Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the Dubai 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 Dubai.

Results: A total of 767 patients were enrolled in the study. Four different insulin analogue regimens were used in the study. Study patients had started on or were switched to biphasic insulin aspart (n = 231), insulin detemir (n = 369), insulin aspart (n = 29), basal insulin plus insulin aspart (n = 111) and other insulin combinations (n = 26). At baseline glycaemic control was poor for both insulin naïve (mean HbA1c: 9.2%) and insulin user (mean HbA1c: 9.1%) groups. After 24 weeks of treatment, both the groups showed improvement in HbA1c (insulin naïve: −1.9%, insulin users: −1.8%). SADRs did not occur in any of the study patients. Major hypoglycaemia was nil similar to that of baseline in insulin naïve group whereas major hypoglycaemic events reduced from 0.3 events/patient-year to 0.1 events/patient-year in insulin users.

Conclusion: Starting or switching to insulin analogues was associated with improvements in glycaemic control with a low rate of hypoglycaemia.

Key words: A1chieve study, Dubai, insulin analogues, type 2 diabetes mellitus

INTRODUCTION

The prevalence of diabetes in United Arab Emirates is estimated to be 12.6%, affecting 768 thousand people.²³ Fear of hypoglycaemia and gain in body weight act as barriers for initiation of insulin therapy.²⁴ Modern insulin analogues are a convenient new approach or tool to glycaemic control, associated with low number of hypoglycaemia and favourable weight change.²⁵ 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.²⁶ This short communication presents the results for patients enrolled from Dubai.

MATERIALS AND METHODS

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

RESULTS

A total of 767 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 (48.1%) started on or were switched to insulin detemir. Other groups were insulin aspart (n = 29), basal insulin plus insulin aspart (n = 111), Biphasic insulin aspart (n = 231) and other insulin combinations (n = 26).
After 24 weeks of treatment, overall hypoglycaemic events reduced from 5.6 events/patient-year to 2.4 events/patient-year in insulin user group whereas hypoglycaemia increased from 0.1 events/patient-year to 0.8 events/patient-year in insulin naive group. However, this hypoglycaemia incidence in insulin naive group at 24 weeks was still lower than that observed in insulin users at baseline. SADRs did not occur in any of the study patients. Major hypoglycaemia was nil similar to that of baseline in insulin naïve group whereas major hypoglycaemic events reduced from 0.3 events/patient-year to 0.1 events/patient-year in insulin users. Blood pressure decreased and overall lipid profile improved at week 24 in the 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, 231 patients started on biphasic insulin aspart ± OGLD, of which 110 (47.6%) were insulin naïve and 121 (52.4%) were insulin users. After 24 weeks of starting or switching to biphasic insulin aspart, hypoglycaemic events reduced from 6.0 events/patient-year to 2.6 events/patient-year in insulin user group, while hypoglycaemia increased from 0.1 events/patient-year to 1.1 events/patient-year in insulin users group. An increase in body weight was also observed at the end of the study [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, 111 patients started on basal + insulin aspart ± OGLD, of which 39 (35.1%) were insulin naïve and 72 (64.9%) were insulin users. After

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**Table 1: Overall demographic data**

| Parameters                        | Insulin naïve | Insulin users | All     |
|-----------------------------------|---------------|---------------|---------|
| Number of participants            | 481           | 286           | 767     |
| Male N (%)                        | 374 (77.8%)   | 192 (67.4%)   | 566 (73.9%) |
| Female N (%)                      | 107 (22.2%)   | 93 (32.6%)    | 200 (26.1%) |
| Age (years)                       | 47.2          | 48.0          | 47.5    |
| Weight (kg)                       | 81.6          | 79.7          | 80.9    |
| BMI (kg/m²)                       | 28.9          | 28.6          | 28.8    |
| Duration of DM (years)            | 6.9           | 11.2          | 8.5     |
| No therapy                        | 42            |               |         |
| >2 OGLD                           | 94            | 15            | 109     |
| HbA₁c (mmol/L)                    | 9.2           | 9.1           | 9.2     |
| FPG (mmol/L)                      | 11.0          | 10.8          | 11.0    |
| PPPG (mmol/L)                     | 16.3          | 14.9          | 15.9    |
| Macrovascular complications, N (%)| 72 (15.0%)    | 82 (28.7%)    | 154 (20.1%) |
| Microvascular complications, N (%)| 250 (52.0%)   | 177 (61.9%)   | 427 (55.7%) |

Pre-study therapy, N (%)

- Insulin users: 286 (37.3%)
- OGLD only: 439 (57.2%)
- No therapy: 42 (5.5%)

Baseline therapy, N (%)

- Insulin detemir±OGLD: 369 (48.1%)
- Insulin aspart±OGLD: 29 (3.8%)
- Basal+insulin aspart±OGLD: 111 (14.5%)
- Biphasic insulin aspart±OGLD: 231 (30.1%)
- Others: 26 (3.4%)
- Missing: 1 (0.1%)

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                                    | 481   | 0.1      | 0.8     | 0.7                  |
| Nocturnal                              | 481   | 0.1      | 0.2     | 0.1                  |
| Major                                  | 481   | 0.0      | 0.0     | 0.0                  |
| Hypoglycaemia (insulin users), events/patient-year |       |          |         |                      |
| All                                    | 286   | 5.6      | 2.4     | −3.2                 |
| Nocturnal                              | 286   | 1.3      | 0.9     | −0.4                 |
| Major                                  | 286   | 0.3      | 0.1     | −0.2                 |
| Body weight, kg                        |       |          |         |                      |
| Insulin naïve                          | 481   | 81.8     | 81.0    | −0.9                 |
| Insulin users                          | 286   | 78.1     | 78.1    | 0.0                  |
| Lipids and BP (insulin naïve)          |       |          |         |                      |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L) | 378   | 3.3 (76, 20.1) | 2.8 (79, 28.2) | −0.5               |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L) | 379   | 1.1 (208, 54.9) | 1.1 (184, 70.0) | 0.0                 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L)  | 373   | 2.2 (240, 64.3) | 1.7 (237, 88.1) | −0.5               |
| SBP, mean (mmHg), (N, % <130 mmHg)     | 474   | 135.6 (158, 33.3) | 127.9 (201, 53.3) | −7.6               |
| Lipids and BP (insulin users)          |       |          |         |                      |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L) | 210   | 3.2 (68, 32.4) | 2.6 (54, 40.3) | −0.6               |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L) | 206   | 1.1 (124, 60.2) | 1.1 (93, 72.7) | 0.1                 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L)  | 211   | 2.0 (148, 70.1) | 1.7 (116, 87.9) | −0.4               |
| SBP, mean (mmHg), (N, % <130 mmHg)     | 286   | 132.2 (111, 38.8) | 127.9 (121, 54.8) | −4.3               |

BP: Blood pressure, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TG: Triglycerides, SBP: Systolic blood pressure.
24 weeks of starting or switching to basal + insulin aspart, hypoglycaemic events reduced from 6.3 events/patient-year to 4.3 events/patient-year in insulin user group, whereas hypoglycaemic events increased from 0.0 events/patient-year to 3.6 events/patient-year in insulin naïve group. A decrease in body weight was observed in insulin naïve group 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].

**Table 3: Insulin dose**

| Insulin dose, U/day | N | Pre-study | N | Baseline | N | Week 24 |
|---------------------|---|-----------|---|----------|---|--------|
| Insulin naïve       | 0 | 0.0       | 481| 26.1     | 368| 38.7   |
| Insulin users       | 286| 46.1      | 285| 49.6     | 221| 57.7   |

**Table 4: Overall efficacy data**

| Parameter                                    | N | Baseline | Week 24 | Change from baseline |
|----------------------------------------------|---|----------|---------|----------------------|
| Glycaemic control (insulin naïve)            |   |          |         |                      |
| HbA1c, mean (%)                              | 343| 9.2      | 7.3     | −1.9                 |
| FPG, mean (mmol/L)                           | 303| 11.0     | 6.7     | −4.3                 |
| PPPG, mean (mmol/L)                          | 229| 16.3     | 9.3     | −7.0                 |
| Glycaemic control (insulin users)            |   |          |         |                      |
| HbA1c, mean (%)                              | 181| 9.1      | 7.4     | −1.8                 |
| FPG, mean (mmol/L)                           | 164| 10.8     | 6.8     | −4.0                 |
| PPPG, mean (mmol/L)                          | 87 | 14.9     | 9.0     | −6.0                 |
| Achievement of HbA1c <7.0% at week 24        |   |          |         |                      |
| Insulin naïve (% of patients)                | 362| 40.3     |         |                      |
| Insulin users (% of patients)                | 196| 37.2     |         |                      |

**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                                | 110| 0.1      | 1.1     | 1.0                  |
| Insulin users                                | 121| 6.0      | 2.6     | −3.4                 |
| Body weight, kg                              | 78 | 78.6     | 79.1    | 0.5                  |
| Insulin naïve                                | 86 | 78.7     | 79.2    | 0.5                  |

**Table 6: Insulin dose**

| Insulin dose, U/day | N | Pre-study | N | Baseline | N | Week 24 |
|---------------------|---|-----------|---|----------|---|--------|
| Insulin naïve       | 0 | 0.0       | 110| 32.5     | 80| 47.4   |
| Insulin users       | 121| 42.9      | 121| 48.9     | 95| 55.6   |

**Insulin detemir ± OGLD**

Of the total cohort, 369 patients started on insulin detemir ± OGLD was 369, of which 315 (85.4%) were insulin naïve and 54 (14.6%) were insulin users. After 24 weeks of starting or switching to insulin detemir, hypoglycaemic events reduced from 5.3 events/patient-year to 0.8 events/patient-year in insulin user group, whereas
hypoglycaemia increased from 0.2 events/patient-year to 0.4 events/patient-year in insulin naïve group. A decrease in body weight was also observed 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, 29 patients started on insulin aspart ± OGLD, of which 8 (27.6%) were insulin naïve and 21 (72.4%) were insulin users. After 24 weeks of treatment starting or switching to insulin aspart, hypoglycaemic events reduced from 1.9 events/patient-year to 0.0 events/patient-year in insulin user group whereas no change in hypoglycaemia was observed in insulin naïve group similar to that of baseline. An increase in body weight was observed in insulin user group at the end of the study [Tables 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 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 HbA1c, FPG and PPPG, this improvement was higher in insulin naïve group compared to insulin users group. SADRs did not occur in any of the study patients. Major hypoglycaemia was nil similar to that of baseline in insulin naïve group whereas major hypoglycaemic events reduced from 0.3 events/patient-year to 0.1 events/patient-year in insulin users. A small weight reduction was observed in insulin naïve group. Though the findings are limited by number of patients, still the trend indicates that insulin analogues

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

| Parameter                              | N     | Baseline | Week 24 | Change from baseline |
|----------------------------------------|-------|----------|---------|----------------------|
| Hypoglycaemia, events/patient-year     |       |          |         |                      |
| Insulin naïve                          | 315   | 0.2      | 0.4     | 0.2                  |
| Insulin users                          | 54    | 5.3      | 0.8     | -4.5                 |
| Body weight, kg                        |       |          |         |                      |
| Insulin naïve                          | 230   | 82.3     | 81.2    | -1.1                 |
| Insulin users                          | 42    | 81.9     | 81.0    | -0.9                 |

**Table 12: Insulin dose**

| Insulin dose, U/day                   | N Pre-study | N Baseline | N Week 24 |
|---------------------------------------|-------------|------------|-----------|
| Insulin naïve                         | 0           | 315        | 247       | 33.2      |
| Insulin users                         | 54          | 27.7       | 247       | 41.1      |

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

| Parameter                              | N     | Baseline | Week 24 | Change from baseline |
|----------------------------------------|-------|----------|---------|----------------------|
| Glycaemic control (insulin naïve)      |       |          |         |                      |
| HbA1c, mean (%)                        | 232   | 9.0      | 7.2     | -1.8                 |
| FPG, mean (mmol/L)                     | 210   | 10.8     | 6.7     | -4.1                 |
| PPPG, mean (mmol/L)                    | 160   | 16.2     | 9.4     | -6.7                 |
| Glycaemic control (insulin users)      |       |          |         |                      |
| HbA1c, mean (%)                        | 42    | 8.3      | 7.0     | -1.3                 |
| FPG, mean (mmol/L)                     | 35    | 9.4      | 6.4     | -3.0                 |
| PPPG, mean (mmol/L)                    | 13    | 12.6     | 8.6     | -4.0                 |

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

| Parameter                              | N     | Baseline | Week 24 | Change from baseline |
|----------------------------------------|-------|----------|---------|----------------------|
| Hypoglycaemia, events/patient-year     |       |          |         |                      |
| Insulin naïve                          | 8     | 0.0      | 0.0     | 0.0                  |
| Insulin users                          | 21    | 1.9      | 0.0     | -1.9                 |
| Body weight, kg                        |       |          |         |                      |
| Insulin naïve                          | 6     | 77.3     | 77.3    | 0.0                  |
| Insulin users                          | 7     | 62.4     | 63.1    | 0.7                  |

**Table 15: Insulin dose**

| Insulin dose, U/day                   | N Pre-study | N Baseline | N Week 24 |
|---------------------------------------|-------------|------------|-----------|
| Insulin naïve                         | 0           | 315        | 247       | 33.2      |
| Insulin users                         | 21          | 50.8       | 47        | 73.6      |

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

| Parameter                              | N     | Baseline | Week 24 | Change from baseline |
|----------------------------------------|-------|----------|---------|----------------------|
| Glycaemic control (insulin naïve)      |       |          |         |                      |
| HbA1c, mean (%)                        | 4     | 8.6      | 7.3     | -1.4                 |
| FPG, mean (mmol/L)                     | 2     | 9.7      | 6.7     | -3.0                 |
| PPPG, mean (mmol/L)                    | 1     | 10.0     | 8.3     | -1.7                 |
| Glycaemic control (insulin users)      |       |          |         |                      |
| HbA1c, mean (%)                        | 7     | 9.3      | 7.1     | -2.2                 |
| FPG, mean (mmol/L)                     | 8     | 11.3     | 8.1     | -3.2                 |
| PPPG, mean (mmol/L)                    | 3     | 12.0     | 11.0    | -1.0                 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPPG: Postprandial plasma glucose
can be considered effective and possess a safe profile for treating type 2 diabetes in Dubai.

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