Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the Northern Tunisia cohort of the A_1chieve study

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ABSTRACT

Background: The A_1chieve, 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 Northern Tunisia. Results: A total of 443 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 = 137), insulin detemir (n = 243), insulin aspart (n = 11), basal insulin plus insulin aspart (n = 39) and other insulin combinations (n = 13). At baseline glycaemic control was poor for both insulin naïve (mean HbA1c: 10.2%) and insulin user (mean HbA1c: 9.8%) groups. After 24 weeks of treatment, both the study groups showed improvement in HbA1c (insulin naïve: −2.1%, insulin users: −0.9%). SADRs including major hypoglycaemic events or episodes 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: A_1chieve study, insulin analogues, Northern Tunisia, type 2 diabetes mellitus

INTRODUCTION

The incidence of diabetes in Tunisia is estimated to be 8.9%. Fear of hypoglycaemia and gain in body weight act as 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. A_1chieve, 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 Northern Tunisia.

MATERIALS AND METHODS

Please refer to editorial titled: The A_1chieve study: Mapping the Ibn Battuta trail.

RESULTS

A total of 443 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 (54.9%) started on or were switched to insulin detemir. Other groups were insulin aspart (n = 11), basal insulin plus insulin aspart (n = 39), biphasic insulin aspart (n = 137), and other insulin combinations (n = 13).
After 24 weeks of treatment, overall hypoglycaemia reduced from 18.4 events/patient-year to 3.2 events/patient-year in insulin user group whereas hypoglycaemic events increased from 0.8 events/patient-year to 1.5 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 including major hypoglycaemic events did not occur in any of the study patients [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, 137 patients starting on biphasic insulin aspart ± OGLD, of which 13 (9.5%) were insulin naïve and 124 (90.5%) were insulin users. After 24 weeks of starting or switching to biphasic insulin aspart, hypoglycaemic events reduced from 1.0 events/patient-year to 0.0 events/patient-year in insulin naïve group and from 13.7 events/patient-year to 1.1 events/patient-year in insulin users group. A decrease in body weight was observed in insulin user group [Tables 5 and 6].

Mean HbA₁c and FPG values improved from baseline to study end in those who started on or were switched to biphasic insulin aspart for insulin naïve group whereas all parameters of glycaemic control improved in insulin user group [Table 7].

**Basal + insulin aspart ± OGLD**

Of the total cohort, 39 patients started on basal + insulin aspart ± OGLD, of which 1 (2.6%) was insulin naïve and 38 (97.4%) were insulin users. All parameters of glycaemic control improved in both insulin user and insulin naïve groups [Table 7].

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**Table 1: Overall demographic data**

| Parameters | Insulin naïve | Insulin users | All |
|------------|--------------|---------------|-----|
| Number of participants | 144          | 299           | 443 |
| Male N (%) | 83 (57.6)    | 141 (47.2)    | 224 (50.6) |
| Female N (%) | 61 (42.4)    | 158 (52.8)    | 219 (49.4) |
| Age (years) | 60.1         | 57.8          | 58.5 |
| Weight (kg) | 77.2         | 79.6          | 78.8 |
| BMI (kg/m²) | 28.3         | 29.5          | 29.1 |
| Duration of DM (years) | 11.7         | 15.1          | 14.0 |
| No therapy | 5            |               |     |
| >2 OGLD   | 2            | 2             | 4   |
| HbA₁c     | 10.2         | 9.8           | 9.9 |
| FPG (mmol/L) | 13.4        | 11.2          | 11.9 |
| PPPG (mmol/L) | 15.8       | 14.7          | 15.0 |
| Macrovascular complications, N (%) | 53 (36.8) | 121 (40.5) | 174 (39.3) |
| Microvascular complications, N (%) | 86 (59.7) | 226 (75.6) | 312 (70.4) |
| Pre-study therapy, N (%) | 443 | | |
| Insulin users | 299 (67.5) | 139 (31.4) | 5 (1.1) |
| OGLD only | 11 (3.9) | | |
| No therapy | 5 (1.1) | | |
| Baseline therapy, N (%) | 243 (54.9) | | |
| Insulin detemixOGLD | | | |
| Insulin aspartOGLD | 11 (16.3) | | |
| Basal+insulin aspartOGLD | 39 (8.8) | | |
| Biphasic insulin aspartOGLD | 137 (30.9) | | |
| Others | 13 (2.9) | | |

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 | 144 | 0.8 | 1.5 | 0.7 |
| Nocturnal | | 0.4 | 0.9 | 0.5 |
| Major | | 0.0 | 0.0 | 0.0 |
| Hypoglycaemia (insulin users), events/patient-year | | | | |
| All | 299 | 18.4 | 3.2 | −15.2 |
| Nocturnal | | 8.2 | 1.6 | −6.6 |
| Major | | 1.2 | 0.0 | −1.2 |
| Body weight, kg | | | | |
| Insulin naïve | 101 | 76.2 | 77.9 | 1.7 |
| Insulin users | 220 | 79.2 | 78.9 | −0.4 |
| Lipids and BP (insulin naïve) | | | | |
| LDL-C, mean (mmol/L), (N, %<2.5 mmol/L) | 46 | 1.7 (30, 65.2) | 3.7 (11, 47.8) | 2.0 |
| HDL-C, mean (mmol/L), (N, %>1.0 mmol/L) | 65 | 0.9 (21, 32.3) | 1.0 (16, 45.7) | 0.1 |
| TG, mean (mmol/L), (N, %<2.3 mmol/L) | 60 | 1.6 (52, 86.7) | 1.6 (42, 89.4) | 0.0 |
| SBP, mean (mmHg), (N, %<130 mmHg) | 141 | 132.4 (39, 27.7) | 133.8 (28, 28.0) | 1.4 |
| Lipids and BP (insulin users) | | | | |
| LDL-C, mean (mmol/L), (N, %<2.5 mmol/L) | 80 | 2.0 (53, 66.3) | 3.1 (19, 50.0) | 1.1 |
| HDL-C, mean (mmol/L), (N, %>1.0 mmol/L) | 144 | 0.9 (63, 43.8) | 1.0 (51, 58.0) | 0.1 |
| TG, mean (mmol/L), (N, %<2.3 mmol/L) | 149 | 2.0 (130, 87.2) | 3.1 (108, 90.8) | 1.1 |
| SBP, mean (mmHg), (N, %<130 mmHg) | 292 | 134.4 (84, 28.8) | 133.3 (70, 30.4) | −1.2 |
| Quality of life, VAS scale (0-100) | | | | |
| Insulin naïve | 15 | 55.9 | 70.3 | 14.4 |
| Insulin users | 62 | 61.4 | 67.4 | 5.9 |

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
38 (97.4%) were insulin users. After 24 weeks of starting or switching to basal + insulin aspart, hypoglycaemic events reduced from 55.8 events/patient-year to 9.9 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 switched to basal + insulin aspart ± OGLDs for insulin user group [Table 10].

### Insulin detemir ± OGLD

Of the total cohort, 243 patients started on insulin detemir ± OGLD, of which 130 (53.5%) were insulin naïve and 113 (46.5%) were insulin users. After 24 weeks of starting or switching to insulin detemir, hypoglycaemic events increased from 0.8 events/patient-year to 1.6 events/patient-year in insulin naïve group whereas hypoglycaemic events reduced from 11.7 events/patient-year to 1.7 events/patient-year in insulin users. A decrease in body weight was observed in insulin user group. An improvement in

### Table 3: Insulin dose

| Insulin dose, U/day | N Pre-study | N Baseline | N Week 24 |
|---------------------|------------|------------|-----------|
| Insulin naïve       | 0          | 0          | 144       |
|                     | 15.8       | 107        | 25.7      |
| Insulin users       | 299        | 48.7       | 299       |
|                     | 41.8       | 238        | 50.2      |

### Table 4: Overall efficacy data

| Parameter | N Baseline | Week 24 Change from baseline |
|-----------|------------|-------------------------------|
| Glycaemic control (insulin naïve) HbA1c, mean (%) | 85 | 10.2 | 8.1 | −2.0 |
| FPG, mean (mmol/L) | 96 | 13.4 | 8.1 | −5.2 |
| PPPG, mean (mmol/L) | 23 | 15.8 | 9.6 | −6.1 |
| Glycaemic control (insulin users) HbA1c, mean (%) | 180 | 9.8 | 8.9 | −0.9 |
| FPG, mean (mmol/L) | 208 | 11.2 | 9.1 | −2.0 |
| PPPG, mean (mmol/L) | 74 | 14.7 | 11.5 | −3.3 |

Achievement of HbA1c <7.0% at week 24

| (insulin naïve) | % of patients | (insulin users) | % of patients |
|----------------|---------------|----------------|---------------|
| Insulin naïve | 144 | 15.6 | Insulin users | 299 | 5.6 |

HbA1c: Glycated hemoglobin 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 | 13 | 1.0 | 0.0 | −1.0 |
| Insulin users | 124 | 13.7 | 1.1 | −12.6 |
| Body weight, kg Insulin naïve | 8 | 77.6 | 81.3 | 3.7 |
| Insulin users | 94 | 80.4 | 80.2 | −0.3 |
| Quality of life, VAS scale (0-100) Insulin naïve | 1 | 50.0 | 70.0 | 20.0 |
| Insulin users | 29 | 58.9 | 67.1 | 8.1 |

VAS: Visual analogue scale

### Table 6: Insulin dose

| Insulin dose, U/day | N Pre-study | N Baseline | N Week 24 |
|---------------------|------------|------------|-----------|
| Insulin naïve       | 0          | 0          | 13        |
|                     | 36.6       | 8          | 50.0      |
| Insulin users       | 124        | 54.0       | 124       |
|                     | 51.3       | 98         | 58.4      |

### 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 (%) | 4 | 11.4 | 8.7 | −2.7 |
| FPG, mean (mmol/L) | 7 | 15.7 | 10.4 | −5.3 |
| PPPG, mean (mmol/L) | 1 | 8.8 | 9.5 | 0.7 |
| Glycaemic control (insulin users) HbA1c, mean (%) | 77 | 10.2 | 8.8 | −1.4 |
| FPG, mean (mmol/L) | 90 | 12.1 | 9.2 | −2.8 |
| PPPG, mean (mmol/L) | 30 | 15.6 | 12.1 | −3.5 |

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 users | 38 | 55.8 | 9.9 | −45.9 |
| Body weight, kg Insulin users | 28 | 80.8 | 81.1 | 0.2 |
| Quality of life, VAS scale (0-100) Insulin users | 6 | 52.5 | 56.0 | 3.5 |

VAS: Visual analogue scale

### Table 9: Insulin dose

| Insulin dose, U/day | N Pre-study | N Baseline | N Week 24 |
|---------------------|------------|------------|-----------|
| Insulin users       | 38          | 58.7       | 38        |
|                     | 53.6       | 29         | 65.6      |

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

| Parameter | N Baseline | Week 24 Change from baseline |
|-----------|------------|-------------------------------|
| Glycaemic control (insulin users) HbA1c, mean (%) | 21 | 9.5 | 8.7 | −0.7 |
| FPG, mean (mmol/L) | 25 | 10.8 | 8.1 | −2.6 |
| PPPG, mean (mmol/L) | 15 | 13.2 | 9.9 | −3.2 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPPG: Postprandial plasma glucose
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 ± OGGLDs for both insulin-naïve and insulin user groups [Table 13].

### Insulin aspart ± OGGLD

Of the total cohort, 11 patients were started on basal + insulin aspart ± OGGLD group and all were insulin users. After 24 weeks of treatment starting or switching to insulin aspart hypoglycaemic events reduced from 8.3 events/patient-year to 0.0 events/patient in insulin user group [Table 14].

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

### Conclusion

Our study reports improved glycaemic control (HbA1c, FPG, PPPG) following 24 weeks of treatment with any of the insulin analogues (basal + insulin aspart; insulin detemir; insulin aspart) with or without OGGLD. In patients who started on or switched to biphasic insulin aspart, mean HbA1c and FPG values improved in insulin naïve group whereas all parameters of glycaemic control improved in insulin user group. SADRs including major hypoglycaemic events or episodes did not occur in any of the study patients after 24 week of treatment. Overall, body weight increased in insulin naïve population while a decrease in body weight was observed in insulin users. Quality of life improved in total cohort. 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 Northern Tunisia.
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