Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the Chennai cohort of the A\textsubscript{1}chieve study

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ABSTRACT

Background: The A\textsubscript{1}chieve, 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 Chennai, India.

Results: A total of 1334 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 \((n = 983)\), insulin detemir \((n = 205)\), insulin aspart \((n = 42)\), basal insulin plus insulin aspart \((n = 41)\) and other insulin combinations \((n = 63)\). At baseline glycaemic control was poor for both insulin naïve (mean HbA\textsubscript{c}: 9.4\%) and insulin users (mean HbA\textsubscript{c}: 9.3\%) groups. After 24 weeks of treatment, both groups showed improvement in HbA\textsubscript{c} (insulin naïve: −2.1\%, insulin users: −1.9\%). 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: A\textsubscript{1}chieve study, Chennai, insulin analogues, 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.\textsuperscript{[1,2]} Fear of hypoglycaemia and gain in body weight are barriers for initiation of insulin therapy.\textsuperscript{[3]} Modern insulin analogues are a convenient new approach or tool to glycaemic control, associated with low number of hypoglycaemia and favourable weight change.\textsuperscript{[4]} A\textsubscript{1}chieve, 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.\textsuperscript{[5]} This short communication presents the results for patients enrolled from Chennai, India.

MATERIALS AND METHODS

Please refer to editorial titled: The A\textsubscript{1}chieve study: Mapping the Ibn Battuta trail.

RESULTS

A total of 1334 patients were enrolled in the study. The patient characteristics for the entire cohort divided as insulin-naïve and insulin users is shown in Table 1. Glycaemic control at baseline was poor in this population. The majority of patients (73.7\%) started on or were switched to biphasic insulin aspart. Other groups were insulin detemir \((n = 205)\), insulin aspart \((n = 42)\), basal insulin plus insulin aspart \((n = 41)\) and other insulin combinations \((n = 63)\).
After 24 weeks of treatment, overall hypoglycaemic events reduced in both insulin naïve (from 1.2 events/patient-year to 0.9 events/patient-year) and insulin user (from 2.9 events/patient-year to 2.5 events/patient-year) groups. 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 or episodes 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 the total cohort [Tables 2 and 3].

All parameters of glycaemic control improved from baseline to study end in the total cohort [Table 4]. Approximately 30.0% of patients achieved HbA1c < 7.0% at week 24.

**Table 1: Overall demographic data**

| Parameters | Insulin naïve | Insulin users | All |
|------------|---------------|--------------|-----|
| Number of participants | 902 | 432 | 1334 |
| Male N (%) | 506 (56.1) | 250 (58.0) | 756 (56.7) |
| Female N (%) | 396 (43.9) | 181 (42.0) | 577 (43.3) |
| Age (years) | 52.7 | 56.4 | 53.9 |
| Weight (kg) | 68.7 | 70.8 | 69.4 |
| BMI (kg/m²) | 25.9 | 27.4 | 26.4 |
| Duration of DM (years) | 5.3 | 5.8 | 5.7 |
| No therapy | 80 | 150 | 230 |
| >2 OGLD | 303 | 181 | 484 |
| HbA1c (mmol/L) | 9.4 | 9.3 | 9.4 |
| FPG (mmol/L) | 10.9 | 10.8 | 10.9 |
| PPPG (mmol/L) | 16.4 | 15.8 | 16.2 |
| Macrovascular complications, N (%) | 130 (14.6) | 100 (23.1) | 230 (17.4) |
| Microvascular complications, N (%) | 571 (64.1) | 335 (77.5) | 906 (68.5) |

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 | 902 | 1.2 | 0.9 | -0.3 |
| Nocturnal | 0.2 | 0.1 | -0.1 |
| Major | 0.2 | 0.0 | -0.2 |
| Hypoglycaemia (insulin users), events/patient-year | | | | |
| All | 432 | 2.9 | 2.5 | -0.4 |
| Nocturnal | 0.5 | 0.4 | -0.1 |
| Major | 0.1 | 0.0 | -0.1 |
| Body weight, kg | | | | |
| Insulin naïve | 710 | 68.6 | 68.9 | 0.4 |
| Insulin users | 351 | 70.3 | 70.8 | 0.5 |
| Lipids and BP (insulin naïve) | | | | |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L) | 596 | 3.0 (193, 32.4) | 2.6 (206, 45.7) | -0.5 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L) | 592 | 1.0 (314, 53.0) | 1.1 (296, 66.1) | 0.1 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L) | 586 | 2.0 (414, 70.6) | 1.6 (379, 91.3) | -0.4 |
| SBP, mean (mmHg), (N, % <130 mmHg) | 800 | 133.7 (260, 32.5) | 128.0 (388, 48.1) | -5.7 |
| Lipids and BP (insulin users) | | | | |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L) | 361 | 2.7 (168, 46.5) | 2.4 (163, 61.0) | -0.3 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L) | 363 | 1.0 (977, 54.3) | 1.1 (766, 65.9) | 0.0 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L) | 358 | 2.0 (267, 74.6) | 1.7 (232, 98.2) | -0.3 |
| SBP, mean (mmHg), (N, % <130 mmHg) | 409 | 137.3 (97, 23.7) | 131.3 (124, 31.7) | -6.0 |
| Quality of life, VAS scale (0-100) | | | | |
| Insulin naïve | 772 | 66.0 | 76.4 | 10.4 |
| Insulin users | 402 | 64.4 | 77.0 | 12.6 |

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, 41 patients started on basal + insulin aspart ± OGLD, of which 10 (24.4%) were insulin naïve and 31 (75.6%) were insulin users. After 24 weeks of treatment, hypoglycaemic events reduced from 2.9 events/patient-year to 2.4 events/patient-year in insulin user group whereas hypoglycaemia increased from 2.6 events/patient-year to 3.3 events/patient-year in insulin naïve group. Body weight decreased and quality of life improved after 24 weeks of treatment [Tables 8 and 9].

### Insulin detemir ± OGLD

Of the total cohort, 205 patients started on insulin detemir ± OGLD, of which 167 (81.5%) were insulin naïve and 38 (18.5%) were insulin users. After 24 weeks of treatment, hypoglycaemic events reduced from...
2.6 events/patient-year to 1.0 events/patient-year in insulin naive group whereas hypoglycaemia increased from 1.7 events/patient-year to 2.5 events/patient-year in insulin users. Quality of life improved after 24 weeks of treatment [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-naive and insulin user groups [Table 13].

### Insulin aspart ± OGLD

Of the total cohort, 42 patients started on insulin aspart ± OGLD, of which 29 (69.0%) were insulin naïve and 13 (31.0%) were insulin users. After 24 weeks of treatment, hypoglycaemic events reduced from 19.0 events/patient-year to 6.5 events/patient-year in insulin user group whereas hypoglycaemia increased from 0.0 events/patient-year to 0.5 events/patient-year in insulin naïve group. Body weight decreased and quality of life improved after 24 weeks of treatment [Tables 14 and 15].

### 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

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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                  |    |          |         |                      |
| HbA1c, mean (%)                    | 8  | 10.0     | 7.3     | −2.6                 |
| FPG, mean (mmol/L)                 | 7  | 13.1     | 7.0     | −6.1                 |
| PPPG, mean (mmol/L)                | 7  | 19.4     | 10.4    | −9.0                 |
| Glycaemic control                  |    |          |         |                      |
| HbA1c, mean (%)                    | 27 | 9.6      | 7.4     | −2.2                 |
| FPG, mean (mmol/L)                 | 26 | 11.9     | 6.5     | −5.4                 |
| PPPG, mean (mmol/L)                | 26 | 17.1     | 8.8     | −8.3                 |

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 naive                      | 167| 2.6      | 1.0     | −1.6                 |
| Insulin users                      | 38 | 1.7      | 2.5     | 0.8                  |
| Body weight, kg                    | 139| 68.6     | 68.6    | 0.0                  |
| Insulin users                      | 27 | 69.8     | 70.2    | 0.3                  |
| Quality of life, VAS scale (0-100) |    |          |         |                      |
| Insulin naive                      | 157| 65.6     | 75.8    | 10.2                 |
| Insulin users                      | 37 | 63.5     | 76.2    | 12.7                 |

VAS: Visual analogue scale

**Table 12: Insulin dose**

| Insulin dose, U/day | N Pre-study | N Baseline | N Week 24 |
|---------------------|-------------|------------|-----------|
| Insulin naïve       | 0           | 0          | 167       |
|                     | 38          | 18.2       | 38        |

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

| Parameter                          | N  | Baseline | Week 24 | Change from baseline |
|------------------------------------|----|----------|---------|----------------------|
| Glycaemic control                  |    |          |         |                      |
| HbA1c, mean (%)                    | 162| 9.3      | 7.3     | −2.0                 |
| FPG, mean (mmol/L)                 | 158| 10.9     | 6.4     | −4.5                 |
| PPPG, mean (mmol/L)                | 158| 15.7     | 9.6     | −6.1                 |
| Glycaemic control                  |    |          |         |                      |
| HbA1c, mean (%)                    | 37 | 9.0      | 7.3     | −1.7                 |
| FPG, mean (mmol/L)                 | 36 | 9.7      | 6.7     | −3.0                 |
| PPPG, mean (mmol/L)                | 36 | 13.8     | 9.9     | −3.9                 |

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 naive                      | 29 | 0.0      | 0.5     | 0.5                  |
| Insulin users                      | 13 | 19.0     | 6.5     | 12.5                 |
| Body weight, kg                    | 28 | 66.1     | 66.0    | −0.1                 |
| Insulin users                      | 12 | 76.0     | 75.2    | −0.8                 |
| Quality of life, VAS scale (0-100) |    |          |         |                      |
| Insulin naive                      | 27 | 66.5     | 78.4    | 11.9                 |
| Insulin users                      | 12 | 63.5     | 78.6    | 15.1                 |

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        | 29        |
|                     | 13          | 43.9       | 13        |
hypoglycaemic events or episodes did not occur in any of the study patients. A slight increase in body weight was noted for overall cohort. 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 Chennai, 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 (%)                    | 28 | 9.1      | 7.2     | −1.9                 |
| FPG, mean (mmol/L)                 | 29 | 9.3      | 6.2     | −3.1                 |
| PPPG, mean (mmol/L)                | 29 | 17.2     | 9.9     | −7.2                 |
| **Glycaemic control (insulin users)** |    |          |         |                      |
| HbA1c, mean (%)                    | 11 | 9.4      | 7.8     | −1.6                 |
| FPG, mean (mmol/L)                 | 12 | 11.4     | 7.0     | −4.4                 |
| PPPG, mean (mmol/L)                | 11 | 14.0     | 11.1    | −2.9                 |

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

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