Clinical experience with insulin detemir, biphasic insulin aspart and insulin aspart in people with type 2 diabetes: Results from the Central Saudi Arabia cohort of the Achieve study

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ABSTRACT
Background: The Achieve, 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 Central Saudi Arabia. Results: A total of 2819 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 = 1100), insulin detemir (n = 1156), insulin aspart (n = 34), basal insulin plus insulin aspart (n = 314) and other insulin combinations (n = 170). At baseline glycaemic control was poor for both insulin naïve (mean HbA1c: 9.9%) and insulin user (mean HbA1c: 9.8%) groups. After 24 weeks of treatment, both the groups showed improvement in HbA1c (insulin naïve: −2.6%, insulin users: −2.5%). SADRs including major hypoglycaemic events did not occur in 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: Achieve study, Central 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%. 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. Achieve, 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 Central Saudi Arabia.

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

RESULTS
A total of 2819 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 started on or switched to insulin detemir (41.0%). Other groups were biphasic insulin aspart (1100), Basal plus insulin aspart (n = 314), insulin aspart (n = 34) and other insulin combinations (n = 170).
After 24 weeks of treatment, overall hypoglycaemic events reduced from 13.0 events/patient-year to 2.1 events/patient-year in insulin user group and from 1.4 events/patient-year to 0.7 events/patient-year in insulin naive group. The hypoglycaemia incidence in insulin naive group at 24 weeks was lower than that observed in insulin users at baseline. SADRs including major hypoglycaemic events did not occur in any of the study patients. A decrease in body weight was noted at the end of the study. Blood pressure decreased and lipid profile improved at week 24 in the complete cohort [Tables 2 and 3].

All parameters of glycaemic control improved from baseline to study end in the total cohort. More than one third of patients achieved HbA1c < 7.0% at week 24 [Table 4].

**Biphasic insulin aspart ± OGLD**

Of the total cohort, 1100 patients started on biphasic insulin aspart ± OGLD, of which 605 (55%) were insulin naïve and 495 (45%) were insulin users. After 24 weeks of starting or switching to biphasic insulin aspart, hypoglycaemic events reduced from 0.8 events/patient-year to 0.7 events/patient-year in insulin naïve group and from 5.5 events/patient-year to 1.0 events/patient-year in insulin users group. Body weight decreased in insulin naïve group 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].

**Basal + insulin aspart ± OGLD**

Of the total cohort 314 patients started on basal + insulin aspart ± OGLD, of which 103 (32.8%) were insulin naïve and 211 (67.2%) were insulin users. After 24 weeks of starting or switching to basal + insulin aspart, hypoglycaemic events reduced from 4.0 events/patient-year to 2.3 events/patient-year [Table 8].

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**Table 1: Overall demographic data**

| Parameters | Insulin naïve | Insulin users | All |
|------------|--------------|--------------|-----|
| Number of participants | 1718 | 1101 | 2819 |
| Male N (%) | 1132 (66.4) | 602 (54.9) | 1734 (61.9) |
| Female N (%) | 574 (33.6) | 494 (45.1) | 1068 (38.1) |
| Age (years) | 50.8 | 51.9 | 51.2 |
| Weight (kg) | 88.7 | 88.3 | 88.6 |
| BMI (kg/m²) | 31.8 | 32.4 | 32.0 |
| Duration of DM (years) | 8.2 | 11.6 | 9.5 |
| No therapy | 37 |
| >2 OGLD | 262 | 62 | 324 |
| HbA1c (mmol/L) | 9.9 | 9.8 | 9.8 |
| FPG (mmol/L) | 11.4 | 10.3 | 11.0 |
| PPPG (mmol/L) | 15.8 | 14.9 | 15.5 |
| Microvascular complications, N (%) | 459 (26.7) | 448 (40.7) | 907 (32.2) |
| Microvascular complications, N (%) | 1147 (66.8) | 873 (79.3) | 2020 (71.7) |
| Pre-study therapy, N (%) | |
| Insulin users | 1101 (39.1) |
| OGLD only | 1681 (59.6) |
| No therapy | 37 (1.3) |
| Baseline therapy, N (%) | |
| Insulin detemir±OGLD | 1156 (41.0) |
| Insulin aspart±OGLD | 34 (1.2) |
| Basal+insulin aspart±OGLD | 314 (11.1) |
| Biphasic insulin aspart±OGLD | 1100 (39.0) |
| Others | 170 (6.0) |
| Missing | 45 (1.6) |

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 | 1283 | 1.4 | 0.7 | −0.7 |
| Nocturnal | 0.2 | 0.2 | 0.0 |
| Major | 0.1 | 0.0 | −0.1 |
| Hypoglycaemia (insulin users), events/patient-year | | | | |
| All | 1101 | 13.0 | 2.1 | −10.1 |
| Nocturnal | 3.7 | 0.7 | −3.09 |
| Major | 3.0 | 0.0 | −3.0 |
| Body weight, kg | | | | |
| Insulin naïve | 1718 | 89.6 | 88.4 | −1.2 |
| Insulin users | 1101 | 89.1 | 88.2 | −0.8 |
| Lipids and BP (insulin naïve) | | | | |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L) | 1222 | 3.2 (282, 23.1) | 2.7 (353, 34.3) | −0.5 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L) | 1220 | 1.1 (767, 62.9) | 1.2 (747, 73.1) | 0.1 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L) | 1283 | 2.0 (877, 68.4) | 1.8 (900, 85.1) | −0.2 |
| SBP, mean (mmHg), (N, % <130 mmHg) | 1690 | 133.0 (555, 32.8) | 127.4 (666, 44.3) | −5.6 |
| Lipids and BP (insulin users) | | | | |
| LDL-C, mean (mmol/L), (N, % <2.5 mmol/L) | 768 | 2.9 (274, 35.7) | 2.6 (247, 44.9) | −0.3 |
| HDL-C, mean (mmol/L), (N, % >1.0 mmol/L) | 757 | 1.1 (443, 58.5) | 1.1 (344, 63.4) | 0.0 |
| TG, mean (mmol/L), (N, % <2.3 mmol/L) | 802 | 1.9 (590, 73.6) | 1.7 (489, 85.5) | −0.2 |
| SBP, mean (mmHg), (N, % <130 mmHg) | 1085 | 132.2 (381, 35.1) | 126.2 (434, 49.9) | −5.9 |

BP: Blood pressure, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TG: Triglycerides, SBP: Systolic blood pressure
patient-year in insulin naïve group and from 22.6 events/patient-year to 3.7 events/patient-year in insulin users group. Body weight decreased at the end of 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, 1156 patients who started on insulin detemir ± OGLD, of which 905 (78.2%) were insulin naïve and 251 (21.8%) were insulin users. After 24 weeks of starting or switching to insulin detemir, hypoglycaemic events reduced from 1.5 events/patient-year to 0.5 events/patient-year in insulin naïve group and from 14.9 events/patient-year to 2.0 events/patient-year in insulin users group. Body weight decreased at the end of 24 weeks [Tables 11 and 12].

### Table 3: Insulin dose

| Parameter                  | N   | Pre-study | Baseline | Week 24 | Change from baseline |
|----------------------------|-----|-----------|----------|---------|----------------------|
| Insulin dose, U/day        |     |           |          |         |                      |
| Insulin naïve              | 0   | 0         | 1704     | 37.1    | 1527                 | 48.7                     |
| Insulin users              | 1101| 61.7      | 1069     | 60.0    | 902                  | 68.4                     |

### Table 4: Overall efficacy data

| Parameter                  | N   | Baseline | Week 24 | Change from baseline |
|----------------------------|-----|----------|---------|----------------------|
| Glycaemic control (insulin naïve) |     |          |         |                      |
| HbA1c, mean (%)            | 1407| 9.9      | 7.3     | −2.6                 |
| FPG, mean (mmol/L)         | 1294| 11.4     | 6.7     | −4.6                 |
| PPPG, mean (mmol/L)        | 1097| 15.8     | 9.1     | −6.8                 |
| Glycaemic control (insulin users) |     |          |         |                      |
| HbA1c, mean (%)            | 823 | 9.8      | 7.3     | −2.5                 |
| FPG, mean (mmol/L)         | 732 | 10.3     | 6.8     | −3.6                 |
| PPPG, mean (mmol/L)        | 590 | 14.9     | 8.9     | −6.0                 |
| Achievement of HbA1c <7.0% at week 24 | | 1463 | 36.4 |                     |
| (%) of patients            |     |          |         |                      |
| Insulin naïve              | 853 | 39.9     |         |                      |
| 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 |     |          |         |                      |
| insulin naïve              | 605 | 0.8      | 0.7     | −0.1                 |
| Insulin users              | 495 | 5.5      | 1.0     | −4.5                 |
| Body weight, kg            |     |          |         |                      |
| Insulin naïve              | 431 | 87.8     | 87.4    | −0.4                 |
| Insulin users              | 330 | 87.3     | 87.3    | 0.0                  |

### Table 6: Insulin dose

| Parameter                  | N   | Pre-study | Baseline | Week 24 | Change from baseline |
|----------------------------|-----|-----------|----------|---------|----------------------|
| Insulin dose, U/day        |     |           |          |         |                      |
| Insulin naïve              | 0   | 0         | 605      | 47.7    | 504                  | 62.3                     |
| Insulin users              | 495 | 61.1      | 494      | 63.2    | 381                  | 73.3                     |

### 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 (%)            | 454 | 10.1     | 7.5     | −2.6                 |
| FPG, mean (mmol/L)         | 392 | 11.9     | 7.1     | −4.9                 |
| PPPG, mean (mmol/L)        | 337 | 17.0     | 9.6     | −7.3                 |
| Glycaemic control (insulin users) |     |          |         |                      |
| HbA1c, mean (%)            | 330 | 9.8      | 7.4     | 2.3                  |
| FPG, mean (mmol/L)         | 285 | 10.9     | 7.1     | −3.8                 |
| PPPG, mean (mmol/L)        | 248 | 14.9     | 9.1     | −5.7                 |

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              | 103 | 4.0      | 2.3     | −1.7                 |
| Insulin users              | 211 | 22.6     | 3.7     | −18.9                |
| Bodyweight, kg             |     |          |         |                      |
| Insulin naïve              | 86  | 88.7     | 87.4    | −1.4                 |
| Insulin users              | 156 | 88.4     | 87.0    | −1.4                 |

### Table 9: Insulin dose

| Parameter                  | N   | Pre-study | Baseline | Week 24 | Change from baseline |
|----------------------------|-----|-----------|----------|---------|----------------------|
| Insulin dose, U/day        |     |           |          |         |                      |
| Insulin naïve              | 0   | 0         | 103      | 54.7    | 97                   | 60.2                    |
| Insulin users              | 211 | 67.1      | 211      | 67.1    | 180                  | 72.1                    |

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

| Parameter                  | N   | Baseline | Week 24 | Change from baseline |
|----------------------------|-----|----------|---------|----------------------|
| Glycaemic control (insulin naïve) |     |          |         |                      |
| HbA1c, mean (%)            | 87  | 10.3     | 7.0     | −3.3                 |
| FPG, mean (mmol/L)         | 90  | 10.5     | 6.2     | −4.4                 |
| PPPG, mean (mmol/L)        | 64  | 16.4     | 8.8     | −7.6                 |
| Glycaemic control (insulin users) |     |          |         |                      |
| HbA1c, mean (%)            | 171 | 9.8      | 7.2     | −2.6                 |
| FPG, mean (mmol/L)         | 160 | 9.7      | 6.1     | −3.6                 |
| PPPG, mean (mmol/L)        | 119 | 15.0     | 8.2     | −6.9                 |

HbA1c: Glycated haemoglobin A1c, FPG: Fasting plasma glucose, PPPG: Postprandial plasma glucose, OGLD: Oral glucose-lowering drug
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].

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

| Parameter                                | N  | Baseline | Week 24 | Change from baseline |
|-------------------------------------------|----|----------|---------|----------------------|
| Hypoglycaemia, events/patient-year        |    |          |         |                      |
| Insulin naïve                             | 905| 1.5      | 0.5     | −1.0                 |
| Insulin users                             | 251| 14.9     | 2.0     | −12.9                |
| Body weight, kg                           |    |          |         |                      |
| Insulin naïve                             | 714| 90.6     | 88.9    | −1.7                 |
| Insulin users                             | 191| 92.7     | 91.0    | −1.7                 |

**Table 12: Insulin dose**

| Insulin dose, U/day | N Pre-study | N Baseline | N Week 24 |
|---------------------|-------------|------------|-----------|
| Insulin naïve       | 0 0         | 28         | 25.4      | 20 24.7 |
| Insulin users       | 251 52.9    | 6 61.3     | 28.7      | 3 66.3 |

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

| Parameter                                | N  | Baseline | Week 24 | Change from baseline |
|-------------------------------------------|----|----------|---------|----------------------|
| Glycaemic control (insulin naïve)         |    |          |         |                      |
| HbA1c, mean (%)                           | 790| 9.7      | 7.2     | −2.5                 |
| FPG, mean (mmol/L)                        | 735| 11.1     | 6.5     | −4.6                 |
| PPPG, mean (mmol/L)                       | 631| 14.9     | 8.7     | −6.3                 |
| Glycaemic control (insulin users)         |    |          |         |                      |
| HbA1c, mean (%)                           | 204| 9.6      | 7.3     | −2.3                 |
| FPG, mean (mmol/L)                        | 180| 9.6      | 6.7     | −2.9                 |
| PPPG, mean (mmol/L)                       | 133| 13.6     | 9.2     | −4.4                 |

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

| Parameter                                | N  | Baseline | Week 24 | Change from baseline |
|-------------------------------------------|----|----------|---------|----------------------|
| Hypoglycaemia, events/patient-year        |    |          |         |                      |
| Insulin naïve                             | 28 | 0.0      | 0.0     | 0.0                  |
| Insulin users                             | 6  | 23.8     | 0.0     | −23.8                |
| Body weight, kg                           |    |          |         |                      |
| Insulin naïve                             | 20 | 87.1     | 87.4    | 0.3                  |
| Insulin users                             | 3  | 110.2    | 110.3   | 0.1                  |

**Table 15: Insulin dose**

| Insulin dose, U/day | N Pre-study | N Baseline | N Week 24 |
|---------------------|-------------|------------|-----------|
| Insulin naïve       | 0 0         | 28         | 25.4      | 20 24.7 |
| Insulin users       | 251 52.9    | 6 61.3     | 28.7      | 3 66.3 |

**Insulin aspart ± OGLD**

Of the total cohort, 34 patients who started on insulin aspart ± OGLD, of which 28 (82.3%) were insulin naïve and 6 (17.7%) were insulin users. After 24 weeks of starting or switching to insulin aspart, hypoglycaemic events reduced from 23.8 events/patient-year to 0.0 events/patient-year in insulin user group, while hypoglycaemic events remained nil similar to that of baseline in insulin naïve 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. SADRs including major hypoglycaemic events or episodes did not occur in any of the study patients. A small weight reduction was noted for all regimens except for insulin aspart group. 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 Central Saudi Arabia.

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