Diabetes Research and Clinical Practice 101, suppl. S1 (2013) S15–S26

Contents available at Sciverse ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

Safety and effectiveness of insulin analogues in type 2 diabetic patients from Algeria: a sub-analysis of the A_1chieve study

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ARTICLE INFO

Keywords:
Insulin analogues
Algeria
Type 2 diabetes
Insulin aspart
Insulin detemir

ABSTRACT

Aim: To determine the safety and effectiveness of insulin analogues in type 2 diabetes (T2D) patients in the Algerian cohort of the A_1chieve study and to examine the status of T2D management across different regions in Algeria.

Methods: Patients starting therapy with biphasic insulin aspart 30, insulin detemir, insulin aspart (IAsp) or IAsp + basal insulin at their physicians' decision were included. The primary outcome was the incidence of serious adverse drug reactions (SADRs), including major hypoglycaemia. Secondary outcomes included changes from baseline to Week 24 in hypoglycaemia, glycated haemoglobin A_{1c} (HbA_{1c}), fasting plasma glucose (FPG), postprandial plasma glucose (PPPG), weight and quality of life (QoL, evaluated using the EQ-5D questionnaire).

Results: Overall, 1494 patients (mean±SD age: 60.1±10.3 years; body mass index: 28.1±4.9 kg/m^2; HbA_{1c}: 9.2±1.8%) were enrolled. Poor baseline glucose control was revealed across the different Algerian regions with mean HbA_{1c} varying from 8.9% to 9.6%. Two SADRs were reported during the study. The proportion of patients reporting major hypoglycaemic events decreased from 1.1% at baseline to 0.2% at Week 24 ($p = 0.0017$). Significant improvements in mean HbA_{1c} (–1.3±2.0%), FPG (–38.8±79.9 mg/dL) and post-breakfast PPPG (–51.4±97.1 mg/dL) were observed in the entire cohort (all $p < 0.001$). The mean body weight increased by 0.9±3.8 kg, while QoL increased by 9.2±16.7 points after 24 weeks.

Conclusions: Insulin analogue therapy was well-tolerated and significantly improved blood glucose control over 24 weeks in the Algerian cohort.

1. Introduction

Along with the rest of the world, Algeria has also witnessed a major rise in the prevalence of type 2 diabetes (T2D) with a national prevalence of 6.9% in 2011 [1]. The increased T2D prevalence is linked to a rise in obesity rates resulting from rapid urbanization and the change from an active lifestyle to a more sedentary one [2]. By 2030, the International Diabetes Federation estimates that Algeria will have 2.3 million people with T2D, corresponding to a prevalence of 7.7% [1]. Some regional variations in T2D prevalence have been detected in Algeria. A study in Setif, Centre East Algeria, found a disease prevalence of 8.8% using the American Diabetes Association (ADA) criteria for diagnosis of T2D and prevalence did not differ between urban and rural areas [3]. However, in Tlemcen, Western Algeria, a T2D prevalence of 10.5% was detected with a higher diabetes prevalence in urban areas compared to rural areas [4].

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0168-8227/$ – see front matter

The ADA recommends targeting a glycated haemoglobin A_{1c} (HbA_{1c}) level below 7.0%, above which the risk of incurring long-term microvascular complications increases [5,6]. Consequently, it is recommended to intensify therapies when the HbA_{1c} target is not met [5].

However, in spite of treatment, many people with T2D have high blood glucose levels in clinical practice across the world [7]. Patients and healthcare providers (HCPs) often delay starting or intensifying insulin therapy over concerns of hypoglycaemia, weight gain and complicated treatment regimens that are difficult to follow [8]. Increased patient and HCP awareness regarding the risks of uncontrolled hyperglycaemia and the benefits of insulin therapy is essential to managing T2D successfully.

Insulin analogues, such as premix biphasic insulin aspart 30 (BIAsp 30), basal insulin detemir (IDet) and bolus insulin aspart (IAsp), were designed to provide safe and effective blood glucose control. These insulin analogues have shown positive treatment results that correlate with improved glycaemic control and low risks of hypoglycaemia in clinical trials as well as observational studies [9–12]. Also, the premix, basal and bolus formulations offer different dosing options and regimens that can be customised to suit the needs of individual patients. This could help improve treatment compliance among patients facing difficulties adhering to schedules or those with fears of multiple injections.

The non-interventional A_1chieve study [13] offered a unique opportunity to examine real-life clinical practices involving insulin analogue treatment in 66,726 T2D patients from 28 countries. Complete A_1chieve study results are available online under www.A1chieve.com. This sub-analysis aimed to determine the safety and effectiveness of insulin analogue therapy in routine clinical practice and also to examine the status of T2D management across different regions in Algeria.

2. Methods

2.1. Study design

A_1chieve was a prospective, open-label, non-interventional, 24-week study in T2D patients who had been using oral glucose-lowering drugs [OGLDs] and/or insulin and started treatment with BIAsp 30 (NovoMix® 30, Novo Nordisk A/S, Denmark), IDet (Levemir®, Novo Nordisk A/S, Denmark) or IAsp (NovoRapid®, Novo Nordisk A/S, Denmark), alone or in combination, in routine clinical practice [13]. Here, data from Algerian patients who started treatment with the study insulins, with or without OGLDs, were analysed. Patients were recruited from 90 centres in Algeria between March 2009 and September 2010.

Commercially available study insulins were prescribed by the physicians in accordance with the locally approved label. All procedures were performed according to routine clinical practice at the baseline, interim (Week 12) and final (Week 24) visits. Data collected from the physicians' records and patient diaries were entered in standard case report forms.

Data were examined for all enrolled Algerian patients (entire cohort) and patients grouped by pre-study therapy type (insulin-naive and insulin-experienced). Patients were further stratified by the study insulin started (BIAsp 30, IDet, IAsp and IAsp + basal insulin) and by region (Centre East, Centre West, East and West). Centre East comprised the following cities: Bejaia, Setif and Tizi Ouzou; Centre West: Ain Defla, Alger, Blida, Ghardaia and Kolea; East: Ain M'lila, Annaba, Constantine and Souk Ahras; and West: Ain Temouchent, Mascara, Oran, Sidi Bel Abbes and Tlemcen.

2.2. Patient selection

Algerian T2D patients who started treatment with any of the study insulins within the 4 weeks preceding the start of the study were included. Women who were pregnant, breastfeeding or intended to become pregnant were excluded.

Study approval was granted by the ethics committee of Algeria and the study was conducted in accordance with local regulatory requirements. Informed consent was obtained from all patients participating in the study.

2.3. Outcomes

The primary safety outcome was the number of serious adverse drug reactions (SADRs), including major hypoglycaemic events considered related to the study insulins, from baseline to the final visit. Secondary safety outcomes included the change in the number of hypoglycaemic events (overall and nocturnal) in the last 4 weeks before the final visit compared to the last 4 weeks before the baseline visit, serious adverse events (SAEs) and adverse drug reactions.

Other outcomes included the change from baseline in HbA_{1c}, fasting plasma glucose (FPG), postprandial plasma glucose (PPPG), body weight, systolic blood pressure (SBP), blood lipids and quality of life (QoL). QoL was measured using the visual analogue scale (VAS) of the EQ-5D questionnaire. Also, the proportion of patients who achieved HbA_{1c} <7.0% at Week 24 was analysed. Laboratory tests were performed in accordance with local standardisation and quality control.

2.4. Statistical analysis

Statistical analyses were performed for the entire cohort and by pre-study insulin therapy type, i.e., insulin-naive and insulin-experienced patients. Between-group and between-region differences were not statistically tested. The number of patients on IAsp was very low; hence, these results are not presented in this paper. Also, the regional data for patients on IAsp + basal insulin are not presented as the numbers were low. P-values are not presented when the number of patients analysed was less than 100.

Continuous variables were summarised using descriptive statistics (n, mean, SD) and discrete variables were summarised using frequency tables (n, %). McNemar's test

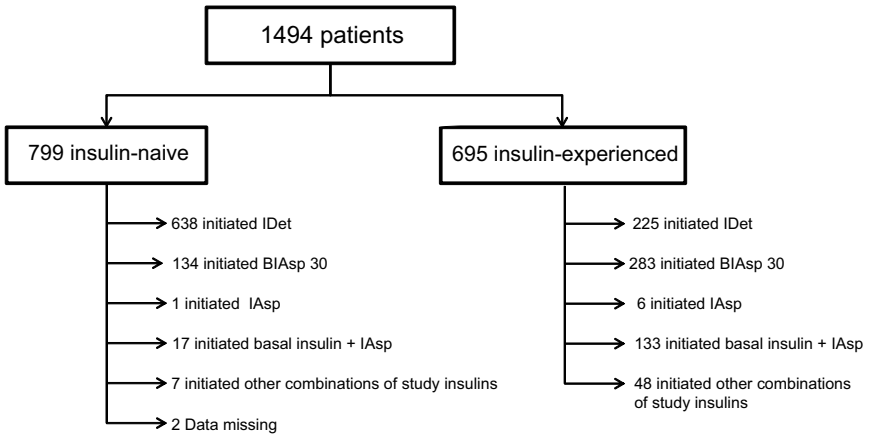

Fig. 1 – Algerian cohort – split by pre-study therapy type. BIAsp 30: biphasic insulin aspart 30; IAsp: insulin aspart; IDet: insulin detemir.

was used to analyse the change from baseline in the proportion of patients reporting at least one hypoglycaemic event. A paired t-test was used to analyse 24-week changes in HbA_{1c}, FPG, PPPG, body weight, SBP, blood lipids and QoL. Two-sided testing with a 5% significance level was used. All data analyses were performed by Novo Nordisk A/S using SAS® Version 9.1.3.

3. Results

3.1. General characteristics

A total of 1494 patients (799 insulin-naive and 695 insulin-experienced) were included (Fig. 1). Patients were, on average, 60.1 years old with a mean BMI of 28.1 kg/m^2 and mean diabetes duration of 11.8 years (Table 1). The mean±SD HbA_{1c} level at baseline was 9.2±1.8% (77±20 mmol/mol, Table 2).

In the entire cohort, 417 patients started BIAsp 30, 863 patients started IDet, 7 patients started IAsp and 150 patients started IAsp + basal insulin therapy at baseline. Data was missing for 2 patients while 55 patients started other combinations of study insulin and are not discussed here.

Of the 1494 patients enrolled, 177 patients were recruited from Centre East Algeria, 701 patients from Centre West Algeria, 294 patients from East Algeria and 322 patients from West Algeria. Demographic and baseline characteristics for these regions are also presented in Table 1. The average diabetes duration varied from 9.9 years in Centre East Algeria to 12.9 years in Centre West Algeria.

The mean±SD HbA_{1c} level at baseline was 9.6±2.0% (81±22 mmol/mol) in Centre East Algeria, 9.2±1.8% (77±20 mmol/mol) in Centre West Algeria, 9.2±1.7% (77±19 mmol/mol) in East Algeria and 8.9±1.8% (74±20 mmol/mol) in West Algeria (Table 1).

For the entire cohort, the majority of physicians (92.6%) reported the need to improve glycaemic control as the reason for prescribing the study insulins.

3.2. OGLDs

At baseline in the entire Algerian cohort, metformin (84.3%) and sulphonylureas (52.7%) were the most commonly used OGLDs. At Week 24, 86.6% of patients continued metformin (87.8% insulin-naive and 84.8% insulin-experienced) and 49.0% were on sulphonylureas (61.6% insulin-naive and 30.2% insulin-experienced).

3.3. Insulin dose and frequency of administration

Pre-study, the average insulin dose was 37.3±21.2 U/day amongst insulin-experienced patients in the entire cohort (Table 2). At baseline, insulin-experienced patients received an average dose of 39.0±20.9 U/day, titrated up to 51.3±28.5 U/day over 24 weeks.

Insulin-naive patients received an average starting dose of 15.5±11.1 U/day, titrated up to 28.0±16.7 U/day over 24 weeks (Table 2).

The mean insulin doses by regimen and by region are presented in Tables 3 and 4, respectively.

At Week 24, 79.6% of patients on BIAsp 30 dosed twice daily, 89.7% of patients on IDet dosed once daily and 78.3% of patients on IAsp + basal insulin dosed more than three times daily.

3.4. SADRs and SAEs

Two SADRs (hypoglycaemic unconsciousness and diabetes mellitus inadequately controlled) were reported by 2 patients taking IAsp + basal insulin in the entire cohort. One event was considered probably related to the study treatment and the other possibly related.

A total of 17 SAEs were reported by 17 patients in the entire Algerian cohort.

3.5. Hypoglycaemia

There was no statistically significant change in the proportions of patients reporting overall hypoglycaemia and minor hypoglycaemia from baseline to Week 24 in the entire cohort (Table 2). The proportions of patients reporting major

Table 1 – Baseline demographics and characteristics of Algerian patients – entire cohort and by region

	All patients	Insulin-naive	Insulin-experienced
Entire cohort			
N (%)	1494 (100)	799 (53.5)	695 (46.5)
Gender (male/female), %	35.0/65.0	39.1/60.9	30.3/69.7
Age, years	60.1 (10.3)	59.6 (10.0)	60.6 (10.7)
Body weight, kg	74.3 (13.1)	73.1 (13.3)	75.6 (12.8)
Body mass index, kg/m^2	28.1 (4.9)	27.5 (4.9)	28.8 (4.8)
Duration of diabetes, years	11.8 (6.9)	10.3 (6.4)	13.6 (7.2)
HbA_{1c}, %/mmol/mol	9.2 (1.8)/77 (20)	9.5 (1.8)/80 (20)	8.9 (1.7)/74 (19)
OGLDs, n (%)			
1	545 (45.2)	239 (33.0)	306 (63.5)
2	618 (51.2)	453 (62.6)	165 (34.2)
>2	43 (3.6)	32 (4.4)	11 (2.3)
Centre East Algeria			
N (%)	177 (100)	96 (54.2)	81 (45.8)
Gender (male/female), %	44.3/55.7	51.6/48.4	35.8/64.2
Age, years	58.6 (9.8)	57.9 (8.9)	59.5 (10.8)
Body weight, kg	71.0 (11.2)	70.6 (11.2)	71.6 (11.2)
Body mass index, kg/m^2	27.0 (4.6)	26.1 (3.8)	28.0 (5.3)
Duration of diabetes, years	9.9 (5.9)	9.1 (5.6)	10.9 (6.1)
HbA_{1c}, %/mmol/mol	9.6 (2.0)/81 (22)	9.9 (2.1)/85 (23)	9.2 (1.8)/77 (20)
OGLDs, n (%)			
1	91 (60.7)	46 (52.3)	45 (72.6)
2	58 (38.7)	41 (46.6)	17 (27.4)
>2	1 (0.7)	1 (1.1)	–
Centre West Algeria			
N (%)	701 (100)	394 (56.2)	307 (43.8)
Gender (male/female), %	37.1/62.9	39.6/60.4	34.0/66.0
Age, years	60.8 (10.4)	60.4 (9.9)	61.4 (11.0)
Body weight, kg	75.6 (13.6)	73.9 (13.7)	77.9 (13.1)
Body mass index, kg/m^2	28.3 (4.9)	27.6 (5.0)	29.2 (4.7)
Duration of diabetes, years	12.9 (7.3)	11.4 (6.6)	14.7 (7.6)
HbA_{1c}, %/mmol/mol	9.2 (1.8)/77 (20)	9.4 (1.8)/79 (20)	9.0 (1.7)/75 (19)
OGLDs, n (%)			
1	214 (36.3)	79 (21.9)	135 (59.2)
2	350 (59.4)	263 (72.9)	87 (38.2)
>2	25 (4.2)	/19 (5.3)	6 (2.6)
East Algeria			
N (%)	294 (100)	158 (53.7)	136 (46.3)
Gender (male/female), %	34.7/65.3	38.0/62.0	30.9/69.1
Age, years	59.6 (10.3)	59.5 (10.1)	59.8 (10.6)
Body weight, kg	73.5 (13.1)	73.0 (13.2)	74.2 (12.9)
Body mass index, kg/m^2	27.9 (4.6)	27.5 (4.7)	28.3 (4.5)
Duration of diabetes, years	10.7 (6.4)	9.5 (6.3)	12.2 (6.3)
HbA_{1c}, %/mmol/mol	9.2 (1.7)/77 (19)	9.5 (1.7)/80 (19)	9.0 (1.7)/75 (19)
OGLDs, n (%)			
1	111 (46.4)	61 (39.9)	50 (58.1)
2	123 (51.5)	90 (58.8)	33 (38.4)
>2	5 (2.1)	2 (1.3)	3 (3.5)

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Table 1 – *(continued)*

	All patients	Insulin-naive	Insulin-experienced
West Algeria			
N (%)	322 (100)	151 (46.9)	171 (53.1)
Gender (male/female), %	25.5/74.5	31.1/68.9	20.5/79.5
Age, years	59.6 (10.3)	58.7 (10.4)	60.4 (10.1)
Body weight, kg	73.8 (12.8)	73.0 (13.4)	74.4 (12.4)
Body mass index, kg/m^2	28.4 (5.1)	27.9 (5.3)	28.8 (4.9)
Duration of diabetes, years	11.7 (6.9)	9.2 (6.0)	14.0 (6.9)
HbA_{1c}, %/mmol/mol	8.9 (1.8)/74 (20)	9.2 (1.8)/77 (20)	8.6 (1.8)/70 (20)
OGLDs, n (%)			
1	129 (56.6)	53 (43.4)	76 (71.7)
2	87 (38.2)	59 (48.4)	28 (26.4)
>2	12 (5.3)	10 (8.2)	2 (1.9)

HbA_{1c}, glycated haemoglobin A_{1C}; OGLDs, oral glucose-lowering drugs.
Data are presented as mean (SD) unless specified otherwise.

hypoglycaemia and nocturnal hypoglycaemia significantly decreased at Week 24 in the entire cohort ($p = 0.0017$ and $p = 0.0008$, respectively).

Across regimens, there was no statistically significant change in the proportion of patients reporting overall hypoglycaemia at Week 24 compared to baseline (Table 3). At Week 24, major hypoglycaemic events were reported only in the BIAsp 30 group (Table 3).

The highest baseline incidence rate of overall hypoglycaemia was noted in East Algerian patients (8.05 events/patient-year). The baseline incidence rates of overall hypoglycaemia in Centre East, Centre West and West Algeria were 5.07, 4.73 and 5.17 events per patient-year, respectively. At Week 24, there were no statistically significant changes in the proportion of patients reporting overall hypoglycaemia in any region, excepting a decrease in West Algerian patients on IDet (Table 4).

3.6. Blood glucose control

In the entire cohort, the mean HbA_{1c} improved significantly by −1.3±2.0% (−14±22 mmol/mol) at Week 24 ($p < 0.001$, Table 2). The mean FPG and PPPG also improved significantly by −38.8±79.9 mg/dL and −51.4±97.1 mg/dL, respectively ($p < 0.001$). The proportion of patients reporting HbA_{1c} <7.0% was 27.5% at Week 24 compared to 6.9% at baseline.

Statistically significant reductions in glucose parameters were also noted in insulin-naive and insulin-experienced patients (Table 2). Improvements in glucose control were also seen in the different regimens and across the different regions (Tables 3 and 4, respectively). The largest reductions in HbA_{1c} were observed in the BIAsp 30 and IDet groups in Centre East Algeria (−1.9±2.6% and −1.9±2.2%, reported for 28 and 82 patients, respectively) (Table 4).

3.7. Body weight, SBP and blood lipids

The mean body weight increased by 0.9±3.8 kg over 24 weeks in the entire cohort (Table 2, $p < 0.001$). Body weight also increased significantly across the different regimens (Table 3). Across regions, the highest weight gain at Week 24 was seen in West Algerian patients on BIAsp 30 (2.4±4.6 kg, Table 4).

From baseline to Week 24, there was no statistically significant change in the mean SBP in the entire cohort (Table 2) or across regimens (Table 3). Results for SBP by region are presented in Table 4.

The mean total cholesterol and triglyceride levels decreased significantly from baseline to Week 24 in the entire cohort (Table 2, $p < 0.05$). There were no statistically significant changes in the mean HDL and LDL cholesterol levels from baseline to Week 24 in the entire cohort (Table 2). Lipid results across regimens and by region are presented in Tables 3 and 4, respectively.

3.8. Quality of life

Patient QoL improved significantly in the entire cohort from baseline to Week 24 (mean change in VAS scores: +9.2±16.7 points, $p < 0.001$). Significant improvements were also noted in both insulin-naive and insulin-experienced patients (mean change: +10.3±16.9 points and +7.9±16.5 points, respectively, $p < 0.001$).

4. Discussion

This cohort analysis demonstrated the safety and effectiveness of insulin analogue treatment in Algerian T2D patients. Overall, a low number of SADRs and SAEs was noted in this cohort. The findings are in accordance with the reported safety profiles of the study insulins in previous studies [9–12] and with the overall A_1chieve results [13].

At baseline, poor blood glucose control was prevalent in the entire Algerian cohort. The mean baseline HbA_{1c} level was 9.2% (77 mmol/mol), exceeding the ADA-recommended target of <7.0% (<53 mmol/mol). The mean FPG and post-breakfast PPPG values were also higher than the recommended levels of <130 mg/dL and <180 mg/dL, respectively [5]. Moreover, patients had an average T2D duration

Table 2 – Baseline and 24-week data for effectiveness and safety outcomes – entire cohort

Parameter		Entire cohort	Insulin naive	Insulin experienced
Insulin dose, U/day	n	1492	797	695
	Pre-study	37.3 (21.2)	–	37.3 (21.2)
	Baseline	26.4 (20.2)	15.5 (11.1)	39.0 (20.9)
	Week 24	38.8 (25.7)	28.0 (16.7)	51.3 (28.5)
HbA_{1c}, %/mmol/mol	n	1077	599	478
	Baseline	9.2 (1.8)/77 (20)	9.5 (1.8)/80 (20)	8.9 (1.7)/74 (19)
	Week 24	7.9 (1.5)/63 (16)	7.8 (1.4)/62 (15)	8.0 (1.6)/64 (17)
	Change	−1.3 (2.0)/−14 (22)	−1.6 (2.0)/−17 (22)	−0.9 (2.0)/−10 (22)
	p	<0.001	<0.001	<0.001
FPG, mg/dL	n	1224	666	558
	Baseline	184.7 (65.9)	196.3 (64.5)	170.8 (64.9)
	Week 24	145.8 (53.6)	141.9 (49.6)	150.5 (57.7)
	Change	−38.8 (79.9)	−54.4 (75.1)	−20.3 (81.6)
	p	<0.001	<0.001	<0.001
PPPG, mg/dL	n	819	440	379
	Baseline	251.1 (78.2)	259.6 (79.6)	241.2 (75.5)
	Week 24	199.7 (68.7)	197.2 (67.6)	202.7 (69.9)
	Change	−51.4 (97.1)	−62.4 (97.1)	−38.6 (95.6)
	p	<0.001	<0.001	<0.001
Weight, kg	n	1369	735	634
	Baseline	74.6 (13.1)	73.5 (13.3)	75.8 (12.8)
	Week 24	75.5 (12.8)	74.7 (12.8)	76.3 (12.8)
	Change	0.9 (3.8)	1.2 (3.8)	0.5 (3.9)
	p	<0.001	<0.001	<0.001
SBP, mmHg	n	1355	729	626
	Baseline	131.2 (18.6)	131.7 (18.1)	130.7 (19.3)
	Week 24	129.9 (24.1)	131.2 (28.8)	128.4 (17.0)
	Change	−1.3 (24.4)	−0.4 (29.1)	−2.3 (17.5)
	p	0.05	0.692	<0.001
Total cholesterol, mmol/L	n	897	497	400
	Baseline	4.5 (1.1)	4.5 (1.1)	4.5 (1.1)
	Week 24	4.4 (1.0)	4.4 (1.0)	4.4 (0.9)
	Change	−0.1 (1.2)	−0.1 (1.2)	−0.1 (1.1)
	p	0.025	0.048	0.256
Triglycerides, mmol/L	n	953	524	429
	Baseline	1.6 (0.9)	1.6 (0.9)	1.5 (0.9)
	Week 24	1.5 (0.7)	1.5 (0.7)	1.4 (0.6)
	Change	−0.1 (0.9)	−0.1 (0.8)	−0.0 (1.0)
	p	0.003	<0.001	0.374
HDL cholesterol, mmol/L	n	532	276	256
	Baseline	1.1 (0.4)	1.2 (0.4)	1.1 (0.5)
	Week 24	1.2 (0.4)	1.2 (0.4)	1.2 (0.4)
	Change	0.0 (0.5)	−0.0 (0.5)	0.0 (0.6)
	p	0.446	0.933	0.264
LDL cholesterol, mmol/L	n	532	273	259
	Baseline	2.8 (1.3)	2.8 (1.2)	2.8 (1.4)
	Week 24	2.7 (1.1)	2.7 (1.0)	2.7 (1.2)
	Change	−0.1 (1.6)	−0.1 (1.3)	−0.1 (1.8)
	p	0.291	0.277	0.619

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Table 2 – *(continued)*

Parameter		Entire cohort	Insulin naive	Insulin experienced
Hypoglycaemia (events per patient-year/percent with at least one event)				
Overall	Baseline	5.52/14.0	1.82/4.4	9.76/25.0
	Week 24	3.92/12.2	2.61/8.3	5.45/16.7
	p[a]	0.0792	0.0003	<0.0001
Major	Baseline	0.28/1.1	0.03/0.1	0.56/2.3
	Week 24	0.09/0.2	0.02/0.1	0.18/0.3
	p[a]	0.0017	1	0.001
Minor	Baseline	5.24/13.6	1.79/4.3	9.20/24.3
	Week 24	3.83/12.0	2.60/8.2	5.26/16.5
	p[a]	0.126	0.0002	<0.0001
Nocturnal	Baseline	2.21/7.3	0.39/1.8	4.30/13.7
	Week 24	1.30/4.5	0.82/2.9	1.86/6.4
	p[a]	0.0008	0.0863	<0.0001

FPG, fasting plasma glucose; HbA_{1c}, glycated haemoglobin A_{1c}; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PPPG, postprandial plasma glucose; SBP, systolic blood pressure.
Baseline, Week 24 and change values are mean (SD).
[a] p-value is from McNemar's test on paired proportions of patients experiencing hypoglycaemia.

of 11.8 years. Patients from all four regions in Algeria also presented with poor blood glucose levels with mean HbA_{1c} values varying from 8.9% to 9.6%. These findings indicate that timely treatment intensification is still an area for improvement in routine clinical practice in Algeria. Continued health education on the dangers of prolonged hyperglycaemia and the need for suitable therapeutic intervention therefore remains a requirement for Algerian patients and HCPs.

Overall blood glucose control improved significantly after 24 weeks as was also observed in the main A_1chieve study [13]. However, despite the marked reductions in blood glucose levels, the overall mean values still failed to match the ADA recommendations [5]. The 2008 DiabCare Algeria study had noted a lack of dose optimisation in routine practice [14]. It is possible that continued up-titration of doses and active treatment intensification may further improve blood glucose control for these Algerian patients.

Hypoglycaemia rates did not increase significantly in the entire cohort, although an anticipated rise among insulin-naive patients and a reduction for insulin-experienced patients were noted. Swinnen et al. [15] have previously reported that a treatment regimen of sulphonylureas in combination with insulin is linked to an increased incidence of hypoglycaemia. It is possible that the high proportion of sulphonylurea users (over 60% at Week 24) among those new to insulin may also have contributed to the increased incidence of overall hypoglycaemia seen in insulin-naive patients.

The small improvements in mean total cholesterol and triglyceride levels seen in this sub-analysis with no change in SBP, and only modest weight gain in spite of significant reductions in HbA_{1c} levels, may be linked to the increased engagement of physicians and patients in their diabetes care after entering the study.

QoL improved significantly in the Algerian cohort following the initiation of study insulins. Significant improvements in QoL after 24 weeks of insulin analogue therapy were also noted in the overall A_1chieve study [16]. It is recognised that blood glucose control and hypoglycaemia can influence reported QoL [17,18]; hence, it is encouraging to note the improvements seen in this cohort.

Constraints of this observational study include the absence of a control arm, retrospective data collection (particularly in the reporting of hypoglycaemia) and the lack of standardization of treatment practices across sites. However, this study was designed to follow the methodologies used in routine clinical practice with the aim of obtaining a perspective on T2D management strategies in Algeria. The study duration was sufficient to show the early response to treatment modification. Furthermore, all laboratory data were processed in accordance with local quality control procedures.

In conclusion, this cohort analysis revealed the vital need to heighten awareness and improve the current situation of T2D management in Algeria. Starting insulin analogue therapy was associated with significant improvements in blood glucose levels and low incidences of SADRs and hypoglycaemia in the Algerian cohort. Further intensification of treatment regimens and continued dose optimisation may be necessary to sustain the therapeutic benefits seen in this study.

Conflict of interest statement

Rachid Malek is a board member and speaker for Novo Nordisk and has received funding for advisory and educational activities. Zakia Arbouche is a board member and speaker for Novo Nordisk. Malika Bachaoui is a speaker for Novo Nordisk. Amine Dahaoui is employed by Novo Nordisk. This study was sponsored by Novo Nordisk A/S, Denmark. The sponsor took part in the development of the protocol, the process of data collection and analysis, funding

Table 3 – Safety and effectiveness outcomes by regimen – entire cohort

Parameter		BIAsp 30	IDet	IAsp + basal
Insulin dose, U/day	n	417	863	150
	Pre-study	38.2 (17.3)	24.5 (13.6)	52.0 (25.4)
	Baseline	37.0 (15.9)	14.2 (7.7)	56.3 (21.8)
	Week 24	47.8 (18.7)	25.8 (14.3)	78.5 (32.1)
HbA_{1c}, %/mmol/mol	n	262	660	115
	Baseline	9.3 (2.0)/78 (22)	9.1 (1.8)/76 (20)	9.3 (1.7)/78 (19)
	Week 24	8.0 (1.5)/64 (16)	7.9 (1.5)/63 (16)	7.9 (1.8)/63 (20)
	Change	–1.3 (2.2)/–14 (24)	–1.3 (1.9)/–14 (21)	–1.4 (2.3)/–15 (25)
	p	<0.001	<0.001	<0.001
FPG, mg/dL	n	322	732	125
	Baseline	185.7 (75.3)	184.9 (62.0)	177.5 (59.5)
	Week 24	157.9 (58.5)	140.0 (50.3)	141.5 (48.8)
	Change	–27.8 (92.5)	–44.9 (73.3)	–36.0 (67.4)
	p	<0.001	<0.001	<0.001
PPPG, mg/dL	n	233	481	74
	Baseline	254.4 (85.7)	246.7 (74.2)	255.7 (74.6)
	Week 24	204.0 (69.4)	198.9 (68.2)	183.4 (66.4)
	Change	–50.4 (103.4)	–47.8 (94.3)	–72.4 (92.5)
	p	<0.001	<0.001	–
Weight, kg	n	374	803	135
	Baseline	74.0 (12.9)	74.5 (13.2)	75.6 (12.2)
	Week 24	75.9 (12.8)	75.0 (12.9)	76.4 (11.5)
	Change	1.9 (4.2)	0.4 (3.4)	0.8 (4.2)
	p	<0.001	<0.001	0.023
SBP, mmHg	n	375	794	131
	Baseline	129.1 (17.6)	132.0 (19.0)	131.4 (17.9)
	Week 24	127.9 (16.9)	131.0 (28.2)	129.6 (16.8)
	Change	–1.2 (17.3)	–1.0 (28.4)	–1.7 (16.8)
	p	0.177	0.317	0.246
Total cholesterol, mmol/L	n	237	528	99
	Baseline	4.5 (1.1)	4.5 (1.1)	4.6 (1.1)
	Week 24	4.5 (1.0)	4.3 (1.0)	4.3 (1.0)
	Change	0.0 (1.2)	–0.1 (1.2)	–0.2 (1.2)
	p	0.842	0.018	–
Triglycerides, mmol/L	n	252	560	107
	Baseline	1.5 (0.9)	1.6 (0.9)	1.5 (0.7)
	Week 24	1.4 (0.6)	1.5 (0.7)	1.5 (0.6)
	Change	–0.1 (0.9)	–0.1 (0.9)	–0.0 (0.8)
	p	0.25	0.003	0.687
HDL cholesterol, mmol/L	n	152	296	62
	Baseline	1.2 (0.5)	1.1 (0.4)	1.2 (0.5)
	Week 24	1.2 (0.3)	1.1 (0.4)	1.2 (0.4)
	Change	0.0 (0.5)	0.0 (0.5)	–0.0 (0.6)
	p	0.939	0.56	–
LDL cholesterol, mmol/L	n	153	297	60
	Baseline	2.8 (1.7)	2.8 (1.2)	2.8 (1.1)
	Week 24	2.8 (1.5)	2.7 (0.9)	2.7 (0.8)
	Change	0.0 (2.2)	–0.1 (1.3)	–0.1 (1.0)
	p	0.942	0.073	–

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Table 3 – (*continued*)

Parameter		BIAsp 30	IDet	IAsp + basal
Hypoglycaemia (events per patient-year/percent with at least one event)				
Overall	Baseline	6.45/19.2	3.59/9.8	10.40/20.7
	Week 24	6.22/19.0	2.46/7.6	6.59/20.3
	p[a]	0.9191	0.0522	0.6547
Major	Baseline	0.22/1.2	0.26/0.9	0.35/2.0
	Week 24	0.34/0.8	0.00/0.0	0.00/0.0
	p[a]	0.4795	0.0047	0.0833
Minor	Baseline	6.24/18.9	3.33/9.4	10.05/20.0
	Week 24	5.88/18.5	2.46/7.6	6.59/20.3
	p[a]	1	0.1129	0.763
Nocturnal	Baseline	3.02/10.3	1.22/4.5	4.68/12.0
	Week 24	2.20/7.9	0.97/2.9	1.22/5.8
	p[a]	0.3452	0.0469	0.0253

BIAsp 30, biphasic insulin aspart 30; FPG, fasting plasma glucose; HbA_{1c}, glycated haemoglobin A_{1c}; HDL, high-density lipoprotein; IAsp, insulin aspart; IDet, insulin detemir; LDL, low-density lipoprotein; PPPG, postprandial plasma glucose; SBP, systolic blood pressure.
Only 7 patients were treated with IAsp; hence, the results are not reported here.
Baseline, Week 24 and change values are mean (SD).
p-values are not presented when the number of patients analysed was less than 100.
[a] p-value is from McNemar's test on paired proportions of patients experiencing hypoglycaemia.

of medical writing services, and in reviewing the manuscript, but not in participant selection, choice of therapies (study or otherwise), provision of therapies including insulin or continuing clinical management of the participants.

Acknowledgements

The authors would like to thank all participants who provided data, and all investigators involved in the A_1chieve study. The authors would like to thank Chunduo Shen of Novo Nordisk for providing statistical analysis. The authors would also like to thank Anjali Philip of Cognizant Technology Solutions for writing assistance, funded by Novo Nordisk.

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Table 4 – Safety and effectiveness outcomes by regimen – regional data for Algeria

Parameter		Centre East Algeria		Centre West Algeria		East Algeria		West Algeria	
		BIAsp 30	IDet	BIAsp 30	IDet	BIAsp 30	IDet	BIAsp 30	IDet
Insulin dose, U/day	n	40	107	173	413	60	188	144	155
	Pre-study	35.7 (14.5)	20.4 (8.5)	36.2 (16.7)	22.4 (11.7)	32.1 (16.0)	29.2 (16.2)	44.3 (17.8)	26.1 (15.0)
	Baseline	38.3 (11.7)	14.1 (6.3)	36.6 (16.4)	13.5 (7.1)	31.5 (16.0)	15.3 (8.4)	39.5 (15.9)	15.1 (9.1)
	Week 24	52.0 (16.8)	28.2 (14.4)	47.6 (18.6)	23.8 (11.7)	43.8 (21.9)	28.1 (16.7)	48.9 (17.6)	26.5 (16.1)
HbA_{1c}, %/mmol/mol	n	28	82	119	321	41	162	74	95
	Baseline	9.7 (2.4)/83 (26)	9.4 (1.9)/79 (21)	9.3 (1.9)/78 (21)	9.2 (1.7)/77 (19)	9.4 (1.9)/79 (21)	9.2 (1.8)/77 (20)	9.2 (2.1)/77 (23)	8.6 (1.6)/70 (17)
	Week 24	7.8 (1.6)/62 (17)	7.5 (1.3)/58 (14)	8.1 (1.3)/65 (14)	7.9 (1.5)/63 (16)	7.9 (1.6)/63 (17)	7.9 (1.6)/63 (17)	8.0 (1.7)/64 (19)	8.0 (1.6)/64 (17)
	Change	−1.9 (2.6)/−21 (28)	−1.9 (2.2)/−21 (24)	−1.2 (2.0)/−13 (22)	−1.3 (1.7)/−14 (19)	−1.5 (2.1)/−16 (23)	−1.3 (2.1)/−14 (23)	−1.1 (2.5)/−12 (27)	−0.5 (1.8)/−5 (20)
		–	–	<0.001	<0.001	–	<0.001	–	–
FPG, mg/dL	n	19	78	134	347	54	174	115	133
	Baseline	194.8 (72.2)	195.0 (61.7)	181.9 (71.7)	189.0 (59.9)	183.8 (66.5)	191.2 (65.4)	189.6 (84.1)	159.8 (57.2)
	Week 24	153.9 (51.1)	134.8 (47.5)	159.6 (59.5)	140.1 (50.3)	139.6 (48.2)	137.2 (49.7)	165.3 (61.7)	146.4 (52.7)
	Change	−41.0 (89.8)	−60.2 (66.7)	−22.2 (92.6)	−48.9 (70.8)	−44.2 (83.6)	−54.0 (74.3)	−24.4 (96.7)	−13.4 (74.2)
	p	–	–	0.006	<0.001	–	<0.001	0.008	0.039
PPPG, mg/dL	n	16	54	87	169	42	159	88	99
	Baseline	246.9 (86.3)	249.0 (66.2)	264.0 (79.2)	245.9 (64.2)	238.9 (87.9)	260.5 (85.2)	253.7 (90.9)	224.6 (70.9)
	Week 24	232.2 (66.3)	193.8 (44.1)	201.5 (67.2)	191.7 (67.8)	194.3 (77.6)	206.0 (72.3)	205.9 (67.7)	202.5 (72.3)
	Change	−14.7 (116.3)	−55.2 (64.6)	−62.5 (90.8)	−54.2 (84.1)	−44.6 (110.8)	−54.5 (107.2)	−47.8 (108.8)	−22.1 (98.8)
	p	–	–	–	<0.001	–	<0.001	–	–
Weight, kg	n	32	100	158	371	56	184	128	148
	Baseline	68.2 (10.3)	72.6 (11.1)	76.1 (13.7)	75.3 (13.4)	74.3 (10.8)	73.9 (13.6)	72.8 (12.8)	74.9 (13.6)
	Week 24	69.2 (10.7)	73.1 (11.2)	77.9 (13.6)	75.7 (12.9)	75.5 (10.5)	74.5 (13.6)	75.1 (12.6)	75.3 (13.0)
	Change	1.0 (2.8)	0.4 (2.5)	1.9 (4.2)	0.4 (3.5)	1.2 (3.5)	0.6 (3.1)	2.4 (4.6)	0.4 (4.2)
	p	–	0.095	<0.001	0.027	–	0.007	<0.001	0.297
SBP, mmHg	n	32	101	157	362	58	183	128	148
	Baseline	131.7 (15.7)	132.6 (20.8)	130.5 (14.5)	131.3 (15.7)	132.2 (24.6)	135.3 (21.4)	125.4 (17.3)	129.4 (21.6)
	Week 24	130.9 (18.3)	138.7 (65.5)	131.2 (16.0)	131.2 (15.4)	128.1 (20.8)	130.3 (19.0)	123.1 (14.4)	126.0 (16.4)
	Change	−0.8 (14.6)	6.2 (62.8)	0.6 (16.5)	−0.1 (16.4)	−4.1 (21.8)	−4.9 (20.7)	−2.3 (16.5)	−3.3 (20.4)
	p	–	0.326	0.623	0.913	–	0.002	0.123	0.05
Total cholesterol, mmol/L	n	8	29	113	272	42	148	74	79
	Baseline	4.9 (0.8)	4.3 (1.0)	4.5 (1.2)	4.4 (1.1)	4.5 (1.2)	4.6 (1.1)	4.5 (1.0)	4.6 (1.2)
	Week 24	4.6 (1.4)	4.1 (1.3)	4.5 (1.0)	4.3 (1.0)	4.4 (1.0)	4.3 (0.9)	4.7 (1.0)	4.4 (1.0)
	Change	−0.3 (1.9)	−0.2 (1.6)	−0.0 (1.1)	−0.0 (1.2)	−0.1 (1.3)	−0.2 (1.0)	0.2 (1.1)	−0.1 (1.2)
	p	–	–	0.909	0.504	–	0.006	–	–

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Table 4 – *(continued)*

Parameter		Centre East Algeria		Centre West Algeria		East Algeria		West Algeria	
		BIAsp 30	IDet	BIAsp 30	IDet	BIAsp 30	IDet	BIAsp 30	IDet
Triglycerides, mmol/L	n	7	31	128	297	42	152	75	80
	Baseline	1.8 (0.9)	1.7 (0.9)	1.6 (1.1)	1.7 (1.1)	1.3 (0.5)	1.6 (0.8)	1.4 (0.7)	1.4 (0.7)
	Week 24	1.3 (0.7)	1.6 (0.9)	1.4 (0.6)	1.5 (0.7)	1.4 (0.7)	1.5 (0.7)	1.3 (0.6)	1.3 (0.6)
	Change	–0.5 (0.7)	–0.1 (1.1)	–0.1 (1.1)	–0.1 (1.0)	0.1 (0.7)	–0.1 (0.8)	–0.0 (0.6)	–0.1 (0.7)
	p	–	–	0.212	0.04	–	0.124	–	–
HDL cholesterol, mmol/L	n	5	19	67	109	36	127	44	41
	Baseline	1.1 (0.3)	1.0 (0.3)	1.1 (0.4)	1.1 (0.4)	1.1 (0.5)	1.1 (0.3)	1.3 (0.6)	1.3 (0.5)
	Week 24	1.1 (0.5)	1.0 (0.3)	1.2 (0.3)	1.2 (0.5)	1.2 (0.4)	1.1 (0.3)	1.1 (0.3)	1.2 (0.4)
	Change	0.0 (0.2)	–0.0 (0.4)	0.1 (0.5)	0.0 (0.6)	0.1 (0.5)	0.0 (0.4)	–0.2 (0.6)	–0.1 (0.7)
	p	–	–	–	0.468	–	0.153	–	–
LDL cholesterol, mmol/L	n	5	18	70	114	36	127	42	38
	Baseline	2.4 (0.6)	2.6 (1.0)	3.1 (2.2)	2.9 (1.4)	2.5 (1.2)	2.8 (0.9)	2.6 (0.8)	2.7 (1.3)
	Week 24	2.8 (1.7)	2.5 (0.9)	3.0 (1.9)	2.7 (1.0)	2.4 (0.8)	2.6 (0.9)	2.9 (0.8)	2.8 (1.0)
	Change	0.4 (1.9)	–0.1 (1.2)	–0.1 (2.9)	–0.2 (1.7)	–0.1 (1.5)	–0.2 (1.0)	0.3 (0.9)	0.2 (1.1)
	p	–	–	–	0.226	–	0.041	–	–
Hypoglycaemia (events per patient-year/percent with event)									
Overall	Baseline	6.83/20.0	4.01/8.4	6.46/16.2	2.05/7.0	7.58/25.0	6.85/13.8	5.87/20.1	3.44/13.5
	Week 24	4.06/15.6	1.91/4.9	7.85/18.9	2.36/6.8	8.07/29.3	3.82/11.4	3.93/15.5	1.40/6.7
	p[a]	0.5271	0.285	0.5465	0.884	0.285	0.398	0.3532	0.0164
Major	Baseline	0.00/0.0	0.12/0.9	0.30/1.7	0.09/0.5	0.00/0.0	0.76/1.6	0.27/1.4	0.17/1.3
	Week 24	0.00/0.0	0.00/0.0	0.82/1.9	0.00/0.0	0.00/0.0	0.00/0.0	0.00/0.0	0.00/0.0
	p[a]	–	0.3173	1	0.1573	–	0.0833	0.1573	0.1573
Minor	Baseline	6.83/20.0	3.89/7.5	6.16/16.2	1.95/6.8	7.58/25.0	6.09/13.3	5.60/19.4	3.27/12.9
	Week 24	4.06/15.6	1.91/4.9	7.03/17.6	2.36/6.8	8.07/29.3	3.82/11.4	3.93/15.5	1.40/6.7
	p[a]	0.5271	0.4054	0.7576	1	0.285	0.4927	0.4497	0.033
Nocturnal	Baseline	1.95/7.5	1.94/3.7	3.31/10.4	0.76/3.6	3.03/11.7	1.66/5.9	2.98/10.4	1.43/5.8
	Week 24	0.41/3.1	1.27/3.9	3.19/9.4	1.16/3.2	2.47/10.3	1.13/3.8	1.31/6.2	0.09/0.7
	p[a]	0.5637	1	0.8474	0.5485	1	0.3173	0.2253	0.0047

BIAsp 30, biphasic insulin aspart 30; FPG, fasting plasma glucose; HbA_{1c}, glycated haemoglobin A_{1c}; HDL, high-density lipoprotein; IDet, insulin detemir; LDL, low-density lipoprotein; PPPG, postprandial plasma glucose; SBP, systolic blood pressure.
Baseline, Week 24 and change values are mean (SD).
p-values are not presented when the number of patients analysed was less than 100.
[a] p-value is from McNemar's test on paired proportions of patients experiencing hypoglycaemia.

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