Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the Punjab 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 Punjab, India. Results: A total of 655 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 = 587), insulin detemir (n = 28), insulin aspart (n = 24), basal insulin plus insulin aspart (n = 13) and other insulin combinations (n = 3). At baseline glycaemic control was poor for both insulin naïve (mean HbA1c: 9.1%) and insulin user (mean HbA1c: 9.1%) groups. After 24 weeks of treatment, both the groups showed improvement in HbA1c (insulin naïve: −0.8%, insulin users: −1.0%). 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, Punjab, type 2 diabetes mellitus
After 24 weeks of treatment, overall hypoglycaemic events reduced from 0.8 events/patient-year to 0.0 events/patient-year in insulin naïve group and from 1.0 events/patient-year to 0.0 events/patient-year in insulin user group. No hypoglycaemic episode in insulin naïve 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. Though blood pressure has shown a decreasing trend in the total cohort, but the finding was limited by number of observations. Quality of life improved at 24 weeks [Table 2 and 3].

Mean HbA1c and FPG values improved from baseline to study end in the total cohort [Table 4]. More than 46.0% of patients achieved HbA1c < 7.0% at week 24.

**Biphasic insulin aspart ± OGLD**

Of the total cohort, 587 patients started on biphasic insulin aspart ± OGLD, of which 355 (60.5%) were insulin naïve and 232 (39.5%) were insulin users. After 24 weeks of starting or switching to biphasic insulin aspart, hypoglycaemic events reduced from 0.9 events/patient-year to 0.0 events/patient-year in insulin naïve group and from 1.0 events/patient-year to 0.0 events/patient-year in insulin user group. Quality of life also improved at the end of the study [Table 5 and 6].

Mean HbA1c and FPG values 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, 13 patients started on basal + insulin aspart ± OGLD of which 7 (53.8%) were insulin naïve and 6 (46.2%) were insulin users. After 24 weeks of starting or switching to biphasic insulin aspart, hypoglycaemic events reduced from 4.3 events/patient-year to 0.0 events/patient-year in insulin naïve group while hypoglycaemia was nil in insulin naïve group, similar to baseline. An improvement in quality of life was observed after 24 weeks [Table 8 and 9].

Mean HbA1c and FPG values improved from baseline to study end in those who started on or were switched to

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**Table 1: Overall demographic data**

| Parameters                     | Insulin naïve | Insulin users | All          |
|--------------------------------|---------------|---------------|--------------|
| Number of participants         | 395           | 260           | 655          |
| Male N (%)                     | 245 (62.0)    | 171 (66.0)    | 416 (63.6)   |
| Female N (%)                   | 150 (38.0)    | 88 (34.0)     | 238 (36.4)   |
| Age (years)                    | 52.8          | 55.2          | 53.8         |
| Weight (kg)                    | 72.2          | 73.6          | 72.8         |
| BMI (kg/m2)                    | 24.1          | 24.3          | 24.2         |
| Duration of DM (years)         | 6.7           | 7.9           | 7.2          |
| No therapy                     | 7             |               |              |
| HbA1c                          | 9.1           | 9.1           | 9.1          |
| FPG (mmol/L)                   | 9.7           | 10.7          | 10.1         |
| PPPG (mmol/L)                  | -             | -             | -            |
| Macrovascular complications, N (%) | 105 (26.6) | 98 (37.7)    | 203 (31.0)   |
| Microvascular complications, N (%) | 310 (78.5) | 216 (83.1)   | 526 (80.3)   |
| Pre-study therapy, N (%)       |               |               |              |
| Insulin users                  | 260 (39.70)   |               |              |
| OGLD only                      | 388 (59.24)   |               |              |
| No therapy                     | 7 (1.07)      |               |              |
| Baseline therapy, N (%)        |               |               |              |
| Insulin detemir±OGLD           | 28 (4.28)     |               |              |
| Insulin aspart±OGLD            | 24 (3.66)     |               |              |
| Basal+insulin aspart±OGLD      | 13 (1.99)     |               |              |
| Biphasic insulin aspart±OGLD   | 587 (89.62)   |               |              |
| Others                         | 3 (0.46)      |               |              |

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                                           | 395   | 0.8      | 0.0     | -0.8                |
| Nocturnal                                     | 0.5   | 0.0      | -0.5    |                     |
| Major                                         | 0.5   | 0.0      | -0.5    |                     |
| Hypoglycaemia (insulin users), events/patient-year |       |          |         |                     |
| All                                           | 260   | 1.0      | 0.0     | -1.0                |
| Nocturnal                                     | 0.4   | 0.0      | -0.4    |                     |
| Major                                         | 0.4   | 0.0      | -0.4    |                     |
| Body weight, kg                               |       |          |         |                     |
| Insulin naïve                                 | 341   | 71.8     | 71.8    | 0.0                 |
| Insulin users                                 | 211   | 73.5     | 73.5    | 0.0                 |
| Lipids and BP (insulin naïve)                 |       |          |         |                     |
| SBP, mean (mmHg), {N, % <130 mmHg}            | 367   | 133.3 (87, 23.7) | 122.4 (92, 69.7) | -10.9 |
| BP (insulin users)                            |       |          |         |                     |
| SBP, mean (mmHg), {N, % <130 mmHg}            | 230   | 130.7 (43, 18.7) | 122.6 (53, 69.7) | -8.1 |
| Quality of life, VAS scale (0-100)            |       |          |         |                     |
| Insulin naïve                                 | 337   | 47.5     | 72.9    | 25.5                |
| Insulin users                                 | 202   | 47.8     | 72.4    | 24.6                |

BP: Blood pressure, SBP: Systolic blood pressure, VAS: Visual analogue scale
basal + insulin aspart ± OGLDs for both insulin naïve and insulin user groups [Table 10].

**Insulin detemir ± OGLD**

Of the total cohort, 28 patients started on insulin detemir ± OGLD, of which 13 (46.4%) were insulin naïve and 15 (53.6%) were insulin users. After 24 weeks of treatment, hypoglycaemic events reduced from 1.0 events/patient-year to 0.0 events/patient-year in insulin naïve group, whereas hypoglycaemia was nil in insulin user group, similar to baseline. Quality of life improved after 24 weeks of treatment [Table 11 and 12].

Mean HbA1c and FPG values 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].

**Table 3: Insulin dose**

| Insulin dose, U/day | N | Pre-study | N | Baseline | N | Week 24 |
|---------------------|---|-----------|---|----------|---|---------|
| Insulin naïve       | 0 | 0.0       | 395| 32.7     | 359| 35.3    |
| Insulin users       | 260| 30.9      | 260| 32.3     | 222| 35.3    |

**Table 4: Overall efficacy data**

| Parameter | N | Baseline | Week 24 | Change from baseline |
|-----------|---|----------|---------|----------------------|
| Glycaemic control (insulin naïve) | 354| 9.1 | 7.0 | −2.1 |
| HbA1c, mean (%) | 263| 9.7 | 5.6 | −4.1 |
| Glycaemic control (insulin users) | 221| 9.1 | 7.0 | −2.1 |
| HbA1c, mean (%) | 164| 10.7 | 5.6 | −5.1 |
| Achievement of HbA1c <7.0% at week 24 | 358| 46.6% | | |
| (%) of patients | 222| 46.8% | | |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting 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 | 355| 0.9 | 0.0 | −0.9 |
| Insulin naïve | 232| 1.0 | 0.0 | −1.0 |
| Body weight, kg | 303| 71.4 | 71.4 | 0.0 |
| Insulin naïve | 193| 73.4 | 73.4 | 0.0 |
| Quality of life, VAS scale (0-100) | 301| 47.6 | 72.8 | 25.2 |
| Insulin naïve | 184| 47.8 | 72.4 | 24.6 |

VAS: Visual analogue scale

**Table 6: Insulin dose**

| Insulin dose, U/day | N | Pre-study | N | Baseline | N | Week 24 |
|---------------------|---|-----------|---|----------|---|---------|
| Insulin naïve       | 0 | 0.0       | 355| 33.1     | 320| 35.6    |
| Insulin users       | 232| 31.4      | 232| 33.3     | 203| 35.7    |

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

| Parameter | N | Baseline | Week 24 | Change from baseline |
|-----------|---|----------|---------|----------------------|
| Glycaemic control (insulin naïve) | 264| 9.6 | 7.9 | −1.7 |
| HbA1c, mean (%) | 273| 12.2 | 5.9 | −6.3 |
| Glycaemic control (insulin users) | 202| 9.1 | 7.0 | −2.1 |
| HbA1c, mean (%) | 150| 10.7 | 5.6 | −5.1 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting 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 | 7 | 0.0 | 0.0 | 0.0 |
| Insulin naïve | 6 | 4.3 | 0.0 | −4.3 |
| Body weight, kg | 7 | 76.4 | 76.4 | 0.0 |
| Insulin naïve | 2 | 73.5 | 73.5 | 0.0 |
| Quality of life, VAS scale (0-100) | 7 | 45.4 | 74.0 | 28.6 |
| Insulin naïve | 3 | 46.3 | 71.3 | 25.0 |

VAS: Visual analogue scale

**Table 9: Insulin dose**

| Insulin dose, U/day | N | Pre-study | N | Baseline | N | Week 24 |
|---------------------|---|-----------|---|----------|---|---------|
| Insulin naïve       | 0 | 0.0       | 7 | 41.7     | 7 | 38.6    |
| Insulin users       | 6 | 31.7      | 6 | 43.5     | 3 | 48.3    |

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

| Parameter | N | Baseline | Week 24 | Change from baseline |
|-----------|---|----------|---------|----------------------|
| Glycaemic control (insulin naïve) | 7 | 9.0 | 7.2 | −1.8 |
| HbA1c, mean (%) | 2 | 11.4 | 5.6 | −5.8 |
| Glycaemic control (insulin users) | 3 | 7.9 | 7.1 | −0.8 |
| HbA1c, mean (%) | 3 | 11.2 | 5.8 | −5.3 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose
Of the total cohort, 24 patients started on insulin aspart ± OGLD, of which 18 (75%) were insulin naïve and 06 (25%) were insulin users. After 24 weeks of treatment, hypoglycaemic events remained nil in both insulin naïve and insulin user groups similar to that of baseline. Quality of life improved at the end of 24 weeks [Table 14 and 15].

Mean HbA1C and FPG values 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 (HbA1C, FPG) 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. After 24 weeks, no change in body weight was noted in the total 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 Punjab, India.

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