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# The IMPROVE™ study — a multinational, observational study in type 2 diabetes: data from the Polish cohort

## Badanie IMPROVE™ — międzynarodowe badanie obserwacyjne w cukrzycy typu 2: wyniki dotyczące populacji Polski

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### Abstract

**Introduction:** Observational studies are valuable tools for assessing the applicability of results from randomised controlled trials to broader patient populations. They are especially important in chronic diseases such as diabetes, as they can provide a comprehensive picture of the safety and effectiveness of a particular therapy across cultures and phenotypes.

**Material and methods:** Patients with type 2 diabetes who required insulin and whose physician had decided to initiate biphasic insulin aspart 30 (BIAsp 30) were eligible. A total of 4117 type 2 diabetic patients were recruited to the study in Poland, and 809 primary and secondary care physicians were involved. The aim of this study was to assess the safety and effectiveness of BIAsp 30 treatment in type 2 diabetes in routine clinical practice.

**Results:** Baseline glycaemic control was poor in the Polish cohort enrolled in the IMPROVE™ study, with a mean $HbA_{1c}$ value of 9.0 ± ± 1.7%. A very high proportion of patients were thus at risk of macrovascular and microvascular complications. A twice-daily regimen for the start of BIAsp 30 therapy was the most common choice, including 72.2% of patients at baseline. $HbA_{1c}$ was significantly reduced by 1.66% for the total cohort and by 3.07% and 1.55% in the pre-study no-therapy or oral antidiabetic drug group respectively ($p < 0.001$). The rates (episodes per subject year) of overall major hypoglycaemia were 0.012 and 0.12 at follow-up and final visits respectively. For minor hypoglycaemia rates of 5.12 per subject per year at follow-up visit and 4.54 episodes per subject per year at final visit were recorded.

**Conclusions:** BIAsp 30 appears to be an effective and flexible treatment approach and can be safely intensified to achieve glycaemic control in a majority of patients with type 2 diabetes. **(Pol J Endocrinol 2008; 59 (6): 460–466)**

***Key words:*** *type 2 diabetes, biphasic insulin aspart 30, observational study*

### Streszczenie

**Wstęp:** Badania obserwacyjne stanowią wartościowe narzędzie uzupełniające informacje uzyskane z badań RCT (*randomised controlled trials*). Odgrywają one szczególnie ważną rolę w przypadku schorzeń przewlekłych, takich jak cukrzyca, w przypadku których, w odniesieniu do dużych populacji, dostarczają istotnych danych dotyczących skuteczności i bezpieczeństwa stosowanych terapii.

**Materiał i metody:** Grupa badana obejmowała chorych na cukrzycę typu 2, którzy w opinii lekarza prowadzącego wymagali rozpoczęcia insulinoterapii i kwalifikowali się do włączenia dwufazowej insuliny aspart 30 (BIAsp 30) w celu poprawy wyrównania metabolicznego. Do badania, którego celem była ocena bezpieczeństwa i skuteczności leczenia cukrzycy typu 2 przy użyciu BIAsp 30 zakwalifikowano w Polsce łącznie 4117 chorych.

**Wyniki:** Wyrównanie metaboliczne polskiej grupy wchodzącej w skład globalnego badania IMPROVE™, w momencie rozpoczęcia obserwacji, było wysoce niezadowalające — średnia wartość $HbA_{1c}$ wynosiła 9,0 ± 1,7%. W konsekwencji istotny odsetek pacjentów prezentował powikłania naczyniowe o typie mikro- i makroangiopatii. Najczęściej stosowanym schematem rozpoczęcia terapii BIAsp 30, w 72,2% przypadków, było zastosowanie dwóch wstrzyknięć na dobę. W trakcie 26-tygodniowej obserwacji redukcja $HbA_{1c}$ wynosiła 1,66% dla całej populacji oraz odpowiednio 3,07% i 1,55% dla osób wyjściowo nie leczonych farmakologicznie oraz otrzymujących doustne leki przeciwcukrzycowe. Ryzyko epizodów ciężkiej hipoglikemii w trakcie całego badania (epizody/pacjenta/rok) wynosiło 0,012, natomiast lekkiej hipoglikemii odpowiednio 5,12/pacjenta/rok w trakcie wizyty kontrolnej oraz 4,54/pacjenta/rok na wizycie końcowej.

**Wnioski:** Dwufazowa insulina aspart 30 stosowana w codziennej praktyce jest bezpieczną i skuteczną insuliną w terapii cukrzycy typu 2. **(Endokrynol Pol 2008; 59 (6): 460–466)**

***Słowa kluczowe:*** *cukrzyca typu 2, dwufazowa insulina aspart 30, badania obserwacyjne*

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## Introduction

Despite evidence that normalising blood glucose levels as far as is practicable minimises the risk of diabetic complications, glycaemic control in patients with type 2 diabetes is commonly poor in clinical practice [1, 2]. In type 2 diabetes, as endogenous insulin secretion continues to decline, oral antidiabetic drugs (OADs) or insulin may be initiated. Premixed insulins have been recommended for the initiation of insulin therapy, as they provide peaks of insulin in the blood that can be timed to limit the rise in blood glucose level following a meal, as well as basal insulin to control blood glucose between meals [3, 4]. A number of randomised controlled trials, considered the gold standard for assessing treatment effects, have shown that biphasic insulin aspart 30 (BIAsp 30) treatment is associated with significant improvements in glycaemic control without increasing the risk of hypoglycaemia [5–9]. However, randomised controlled trials employ stringent selection criteria, which may not make them fully representative of the patient population in question and in such cases observational studies provide essential sources of "real-life" clinical data and complement those from randomised controlled trials [10]. The key contributions of well-designed large observational studies such as the IMPROVE™ study are the detection of rare adverse drug reactions and the provision of data about the performance of a treatment or strategy in routine clinical practice

Two observational studies have been undertaken recently to assess how the benefits observed in the populations of the BIAsp 30 clinical trial programme translate into clinical practice. These studies are the Physician's Routine Evaluation of Safety and Efficacy of NovoMix® 30 Therapy (PRESENT) study and the IMPROVE™ study [11, 12].

The data presented in this paper form the first full report from the Polish cohort enrolled into the global IMPROVE™ study. The aim of the IMPROVE™ study, a multinational, open-label, non-randomised 26-week observational study, was to assess the safety and effectiveness of BIAsp 30 treatment in type 2 diabetes in routine clinical practice.

## Material and methods

### *Study design*

IMPROVE™ was an open-label, non-randomised 26-week observational study conducted with almost 58,000 type 2 diabetes patients enrolled in 11 countries in North America, Europe and Asia, making it the largest study of patients with type 2 diabetes ever undertaken. Patients were followed up after 13 weeks, with a final visit after 26 weeks. Physicians made decisions about the dose and timing of BIAsp 30 plus any concomitant medication according to their routine clinical practice. Any changes in BIAsp 30 treatment were recorded at the two follow-up visits. Physicians also completed the resource utilisation questionnaires, which addressed the time spent teaching patients to monitor blood glucose and inject BIAsp 30. The objective of this study was to assess the safety of BIAsp 30 treatment in patients with type 2 diabetes in routine clinical practice. Effectiveness and quality of life were secondary endpoints. Here we report data from Poland.

The study was conducted in accordance with the Declaration of Helsinki. Study procedures complied with local regulations and practice governing observational studies, and were subject to health authority approval, ethics committee approval and the informed consent of the patients. The prescription and purchase of study medication followed routine practice at each study site.

### *Study population*

Any patient with type 2 diabetes who, according to their physician, needed insulin treatment with BIAsp 30 was eligible for the study, including newly-diagnosed patients and those receiving OADs. In order to minimise selection bias, patients were enrolled on a consecutive basis, until the quota for each participating physician was reached. Patients were excluded if they were unable to comply with protocol requirements or were hypersensitive to BIAsp 30. Women who were pregnant, breastfeeding or intending to become pregnant within the next 12 months were also excluded. BIAsp 30 was prescribed by the physician as part of routine treatment depending on the patient's needs, and the dosage was also adjusted individually.

Finally 4117 eligible type 2 diabetic patients were recruited to the study in Poland. The study involved 809 primary and secondary care physicians. A total of 181 patients withdrew from the study (130 as a result of loss of contact, 3 because of adverse drug reaction and 50 for other reasons)

### *Assessments and outcome measures*

After patients had signed the informed consent form, assessments were made. The primary outcome measure was the incidence of major hypoglycaemic events reported as serious adverse drug reactions (SADRs). One of the secondary outcome measures was safety: SADRs, adverse drug reactions (ADRs), the number of major and minor hypoglycaemic events (daytime and nocturnal), weight and body mass index (BMI) change. Another was effectiveness: $HbA_{1c}$, proportions of patients reaching targets of $HbA_{1c} < 6.5\%$ and $< 7.0\%$, as well as physician-set targets, fasting plasma glucose (FPG) and postprandial plasma glucose (PPG) after all main meals.

Data were collected from medical records, patient recall, and patient diaries at baseline, follow-up visit (13 weeks) and final visit (26 weeks) and summarised for the global cohort, for each country and for each of two pre-study treatment groups ("no-therapy" and "OADs only"). At these visits, physicians recorded the following information: demographics, medical history (diabetes duration, pre-study treatment and medication, macrovascular and microvascular complications hypoglycaemic events), measures of glycaemic control ($HbA_{1c}$, FPG, PPG) and reasons for starting a new therapy (baseline only), as well as the dose and timing of BIAsp 30.

A major hypoglycaemic event was defined as an event with severe central nervous system symptoms consistent with hypoglycaemia in which the patient was unable to treat himself/herself and had either blood glucose < 3.1 mmol/L or reversal of symptoms after either carbohydrate intake, glucagon or intravenous glucose administration. A minor hypoglycaemic event was defined as an event with either symptoms of hypoglycaemia with a blood glucose measurement < 3.1 mmol/L which was handled by the patient himself/herself, or any asymptomatic blood glucose measurement < 3.1 mmol/L. A nocturnal hypoglycaemic event was defined as an event occurring while the patient was asleep, between the evening insulin injection and before waking in the morning.

### *Statistical analyses*

Statistics were based on patients with a complete set of values. Descriptive statistics were used to summarise baseline data from the full analysis set (patients receiving at least one dose of study medication and reporting safety information). Mean and standard deviations were prepared for continuous variables and frequencies and percentages for categorical variables. Comparisons were performed by ANOVAs for continuous variables and by $\chi^2$ tests for categorical variables. Linear correlations between continuous variables were calculated. Statistical comparisons of BIAsp 30 outcome measures at baseline, follow-up and final visit were performed with paired t-tests for continuous variables and with Wilcoxon tests for discrete variables. The influence of predictor variables on the change in outcome variables was evaluated with analysis of covariance models (ANCOVA) for continuous outcome variables and logistic models for discrete outcome variables. In all cases significance was set at $p < 0.05$.

## Results

Demographic and disease characteristics of the study population are shown in Table I. Baseline glycaemic control was poor in the Polish cohort enrolled in the IMPROVE™ study, with a mean $HbA_{1c}$ value of 9.0 ± ± 1.7%. A very high proportion of patients were thus at risk of macrovascular and microvascular complications (Table I).

**Table I.** *Demographic and disease characteristics at baseline*

**Tabela I.** *Dane demograficzne i charakterystyka kliniczna*

| Parameter | Poland (n = 4117) |
|---|---|
| Age (years) | 60.7 (10.5) |
| Proportion of men/women (%) | 48/52 |
| Weight [kg] | 84.9 (16.5) |
| BMI [kg/m$^2$] | 30.5 (5.4) |
| Duration of diabetes [years] | 7.1 (5.5) |
| $HbA_{1c}$ (%) | 9.0 (1.7) |
| Proportion of patients with $HbA_{1c} \geq 9\%$ (%) | 42.0 |
| Fasting blood glucose [mmol/l] | 10.2 (3.1) |
| **Postprandial blood glucose [mmol/l]** | |
| Breakfast | 11.6 (3.3) |
| Lunch | 11.7 (3.3) |
| Dinner | 11.0 (2.9) |
| **Proportion with macrovascular complications (%)** | |
| Any | (n = 2181) 53.1 |
| Peripheral vascular disease | 20.9 |
| Coronary heart disease | 41.3 |
| Stroke | 4.5 |
| **Proportion with microvascular complications (%)** | |
| Any | (n = 1783) 43.4 |
| Retinopathy | 28.6 |
| Diabetic nephropathy | 9.3 |
| Peripheral neuropathy | 20.6 |
| Autonomic neuropathy | 3.9 |

BMI — body mass index; Data are mean ± SD

A total of 89.2% (3669) of patients had received OAD therapy for diabetes prior to the study, while 10.8% had received no pharmaceutical therapy at baseline (Table II, IIa). Physicians' treatment decisions by pre-study treatment groups both at baseline and final visits are also shown in Table II. A twice-daily regimen for the start of BIAsp 30 therapy was the most common choice, including 72.2% of patients at baseline (Table III).

### *Efficacy*

$HbA_{1c}$ was significantly reduced by 1.66% for the total cohort and by 3.07% and 1.55% in the pre-study no-therapy and OADs group respectively ($p < 0.001$; Table IV). At the final visit (week 26) $HbA_{1c}$ values were 7.29%, 7.21% and 7.29% in the total cohort, pre-study no-therapy and OADs groups, respectively. As expected, subjects with no previous pharmaceutical therapy

**Table II.** *Diabetes therapy — Initiation: Pre-study* **vs.** *New therapy (baseline)*

**Tabela II.** *Zastosowany schemat terapii cukrzycy z użyciem BIAsp 30 w zależności od terapii wyjściowej*

| **Full Analysis Set** | | | **New therapy (Baseline)** | | |
|---|---|---|---|---|---|
| | **Therapy** | **NovoMix 30 alone** | **NovoMix 30 +OAD** | **NovoMix 30 + Insulin ± OAD** | **Total** |
| **Pre-study** | No therapy | 342 (8.3%) | 82 (2.0%) | 21 (0.5%) | **445 (10.8%)** |
| | OAD only | 1228 (29.8%) | 2340 (56.8%) | 98 (2.4%) | **3669 (89.2%)** |
| | **Total** | **1570 (38.1%)** | **2422 (58.8%)** | **119 (2.9%)** | **4117 (100%)** |

**Table IIa.** *Diabetes therapy — Pre-study* **vs.** *Final visit*

**Tabela IIa.** *Zastosowany schemat terapii cukrzycy w trakcie wizyty kontrolnej*

| **Full Analysis Set** | | | **New therapy (Final visit)** | | |
|---|---|---|---|---|---|
| | **Therapy** | **NovoMix 30 alone** | **NovoMix 30 +OAD** | **NovoMix 30 + Insulin ± OAD** | **Total** |
| **Pre-study** | No therapy | 276 (6.7%) | 97 (2.4%) | 26 (0.6%) | **445 (10.8%)** |
| | OAD only | 1104 (26.8%) | 2163 (52.5%) | 195 (4.7%) | **3669** (89.1%) |
| | **Total** | **1381 (33.5%)** | **2262 (54.9%)** | **221 (5.4%)** | **4117 (100%)** |

**Table III.** *BIAsp 30 regimens prescribed at baseline and at follow-up and final visits*

**Tabela III.** *Zastosowane dawki oraz liczba wstrzyknięć insuliny BIAsp 30, wartości wyjściowe, w trakcie wizyty kontrolnej, w trakcie wizyty końcowej*

| | **Baseline** | **Follow-up** | **Final** |
|---|---|---|---|
| Total dose [IU] | 26.4 (n = 4111) | 32.6 (n = 3928) | 34.5 (n = 3864) |
| Total dose [IU/kg] | 0.32 (n = 4107) | 0.39 (n = 3922) | 0.42 (n = 3854) |
| Proportion of patients receiving (%) | **Baseline (n = 4112)** | **Follow-up (n = 3929)** | **Final (n = 3865)** |
| One injection | 25.1 | 14.8 | 13.0 |
| Two injections | 72.2 | 79.1 | 78.5 |
| Three injections | 2.7 | 6.1 | 8.4 |

**Table IV.** *Efficacy at baseline and at follow-up and final visits*

**Tabela IV.** *Skuteczność terapii, wartości wyjściowe, w trakcie wizyty kontrolnej, w trakcie wizyty końcowej*

| | **Baseline** | **Follow-up** | **Final** | **Mean change** | **p-Value** |
|---|---|---|---|---|---|
| **$HbA_{1c}$ (%)** | | | | | |
| Total cohort | 8.95 (n = 1768) | 7.7 (n = 1237) | 7.29 (n = 1768) | –1.66 | < 0.001 |
| No therapy | 10.28 (n = 126) | | 7.21 (n = 126) | –3.07 | < 0.001 |
| OADs only | 8.84 (n = 1633) | | 7.29 (n = 1633) | –1.55 | < 0.001 |
| **Fasting blood glucose [mg/dl]** | 182 (n = 3387) | 129 (n = 3333) | 120 (n = 3387) | – 62 (56) | < 0.001 |
| Fasting blood glucose variability [mg/dl] | 20 (n = 2837) | 12 (n = 2744) | 11 (n = 2837) | – 9 (21) | < 0.001 |
| **Postprandial blood glucose [mg/dl]** | | | | | |
| Breakfast (n = 2533) | 207 (58) | | 139 (26) | – 69 (61) | < 0.001 |
| Lunch (n = 2387) | 209 (58) | | 148 (27) | – 61 (61) | < 0.001 |
| Dinner (n = 2212) | 199 (50) | | 141 (27) | – 58 (54) | < 0.001 |

**Table V.** *Efficacy — proportion reaching therapeutic goals at final visit*

**Tabela V.** *Skuteczność terapii — odsetek chorych osiągających cel terapeutyczny*

| | No therapy (n = 398) | OADs (n = 3423) |
|---|---|---|
| $HbA_{1c} \leq 6.5\%$ | 23 | 15 |
| $HbA_{1c} < 7.0\%$ | 51 | 38 |
| $HbA_{1c}$ (physician given target) | 37 | 27 |
| FBG | 36 | 27 |
| PPBG — Breakfast | 54 | 45 |
| PPBG — Lunch | 45 | 36 |
| PPBG — Dinner | 45 | 41 |

achieved a greater reduction in $HbA_{1c}$ compared with those treated with OADs. The improvement in glycaemic control included both FPG and PPG values after all main meals (Table IV).

At the end of the observation period (the final visit) 23% and 15% of patients reached the target $HbA_{1c} \leq 6.5\%$, 23% and 15% reached the target $HbA_{1c} < 7\%$ and 37% and 27% reached the physician-given $HbA_{1c}$ in the pre-study no-therapy and OADs groups respectively (Table V).

### *Safety*

The rates (episodes per subject year) of overall major hypoglycaemia were 0.012 and 0.12 at follow-up and final visits respectively. For minor hypoglycaemia rates of 5.12 per subject per year at follow-up visit and 4.54 episodes per subject per year at final visit, were recorded. No significant difference was observed in relation to pre-study therapy (Tables VI, VIa, VIb).

### *Insulin doses and weight gain*

Overall insulin the BIAsp 30 dose increased from 26.4 IU (0.32 IU/kg) at baseline to 34.5 IU (0.42 IU/kg) at final visit and the proportion of patients receiving one, two or three injections per day at the final visit was 13.0%; 78.5%; 8.5% respectively (Table III).

There was no significant difference in weight gain and BMI during the observation period (Table VII).

## Discussion

Despite evidence that normalising blood glucose levels as far as is practicable minimises the risk of diabetic complications, glycaemic control in patients with type 2 diabetes is commonly poor in clinical practice. The principal aim of antidiabetic therapy is to normalise, as far as is practicable, blood glucose levels, thus minimising the complications associated with hyperglycaemia [1, 2]. As type 2 diabetes progresses, the need for insulin therapy increases in order to improve glycaemic control, but there is no consensus on how or, to be precise, when to start insulin treatment, and insulin regimens are known to vary from country to country [4, 13]. There is also persistent reluctance among physicians and patients worldwide to initiate insulin therapy [14], often due to concerns over hypoglycaemia and/or weight gain. Hence, the initiation of insulin therapy at $HbA_{1c}$ levels, at 9%, as in our study, is probably not unusual. For patients not receiving prior pharmaceutical therapy, physicians have commonly considered BIAsp 30 an easy way to start insulin treatment. Generally, however, the key reason for the choice of BIAsp 30 has been improved glycaemic control. According to the National Health Interview Survey, 28% of type 2 diabetic patients are using insulin, either alone (16%) or in combination with OADs (12%) [15]. While basal insulins are often first-line therapy, premixed insulins such as BIAsp 30 address both basal and mealtime requirements. According to Monnier and colleagues the contribution of postprandial glucose control has been shown to have an impact on overall glycaemic control as glycaemic targets are approached [16]. Such a model implies that current glycaemic control targets in the treatment of diabetes may frequently prove difficult to achieve unless therapy includes the control of postprandial glucose levels.

Given the importance of glycaemic control in decreasing mortality and morbidity, we aimed to assess the safety and effectiveness of BIAsp 30 treatment in type 2 diabetes in routine clinical practice in Poland. Our study is part of the global IMPROVE™ study, in which almost 58,000 patients with type 2 diabetes from 11 countries in North America, Europe and Asia have been observed. It could be said to be unfortunate that the populations of observational studies are highly heterogeneous, particularly compared with those of randomised controlled trials, which are a valuable tool for assessing the performance and safety of a drug. On the other hand, the body of data generated even by the Polish cohort alone as presented in this study is large and in our opinion provides information complementary to that of controlled trials.

Initiating insulin therapy with BIAsp 30 provided significantly improved overall glycaemic control compared with baseline, as measured by $HbA_{1c}$, FPG and PPG values after all main meals, allowing significantly more treated patients to achieve the $HbA_{1c}$ targets established by the European Association for the Study of Diabetes (EASD), the American Diabetes Association (ADA) or by physicians. In a study of patients with type 2 diabetes and $HbA_{1c}$ levels of 7.5–10.0%, Garber and colleagues showed that 70% of patients achieved the American Diabetes Association target $HbA_{1c}$ level with

**Table VI.** *Safety: rate of hypoglycaemic events at baseline and at follow-up and final visits*

**Tabela VI.** *Ryzyko epizodów hipoglikemii; wartości wyjściowe, w trakcie wizyty kontrolnej, w trakcie wizyty końcowej*

| Events/Patient/Year | Baseline | Follow-up | Final |
|---|---|---|---|
| Major | 0.056 (n = 3864) | 0.012 (n = 1779) | 0.012 (n = 3864) |
| Minor | 2.38 (n = 3861) | 5.12 (n = 3852) | 4.54 (n = 3861) |
| Nocturnal | 0.68 (n = 3861) | 0.75 (n = 3852) | 0.75 (n = 3861) |
| Daytime | 1.72 (n = 3861) | 4.37 (n = 3852) | 3.78 (n = 3861) |

**Table VIa.** *Safety: rate of major hypoglycaemic events in relation to by pre-study therapy*

**Tabela VIa.** *Ryzyko epizodów ciężkiej hipoglikemii w zależności od terapii wyjściowej*

| Events/Patient/Year | Total cohort (n = 3864) | No therapy (n = 399) | OAD only (n = 3465) |
|---|---|---|---|
| Baseline | 0.056 | 0.110 | 0.050 |
| Final | 0.012 | 0.015 | 0.012 |

**Table VIb.** *Safety: rate of minor hypoglycaemic events in relation to pre-study therapy*

**Tabela VIb.** *Ryzyko epizodów lekkiej hipoglikemii w zależności od terapii wyjściowej*

| Events/Patient/Year | Total cohort (n = 3861) | No therapy (n = 399) | OAD only (n = 3462) |
|---|---|---|---|
| Baseline | 2.38 | 2.15 | 2.41 |
| Final | 4.54 | 5.15 | 4.46 |

**Table VII.** *Body weight and BMI*

**Tabela VII.** *Masa ciała i BMI*

| | Baseline | Follow-up | Final | Mean change |
|---|---|---|---|---|
| Weight [kg] | 85.0 (n = 3853) | 84.8 (n = 3841) | 84.6 (n = 3853) | – 0.3 (4.5) |
| BMI [kg/m$^2$] | 30.5 (n = 3849) | 30.5 (n = 3837) | 30.4 (n = 3849) | – 0.10 (1.63) |

BMI — body mass index

a twice-daily injection regimen and with a three-times-daily injection regimen the proportion rose to 77% [17].

The rate of hypoglycaemia typically increases as patients use or intensify their use of insulin to attain better glycaemic control and defined glycaemic targets. In general, the better the glycaemic control, the greater the risk of hypoglycaemia. It is therefore not surprising that the overall rate of minor hypoglycaemic episodes per subject year was greater after starting BIAsp 30 treatment compared to baseline, but the most important fact is that hypoglycaemia was not a barrier to achieving glycaemic targets in this population.

Initiation of insulin therapy, besides increasing the risk of hypoglycaemia, is also often accompanied by an increase in weight as glycaemic control improves. In our population no significant difference in weight gain or BMI was observed during the 26 weeks' duration of this study, but of course a study of longer duration might be required to determine a realistic treatment effect.

## Conclusions

In conclusion, our observations, as part of the global IMPROVE™ study, provide the valuable information that the initiation of insulin therapy with BIAsp 30 is a viable treatment approach and can be safely intensified to achieve glycaemic control in the majority of patients who have failed to achieve glycaemic control with previous no pharmaceutical or OADs therapy. Ultimately, effective diabetes management can reduce diabetes-related complications and improve patients' quality of life.

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The authors declare that they have no competing interests.

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