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

Uday Phadke, Sunil Gupta1, Vaishali Deshmukh2
Ruby Hall Clinic, Pune, 1Sunil’s Diabetes Care ‘n’ Research Centre Pvt. Ltd, Nagpur; 2Deshmukh Clinic and Research Center, Pune, Maharashtra, India

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 Maharashtra, India. Results: A total of 3069 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 = 2115), insulin detemir (n = 461), insulin aspart (n = 333), basal insulin plus insulin aspart (n = 92) and other insulin combinations (n = 61). At baseline glycaemic control was poor for both insulin naïve (mean HbA1c: 8.8) and insulin user (mean HbA1c: 9.1%) groups. After 24 weeks of treatment, both the groups showed improvement in HbA1c (insulin naïve: −1.4%, insulin users: −1.4%). 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, Maharashtra, 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.3 This short communication presents the results for patients enrolled from Maharashtra, India.

MATERIALS AND METHODS

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

RESULTS

A total of 3069 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 (68.92%) started on or were switched to biphasic insulin aspart. Other groups were insulin detemir (n = 461), insulin aspart (n = 333), basal

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Corresponding Author: Dr. Uday Phadke, Ruby Hall Clinic, Pune, India. E-mail: uday.instride@gmail.com
After 24 weeks of treatment, overall hypoglycaemic events reduced from 0.2 events/patient-year to 0.0 events/patient-year in insulin naive group and from 2.8 events/patient-year to 0.3 events/patient-year in insulin user 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 while 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, 2115 patients started on biphasic insulin aspart ± OGLD, of which 1845 (87.2%) were insulin naïve and 270 (12.8%) were insulin users. After 24 weeks of starting or switching to biphasic insulin aspart, hypoglycaemic events reduced from 0.2 events/patient-year to 0.0 events/patient-year in insulin naïve group and from 2.2 events/patient-year to 0.1 events/patient-year in insulin users group. 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].

| Table 1: Overall demographic data |
|----------------------------------|
| Parameters | Insulin naïve | Insulin users | All |
|-----------|---------------|---------------|-----|
| Number of participants | 2572 | 497 | 3069 |
| Male N (%) | 1444 (56.2) | 332 (66.9) | 1776 (57.9) |
| Female N (%) | 1127 (43.8) | 164 (33.1) | 1291 (42.1) |
| Age (years) | 51.5 | 54.4 | 52.0 |
| Weight (kg) | 69.2 | 70.2 | 69.4 |
| BMI (kg/m²) | 26.7 | 26.4 | 26.6 |
| Duration of DM (years) | 6.3 | 10.5 | 7.0 |
| No therapy | 119 |
| >2 OGLD | 94 | 57 | 151 |
| HbA1c | 8.8 | 9.1 | 8.9 |
| FPG (mmol/L) | 11.5 | 9.7 | 11.3 |
| PPPG (mmol/L) | 16.8 | 14.1 | 16.4 |
| Macrovascular complications, N (%) | 544 (36.1) | 214 (46.4) | 758 (38.6) |
| Microvascular complications, N (%) | 1109 (73.7) | 366 (79.4) | 1475 (75.0) |
| Pre-study therapy, N (%) | 497 (16.19) |
| OGLD only | 2453 (79.93) |
| No therapy | 119 (3.88) |
| Baseline therapy, N (%) | 461 (15.02) |
| Insulin detemrinsOGLD | 333 (10.85) |
| Basal+insulin aspart±OGLD | 92 (3.0) |
| Biphasic insulin aspart±OGLD | 2115 (68.92) |
| Others | 61 (1.99) |
| Missing | 7 (0.23) |

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 | | | | |
| All | 2572 | 0.2 | 0.0 | −0.2 |
| Nocturnal | | 0.1 | 0.0 | −0.1 |
| Major | | 0.0 | 0.0 | 0.0 |
| Hypoglycaemia (insulin users), events/patient-year | | | | |
| All | 497 | 2.8 | 0.3 | −2.5 |
| Nocturnal | | 1.1 | 0.1 | −1.0 |
| Major | | 0.7 | 0.0 | −0.7 |
| Body weight, kg | | | | |
| Insulin naïve | 2158 | 69.0 | 69.1 | 0.2 |
| Insulin users | 374 | 69.6 | 69.7 | 0.1 |
| Lipids and BP (insulin naïve) | | | | |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L) | 357 | 2.3 (42, 11.8) | 2.4 (8, 47.1) | 0.1 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L) | 357 | 1.1 (303, 84.9) | 1.1 (14, 82.4) | 0.0 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L) | 424 | 1.9 (120, 28.3) | 1.8 (14, 82.4) | −0.1 |
| SBP, mean (mmHg), (N, % <130 mmHg) | 2399 | 131.5 (813, 33.9) | 125.7 (1440, 67.4) | −5.8 |
| Lipids and BP (insulin users) | | | | |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L) | 124 | 2.7 (42, 33.9) | 2.7 (20, 50.0) | 0.0 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L) | 123 | 1.2 (91, 74.0) | 1.2 (35, 89.7) | 0.0 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L) | 123 | 1.7 (93, 75.6) | 1.5 (40, 100) | −0.1 |
| SBP, mean (mmHg), (N, % <130 mmHg) | 483 | 136.0 (97, 20.1) | 131.1 (160, 42.7) | −4.9 |
| Quality of life, VAS scale (0-100) | | | | |
| Insulin naïve | 2089 | 42.6 | 78.4 | 35.8 |
| Insulin users | 351 | 50.3 | 75.7 | 25.4 |

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, 92 patients started on basal + insulin aspart ± OGLD, of which 41 (44.6%) were insulin naïve and 51 (55.4%) were insulin users. After 24 weeks of starting or switching to basal + insulin aspart, hypoglycaemic events reduced from 0.8 events/patient-year to 0.0 events/patient-year in insulin user group, while hypoglycaemia was nil in insulin naïve group, similar to baseline. Quality of life improved after 24 weeks of treatment [Table 8 and 9].

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

Insulin detemir ± OGLD

Of the total cohort, 461 patients started on insulin detemir ± OGLD, of which 399 (86.6%) were insulin naïve and 62 (13.4%) were insulin users. After 24 weeks of starting or switching to insulin detemir, hypoglycaemic events reduced from 0.2 events/patient-year to 0.0 events/patient-year in insulin naïve group and from 2.7 events/patient-year to 0.0 events/patient-year in insulin users. Body weight decreased and quality of life improved at 24 weeks [Table 11 and 12].

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### Table 3: Insulin dose

| Parameter | N | Pre-study | N | Baseline | N | Week 24 |
|-----------|---|-----------|---|----------|---|---------|
| Insulin naïve | 0 | 0.0 | 2565 | 25.1 | 2328 | 24.2 |
| Insulin users | 497 | 28.4 | 497 | 28.4 | 423 | 26.9 |

### Table 4: Overall efficacy data

| Parameter | N | Baseline | Week 24 | Change from baseline |
|-----------|---|----------|---------|----------------------|
| Glycaemic control (insulin naïve) | | | |
| HbA1c, mean (%) | 1877 | 8.8 | 7.4 | −1.5 |
| FPG, mean (mmol/L) | 2156 | 11.5 | 7.0 | −4.5 |
| PPG, mean (mmol/L) | 1433 | 16.8 | 9.8 | −7.0 |
| Glycaemic control (insulin users) | | | |
| HbA1c, mean (%) | 351 | 9.1 | 7.7 | −1.4 |
| FPG, mean (mmol/L) | 331 | 9.7 | 7.1 | −2.6 |
| PPG, mean (mmol/L) | 239 | 14.1 | 10.1 | −4.0 |
| Achievement of HbA1c <7.0% at week 24 | | | |
| Insulin naïve | 2162 | 15.7% |
| % of patients | | |
| Insulin users | 388 | 12.9% |
| % of patients | | |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPG: 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 | 1845 | 0.2 | 0.0 | −0.2 |
| Insulin users | 270 | 2.2 | 0.1 | −2.1 |
| Body weight, kg | | | |
| Insulin naïve | 1586 | 68.5 | 68.8 | 0.3 |
| Insulin users | 209 | 68.8 | 69.0 | 0.2 |
| Quality of life, VAS scale (0-100) | | | |
| Insulin naïve | 1546 | 42.4 | 78.4 | 36.0 |
| Insulin users | 215 | 49.7 | 76.1 | 26.3 |

VAS: Visual analogue scale

### Table 6: Insulin dose

| Parameter | N | Pre-study | N | Baseline | N | Week 24 |
|-----------|---|-----------|---|----------|---|---------|
| Insulin naïve | 0 | 0.0 | 1845 | 25.2 | 1683 | 25.1 |
| Insulin users | 270 | 28.4 | 270 | 28.1 | 239 | 28.1 |

### 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 (%) | 1360 | 8.8 | 7.4 | −1.5 |
| FPG, mean (mmol/L) | 1563 | 11.6 | 7.0 | −4.6 |
| PPG, mean (mmol/L) | 1037 | 16.7 | 9.6 | −7.1 |
| Glycaemic control (insulin users) | | | |
| HbA1c, mean (%) | 194 | 9.1 | 7.7 | −1.4 |
| FPG, mean (mmol/L) | 184 | 9.7 | 7.2 | −2.5 |
| PPG, mean (mmol/L) | 140 | 14.2 | 9.9 | −4.3 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPG: 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 | 41 | 0.0 | 0.0 | 0.0 |
| Insulin users | 51 | 0.8 | 0.0 | −0.8 |
| Body weight, kg | | | |
| Insulin naïve | 36 | 68.9 | 69.4 | 0.5 |
| Insulin users | 41 | 71.0 | 71.4 | 0.4 |
| Quality of life, VAS scale (0-100) | | | |
| Insulin naïve | 35 | 43.5 | 78.0 | 34.5 |
| Insulin users | 33 | 45.7 | 75.5 | 29.8 |

VAS: Visual analogue scale

### Table 9: Insulin dose

| Parameter | N | Pre-study | N | Baseline | N | Week 24 |
|-----------|---|-----------|---|----------|---|---------|
| Insulin naïve | 0 | 0.0 | 41 | 44.1 | 38 | 30.0 |
| Insulin users | 51 | 32.2 | 51 | 39.2 | 43 | 31.5 |
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, 333 patients started on insulin aspart ± OGLD, of which 242 (72.7%) were insulin naïve and 91 (27.3%) were insulin users. After 24 weeks of treatment starting or switching to insulin aspart a decrease in hypoglycaemic events was observed in both insulin naïve (from 0.5 events/patient-year to 0.0 events/patient-year) and insulin user (from 5.6 events/patient-year to 1.5 events/patient-year) groups. A decrease in body weight and improvement in quality of life was observed at the end of the study [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. All four insulin regimens showed a decrease in FPG and PPPG; however this improvement was higher in insulin naïve compared to insulin users. SADRs including major hypoglycaemic events or episodes did not occur in any of the study patients. A small weight reduction was noted for insulin detemir and insulin aspart groups. Though

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**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 (%)             | 35 | 9.3      | 8.3     | −1.0                 |
| FPG, mean (mmol/L)          | 35 | 12.6     | 8.5     | −4.2                 |
| PPPG, mean (mmol/L)         | 29 | 18.5     | 12.4    | −6.1                 |
| **Glycaemic control**       |    |          |         |                      |
| (insulin users)             |    |          |         |                      |
| HbA1c, mean (%)             | 37 | 8.9      | 7.7     | −1.2                 |
| FPG, mean (mmol/L)          | 29 | 10.0     | 6.4     | −3.6                 |
| PPPG, mean (mmol/L)         | 11 | 15.6     | 10.7    | −4.9                 |

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               | 399| 0.2      | 0.0     | −0.2                |
| Insulin users               | 62 | 2.7      | 0.0     | −2.7                |
| Body weight, kg             |    |          |         |                      |
| Insulin naïve               | 330| 71.2     | 71.1    | −0.1                |
| Insulin users               | 32 | 71.5     | 71.2    | −0.3                |
| Quality of life, VAS scale (0-100) |    |          |         |                      |
| Insulin naïve               | 317| 41.3     | 79.2    | 37.9                |
| Insulin users               | 32 | 54.2     | 75.3    | 21.1                |

VAS: Visual analogue scale

**Table 12: Insulin dose**

| Insulin dose, U/day | N  | Pre-study | Baseline | N  | Week 24 |
|---------------------|----|-----------|----------|----|---------|
| Insulin naïve       | 0  | 0.0       | 399      | 19.0| 358     | 19.3   |
| Insulin users       | 62 | 20.9      | 62       | 15.5| 42      | 16.5   |

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

| Parameter                   | N  | Baseline | Week 24 | Change from baseline |
|-----------------------------|----|----------|---------|----------------------|
| **Glycaemic control**       |    |          |         |                      |
| (insulin naïve)             |    |          |         |                      |
| HbA1c, mean (%)             | 282| 8.9      | 7.3     | −1.5                 |
| FPG, mean (mmol/L)          | 338| 11.6     | 6.8     | −4.8                 |
| PPPG, mean (mmol/L)         | 198| 17.0     | 9.5     | −7.5                 |
| **Glycaemic control**       |    |          |         |                      |
| (insulin users)             |    |          |         |                      |
| HbA1c, mean (%)             | 31 | 9.2      | 7.5     | −1.7                 |
| FPG, mean (mmol/L)          | 28 | 9.8      | 7.1     | −2.7                 |
| PPPG, mean (mmol/L)         | 19 | 13.8     | 10.5    | −3.3                 |

HbA1c: Glycated haemoglobin A1c, 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               | 242| 0.5      | 0.0     | −0.5                |
| Insulin users               | 91 | 5.6      | 1.5     | −4.1                |
| Body weight, kg             |    |          |         |                      |
| Insulin naïve               | 174| 69.3     | 69.2    | −0.1                |
| Insulin users               | 70 | 70.4     | 70.3    | −0.1                |
| Quality of life, VAS scale (0-100) |    |          |         |                      |
| Insulin naïve               | 163| 45.7     | 76.8    | 31.1                |
| Insulin users               | 62 | 54.1     | 74.8    | 20.7                |

VAS: Visual analogue scale

**Table 15: Insulin dose**

| Insulin dose, U/day | N  | Pre-study | Baseline | N  | Week 24 |
|---------------------|----|-----------|----------|----|---------|
| Insulin naïve       | 0  | 0.0       | 242      | 28.1| 209     | 24.0   |
| Insulin users       | 91 | 28.7      | 91       | 28.8| 77      | 25.3   |
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 Maharashtra, India.

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

| Parameter                      | N  | Baseline | Week 24 | Change from baseline |
|-------------------------------|----|----------|---------|----------------------|
| Glycaemic control (insulin naïve) |    |          |         |                      |
| HbA1c, mean (%)                | 169| 8.9      | 7.5     | −1.4                 |
| FPG, mean (mmol/L)             | 187| 10.6     | 7.3     | −3.3                 |
| PPPG, mean (mmol/L)            | 147| 16.6     | 10.7    | −5.9                 |
| Glycaemic control (insulin users) |   |          |         |                      |
| HbA1c, mean (%)                | 69 | 9.3      | 7.8     | −1.5                 |
| FPG, mean (mmol/L)             | 69 | 9.6      | 7.4     | −2.2                 |
| PPPG, mean (mmol/L)            | 60 | 13.4     | 10.4    | −3.0                 |

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

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