Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the West 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 West India. Results: A total of 4192 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 = 2846), insulin detemir (n = 596), insulin aspart (n = 517), basal insulin plus insulin aspart (n = 140) and other insulin combinations (n = 83). 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: −1.6%, 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: A₁chieve study, insulin analogues, type 2 diabetes mellitus, West India

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 West India.

MATERIALS AND METHODS

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

RESULTS

A total of 4192 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 (67.9%) started on
or switched to biphasic insulin aspart. Other groups were insulin detemir \((n = 596)\), insulin aspart \((n = 517)\), basal insulin plus insulin aspart \((n = 140)\) and other insulin combinations \((n = 83)\).

After 24 weeks of treatment, overall hypoglycaemic events reduced from 0.4 events/patient-year to 0.0 events/patient-year in insulin naive group and from 3.3 events/patient-year to 0.3 events/patient-year in insulin user 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. Blood pressure decreased while overall lipid profile and quality of life improved at week 24 in the total cohort [Tables 2 and 3].

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

**Biphasic insulin aspart ± OGLD**

Of the total cohort, 2846 patients started on biphasic insulin aspart ± OGLD, of which 2391 (84.0%) were insulin naïve and 455 (16.0%) were insulin users. After 24 weeks of starting or switching to biphasic insulin aspart, hypoglycaemic events reduced from 0.4 events/patient-year to 0.1 events/patient-year in insulin naïve group and from 3.2 events/patient-year to 0.2 events/patient-year in insulin users group. Body weight decreased and quality of life improved after 24 weeks of treatment [Tables 5 and 6].

### Table 1: Overall demographic data

| Parameters | Insulin naive | Insulin users | All |
|------------|---------------|---------------|-----|
| Number of patients | 3419 | 773 | 4192 |
| Male N (%) | 1983 (58.0) | 502 (65.0) | 2485 (40.7) |
| Female N (%) | 1435 (42.0) | 270 (35.0) | 1705 (59.3) |
| Age (years) | 51.9 | 55.3 | 52.5 |
| Weight (kg) | 69.0 | 70.4 | 69.3 |
| BMI (kg/m²) | 26.5 | 26.4 | 26.5 |
| Duration of DM (years) | 6.3 | 10.3 | 7.1 |
| No therapy | | | 137 |
| >2 OGLD | 139 | 75 | 214 |
| HbA₁c | 8.8 | 9.1 | 8.9 |
| FPG (mmol/L) | 11.1 | 9.8 | 10.9 |
| PPG (mmol/L) | 16.7 | 14.2 | 16.3 |
| Macrovascular complications, N (%) | 906 (39.9) | 382 (52.1) | 1288 (42.8) |
| Microvascular complications, N (%) | 1383 (60.8) | 512 (69.8) | 1895 (57.2) |

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 | 3419 | 0.4 | 0.0 | 0.0 |
| Nocturnal | | 0.1 | 0.0 | −0.7 |
| Major | | 0.3 | 0.0 | −0.3 |

| Hypoglycaemia (insulin users), events/patient-year | | | | |
| All | 773 | 3.3 | 0.3 | −2.9 |
| Nocturnal | | 1.2 | 0.1 | −1.2 |
| Major | | 0.7 | 0.0 | −0.7 |

| Body weight, kg | | | |
| Insulin naïve | 2809 | 69.0 | 69.0 | 0.1 |
| Insulin users | 597 | 70.2 | 70.2 | −0.1 |

| Lipids and BP (insulin naïve) | | | |
| LDL-C, mean (mmol/L), \(N, \% <2.5\) mmol/L | 692 | 3.8 (78, 11.3) | 3.2 (16, 11.6) | −0.6 |
| HDL-C, mean (mmol/L), \(N, \% >1.0\) mmol/L | 692 | 1.0 (104, 75.4) | 1.0 (145, 75.4) | −0.1 |
| TG, mean (mmol/L), \(N, \% <2.3\) mmol/L | 753 | 2.3 (265, 35.2) | 2.0 (117, 85.4) | −0.3 |
| SBP, mean (mmHg), \(N, \% <130\) mmHg | 3240 | 125.2 (1080, 68.6) | 125.2 (1076, 33.2) | 7.3 |

| Lipids and BP (insulin users) | | | |
| LDL-C, mean (mmol/L), \(N, \% <2.5\) mmol/L | 228 | 3.2 (55, 24.1) | 2.8 (27, 36.5) | −0.4 |
| HDL-C, mean (mmol/L), \(N, \% >1.0\) mmol/L | 227 | 1.1 (145, 63.9) | 1.1 (145, 63.9) | 0.1 |
| TG, mean (mmol/L), \(N, \% <2.3\) mmol/L | 226 | 1.9 (145, 64.2) | 1.7 (70, 95.9) | −0.3 |
| SBP, mean (mmHg), \(N, \% <130\) mmHg | 756 | 136.3 (166, 22.0) | 128.8 (278, 52.0) | −7.5 |

| Quality of life, VAS scale (0-100) | | | |
| Insulin naïve | 2605 | 44.7 | 79.7 | 35.0 |
| Insulin users | 531 | 51.4 | 79.3 | 27.9 |

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
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, 140 patients who started on basal + insulin aspart ± OGLD, of which 74 (52.9%) were insulin naïve and 66 (47.1%) were insulin users. After 24 weeks of starting or switching to insulin aspart, hypoglycaemic events reduced from 0.2 events/patient-year to 0.0 events/patient-year in insulin naïve group and from 2.0 events/patient-year to 0.0 events/patient-year in insulin users. Body weight decreased and quality of life improved at the end of the study [Tables 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, 596 patients who started on insulin detemir ± OGLD, of which 503 (84.4%) were insulin naïve and 93 (15.6%) were insulin users. After 24 weeks of starting or switching to insulin detemir, hypoglycaemic

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**Table 3: Insulin dose**

| Insulin dose, U/day | Pre-study | N | Baseline | N | Week 24 | N |
|---------------------|-----------|---|----------|---|---------|---|
| Insulin naïve       | 773       | 0 | 3410     | 10.6 | 2996    | 23.8 |
| Insulin users       | 772       | 29.1 | 29.3 | 649 | 26.0 |

**Table 4: Overall efficacy data**

| Parameter | N | Baseline | Week 24 | Change from baseline |
|-----------|---|----------|---------|----------------------|
| Glycaemic control (insulin naïve) | HbA1c, mean (%) | 2527 | 8.8 | 7.3 | −1.6 |
| FPG, mean (mmol/L) | 2754 | 11.1 | 6.8 | −4.3 |
| PPG, mean (mmol/L) | 1484 | 16.7 | 9.7 | −6.9 |
| Glycaemic control (insulin users) | HbA1c, mean (%) | 567 | 9.1 | 7.4 | −1.7 |
| FPG, mean (mmol/L) | 538 | 9.8 | 6.8 | −3.0 |
| PPG, mean (mmol/L) | 255 | 14.2 | 10.0 | −4.2 |
| Achievement of HbA1c <7.0% at week 24 | Insulin naïve | 2816 | 24.2 |
| (% of patients) | Insulin users | 605 | 26.3 |
| (percentage) | |

**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 | 2391 | 0.4 | 0.1 | −0.3 |
| | Insulin users | 455 | 3.2 | 0.2 | −3.0 |
| Body weight, kg | Insulin naïve | 2008 | 68.7 | 68.9 | 0.2 |
| | Insulin users | 362 | 69.4 | 69.5 | 0.1 |
| Quality of life, VAS scale (0-100) | Insulin naïve | 1884 | 44.2 | 79.5 | 35.3 |
| | Insulin users | 337 | 50.7 | 79.6 | 28.9 |
| VAS: Visual analogue scale |

**Table 6: Insulin dose**

| Insulin dose, U/day | Pre-study | N | Baseline | N | Week 24 | N |
|---------------------|-----------|---|----------|---|---------|---|
| Insulin naïve       | 0         | 0.0 | 2391     | 25.2 | 2117    | 24.9 |
| Insulin users       | 455       | 29.4 | 455 | 29.3 | 395 | 27.4 |

**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 (%) | 1782 | 8.8 | 7.3 | −1.6 |
| FPG, mean (mmol/L) | 1941 | 11.2 | 6.8 | −4.4 |
| PPG, mean (mmol/L) | 1075 | 16.6 | 9.6 | −7.0 |
| Glycaemic control (insulin users) | HbA1c, mean (%) | 343 | 9.1 | 7.4 | −1.7 |
| FPG, mean (mmol/L) | 326 | 9.7 | 6.8 | −2.9 |
| PPG, mean (mmol/L) | 156 | 14.4 | 9.8 | −4.6 |

**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 | 74 | 0.2 | 0.0 | −0.2 |
| | Insulin users | 66 | 2.0 | 0.0 | −2.0 |
| Bodyweight, kg | Insulin naïve | 67 | 73.6 | 73.2 | −0.4 |
| | Insulin users | 53 | 72.2 | 72.2 | −0.1 |
| Quality of life, VAS Scale (0-100) | Insulin naïve | 66 | 49.7 | 82.8 | 33.1 |
| | Insulin users | 42 | 47.9 | 78.1 | 30.1 |
| VAS: Visual analogue scale |

**Table 9: Insulin dose**

| Insulin dose, U/day | Pre-study | N | Baseline | N | Week 24 | N |
|---------------------|-----------|---|----------|---|---------|---|
| Insulin naïve       | -         | - | 74 | 47.9 | 69 | 26.6 |
| Insulin users       | 66 | 31.2 | 66 | 40.9 | 69 | 26.6 |
events reduced from 0.3 events/patient-year to 0.0 events/patient-year in insulin naive group and from 2.1 events/patient-year to 0.0 events/patient-year in insulin user group. Body weight decreased in insulin naive group. Quality of life improved at the end of the study [Tables 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, 517 patients who started on insulin aspart ± OGLD, of which 390 (75.4%) were insulin naïve and 127 (24.6%) were insulin users. After 24 weeks of treatment starting or switching to insulin aspart, hypoglycaemic events reduced from 0.5 events/patient-year to 0.0 events/patient-year in insulin naive group and from 4.7 events/patient-year to 1.1 events/patient-year in insulin users. Body weight decreased and quality of life improved after 24 weeks of treatment [Tables 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 (%)                    | 66 | 9.2      | 7.6     | −1.6                 |
| FPG, mean (mmol/L)                | 66 | 11.3     | 7.4     | −3.8                 |
| PPGG, mean (mmol/L)               | 29 | 18.5     | 12.4    | −6.1                 |
| Glycaemic control (insulin users)  |    |          |         |                      |
| HbA1c, mean (%)                    | 49 | 8.9      | 7.5     | −1.4                 |
| FPG, mean (mmol/L)                | 40 | 10.0     | 6.4     | −3.6                 |
| PPGG, mean (mmol/L)               | 11 | 15.6     | 10.7    | −4.9                 |

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

| Parameter                          | N  | Baseline | Week 24 | Change from baseline |
|------------------------------------|----|----------|---------|----------------------|
| Hypoglycaemia, events/patient-year |    |          |         |                      |
| Insulin naïve                      | 503| 0.3      | 0.0     | −0.3                 |
| Insulin users                      | 93 | 2.1      | 0.0     | −2.1                 |
| Body weight, kg                    |    |          |         |                      |
| Insulin naïve                      | 414| 70.6     | 70.5    | −0.1                 |
| Insulin users                      | 57 | 73.4     | 73.4    | 0.0                  |
| Quality of life, VAS scale (0-100) |    |          |         |                      |
| Insulin naïve                      | 373| 43.0     | 80.3    | 37.3                 |
| Insulin users                      | 53 | 53.0     | 79.6    | 26.6                 |

### Table 12: Insulin dose

| Insulin                          | N  | Pre-study | N  | Baseline | N  | Week 24 |
|----------------------------------|----|-----------|----|----------|----|---------|
| Insulin naïve                    | 0  | 0         | 503| 17.9     | 445| 18.3    |
| Insulin users                    | 93 | 22.4      | 93 | 15.4     | 67 | 14.9    |

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

| Parameter                          | N  | Baseline | Week 24 | Change from baseline |
|------------------------------------|----|----------|---------|----------------------|
| Glycaemic control (insulin naïve)  |    |          |         |                      |
| HbA1c, mean (%)                    | 368| 8.8      | 7.2     | −1.6                 |
| FPG, mean (mmol/L)                | 418| 11.2     | 6.7     | −4.5                 |
| PPGG, mean (mmol/L)               | 208| 16.8     | 9.4     | −7.4                 |
| Glycaemic control (insulin users)  |    |          |         |                      |
| HbA1c, mean (%)                    | 54 | 9.2      | 7.2     | −1.9                 |
| FPG, mean (mmol/L)                | 50 | 9.8      | 6.6     | −3.2                 |
| PPGG, mean (mmol/L)               | 19 | 13.8     | 10.5    | −3.3                 |

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

| Parameter                          | N  | Baseline | Week 24 | Change from baseline |
|------------------------------------|----|----------|---------|----------------------|
| Hypoglycaemia, events/patient-year |    |          |         |                      |
| Insulin naïve                      | 390| 0.5      | 0.0     | −0.5                 |
| Insulin users                      | 127| 4.7      | 1.1     | −3.6                 |
| Body weight, kg                    |    |          |         |                      |
| Insulin naïve                      | 275| 67.2     | 67.0    | −0.2                 |
| Insulin users                      | 96 | 70.8     | 70.3    | −0.5                 |
| Quality of life, VAS scale (0-100) |    |          |         |                      |
| Insulin naïve                      | 244| 49.2     | 79.6    | 30.5                 |
| Insulin users                      | 84 | 55.3     | 78.0    | 22.7                 |

### Table 15: Insulin dose

| Insulin dose, U/day                | N  | Pre-study | N  | Baseline | N  | Week 24 |
|-----------------------------------|----|-----------|----|----------|----|---------|
| Insulin naïve                     | 0  | 0         | 390| 27.2     | 312| 23.7    |
| Insulin users                      | 127| 29.5      | 127| 30.6     | 103| 24.9    |

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

| Parameter                          | N  | Baseline | Week 24 | Change from baseline |
|------------------------------------|----|----------|---------|----------------------|
| Glycaemic control (insulin naïve)  |    |          |         |                      |
| HbA1c, mean (%)                    | 269| 9.0      | 7.3     | −1.7                 |
| FPG, mean (mmol/L)                | 284| 10.5     | 6.9     | −3.5                 |
| PPGG, mean (mmol/L)               | 149| 16.5     | 10.7    | −5.9                 |
| Glycaemic control (insulin users)  |    |          |         |                      |
| HbA1c, mean (%)                    | 94 | 9.4      | 7.6     | −1.9                 |
| FPG, mean (mmol/L)                | 94 | 9.9      | 7.1     | −2.8                 |
| PPGG, mean (mmol/L)               | 60 | 13.4     | 10.4    | −3.0                 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPGG: Postprandial plasma glucose
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. SADRs including major hypoglycaemic events or episodes did not occur in any of the study patients. Except for biphasic insulin aspart, a small weight reduction was noted for the other three regimens. 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 West India.

**REFERENCES**

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047-53.
2. Shetty P. Public health: India’s diabetes time bomb. Nature 2012;485:S14-6.
3. Korytkowski M. When oral agents fail: Practical barriers to starting insulin. Int J Obes Relat Metab Disord 2002;26 Suppl 3:S18-24.
4. Hirsch IB. Insulin analogues. N Engl J Med 2005;352:174-83.
5. Shah SN, Litwak L, Haddad J, Chakkarwar PN, Hajjaji I. The A1chieve study: A 60 000-person, global, prospective, observational study of basal, meal-time, and biphasic insulin analogs in daily clinical practice. Diabetes Res Clin Pract 2010;88 Suppl 1:S11-6.

Cite this article as: Jain SM, Jindal S, Malve H, Shetty R, Bhoraskar A. Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the West India cohort of the A1chieve study. Indian J Endocr Metab 2013;17:S486-90.

Source of Support: Nil, Conflict of Interest: None declared.