypoglycemia among insulin-naïve subjects, while there was a marked reduction in hypoglycemia (4.93 to 2.53 events/person-year) among prior insulin users at 24 weeks.

Conclusion: BIAsp 30 is safe and efficacious for initiating and intensifying insulin therapy for Filipino T2DM patients.

Keywords: A₁chieve, HbA_{1c}, glucose control, type 2 diabetes mellitus, BIAsp 30, Philippines.

Introduction

Chronic hyperglycemia often precedes diagnosis of type 2 diabetes mellitus (T2DM), leading to extensive vascular damage and early development of clinical complications.¹ In addition, absence of good glycemic control while on therapy, and the resulting metabolic imbalances further deteriorate the clinical condition of these patients.^{2,3} The Philippines has an estimated diabetes prevalence of 4.6%, affecting around 3.9 million individuals. Peripheral arterial disease, a macrovascular complication, is also widespread among the Filipinos.⁴ Diabetes mellitus (DM) caused 8,819 deaths in 1998 and was ranked the eighth leading cause of

mortality in the Philippines.⁵ In a developing country like the Philippines, suboptimal management of T2DM and subsequent complications impose a significant burden on the existing healthcare resources.

β-cell function in T2DM declines progressively and eventually fail, thereby, requiring most patients to receive insulin therapy.⁶ It has been reported that about 80% of T2DM require some form of insulin therapy within nine years of diagnosis.^{4,7} The joint consensus of the European Association for the Study of Diabetes and the American Diabetes Association (EASD-ADA) recommends that HbA_{1c} above 7.0% warrants an action to initiate or change therapy to achieve target HbA_{1c}.⁶ Thus, early initiation of insulin to reach glycemic targets without compromising safety should be considered as an alternative option.

An increasing body of evidence also suggests that early intensive glycemic control reduces long-term vascular outcomes and may potentially prolong β-cell lifespan and function.⁶ In view of the progressive nature of the disease, continuous monitoring of glycaemia and, when necessary, intensification of existing treatment is imperative for achieving HbA_{1c} control. One option is to intensify to a modern premixed insulin analogue, without increasing the number of injections as in the basal-bolus regimen.⁷

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The premixed insulin analogue, biphasic insulin aspart 30 (BIAsp 30), consists of a rapid-acting soluble insulin (30%) which effectively controls post-prandial glucose (PPG) and a long-acting protaminated insulin (70%) which controls basal glucose.⁸ BIAsp 30 has a low incidence of hypoglycemia and therefore allows for convenient and flexible mealtime dosing.^{8,9} Although many randomised controlled trials (RCTs) have shown the beneficial effects of BIAsp 30, this needs to be confirmed in routine clinical practice among different patient populations, varying stages of disease, co-morbidities, and multiple medications.⁹ Observational studies can complement data from RCTs by providing insight on how a well-studied treatment regimen perform or vary in more clinically representative patient populations.^{10,11} The A₁chieve study is one of the largest observational studies on insulin therapy to date. It is designed to assess the real-life safety and effectiveness of insulin analogues in large diabetic populations (more than 65,000 insulin-naïve patients and prior insulin users from 28 countries). A₁chieve also evaluated the effect of insulin analogues on health-related quality of life (HRQoL) scores in these patients.¹²

The safety and efficacy of BIAsp 30 in the Philippine population is not well established with limited published data exploring its use in routine clinical practice. Therefore, the objective of the present analysis was to evaluate the safety, effectiveness, and HRQoL parameters of A₁chieve study participants in the Philippine cohort who were treated with BIAsp 30.

Materials and Methods

Overview of the A₁chieve study

The A₁chieve study was a 24-week, multinational, prospective, multi-center, non-randomized, observational study of people with T2DM who were started on basal insulin detemir (Levemir®, Novo Nordisk, Denmark), bolus insulin aspart (NovoRapid®, Novo Nordisk), and biphasic insulin aspart 30 - BIAsp 30 (NovoMix® 30, Novo Nordisk), alone or in combination with oral antidiabetic drugs (OADs), to evaluate their safety and effectiveness in routine clinical use.^{12,13} The study was carried out in 28 countries across Asia, Africa, Latin America and Europe. In the Philippines, this study was carried out by specialists (endocrinologist, physicians with special interest in diabetes (internists and general practitioners) at clinics and hospitals. A total of 252 investigators from 120 investigative sites participated in this study. The list of investigators and sites is in Appendix 1.

Study eligibility

The study was conducted in accordance with the principles of Declaration of Helsinki. Ethics committee

approval was obtained before study commencement, and all participants signed an informed consent prior to enrolment in the study. Inclusion and exclusion criteria were minimal in order to reflect real-life clinical practice. Patients with T2DM on any current and prior medications other than the insulin analogue being evaluated were included. Patients who had been started on the study insulin (Levemir®, NovoRapid® or NovoMix® 30) within four weeks prior to the study start were also included. Patients with hypersensitivity to the study drug or excipients, women who were pregnant, breast-feeding or with planned pregnancy within six months of the study were excluded. Participants were free to withdraw at will at any time during the study and the data collected were used for analysis until the part when consent was withdrawn.

Study objectives and assessment

The primary objective was to evaluate safety and effectiveness of the insulin analogues. The incidence of serious adverse drug reactions (SADRs), including major hypoglycemic events was recorded from baseline to final visit. Minor hypoglycemic episodes and nocturnal hypoglycemia were also assessed. The rate of hypoglycemia was measured in events per patient years and was calculated as number of hypoglycemic events happened during four weeks prior to each visit/number of patients *52/4. Major hypoglycemic events were defined as events with severe central nervous system symptoms, consistent with hypoglycemia, requiring the assistance of another person and accompanied by plasma glucose <3.1 mmol/L or 56 mg/dL, with reversal of symptoms after food intake, intravenous glucose, or glucagon administration. Minor hypoglycemia was any event, with or without symptoms of hypoglycemia, with a plasma glucose reading below 3.1 mmol/L or 56 mg/dL that the participant was able to self-treat. Nocturnal hypoglycemia was defined as a symptomatic event consistent with hypoglycemia that occurred during sleep between bedtime after the evening insulin injection and before getting up in the morning. Effectiveness was determined from changes in HbA_{1c}, fasting plasma glucose (FPG), PPG and body weight between baseline, interim and final visits. Changes in systolic blood pressure (SBP) and lipid profile from baseline to final visit were also assessed. In addition, the effect of insulin analogue therapies on HRQoL of the participants was also evaluated.

The various insulin analogues prescribed by the physician during routine clinical practice were commercially available and funded according to local practice. Insulin analogues were administered by the patients themselves as per routine clinical practice. There were no defined study-related procedures and no medications or blood glucose monitoring equipment/

test strips were provided as part of study participation. The clinical and biochemical measurements made by the treating physician were those required in routine clinical practice. Data points were captured at baseline, 12 weeks and 24 weeks. The pre-study period was defined as the period four weeks prior to the baseline visit. Data was collected from the physicians' clinical notes, participants' recall and self-monitoring diary/meter at each visit and transferred to a standard case report form (CRF). The clinical and biochemical measurements made by the treating physician were those required in routine clinical practice, including weight, blood pressure, plasma glucose levels, HbA_{1c}, etc.

HRQoL was measured using the EQ-5D questionnaire and EQ visual analogue scale (EQ VAS) at baseline and 24 weeks. EQ VAS is a rating for an individual's current state, measured by a standard vertical 20 cm scale ranging from 0 (worst imaginable health) to 100 (best imaginable health). The EQ-5D questionnaire consisted of five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) and scored as 1, 2 or 3 depending on the level of severity. These different dimensions were converted to a single utility value, anchored by '1.00' representing "full health" and '0.00' representing the state "dead".

The participants were recruited between January 2009 and June 2010 and a total of 66,726 people were included in the study. In the Philippines, the patients were recruited from private, public and university clinics or hospitals referred by endocrinologists or internists or physicians treating diabetes mellitus. In this paper, we present the results of analysis from 1,252 Filipino participants treated with biphasic insulin aspart 30-BIAsp 30 (NovoMix 30, Novo Nordisk, Denmark).

Statistical methods

The sample size calculation for the entire global cohort was based on the number of patients (60,000) exposed for six months required to confirm a frequency of ≥ 15 events/100,000 patient-years of any one SADR, including major hypoglycemic events, at the 95% confidence level. No specific sample size calculation was conducted for each country.

Statistical analyses were performed for the entire cohort and for the insulin-naïve and prior insulin user cohorts. Descriptive statistics were used to summarize continuous variables and frequency tables (number and percentage) were used for discrete variables. All statistical analyses were two-sided, with 5.0% significance level, unless otherwise stated. For the change in hypoglycemia from baseline, the percentage of patients reporting at least one event was analyzed using McNemar's test. The change from baseline in HbA_{1c}, FPG, PPG, SBP, body weight, blood lipids and HRQoL was analyzed using a paired t-test using

baseline and end-of-study values. Data analyses were performed by Novo Nordisk using SAS (Version 9.1.3).

Results

Statistical methods

A total of 1,252 patients were included in the subgroup analysis, with 978 patients (78%) being insulin-naïve and 274 patients (22%) on prior insulin therapy (mean age of total cohort was 55.5 ± 11.7 years). Females comprised 55.6% of the entire cohort. The duration of DM in the insulin-naïve group was 6.6 ± 5.1 years and 9.6 ± 6.6 years among prior insulin users. The baseline HbA_{1c} level was $10.0 \pm 2.2\%$ in insulin-naïve patients and $9.5 \pm 2.3\%$ in prior insulin users, indicating poor glycemic control (Table I). There were withdrawal of 188 patients in the entire cohort during the study period – two (0.2%) patients due to adverse drug reaction, 117 (9.3%) due to lost contact and 69 (5.5%) patients due to other reasons. As this study was non-interventional in nature, we did not obtain the educational status and religion of the participated patients.

Table I: Baseline characteristics of the Philippine cohort, N=1,252

	Entire cohort	Insulin-naïve	Prior insulin users
N (%)	1252 (100)	978 (78.1)	274 (21.9)
Sex, M/F † (%)	555 (44.4) / 696 (55.6)	448 (45.9) / 529 (54.1)	107 (39.1) / 167 (60.9)
Age (yrs)	55.5 (11.7)	54.9 (11.2)	57.6 (13.0)
Duration of diabetes (yrs)	7.2 (5.6)	6.6 (5.1)	9.6 (6.6)
Body weight (kgs)	65.1 (14.7)	65.3 (15.1)	64.3 (13.1)
BMI § (kg/m ²)	25.4 (5.3)	25.4 (5.4)	25.3 (4.9)
HbA _{1c} (%)	9.9 (2.2)	10.0 (2.2)	9.5 (2.3)

†- male/female; §- body mass index; Data expressed in Mean (Standard deviation) for all variables except N and Sex

Metformin was the most commonly prescribed OAD at pre-study (81.4%), at baseline (77.0%), and at 24 weeks (77.1%) of the study. Sulfonylureas were the second most commonly prescribed OAD (61.4%) at the pre-study period, dropping to 19.2% at baseline and further reduced to 17.6% at study end. DPP-4 inhibitor use increased from 10.9% (pre-study period) to 24.4% at study end. Thiazolidinediones were prescribed to 19.1% of the patients pre-study and was reduced to 13.4% at study end.

Safety and effectiveness

Glycemic control and insulin dose

Treatment with BIAsp 30 for 24 weeks led to statistically significant improvement in the magnitude of glycemic control ($p < 0.001$). In the entire cohort, the mean reduction for HbA_{1c} was 2.7% and for FPG and PPG were 5.4mmol/L and 6.5mmol/L respectively.

In insulin naïve cohort, mean HbA_{1c} reduction was 2.8%; in prior insulin users, it was 2.4%. About 44% of the entire cohort achieved target HbA_{1c} level of <7%, after 24 weeks of BIAsp 30 therapy. Target HbA_{1c} <7% was achieved by 44.7% of insulin-naïve and 42.4% of prior insulin users following BIAsp 30 treatment (Table II). An analysis further into the treatment naïve patients (no insulin, no OAD given to patient) revealed a reduction of 3.6% in HbA_{1c} from baseline (10.7 ± 2.6). FPG and PPG also showed similar reductions for the entire cohort, the insulin-naïve patients and prior insulin users. HbA_{1c} was evaluated or available for only 630 of the 1,252 patients originally enrolled in the study.

Table II: Efficacy of BIAsp 30 in controlling hyperglycemia

		Entire cohort	Insulin naïve	Prior insulin
HbA _{1c} (%)	N	630	492	138
	Baseline	9.9 (2.2)	10.0 (2.2)	9.5 (2.3)
	24 weeks	7.2 (1.0)	7.2 (1.0)	7.2 (1.0)
	Change	-2.7 (2.1)*	-2.8 (2.0)*	-2.4 (2.1)*
	Proportion (%) with HbA _{1c} <7%			
	Baseline	5.2	4.6	7.1
	24 weeks	44.2	44.7	42.4
Fasting plasma glucose (mmol/l)	N	774	596	178
	Baseline	12.2 (4.1)	12.6 (4.0)	10.9 (3.8)
	24 weeks	6.8 (1.9)	6.9 (2.0)	6.5 (1.6)
	Change	-5.4 (4.0)*	-5.7 (4.0)*	-4.4 (3.9)*
	Post prandial plasma glucose (mmol/l)	N	116	83
Baseline		14.3 (5.4)	14.4 (5.4)	14.1 (5.6)
24 weeks		7.8 (1.7)	7.8 (1.7)	7.8 (1.7)
Change,p		-6.5 (5.3)*	-6.6 (5.2)*	-6.3 (5.8)*

*p<0.001 compared to baseline; Data expressed in Mean (Standard deviation) for all variables unless mentioned otherwise

During the study, the dose of insulin in insulin-naïve patients was up-titrated from 32.9 ± 13.5 (0.52 U/Kg) at baseline to 40.5 ± 15.3 U/day (0.64 U/Kg) at 24 weeks. In prior insulin users, the pre-study insulin dose

was 37.6 ± 18.1 U/day, adjusted to 40.7 ± 17.1 U/day at baseline and increased to 47.4 ± 19.6 U/day at study end.

Hypoglycemia

At baseline, overall 149 hypoglycemic events (1.55 events/person-year) were observed in 60 (4.8%) individuals in the entire cohort. Treatment with BIAsp 30 led to a reduction in the rate of overall hypoglycemia in the entire cohort, with 93 (1.14 events/person-year) events occurring in 41 (3.9%) patients. In prior insulin users, there was a remarkable reduction in overall hypoglycemic events from 4.93 events/person-year at baseline to 2.53 events/person year at 24 weeks. Although these reductions were clinically important, they did not reach statistical significance. There was a marginal non-statistically significant increase in the rate of hypoglycemia in insulin-naïve patients from 0.60 events/person year to 0.75 events/person-year. Twelve major hypoglycemic episodes (0.12 events/person-year) in five patients were reported from the entire cohort at baseline. The incidence of major hypoglycemia at baseline was higher in prior insulin users (0.52 events/person-year) compared to insulin-naïve patients (0.01 events/person-year). After 24 weeks of BIAsp 30 therapy, there was reduction in major hypoglycemic episodes with no report of such an event occurring in any participant, including the treatment-naïve patients. Minor hypoglycemic events in the entire cohort decreased from 1.42 events/person year to 1.14 events/person year. Nocturnal hypoglycemia was also reduced mainly in prior insulin users from 1.95 events/person-year to 0.79 events/person-year (Table III).

Body weight, blood lipids and blood pressure

Following treatment with BIAsp 30 for 24 weeks, there was no significant change in body weight in either insulin-naïve patients or prior-insulin users (Table II). In the entire cohort, total cholesterol level decreased significantly from 5.7 ± 1.5 mmol/L to 4.8 ± 0.9 mmol/L (p<0.001) at study end. There was a significant reduction in level of LDL cholesterol from baseline value of 3.7 ± 1.3 mmol/L to 2.9 ± 0.9 mmol/L (p< 0.001). Serum triglyceride level also decreased significantly from 2.0 ± 1.1 mmol/L at baseline to 1.6 ± 1.1 mmol/L (p< 0.001). Statistically significant increase in the HDL level was observed in prior insulin users, from 1.2 ± 0.3 mmol/L at baseline to 1.4 ± 0.4 mmol/L at 24 weeks (p=0.014). However, no statistically significant change in the HDL level was observed in the insulin-naïve patients. A reduction in SBP from 129.3 ± 19.3 mmHg at baseline to 123.0 ± 12.9 mmHg at 24 weeks (p<0.001) was observed in the entire cohort. The reductions in SBP following BIAsp 30 therapy were similar in insulin-naïve patients and prior insulin users.

Table III: Hypoglycemia and effect on body weight

(Percent with event/event per person-year)		Entire cohort	Insulin-naïve	Prior insulin
N		(Baseline, 1252/24-weeks, 1064)	(Baseline, 978/24-weeks, 833)	(Baseline, 274/24-weeks, 231)
Overall Hypoglycemia ‡	Baseline	4.8 / 1.55	2.2 / 0.60	13.9 / 4.93
	24 weeks	3.9 / 1.14	2.4 / 0.75	9.1 / 2.53
	p-value	0.1385	1	0.0374
Minor Hypoglycemia ‡	Baseline	4.8 / 1.42	2.2 / 0.58	13.9 / 4.41
	24 weeks	3.9 / 1.14	2.4 / 0.75	9.1 / 2.53
	p-value	0.1385	1	0.0374
Major Hypoglycemia ‡	Baseline	0.4 / 0.12	0.1 / 0.01	1.5 / 0.52
	24 weeks	0.00 / 0.000	0.00 / 0.000	0.00 / 0.000
	p-value	0.0455	0.3173	0.0833
Nocturnal Hypoglycemia ‡	Baseline	2.2 / 0.56	0.6 / 0.17	7.7 / 1.95
	24 weeks	1.9 / 0.37	1.2 / 0.25	4.3 / 0.79
	p-value	0.3173	0.3173	0.0253
Body weight (kg)	N	918	717	201
	Baseline	64.5 (13.8)	64.9 (14.1)	63.0 (12.5)
	24 weeks	64.8 (13.3)	65.2 (13.5)	63.6 (12.5)
	Change	0.3 (4.5)*	0.2 (4.4)	0.6 (4.7)

‡- Patients experiencing at least one episode of hypoglycemia; * p<0.05 compared to baseline; Body weight is expressed in Mean (Standard deviation)

Health-related quality of life (HRQoL)

There was marked improvement in the quality of life measures of the participants following BIAsp 30 therapy. At baseline, the EQ VAS scores were similar for both insulin-naïve patients and prior insulin users. Significant improvement was noted following BIAsp 30 therapy with an increase of 13.8 points in insulin-naïve patients [68.4 at baseline (p<0.001)] and 6.3 points in prior insulin users (70.6 at baseline (p<0.001)). Across all the summary dimensions of EQ-5D (scale 0-1), significant improvements were observed. Prior insulin users improved by 0.110 points (0.764 at baseline (p<0.001) while there was an increase of 0.139 points [0.782 at baseline (p<0.001)] in insulin-naïve patients.

Discussion

The present subgroup analysis assessed the safety, effectiveness, and HRQoL parameters in A₁chieve study participants from the Philippines treated with BIAsp 30 for six months. There were significant reductions in

HbA_{1c} by 2.8% in insulin-naïve patients and 2.4% in prior insulin users. These were consistent with the results observed in the global analysis of the A₁chieve study (2.2% in insulin-naïve patients; 1.8% in prior insulin users).¹³ Although there were significant reductions in FPG and PPG in insulin-naïve and prior insulin users, the evaluation was based on a very small number of patients (FPG - 774 and PPG - 116) and therefore, should be carefully interpreted. The decrease in HbA_{1c} levels was similar to the results of the PRESENT and the ACTION studies. In the subpopulation analysis of the PRESENT study, patients with uncontrolled (HbA_{1c} ≥ 7.0%) on previous treatment (human insulin ± OAD or OAD only) reported significant reduction in HbA_{1c} level (2.2% in insulin-naïve patients and 1.60% in prior insulin users) after a six-month treatment with BIAsp 30.⁶ Similarly, the patients in the ACTION study decreased HbA_{1c} level by 1.5% when BIAsp 30 was added to their existing regimen of metformin and pioglitazone.¹⁴

Bebakar et al, (2008), studied the effect of

adding BIAsp 30 to existing OADs vs. optimizing OADs in Western Pacific T2DM patients. Addition of BIAsp 30 once or twice daily for 26 weeks led to a 1.24% and 1.34% reduction in HbA_{1c} respectively, compared to a 0.67% reduction with OADs only.¹⁵ Reduction in HbA_{1c} has been shown to correlate well with improved glycemic control and subsequent reductions in diabetic complications.^{12,16} In an earlier multi-centric, multi-country survey in the secondary and tertiary health care setting, nearly 60% of Philippine participants found to have HbA_{1c} levels of >8%.¹⁷ In the entire cohort of Filipino patients of the A₁chieve study, an overall reduction of 2.7% in HbA_{1c} led to a 44.2% achievement of target HbA_{1c} <7.0%. Importantly, 42.4% of prior insulin users reached target HbA_{1c} <7.0%, suggesting the benefit of switching to BIAsp 30 from other insulin therapies. The present analysis indicates that clinically significant glycemic control would be achievable with BIAsp 30 in Filipino patients within a six-month period, which would be at par with other diabetic populations across the world receiving this agent. There was a statistically marginal, but clinically irrelevant increase in body weight in the entire cohort.

Intensive insulin therapy while improving glycemic control is associated with increased risk of hypoglycemia, leading to significant morbidity and mortality, particularly in elderly and frail T2DM patients.¹⁸ The UK Hypoglycemia Study Group which examined the frequency of hypoglycemia prospectively for nine to 12 months in T2DM patients who were being treated in secondary care reported the prevalence of severe hypoglycemia to be 25% in patients who were using insulin for more than five years.^{18,19} In the present analysis of the Filipino cohort of A₁chieve study, no major hypoglycemic event was observed even among prior insulin users. In addition, the incidence of minor and nocturnal hypoglycemic events also decreased. However, while the reduction in hypoglycemic events were clinically significant, they did not achieve statistical significance. This is comparable with the global analysis of A₁chieve study data where the rate of major hypoglycemic episodes in prior insulin users decreased from 0.52 events/person-year at baseline to 0.02 events/person-year.¹³ Our observations regarding safety of BIAsp 30 are consistent with that of other studies. A subgroup analysis of the PRESENT study reported a statistically significant reduction of daytime hypoglycemia from 3.9 events/person-year to 1.6 events/person-year following the switch from human basal insulin analogues to BIAsp 30. Similarly, nocturnal hypoglycemia also decreased from two events/person-year to 0.57 events/person-year.⁷ Low rates of hypoglycemia with BIAsp 30 therapy have been reported in T2DM from the Western Pacific region by Bebakar et al, (2008)

and Yoshioka et al, (2009) in Japanese patients.²⁰ However, this is in contrast with the 1-2-3 Study, an RCT carried out Western T2DM, which reported higher minor hypoglycemia rates of 15.4, 22.4 and 12.0 events/patient year with once-daily, twice-daily, and thrice-daily BIAsp 30 respectively.²¹ The safety data of A₁chieve reassures the use of BIAsp 30 in clinical practice. Similar sub-group analysis on BIAsp 30 was published for Pakistani T2DM patients which showed similar effectiveness and safety profile of BIAsp 30.²²

The EQ-5D instrument used in the study has been previously validated for use in diabetic patients.²³ The statistically significant improvement in EQ VAS score and EQ-5D scores at six months reflected the positive overall experience with BIAsp 30 therapy. The improvement in the EQ VAS score and EQ-5D score paralleled the improvement in glycemic control, and HRQoL scores in participants of the global A₁chieve cohort.²⁴ Our observations also echo the findings of the IMPROVE study which reported significantly higher satisfaction scores in patients with T2DM following the use of BIAsp30.²⁵

Even though the large body of data generated by this study offers the opportunity to explore other important disease and therapy-related questions, there were limitations inherent in the study design. In particular, concomitant medication and dietary intake were not controlled, and the latter remains largely unmeasurable. The study was non-randomized and lacked a standardized treatment protocol and a control arm, with most safety and effectiveness parameters based on participant recall, diverse diaries or self-reported information. The circumstances under which participants came under the care of the investigators are not known, and these could have been a trigger for starting modern insulin therapy while at the same time improving other aspects of diabetes care. Additionally, the findings could have been influenced by a study effect as, although entry was retrospective, further data collection was prospective following informed consent. Further, due to the non-interventional nature of the study, there are a lot of missing values in effectiveness variables like HbA_{1c}, FPG and PPG.

Conclusions

The present subset analysis of the A₁chieve study showed that administration of BIAsp 30 among Filipino patients (both insulin-naïve and prior insulin users) improved glycemic control without concomitant risk of hypoglycemia or weight gain. BIAsp 30 is safe and efficacious for initiating and intensifying insulin therapy for T2DM patients in Philippines.

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APPENDIX 1
List of Investigators

Centre No.	Investigator	
0011	Quintin Cocoon Mariano Marcos Memorial Hospital and Medical Center Barangay 6 San Julian, Batac, Ilocos Norte, Philippines 2606	0068
0012	Rose Marie Dominguez Notre Dame De Chartres Hospital 25 General Luna Road, Baguio City Benguet, Philippines 2600	0070
0013	Lani Flor 4 McKinley Street, Brgy. 10 Laogay City, Ilocos Norte Philippines 2900	0071
0015	Elizabeth Gonzales Bethany Hospital #2210 North Wing Annex Bldg. Real Street Tacloban City, Leyte Philippines 6500	0072
0016	Werner Paul Irmacher Saint Louis University Hospital Assumption Road, Baguio City 2600 Benguet, Philippines 2600	0082
0017	Raymond Ordoño Notre Dame De Chartres Hospital Room 218 - 25 General Luna Road, Baguio City, Benguet, Philippines 2600	0084
0018	Liza Marie Paz-Tan Ground Floor Savellano Bldg. General Luna St., Laogay City Ilocos Norte, Philippines 2900	0085
0019	Franco Pizamo Notre Dame De Chartres Hospital 25 General Luna Road, Baguio City Benguet, Philippines 2600	0092
0020	Melaine Croce-Valdes Vallejos Bldg., Laogay City Ilocos Norte, Philippines 2900	0093
0021	Julieta De Guzman Dagupan Doctors Villafor Memorial Hospital Rm 2010 Medical Arts Tower Mayomboc District, Dagupan City Pangasinan, Philippines 2400	0094
0023	Cleczel Montarito Monsanto Clinic 2nd Floor EF Square Bldg., Urdaneta, Pangasinan, Philippines 2428	0096
0024	Cristina Pascual Cristina Pascual Zamorra Street, San Roque Tarlac City, Philippines 2300	0098
0025	Lynette Bellocera Orthomed Clinic Rizal Street, Mangaldan Pangasinan, Philippines 2432	0099
0026	Jovillo Rivera Sabero Naminos Pangasinan Philippines 2404	1000
0028	Toledo Ronaldo Sector Sto. Niño Hospital P. Burgos St., Cerning, Tarlac Philippines 2306	0091
0029	Mary Rose Tongpal Ramos General Hospital Rm 202 RAMDOCS 769 P. Hlado Street, Ligasan Tarlac City, Philippines 2300	0101
0030	Elmer Tumacader Specialist Group Hospital & Trauma Center Tigayao District, Dagupan City Philippines 2400	0106
0031	Mary Ann Balongpabal Nazareno Hospital Brgy. Ibayo, Maricao, Bulacan Philippines 3019	0107
0037	Tiniedad Doria Cruz Sta. Clara de Montefalco Medical Center Km. 20 North, Service Road, Meycauayan City, Bulacan Philippines 3020	0109
0111	John Nazareno Nazareno Family Clinic Poblacion, Hagonoy, Bulacan Philippines 3002	0078
0112	Gorgonia Salazar Salazar Clinic M de Leon cor R Mercado Streets, Poblacion, Sta Maria, Bulacan Philippines 3022	0121
0113	Leticia May Uñe Meycauayan Doctors Hospital LS Pavilion, Banga, Meycauayan, Bulacan, Philippines 3020	0122
0114	Criselda Vileral Real CMV Clinic Paraiso, Sta. Maria, Bulacan Philippines 3020	0123
0046	Ariel Raya Bataan Doctors Hospital Cuaderno St., Balanga City, Bataan Philippines 2100	0124
0047	Maurice Sanosa St. Luke's Medical Center Rm 807 CHCC Bldg. 279 E. Rodriguez St. Boulevard Quezon City, Philippines 1112	0125
0049	Agnes Soriano St. Agnes Polymedic #15 20th St., West Bago-Bajac, Olongapo City, Philippines 2200	0126
0051	Daniel Baldeamor Center for Diabetes Care Sotoperña Drive, San Jose City Nueva Ecija, Philippines 3121	0127
0052	Edwin Borja 2nd Floor Centro Bldg., Tiro Street San Vicente, Gapan City Nueva Ecija, Philippines 3105	0128
0054	Rashy Mejia Premiere Medical Center Marikina Highway, Daan Sanle Cabanatuan City, Nueva Ecija Philippines 3100	0129
0055	Reilo Ignacio CT Ignacio Pharmacy Sacred Heart of Jesus, San Jose Nueva Ecija, Philippines 3121	0130
0057	Manuel Martinez Maharlika Highway, Matias District Talavera, Nueva Ecija Philippines 3114	0131
0060	Reynaldo Yang Premiere Medical Center Marikina Highway, Daan Sanle Cabanatuan City, Nueva Ecija Philippines 3100	0133
0061	Mercedita Amansec Mother of Calcutta Medical Center Barangay Malmpis, San Fernando, Pampanga, Philippines 2000	0138
0062	Carlo Rodrigo Carreron Angelic University Foundation Medical Center (AUFMC) Rm 207 Medical Tower Bldg. MacArthur Highway Barangay Salapangan Angeles City Philippines 2009	0141
0063	Jocelyn Cordero Angelic University Foundation Medical Center (AUFMC) MacArthur Highway Barangay Salapangan Angeles City Philippines 2009	0142
0064	Wilner Reinel De Guzman W. De Guzman Medical Clinic Angeles City, Pampanga Philippines 2009	0143
0065	Fernando Guerrero Garcia Medical Center Rizal Street, Angeles City Pampanga, Philippines 2009	0147
0066	John Ki Angelic University Foundation Medical Center (AUFMC) MacArthur Highway Barangay Salapangan Angeles City Philippines 2009	0148
0067	Rommel Malonzo 1232 Miranda Street Angeles City, Pampanga Philippines 2009	0149
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0152	Don Bosco, Paranaque City Philippines 1711 Cardinal Hipolito Olivarez General Hospital Dr. A. Santos Ave. (Sucat) Paranaque City, Metro Manila, Philippines 1700	0215	Rm 203 Medical Arts Bldg. E. Rodriguez Sr. Avenue Quezon City, Philippines 1102 Gabriel Jesus St. Luke's Medical Center 201 E. Rodriguez Sr. Avenue Quezon City, Philippines 1102
0154	Ma. Luisa Licaros Manila Adventist Medical Center 1975 Conrada Street Pasay City, Metro Manila Philippines 1300	0216	Cherie Lumagas St. Luke's Medical Center 201 E. Rodriguez Sr. Avenue Quezon City, Philippines 1102
0155	Rachel Magno Lantoc Manila Naval Hospital Fort Bonifacio, Taguig City, Taguig City 1201	0219	Jose Yason Delos Santos Medical Center No. 201 E. Rodriguez Sr. Blvd., Quezon City, Metro Manila Philippines 1102
0157	Maria Josephine Valerio Air Force General Hospital Col. Jesus Villamor Air Base Pasay Metro Manila 1350	0222	Arlene Francisco Twin Hearts Clinic Fairview Quezon City
0158	Arlene Yason Paranaque Doctors Hospital 175 Dofra Soledad Avenue Better Living Subdivision, Don Bosco, Paranaque City Philippines 1711	0223	Janelle Liban FEU - NRMF Medical Center Regalado Ave. cor Dahlia, West Fairview Q.C., Philippines 1118
0161	Ernesto Ang Cardinal Santos Medical Center Wilson Street, Greenhills, San Juan, Metro Manila, Philippines 1503	0224	Deana Licop Christian Medical Clinic # 7 BF Road, Commonwealth Quezon City, Philippines 1121
0162	Eduardo Thomas Aquino Victor R. Potenciano Medical Center No.163 EDSA (Southbound Side) Mandaluyong City, Philippines 1556	0225	Rozema Linga FEU - NRMF Medical Center Regalado Ave. cor Dahlia, West Fairview Q.C., Philippines 1118
0164	Alfredo Gatmaitan Victor R. Potenciano Medical Center No.163 EDSA (Southbound Side) Mandaluyong City, Philippines 1556	0226	John Malando Well of Life Medical Specialist Center # 86 Fairview Ave., Cor. Winston St., Fairview Subd., Q.C., Philippines 1118
0165	Ruby Go Cardinal Santos Medical Center Wilson Street, Greenhills, San Juan, Metro Manila, Philippines 1503	0227	Don Maringas FEU - NRMF Medical Center Regalado Ave. cor Dahlia, West Fairview Q.C., Philippines 1118
0166	Griselda Ishiwata Mandaluyong City Medical Center Boni Avenue cor. Sta. Rosario Street Barangay Plainview, Mandaluyong City, Philippines 1550	0230	Arlette Samaniego FEU - NRMF Medical Center Regalado Ave. cor Dahlia, West Fairview Q.C., Philippines 1118
0167	Ramon Mariano Victor R. Potenciano Medical Center No.163 EDSA (Southbound Side) Mandaluyong City, Philippines 1556	0393	Arnel Santos San Lorenzo General Hospital Quirino Highway, Brgy. Pasong Putik, Lagro, Novaliches, Quezon City Philippines 1123
0168	Ma. Concepcion Marcelo Cardinal Santos Medical Center Wilson Street, Greenhills, San Juan, Metro Manila, Philippines 1503	0395	Estopa Victoria Medical Specialist Clinic 483 Quirino Highway in Novaliches, Quezon City, Philippines 1123
0169	Ma. Isabel Savillo Our Lady of Lourdes Hospital 46 P Sanchez St., Sta. Mesa Manila, Philippines, Philippines 1016	0231	Cynthia Fabregas Starmed Clinic Acre Bldg., Malakas Street Diliman, Quezon City Philippines 1101
0170	Rosa Ally Sy Cardinal Santos Medical Center Wilson Street, Greenhills, San Juan, Metro Manila, Philippines 1503	0233	Vivian Tagle SSS Medical Department East Avenue Diliman, Quezon City Philippines 1101
0171	Maria Grace Ararata Ramiro Medical Center Tagbilaran City, Bohol Philippines 6300	0235	Maybelle Yasuista V. Luna Hospital V. Luna Rd., Quezon City Philippines 1100
0172	Manoel Cardino Tagbilaran Community Hospital Miguel Parais street, Tagbilaran City, Bohol, Philippines 6300	0243	Gerardo Nallas Cisdoctors Polyclinic 742 M. Naval St., , Novotas, Metro Manila, Philippines 1485
0173	Kevin Conrañan Perpetual Succour Hospital Gorordo Avenue, Lahug, Cebu City Philippines 6000	0245	Alan Ong Diabetes Clinic A Bonifacio Street, Quezon City Philippines 1100
0174	Luisa de los Santos Ramiro Medical Center Tagbilaran City, Bohol Philippines 6300	0246	Vicente Ortiz Perlas Polyclinic Specialist's Center 171-173 cor F. Roxas St., 4th Ave., Calococan City, Philippines 1405
0175	Renan Dungog Perpetual Succour Hospital Gorordo Avenue, Lahug, Cebu City Philippines 6000	0247	Antonio David Medicare Specialists Clinic 120 McArthur Highway Valenzuela City, Philippines 1440
0177	Liliosa Patindol Ramiro Medical Center Tagbilaran City, Bohol Philippines 6300	0248	Edwin Fortuno Fatima Medical Center 120 Mc Arthur Hwy., Valenzuela, Metro Manila, Philippines 1440
0178	Enriqueta Sepso Ramiro Medical Center Tagbilaran City, Bohol Philippines 6300	0249	Virginia Tolentino Clinica Nazal Sangandaan Calococan City Philippines 2081
0179	Maretha Tolentino Perpetual Succour Hospital Gorordo Avenue, Lahug, Cebu City Philippines 6000	0251	Yvette Amante Asian Hospital and Medical Center 2205 Civic Drive, Filinvest Corporate City, Alabang, Muntinlupa City, Metro Manila, Philippines 1780
0180	Marc Udaete Silliman University Medical Center Aldecoa Road, Dumaguete City, Philippines 6200	0252	Carmen Babaran Healthway Medical Clinic Filinvest Corporate City Alabang, Muntinlupa, Philippines 1780
0181	Elma Bascoles Visayas Community Medical Center No. 85 Osmeña Boulevard, Cebu City Philippines 6000	0253	Arlene Crisaldo Optical City Muntinlupa Civic Drive, Filinvest, Alabang, Muntinlupa City, Metro Manila Philippines 1780
0182	Imelda Bilocura Chong Hua Hospital Lorente St., Capitol Site Cebu City Philippines 6000	0256	Ignacia Pajardo Las Piñas District Hospital Real St., Pulang Lupa, Las Piñas City, Metro Manila, Philippines 1742
0183	Consolacion Cullitar Cebu Venet General Hospital corner of F. Ramos and V. Ramado Street, Cebu City Philippines 6000	0258	Aurora Macaballag Perennial Help Hospital Alabang Zapote Rd., Pampona, Las Piñas City, Philippines 1742
0184	Deanna Paz Del Mar Chong Hua Hospital Lorente St., Capitol Site Cebu City Philippines 6000	0260	Gabriel Tan Las Piñas City Medical Center 1314 Marcos Alvarez Ave., Taton V, Las Piñas City, Metro Manila Philippines 1747
0185	Marian Denopol Visayas Community Medical Center No. 85 Osmeña Boulevard, Cebu City Philippines 6000	0261	Oliver Bautista One Stop Diabetes Center National Highway San Antonio, San Pascual, Batangas City Philippines 4204
0186	Evelyn Gamallo Visayas Community Medical Center No. 85 Osmeña Boulevard, Cebu City Philippines 6000	0262	Tereisa Andral St. Therese of the Child Jesus Clinic 75 TM Kalaw St., Brgy. Tres Lipa City, Philippines 4217
0187	Athena Mapa Chong Hua Hospital Lorente St., Capitol Site Cebu City Philippines 6000	0263	Eden Carriaga Most Holy Trinity Clinic Rozal Avenue, Batangas City Philippines 4200
0188	Chela Marie Romero South General Hospital Tuyasan, Naga Cebu Philippines 6037	0264	Christia Goco Maria Eleanora Hospital Telfiran, Calapan City, Oriental Mindoro, Philippines 5200
0189	Jesus Santos Kainos Medical Clinic 10th Floor Metrobank Plaza, Fuente Osmeña, Cebu City Philippines 6000	0265	Gloria Malaluan-Craig Palma Malaluan Hospital J. Magbway St., Rosario Batangas Philippines 4225
0190	Gerry Tan Cebu Doctors Hospital Osmena Boulevard, Cebu City Philippines 6000	0266	Simon Maljan Daniel Mercado Memorial Medical Center #1 Pres. Laurel Highway, Tanzaun City, Batangas Philippines 4232
0191	Caral Balagot S.R Diagnostic Clinic M.H. Del Pilar Street Tagbilaran City, Leyte Philippines 6500	0267	Carmelyn Montano Daniel Mercado Memorial Medical Center Rm 116 #1 Pres. Laurel Highway, Tanzaun City, Batangas Philippines 4232
0192	Edwin Carlele Calleña Medical Clinic Burgos Street Ormoc City, Leyte, Philippines 6541	0268	Francisca Paginawan Holy Queen Medical Clinic # 18 Binay St. Poblacion 4 Bauan Batangas, Philippines 4201
0193	Oliga Chavez Divine Word Hospital Avenida Veteranos, Tacloban City Leyte, Philippines 6500	0269	Florence Santos Marignia Bldg., Apacible St. Tanzaun, Batangas, Philippines 4232
0194	Nelson Chiu Chu Medical Clinic Lopez Jaena Street Ormoc City, Leyte, Philippines 6541	0270	Agonina Livia Vilares St. Therese of the Child Jesus Clinic 75 TM Kalaw St., Brgy. Tres Lipa City, Philippines 4217
0195	Conchito dela Cruz Divine Word Hospital Avenida Veteranos, Tacloban City Leyte, Philippines 6500	0271	Amr Aweyan St. Gerard Polyclinic and Diagnostic Laboratory Gombarua Street, San Pablo City Laguna, Philippines 4000
0200	Pablo Tan Jr. Samar Provincial Hospital Cathalogan City, Eastern Samar Philippines 6700	0272	Angelito Belen Belcast Clinic 53 Barangay, San Pablo City Laguna, Philippines 4000
0201	Gisela Adolor Lung Center of the Philippines Quezon Avenue, Quezon City, Philippines 1104	0273	Josephine Briones MMC Medical Plaza Kinika Briones, 4th Unit Aviso Bldg., Valdeera St. Sanitary, Quezon, Philippines 4322
0203	Bernardo Carpio Veterans Memorial Medical Center North Ave., Diliman Quezon City, Metro Manila Philippines 1101	0274	Jocelyn Chua Mother of Grace Polyclinic Rozal St., Candiana, Quezon Philippines 4323
0204	Princessa Concepcion Neo Medica Clinic Congressional Avenue Quezon City, Philippines 1100	0275	Marilyn Coronacion Quezon Medical Center Ciudad Maharika, Iyam, Lucena City Philippines 4301
0210	Balthazar Vitaraza Veterans Memorial Medical Center North Ave., Diliman Quezon City, Metro Manila Philippines 1100	0276	Prospero Esclanda P. Zuñiga Street, San Pablo City, Laguna, Philippines 4000
0213	Dionisio Cabañatan St. Luke's Medical Center 201 E. Rodriguez Sr. Avenue Quezon City, Philippines 1102	0277	Maria Lourdes Gonzales Lucena United Doctors Hospital 178 Merchan St., Lucena City
0214	Richard Elwyn Fernando St. Luke's Medical Center		

0278	Philippines 4301 Jean Frances Nobajas Immaculate Conception Hospital P. Alcantara Street, San Pablo City Laguna, Philippines 4000	0325	Philippines 7207 Babelonia Kanglion Dipolog Medical Center Sta. Filomena, Dipolog City Philippines 7100
0279	Roman Oabel Lucena MMG General Hospital Maharlika Highway, Ibabang Dupay, Lucena City, Quezon Philippines 4301	0326	Jo Ann Lao-Go Ozamis Laboratory and Clinic 104 Metro Lab Building, Burgos St. Ozamis City, Misamis Occidental Philippines 7200
0280	Romane Jesus Pilar Emil and Joana Hospital Quezon Street, Almonan Quezon Philippines 4331	0327	Auranciano Arce Lomanta Jr. Lomanta Diabetes Clinic Ozamis City, Misamis Occidental Philippines 7200
0397	Roy Roxas Lucena MMG General Hospital Maharlika Highway, Ibabang Dupay Lucena City, Quezon Philippines 4301	0328	Agnes Jane Santillanes Our Lady of Carmel Family Medical Clinic Herrera Street, Dipolog City Philippines 7100
0398	Cynthia Sanchez San Pablo Community Medical Center Brgy. San Rafael Maharlika Highway, San Pablo City, Laguna Philippines 4000	0331	Angel Aranteta Riverside Medical Center B.S. Aquino Drive Bacolod City Philippines 6100
0399	Nenita Tan Quezon Medical Center 69 Osmenia Street, Lucena City Quezon, Philippines 4301	0332	Marian Joyce Co Acoutrack 21st North Drive, Bacolod City Philippines 6100
0400	Mariasona Tan San Pablo Doctors Hospital 55 A. Mabini St., Maharlika Highway, Barangay San Rafael San Pablo City Philippines 4000	0340	Roberto Salvator Riverside Medical Center B.S. Aquino Drive Bacolod City Philippines 6100
0281	Amor Antonio Amor Antonio Clinic Pacita, San Pedro, Laguna Philippines 4023	0345	Judy Anne Galatin-Yuzon Davao Medical School Foundation Hospital Suite 201-202 2nd Flr. Medical Arts Bldg., San Pedro Hospital Davao City, Philippines 8000
0282	Lynn Bilal St. James Hospital Marikita Pecho Dita Sta. Rosa, Laguna Philippines 4028	0347	Veronica Racho Davao Doctor Medical Clinic 8th Floor Davao Doctor Medical Clinic Tower, Malvar, Davao City Philippines 8000
0283	Antonio Chua Emmanuel Clinic Brgy. Pagaawalan, Sta. Cruz, Laguna Philippines 4009	0348	Yvette Tan CHCC Hospital Rm 109 CHDC Hospital Andia Riverside, Davao City Philippines 8000
0284	Victorino de las Reyes Evangelical Medical Specialty Hospital J. P. Rizal St., cor. Macarita Ave., Pacita 1, San Pedro, Laguna Philippines 4023	0349	Hector Quimbao San Pedro College Doctors Clinic Rm 18 SPCDC Davao City Philippines 8000
0285	Ronald Ningsun Perpetual Help Hospital Jubilation New Binan, Mampalasan, Binan, Laguna, Philippines 4024	0350	Francis Lee Ho Brokership Hospital Madapo Hills, Davao City Philippines 8000
0286	Elaene Gayle Lopez Bifan Doctors Hospital Segunda Village Platero Laguna, Philippines 4024	0351	Jaime Acorin ZACC Hospital 291 Caneler St., Zamboanga City Philippines 7000
0287	Marie Gertrude Santos Bifan Doctors Hospital Segunda Village Platero Laguna, Philippines 4024	0352	Cynthia Pollisco Western Mindanao Medical Center Rm 122 Veterans Avenue Extension, Zamboanga City, Philippines 7000
0288	Venus Seron Green Pasture Diabetes Center Ph 4 Block 5 Lot 31 Gold ave., Golden City Subd., Brgy. Dita, Sta. Rosa, Laguna, Philippines 4026	0353	Jamasal Usman Cidadal Medical Hospital Nufez Extension, Zamboanga City, Philippines 7000
0289	Cynthia Talia Calamba Medical Center Crossing, Calamba City Calamba Laguna, Philippines 4029	0354	Troy Abudhmanan ZACC Hospital 291 Caneler St., Zamboanga City Philippines 7000
0290	Ma. Victoria Valdez San Pedro Doctors Hospital Old National Highway, San Pedro Laguna, Philippines 4023	0355	Falma Tu Zamboanga Doctors Hospital Veterans Avenue, Zamboanga City Philippines 7000
0402	Vicente Escarlante Calamba Medical Center Crossing, Calamba City Calamba Laguna, Philippines 4029	0356	Roger Fernandez Diabetes Clinic, Veterans Avenue Zamboanga City, Philippines 7000
0291	Arthur Alvarez Alvarez Medical Clinic V. Demetriou St., Tabaco, Albay Philippines 4511	0357	Cidadal Medical Hospital Nufez Extension, Zamboanga City, Philippines 7000
0293	Royanito Cairesasa Naga City Hospital Naga City, Camarines Sur Philippines 4000	0361	Ma. Ester Legaspi St. Jude's Hospital F. Quiroga Street, Kalibo, Aklan Philippines 5600
0294	Rosemen Fernando Estevan Memorial Hospital Legaspi City, Albay Philippines 4500	0362	Faye Maria Blancaver St. Anthony College Hospital San Roque Ext., Roxas City Capiz, Philippines 5800
0296	Christopher Giaman Daddy's Little Angel Door #5 Cocoon Bldg., Old Bldg. Legaspi City, Albay Philippines 4500	0363	Diana Marie Cacho St. Paul's Hospital Rm 212 PLCC St., Iloilo City Philippines 5000
0297	Justin Noveta Rinconada Diagnostic Center Camarines Sur, Bonanza Bldg., Guevarra St., San Roque Iriga City, Philippines 4431	0365	Lenny Malaki St. Paul's Hospital Spice Bldg., Gen. Luna Street Iloilo City, Philippines 5000
0298	Paul Luis Palencia Our Lady of Lourdes Hospital Dact, Camarines Norte Philippines 4000	0367	Ma. Dovie Ygnara Rm 212 Healthlink, Mabini Street Iloilo City, Philippines 5000
0299	Fioranie Paredes Paredes Medical Clinic Montana Arcade, Pangasinan Drive Naga City, Camarines Sur Philippines 4000	0368	Gregory Ardena Panay Healthcare Estancia, Kalibo, Aklan Philippines 5800
0301	Nasarciano Alaban St. Dominic Medical Center Tababa, Bacoor, Cavite Philippines 4102	0369	Louella Araca Plaza Libertad Medical Specialists Yulo Bldg., JM Basa St., Iloilo City Philippines 5000
0302	Suzette Ambagan De La Salle University Medical Center Congressional Avenue Dasmarinas Cavite, Philippines 4114	0372	Ma. Theresa Pascual Cerezo Clinic Alunan Avenue, Koronadal City Philippines 9508
0303	Gina Amosco Fortune Care Imus Cavite Blk. 1 Lt. 22 England St., Barcelona Phase 2, Buhay Na Tubig Imus Cavite, Philippines 4103	0373	Gleicy Forman Forman Clinic National Highway, Isulan Sultan Kudarat, Philippines 9805
0304	Merissa Calma Rural Health Center Divine Grace, Bacab, Cavite Philippines 4100	0374	Fiona Mae Jacobo Jacobco Clinic Midayap, Cotabato City Philippines 9410
0305	Asamedic Diagnostic & Specialty Center E. Aguinaldo Highway, Anabu II, Imus Cavite, Philippines 4103	0376	Joylye Mazo AJM Bldg., Magsaysay Avenue General Santos City, Cotabato Philippines 9500
0306	Jose Carlos Miranda Our Lady of Pilar Medical Center Tenua Ave. Bayan Luma, Imus, Cavite, Philippines 4103	0377	Vinaylny Nobasco Demonstario Multi-Specialty Clinics Demonstario Bldg., Santiago Blvd. General Santos City, Cotabato Philippines 9500
0307	Ruth Punzalan Municipal Health Center A. Soriano Highway, Tarca, Cavite Philippines 4108	0378	Belen Pascasio Pascasio Clinic Tacouron, Sultan Kudarat Philippines 9800
0308	Josefino Rebrancos De La Salle University Medical Center Congressional Avenue Dasmarinas Cavite, Philippines 4114	0379	Ruth Peralta Demonstario Multi-Specialty Clinics Demonstario Bldg., Santiago Blvd. General Santos City, Cotabato Philippines 9500
0309	Michelle Santiago De La Salle University Medical Center Congressional Avenue Dasmarinas Cavite, Philippines 4114	0380	Lucy Ann Yap Yap's Clinic Roxas East Avenue General Santos City, Cotabato Philippines 9500
0310	Maria Esperanza Uy De La Salle University Medical Center Congressional Avenue Dasmarinas Cavite, Philippines 4114	0381	Louren Apotadera Apotadera Bldg., Commission Civil St. Jaro, Iloilo City Philippines 5000
0317	Emilia Paliana Cagayan De Oro Polymedic Hospital Don Apolinar Velez St., Cagayan de Oro City, Philippines 9000	0385	Fe Hialdo Iloilo Doctors Hospital 311 MAJ Condominium Iloilo City Philippines 5000
0319	Ericason San Juan St. Ignatius Medical Clinic Petez Sports Center A. Velez St., Cagayan de Oro City, Philippines 9000	0386	Aretha Ann Liwag J&B Clinics Quezon St., Iloilo City Philippines 5000
0320	Arthur Tan Cagayan De Oro Polymedic Hospital Don Apolinar Velez St., Cagayan de Oro City, Philippines 9000	0387	Suzette Labrador Healthlink Clinic Rm 221 Healthlink Bldg., Mabini St. Iloilo City, Philippines 5000
0321	Jeanette Abucayon FK Polyclinic Iriga City, Lanao del Norte Philippines 9200	0388	Christina Etum Iloilo Doctors Hospital 2nd floor, Gonda Wing, Molo Iloilo City, Philippines 5000
0322	Lilo Buenañada Buenañada Clinic Malvar St. Dipolog City, Zamboanga Del Norte, Philippines 7100	0390	Rollin Tabuena Jalandonis Street, Iloilo City Philippines 5000
0323	Agnes Fernandez F. Susana Polyclinic Ozamis City, Misamis Occidental Philippines 7200		
0324	Faith Go Go Clinic Oroquieta City, Misamis Occidental		