Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the Taif, Saudi Arabia 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 participants enrolled from Taif, Saudi Arabia. Results: A total of 791 subjects were enrolled in the study. Four different insulin analogue regimens were used in the study. Study patients were started on or were switched to biphasic insulin aspart (n = 238), insulin detemir (n = 325), insulin aspart (n = 9), basal insulin plus insulin aspart (n = 85) and other insulin combinations (n = 127). At baseline glycaemic control was poor for both insulin naïve (mean HbA1c: 9.7%) and insulin user (mean HbA1c: 9.8%) groups. After 24 weeks of treatment, both the study groups showed improvement in HbA1c (insulin naïve: −2.3%, insulin users: −2.6%). SADRs including major hypoglycaemic events did not occur in 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, Taif, Saudi Arabia

INTRODUCTION

2.7 million people are estimated to have diabetes in Saudi Arabia, with estimated prevalence of 16.2%. Fear of hypoglycaemia and gain in body weight are barriers for initiation of insulin therapy. Modern insulin analogues are a convenient new approach or tool to glycaemic control, associated with low number of hypoglycaemia and favourable weight change. 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. This short communication presents the results for participants enrolled from Taif, Saudi Arabia.

MATERIALS AND METHODS

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

RESULTS

A total of 791 subjects were enrolled in the study. The patient characteristics for the entire cohort divided as insulin-naïve and insulin user is shown in the Table 1. Glycaemic control at baseline was poor in this population. The majority of patients (41.1%) were started on or were switched to insulin detemir. Other groups were biphasic insulin aspart (n = 238), insulin aspart (n = 9), basal insulin plus insulin aspart (n = 85) and other insulin combinations (n = 127).

After 24 weeks of treatment, overall hypoglycaemia reduced...
for both insulin naïve (from 0.6 to 0.3 events/patient-year) and insulin user (2.3 to 0.5 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 did not occur in any of the study patients. A decrease in body weight was observed after 24 weeks. Blood pressure and lipid profile improved 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].

### Biphasic insulin aspart ± OGLD

Of the total cohort, 238 patients started on biphasic insulin aspart ± OGLD, of which 131 (55%) were insulin naïve and 107 (45%) were insulin users. After 24 weeks of starting or switching to biphasic insulin aspart, hypoglycaemic events or episodes reduced for both insulin naïve and user groups (insulin naïve: from 1.0 to 0.5 events/patient-year, insulin users: from 1.1 to 0.5 events/patient-year) [Tables 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, 85 patients started on basal + insulin aspart ± OGLD, 28 (32.9%) were insulin naïve and 57 (67.1%) were insulin users. After 24 weeks, hypoglycaemic events reduced from 7.5 to 0.2 events/patient-year in insulin user group. Hypoglycaemia was nil in insulin naïve group similar to that of baseline. A decrease in body weight was also observed in both the groups. [Tables 8 and 9]

#### Table 1: Overall demographic data

| Parameters               | Insulin naïve | Insulin users | All          |
|--------------------------|---------------|---------------|--------------|
| Number of participants   | 403           | 388           | 791          |
| Male N (%)               | 230 (57.2)    | 207 (53.5)    | 437 (55.4)   |
| Female N (%)             | 172 (42.8)    | 180 (46.5)    | 352 (44.6)   |
| Age (years)              | 52.2          | 53.1          | 52.6         |
| Weight (kg)              | 83.8          | 82.5          | 83.2         |
| BMI (kg/m²)              | 31.2          | 31.3          | 31.3         |
| Duration of DM (years)   | 9.2           | 12.0          | 10.6         |
| No therapy               | 5             | 5             | 5            |
| >2 OGLD                  | 28            | 14            | 42           |
| HbA₁c                    | 9.7           | 9.8           | 9.7          |
| FPG (mmol/L)             | 11.7          | 11.6          | 11.7         |
| PPPG (mmol/L)            | 17.0          | 15.6          | 16.4         |
| Macrovascular complications, N (%) | 120 (29.8) | 151 (38.9) | 271 (34.3) |
| Microvascular complications, N (%) | 270 (67.0) | 273 (70.4) | 543 (68.6) |
| Pre-study therapy, N (%) | 388 (49.1)    | 398 (50.3)    | 786 (99.0)   |
| Insulin users            |               |               |              |
| OGLD only                |               |               |              |
| No therapy               |               |               |              |
| Baseline therapy, N (%)  | 325 (41.1)    | 9 (1.1)       | 334 (41.6)   |
| Insulin detemir±OGLD     |               |               |              |
| Insulin aspart±OGLD      |               |               |              |
| Basal±insulin aspart±OGLD|               |               |              |
| Biphasic insulin aspart±OGLD | 238 (30.1) |               |              |
| Others                   | 127 (16.1)    |               |              |
| Missing                  | 7 (0.9)       |               |              |

 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                                    | 403 | 0.6      | 0.3     | −0.3                 |
| Nocturnal                              |     | 0.3      | 0.1     | −0.2                 |
| Major                                  |     | 0.1      | 0.0     | −0.1                 |
| Hypoglycaemia (insulin users), events/patient-year | 388 | 2.3      | 0.5     | −1.8                 |
| Nocturnal                              |     | 0.6      | 0.1     | −0.5                 |
| Major                                  |     | 0.5      | 0.0     | −0.5                 |
| Body weight, kg                        |     |          |         |                      |
| Insulin naïve                          | 403 | 83.9     | 82.9    | −1.0                 |
| Insulin users                          | 388 | 82.8     | 82.0    | −0.8                 |
| Lipids and BP (insulin naïve)          |     |          |         |                      |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L) | 276 | 3.6 (28, 10.1) | 2.7 (98, 39.8) | −0.9 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L) | 272 | 1.0 (135, 49.6) | 1.1 (156, 63.9) | 0.1 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L)  | 338 | 2.4 (70, 50.3) | 1.8 (268, 90.5) | −0.6 |
| SBP, mean (mmHg), (N, % <130 mmHg)     | 400 | 137.6 (109, 27.3) | 132.0 (122, 33.1) | −5.6 |
| Lipids and BP (insulin users)          |     |          |         |                      |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L) | 257 | 3.5 (24, 9.3) | 2.7 (78, 32.1) | −0.8 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L) | 255 | 1.1 (130, 51.0) | 1.1 (168, 70.6) | 0.0 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L)  | 329 | 2.3 (184, 55.9) | 1.8 (264, 92.3) | −0.5 |
| SBP, mean (mmHg), (N, % <130 mmHg)     | 355 | 139.1 (118, 33.2) | 129.5 (148, 43.4) | −9.5 |

 BP: Blood pressure, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TG: Triglycerides, SBP: Systolic blood pressure
All parameters of glycaemic control improved from baseline to study end in those who started on or were basal + insulin aspart ± OGLDs for both insulin naïve and insulin user groups [Table 10].

**Insulin detemir ± OGLD**

Of the total cohort, 325 patients started on insulin detemir ± OGLD, of which 202 (62.1%) were insulin naïve and 123 (37.9%) were insulin users. After 24 weeks of starting or switching to insulin detemir, hypoglycaemic events reduced from 0.7 to 0.0 events/patient-year in insulin users while hypoglycaemia increased from 0.1 to 0.3 events/patient-year in insulin naïve group [Tables 11 and 12]. Body weight decreased in both the groups.

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].

### Table 3: Insulin dose

| Insulin dose, U/day | Pre-study | Baseline | Week 24 |
|---------------------|-----------|----------|---------|
| Insulin naïve       | 0         | 0        | 398     |
| Insulin users       | 388       | 55.0     | 384     |

### Table 4: Overall efficacy data

| Parameter                | N  | Baseline | Week 24 | Change from baseline |
|--------------------------|----|----------|---------|----------------------|
| Glycaemic control (insulin naïve) |    |          |         |                      |
| HbA1c, mean (%)          | 365| 9.7      | 7.4     | -2.3                 |
| FPG, mean (mmol/L)       | 326| 11.7     | 7.0     | -4.7                 |
| PPPG, mean (mmol/L)      | 275| 17.0     | 9.6     | -7.3                 |
| Glycaemic control (insulin users) |    |          |         |                      |
| HbA1c, mean (%)          | 348| 9.8      | 7.2     | -2.6                 |
| FPG, mean (mmol/L)       | 275| 11.6     | 6.6     | -5.0                 |
| PPPG, mean (mmol/L)      | 222| 15.6     | 9.1     | -6.5                 |
| Achievement of HbA1c <7.0% at week 24 | | | |
| Insulin naïve (%)        | 374| 32.9     |         |                      |
| Insulin users (%)        | 366| 40.7     |         |                      |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPPG: 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            | 131| 1.0      | 0.5     | -0.5                 |
| Insulin users            | 107| 1.1      | 0.5     | -0.6                 |
| Body weight, kg          |    |          |         |                      |
| Insulin naïve            | 101| 77.8     | 78.7    | 1.0                  |
| Insulin users            | 91 | 79.1     | 78.1    | -1.0                 |

### Table 6: Insulin dose

| Insulin dose, U/day | Pre-study | Baseline | Week 24 |
|---------------------|-----------|----------|---------|
| Insulin naïve       | 0         | 121      | 35.3    |
| Insulin users       | 110       | 41.8     | 45.0    |

### 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 (%)          | 118| 10.0     | 7.7     | -2.3                 |
| FPG, mean (mmol/L)       | 105| 12.3     | 7.4     | -5.0                 |
| PPPG, mean (mmol/L)      | 97 | 18.1     | 10.0    | -8.0                 |
| Glycaemic control (insulin users) |    |          |         |                      |
| HbA1c, mean (%)          | 105| 9.4      | 6.9     | -2.4                 |
| FPG, mean (mmol/L)       | 82 | 10.5     | 6.2     | -4.3                 |
| PPPG, mean (mmol/L)      | 79 | 13.3     | 8.0     | -5.3                 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPPG: 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            | 28 | 0.0      | 0.0     | 0.0                  |
| Insulin users            | 57 | 7.5      | 0.2     | -7.3                 |
| Body weight, kg          |    |          |         |                      |
| Insulin naïve            | 23 | 98.4     | 93.4    | -5.0                 |
| Insulin users            | 41 | 82.3     | 81.1    | -1.2                 |

### Table 9: Insulin dose

| Insulin dose, U/day | Pre-study | Baseline | Week 24 |
|---------------------|-----------|----------|---------|
| Insulin naïve       | 0         | 121      | 35.3    |
| Insulin users       | 110       | 41.8     | 45.0    |

### 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 (%)          | 27 | 9.4      | 7.1     | -2.3                 |
| FPG, mean (mmol/L)       | 23 | 11.2     | 6.8     | -4.4                 |
| PPPG, mean (mmol/L)      | 17 | 15.5     | 9.5     | -6.0                 |
| Glycaemic control (insulin users) |    |          |         |                      |
| HbA1c, mean (%)          | 50 | 9.5      | 7.4     | -2.1                 |
| FPG, mean (mmol/L)       | 40 | 11.9     | 6.7     | -5.2                 |
| PPPG, mean (mmol/L)      | 37 | 17.0     | 9.6     | -7.4                 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPPG: Postprandial plasma glucose
Of the total cohort, 9 patients started on insulin aspart ± OGLD of which 5 (55.5%) were insulin naïve and 4 (44.5%) were insulin users. After 24 weeks of treatment, hypoglycaemic events decreased from 13.0 to 0.0 events/patient-year in insulin naïve group. Hypoglycaemia was nil in insulin user group similar to that of baseline. A decrease in body weight was noted for both insulin naïve and user groups [Tables 14 and 15].

**Conclusion**

Our study reports improved glycaemic control 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. Their administration even caused a small weight reduction. SADRs including major hypoglycaemic events did not occur in the study patients. 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 in Taif, Saudi Arabia.

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