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Safety and effectiveness of BIAsp 30 treatment: Data from the Moroccan cohort of the A_1chieve study

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This sub-analysis aimed to determine the safety and effectiveness of biphasic insulin aspart30 (BIAsp30) therapy in people with type 2 diabetes (T2D) from Morocco as a part of the global, 24-week, non-interventional A_1chieve study. A total of 770 Moroccan T2D patients, both insulin-naïve patients and prior insulin users, who started BIAsp 30 therapy at their physicians' discretion, were included. Baseline glycaemic control was poor in the Moroccan cohort with a mean (±SD) glycated haemoglobin A_{1c}(HbA_{1c}) of 9.8 ± 1.8%. After 24 weeks, mean HbA_{1c} significantly reduced by -2.2 ± 1.7% in the Moroccan cohort (-2.5 ± 1.8% in insulin-naïve patients and -1.9 ± 1.5% in prior insulin users, all p<0.001). In the entire cohort, there was no significant difference from baseline to Week 24 in the percentage of patients with at least one event of overall or minor hypoglycaemia, while there was a significant reduction in the percentage of patients reporting at least one event of major or nocturnal hypoglycaemia (p<0.0001). Mean body weight increased (1.4 ± 4.3 kg), while the lipid profile and systolic blood pressure improved over 24 weeks. Overall, BIAsp 30 therapy was well-tolerated and improved glycaemic control in Moroccan T2D patients.

Key words: Type 2 diabetes, BIAsp 30, Morocco, non-interventional study, glycaemic control.

INTRODUCTION

The International Diabetes Federation forecasts a global increase in the number of diabetes cases from 366 million affected people in 2011 to 552 million in 2030, with type 2 diabetes (T2D) comprising between 90 and 95% of all cases (Whiting et al., 2011; Das and Chakrabarti, 2005). The Middle East and North Africa (MENA) region is heavily impacted by the disease burden with a predicted 83% increase in diabetes prevalence over the next 20 years (Whiting et al., 2011).

In Morocco, as in other developing countries, increasing urbanization has led to lifestyle and dietary changes that adversely affect metabolism, resulting in the

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rapid emergence of diabetes during the last decade (Rguibi and Belahsen, 2006; Benjelloun, 2002). A total of 1.4 million Moroccan adults have been diagnosed with diabetes and Morocco ranks seventh among the 10 countries with the highest diabetes prevalence in the MENA region (IDF Diabetes Atlas, 2011). A survey by the Ministry of Health in 2000 showed that diabetes equally affected men and women nationwide with a higher prevalence in urban areas compared to rural areas (Benjelloun, 2002).

Regular assessment of glycaemic control status plays an important role in the management of T2D. Maintaining a glycated haemoglobin A_{1c}(HbA_{1c}) level of <53 mmol/L (<7.0%) is recommended for optimal glycaemic control and to minimize the risk of experiencing diabetes-related complications later in life (Saydah et al., 2004; Nathan et al., 2009). Appropriate intensification of treatment regimens, including the timely initiation of insulin, is highly recommended to maintain adequate glycaemic control (Inzucchi et al., 2012).

However, despite the known effectiveness of insulin treatment in T2D management, patients and physicians tend to delay initiating or intensifying insulin therapy due to apprehensions of weight gain, hypoglycaemia, high number of injections and lifestyle restrictions (Peyrot et al., 2005). Premixed insulin formulations were designed to improve the convenience and practicality of dosing for patients as they combine a long-acting basal component with a fast-acting mealtime component, thus requiring fewer daily injections than basal-bolus regimens (Raja Khan et al., 2007). The premixed insulin analogue, biphasic insulin aspart 30 (BIAsp 30), was developed to provide a more predictable pharmacological profile than biphasic human insulin. BIAsp 30 has demonstrated efficacy in controlling HbA_{1c} and PPPG levels with a low incidence of major hypoglycaemia and is commonly prescribed (Raja Khan et al., 2007; Valensi, 2009a).

The A_1chieve study aimed to determine the safety and effectiveness of insulin analogues prescribed in local clinical care settings in diverse populations in 28 countries (Home et al., 2011). Data from such large observational studies can provide important evidence to support prescribing decisions and guidelines for T2D management. Currently, there is limited efficacy and safety information regarding the routine clinical use of insulin analogues such as BIAsp 30 in treating T2D in Morocco; hence, this sub-analysis was performed to evaluate outcomes data from Moroccan patients on BIAsp 30 therapy. This sub-analysis was also expected to provide information on the current scenario of T2D management in this region.

MATERIALS AND METHODS

Study design

The 24-week, international, prospective, multi-centre, non-interventional A_1chieve study aimed to assess the clinical safety and effectiveness of BIAsp 30 (NovoMix 30®, Novo Nordisk A/S, Denmark), insulin detemir (Levemir®, Novo Nordisk A/S, Denmark) or insulin aspart (NovoRapid®, Novo Nordisk A/S, Denmark) in routine clinical use outside the Western economies (Home et al., 2010). In this sub-analysis, we examined the clinical safety and effectiveness of BIAsp 30 in 770 Moroccan T2D patients, recruited between 15 October, 2009 and 15 July, 2010, at 76 centres in Morocco.

BIAsp 30 was commercially available and funded according to local practice in clinical care. The choice of BIAsp 30 was decided jointly by the patient and physician. The physician determined the dose and frequency of administration of BIAsp 30, in accordance with the licensed approval from the local regulatory authority. Concurrent oral glucose-lowering drugs (OGLDs) were permitted, at the discretion of the physician, throughout the study.

All measurements were made by the treating physician during routine clinical care; there were no pre-defined study-related procedures. Data were collected from the physicians' records and from the patients' recall and self-monitoring diaries/blood glucose meters at baseline and Week 24. All information was transferred to standard case report forms (CRFs).

Patient population

Any Moroccan T2D patient prescribed BIAsp 30 at the discretion of the physician was eligible for this sub-analysis. Patients who were treated with insulin analogues (alone or in combination) for more than 4 weeks prior to the study were excluded. Pregnant women and women who were breast-feeding or had the intention of becoming pregnant were also excluded. Signed informed consent was obtained from all patients and ethics committee approval was obtained for Morocco. Patients could withdraw at any time. Following withdrawal, the data collected were used for analysis until the point when consent was withdrawn. All investigators were trained on the study protocol, CRF completion, informed consent and safety reporting procedures.

Assessments and outcome measures

The primary objective was to evaluate the clinical safety of BIAsp 30 based on the number of serious adverse drug reactions (SADRs), including major hypoglycaemic events, considered related to BIAsp 30 from baseline to Week 24. The secondary safety assessments included changes in the occurrence and frequency of hypoglycaemic events and the number of adverse drug reactions (ADRs) and adverse events from baseline to Week 24.

Efficacy assessments included the change from baseline to final visit in HbA_{1c}, pre-breakfast fasting plasma glucose (FPG), post-breakfast postprandial plasma glucose (PPPG), body weight, systolic blood pressure (SBP) and lipid profile.

Local laboratories were used for all laboratory measurements with local standardisation and quality control procedures.

Health-related quality-of-life (QoL) was assessed using the five-dimensional EQ-5D questionnaire at baseline and after 24 weeks of therapy with BIAsp 30. Current health-related QoL was measured on a standard vertical 20 cm visual analogue scale (VAS) with scores ranging from 0 (worst imaginable health) to 100 (best imaginable health).

Statistical methods

Statistical analyses were performed for the entire Moroccan cohort, insulin-naïve patients and prior insulin users. No statistical analyses were performed to compare differences between insulin-naïve patients and prior insulin users.

Table 1. Patient numbers and characteristics for the entire cohort and by pre-study therapy.

Parameter	Entire cohort	Insulin-naïve	Prior insulin users
n (%)	770 (100)	435 (56.5)	335 (43.5)
Sex, M/F (%)	47.4/52.6	49.7/50.3	44.5/55.5
Mean (SD)			
Age (years)	57.2 (12.4)	57.3 (11.9)	57.0 (13.0)
Body weight (kg)	72.9 (12.4)	72.0 (13.1)	74.1 (11.4)
BMI (kg/m^2)	26.7 (4.3)	26.0 (4.0)	27.5 (4.5)
Diabetes duration (years)	9.6 (7.0)	8.2 (6.4)	11.3 (7.4)
HbA_{1c} (mmol/mol)	84 (20)	88 (22)	79 (17)
HbA_{1c} (%)	9.8 (1.8)	10.2 (2.0)	9.4 (1.6)
Prior OGLDs; n (%)			
Metformin	339 (66.5)	248 (64.9)	91 (71.1)
Sulfonylureas	360 (70.6)	308 (80.6)	52 (40.6)
Thiazolidinediones	13 (2.5)	13 (3.4)	-
One/two/>two	229 (44.9)/249 (48.8)/32 (6.3)	137 (35.9)/215 (56.3)/30 (7.9)	92 (71.9)/34 (26.6)/2 (1.6)

BMI: body mass index; F: female; M: male. Data are n (%), % or mean (SD).

Continuous and discrete variables were summarized using descriptive statistics and frequency tables (number and percentage), respectively. All statistical analyses were conducted using two-sided tests with a pre-specified 5% significance level, unless otherwise stated.

The change from baseline in HbA_{1c}, FPG, PPPG, SBP, body weight, blood lipids and QoL was analyzed using a paired t-test with baseline and Week 24 values. The change from baseline to Week 24 in the percentage of patients reporting at least one hypoglycaemic event was analyzed using Fisher's exact test. Data were analyzed by Novo Nordisk using SAS (Version 9.1.3).

RESULTS

Study patients

A total of 770 Moroccan T2D patients started BIAsp 30 treatment. Patient characteristics and prior OGLD use are presented in Table 1. Prior to study enrolment, 49.6% of patients were on OGLDs alone, 16.6% on OGLDs + insulin therapy, 26.9% on insulin only and 6.9% did not report any prior T2D medication.

Fewer males (47.4%) than females (52.6%) were enrolled. The average age was 57.2 years and the mean body mass index (BMI) was 26.7 kg/m^2 with a mean diabetes duration of 9.6 years.

The most common reasons reported by the physicians for starting BIAsp 30 therapy were to improve glycaemic control (94%), patient dissatisfaction with current therapy (48%), and to reduce plasma glucose variability (43%).

A total of 126 (16.4%) patients withdrew from the study; the most common reason being failure to maintain contact with their physician, 95 patients (12.3%), and the remaining 31 patients (4.0%) withdrew for a variety of other reasons. No withdrawals due to ADRs occurred.

Entire cohort and by prior insulin use

Blood glucose lowering and insulin dose

The total daily insulin dose at 24 weeks was titrated up to47.1 ± 14.8 U/day in the entire cohort and up to 45.2 ± 14.9 U/day for insulin-naïve patients. In prior insulin users, the pre-study insulin dose was 41.0 ± 17.3 U/day2, the total starting insulin dose was 43.6 ± 14.4 U/day titrated up to 49.5 ± 14.5 U/day over 24 weeks.

Blood glucose parameters improved significantly after 24 weeks (Table 2: HbA_{1c} -24 mmol/mol [-2.2%], FPG -5.5 mmol/L, PPPG -6.8 mmol/L, all p<0.001).

Overall, the percentage of patients achieving an HbA_{1c} level of <53 mmol/mol (<7.0%) increased from 2.8% at baseline to 19.7% at Week 24.

The OGLDs most commonly continued at baseline by insulin-naïve patients after initiating BIAsp 30 treatment were metformin (83.9%), alpha-glucosidase inhibitors (15.1%) and sulphonylurea (6.5%). The OGLDs most commonly continued by prior insulin users after transferring to BIAsp 30 treatment were metformin (86.0%), alpha-glucosidase inhibitors (9.3%) and glinides (8.1%).

Hypoglycaemia

The incidence of hypoglycaemia in the entire cohort and

Table 2. Safety and effectiveness outcomes for the entire cohort and by pre-study therapy at baseline and after 24 weeks of BIAsp 30 therapy

Parameter		Entire cohort	Insulin-naïve	Prior insulin users
Insulin dose (U/day)	n	770	435	335
	Pre-study	41.0 (17.3)	-	41.0 (17.3)
	Baseline	39.5 (12.8)	36.4 (10.3)	43.6 (14.4)
	Week 24	47.1 (14.8)	45.2 (14.9)	49.5 (14.5)
HbA_{1c} (mmol/mol/%)	n	443	241	202
	Baseline	84 (20)/9.8 (1.8)	88 (22)/10.2 (2.0)	79 (17)/9.4 (1.6)
	Week 24	60 (10)/7.6 (0.9)	60 (10)/7.6 (0.9)	58 (10)/7.5 (0.9)
	Change, p	-24 (19)/-2.2 (1.7), <0.001	-27 (20)/-2.5 (1.8), <0.001	-21 (16)/-1.9 (1.5), <0.001
FPG (mmol/L)	n	532	308	224
	Baseline	12.8 (4.4)	13.8 (4.4)	11.5 (4.0)
	Week 24	7.4 (2.1)	7.5 (2.2)	7.3 (2.0)
	Change, p	-5.5 (4.5), <0.001	-6.4 (4.6), <0.001	-4.2 (4.1), <0.001
PPPG (mmol/L)	n	349	184	165
	Baseline	16.5 (4.7)	17.4 (4.5)	15.5 (4.8)
	Week 24	9.7 (2.8)	9.8 (2.9)	9.6 (2.8)
	Change, p	-6.8 (5.2), <0.001	-7.6 (5.3), <0.001	-5.9 (5.0), <0.001
Weight (kg)	n	576	323	253
	Baseline	73.2 (12.3)	72.2 (12.7)	74.5 (11.6)
	Week 24	74.6 (11.3)	74.0 (11.3)	75.2 (11.2)
	Change, p	1.4 (4.3), <0.001	1.9 (4.6), <0.001	0.7 (3.7), 0.002
SBP (mmHg)	n	461	249	212
	Baseline	135.4 (17.0)	136.0 (18.1)	134.6 (15.7)
	Week 24	131.9 (13.3)	131.6 (13.2)	132.2 (13.4)
	Change, p	-3.5 (16.7), <0.001	-4.4 (16.6), <0.001	-2.4 (16.8), 0.037
Total cholesterol (mmol/L)	n	142	74	68
	Baseline	5.2 (1.2)	5.3 (1.2)	5.2 (1.1)
	Week 24	4.7 (0.7)	4.7 (0.7)	4.7 (0.8)
	Change, p	-0.6 (1.1)), <0.001	-0.6 (0.9), -	-0.5 (1.2), -
Triglycerides (mmol/L)	n	142	73	69
	Baseline	1.8 (1.0)	2.0 (1.1)	1.7 (0.8)
	Week 24	1.6 (0.5)	1.6 (0.5)	1.6 (0.5)
	Change, p	-0.2 (0.9), 0.002	-0.3 (1.0), -	-0.1 (0.7), -
HDL cholesterol (mmol/L)	n	118	61	57
	Baseline	1.2 (0.3)	1.1 (0.3)	1.2 (0.3)
	Week 24	1.2 (0.4)	1.2 (0.4)	1.2 (0.3)
	Change, p	0.0 (0.4), 0.211	0.1 (0.4), -	-0.0 (0.3), -
LDL cholesterol (mmol/L)	n	123	62	61
	Baseline	3.3 (1.1)	3.3 (1.3)	3.3 (0.9)
	Week 24	2.9 (0.6)	2.8 (0.6)	2.9 (0.6)
	Change, p	-0.4 (0.9), <0.001	-0.5 (1.0), -	-0.4 (0.8), -

Table 2. Contd.

Hypoglycaemia (event per patient-year/percent with at least one event)				
Overall	Baseline	10.08/24.7	6.49/17.9	14.75/33.4
	Week 24	5.77/23.4	5.17/24.6	6.55/22.0
	p[a]	0.6177	0.0232	0.0017
Minor	Baseline	7.60/23.9	4.66/17.9	11.41/31.6
	Week 24	5.75/23.4	5.14/24.6	6.55/22.0
	p[a]	0.8508	0.0232	0.0084
Nocturnal	Baseline	4.17/18.1	2.93/14.0	5.78/23.3
	Week 24	1.43/ 9.2	1.33/9.4	1.57/8.9
	p[a]	<0.0001	0.0483	<0.0001
Major	Baseline	2.48/11.7	1.82/9.9	3.34/14.0
	Week 24	0.02/0.2	0.04/0.3	0
	p[a]	<0.0001	<0.0001	<0.0001

FPG: fasting plasma glucose; HbA_{1c}: glycated haemoglobin A_{1c}; HDL: high-density lipoprotein cholesterol; LDL: low-density lipoprotein cholesterol; PPPG: postprandial plasma glucose; SBP: systolic blood pressure. [a]p-value is for difference in percent of patients with at least one event. [b]Data are mean (SD) unless otherwise specified.

by pre-study therapy is presented in Table 2. The incidence of major hypoglycaemia decreased in the entire cohort (with a statistically significant difference in the percentage of patients reporting at least one event, p<0.0001). In the insulin-naïve patients, the reported rate of overall hypoglycaemia decreased marginally from 6.49 to 5.17 events/patient-year, with a statistically significant increase in the percentage of patients reporting at least one event (p<0.05). In the prior insulin users, the reported rate decreased from 14.75 to 6.55 events/patient-year after 24 weeks, associated with a statistically significant reduction (p<0.005) in the percentage of patients reporting at least one event.

For insulin-naïve patients, the rate of minor hypoglycaemic events increased from 4.66 to 5.14 events/patient-year (percentage of patients reporting at least one event, p<0.05) while the rate of nocturnal hypoglycaemia decreased from 2.93 to 1.33 events/ patient-year (percentage of patients reporting at least one event, p<0.05). In the prior insulin users, the incidence of minor and nocturnal hypoglycaemic events decreased from 11.41 to 6.55 events/patient-year (percentage of patients reporting at least one event, p<0.01) and 5.78 to 1.57 events/patient-year (percentage of patients reporting at least one event, p<0.0001), respectively, during the study period.

Body weight, blood lipids and blood pressure control

Mean body weight change over 24 weeks was statistically significant (Table 2, p<0.001 for the entire cohort and insulin-naïve patients; p<0.005 for prior insulin users). The mean body weight increase for the entire cohort was 1.4 kg (1.9 kg for insulin-naïve patients and 0.7 kg for prior insulin users).

Total cholesterol levels reduced in the entire cohort from a mean of 5.2 mmol/L at baseline to 4.7 mmol/L at Week 24 (Table 2, -0.6 mmol/L, p<0.001). Low-density lipoprotein cholesterol levels reduced from a mean of 3.3 to 2.9 mmol/L after 24 weeks (-0.4 mmol/L, p<0.001) and a statistically significant reduction was also seen in triglycerides levels (-0.2 mmol/L, p<0.005) in the entire cohort. No change in high-density lipoprotein cholesterol levels was noted during the study.

Mean SBP reduced in the entire cohort, from 135.4 mmHg at baseline to 131.9 mmHg after 24 weeks of treatment (Table 2, -3.5 mmHg; p<0.001).

SADRs and serious adverse events

Overall, the incidence of SADRs was low; 4 SADRs (all hypoglycaemic events) were reported by 4 patients (0.01 events/patient-year).

The event rate of serious adverse events (SAEs) was also low (0.02 events/patient-year); 8 patients had 11 SAEs and 7 events had fatal outcomes. The majority of SAEs were reported under metabolism and nutrition disorders (4 events in 4 patients), of which all events were hypoglycaemia-related.

Quality of life assessments

As measured by the VAS from the EQ-5D questionnaire (on a scale of 0–100), QoL increased significantly by 16

points from 60.1 points at baseline to 76.1 points at Week 24 for the entire cohort (p<0.001).

DISCUSSION

This sub-analysis demonstrated the safety and effectiveness of BIAsp 30 treatment in T2D in routine clinical practice in Morocco.

International data from routine clinical practice reveal that glycaemic control in T2D patients is generally poor (Davidson et al., 2008). In the IMPROVE observational study, almost 50% of patients had an HbA_{1c}> 9.0% at baseline (Valensi et al., 2009b). This was reflected in the global A_1chieve study where the mean baseline HbA_{1c} value was 9.5% (Home et al., 2011) and in the Moroccan data in this paper where the mean baseline HbA_{1c} value was 9.8%.

For the Moroccan cohort, BIAsp 30 therapy significantly improved overall glycaemic control over 24 weeks, as measured by HbA_{1c}, pre-breakfast FPG and post-breakfast PPPG values. These results are similar to the global A_1chieve study results (Home et al., 2011) and the results of two other large observational studies, IMPROVE and PRESENT (Valensi et al., 2009b; Khutsoane et al., 2008). Overall, 19.7% of Moroccan patients achieved HbA_{1c} levels <53 mmol/mol (<7.0%) with BIAsp 30 treatment after 24 weeks. It is possible that earlier insulin initiation and more active intensification of treatment may be helpful in allowing a greater proportion of T2D patients to attain long-term glycaemic goals.

The marked improvement in glycaemic control was accompanied by a low incidence of SADRs and hypoglycaemia. The risk of hypoglycaemia typically increases when insulin is used to attain better glycaemic control and defined glycaemic targets (Gerstein et al., 2008). As expected following the initiation of BIAsp 30 therapy, overall and minor hypoglycaemia increased slightly in the insulin-naïve patients. For prior insulin users, overall and minor hypoglycaemia reduced significantly with BIAsp 30 therapy as also observed in the IMPROVE and PRESENT studies (Valensi et al., 2009b; Khutsoane et al., 2008). In the entire Moroccan cohort, the percentage of patients reporting nocturnal hypoglycaemia decreased significantly and the reduction in major hypoglycaemia was also marked.

Statistically significant reductions in blood lipids and SBP were also noted in the entire cohort. These results are similar to the findings from the global A_1chieve study (Home et al., 2011) and other studies on BIAsp 30 (Gero et al., 2009; Schmoelzer et al., 2005). It is possible that physicians and patients may have taken advantage of the start of insulin analogue therapy to augment self-management behaviours (Home et al., 2011); however, as diet, lifestyle and concomitant disease and medication were not controlled, detailed information on the likely changes initiated is not available.

Initiating BIAsp 30 was shown to positively impact QoL as significant improvements in QoL were reported after 24 weeks for Moroccan patients, as also observed in the global A_1chieve study (Home et al., 2011).

As this observational study was not randomized and lacked a standardized design, limiting factors such as the absence of a control group, retrospective data collection methods and the potential for recall bias in observations such as the occurrence of hypoglycaemia may not be excluded. However, all measurements were performed in accordance with local regulations and by methods that are NGSP-certified. The 24-week study duration was considered suitable to evaluate patient responses to the regulatory-approved BIAsp 30 therapy. In contrast to a more stringent randomized clinical trial setting, this study provided a valuable opportunity to collect real-life data on the safety and effectiveness of BIAsp 30 from a heterogeneous patient group in Morocco.

Conclusions

In conclusion, starting BIAsp 30 therapy was well-tolerated in this Moroccan cohort and resulted in significant improvements in glycaemic control. The poor baseline glycaemic control evinced in this cohort also points to the urgent need to reconsider current healthcare practices for T2D management in Morocco.

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REFERENCES

Benjelloun S (2002). Nutrition transition in Morocco.Public Health Nutr. 5(1A): 135–140.

Das SK, Chakrabarti R (2005). Non-insulin dependent diabetes mellitus: present therapies and new drug targets. Mini Rev. Med. Chem. 5(11):1019–1034.

Davidson J, Koro C, Arondekar B, Lee BH, Fedder D (2008). A retrospective analysis of the fasting plasma glucose and glycosylated hemoglobin and pharmacotherapy change patterns among type 2 diabetes mellitus patients.Clin.Ther. 30(2):287–293.

Gero L, Gyimesi A, Hidvégi T, Jánosi I (2009). [Improvement in glycemic control, cardiovascular risk factors and anthropometric data in type 2 diabetic patients after the switch from biphasic human insulin to biphasic premix analog insulin aspart]. Orv. Hetil. 150(35):1637–1647.

Gerstein HC, Miller ME, Byington RP, Goff DC Jr, Bigger JT, Buse JB, Cushman WC, Genuth S, Ismail-Beigi F, Grimm RH Jr, Probstfield JL, Simons-Morton DG, Friedewald WT, on behalf of the Action to Control Cardiovascular Risk in Diabetes Study Group (2008). Effects of intensive glucose lowering in type 2 diabetes. N. Engl. J. Med. 358(24):2545–2559.

Home P, Naggar NE, Khamseh M, Gonzalez-Galvez G, Shen C, Chakkarwar P, Wenying Y (2011). An observational non-interventional study of patients with diabetes beginning or changed to insulin analogue therapy in non-Western countries: The A_1chieve study. Diabetes Res. Clin.Pract. 94:352–363.

International Diabetes Federation (2011). IDF Diabetes Atlas, 5th ed. Brussels, Belgium. Updated 14 November 2012.
Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E, Nauck M, Peters AL, Tsapas A, Wender R, Matthews DR (2012). Management of hyperglycaemia in type 2 diabetes: a patient-centered approach. Position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia. 55(6):1577–1596.
Khutsoane D, Sharma SK, Almustafa M, Jang HC, Azar ST, Danciulescu R, Shestakova M, Ayad NM, Guler S, Bech OM; PRESENT Study Group (2008). Biphasic insulin aspart 30 treatment improves glycaemic control in patients with type 2 diabetes in a clinical practice setting: experience from the PRESENT study. Diabetes Obes. Metab. 10(3):212–222.
Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, Zinman B (2009). Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 32(1):193–203.
Peyrot M, Rubin RR, Lauritzen T, Skovlund SE, Snoek FJ, Matthews DR, Landgraf R, Kleinebreil L (2005). International DAWN Advisory Panel. Resistance to insulin therapy among patients and providers: results of the cross-national Diabetes Attitudes, Wishes, and Needs (DAWN) study. Diabetes Care 28(11):2673–2679.
Raja-Khan N, Warehime SS, Gabbay RA (2007). Review of biphasic insulin aspart in the treatment of type 1 and 2 diabetes. Vasc. Health Risk Manag. 3(6):919–935.
Rguibi M, Belahsen R (2006). Prevalence and associated risk factors of undiagnosed diabetes among adult Moroccan Sahraoui women. Public Health Nutr. 9(6):722–727.
Saydah SH, Fradkin J, Cowie CC (2004). Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. JAMA 291(3):335–342.
Schmoelzer I, de Campo A, Pressl H, Stelzl H, Dittrich P, Oettl K, Wascher TC (2005). Biphasic insulin aspart compared to biphasic human insulin reduces postprandial hyperlipidemia in patients with type 2 diabetes. Exp. Clin. Endocrinol. Diabetes 113(3):176–181.
Valensi P (2009a). Biphasic insulin aspart 30/70 (BIAsp 30) in the treatment of type 1 and type 2 diabetes. Diabetes Metab. Syndr. Obes. 2:61–71.
Valensi P, Benroubi M, Borzi V, Gumprecht J, Kawamori R, Shaban J,
Shah S, Shestakova M, Wenying Y; on behalf of the IMPROVE™ Study Group Expert Panel (2009b). Initiating insulin therapy with, or switching existing insulin therapy to, biphasic insulin aspart 30/70 (NovoMix 30) in routine care: safety and effectiveness in patients with type 2 diabetes in the IMPROVE observational study. Int. J. Clin. Pract. 63(3):522–531.
Whiting DR, Guariguata L, Weil C, Shaw J (2011). IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res. Clin. Pract. 94(3):311–321.