Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the Kerala 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 Kerala, India. Results: A total of 1732 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 = 1203), insulin detemir (n = 212), insulin aspart (n = 312), basal insulin plus insulin aspart (n = 1) and other insulin combinations (n = 1). At baseline glycaemic control was poor for both insulin naïve (mean HbA1c: 10.0%) and insulin user (mean HbA1c: 8.3%) groups. After 24 weeks of treatment, both the groups showed improvement in HbA1c (insulin naïve: −2.4%, insulin users: −0.5%). 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, Kerala, 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 act as 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 Kerala, India.

MATERIALS AND METHODS

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

RESULTS

A total of 1732 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 (69.5%) started on or switched to biphasic insulin aspart. Other groups were insulin detemir (n = 212), insulin aspart (n = 312), basal insulin plus insulin aspart (n = 1) and other insulin combinations (n = 1).
After 24 weeks of treatment overall hypoglycaemic events reduced to nil for both insulin naïve (0.2 events/patient-year at baseline) and insulin user (2.0 events/patient-year at baseline) groups. The hypoglycaemia incidence in insulin naïve group at 24 weeks was lower than that observed in insulin users at baseline. SADRsincluding major hypoglycaemic events did not occur in any of the study patients. Blood pressure decreased whereas overall lipid profile and quality of life improved at week 24 in the 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, 1203 patients started on biphasic insulin aspart ± OGLD, of which 1060 (88.1%) were insulin naïve and 143 (11.9%) were insulin users. After 24 weeks of starting or switching to biphasic insulin aspart, hypoglycaemic events reduced from 0.1 events/patient-year to nil in insulin naïve group and from 1.5 events/patient-year to zero events in insulin users. Body weight decreased and 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 groups [Table 7].

**Basal + insulin aspart ± OGLD**

Of the total cohort, only one patient who started on basal + insulin aspart ± OGLD group was insulin naïve. After 24 weeks of starting or switching to insulin

### Table 1: Overall demographic data

| Parameters | Insulin naïve | Insulin users | All |
|------------|---------------|---------------|-----|
| Number of participants | 1532 | 200 | 1732 |
| Male N (%) | 904 (59.0) | 126 (63.0) | 1030 (59.5) |
| Female N (%) | 627 (41.0) | 74 (37.0) | 701 (40.5) |
| Age (years) | 57.4 | 57 | 57.5 |
| Weight (kg) | 69.4 | 62.2 | 68.6 |
| BMI (kg/m²) | 25.3 | 23.1 | 25.1 |
| Duration of DM (years) | 7.1 | 12.0 | 7.7 |
| No therapy | 98 |
| >2 OGLD | 3 |
| HbA₁c | 10.0 | 8.3 | 9.9 |
| FPG (mmol/L) | 11.8 | 10.6 | 11.7 |
| PPPG (mmol/L) | 15.5 | 15.2 | 15.5 |
| Macrovascular complications, N (%) | 782 (51.1) | 37 (18.5) | 819 (47.3) |
| Microvascular complications, N (%) | 1064 (69.5) | 26 (13.0) | 1090 (63.0) |
| Pre-study therapy, N (%) | 200 (11.55) | 1343 (82.79) |
| No therapy | 98 (5.66) |
| Baseline therapy, N (%) | 212 (12.24) | 312 (18.01) |
| Insulin detemir±OGLD | 1 (0.06) |
| Insulin aspart±OGLD | 1203 (69.5) |
| Basal insulin aspart±OGLD | 1 (0.06) |
| Others | 3 (0.17) |
| BMI: Body mass index, OGLD: Oral glucose-lowering drug, HbA₁c: Glycated hemoglobin A₁c, FPG: Fasting plasma glucose, PPPG: 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 | 1532 | 0.2 | 0.0 | −0.2 |
| All | | | | |
| Nocturnal | | | | |
| Major | | | | |
| Hypoglycaemia (insulin users), events/patient-year | 200 | 2.0 | 0.0 | −2.0 |
| All | | | | |
| Nocturnal | | | | |
| Major | | | | |
| Body weight, kg | | | | |
| Insulin naïve | 1402 | 69.6 | 69.5 | −0.1 |
| Insulin users | 154 | 61.6 | 62.5 | 0.9 |
| Lipids and BP (insulin naïve) | | | | |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L) | 58 | 2.7 (27, 46.6) | 2.4 (14, 46.7) | −0.3 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L) | 57 | 1.3 (52, 91.2) | 1.3 (27, 90.0) | 0.0 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L) | 40 | 1.8 (36, 90.0) | 1.5 (23, 100) | −0.3 |
| SBP, mean (mmHg), (N, % <130 mmHg) | 1503 | 160.3 (201, 13.4) | 131.1 (524, 37.9) | −29.2 |
| Lipids and BP (insulin users) | | | | |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L) | 44 | 2.0 (20, 45.5) | 2.0 (6, 66.7) | 0.0 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L) | 44 | 1.3 (41, 93.2) | 1.3 (9, 100) | 0.0 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L) | 28 | 1.2 (25, 89.3) | 1.1 (6, 100) | −0.1 |
| SBP, mean (mmHg), (N, % <130 mmHg) | 195 | 133.6 (53, 27.2) | 131.0 (53, 42.7) | −2.6 |
| Quality of life, VAS scale (0-100) | | | | |
| Insulin naïve | 1442 | 48.6 | 72.1 | 23.5 |
| Insulin users | 149 | 57.4 | 72.4 | 15.0 |

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
aspart, hypoglycaemic events reduced from 13.0 events/patient-year to 0.0 events/patient-year. Body weight decreased and quality of life improved after 24 weeks of treatment. All parameters of glycaemic control improved from baseline to study end in this patient.

**Insulin detemir ± OGLD**

Of the total cohort, 212 patients started on insulin detemir ± OGLD, of which 188 (88.7%) were insulin naïve and 24 (11.3%) were insulin users. After 24 weeks of starting or switching to insulin detemir, hypoglycaemic events reduced to nil for both insulin naïve (0.1 events/patient-year at baseline) and insulin user (3.3 events/patient-year at baseline) groups. An improvement in quality of life was observed at 24 weeks [Table 8 and 9].

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 10].

**Insulin aspart ± OGLD**

Of the total cohort, 312 patients who started on insulin aspart ± OGLD, of which 279 (89.4%) were insulin naïve and 33 (10.6%) were insulin users. After 24 weeks of treatment starting or switching to insulin aspart, hypoglycaemic events reduced from 0.6 events/patient-year to 0.0 events/patient-year. Body weight decreased and quality of life improved after 24 weeks of treatment. All parameters of glycaemic control improved from baseline to study end in this patient.

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**Table 3: Insulin dose**

| Insulin dose, U/day | N | Pre-study | N | Baseline | N | Week 24 |
|---------------------|---|-----------|---|----------|---|---------|
| Insulin naïve      | 0 | 0.0       | 1060 | 23.5     | 1011 | 20.6    |
| Insulin users      | 143 | 23.2 | 143 | 22.3 | 120 | 22.0 |

**Table 4: Overall efficacy data**

| Parameter                  | N | Baseline | Week 24 | Change from baseline |
|----------------------------|---|----------|---------|----------------------|
| Glycaemic control (insulin naïve) |   |          |         |                      |
| HbA1c, mean (%)            | 1271 | 10.0     | 7.6     | −2.4                 |
| FPG, mean (mmol/L)         | 1365 | 11.8     | 8.5     | −3.3                 |
| PPPG, mean (mmol/L)        | 1358 | 15.5     | 12.0    | −3.5                 |
| Glycaemic control (insulin users) |   |          |         |                      |
| HbA1c, mean (%)            | 110 | 8.3      | 7.8     | −0.5                 |
| FPG, mean (mmol/L)         | 132 | 10.6     | 9.6     | −1.0                 |
| PPPG, mean (mmol/L)        | 132 | 15.2     | 14.1    | −1.1                 |

Achievement of HbA1c <7.0% at week 24

Insulin naïve: 1432 (5.0%)

Insulin users: 147 (1.4%)

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

| Parameter                  | N | Baseline | Week 24 | Change from baseline |
|----------------------------|---|----------|---------|----------------------|
| Glycaemic control (insulin naïve) |   |          |         |                      |
| HbA1c, mean (%)            | 886 | 10.0     | 7.6     | −2.3                 |
| FPG, mean (mmol/L)         | 940 | 10.7     | 7.8     | −2.9                 |
| PPPG, mean (mmol/L)        | 937 | 14.1     | 11.0    | −3.0                 |
| Glycaemic control (insulin users) |   |          |         |                      |
| HbA1c, mean (%)            | 79 | 8.3      | 7.9     | −0.5                 |
| FPG, mean (mmol/L)         | 94 | 10.9     | 9.8     | −1.1                 |
| PPPG, mean (mmol/L)        | 94 | 15.2     | 14.0    | −1.2                 |

**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              | 1060 | 0.1      | 0.0     | −0.1                 |
| Insulin users              | 143  | 1.5      | 0.0     | −1.5                 |
| Body weight, kg            |   |          |         |                      |
| Insulin naïve              | 986  | 69.9     | 69.8    | −0.2                 |
| Insulin users              | 108  | 62.4     | 63.3    | 0.9                  |
| Quality of life, VAS scale (0-100) |   |          |         |                      |
| Insulin naïve              | 995  | 48.2     | 72.2    | 23.9                 |
| Insulin users              | 100  | 56.9     | 72.4    | 15.6                 |

**Table 6: Insulin dose**

| Insulin dose, U/day | N | Pre-study | N | Baseline | N | Week 24 |
|---------------------|---|-----------|---|----------|---|---------|
| Insulin naïve      | 0 | 0.0       | 1060 | 23.5     | 1011 | 20.6    |
| Insulin users      | 143 | 23.2 | 143 | 22.3 | 120 | 22.0 |

**Table 8: Insulin detemir±oral glucose-lowering drug safety data**

| Parameter                  | N | Baseline | Week 24 | Change from baseline |
|----------------------------|---|----------|---------|----------------------|
| Hypoglycaemia, events/patient-year |   |          |         |                      |
| Insulin naïve              | 188 | 0.1      | 0.0     | −0.1                 |
| Insulin users              | 24  | 3.3      | 0.0     | −3.3                 |
| Body weight, kg            |   |          |         |                      |
| Insulin naïve              | 171 | 69.5     | 69.4    | 0.0                  |
| Insulin users              | 18  | 63.9     | 65.1    | 1.1                  |
| Quality of life, VAS scale (0-100) |   |          |         |                      |
| Insulin naïve              | 182 | 49.1     | 71.7    | 22.6                 |
| Insulin users              | 20  | 57.4     | 73.4    | 16.0                 |

**Table 9: Insulin dose**

| Insulin dose, U/day | N | Pre-study | N | Baseline | N | Week 24 |
|---------------------|---|-----------|---|----------|---|---------|
| Insulin naïve      | 0 | 0.0       | 188 | 15.0     | 186 | 14.0    |
| Insulin users      | 24  | 19.8     | 24 | 17.0 | 22 | 15.9 |
patient-year to nil in insulin naïve group and from 3.2 events/patient-year to zero events in insulin users. A slight decrease in body weight was noted for insulin naïve group. Quality of life improved at the end of the study [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 aspart ± OGLDs for both insulin naïve and insulin user groups [Table 13].

**CONCLUSION**

Our study reports improved glycaemic control (HbA1c, FPG and PPPG) 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. Overall, a small

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