Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the Agadir cohort of the A1chieve study

Hicham Boussouf, Mahassine Mouniri1, Maha Oudrhiri2
Hospital Moulay El Hassan Belmehdi, Laayoune, 1Hospital Hassan II, Agadir, 2Prefetoral Hospital of Inezegane, Inzegane, Morocco

ABSTRACT

Background: 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 Agadir, Morocco. Results: A total of 201 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 = 98), insulin detemir (n = 54), insulin aspart (n = 8), basal insulin plus insulin aspart (n = 8) and other insulin combinations (n = 33). At baseline glycaemic control was poor for both insulin naïve (mean HbA1c: 10.7%) and insulin user (mean HbA1c: 9.1%) groups. After 24 weeks of treatment, both groups showed improvement in HbA1c (insulin naïve: −2.7%, insulin users: −1.3%). No major hypoglycaemia was observed at 24 weeks. SADRs were reported in 1.5% of insulin users. Conclusion: Starting or switching to insulin analogues was associated with improvement in glycaemic control with a low rate of hypoglycaemia.

Key words: A1chieve study, Agadir, insulin analogues, 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 Agadir, Morocco.

MATERIALS AND METHODS

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

RESULTS

A total of 201 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 (48.8%) started on or were switched to biphasic insulin aspart. Other groups were insulin detemir (n = 54), insulin aspart (n = 8), basal insulin plus insulin aspart (n = 8) and other insulin combinations (n = 33).

After 24 weeks of treatment, overall hypoglycaemia reduced
from 20.8 events/patient-year to 4.3 events/patient-year in insulin user group whereas hypoglycaemic events increased from 0.3 events/patient-year to 2.0 events/patient-year in 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 did not occur in any of the study patients. SADRs were reported in 1.5% of insulin users. Blood pressure and lipid profile improved in the total cohort, but the findings were limited by number of observations. Quality of life also improved after 24 weeks of treatment [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, 98 patients started on biphasic insulin aspart ± OGLD, of which 69 (70.4%) were insulin naïve and 29 (29.6%) were insulin users. After 24 weeks of treatment, hypoglycaemic events reduced from 21.5 events/patient-year to 1.2 events/patient-year in insulin user group whereas hypoglycaemia increased from 0.4 events/patient-year to 2.4 events/patient-year in insulin naïve group. Quality of life also 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

### Table 1: Overall demographic data

| Parameters                                          | Insulin naïve | Insulin users | All     |
|-----------------------------------------------------|---------------|---------------|---------|
| Number of participants                              | 134           | 67            | 201     |
| Male N (%)                                          | 52 (38.8)     | 26 (38.8)     | 78 (38.8)|
| Female N (%)                                        | 82 (61.2)     | 41 (61.2)     | 123 (61.2)|
| Age (years)                                         | 55.9          | 60.3          | 57.3    |
| Weight (kg)                                         | 74.3          | 75.3          | 74.6    |
| BMI (kg/m²)                                         | 26.1          | 26.9          | 26.4    |
| Duration of DM (years)                              | 7.8           | 14.2          | 10.0    |
| No therapy                                          |               |               | 21      |
| >2 OGLD                                             |               |               |         |
| HbA1c                                               | 10.7          | 9.1           | 10.1    |
| FPG (mmol/L)                                        | 14.5          | 9.8           | 13.0    |
| PPPG (mmol/L)                                       | 16.3          | 14.7          | 15.6    |
| Macrovascular complications, N (%)                  | 21 (15.7)     | 21 (31.3)     | 42 (20.9)|
| Microvascular complications, N (%)                  | 61 (45.5)     | 49 (73.1)     | 110 (54.7)|
| Pre-study therapy, N (%)                            |               |               |         |
| Insulin users                                       | 67 (33.3)     |               |         |
| OGLD only                                           | 113 (56.2)    |               |         |
| No therapy                                          | 21 (10.4)     |               |         |
| Baseline therapy, N (%)                             |               |               |         |
| Insulin detemir±OGLD                                | 54 (26.9)     |               |         |
| Insulin aspart±OGLD                                 | 8 (3.9)       |               |         |
| Basal±insulin aspart±OGLD                           | 8 (3.9)       |               |         |
| Biphasic insulin                                    | 98 (48.8)     |               |         |
| aspart±OGLD                                         |               |               |         |
| Others                                              | 33 (16.4)     |               |         |

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/participant-year                     |       |          |         |                      |
| All                                                                       | 134   | 0.3      | 2.0     | 1.6                  |
| Nocturnal                                                                 |        | 0.0      | 1.0     | 0.9                  |
| Major                                                                     |        | 0.0      | 0.0     | 0.0                  |
| Hypoglycaemia (insulin users), events/participant-year                     | 67    | 20.8     | 4.3     | −16.5                |
| Nocturnal                                                                 |        | 8.9      | 0.3     | −8.6                 |
| Major                                                                     |        | 6.4      | 0.0     | −6.4                 |
| Body weight, kg                                                           | 68    | 74.4     | 75.6    | 1.1                  |
| Insulin naïve                                                             | 36    | 76.6     | 76.1    | −0.5                 |
| Lipids and BP (insulin naïve)                                             |       |          |         |                      |
| LDL-C, mean (mmol/L), (N, %<2.5 mmol/L)                                   | 59    | 2.9 (18, 30.5) | 2.6 (18, 38.3) | −0.3 | |
| HDL-C, mean (mmol/L), (N, %>1.0 mmol/L)                                   | 58    | 1.2 (48, 82.8) | 1.2 (46, 97.9) | 0.0  | |
| TG, mean (mmol/L), (N, %<2.3 mmol/L)                                      | 73    | 2.2 (50, 68.5) | 1.8 (43, 87.8) | −0.4 | |
| SBP, mean (mmHg), (N, %<130 mmHg)                                         | 129   | 140.2 (26, 20.2) | 135.1 (16, 23.2) | −5.0 | |
| Lipids and BP (insulin users)                                             |       |          |         |                      |
| LDL-C, mean (mmol/L), (N, %<2.5 mmol/L)                                   | 37    | 2.9 (10, 27.0) | 2.6 (16, 59.3) | −0.2 | |
| HDL-C, mean (mmol/L), (N, %>1.0 mmol/L)                                   | 36    | 1.2 (28, 77.8) | 1.3 (22, 91.7) | 0.1  | |
| TG, mean (mmol/L), (N, %<2.3 mmol/L)                                      | 38    | 2.1 (32, 84.2) | 1.7 (23, 88.5) | −0.3 | |
| SBP, mean (mmHg), (N, %<130 mmHg)                                         | 64    | 142.1 (7, 10.9) | 139.2 (10, 25.6) | −2.9 | |
| Quality of life, VAS scale (0-100)                                        |       |          |         |                      |
| Insulin naïve                                                             | 93    | 64.6     | 76.7    | 12.2                 |
| Insulin users                                                             | 45    | 54.3     | 74.6    | 20.4                 |

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, 8 patients started on basal + insulin aspart ± OGLD, of which 1 (12.5%) was insulin naïve and 7 (87.5%) were insulin users. After 24 weeks, hypoglycaemic events reduced from 26.0 events/patient-year to 9.3 events/patient-year in insulin user group [Tables 8 and 9].

All parameters of glycaemic control improved from baseline to study end in those who started on or were basal + insulin aspart ± OGLDs for insulin-user group [Table 10].

**Insulin detemir ± OGLD**

Of the total cohort, 54 patients started on insulin detemir ± OGLD, of which 46 (85.2%) were insulin naïve and 8 (14.8%) were insulin users. After 24 weeks of starting

| Table 3: Insulin dose |
|----------------------|
| **Insulin dose, U/day** | **N** | **Pre-study** | **Baseline** | **N** | **Week 24** |
|------------------------|-------|---------------|-------------|-------|------------|
| Insulin naïve          | 0     | 0.0           | 134         | 27.0  | 93         | 33.3       |
| Insulin users          | 67    | 38.1          | 40.5        | 45.0  | 43.6       |

| Table 4: Overall efficacy data |
|-------------------------------|
| **Parameter** | **N** | **Baseline** | **Week 24** | **Change from baseline** |
|----------------|-------|--------------|-------------|-------------------------|
| Glycaemic control (insulin naïve) | 61 | 10.7 | 8.0 | −2.7 |
| HbA1c, mean (%) | 93 | 14.5 | 8.2 | −6.3 |
| FPG, mean (mmol/L) | 25 | 16.3 | 12.3 | −4.0 |
| Glycaemic control (insulin users) | 34 | 9.1 | 7.8 | −1.3 |
| HbA1c, mean (%) | 42 | 9.8 | 7.6 | −2.1 |
| FPG, mean (mmol/L) | 18 | 14.7 | 10.9 | −3.8 |
| Achievement of HbA1c <7.0% at week 24 | 70 | 14.3 |
| Insulin naïve (%) | 38 | 15.8 |
| Insulin users (%) |

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 | 69 | 0.4 | 2.4 | 2.0 |
| Insulin naïve | 29 | 2.15 | 1.2 | −20.3 |
| Body weight, kg | 31 | 74.3 | 75.9 | 1.7 |
| Insulin naïve | 15 | 73.9 | 72.7 | −1.1 |
| Insulin users | 48 | 69.5 | 73.9 | 4.4 |
| Quality of life, VAS scale (0-100) | 21 | 62.0 | 79.3 | 17.3 |
| Insulin naïve (%) | 38 | 15.8 |
| Insulin users (%) |

VAS: Visual analogue scale

| Table 6: Insulin dose |
|----------------------|
| **Insulin dose, U/day** | **N** | **Pre-study** | **Baseline** | **N** | **Week 24** |
|------------------------|-------|---------------|-------------|-------|------------|
| Insulin naïve          | 0     | 0.0           | 69          | 34.6  | 48         | 42.0       |
| Insulin users          | 29    | 36.2          | 29          | 39.8  | 21         | 43.0       |
or switching to insulin detemir, hypoglycaemia reduced from 11.4 events/patient-year to 0.0 events/patient-year in insulin user group whereas hypoglycaemic events increased from 0.0 to 1.1 events/patient-year in insulin naïve group. An improvement in quality of life 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 insulin-naïve group whereas mean HbA1c and FPG values improved for insulin user group [Table 13].

**Insulin aspart ± OGLD**

Of the total cohort, 8 patients started on insulin aspart ± OGLD, of which 5 (62.5%) were insulin naïve and 3 (37.5%) were insulin users. After 24 weeks of treatment, hypoglycaemic events reduced from 65.0 events/patient-year to 6.5 events/patient-year in insulin user group [Table 14]. Quality of life improved in both the groups.

Mean FPG values improved from baseline to study end in those who started on or were switched to insulin aspart ± OGLDs for insulin-naïve group [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. Quality of life improved in the total cohort. Major hypoglycaemic episodes were null at 24 weeks. SADRs were reported in 1.5% of insulin users. Overall, body weight increased in insulin naïve population and decreased in insulin users. 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 Agadir, Morocco.

---

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

| Parameter                          | N   | Baseline | Week 24 | Change from baseline |
|------------------------------------|-----|----------|---------|----------------------|
| Hypoglycaemia, events/patient-year |     |          |         |                      |
| Insulin naïve                      | 46  | 0.0      | 1.1     | 1.1                  |
| Insulin users                      | 8   | 11.4     | 0.0     | −11.4                |
| Body weight, kg                    |     |          |         |                      |
| Insulin naïve                      | 31  | 72.7     | 73.2    | 0.5                  |
| Insulin users                      | 3   | 89.7     | 88.3    | −1.3                 |
| Quality of life, VAS scale (0-100) |     |          |         |                      |
| Insulin naïve                      | 36  | 61.3     | 82.5    | 21.2                 |
| Insulin users                      | 5   | 54.0     | 74.0    | 20.0                 |

VAS: Visual analogue scale

**Table 12: Insulin dose**

| Insulin dose, U/day | Pre-study | N | Baseline | N | Week 24 |
|---------------------|-----------|---|----------|---|---------|
| Insulin naïve       | 0         | 0.0| 46       | 13.7| 36      | 21.9   |
| Insulin users       | 8         | 29.9| 8       | 18.8| 5       | 18.8   |

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

| Parameter                          | N   | Baseline | Week 24 | Change from baseline |
|------------------------------------|-----|----------|---------|----------------------|
| Glycaemic control (insulin naïve)  |     |          |         |                      |
| HbA1c, mean (%)                    | 27  | 9.9      | 7.8     | −2.2                 |
| FPG, mean (mmol/L)                 | 36  | 12.7     | 7.4     | −5.3                 |
| PPPG, mean (mmol/L)                | 9   | 15.5     | 10.0    | −5.5                 |
| Glycaemic control (insulin users)  |     |          |         |                      |
| HbA1c, mean (%)                    | 5   | 7.8      | 7.4     | −0.4                 |
| FPG, mean (mmol/L)                 | 5   | 9.2      | 7.6     | −1.6                 |

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

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

| Parameter                          | N   | Baseline | Week 24 | Change from baseline |
|------------------------------------|-----|----------|---------|----------------------|
| Hypoglycaemia, events/patient-year |     |          |         |                      |
| Insulin naïve                      | 5   | 0.0      | 0.0     | 0.0                  |
| Quality of life, VAS scale (0-100) |     |          |         |                      |
| Insulin naïve                      | 2   | 37.5     | 75.0    | 37.5                 |

VAS: Visual analogue scale

**Table 15: Insulin dose**

| Insulin dose, U/day | Pre-study | N | Baseline | N | Week 24 |
|---------------------|-----------|---|----------|---|---------|
| Insulin naïve       | 0         | 0  | 5        | 15.2| 2       | 30.0   |

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

| Parameter                          | N   | Baseline | Week 24 | Change from baseline |
|------------------------------------|-----|----------|---------|----------------------|
| Glycaemic control (insulin naïve)  |     |          |         |                      |
| FPG, mean (mmol/L)                 | 2   | 15.7     | 13.7    | −2.1                 |

FPG: Fasting plasma glucose
REFERENCES

1. IDF Diabetes Atlas. 5th ed. 2011. Available from: http://www.idf.org/atlasmap/atlasmap [Last accessed on 2013 Jun 10].
2. Korytkowski M. When oral agents fail: Practical barriers to starting insulin. Int J Obes Relat Metab Disord 2002;26 Suppl 3:S18-24.
3. Hirsch IB. Insulin analogues. N Engl J Med 2005;352:174-83.
4. Shah SN, Litwak L, Haddad J, Chakkarwar PN, Hajjaji I. The A1chieve study: A 60,000-person, global, prospective, observational study of basal, meal-time, and biphasic insulin analogs in daily clinical practice. Diabetes Res Clin Pract 2010;88 Suppl 1:S11-6.

Cite this article as: Boussouf H, Mouniri M, Oudrhiri M. Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the Agadir cohort of the A1chieve study. Indian J Endocr Metab 2013;17:S399-403.

Source of Support: Nil, Conflict of Interest: None declared.