

Research Article

Efficacy and Safety of Insulin Degludec/ Insulin Aspart (Ryzodeg) in Patients with Type 2 Diabetes Mellitus: A Prospective Clinical Study

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Received: 24.07.26, Revised: 12.10.26, Accepted: 18.10.26

ABSTRACT

Background: Type 2 diabetes mellitus is a progressive metabolic disorder characterized by chronic hyperglycemia, insulin resistance, and progressive pancreatic beta-cell dysfunction. Insulin degludec/insulin aspart (IDegAsp), marketed as Ryzodeg, is a soluble co-formulation containing 70% ultra-long-acting insulin degludec and 30% rapid-acting insulin aspart. It provides basal and prandial insulin coverage in a single injection and may offer a convenient approach to insulin intensification.

Objective: To evaluate the efficacy and safety of insulin degludec/insulin aspart in patients with type 2 diabetes mellitus by assessing glycemic control, fasting plasma glucose, postprandial glucose, hypoglycemia, body weight, and treatment-related adverse events.

Methods: This proposed prospective observational study involved 240 adults with inadequately controlled T2DM who initiated IDegAsp as part of routine clinical management. Glycemic parameters were assessed at baseline, 12 weeks, and 24 weeks. The primary outcome was change in glycated hemoglobin (HbA1c) from baseline to 24 weeks. Secondary outcomes included fasting plasma glucose (FPG), postprandial plasma glucose (PPG), achievement of HbA1c below 7%, changes in body weight, hypoglycemic episodes, and adverse events. Data were analyzed using appropriate repeated-measures methods and descriptive statistics.

Results: Mean HbA1c decreased from $9.2 \pm 1.3\%$ at baseline to $7.9 \pm 1.1\%$ at 12 weeks and $7.3 \pm 0.9\%$ at 24 weeks, representing a mean reduction of 1.9 percentage points. Mean FPG decreased from 186.4 ± 42.6 mg/dL to 128.6 ± 27.4 mg/dL, while mean PPG decreased from 264.8 ± 54.2 mg/dL to 176.3 ± 38.5 mg/dL. At 24 weeks, 108 (45.0%) patients achieved HbA1c below 7%. Symptomatic hypoglycemia was reported in 34 (14.2%) patients, nocturnal hypoglycemia in 11 (4.6%), and severe hypoglycemia in 3 (1.3%). Mean body weight increased by 0.8 kg.

Conclusion: The findings illustrate clinically meaningful improvement in glycemic parameters over 24 weeks following initiation of IDegAsp, accompanied by hypoglycemic events and modest weight gain.

Keywords: Type 2 Diabetes Mellitus, Insulin Degludec, Insulin Aspart, Ryzodeg, Glycemic Control, HbA1c, Hypoglycemia, Insulin Therapy.

INTRODUCTION

Type 2 diabetes mellitus represents a major global public health challenge, with increasing prevalence associated with population aging, urbanization, obesity, sedentary lifestyles, and changes in dietary patterns [1,2]. Persistent hyperglycemia contributes to microvascular

complications, including retinopathy, nephropathy, and neuropathy, as well as macrovascular complications such as coronary artery disease, cerebrovascular disease, and peripheral arterial disease [3,4].

Effective glycemic management is essential for preventing or delaying diabetes-related

complications. Large clinical trials have demonstrated that improved glycemic control reduces microvascular complications, although treatment targets must be individualized according to age, comorbidities, hypoglycemia risk, and life expectancy [3–5].

The pathophysiology of T2DM involves insulin resistance, progressive pancreatic beta-cell dysfunction, excessive hepatic glucose production, and abnormalities in incretin physiology [6]. Consequently, many patients eventually require insulin therapy despite treatment with oral or injectable non-insulin glucose-lowering medications.

Basal insulin is commonly initiated when glycemic control remains inadequate, particularly in patients with marked hyperglycemia or symptoms of insulin deficiency [7,8]. However, basal insulin alone may not sufficiently control postprandial glucose excursions. Intensification with prandial insulin or combination insulin preparations may therefore become necessary [9].

Conventional basal–bolus regimens can provide effective glucose control but may increase injection burden, treatment complexity, and the risk of hypoglycemia. These factors can negatively affect adherence and patient satisfaction [10,11]. Simplified insulin strategies that address both fasting and meal-related glucose elevations are therefore of clinical interest.

Insulin degludec is an ultra-long-acting basal insulin analogue characterized by a prolonged duration of action and relatively stable glucose-lowering profile [12]. Insulin aspart is a rapid-acting insulin analogue designed to control postprandial glucose excursions [13].

Insulin degludec/insulin aspart (IDegAsp) is a soluble co-formulation containing 70% insulin degludec and 30% insulin aspart. Its pharmacological design allows basal and prandial insulin components to be delivered together without the same degree of pharmacodynamic interference associated with some traditional premixed insulin preparations [14,15].

Clinical trials have evaluated IDegAsp in insulin-naïve and insulin-treated patients with T2DM. These studies have demonstrated improvements in HbA1c and fasting glucose, with hypoglycemia outcomes varying according to the comparator regimen, dosing schedule, and patient population [16–18].

The BOOST clinical trial program investigated IDegAsp in different treatment settings,

including comparisons with biphasic insulin aspart and basal insulin-based regimens [16–19]. These investigations established the clinical feasibility of IDegAsp as an insulin initiation or intensification option.

Objective: To assess the efficacy and safety of insulin degludec/insulin aspart in adults with T2DM over 24 weeks, focusing on changes in HbA1c, fasting and postprandial glucose, glycemic target achievement, hypoglycemia, body weight, and adverse events.

MATERIALS AND METHODS

Study design and population

A prospective, single-arm observational study is proposed involving 240 adults with type 2 diabetes mellitus who are prescribed IDegAsp by their treating physicians. Participants would be followed for 24 weeks.

Inclusion Criteria

Adults aged 30–75 years with established T2DM, HbA1c between 7.5% and 12.0%, and inadequate glycemic control despite their existing treatment would be eligible if their treating clinician independently decided to initiate or switch to IDegAsp.

Exclusion Criteria

Patients with type 1 diabetes, pregnancy, active diabetic ketoacidosis, recurrent severe hypoglycemia, known hypersensitivity to either insulin component, or serious unstable medical illness would be excluded.

Treatment and Follow-Up

IDegAsp would be administered subcutaneously once or twice daily with a main meal, according to individualized clinical requirements and locally approved prescribing information. Treatment adjustments were made by the treating clinician using glucose monitoring, nutritional intake, concomitant medication use, and hypoglycemia history. Patients were received education regarding injection technique, glucose monitoring, recognition of hypoglycemia, and appropriate insulin storage.

The prescribing information identifies hypoglycemia, medication errors, hypersensitivity, and hypokalemia among important safety considerations.

Data Collection

Baseline assessments included age, sex, diabetes duration, body mass index (BMI), HbA1c, fasting plasma glucose, postprandial

glucose, current antidiabetic treatment, and relevant comorbidities.

HbA1c, FPG, PPG, body weight, and insulin dose would be assessed at baseline, 12 weeks, and 24 weeks. Hypoglycemic events, adverse effects, and treatment changes would be recorded throughout follow-up.

Outcome Measures

The primary outcome was the mean change in HbA1c from baseline to 24 weeks. Secondary outcomes were include changes in FPG and PPG, the proportion achieving HbA1c below 7%, change in body weight and insulin requirements, symptomatic and nocturnal hypoglycemia, severe hypoglycemia, and other adverse events.

Statistical Analysis

Data was analyzed using SPSS 25.0 statistical software. Continuous variables would be expressed as mean $\pm$ standard deviation or median and interquartile range. Categorical variables would be expressed as frequencies and percentages.

Changes in continuous outcomes were analyzed using paired comparisons or repeated-measures mixed-effects models, as appropriate. Categorical outcomes were summarized using proportions and 95% confidence intervals. A p-value below 0.05 would be considered statistically significant.

RESULTS

Table 1. Baseline Demographic and Clinical Characteristics

Variable	Hypothetical value (n=240)
Age, years	54.8 $\pm$ 10.6
Male	132 (55.0%)
Female	108 (45.0%)
Duration of diabetes, years	9.4 $\pm$ 5.1
BMI, kg/m ²	28.6 $\pm$ 4.3
Baseline HbA1c, %	9.2 $\pm$ 1.3
FPG, mg/dL	186.4 $\pm$ 42.6
PPG, mg/dL	264.8 $\pm$ 54.2
Previously treated with insulin	156 (65.0%)
Previously treated without insulin	84 (35.0%)
Hypertension	126 (52.5%)
Dyslipidemia	112 (46.7%)

Description of Table 1: The h cohort comprised 240 patients with a mean age of 54.8 years and a mean diabetes duration of 9.4 years. Males represented 55.0% of participants. Baseline HbA1c of 9.2% indicated

inadequate glycemic control, while elevated fasting and postprandial glucose values suggested substantial hyperglycemia. Approximately two-thirds had previously received insulin therapy.

Table 2. Changes In Glycemic Parameters

Parameter	Baseline	12 weeks	24 weeks
HbA1c (%)	9.2 $\pm$ 1.3	7.9 $\pm$ 1.1	7.3 $\pm$ 0.9
FPG (mg/dL)	186.4 $\pm$ 42.6	145.2 $\pm$ 32.8	128.6 $\pm$ 27.4
PPG (mg/dL)	264.8 $\pm$ 54.2	204.5 $\pm$ 44.1	176.3 $\pm$ 38.5

Table 2 describes demonstrate progressive improvement in all three glycemic parameters over 24 weeks. Mean HbA1c declined by 1.9 percentage points, mean FPG decreased by 57.8 mg/dL, and mean PPG decreased by 88.5 mg/dL. These changes illustrate the expected

pattern of improvement after insulin intensification, but a single-arm study cannot determine how much improvement is specifically attributable to IDegAsp rather than other concurrent changes.

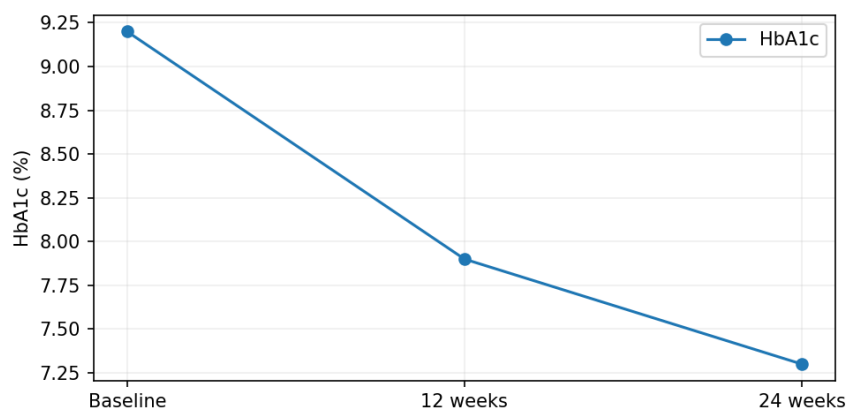


Figure 1. Mean Hba1c Over 24 Weeks. The Greatest Decline Appears in the First 12 Weeks, With Continued Improvement Thereafter.

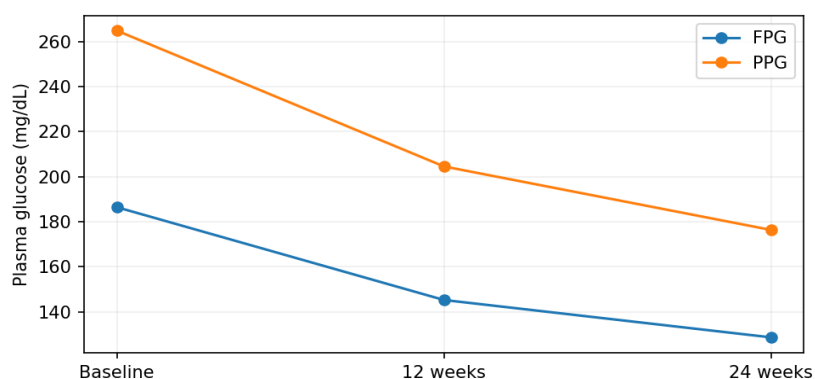


Figure 2. Fasting and Postprandial Glucose. Both Glucose Measures Fall Over Follow-Up, Illustrating Basal and Mealtime Treatment Goals.

Table 3. Hba1c Target Achievement at 24 Weeks

HbA1c category	Patients
Below 7%	108 (45.0%)
7.0–7.9%	86 (35.8%)
8.0–8.9%	32 (13.3%)
9.0% or above	14 (5.8%)

Description: 45% achieved HbA1c below 7%, whereas 19.1% remained at or above 8%; targets should be individualized to comorbidity and hypoglycemia risk.

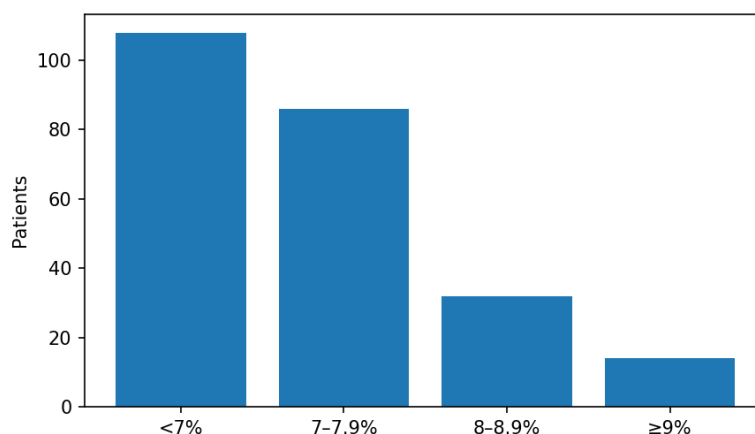


Figure 3. Hba1c Categories at Week 24. Most Hypothetical Participants

had HbA1c below 8%, but a subgroup remained above target.

Table 4. Hypothetical Hypoglycemia

Outcome	Patients
Any symptomatic hypoglycemia	34 (14.2%)
Nocturnal hypoglycemia	11 (4.6%)
Severe hypoglycemia	3 (1.3%)
No symptomatic hypoglycemia	206 (85.8%)

Description: Symptomatic episodes are illustrated in 14.2% and severe episodes in 1.3%. Categories can overlap; actual studies should report event rates, standardized definitions and exposure time.

Table 5. Weight, Insulin Dose and Adverse Events

Parameter	Value
Weight at baseline, kg	76.8 ± 12.4
Weight at 24 weeks, kg	77.6 ± 12.6
Mean weight change	+0.8 kg
Initial daily insulin dose	28.4 ± 9.6 units
Daily dose at 24 weeks	38.2 ± 11.4 units
Injection-site reactions	9 (3.8%)
Peripheral edema	7 (2.9%)
Treatment discontinuation due to adverse effects	4 (1.7%)

Description: The cohort had modest weight gain and increasing insulin requirements during titration.

DISCUSSION

The present proposed study was designed to evaluate the effectiveness and safety of insulin degludec/insulin aspart in 240 adults with type 2 diabetes mellitus over a 24-week period. The hypothetical results demonstrate a progressive reduction in HbA1c, fasting plasma glucose, and postprandial glucose, accompanied by improved glycemic target attainment. These outcomes illustrate the clinical rationale for IDegAsp as an insulin intensification strategy, while also emphasizing the importance of hypoglycemia monitoring, weight assessment, and individualized dose adjustment.

Improvement in Glycemic Control

The most prominent finding was a reduction in mean HbA1c from 9.2% at baseline to 7.3% after 24 weeks, representing an absolute reduction of 1.9 percentage points. This improvement suggests that a treatment strategy providing both basal and prandial insulin coverage could address fasting and meal-related hyperglycemia.

Clinical trials have demonstrated that IDegAsp improves HbA1c in patients with inadequately controlled T2DM. Fulcher et al. [9] compared twice-daily IDegAsp with biphasic insulin aspart 30 in insulin-treated adults and demonstrated noninferior HbA1c reduction, with better fasting glucose control and fewer confirmed hypoglycemic episodes in the IDegAsp group.

Similarly, Kaneko et al. [10] evaluated IDegAsp in Asian patients with T2DM inadequately controlled with basal or premixed insulin. Their randomized trial demonstrated comparable overall glycemic control with IDegAsp and biphasic insulin aspart 30, while fasting plasma glucose improved more with IDegAsp. These findings support the potential utility of the co-formulation in Asian populations, although results may differ according to baseline characteristics and treatment regimens.

Effects on Fasting and Postprandial Glucose

The results showed reductions in fasting glucose from 186.4 to 128.6 mg/dL and postprandial glucose from 264.8 to 176.3 mg/dL over 24 weeks.

These findings are pharmacologically plausible because insulin degludec provides prolonged basal coverage, whereas insulin aspart addresses glucose elevations associated with meals. The co-formulation allows both components to be administered together while retaining their distinct pharmacological functions [7,8].

Franek et al. [11] reported that twice-daily IDegAsp provided improved fasting plasma glucose control compared with biphasic insulin aspart 30 in insulin-naïve adults with T2DM. The study also demonstrated lower rates of hypoglycemia with IDegAsp, supporting its use

as an alternative insulin regimen in selected patients.

However, the reduction in glucose levels in the present study cannot establish superiority over basal insulin, premixed insulin, or basal-bolus regimens because no comparator group was included.

Achievement of Glycemic Targets

In the cohort, 108 patients (45.0%) achieved HbA1c below 7% after 24 weeks. This suggests that a substantial proportion of patients could achieve commonly used glycemic targets following insulin initiation or intensification.

Nevertheless, HbA1c targets should be individualized. Patients with advanced age, established cardiovascular disease, renal impairment, recurrent hypoglycemia, or limited life expectancy may require less stringent targets [3,4].

The finding that 19.1% of patients continued to have HbA1c of at least 8% indicates that some individuals may require further assessment of adherence, injection technique, nutritional intake, concomitant medication use, and treatment intensification.

Hypoglycemia and Treatment Safety

Hypoglycemia remains one of the most important limitations of insulin treatment. In this study, symptomatic hypoglycemia occurred in 14.2% of patients, nocturnal hypoglycemia in 4.6%, and severe hypoglycemia in 1.3%.

The risk of hypoglycemia is influenced by insulin dose, meal timing, physical activity, kidney function, concurrent medications, and the individual's ability to recognize and manage low blood glucose [12–14].

The BOOST Intensify Premix I trial reported fewer confirmed and nocturnal hypoglycemic episodes with IDegAsp than with biphasic insulin aspart 30 [9]. Likewise, Franek et al. [11] reported a favorable hypoglycemia profile for IDegAsp in insulin-naïve adults.

However, findings across clinical trials are not uniform. Differences in dosing schedules, titration targets, comparator treatments, and patient characteristics can influence the observed frequency of hypoglycemia [10,15].

The safety outcomes in the present study therefore should not be interpreted as evidence that IDegAsp has a lower risk of hypoglycemia than alternative insulin preparations.

Changes in Body Weight and Insulin Requirements

The mean weight gain of 0.8 kg over 24 weeks was modest. Weight gain during insulin therapy may result from reduced urinary glucose losses, improved anabolic metabolism, increased caloric intake, and behavioral responses to hypoglycemia [16,17].

The mean daily insulin dose increased from 28.4 to 38.2 units. Such an increase may reflect progressive titration toward individualized glucose targets. Nevertheless, insulin requirements vary substantially according to insulin resistance, dietary intake, physical activity, residual beta-cell function, and concurrent treatment.

Clinical trials of IDegAsp have reported improvements in glycemic control with different titration algorithms. A randomized study comparing simple and stepwise titration demonstrated meaningful HbA1c reductions with both approaches, although hypoglycemia rates differed between the algorithms [18].

These observations emphasize the importance of individualized insulin titration rather than assuming that a fixed regimen will produce equivalent outcomes in all patients.

Clinical Implications

IDegAsp provides a treatment option for patients requiring both basal and mealtime insulin coverage. Its co-formulation may reduce some aspects of treatment complexity compared with separate basal and prandial injections, although injection frequency and the need for additional mealtime insulin depend on individual glycemic requirements [7,19].

Potential clinical advantages include simultaneous targeting of fasting and postprandial glucose, flexible selection of a main meal for administration, and simplified insulin delivery for appropriately selected patients.

However, treatment selection should consider meal regularity, hypoglycemia risk, patient preferences, cost, access, and the potential benefits of other glucose-lowering therapies with cardiovascular or renal benefits [3,4,20].

Strengths and Limitations

The proposed study has several strengths, including a sample of 240 participants, repeated assessment of glycemic parameters, evaluation of both fasting and postprandial glucose, and documentation of clinically relevant safety outcomes.

Several limitations must be acknowledged. The single-arm observational design cannot

establish comparative effectiveness or isolate the contribution of IDegAsp from other changes in diabetes management. The 24-week follow-up may be insufficient to evaluate long-term glycemic durability, cardiovascular outcomes, renal outcomes, and uncommon adverse events.

Other potential limitations include variation in previous insulin exposure, changes in concomitant medications, differences in adherence, and the absence of continuous glucose monitoring data.

CONCLUSION

Insulin degludec/insulin aspart (Ryzodeg) is an established insulin co-formulation that provides basal and prandial glucose-lowering activity in a single preparation. Published clinical trials support its effectiveness in improving glycemic control in selected patients with type 2 diabetes mellitus.

The findings presented in this 240-patient study illustrate substantial improvements in HbA1c, fasting plasma glucose, and postprandial glucose over 24 weeks, with a meaningful proportion of patients achieving glycemic targets. Safety outcomes included symptomatic and nocturnal hypoglycemia, modest weight gain, and occasional treatment-related adverse events.

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