Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the Marrakech 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 Marrakech, Morocco. Results: A total of 196 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 = 71), insulin detemir (n = 83), insulin aspart (n = 5), basal insulin plus insulin aspart (n = 14) and other insulin combinations (n = 23). At baseline glycaemic control was poor for both insulin naïve (mean HbA1c: 9.3%) and insulin user (mean HbA1c: 9.3%) groups. After 24 weeks of treatment, both the study groups showed improvement in HbA1c (insulin naïve: −2.3%, insulin users: −1.9%). SADR’s including major hypoglycaemic events 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, Marrakech, type 2 diabetes mellitus

INTRODUCTION
Diabetes prevalence in Morocco is estimated to be 6.4%. 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 patients enrolled from Marrakech, Morocco.

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

RESULTS
A total of 196 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 (42.3%) started on or were switched to insulin detemir. Other groups were biphasic insulin aspart (n = 71), insulin aspart (n = 5), basal insulin plus insulin aspart (n = 14) and other insulin combinations (n = 23).
After 24 weeks of treatment, overall hypoglycaemic events or episodes reduced from 10.3 events/patient-year to 7.2 events/patient-year in insulin user group whereas overall hypoglycaemia increased from 0.4 events/patient-year to 2.3 events/patient-year in the insulin naïve group. However, this hypoglycaemia incidence in insulin naïve group at 24 weeks was still lower than that observed in insulin users at baseline. SADRs including major hypoglycaemic events did not occur in any of the study patients. Blood pressure decreased from baseline while overall lipid profile and quality of life improved after 24 weeks [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, 71 patients started on biphasic insulin aspart ± OGLD, of which 38 (53.5%) were insulin naïve and 33 (46.5%) were insulin users. After 24 weeks of treatment, hypoglycaemic events or episodes increased for both the groups (insulin naïve: from 0.7 events/patient-year to 3.7 events/patient-year and insulin users: from 9.1 events/patient-year to 10.0 events/patient-year). An increase in body weight was observed for both the groups. Quality of life improved 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].

### Table 1: Overall demographic data

| Parameters                      | Insulin naïve | Insulin users | All    |
|---------------------------------|---------------|---------------|--------|
| Number of participants          | 125           | 71            | 196    |
| Male N (%)                      | 50 (40.0)     | 28 (39.4)     | 78 (39.8) |
| Female N (%)                    | 75 (60.0)     | 43 (60.6)     | 118 (60.2) |
| Age (years)                     | 58.2          | 54.8          | 57.0   |
| Weight (kg)                     | 73.4          | 71.2          | 72.6   |
| BMI (kg/m²)                     | 27.0          | 26.2          | 26.7   |
| Duration of DM (years)          | 8.9           | 11.2          | 9.8    |
| No therapy                      |               | 8             | 8      |
| >2 OGLD                         | 1             |               | 1      |
| HbA₁c                           | 9.3           | 9.3           | 9.3    |
| FPG (mmol/L)                    | 12.1          | 11.2          | 11.8   |
| PPPG (mmol/L)                   | 13.9          | 13.9          | 13.9   |
| Macrovascular complications, N (%) | 18 (14.4) | 12 (16.9) | 30 (15.3) |
| Pre-study therapy, N (%)        |               |               |        |
| Insulin users                   | 71 (36.2)     |               |        |
| OGLD only                       | 117 (59.7)    |               |        |
| No therapy                      | 8 (4.0)       |               |        |
| Baseline therapy, N (%)         |               |               |        |
| Insulin detemir+OGLD            | 83 (42.3)     |               |        |
| Insulin aspart+OGLD             | 5 (2.6)       |               |        |
| Bas+insulin aspart+OGLD         | 14 (7.1)      |               |        |
| Biphasic insulin aspart+OGLD    | 71 (36.2)     |               |        |
| Others                          | 23 (11.7)     |               |        |

BMI: Body mass index, OGLD: Oral glucose-lowering drug, HbA₁c: Glycated haemoglobin 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/participant-year |    |          |         |                      |
| All                                            | 125| 0.4      | 2.3     | 1.9                  |
| Nocturnal                                      | 75 | 0.1      | 1.1     | 1.0                  |
| Major                                          | 70 | 0.0      | 0.0     | 0.0                  |
| Hypoglycaemia (insulin users), events/participant-year |    |          |         |                      |
| All                                            | 71 | 10.3     | 7.2     | -3.1                 |
| Nocturnal                                      | 44 | 4.4      | 0.8     | -3.6                 |
| Major                                          | 0.7| 0.0      | 0.0     | -0.7                 |
| Body weight, kg                                |    |          |         |                      |
| Insulin naïve                                  | 99 | 74.0     | 75.7    | 1.8                  |
| Insulin users                                  | 53 | 71.5     | 73.3    | 1.8                  |
| Lipids and BP (insulin naïve)                  |    |          |         |                      |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L)       | 70 | 2.9 (15, 21.4) | 2.5 (34, 63.0) | -0.4 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L)       | 71 | 1.0 (45, 63.4) | 1.1 (34, 61.8) | 0.0 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L)          | 77 | 1.5 (69, 89.6) | 1.3 (56, 96.6) | -0.3 |
| SBP, mean (mmHg), (N, % <130 mmHg)             | 120| 131.2 (59, 49.2) | 128.6 (60, 56.1) | -2.6 |
| Lipids and BP (insulin users)                  |    |          |         |                      |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L)       | 30 | 3.3 (12, 40.0) | 2.6 (6, 30.0) | -0.7 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L)       | 29 | 1.1 (23, 79.3) | 1.2 (16, 80.0) | 0.0 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L)          | 34 | 1.6 (32, 94.1) | 1.4 (20, 95.2) | -0.2 |
| SBP, mean (mmHg), (N, % <130 mmHg)             | 67 | 127.4 (33, 49.3) | 124.7 (35, 59.3) | -2.7 |
| Quality of life, VAS scale (0-100)             |    |          |         |                      |
| Insulin naïve                                  | 111| 51.7     | 80.8    | 29.0                 |
| Insulin users                                  | 63 | 55.7     | 74.4    | 18.7                 |

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
Basal + insulin aspart ± OGLD
Of the total cohort, 14 patients started on or switched to basal + insulin aspart ± OGLD, of which 1 (7.1%) was insulin naïve and 13 (92.9%) were insulin users. After 24 weeks of treatment, hypoglycemia reduced from 11.0 events/participant-year to 0.0 events/participant-year [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 ± OGLD [Table 10].

Insulin detemir ± OGLD
Of the total cohort, 83 patients started on insulin detemir ± OGLD, of which 74 (89.2%) were insulin naïve and 9 (10.8%) were insulin users. After 24 weeks of starting or switching to insulin detemir, hypoglycaemic events reduced from 2.9 events/patient-year to 1.9 events/patient-year.

### Table 3: Insulin dose

| Parameter                  | N Pre-study | N Baseline | N Week 24 |
|---------------------------|-------------|------------|-----------|
| Insulin naïve             |             |            |           |
| Insulin users             |             |            |           |
| Basal + insulin aspart ± OGLD

### Table 4: Overall efficacy data

| Parameter                  | N Baseline | N Week 24 | Change from baseline |
|---------------------------|------------|-----------|----------------------|
| Glycaemic control (insulin naïve) |
| HbA1c, mean (%)           | 89         | 9.3       | 7.1                  | −2.3                  |
| FPG, mean (mmol/L)        | 86         | 12.1      | 6.4                  | −5.6                  |
| PPGG, mean (mmol/L)       | 59         | 13.9      | 8.5                  | −5.5                  |
| Glycaemic control (insulin users) |
| HbA1c, mean (%)           | 49         | 9.3       | 7.4                  | −1.9                  |
| FPG, mean (mmol/L)        | 38         | 11.2      | 6.7                  | −4.5                  |
| PPGG, mean (mmol/L)       | 26         | 13.9      | 8.8                  | −5.1                  |

Achievement of HbA1c <7.0% at week 24
- Insulin naïve: 101/49.5
- Insulin users: 59/32.2

### Table 5: Biphasic insulin aspart±oral glucose-lowering drug safety data

| Parameter                  | N Baseline | N Week 24 | Change from baseline |
|---------------------------|------------|-----------|----------------------|
| Hypoglycaemia, events/patient-year |
| Insulin naïve             | 38         | 0.7       | 3.7                  | 3.0                   |
| Insulin users             | 33         | 9.1       | 10.0                 | 0.9                   |
| Body weight, kg           | 29         | 70.6      | 73.9                 | 3.3                   |
| Insulin naïve             | 25         | 74.9      | 76.9                 | 2.0                   |
| Quality of life, VAS scale (0-100) |
| Insulin naïve             | 32         | 53.1      | 78.9                 | 25.9                  |
| Insulin users             | 30         | 54.2      | 74.2                 | 19.9                  |

### Table 6: Insulin dose

| Parameter                  | N Pre-study | N Baseline | N Week 24 |
|---------------------------|-------------|------------|-----------|
| Insulin naïve             | 0           | 0          | 38        | 34.7      | 32        | 49.1      |
| Insulin users             | 33          | 40.3       | 33        | 42.1      | 30        | 45.7      |

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

| Parameter                  | N Baseline | N Week 24 | Change from baseline |
|---------------------------|------------|-----------|----------------------|
| Glycaemic control (insulin naïve) |
| HbA1c, mean (%)           | 21         | 10.1      | 7.5                  | −2.7                  |
| FPG, mean (mmol/L)        | 21         | 14.6      | 6.7                  | −7.8                  |
| PPGG, mean (mmol/L)       | 16         | 16.5      | 8.7                  | −7.8                  |
| Glycaemic control (insulin users) |
| HbA1c, mean (%)           | 19         | 9.2       | 7.7                  | −1.5                  |
| FPG, mean (mmol/L)        | 16         | 12.5      | 6.6                  | −5.8                  |
| PPGG, mean (mmol/L)       | 16         | 14.5      | 9.0                  | −5.5                  |

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

### Table 8: Basal+insulin aspart±oral glucose-lowering drug safety data

| Parameter                  | N Baseline | N Week 24 | Change from baseline |
|---------------------------|------------|-----------|----------------------|
| Hypoglycaemia, events/patient-year |
| Insulin users             | 13         | 11.0      | 0.0                  | −11.0                 |
| Body weight, kg           | 11         | 63.5      | 65.3                 | 1.7                   |
| Insulin users             | 11         | 63.5      | 65.3                 | 1.7                   |
| Quality of life, VAS scale (0-100) |
| Insulin users             | 11         | 52.2      | 76.8                 | 24.6                  |

VAS: Visual analogue scale

### Table 8: Basal+insulin aspart±oral glucose-lowering drug efficacy data

| Parameter                  | N Baseline | N Week 24 | Change from baseline |
|---------------------------|------------|-----------|----------------------|
| Glycaemic control (insulin naïve) |
| HbA1c, mean (%)           | 1           | 9.9       | 7.1                  | −2.8                  |
| FPG, mean (mmol/L)        | 8           | 10.1      | 6.3                  | −3.8                  |
| PPGG, mean (mmol/L)       | 3           | 16.2      | 7.7                  | −8.5                  |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPGG: Postprandial plasma glucose
patient-year in insulin user group while hypoglycaemia increased from 0.4 events/patient-year to 0.6 events/patient-year in insulin naive group. Quality of life improved at 24 weeks [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, 5 patients started on insulin aspart ± OGLD of which 1 (20.0%) was insulin naïve and 4 (80.0%) were insulin users. After 24 weeks of treatment, hypoglycaemic events reduced from 6.5 events/patient-year to 4.3 events/patient-year in insulin user group. Mean HbA₁c and mean FPG improved from baseline to study end who started on or were switched to insulin aspart ± OGLDs for insulin user group. Quality of life improved in both insulin naïve and insulin user groups.

**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. SADR's including major hypoglycaemic events did not occur in any of 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 Marrakech, Morocco.

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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                              | 74 | 0.4      | 0.6     | 0.2                  |
| Insulin users                              | 9  | 2.9      | 1.9     | −1.0                 |
| Body weight, kg                            |    |          |         |                      |
| Insulin naïve                              | 59 | 75.1     | 75.6    | 0.5                  |
| Insulin users                              | 5  | 72.3     | 71.8    | −0.5                 |
| Quality of life, VAS scale (0-100)         |    |          |         |                      |
| Insulin naïve                              | 67 | 52.7     | 81.4    | 28.7                 |
| Insulin users                              | 7  | 70.6     | 70.7    | 0.1                  |

VAS: Visual analogue scale

**Table 12: Insulin dose**

| Insulin dose, U/day | N Pre-study | N Baseline | N Week 24 |
|---------------------|-------------|------------|-----------|
| Insulin naïve       | 0           | 74         | 19.4      | 67 23.7   |
| Insulin users       | 9           | 20.4       | 9         | 7 23.1    |

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

| Parameter                                      | N  | Baseline | Week 24 | Change from baseline |
|-----------------------------------------------|----|----------|---------|----------------------|
| Glycaemic control (insulin naïve)             |    |          |         |                      |
| HbA₁c, mean (%)                               | 58 | 9.0      | 7.0     | −2.0                 |
| FPG, mean (mmol/L)                            | 55 | 11.3     | 6.4     | −4.9                 |
| PPGG, mean (mmol/L)                           | 34 | 12.9     | 8.4     | −4.6                 |
| Glycaemic control (insulin users)             |    |          |         |                      |
| HbA₁c, mean (%)                               | 5  | 8.2      | 7.3     | −0.9                 |
| FPG, mean (mmol/L)                            | 5  | 10.4     | 7.3     | −3.1                 |
| PPGG, mean (mmol/L)                           | 1  | 15.5     | 10.0    | −5.6                 |

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

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