Original Article

Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the Karnataka cohort of the A_1chieve study

Neeta Deshpande, Vageesh Ayyar[1], Rajkumar Channabasavaiah[2], Raman Shetty[2], Anish Behl[3]

Belgaum Diabetes Centre, Belgaum, [1]St. John's Medical College, [2]Novo Nordisk India Pvt. Ltd., Bangalore, [3]Apollo BGS Hospitals, Mysore, Karnataka, India

ABSTRACT

Background: The A_1chieve, a multicentric (28 countries), 24-week, non-interventional study evaluated the safety and effectiveness of insulin detemir, biphasic insulin aspart and insulin aspart in people with T2DM (n = 66,726) in routine clinical care across four continents. **Materials and Methods:** Data was collected at baseline, at 12 weeks and at 24 weeks. This short communication presents the results for patients enrolled from Karnataka, India. **Results:** A total of 2243 patients were enrolled in the study. Four different insulin analogue regimens were used in the study. Patients had started on or were switched to biphasic insulin aspart (n = 1855), insulin detemir (n = 211), insulin aspart (n = 111), basal insulin plus insulin aspart (n = 16) and other insulin combinations (n = 40). At baseline glycaemic control was poor for both insulin naïve (mean HbA_1c: 9.2%) and insulin user (mean HbA_1c: 9.0%) groups. After 24 weeks of treatment, both the groups showed improvement in HbA_1c (insulin naïve: −1.4%, insulin users: −1.7%). SADRs including major hypoglycaemic events or episodes did not occur in any of the study patients. **Conclusion:** Starting or switching to insulin analogues was associated with improvement in glycaemic control with a low rate of hypoglycaemia.

Key words: A_1chieve study, insulin analogues, Karnataka, type 2 diabetes mellitus

Introduction

62.4 million Indians were reported to have type 2 diabetes mellitus (T2DM) putting India on the forefront of diabetic epidemic across globe.[1,2] Fear of hypoglycaemia and gain in body weight are barriers for initiation of insulin therapy.[3] Modern insulin analogues are a convenient new approach or tool to glycaemic control, associated with low number of hypoglycaemia and favourable weight change.[4] A_1chieve, a multinational, 24-week, non-interventional study, assessed the safety and effectiveness of insulin analogues in people with T2DM (n = 66,726) in routine clinical care.[5] This short communication presents the results for patients enrolled from Karnataka, India.

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Materials and Methods

Please refer to editorial titled: The A1chieve study: Mapping the Ibn Battuta trail

Results

A total of 2243 patients were enrolled in the study. The patient characteristics for the entire cohort divided as insulin-naïve and insulin users is shown in Table 1. Glycaemic control at baseline was poor in this population. The majority of patients (82.7%) started on or switched to biphasic insulin aspart. Other groups were insulin detemir (n = 211), insulin aspart (n = 111), basal insulin plus insulin aspart (n = 16) and other insulin combinations (n = 40).

Corresponding Author: Dr. Raman Shetty, Novo Nordisk India Pvt. Ltd., Plot No.32, 47 - 50, EPIP Area, Whitefield, Bangalore, India.
E-mail: rasy@novonordisk.com

After 24 weeks of treatment, overall hypoglycaemic events reduced from 0.8 events/patient-year to 0.0 events/patient-year in insulin naïve group and from 6.4 events/patient-year to 0.1 events/patient-year in insulin users group. No hypoglycaemic episode in insulin naive group at 24 weeks suggests low event rate than insulin users at baseline. SADRs including major hypoglycaemic events did not occur in any of the study patients. Though blood pressure has shown a decreasing trend in the total cohort, but the finding was limited by number of observations. Quality of life improved at 24 weeks [Table 2 and 3].

All parameters of glycaemic control improved from baseline to study end in the total cohort [Table 4].

Table 1: Overall demographic data

Parameters	Insulin naïve	Insulin users	All
Number of participants	2035	208	2243
Male *N* (%)	1460 (71.7)	137 (65.9)	1597 (71.2)
Female *N* (%)	575 (28.3)	71 (34.1)	646 (28.8)
Age (years)	50.0	54.3	50.4
Weight (kg)	73.2	72.3	73.1
BMI (kg/m^2)	28.2	27.6	28.2
Duration of DM (years)	5.5	8.9	5.8
No therapy	21		
>2 OGLD	105	43	148
HbA$_1$c	9.2	9.0	9.2
FPG (mmol/L)	13.0	10.4	12.9
PPPG (mmol/L)	18.0	16.3	18.0
Macrovascular complications, *N* (%)	104 (5.1)	65 (31.3)	169 (7.6)
Microvascular complications, *N* (%)	168 (8.3)	91 (43.8)	259 (11.6)
Pre-study therapy, *N* (%)			
Insulin users			208 (9.3)
OGLD only			2014 (89.8)
No therapy			21 (0.9)
Baseline therapy, *N* (%)			
Insulin detemir±OGLD			211 (9.4)
Insulin aspart±OGLD			111 (5.0)
Basal+insulin aspart±OGLD			16 (0.7)
Biphasic insulin aspart±OGLD			1855 (82.7)
Others			40 (1.8)
Missing			10 (0.5)

BMI: Body mass index, OGLD: Oral glucose-lowering drug, HbA$_1$c: Glycated hemoglobin A$_1$c, FPG: Fasting plasma glucose, PPPG: Postprandial plasma glucose, DM: Diabetes mellitus

Biphasic insulin aspart ± OGLD

Of the total cohort, 1855 patients started on biphasic insulin aspart ± OGLD, of which 1682 (90.7%) were insulin naïve and 173 (9.3%) were insulin users. After 24 weeks of starting or switching to biphasic insulin aspart, hypoglycaemic events reduced for both insulin naïve (from 0.8 events/patient-year to 0.0 events/patient-year) and insulin user (from 7.7 events/patient-year to 0.1 events/patient-year) groups. Body weight decreased and quality of life improved at 24 weeks [Table 5 and 6].

All parameters of glycaemic control improved from baseline to study end in those who started on or were switched to biphasic insulin aspart for both insulin naïve and insulin user groups [Table 7].

Basal + insulin aspart ± OGLD

Of the total cohort, 16 patients started on basal + insulin aspart ± OGLD of which 10 (31.2%) were insulin naïve and 6 (68.8%) were insulin users. After 24 weeks of starting or switching to Basal + insulin aspart, hypoglycaemic events reduced from 4.7 events/patient-year to 0.0 events/patient-year in insulin naïve group, whereas hypoglycaemia was nil in insulin users similar to baseline. Quality of life improved after 24 weeks of treatment [Table 8 and 9].

Table 2: Overall safety data

Parameter	*N*	Baseline	Week 24	Change from baseline
Hypoglycaemia (insulin naïve), events/patient-year				
All	2035	0.8	0.0	−0.8
Nocturnal		0.0	0.0	0.0
Major		0.0	0.0	0.0
Hypoglycaemia (insulin users), events/patient-year				
All	208	6.4	0.1	−6.3
Nocturnal		1.8	0.0	−1.8
Major		1.2	0.0	−1.2
Body weight, kg				
Insulin naïve	675	72.6	71.8	−0.8
Insulin users	50	69.4	69.5	0.1
BP (insulin naïve)				
SBP, mean (mmHg), (N, % <130 mmHg)	1338	144.4 (135, 10.1)	131.8 (204, 36.2)	−12.5
BP (insulin users)				
SBP, mean (mmHg), (N, % <130 mmHg)	166	150.0 (27, 16.3)	136.4 (9, 26.5)	−13.6
Quality of life, VAS Scale (0-100)				
Insulin naïve	1416	81.7	84.3	2.6
Insulin users	35	74.4	84.2	9.8

BP: Blood pressure, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TG: Triglycerides, SBP: Systolic blood pressure, VAS: Visual analogue scale

Mean HbA$_1$c and PPPG values improved from baseline to study end in those who started on or were switched to basal + insulin aspart ± OGLDs for insulin naïve group. FPG values deteriorated for this group [Table 10].

Insulin detemir ± OGLD

Of the total cohort, 211 patients started on insulin detemir ± OGLD, of which 203 (78.5%) were insulin naïve and 8 (21.5%) were insulin users. After 24 weeks of starting or switching to insulin detemir, hypoglycaemic events reduced from 0.8 events/patient-year to 0.0 events/patient-year in insulin naïve group, whereas hypoglycaemia was nil in insulin users similar to baseline. A decrease in body weight and improvement in quality of life was also observed at the end of the study [Table 11 and 12].

All parameters of glycaemic control improved from

Table 3: Insulin dose

Insulin dose, U/day	*N*	Pre-study	*N*	Baseline	*N*	Week 24
Insulin naïve	0	0.0	2026	28.8	1724	23.9
Insulin users	208	28.9	207	28.2	125	28.9

Table 4: Overall efficacy data

Parameter	*N*	Baseline	Week 24	Change from baseline
Glycaemic control (insulin naïve)				
HbA$_1$c, mean (%)	1154	9.2	7.8	−1.4
FPG, mean (mmol/L)	1044	13.0	10.6	−2.4
PPPG, mean (mmol/L)	708	18.0	13.3	−4.7
Glycaemic control (insulin users)				
HbA$_1$c, mean (%)	101	9.0	7.3	−1.7
FPG, mean (mmol/L)	46	10.4	8.0	−2.4
PPPG, mean (mmol/L)	32	16.3	10.7	−5.6
Achievement of HbA$_1$c <7.0% at week 24				
Insulin naïve (% of patients)	1513	13.3%		
Insulin users (% of patients)	118	17.8%		

HbA$_1$c: Glycated haemoglobin A$_1$c, FPG: Fasting plasma glucose, PPPG: Postprandial plasma glucose

Table 5: Biphasic insulin aspart±oral glucose-lowering drug safety data

Parameter	*N*	Baseline	Week 24	Change from baseline
Hypoglycaemia, events/patient-year				
Insulin naïve	1682	0.8	0.0	−0.8
Insulin users	173	7.7	0.1	−7.6
Body weight, kg				
Insulin naïve	541	72.5	71.7	−0.8
Insulin users	37	69.2	68.9	−0.3
Quality of life, VAS scale (0-100)				
Insulin naïve	1145	81.9	84.3	2.4
Insulin users	21	80.0	85.1	5.2

VAS: Visual analogue scale

Table 6: Insulin dose

Insulin dose, U/day	*N*	Pre-study	*N*	Baseline	*N*	Week 24
Insulin naïve	0	0.0	1682	30.1	1429	24.1
Insulin users	173	28.0	173	27.3	100	28.8

Table 7: Biphasic insulin aspart±oral glucose-lowering drug efficacy data

Parameter	*N*	Baseline	Week 24	Change from baseline
Glycaemic control (insulin naïve)				
HbA$_1$c, mean (%)	951	9.2	7.7	−1.4
FPG, mean (mmol/L)	870	13.0	10.5	−2.5
PPPG, mean (mmol/L)	583	17.9	13.1	−4.8
Glycaemic control (insulin users)				
HbA$_1$c, mean (%)	82	8.8	7.3	−1.5
FPG, mean (mmol/L)	36	10.2	8.4	−1.9
PPPG, mean (mmol/L)	28	16.2	11.1	−5.1

HbA$_1$c: Glycated haemoglobin A$_1$c, FPG: Fasting plasma glucose, PPPG: Postprandial plasma glucose

Table 8: Basal+insulin aspart±oral glucose-lowering drug safety data

Parameter	*N*	Baseline	Week 24	Change from baseline
Hypoglycaemia, events/patient-year				
Insulin naïve	11	4.7	0.0	−4.7
Insulin users	5	0.0	0	0.0
Body weight, kg				
Insulin naïve	2	75.0	75.4	0.4
Quality of life, VAS scale (0-100)				
Insulin naïve	6	83.2	83.2	0.0

VAS: Visual analogue scale

Table 9: Insulin dose

Insulin dose, U/day	*N*	Pre-study	*N*	Baseline	*N*	Week 24
Insulin naïve	0	0.0	11	36.0	6	27.0
Insulin users	5	47.2	5	28.8	-	-

Table 10: Basal+insulin aspart±oral glucose-lowering drug efficacy data

Parameter	*N*	Baseline	Week 24	Change from baseline
Glycaemic control (insulin naïve)				
HbA$_1$c, mean (%)	6	9.4	7.2	−2.2
FPG, mean (mmol/L)	3	8.4	11.4	3.0
PPPG, mean (mmol/L)	1	21.7	11.6	−10.0

HbA$_1$c: Glycated haemoglobin A$_1$c, FPG: Fasting plasma glucose, PPPG: Postprandial plasma glucose

Table 11: Insulin detemir±oral glucose-lowering drug safety data

Parameter	*N*	Baseline	Week 24	Change from baseline
Hypoglycaemia, events/patient-year				
Insulin naïve	203	0.8	0.0	−0.8
Insulin users	8	0.0	0.0	0.0
Body weight, kg				
Insulin naïve	82	73.2	71.9	−1.2
Insulin users	2	60.5	59.0	−1.5
Quality of life, VAS scale (0-100)				
Insulin naïve	160	82.4	84.8	2.3
Insulin users	3	58.3	85.0	26.7

VAS: Visual analogue scale

Table 12: Insulin dose

Insulin dose, U/day	*N*	Pre-study	*N*	Baseline	*N*	Week 24
Insulin naïve	0	0.0	203	15.2	177	21.5
Insulin users	8	28.6	8	20.1	8	27.8

Table 13: Insulin detemir±oral glucose-lowering drug efficacy data

Parameter	*N*	Baseline	Week 24	Change from baseline
Glycaemic control (insulin naïve)				
HbA_1c, mean (%)	119	9.1	8.0	−1.1
FPG, mean (mmol/L)	118	13.6	11.2	−2.4
PPPG, mean (mmol/L)	88	18.4	14.3	−4.0
Glycaemic control (insulin users)				
HbA_1c, mean (%)	5	7.9	7.2	−0.7
FPG, mean (mmol/L)	1	10.0	6.6	−3.4

HbA_1c: Glycated haemoglobin A_1c, FPG: Fasting plasma glucose, PPPG: Postprandial plasma glucose

baseline to study end in those who started on or were switched to insulin detemir ± OGLDs for insulin-naïve group while mean HbA_1c and FPG values improved in insulin users [Table 13].

Insulin aspart ± OGLD

Of the total cohort, 111 patients started on insulin aspart ± OGLD, of which 106 (95.5%) were insulin naïve and 5 (4.5%) were insulin users. After 24 weeks of starting or switching to insulin aspart, hypoglycaemic events decreased from 0.5 events/patient year to 0.0 in insulin naïve group and from 2.6 events/patient-year to 0.0 events/patient-year in insulin user group. Quality of life improved after 24 weeks of treatment [Table 14 and 15].

All parameters of glycaemic control improved from baseline to study end in those who started on or were switched to insulin aspart ± OGLDs for both insulin naïve and insulin user groups [Table 16].

Table 14: Insulin aspart±oral glucose-lowering drug safety data

Parameter	*N*	Baseline	Week 24	Change from baseline
Hypoglycaemia, events/patient-year				
Insulin naïve	106	0.5	0.0	−0.5
Insulin users	5	2.6	0.0	−2.6
Body weight, kg				
Insulin naïve	39	72.5	71.8	−0.7
Insulin users	3	77.0	77.1	0.1
Quality of life, VAS scale (0-100)				
Insulin naïve	84	81.4	83.9	2.5
Insulin users	1	82.0	90.0	9.0

VAS: Visual analogue scale

Table 15: Insulin dose

Insulin dose, U/day	*N*	Pre-study	*N*	Baseline	*N*	Week 24
Insulin naïve	0	0.0	106	30.1	83	23.5
Insulin users	5	26.8	5	31.6	4	29.5

Table 16: Insulin aspart±oral glucose-lowering drug efficacy data

Parameter	*N*	Baseline	Week 24	Change from baseline
Glycaemic control (insulin naïve)				
HbA_1c, mean (%)	52	9.5	7.9	−1.6
FPG, mean (mmol/L)	43	13.8	11.5	−2.3
PPPG, mean (mmol/L)	29	18.7	14.6	−4.1
Glycaemic control (insulin users)				
HbA_1c, mean (%)	3	9.8	7.1	−2.7
FPG, mean (mmol/L)	3	11.1	6.8	−4.3
PPPG, mean (mmol/L)	3	16.8	9.6	−7.2

HbA_1c: Glycated haemoglobin A_1c, FPG: Fasting plasma glucose, PPPG: Postprandial plasma glucose

Conclusion

Our study reports improved glycaemic control and quality of life following 24 weeks of treatment with any of the insulin analogues (Biphasic insulin aspart; basal + insulin aspart; insulin detemir; insulin aspart) with or without OGLD. SADRs including major hypoglycaemic events or episodes did not occur in any of the study patients. Overall, body weight reduced in insulin naïve group and a small increase in weight was noted for insulin users. Though the findings are limited by number of patients, still the trend indicates that insulin analogues can be considered effective and possess a safe profile for treating type 2 diabetes in Karnataka, India.

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