Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the Eastern Saudi Arabia 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 Eastern Saudi Arabia. Results: A total of 1040 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 = 489), insulin detemir (n = 360), insulin aspart (n = 37), basal insulin plus insulin aspart (n = 96) and other insulin combinations (n = 57). At baseline glycaemic control was poor for both insulin naïve (mean HbA₁c: 10.0%) and insulin user (mean HbA₁c: 9.2%) groups. After 24 weeks of treatment, both the groups showed improvement in HbA₁c (insulin naïve: −2.7%, insulin users: −1.7%). No major hypoglycaemic episodes were observed at 24 weeks. SADR was reported in 0.6% 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, Eastern Saudi Arabia, insulin analogues, type 2 diabetes mellitus

INTRODUCTION

2.7 million people are estimated to have diabetes in Saudi Arabia, with estimated prevalence of 16.2%.¹ Hypoglycaemia and gain in body weight are barriers for initiation of insulin therapy.² Modern insulin analogues are a convenient new approach or tool to glycaemic control, associated with low number of hypoglycaemia and favourable weight change.³ 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.⁴ This short communication presents the results for patients enrolled from Eastern Saudi Arabia.
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After 24 weeks of treatment, overall hypoglycaemic events reduced from 10.1 events/patient-year to 3.9 events/patient-year in insulin user group whereas hypoglycaemia increased from 0.7 events/patient-year to 3.9 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. No major hypoglycaemic episodes were observed at 24 weeks. SADR was reported in 0.6% of insulin users. A slight decrease in body weight was noted. Blood pressure decreased and overall lipid profile improved at week 24 in complete 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, 489 patients started on biphasic insulin aspart ± OGLD, of which 238 (48.6%) were insulin naïve and 251 (51.4%) were insulin users. After 24 weeks of starting or switching to biphasic insulin aspart, hypoglycaemic events reduced from 8.2 events/patient-year to 5.7 events/patient-year in insulin user group while hypoglycaemia increased from 8.2 events/patient-year to 5.7 events/patient-year in insulin naive group. Body weight decreased in both insulin naïve and insulin user groups [Tables 5 and 6].

All parameters of glycaemic control improved from baseline to study end in both insulin naïve and insulin user groups [Table 7].

### Basal + insulin aspart ± OGLD

Of the total cohort, 96 patients started on basal + insulin aspart ± OGLD, of which 16 (16.7%) were insulin naïve and 80 (83.3%) were insulin users. After 24 weeks of starting or switching to basal + insulin aspart hypoglycaemic

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**Table 1: Overall demographic data**

| Parameters | Insulin naive | Insulin users | All |
|-----------|---------------|---------------|-----|
| Number of participants | 560 | 480 | 1040 |
| Male N (%) | 373 (66.7) | 275 (57.5) | 648 (62.5) |
| Female N (%) | 186 (33.3) | 203 (42.5) | 389 (37.5) |
| Age (years) | 48.9 | 47.1 | 48.1 |
| Weight (kg) | 87.4 | 85.3 | 86.4 |
| BMI (kg/m²) | 31.4 | 30.4 | 30.9 |
| Duration of DM (years) | 9.9 | 11.9 | 10.9 |
| No therapy | 20 | | |
| >2 OGLD | 87 | 24 | 111 |
| Hba1c | 10.0 | 9.2 | 9.6 |
| FPG (mmol/L) | 11.9 | 10.3 | 11.1 |
| PPPG (mmol/L) | 16.1 | 14.6 | 15.3 |
| Macrovascular complications, N (%) | 99 (17.7) | 170 (35.4) | 269 (25.9) |
| Microvascular complications, N (%) | 370 (66.1) | 330 (68.8) | 700 (67.3) |
| Pre-study therapy, N (%) | | | |
| Insulin users | 480 (46.6) | | |
| OGLD only | 540 (51.9) | | |
| No therapy | 20 (1.9) | | |
| Baseline therapy, N (%) | | | |
| Insulin detemir±OGLD | 360 (34.6) | | |
| Insulin aspart±OGLD | 37 (3.6) | | |
| Basal+insulin aspart±OGLD | 96 (9.2) | | |
| Biphasic insulin aspart±OGLD | 489 (47.0) | | |
| Others | 57 (5.5) | | |
| 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 | 560 | 0.7 | 3.9 | 3.2 |
| Nocturnal | 0.2 | 1.1 | 0.9 |
| Major | 0.1 | 0.0 | −0.1 |
| Hypoglycaemia (insulin users), events/patient-year | | | | |
| All | 480 | 10.1 | 3.9 | −6.2 |
| Nocturnal | 3.1 | 1.3 | −1.8 |
| Major | 1.8 | 0.0 | −1.8 |
| Body weight, kg | | | | |
| Insulin naïve | 529 | 86.9 | 86.3 | −0.6 |
| Insulin users | 480 | 85.2 | 84.8 | −0.3 |
| Lipids and BP (insulin naïve) | | | | |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L) | 386 | 3.2 (63, 16.3) | 2.7 (100, 30.8) | −0.5 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L) | 406 | 1.0 (231, 56.9) | 1.2 (245, 70.8) | 0.1 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L) | 418 | 2.3 (259, 62.0) | 1.9 (314, 86.3) | −0.4 |
| SBP, mean (mmHg), (N, % <130 mmHg) | 558 | 133.8 (156, 28.0) | 126.5 (265, 50.8) | −7.3 |
| Lipids and BP (insulin users) | | | | |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L) | 335 | 3.2 (60, 17.9) | 2.8 (82, 29.0) | −0.4 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L) | 333 | 1.1 (217, 65.2) | 1.2 (217, 76.7) | 0.1 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L) | 349 | 2.3 (202, 57.9) | 1.9 (238, 79.1) | −0.5 |
| SBP, mean (mmHg), (N, % <130 mmHg) | 479 | 132.7 (159, 33.2) | 126.3 (234, 52.9) | −6.4 |

BP: Blood pressure, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TG: Triglycerides, SBP: Systolic blood pressure
events reduced from 13.7 events/patient-year to 2.3 events/patient-year in insulin user group, whereas hypoglycaemia increased from 0.0 events/patient-year to 8.1 events/patient-year in insulin naive group. A decrease in body weight was observed in insulin naive 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 both insulin naïve and insulin user groups [Table 10].

### Table 3: Insulin dose

| Parameter            | N  | Baseline | Week 24 | Change from baseline |
|----------------------|----|----------|---------|----------------------|
| Insulin dose, U/day  |    |          |         |                      |
| Insulin naïve        | 0  | 0.0      | 560     | 31.7                 |
| Insulin users        | 480| 56.8     | 479     | 56.2                 |

### Table 4: Overall efficacy data

| Parameter            | N  | Baseline | Week 24 | Change from baseline |
|----------------------|----|----------|---------|----------------------|
| Glycaemic control    |    |          |         |                      |
| HbA1c, mean (%)      | 468| 10.0     | 7.3     | −2.7                 |
| FPG, mean (mmol/L)   | 396| 11.9     | 6.7     | −5.2                 |
| PPG, mean (mmol/L)   | 251| 16.1     | 9.0     | −7.1                 |
| Glycaemic control    |    |          |         |                      |
| HbA1c, mean (%)      | 391| 9.2      | 7.4     | −1.7                 |
| FPG, mean (mmol/L)   | 378| 10.3     | 6.9     | −3.4                 |
| PPG, mean (mmol/L)   | 267| 14.6     | 8.9     | −5.7                 |
| Achievement of HbA1c |    |          |         |                      |
| <7.0% at week 24     | 508| 36.2     |         |                      |
| (% of patients)       | 435| 29.0     |         |                      |

### 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        | 238| 0.7      | 4.1     | 3.4                  |
| Insulin users        | 251| 8.2      | 5.7     | −2.5                 |
| Body weight, kg      |    |          |         |                      |
| Insulin naïve        | 202| 86.8     | 85.8    | −1.0                 |
| Insulin users        | 201| 85.7     | 85.4    | −0.2                 |

### Table 6: Insulin dose

| Parameter            | N  | Baseline | Week 24 | Change from baseline |
|----------------------|----|----------|---------|----------------------|
| Insulin dose, U/day  |    |          |         |                      |
| Insulin naïve        | 0  | 0.0      | 238     | 44.1                 |
| Insulin users        | 251| 60.5     | 251     | 61.8                 |

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

| Parameter            | N  | Baseline | Week 24 | Change from baseline |
|----------------------|----|----------|---------|----------------------|
| Glycaemic control    |    |          |         |                      |
| HbA1c, mean (%)      | 204| 10.2     | 7.2     | −3.0                 |
| FPG, mean (mmol/L)   | 193| 12.3     | 6.8     | −5.5                 |
| PPG, mean (mmol/L)   | 114| 17.3     | 9.1     | −8.2                 |
| Glycaemic control    |    |          |         |                      |
| HbA1c, mean (%)      | 187| 9.2      | 7.3     | −1.9                 |
| FPG, mean (mmol/L)   | 181| 11.1     | 7.0     | −4.2                 |
| PPG, mean (mmol/L)   | 106| 15.0     | 9.1     | −6.0                 |

### 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        | 16 | 0.0      | 8.1     | 8.1                  |
| Insulin users        | 80 | 13.7     | 2.3     | −11.4                |
| Body weight, kg      |    |          |         |                      |
| Insulin naïve        | 13 | 93.0     | 92.3    | −0.7                 |
| Insulin users        | 75 | 81.4     | 81.5    | 0.1                  |

### Table 9: Insulin dose

| Parameter            | N  | Baseline | Week 24 | Change from baseline |
|----------------------|----|----------|---------|----------------------|
| Insulin dose, U/day  |    |          |         |                      |
| Insulin naïve        | 0  | 0.0      | 16      | 44.0                 |
| Insulin users        | 80 | 56.0     | 80      | 55.2                 |

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

| Parameter            | N  | Baseline | Week 24 | Change from baseline |
|----------------------|----|----------|---------|----------------------|
| Glycaemic control    |    |          |         |                      |
| HbA1c, mean (%)      | 12 | 10.1     | 7.1     | −3.0                 |
| FPG, mean (mmol/L)   | 6  | 13.3     | 6.9     | −6.4                 |
| PPG, mean (mmol/L)   | 4  | 15.6     | 8.2     | −7.3                 |

### Insulin detemir ± OGLD

Of the total cohort, 360 of patients started on insulin detemir ± OGLD, of which 282 (78.3%) were insulin naïve and 78 (21.7%) were insulin users. After 24 weeks of starting or switching to insulin detemir,
hypoglycaemic events reduced from 6.2 events/patient-year to 2.9 events/patient-year in insulin user group, while hypoglycaemia increased from 0.5 events/patient-year to 3.3 events/patient-year in insulin naive group. A decrease in body weight was observed in both insulin naive and insulin user groups [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 ± O GLD**

Of the total cohort, 37 patients started on insulin aspart ± OGLD, of which 17 (45.9%) were insulin naïve and 20 (54.1%) were insulin users. After 24 weeks of treatment starting or switching to insulin aspart, hypoglycaemic events reduced from 10.4 events/patient-year to 0.0 events/patient-year in insulin user group, whereas hypoglycaemia increased from 3.1 events/patient-year to 8.4 events/patient-year in insulin naive group. A decrease in body weight was observed in insulin user group [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. No major hypoglycaemic episodes were observed at 24 weeks. SADR was reported in 0.6% of insulin users. A small weight reduction was observed at week 24 in the complete 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 Eastern Saudi Arabia.

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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                      | 282| 0.5      | 3.3     | 2.8                  |
| Insulin users                      | 78 | 6.2      | 2.9     | −3.3                 |
| Body weight, kg                    |    |          |         |                      |
| Insulin naïve                      | 229| 87.5     | 87.1    | −0.4                 |
| Insulin users                      | 68 | 85.7     | 85.1    | −0.6                 |

**Table 12: Insulin dose**

| Insulin dose, U/day | N  | Pre-study | N  | Baseline | N  | Week 24 |
|---------------------|----|-----------|----|----------|----|---------|
| Insulin naïve       | 0  | 0.0       | 282| 19.8     | 266| 29.2    |
| Insulin users       | 78 | 40.8      | 78 | 33.4     | 73 | 40.0    |

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

| Glycaemic control (insulin naïve) | N  | Baseline | Week 24 | Change from baseline |
|-----------------------------------|----|----------|---------|----------------------|
| HbA1c, mean (%)                   | 233| 9.8      | 7.3     | −2.5                 |
| FPG, mean (mmol/L)                | 182| 11.3     | 6.7     | −4.6                 |
| PPPG, mean (mmol/L)               | 124| 14.9     | 9.0     | −5.9                 |
| Glycaemic control (insulin users) |    |          |         |                      |
| HbA1c, mean (%)                   | 65 | 8.7      | 7.7     | −1.0                 |
| FPG, mean (mmol/L)                | 65 | 9.3      | 7.0     | −2.3                 |
| PPPG, mean (mmol/L)               | 43 | 14.0     | 8.6     | −5.4                 |

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                      | 17 | 3.1      | 8.4     | −5.3                 |
| Insulin users                      | 20 | 10.4     | 0.0     | −10.4                |
| Body weight, kg                    |    |          |         |                      |
| Insulin naïve                      | 15 | 73.1     | 76.0    | 2.9                  |
| Insulin users                      | 16 | 94.4     | 91.2    | −3.2                 |

**Table 15: Insulin dose**

| Insulin dose, U/day | N  | Pre-study | N  | Baseline | N  | Week 24 |
|---------------------|----|-----------|----|----------|----|---------|
| Insulin naïve       | 0  | 0.0       | 17 | 31.0     | 17 | 45.4    |
| Insulin users       | 20 | 29.4      | 20 | 24.6     | 19 | 46.6    |

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

| Glycaemic control (insulin naïve) | N  | Baseline | Week 24 | Change from baseline |
|-----------------------------------|----|----------|---------|----------------------|
| HbA1c, mean (%)                   | 13 | 9.1      | 7.1     | −2.0                 |
| FPG, mean (mmol/L)                | 9  | 12.7     | 6.2     | −6.6                 |
| PPPG, mean (mmol/L)               | 4  | 15.8     | 7.8     | −8.0                 |
| Glycaemic control (insulin users) |    |          |         |                      |
| HbA1c, mean (%)                   | 18 | 10.8     | 7.6     | −3.2                 |
| FPG, mean (mmol/L)                | 15 | 12.0     | 6.8     | −5.2                 |
| PPPG, mean (mmol/L)               | 9  | 15.1     | 8.2     | −6.9                 |

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