Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the Casablanca 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 Casablanca, Morocco. Results: A total of 495 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 = 151), insulin aspart (n = 19), basal insulin plus insulin aspart (n = 53) and other insulin combinations (n = 41). At baseline glycaemic control was poor for both insulin naïve (mean HbA\textsubscript{1c}: 10.2%) and insulin user (mean HbA\textsubscript{1c}: 9.4%) groups. After 24 weeks of treatment, both groups showed improvement in HbA\textsubscript{1c} (insulin naïve: −2.3%, insulin users: −1.8%). Major hypoglycaemia was observed in the insulin naïve group after 24 weeks. SADRs were reported in 1.2% of insulin naïve and 2.1% of insulin user groups. 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, Casablanca, insulin analogues, type 2 diabetes mellitus

INTRODUCTION

Diabetes prevalence in Morocco is estimated to be 6.4%.\textsuperscript{11} Fear of hypoglycaemia and gain in body weight are barriers for initiation of insulin therapy.\textsuperscript{12} Modern insulin analogues are a convenient new approach or tool to glycaemic control, associated with low number of hypoglycaemia and favourable weight change.\textsuperscript{13} 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{14} This short communication presents the results for patients enrolled from Casablanca, Morocco.

MATERIALS AND METHODS

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

RESULTS

A total of 495 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 (46.7%) started on or were switched to biphasic insulin aspart. Other groups were insulin detemir (n = 151), insulin aspart (n = 19), basal insulin plus insulin aspart (n = 53) and other insulin combinations (n = 41).
After 24 weeks of treatment, overall hypoglycaemic events or episodes reduced from 11.7 events/patient-year to 5.0 events/patient-year in insulin user group whereas overall hypoglycaemia increased from 3.5 events/patient-year to 3.8 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. Major hypoglycaemic events or episodes occurred in the insulin naïve group. SADRs were reported in 1.2% of insulin naïve and 2.1% of insulin user groups. Blood pressure and quality of life improved after 24 weeks. Although lipid profile improved in the total cohort, the finding was limited by number of observations [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 121 (52.4%) were insulin naïve and 110 (47.6%) were insulin users. After 24 weeks of treatment, hypoglycaemic events or episodes reduced from 11.1 events/patient-year to 2.9 events/patient-year in insulin user group whereas hypoglycaemia increased from 1.3 events/patient-year to 3.2 events/patient-year in insulin naïve group. 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

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**Table 1: Overall demographic data**

| Parameters | Insulin naive | Insulin users | All |
|------------|---------------|---------------|-----|
| Number of participants | 253 | 242 | 495 |
| Male N (%) | 115 (45.5) | 107 (44.2) | 222 (44.8) |
| Female N (%) | 138 (54.5) | 135 (55.8) | 273 (55.2) |
| Age (years) | 57.5 | 55.5 | 56.5 |
| Weight (kg) | 71.2 | 75.1 | 73.1 |
| BMI (kg/m²) | 26.3 | 27.5 | 26.9 |
| Duration of DM (years) | 9.2 | 13.2 | 11.2 |
| No therapy | 22 | | |
| >2 OGLD | 4 | 1 | 5 |
| HbA₁c | 10.2 | 9.4 | 9.9 |
| FPG (mmol/L) | 14.3 | 11.9 | 13.2 |
| PPG (mmol/L) | 18.5 | 16.0 | 17.4 |
| Macrovascular complications, N (%) | 56 (22.1) | 56 (23.1) | 112 (22.6) |
| Microvascular complications, N (%) | 136 (53.8) | 133 (55.0) | 269 (54.3) |
| Pre-study therapy, N (%) | | | |
| Insulin users | 242 (48.88) | 231 (46.6) | 22 (4.44) |
| OGLD only | | 231 (46.6) | |
| No therapy | | | |
| Baseline therapy, N (%) | | | |
| Insulin detemir±OGLD | 151 (30.5) | | |
| Insulin aspart±OGLD | 19 (3.8) | | |
| Basal+insulin aspart±OGLD | 53 (10.7) | | |
| Biphasic insulin aspart±OGLD | 231 (46.7) | | |
| Others | 41 (8.3) | | |

BMI: Body mass index, OGLD: Oral glucose-lowering drug, HbA₁c: Glycated haemoglobin A₁c, FPG: Fasting plasma glucose, PPG: 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 | 253 | 3.5 | 3.8 | 0.3 |
| Nocturnal | | 0.9 | 1.6 | 0.7 |
| Major | | 0.7 | 0.1 | −0.6 |
| Hypoglycaemia (insulin users), events/participant-year | | | | |
| All | 242 | 11.7 | 5 | −6.7 |
| Nocturnal | | 4.7 | 1.2 | −3.5 |
| Major | | 2.2 | 0.0 | −2.2 |
| Body weight, kg | | | | |
| Insulin naïve | 185 | 70.9 | 74.3 | 3.4 |
| Insulin users | 166 | 75.1 | 76.2 | 1.1 |
| Lipids and BP (insulin naïve) | | | | |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L) | 102 | 3.3 (23, 22.5) | 2.6 (22, 40.7) | −0.7 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L) | 96 | 1.2 (73, 76.0) | 1.2 (43, 86.0) | 0.0 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L) | 114 | 1.9 (83, 72.8) | 1.6 (55, 88.7) | −0.3 |
| SBP, mean (mmHg), (N, % <130 mmHg) | 245 | 135.6 (73, 29.8) | 132.0 (68, 35.1) | −3.6 |
| Lipids and BP (insulin users) | | | | |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L) | 105 | 3.2 (23, 21.9) | 2.7 (13, 33.3) | −0.5 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L) | 93 | 1.3 (76, 81.7) | 1.4 (36, 94.7) | 0.1 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L) | 110 | 1.6 (95, 86.4) | 1.6 (37, 90.2) | 0.0 |
| SBP, mean (mmHg), (N, % <130 mmHg) | 235 | 133.2 (73, 31.1) | 131.0 (63, 35.2) | −2.2 |
| Quality of life, VAS scale (0-100) | | | | |
| Insulin naïve | 200 | 62.7 | 78.3 | 15.6 |
| Insulin users | 179 | 66.0 | 77.3 | 11.3 |

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, 53 patients started on basal + insulin aspart ± OGLD, of which 10 (18.9%) were insulin naïve and 43 (81.1%) were insulin users. After 24 weeks, hypoglycaemic events reduced from 29.9 events/patient-year to 0.0 events/patient-year in insulin naïve group and from 14.5 events/patient-year to 8.1 events/patient-year in insulin user group. Quality of life improved after 24 weeks [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].

**Insulin detemir ± OGLD**

Of the total cohort, 151 patients started on insulin detemir ± OGLD, of which 111 (73.5%) were insulin naïve and 40 (26.5%) were insulin users. After 24 weeks of starting or switching to insulin detemir, hypoglycaemia reduced from 13.7 events/patient-year to 3.7 events/patient-year in insulin user group while hypoglycaemic events increased from 3.9 events/patient-year to 4.7 events/patient-year.

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**Table 3: Insulin dose**

| Insulin dose, U/day | N | Pre-study | N | Baseline | N | Week 24 |
|---------------------|---|-----------|---|----------|---|---------|
| Insulin naïve       | 0 | 0.0       | 253 | 28.7     | 207| 34.2    |
| Insulin users       | 242| 41.5      | 242 | 42.5     | 184| 49.2    |

**Table 4: Overall efficacy data**

| Parameter                      | N | Baseline | Week 24 | Change from baseline |
|--------------------------------|---|----------|---------|----------------------|
| Glycaemic control (insulin naïve) |   |           |         |                      |
| HbA1c, mean (%)                | 124| 10.2     | 7.9     | −2.3                 |
| FPG, mean (mmol/L)             | 170| 14.3     | 8.1     | −6.2                 |
| PPPG, mean (mmol/L)            | 108| 18.5     | 10.2    | −8.3                 |
| Glycaemic control (insulin users) |   |           |         |                      |
| HbA1c, mean (%)                | 112| 9.4      | 7.6     | −1.8                 |
| FPG, mean (mmol/L)             | 139| 11.9     | 7.5     | −4.4                 |
| PPPG, mean (mmol/L)            | 87 | 16.0     | 10.1    | −5.9                 |
| Achievement of HbA1c <7.0% at week 24 |   |           |         |                      |
| Insulin naïve (%)              | 159| 21.4     |         |                      |
| Insulin users (%)              | 140| 20.7     |         |                      |

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                  | 121| 1.3      | 3.2     | 1.9                  |
| Insulin users                  | 110| 1.1      | 2.9     | −8.2                 |
| Body weight, kg                |   |           |         |                      |
| Insulin naïve                  | 86 | 69.1     | 74.1    | 5.0                  |
| Insulin users                  | 76 | 74.8     | 77.0    | 2.2                  |
| Quality of life, VAS scale (0-100) |   |           |         |                      |
| Insulin naïve                  | 92 | 64.1     | 81.1    | 17.0                 |
| Insulin users                  | 82 | 65.6     | 79.4    | 13.9                 |

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       | 121| 35.3     | 95 | 40.2    |
| Insulin users        | 110| 41.8      | 110| 45.0     | 86 | 50.1    |

| 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 (%)                | 51 | 10.5     | 7.8     | −2.7                 |
| FPG, mean (mmol/L)             | 78 | 14.4     | 8.1     | −6.3                 |
| PPPG, mean (mmol/L)            | 48 | 19.4     | 10.2    | −9.2                 |
| Glycaemic control (insulin users) |   |           |         |                      |
| HbA1c, mean (%)                | 55 | 9.6      | 7.6     | −2.0                 |
| FPG, mean (mmol/L)             | 67 | 12.3     | 7.5     | −4.8                 |
| PPPG, mean (mmol/L)            | 43 | 16.0     | 10.1    | −5.9                 |

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                  | 10 | 29.9     | 0.0     | −29.9                |
| Insulin users                  | 43 | 14.5     | 8.1     | −6.4                 |
| Body weight, kg                |   |           |         |                      |
| Insulin naïve                  | 9  | 72.7     | 73.7    | 1.0                  |
| Insulin users                  | 29 | 77.6     | 78.3    | 0.7                  |
| Quality of life, VAS scale (0-100) |   |           |         |                      |
| Insulin naïve                  | 9  | 73.3     | 83.9    | 10.6                 |
| Insulin users                  | 32 | 70.4     | 77.2    | 6.8                  |

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       | 10 | 42.1     | 9 | 49.0    |
| Insulin users        | 43 | 47.3      | 43 | 54.7     | 32| 59.3    |
in insulin naïve group. Quality of life also improved after 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, 19 patients started on insulin aspart ± OGLD and all of them were insulin users. After 24 weeks of treatment, hypoglycaemic events increased from 10.3 events/patient-year to 13.9 events/patient-year. Quality of life improved at 24 weeks [Tables 14 and 15].

All parameters of glycaemic control improved from baseline to study end in those who started on or were switched insulin aspart ± OGLDs for insulin user group [Table 16].

**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. Major hypoglycaemia was observed in the insulin naïve group after 24 weeks. SADRs were reported in 1.2% of insulin naïve and 2.1% of insulin user groups. Overall, increase in weight was noted for both insulin naïve and

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

| Parameter                  | N  | Baseline | Week 24 | Change from baseline |
|----------------------------|----|----------|---------|----------------------|
| Glycaemic control (insulin naïve) | 5  | 10.9     | 7.3     | −3.6                 |
| HbA1c, mean (%)            |    | 8        | 15.9    | −8.1                 |
| FPG, mean (mmol/L)        | 6  | 18.7     | 8.3     | −10.4                |
| Glycaemic control (insulin users) | 16 | 9.6     | 7.6     | −2.0                 |
| HbA1c, mean (%)          | 28 | 12.3     | 8.2     | −4.1                 |
| FPG, mean (mmol/L)        | 16 | 17.3     | 9.6     | −7.7                 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPGL: 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 | 111 | 3.9     | 4.7     | 0.8                  |
| Insulin naïve              | 40 | 13.7     | 3.7     | −10.0                |
| Body weight, kg            | 82 | 73.2     | 75.2    | 2.0                  |
| Insulin naïve              | 30 | 75.9     | 75.1    | −0.8                 |
| Quality of life, VAS scale (0-100) | 91 | 60.2     | 75.2    | 15.1                 |
| Insulin naïve              | 31 | 66.6     | 74.9    | 8.3                  |

VAS: Visual analogue scale

### Table 12: Insulin dose

| Insulin dose, U/day | Pre-study | N  | Baseline | N  | Week 24 |
|---------------------|-----------|----|----------|----|---------|
| Insulin naïve       | 0         | 0  | 111      | 18.9| 94      | 25.8   |
| Insulin users       | 40        | 29.5| 40       | 23.0| 32      | 30.3   |

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

| Parameter                  | N  | Baseline | Week 24 | Change from baseline |
|----------------------------|----|----------|---------|----------------------|
| Glycaemic control (insulin naïve) | 65 | 9.9     | 8.1     | −1.8                 |
| HbA1c, mean (%)            | 77 | 13.6    | 7.9     | −5.7                 |
| FPG, mean (mmol/L)        | 52 | 17.8    | 10.6    | −7.2                 |

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

| Parameter                  | N  | Baseline | Week 24 | Change from baseline |
|----------------------------|----|----------|---------|----------------------|
| Hypoglycaemia, events/patient-year | 19 | 10.3    | 13.9    | 3.6                  |
| Insulin users              | 15 | 69.8    | 70.1    | 0.3                  |
| Body weight, kg            | 9  | 68.1    | 80.7    | 12.6                 |

### Table 15: Insulin aspart±oral glucose-lowering drug efficacy data

| Parameter                  | N  | Baseline | Week 24 | Change from baseline |
|----------------------------|----|----------|---------|----------------------|
| Glycaemic control (insulin users) | 11 | 9.3     | 7.6     | −1.7                 |
| HbA1c, mean (%)            | 7  | 12.4    | 7.5     | −4.9                 |
| FPG, mean (mmol/L)        | 10 | 15.1    | 10.3    | −4.8                 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPGL: Postprandial plasma glucose
insulin user groups. 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 Casablanca, Morocco.

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