Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the North East India cohort of the A1chieve study

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ABSTRACT

Background: The A1chieve, 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 North East, India. Results: A total of 730 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 = 518), insulin detemir (n = 88), insulin aspart (n = 74), basal insulin plus insulin aspart (n = 19) and other insulin combinations (n = 30). At baseline glycaemic control was poor for both insulin naïve (mean HbA₁c: 9.5%) and insulin users (mean HbA₁c: 9.2%) groups. After 24 weeks of treatment, both groups showed improvement in HbA₁c (insulin naïve: −1.6%, insulin users: −1.5%). 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: A1chieve study, insulin analogues, North East India, 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] A1chieve, 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 North East, India.
insulin plus insulin aspart ($n = 19$) and other insulin combinations ($n = 30$).

After 24 weeks of treatment, overall hypoglycaemic events reduced from 0.9 events/patient-year to 0.5 events/patient-year and from 20.5 events/patient-year to 0.7 events/patient-year in insulin users. The hypoglycaemia incidence in insulin naïve 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 and overall lipid profile improved in the total cohort, but the findings were limited by number of observations. Quality of life improved at the end of the study [Table 2 and 3].

All parameters of glycaemic control improved from baseline to study end in those who started on or were

### Table 1: Overall demographic data

| Parameters                      | Insulin naïve | Insulin users | All     |
|---------------------------------|--------------|--------------|---------|
| Number of participants          | 505          | 225          | 730     |
| Male N (%)                      | 304 (60.2%)  | 162 (72.0%)  | 466 (63.8) |
| Female N (%)                    | 201 (39.8%)  | 63 (28.0%)   | 264 (36.2) |
| Age (years)                     | 52.4         | 56.6         | 53.7    |
| Weight (kg)                     | 63.0         | 64.1         | 63.3    |
| BMI (kg/m²)                     | 23.7         | 23.4         | 23.6    |
| Duration of DM (years)          | 6.0          | 10.0         | 7.3     |
| No therapy                      | 44           |              |         |
| >2 OGLD                         | 12           | 9            | 21      |
| HbA₁c, %                        | 9.5          | 9.2          | 9.4     |
| FPG (mmol/L)                    | 11.8         | 10.5         | 11.4    |
| PPG (mmol/L)                    | 16.5         | 14.9         | 15.6    |
| Macrovascular complications N (%)| 36 (7.1)     | 51 (22.7)    | 87 (11.9) |
| Microvascular complications N (%)| 257 (50.9)   | 174 (77.3)   | 431 (59.0) |
| Pre-study therapy, N (%)        |              |              |         |
| Insulin users                   | 225 (30.82)  |              |         |
| OGLD only                       | 461 (63.15)  |              |         |
| No therapy                      | 44 (6.03)    |              |         |
| Baseline therapy, N (%)         |              |              |         |
| Insulin detemir±OGLD            | 88 (12.05)   |              |         |
| Insulin aspart±OGLD             | 74 (10.14)   |              |         |
| Basal+insulin aspart±OGLD       | 19 (2.60)    |              |         |
| Biphasic insulin aspart±OGLD    | 518 (70.96)  |              |         |
| Others                          | 30 (4.11)    |              |         |
| Missing                         | 1 (0.14)     |              |         |

BMi: Body mass index, OGLD: Oral glucose-lowering drug, HbA₁c: Glycated hemoglobin A₁c, FPG: Fasting plasma glucose, PPG: Postprandial plasma glucose, DM: Diabetes mellitus

### Table 2: Overall safety data

| Parameter                                      | N       | Baseline | Week 24 | Change from baseline |
|------------------------------------------------|---------|----------|---------|----------------------|
| Hypoglycaemia (insulin naïve), events/patient-year |         |          |         |                      |
| All                                            | 505     | 0.9      | 0.5     | −0.4                 |
| Nocturnal                                      |         | 0.3      | 0.2     | −0.1                 |
| Major                                          |         | 0.0      | 0.0     | 0.0                  |
| Hypoglycaemia (insulin users), events/patient-year |         |          |         |                      |
| All                                            | 225     | 20.5     | 0.7     | −19.8                |
| Nocturnal                                      |         | 6.8      | 0.3     | −6.5                 |
| Major                                          |         | 0.9      | 0.0     | −0.9                 |
| Body weight, kg                                |         |          |         |                      |
| Insulin naïve                                  | 308     | 62.0     | 62.1    | 0.1                  |
| Insulin users                                  | 138     | 64.7     | 65.0    | 0.3                  |
| Lipids and BP (insulin naïve)                  |         |          |         |                      |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L)       | 203     | 2.4 (106, 52.2) | 2.3 (49, 77.8) | −0.1 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L)       | 201     | 1.2 (163, 81.1) | 1.2 (60, 95.2) | 0.0 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L)          | 204     | 1.8 (153, 75.0) | 1.5 (55, 91.7) | −0.3 |
| SBP, mean (mmHg), (N, % <130 mmHg)             | 378     | 133.8 (106, 28.0) | 125.6 (128, 68.8) | −8.2 |
| Lipids and BP (insulin users)                  |         |          |         |                      |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L)       | 103     | 2.5 (53, 51.5) | 2.3 (26, 78.8) | −0.2 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L)       | 105     | 1.1 (89, 84.8) | 1.2 (31, 91.2) | 0.1 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L)          | 105     | 1.9 (82, 78.1) | 1.6 (29, 90.6) | −0.3 |
| SBP, mean (mmHg), (N, % <130 mmHg)             | 186     | 130.5 (67, 36.0) | 124.8 (64, 63.4) | −5.7 |
| Quality of life, VAS scale (0-100)             | 9       | 57.6     | 67.6    | 10.0                 |
| Insulin naïve                                  | 9       | 57.1     | 67.2    | 10.1                 |

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
switched to biphasic insulin aspart for both insulin naïve and insulin user groups [Table 7].

**Basal + insulin aspart ± OGLD**

Of the total cohort, 19 patients on started on basal + insulin aspart ± OGLD, of which 5 (26.3%) were insulin naïve and 14 (73.7%) were insulin users. After 24 weeks of treatment, hypoglycaemic events reduced from 17.6 events/patient-year to 0.0 events/patient-year in insulin user group, whereas hypoglycaemia remained nil in insulin naïve group similar to that of baseline. Body weight increased in insulin naïve group whereas it decreased in insulin users. Quality of life improved after 24 weeks of treatment [Table 8 and 9].

Mean HbA1c and FPG values improved from baseline to study end in those who started on or were switched to basal + insulin aspart ± OGLDs for insulin naïve group whereas all aspects of glycaemic control improved in the insulin user group [Table 10].

**Insulin detemir ± OGLD**

Of the total cohort, 88 patients started on insulin detemir ± OGLD, of which 83 (94.3%) were insulin naïve and 05 (5.7%) were insulin users. After 24 weeks of starting or switching to insulin detemir, hypoglycaemic events reduced from 0.3 events/patient-year to 0.0 events/patient-year in

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**Table 3: Insulin dose**

| Insulin dose, U/day | Insulin naïve N | Baseline N | Week 24 N |
|---------------------|----------------|------------|-----------|
| Pre-study 0         | 504            | 20.2       | 349       |
| Baseline 225        | 29.6           | 148        |

**Table 4: Overall efficacy data**

| Parameter | N Baseline | Week 24 | Change from baseline |
|-----------|------------|---------|----------------------|
| HbA1c, mean (%) | 9.5 | 7.9 | -1.5 |
| FPG, mean (mmol/L) | 11.8 | 5.9 | -5.9 |
| PPPG, mean (mmol/L) | 16.5 | 8.6 | -7.9 |

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

| Parameter | N Baseline | Week 24 | Change from baseline |
|-----------|------------|---------|----------------------|
| HbA1c, mean (%) | 9.6 | 7.9 | -1.7 |
| FPG, mean (mmol/L) | 12.2 | 5.9 | -6.3 |
| PPPG, mean (mmol/L) | 17.3 | 8.6 | -8.7 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPPG: Postprandial plasma glucose

**Table 6: Insulin dose**

| Insulin dose, U/day | Pre-study N | Baseline N | Week 24 N |
|---------------------|-------------|------------|-----------|
| Insulin naïve 0     | 365         | 20.3       | 275       |
| Insulin users 153   | 153         | 28.1       | 117       |

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

| Parameter | N Baseline | Week 24 | Change from baseline |
|-----------|------------|---------|----------------------|
| Hypoglycaemia, events/patient-year | 0.0 | 0.0 | 0.0 |
| Insulin naïve 14 | 17.6 | 0.0 | -17.6 |
| Insulin users 2 | 68.0 | 69.5 | 1.5 |

Body weight, kg

| Parameter | N Baseline | Week 24 | Change from baseline |
|-----------|------------|---------|----------------------|
| Insulin naïve 5 | 75.9 | 75.5 | -0.4 |
| Insulin users 6 | 56.5 | 69.2 | 12.7 |

Quality of life, VAS scale (0-100)

| Parameter | N Baseline | Week 24 | Change from baseline |
|-----------|------------|---------|----------------------|
| Insulin naïve 2 | 57.0 | 67.5 | 10.5 |
| Insulin users 6 | 56.5 | 69.2 | 12.7 |

HbA1c: Glycated haemoglobin A1c, 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 | 0.0 | 0.0 | 0.0 |
| Insulin naïve 14 | 17.6 | 0.0 | -17.6 |
| Insulin users 2 | 68.0 | 69.5 | 1.5 |

Body weight, kg

| Parameter | N Baseline | Week 24 | Change from baseline |
|-----------|------------|---------|----------------------|
| Insulin naïve 5 | 75.9 | 75.5 | -0.4 |
| Insulin users 6 | 56.5 | 69.2 | 12.7 |

Quality of life, VAS scale (0-100)

| Parameter | N Baseline | Week 24 | Change from baseline |
|-----------|------------|---------|----------------------|
| Insulin naïve 2 | 57.0 | 67.5 | 10.5 |
| Insulin users 6 | 56.5 | 69.2 | 12.7 |

VAS: Visual analogue scale

**Table 9: Insulin dose**

| Insulin dose, U/day | Pre-study N | Baseline N | Week 24 N |
|---------------------|-------------|------------|-----------|
| Insulin naïve 0     | 5           | 40.8       | 2         |
| Insulin users 14    | 14          | 47.7       | 6         |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPPG: Postprandial plasma glucose
insulin naïve group and from 26.0 events/patient-year to 0.0 events/patient-year in insulin users. Quality of life improved after 24 weeks of treatment [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, 74 patients started on insulin aspart ± OGLD was 74, of which 41 (55.4%) were insulin naïve and 33 (44.6%) were insulin users. After 24 weeks of treatment, hypoglycaemic events reduced from 24.0 to 0.0 in insulin users group whereas hypoglycaemia increased from 0.6 events/patient-year to 1.5 events/patient-year in insulin naïve group. Quality of life improved after 24 weeks [Table 14 and 15].

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

| Parameter               | N  | Baseline | Week 24 | Change from baseline |
|-------------------------|----|----------|---------|----------------------|
| Glycaemic control       |    |          |         |                      |
| (insulin naïve)         |    |          |         |                      |
| HbA1c, mean (%)         | 2  | 11.2     | 8.7     | −2.5                 |
| FPG, mean (mmol/L)      | 2  | 12.2     | 5.8     | −6.4                 |
| Glycaemic control       |    |          |         |                      |
| (insulin users)         |    |          |         |                      |
| HbA1c, mean (%)         | 6  | 9.8      | 8.6     | −1.2                 |
| FPG, mean (mmol/L)      | 6  | 12.3     | 5.5     | −6.8                 |
| PPPG, mean (mmol/L)     | 1  | 16.2     | 7.2     | −9.0                 |

HbA1c: Glycated haemoglobin A1c, 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           | 83 | 0.3      | 0.0     | −0.3                 |
| Insulin users           | 5  | 26.0     | 0.0     | −26.0                |
| Body weight, kg         |    |          |         |                      |
| Insulin naïve           | 29 | 66.3     | 64.8    | −1.5                 |
| Insulin users           | 1  | 82.5     | 83.5    | 1.0                  |
| Quality of life, VAS scale (0-100) |    |          |         |                      |
| Insulin naïve           | 40 | 57.7     | 67.6    | 9.9                  |
| Insulin users           | 1  | 55.0     | 66.0    | 11.0                 |

VAS: Visual analogue scale

### Table 12: Insulin dose

| Insulin dose, U/day | N Pre-study | N Baseline | N Week 24 |
|--------------------|------------|------------|-----------|
| Insulin naïve      | 0          | 83         | 43        | 14.3      |
| Insulin users      | 5          | 17.2       | 5         | 15.2      | 1 | 20.0 |
mean HbA1c and FPG values improved in the insulin user population [Table 16].

CONCLUSION

Our study reports improved glycaemic control 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. Quality of life improved in biphasic insulin aspart, insulin detemir and insulin aspart groups. Overall, an increase in body weight was noted for both insulin naïve and users group. 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 North East India.

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