Original Article

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

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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 Tamil Nadu, India. **Results:** A total of 2221 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 = 1707), insulin detemir (n = 270), insulin aspart (n = 85), basal insulin plus insulin aspart (n = 79) and other insulin combinations (n = 80). At baseline glycaemic control was poor for both insulin naïve (mean HbA_1c: 9.2%) and insulin user (mean HbA_1c: 9.2%) groups. After 24 weeks of treatment, both the groups showed improvement in HbA_1c (insulin naïve: –1.7%, insulin users: –1.7%). SADRs including major hypoglycaemic events 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, Tamil Nadu, 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 Tamil Nadu, 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 2221 patients were enrolled in the study. The patient characteristics for the entire cohort divided as insulin-naïve and insulin users is shown in the Table 1. Glycaemic control at baseline was poor in this population. The majority of patients (76.86%) started on or were switched to biphasic insulin aspart. Other groups were insulin detemir (n = 270), insulin aspart (n = 85), basal

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insulin plus insulin aspart (n = 79) and other insulin combinations (n = 80).

Table 1: Overall demographic data

Parameters	Insulin naïve	Insulin users	All
Number of participants	1664	557	2221
Male *N* (%)	1003 (60.3)	329 (59.2)	1332 (60.1)
Female *N* (%)	659 (39.7)	227 (40.8)	886 (39.9)
Age (years)	51.3	55.7	52.4
Weight (kg)	67.8	70.4	68.4
BMI (kg/m^2)	26.1	27.2	26.4
Duration of DM (years)	7.9	12.8	9.2
No therapy	-	-	158
>2 OGLD	356	220	576
HbA$_1$c	9.2	9.2	9.2
FPG (mmol/L)	10.3	10.7	10.4
PPPG (mmol/L)	15.7	15.5	15.6
Macrovascular complications, *N* (%)	228 (13.8)	163 (29.3)	391 (17.7)
Microvascular complications, *N* (%)	845 (51.2)	430 (77.3)	1275 (57.7)
Pre-study therapy, *N* (%)			
Insulin users			557 (25.08)
OGLD only			1506 (67.81)
No therapy			158 (7.11)
Baseline therapy, *N* (%)			
Insulin detemir±OGLD			270 (12.16)
Insulin aspart±OGLD			85 (3.83)
Basal+insulin aspart±OGLD			79 (3.56)
Biphasic insulin aspart±OGLD			1707 (76.86)
Others			80 (3.60)

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

After 24 weeks of treatment, overall hypoglycaemia reduced from 1.1 events/patient-year to 0.6 events/patient-year in insulin naïve group and from 3.9 events/patient-year to 2.0 events/patient-year in insulin users group. The hypoglycaemia incidence in insulin naive group at 24 weeks was lower than that observed in insulin users at baseline. SADRs including major hypoglycaemic events did not occur in any of the study patients. Blood pressure decreased from baseline, while overall lipid profile and quality of life improved at week 24 in total cohort [Table 2 and 3].

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

Biphasic insulin aspart ± OGLD

Of the total cohort, 1707 patients started on biphasic insulin aspart ± OGLD, of which 1314 (77.0%) were insulin naïve and 393 (23.0%) were insulin users. After 24 weeks of starting or switching to biphasic insulin aspart, hypoglycaemic events reduced from 0.9 events/patient-year to 0.6 events/patient-year in insulin naïve group and from 3.4 events/patient-year to 1.8 events/patient-year in insulin users. Quality of life improved at the end of the study [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 group [Table 7].

Table 2: Overall safety data

Parameter	*N*	Baseline	Week 24	Change from baseline
Hypoglycaemia (insulin naïve), events/patient-year				
All	1664	1.1	0.6	−0.5
Nocturnal		0.1	0.0	−0.1
Major		0.1	0.0	−0.1
Hypoglycaemia (insulin users), events/patient-year				
All	557	3.9	2.0	−1.9
Nocturnal		0.8	0.4	−0.4
Major		0.7	0.0	−0.7
Body weight, kg				
Insulin naïve	1382	67.6	67.9	0.3
Insulin users	459	69.8	70.2	0.4
Lipids and BP (insulin naïve)				
LDL-C, mean (mmol/L), (*N*, % <2.5 mmol/L)	687	3.0 (217, 31.6%)	2.6 (221, 46.1%)	−0.4
HDL-C, mean (mmol/L), (*N*, % >1.0 mmol/L)	683	1.0 (356, 52.1)	1.1 (313, 65.9)	0.1
TG, mean (mmol/L), (*N*, % <2.3 mmol/L)	663	2.0 (468, 70.6)	1.6 (381, 91.1)	−0.4
SBP, mean (mmHg), (*N*, % <130 mmHg)	1503	131.4 (694, 46.2)	127.4 (803, 56.7)	−4.0
Lipids and BP (insulin users)				
LDL-C, mean (mmol/L), (*N*, % <2.5 mmol/L)	398	2.7 (171, 43.0%)	2.4 (169, 60.4)	−0.3
HDL-C, mean (mmol/L), (*N*, % >1.0 mmol/L)	401	1.0 (210, 52.4)	1.1 (182, 65.2)	0.1
TG, mean (mmol/L), (*N*, % <2.3 mmol/L)	394	2.0 (282, 71.6)	1.7 (238, 88.5)	-0.3
SBP, mean (mmHg), (*N*, % <130 mmHg)	530	137.2 (140, 26.4)	131.6 (183, 36.5)	−5.6
Quality of life, VAS scale (0-100)				
Insulin naïve	1388	60.9	79.4	18.5
Insulin users	489	62.8	77.9	15.2

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

Basal + insulin aspart ± OGLD

Of the total cohort, 79 patients who started on basal + insulin aspart ± OGLD, of which 35 (44.3%) were insulin naïve and 44 (55.7%) were insulin users. After 24 weeks of starting or switching to insulin aspart, hypoglycaemic events reduced from 2.2 events/patient-year to 0.8 events/patient-year in insulin naïve group and from 6.5 events/patient-year to 1.7 events/patient-year in insulin users. Quality of life improved after 24 weeks of treatment [Table 8 and 9].

Table 3: Insulin dose

Insulin dose, U/day	*N*	Pre-study	*N*	Baseline	*N*	Week 24
Insulin naïve	0	0.0	1664	20.0	1529	19.2
Insulin users	557	28.3	557	31.1	521	27.0

Table 4: Overall efficacy data

Parameter	*N*	Baseline	Week 24	Change from baseline
Glycaemic control (insulin naïve)				
HbA$_1$c, mean (%)	1472	9.2	7.5	−1.7
FPG, mean (mmol/L)	1421	10.3	6.7	−3.6
PPPG, mean (mmol/L)	1442	15.7	9.8	−5.9
Glycaemic control (insulin users)				
HbA$_1$c, mean (%)	507	9.2	7.5	−1.7
FPG, mean (mmol/L)	495	10.7	6.8	−3.9
PPPG, mean (mmol/L)	502	15.5	9.9	−5.6
Achievement of HbA$_1$c <7.0% at week 24				
Insulin naïve (% of patients)	1515	23.2%		
Insulin users (% of patients)	511	28.2%		

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	1314	0.9	0.6	−0.3
Insulin users	393	3.4	1.8	1.6
Body weight, kg				
Insulin naïve	1083	67.6	67.9	0.3
Insulin users	324	68.3	68.9	0.6
Quality of life, VAS scale (0-100)				
Insulin naïve	1100	60.6	79.5	18.9
Insulin users	354	62.8	77.9	15.2

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	1314	19.9	1197	19.9
Insulin users	393	25.7	393	26.9	368	25.2

All parameters of glycaemic control improved from baseline to study end in those who started on or switched to basal + insulin aspart ± OGLDs for both insulin naïve and insulin user groups [Table 10].

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 (%)	1149	9.2	7.4	−1.7
FPG, mean (mmol/L)	1107	10.2	6.8	−3.5
PPPG, mean (mmol/L)	1124	15.7	9.8	−5.9
Glycaemic control (insulin users)				
HbA$_1$c, mean (%)	358	9.1	7.4	−1.7
FPG, mean (mmol/L)	349	10.5	6.8	−3.7
PPPG, mean (mmol/L)	355	15.5	9.9	−5.6

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	35	2.2	0.8	−1.4
Insulin users	44	6.5	1.7	−4.8
Bodyweight, kg				
Insulin naïve	28	69.5	69.6	0.1
Insulin users	34	75.3	75.2	−0.1
Quality of life, VAS Scale (0-100)				
Insulin naïve	16	55.6	84.8	29.2
Insulin users	29	62.1	78.0	16.0

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	35	44.5	32	26.9
Insulin users	44	42.2	44	56.5	38	39.8

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 (%)	32	9.6	8.2	−1.4
FPG, mean (mmol/L)	28	11.0	7.6	−3.4
PPPG, mean (mmol/L)	30	15.8	10.4	−5.4
Glycaemic control (insulin users)				
HbA$_1$c, mean (%)	35	9.6	7.7	−1.9
FPG, mean (mmol/L)	37	11.6	6.8	−4.8
PPPG, mean (mmol/L)	37	16.2	9.2	−7.0

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

Insulin detemir ± OGLD

On the total cohort, 270 patients who started on insulin detemir ± OGLD, of which 224 (83.0%) were insulin naïve and 46 (17.0%) were insulin users. After 24 weeks of starting or switching to biphasic insulin detemir, hypoglycaemic events reduced from 2.2 events/patient-year to 0.7 events/patient-year in insulin naïve group and from 4.8 events/patient-year to 2.1 events/patient-year in insulin users group. A small increase in body weight was observed. Quality of life improved at 24 weeks [Table 11 and 12].

All parameters of glycaemic control improved from baseline to study end in those who started on or were switched to insulin detemir ± OGLDs for both insulin-naïve and insulin user groups [Table 13].

Insulin aspart ± OGLD

Of the total cohort, 85 patients who started on insulin aspart ± OGLD, of which 69 (81.2%) were insulin naïve and 16 (18.8%) were insulin users. After 24 weeks of treatment starting or switching to insulin aspart hypoglycaemic events reduced from 15.4 events/patient-year to 5.2 events/patient-year in insulin users group, while hypoglycaemia increased from 0.0 events/patient-year to 0.2 events/patient-year in insulin naïve group. An improvement in quality of life was observed after 24 weeks [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].

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.

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

Parameter	*N*	Baseline	Week 24	Change from baseline
Hypoglycaemia, events/patient-year				
Insulin naïve	224	2.2	0.7	−1.5
Insulin users	46	4.8	2.1	−2.7
Body weight, kg				
Insulin naïve	187	68.1	68.2	0.1
Insulin users	34	70.2	70.4	0.2
Quality of life, VAS scale (0-100)				
Insulin naïve	191	63.8	77.2	13.5
Insulin users	40	62.4	76.7	14.3

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	224	13.4	211	13.5
Insulin users	46	19.8	46	15.3	44	16.3

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

Parameter	*N*	Baseline	Week 24	Change from baseline
Glycaemic control (insulin naïve)				
HbA$_1$c, mean (%)	208	9.2	7.4	−1.8
FPG, mean (mmol/L)	205	10.6	6.4	−4.2
PPPG, mean (mmol/L)	206	15.2	9.5	−5.7
Glycaemic control (insulin users)				
HbA$_1$c, mean (%)	44	9.1	7.5	−1.6
FPG, mean (mmol/L)	43	10.2	6.7	−3.5
PPPG, mean (mmol/L)	43	14.1	9.8	−4.3

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

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

Parameter	*N*	Baseline	Week 24	Change from baseline
Hypoglycaemia, events/patient-year				
Insulin naïve	69	0.0	0.2	0.2
Insulin users	16	15.4	5.2	−10.2
Body weight, kg				
Insulin naïve	67	64.9	65.1	0.1
Insulin users	15	75.7	75.1	−0.6
Quality of life, VAS scale (0-100)				
Insulin naïve	64	58.1	82.0	23.9
Insulin users	15	62.9	80.2	17.3

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	69	22.2	69	18.7
Insulin users	16	40.9	16	37.9	15	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$_1$c, mean (%)	63	9.0	7.4	−1.6
FPG, mean (mmol/L)	63	8.5	6.4	−2.1
PPPG, mean (mmol/L)	64	15.4	9.5	−5.9
Glycaemic control (insulin users)				
HbA$_1$c, mean (%)	14	9.2	7.6	−1.6
FPG, mean (mmol/L)	13	11.2	6.9	−4.3
PPPG, mean (mmol/L)	14	14.8	10.5	−4.2

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

A slight increase in body weight was observed for the total cohort. SADRs including major hypoglycaemic events did not occur in any of the study patients. 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 Tamil Nadu, India.

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