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IDegLira fixed-ratio combination in the real world: a retrospective observational single-center Italian experience

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Abstract. – OBJECTIVE: An improvement of type 2 diabetes treatment is represented by the recent availability of a fixed-ratio combination of slow insulin degludec and GLP-1 RA liraglutide (IDegLira), which shows encouraging clinical trial results. This work represents a real-world evidence study to evaluate if the obtained clinical results are also confirmed in the clinical practice, in an Italian type 2 diabetes patients' population.

PATIENTS AND METHODS: This retrospective observational study was conducted in the Diabetology Service of the Umbria local sanitary agency (USL Umbria 1) in Perugia. The study investigated all diabetic patients >18 years, who underwent anti-diabetic treatment with basal insulin with or without the concomitant consumption of one or more oral anti-diabetic agent (BOT group) or GLP-1 RA or rapid-acting insulin bolus (BB group), with unsatisfactory glycemic control for either hypoglycemic episodes or weight gain. The observation period was February 2018 to April 2019.

RESULTS: IDegLira results to be effective in reducing HbA1c and fasting plasma glucose, especially among GLP-1 RA and BOT subgroup. In BOT group, a statistical difference was noted from the first month of treatment, also for post-prandial glycemia. Obtained results were achieved at a moderate dose of IDegLira reported during the study, which also represents a significant reduction of the amount of basal insulin in BB patients.

CONCLUSIONS: Obtained results suggest that in a real-world setting, the switch to IDegLira treatment is a valid option for patients with unsatisfactory glycemic control, or who experienced side effects such as weight gain and hypoglycemia of other insulin therapies.

Key Words:

Insulin degludec, Liraglutide, IDegLira, Fixed-ratio combination, Diabetes, Basal bolus, Oral anti-diabetic therapy.

Introduction

According to the American Diabetes Association (ADA)/European Association for the Study of Diabetes (EASD), one of the main goals of anti-diabetes treatment is an individualized glycemic target, and a personalized approach to therapy, which is based on patient- and disease-related characteristics[1,2]. Basal insulin (BI) is a recommended option at many stages of type 2 diabetes and is often added to oral anti-diabetic drugs (OADs) to achieve target fasting plasma glucose levels. However, it increases the risk of hypoglycemia and weight gain, and its dosage must be titrated effectively to achieve glycemic targets[3].

The use of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) strongly reduces hypoglycemic episodes, and a therapeutic strategy based on GLP-1 RAs may reduce glycated hemoglobin (HbA1c) more than a strategy based on BI[4,5]. Furthermore, GLP-1 RAs and BI potentiate each other, and they may be used together for therapy intensification[6]. In this case, a strategy of either flexible or fixed-ratio combinations (FRCs) of BI and GLP-1 RAs may be selected.

The fixed-ratio therapy has recently been improved with the availability of the combination of insulin degludec and liraglutide (IDegLira).

Insulin degludec is a BI administered via subcutaneous injection, which is slowly absorbed into the circulation for a stable glucose-lowering effect[7]. Liraglutide is a GLP-1 analogue (administered subcutaneously) with a protracted action and a long plasma half-life. This improves glycemic control by lowering both fasting and postprandial blood glucose levels, stimulating insulin secretion and lowering inappropriately

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high glucagon secretion, in a glucose-dependent way[8]. Thus, liraglutide improves glycemic control and reduces both hypoglycemia and weight gain.

IDegLira has been available in Italy since January 2018 and is administered once daily, independent of meals, as dose steps (DS) of 1 unit of insulin degludec and 0.036 mg of liraglutide[9]. The use of IDegLira has recently been extended to all type 2 diabetes patients who do not reach an adequate glycemic control with previous line of BI therapy plus OADs or rapid insulin. The consistent and robust data of the phase III DUAL I-VII clinical trial program contribute to this extension of use. In particular, DUAL V and DUAL VII trials included patients that respectively switched from glargine treatment or were subjected to the therapeutic intensification with the rapid-acting insulin analogue (basal-bolus protocol). These trials demonstrated a greater reduction in HbA1c, hypoglycemia and weight in the IDegLira-treated groups. In DUAL VII, HbA1c levels in IDegLira group were comparable to the basal-bolus group at the end of the study[10-17].

Despite a large amount of literature on IDegLira from randomized trials, real-world evidence is limited. This literature type is useful as it comprehends a heterogeneous population of patients, commonly seen in routine clinical practice. A few real-world retrospective observational experiences[18-21] have already compared the fixed and flexible BI/GLP-1 RA combinations' effectiveness. In particular, Morieri et al[21] recently showed that both the flexible and FRC are safe and effective for controlling blood glucose levels, although a better weight reduction was obtained with the flexible combination, due to lower insulin and higher GLP-1 RA doses used in the flexible combination. Of note, the single daily injection needed with the FRC, increases the patient's compliance to therapy as opposed to multiple injections of other therapies[20]. Moreover, in real-world experiences, the use of IDegLira was also associated with the reduction of at least one class of concomitant diabetic medications compared to baseline[19-21].

The aim of the present real-world cohort study is to confirm in real clinical practice, whether results from IDegLira trials are confirmed in an Italian population of diabetic patients with poor glycemic control, during 18 months of follow-up, with the specific intent to reach the guidelines recommended target glycaemic control of patients, without increasing the risk of hypoglycemia compared to titration of BI alone, and without worsening the extra-glycemic parameters indicative of cardiovascular risk.

Patients and Methods

Study Design

This study was a retrospective observational investigation conducted in the Diabetology Service of the Umbria local sanitary agency (USL Umbria 1) in Perugia. The study was conducted according to the Declaration of Helsinki and was approved by the local Ethics Committee.

Patients Population

All diabetic patients who were >18 years, undergoing anti-diabetic treatment with BI with or without the concomitant consumption of one or more OADs (BOT group) or GLP-1 RA or rapid BI (basal + rapid-acting boluses; BB group), with unsatisfactory glycemic control for either hypoglycemic episodes or weight gain were screened for participation in this study. Patients were treated in the Diabetology Service of the Umbria USL in Perugia (Italy), during the period February 2018 to April 2019. Reasons for study exclusion were the contraindications to IDegLira administration (personal or family history of medullary thyroid carcinoma, or history of pancreatitis), or therapeutic strategies not allowed in the IDegLira summary of product characteristics. Insulin-naïve subjects were also excluded.

Study Measures

Information on gender, age, diabetes duration, HbA1c levels, fasting plasma glucose (FPG), post-prandial plasma glucose (PPG), body mass index (BMI), body weight, waist circumference, height, anti-diabetic treatment with either insulin or other OADs and existing comorbidities were collected for each patient at baseline (V0; i.e., when patients were switched to IDegLira from their previous treatments). HbA1c levels, FPG, PPG, BMI, body weight and waist circumference were followed-up at regular intervals at 6 (V1), 12 (V2) and 18 months (V3).

Additional information was recorded, such as the average IDegLira dosage reached during up-titration and the mean time needed to have an HbA1c reduction of 0.4% (defined as time to efficacy).

We evaluated three groups of patients: the BOT group comprised patients undergoing treat-

ment with BI alone or plus at least one OAD; the GLP-1 RAs group consisted of patients treated with BI plus a GLP-1 RA; and the BB group consisted of the patients receiving basal plus rapid BI. Comparisons of follow-up visits results are always referred to the respective baseline group.

Statistical Analysis

Results are expressed as mean and standard deviation (SD) or standard error (SE) for continuous variables, and proportion and percentages for categorical measures, respectively. Between-group patient characteristics were compared with a Wilcoxon signed-rank test or Paired *t*-test (as appropriate) for continuous variables, or a McNemar's test for categorical variables. Time to efficacy was estimated with Kaplan-Meier curves. All data were collected from electronic medical records.

Analyses were performed with IBM SPSS Statistics for Windows version 26 and MedCalc Statistical Software version 19.4.0.

Results

Study Population and Clinical Characteristics

161 patients were screened for the present study. Among them, 24 were excluded because they were naïve to insulin therapy. Thus, 137 patients were included in the present study: 104 in the BOT group, 13 in the GLP-1 RA group, and 20 in the BB group. The patients characteristics at baseline are listed in Table I.

The main existing comorbidities were kidney failure with either reduced creatinine clearance (mean cc = 44.8±18.2 ml/min, n=17) or microalbuminuria (mean = 68.4±170.5 mg/dL, n=75), renal insufficiency (n=18, 13.1% of patients) and major cardiovascular events (n=20, 14.6% of patients). In Table II, the previous diabetic therapies followed by patients were summarized.

Before the switch to IDegLira, most of BOT patients were treated with one additional OAD (n=63, 63%). A total of 36% of patients (n=36) were treated with two additional OADs and 1% (one patient) with three OADs. The reasons for the switch to IDegLira therapy were reported in Table III.

Effectiveness Outcomes

Table IV shows the mean values of HbA1c (%), FPG, BMI, body weight and waist circumference at V1 (6 months), V2 (12 months) and V3 (18 months), for each subgroup.

HbA1c was significantly reduced at each follow-up visits in the BOT and GLP-1 RA populations (BOT: 6 months mean±SD reduction = -1.1±1.4%; 12 months mean±SD reduction = -0.9±1.1%; 18 months mean±SD reduction = -0.9±1.0%; $p<0.001$. GLP-1 RA: 6 months mean±SD reduction = -1.4±1.0%, $p=0.005$; 12 months mean±SD reduction = -1.2±0.5%, $p=0.001$; 18 months mean±SD reduction = -1.2±0.4%, $p=0.012$). In the BB group, HbA1c was significantly reduced at 6 months (mean±SD reduction = -1.2±1.1%; $p=0.025$) (Table IV and Figure 1).

In the BOT group, the frequency of patients with HbA1c<7% is significantly increased at each visit, respectively of +37% at 6 months, +27% at 12 months and +25% at 18 months (Table IV).

The mean±SE times to efficacy were 8.1±0.6 months (95% CI: 7.0-9.2; n=84) for BOT patients, 6.2±1.3 months (95% CI: 3.5-8.8; n=10) for GLP-1 RA patients and 10.4±1.7 months (95% CI: 7.0-13.8; n=10) for BB patients. Cumulative proportion of patients with efficacy for all the populations are reported in Figure 2.

Table I. Patient characteristics at baseline.

Characteristic	BOT	GLP-1 RA	BB
Full analysis set (n)	104	13	20
Male, n (%)	73 (70)	8 (61)	13 (65)
Age (years), mean (SD)	65 (9) n = 104	65 (11) n = 13	65 (13) n = 20
Duration of diabetes, years mean (SD)	11 (7) n = 103	11 (6) n = 13	5 (4) n = 17
HbA1c %, mean (SD)	8.4 (1.2) n = 104	8.6 (0.9) n = 13	8.4 (1.5) n = 20
FPG (mg/dL), mean (SD)	163.2 (53.4) n = 95	171.8 (40.9) n = 13	162.0 (65.8) n = 16
BMI (kg/m^2), mean (SD)	30.5 (5.2) n = 102	34.7 (5.7) n = 13	34.6 (3.9) n = 19
Weight (kg), mean (SD)	88.0 (17.4) n = 102	98.2 (21.8) n = 13	96.4 (15.7) n = 19
Waist circumference (cm), mean (SD)	108.0 (12.6) n = 99	113.9 (15.1) n = 13	117.1 (9.2) n = 17
Height (cm), mean (SD)	167.7 (9.6) n = 103	167.5 (9.3) n = 12	166.6 (10.6) n = 20

Table II. Previous diabetic therapies.

Type	Mean insulin dose (SD)	
	IU	U/Kg)
Basal insulin (n = 137):	26.3 (22.8)	0.29 (0.2)
Detemir (n = 8)	21.3 (13.9)	0.27 (0.2)
Degludec (n = 42)	33.9 (32.3)	0.34 (0.3)
Glargine U100 (n = 74)	23.6 (15.0)	0.27 (0.16)
Glargine U300 (n = 13)	19.8 (9.7)	0.23 (0.11)
BOT group:		
Basal insulin (n = 104)	18.8 (7.5)	
Metformin (n = 96)	0.22 (0.1)	
DPP-4i (n = 24)		
Sulfonylurea (n = 10)		
SGLT-2i (n = 8)		
GLP-1 RA (n = 13)	29.6 (14.0)	0.31 (0.1)
Basal bolus (n = 20)	63.0 (39.7)	0.62 (0.33)

Table III. Reasons for switch to IdegLira.

	BOT, n (%)	GLP-1 RA, n (%)	BB, n (%)
Glycemic variability	11 (10.6)	–	20 (100)
Hypoglycemic episodes	11 (10.6)	–	20 (100)
Low adherence to therapy	6 (5.8)	13 (100.0)	20 (100)
Weight gain	5 (4.8)	–	20 (100)
Inefficacy of current therapy	93 (89.4)	13 (100.0)	–
Need more intensification	97 (93.3)	13 (100.0)	–
Adverse events of previous therapy	2 (1.9)	–	–

Table IV. Effectiveness outcomes.

Group	Outcome, mean (SD)	V1			V2			V3		
		N	Baseline	Follow-up	N	Baseline	Follow-up	N	Baseline	Follow-up
BOT	HbA1c (%)	54	8.3 (1.2)	7.2 (1.0)***	100	8.4 (1.3)	7.5 (1.1)***	28	8.3 (0.9)	7.4 (0.9)***
	HbA1c<7%, n (%)	54	3 (5.6)	23 (42.6)***	100	9.0 (9.0)	36.0 (36.0)***	28	1 (3.6)	8.0 (28.6)*
	FPG (mg/dL)	36	154.5 (40.3)	129.4 (36.2)***	52	159.2 (57.5)	130.5 (28.1)***	20	163.3 (40.2)	141.6 (41.7)*
	BMI (kg/m^2)	49	30.6 (5.3)	30.4 (5.3)	60	32.3 (5.6)	32.3 (5.6)	23	31.6 (5.4)	32.3 (5.7)*
	Weight (kg)	53	86.0 (16.5)	85.6 (16.8)	62	91.8 (19.2)	91.7 (19.3)	24	91.9 (18.2)	92.8 (18.4)
	Waist circumference (cm)	41	105.4 (13.4)	105.0 (12.6)	54	111.7 (13.6)	111.1 (14.4)	21	112.9 (14.8)	112.5 (15.5)
GLP-1 RA	HbA1c (%)	8	8.9 (1.1)	7.5 (1.1)**	7	8.4 (0.8)	7.2 (0.6)***	4	8.2 (0.8)	7.0 (0.4)*
	HbA1c<7%, n (%)	8	0	4 (50)	7	0	2 (28)	4	0	1 (25)
	FPG (mg/dL)	4	190.8 (43.3)	126.0 (42.1)	4	197.3 (25.0)	129.5 (22.7)	2	170.0 (9.9)	101.0 (41.0)
	BMI (kg/m^2)	7	33.5 (5.9)	33.7 (5.6)	7	34.0 (4.3)	33.8 (4.8)	3	32.2 (6.6)	31.4 (6.2)
	Weight (kg)	7	94.6 (22.0)	95.4 (21.6)	7	96.7 (21.2)	96.3 (22.4)	3	86.7 (30.7)	84.5 (29.0)
	Waist circumference (cm)	5	117.2 (12.0)	117.0 (11.0)	6	114.0 (14.3)	115.5 (12.4)	1	90.0	91.0
BB	HbA1c (%)	7	8.4 (0.7)	7.2 (0.6)*	9	8.1 (1.8)	7.9 (1.9)	2	9.5 (0.2)	9.0 (0.3)
	HbA1c<7%, n (%)	8	–	3 (42.9)	9	3 (33.3)	3 (33.3)	2	0	0
	FPG (mg/dL)	4	161.0 (14.2)	107.5 (22.2)	7	155.1 (55.5)	136.9 (32.2)	–	–	–
	BMI (kg/m^2)	6	33.3 (4.3)	32.0 (3.8)*	8	35.1 (4.4)	34.0 (4.6)**	2	36.5 (2.6)	35.1 (2.9)
	Weight (kg)	6	89.6 (10.8)	86.2 (11.5)	8	93.5 (15.6)	90.5 (16.6)**	2	104.5 (2.1)	100.5 (0.7)
	Waist circumference (cm)	4	113.8 (6.7)	111.8 (5.2)	7	116.6 (7.1)	114.4 (9.0)	2	119.0 (1.4)	114.5 (2.1)

Statistical significance: *p<0.05; **p<0.01; ***p<0.001.

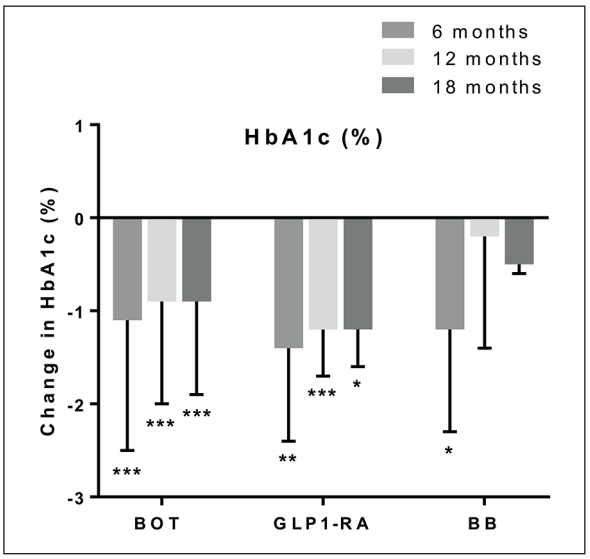

Figure 1. Delta reduction of HbA1c (%) by visit in BOT, GLP-1 RA and BB populations compared to baseline values. Mean±SD are represented. Statistical significance: *p<0.05; **p<0.01; ***p<0.001.

Similarly, FPG was significantly reduced at each follow-up visit in BOT group (6 months mean±SD reduction = -25.1±40.9 mg/dL, p<0.001; 12 months mean±SD reduction = -28.7±50.6 mg/dL, p<0.001; 18 months mean±SD reduction = -21.7±41.6 mg/dL, p=0.031). The reduction of FPG in BOT group has been observed already from the first month of treatment (Figure 3A). A slight reduction of FPG is also reported for GLP-1 RA and BB groups (Table IV).

Considering PPG, a reduction has been observed in BOT group during the first 4 weeks of treatment (Figure 3B). FPG weekly trends and PPG have not been analyzed for the other populations because of a reduced number of patients.

A significant reduction of BMI was reported at 6 and 12 months in the BB group (6 months mean±SD reduction = -1.3±1.0 kg/m^2, p=0.023; 12 months mean±SD reduction = -1.1±0.88 kg/m^2, p=0.009).

A significant variation of body weight has been reported at 12 months in the BB group (mean±SD reduction = -3.0±2.1 kg, p=0.004).

Considering the waist circumference, a not significant reduction has been reported in BOT and BB group at each follow-up, and at 6 months in the GLP-1 RA group (Table IV).

Variation of IDegLira Dose and Concomitant OADs During the Study

Previous to the switch to IDegLira treatment, the mean dose of BI was 0.22±0.1 U/kg (18.8±7.5 IU) in the BOT group, 0.31±0.1 U/kg (29.5±14.0 IU) in the GLP-1 RA group and 0.62±0.3 U/kg (63.0±39.7 IU) in BB group (Figure 4 and Table V). The mean starting dose of IDegLira in BOT group was 16.6±2.2 DS, 27.0±12.2 DS in the GLP-1 RA group and 17.9±4.3 DS in BB group (Table V).

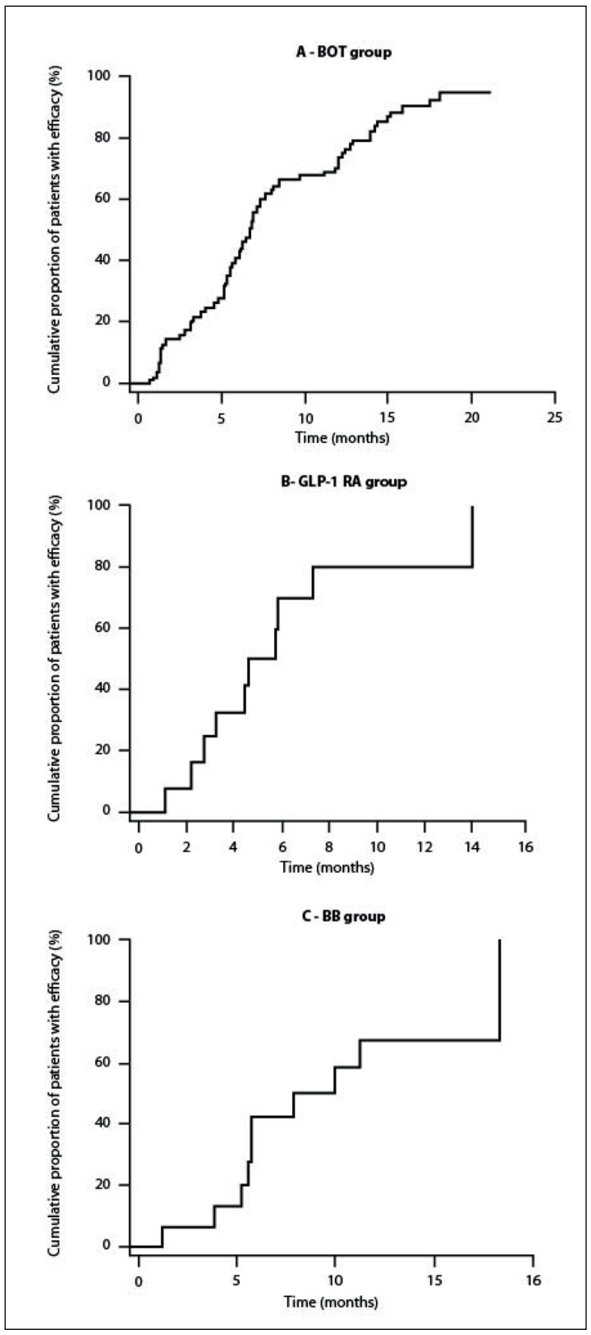

Figure 2. Time to efficacy (mean time needed to have an HbA1c reduction of 0.4%) in BOT group (**A**), GLP-1 RA group (**B**) and BB group (**C**).

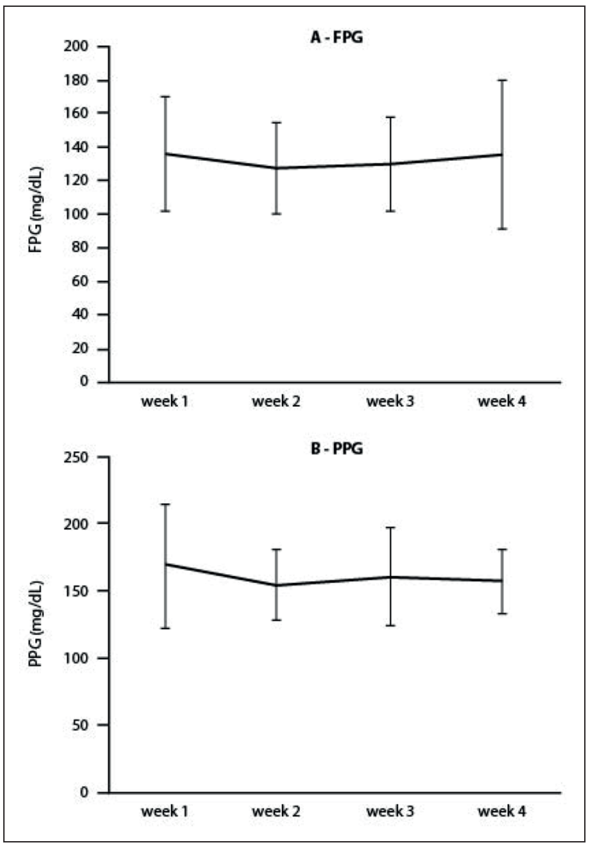

Figure 3. Analysis of FPG (A, n=25) and PPG (B, n=18) trends by week in BOT group of patients. Mean±SD are represented.

In BOT group, the mean dose of BI (IDegLira) significantly increased to 22.4±7.9 DS, 25.5±10.0 DS and 28.2±9.5 DS after 6, 12 and 18 months of treatment, respectively ($p \leq 0.001$) (Figure 4 and Table V).

In GLP-1 RA group, the mean dose of BI (IDegLira) was 35.0±11.5 DS, 34.6±16.8 DS and 25.8±16.2 DS after 6, 12 and 18 months of treatment, respectively, without significant variations compared to previous BI therapy (Figure 4, Table V).

In BB group, the mean dose of BI (IDegLira) significantly decreased to 25.5±7.5 DS (p=0.004), 27.3±10.7 DS (p=0.05) and 33.0±9.9 DS (p=0.03) after 6, 12 and 18 months of treatment, respectively, compared to previous BI therapy (Figure 4 and Table V).

The reference IDegLira maximum dose of 50 DS daily was prescribed to only one patient of the GLP-1 RA group as starting dose and was reached by one BOT patient (1.8%) and one GLP-1 RA patient (11.1%) at 6 months, by four BOT patients (5.7%) and two GLP-1 RA patients (28.6%) at 12 months and by one BOT patient (3.7%) and one GLP-1 RA patient (25.0%) at 18 months. No patients from the BB group reached the 50 DS daily dose of IDegLira during the study.

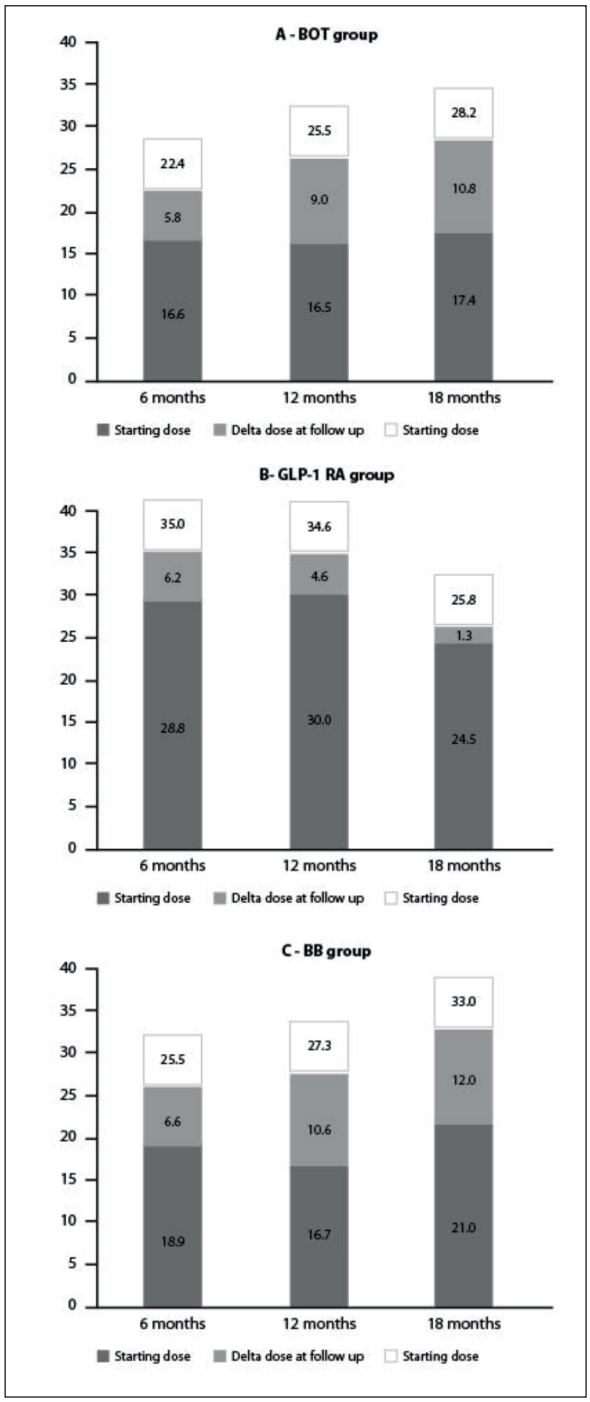

Figure 4. IDegLira mean dose steps (DS) by visit in BOT (**A**), GLP-1 RA (**B**) and BB (**C**) groups. Final mean dosages (DS) at visit are reported above columns, considering the relative baseline values of patients.

Table V. Insulin dose (mean [SD]) before and post switch to IDegLira.

Group		N	Insulin (IU) (before switch)	IDegLira dose (DS)	Delta
BOT	Baseline	102	18.8 (7.5)	16.6 (2.2)	-2.3 (7.1)***
	6 months	53	18.3 (6.4)	22.3 (7.9)	4.0 (7.5)***
	12 months	62	18.8 (7.4)	25.6 (10.0)	6.8 (10.3)***
	18 months	23	19.7 (7.2)	28.2 (9.5)	8.5 (9.3)***
GLP-1 RA	Baseline	13	29.5 (14.0)	27.0 (12.2)	-2.5 (11.1)
	6 months	7	31.1 (16.4)	35.0 (11.5)	3.9 (12.6)
	12 months	7	32.9 (15.7)	34.6 (16.8)	1.7 (11.6)
	18 months	3	25.5 (13.3)	25.8 (16.2)	0.3 (9.0)
BB	Baseline	19	63.0 (39.7)	17.9 (4.3)	-45.1 (40.7)***
	6 months	6	52.4 (20.7)	25.4 (7.5)	-27.0 (15.6)**
	12 months	8	66.7 (54.3)	27.2 (10.7)	-39.4 (52.1)*
	18 months	2	71.0 (7.1)	33.0 (9.9)	-38.0 (2.8)*

Statistical significance: *p<0.05; **p<0.01; ***p<0.001.

At the baseline visit (switch to IDegLira therapy), a total of 96 out of 104 patients of the BOT group was treated with one concomitant OAD. At the first visit post-switch to IDegLira, the number of BOT patients treated with one BOT was 48 out of 104, and one patient was treated with two concomitant OADs.

Discussion

In this analysis, we compared changes in glycemic (HbA1c, FPG, PPG) and extra-glycemic (BMI, body weight, waist circumference) effectiveness parameters among patients who switched to IDegLira, based on their previous treatment regimen (BOT, GLP-1 RA, BB). We also evaluated the effectiveness of the therapeutic switch by means of the fewer number of OADs needed after the introduction of IDegLira (BOT classes).

The results of our investigation show that IDegLira is effective in reducing HbA1c and FPG during follow-up, especially among the patients in the BOT subgroup, where a statistical difference was noted from the first month of treatment, also for PPG. HbA1c was significantly reduced at all time points also in the GLP-1 RA subgroup. Due to the limited sample of patients in the BB subgroup, no statistical difference was found in this case.

Obtained results were achieved at a moderate dose of IDegLira reported during the study (mean±SD IDegLira dose at the end of the study = 28.2±9.5 DS for the BOT group, 25.8±16.2 DS for the GLP-1 RA group and 33.0±9.9 DS for the BB group). For instance, this mean dose also represents a significant reduction of the amount of BI in BB patients (-38.0±2.8 IU at the end of the study, compared to previous treatment) and no BB patients reached the reference IDegLira maximum dose of 50 DS daily.

Our results are in line with previous data from phase III clinical studies, in which IDegLira significantly reduced HbA1c and FPG compared to OADs and glargine, showing a non-inferiority to these treatments. In the DUAL program trials[14-17], IdegLira reduced the episodes of symptomatic hypoglycemia and allowed for a better glycemic control, with a lower basal and total insulin dose compared to glargine[22,23].

Our findings also show that anti-diabetic therapy titration may be obtained not only with the increase of the BI dose. Despite the fact that ‘‘over-basalization’’ is a frequent option in clinical practice[24], it may lead to an increase in the number of hypoglycemic episodes and to weight gain, without improving glycemic control[25]. In this regard, combining different molecules involved in multiple pathways represents a more useful way to address a complex and global disease, such as type 2 diabetes[26]. Importantly, BI and GLP-1 RA are strictly complementary[27], with an additional action on the gastric emptying and feeling of satiation.

Clinical studies have demonstrated the enhanced glycemic control of the FRC of BI and GLP-1 RA in both insulin-naïve and insulin-treated patients with type 2 diabetes not adequately controlled on their current treatment, regardless of patients’ baseline HbA1c or disease duration[28]. Furthermore, it is important to underline that

glycemic fluctuations are reduced with the FRC compared to each individual component, with more in-target-range time[29].

Due to the reimbursement criteria for IDegLira in Italy (reserved to BOT and GLP-1 RA patients), the switch to this treatment is not possible for insulin-naïve patients. Thus, our study, which reflects common clinical practice, was limited to patients already receiving insulin. However, this limitation does not reduce the impact of our results.

GLP-1 RAs may often cause gastrointestinal side-effects, which, in turn, may cause therapy discontinuation. However, it has been shown that also this type of side-effects can be reduced with the FRC of insulin degludec and liraglutide[30]. In our population, adverse events were a cause to switch from previous BOT to IDegLira (two patients), but no side-effects were reported during follow-up.

Conclusions

In this investigation, conducted in a real-life clinical setting, we showed the results of previously published literature on IDegLira in a population of insulin-treated patients undergoing three different therapeutic regimens (BOT, GLP-1 RAs and BB). Thus, we indicated that IDegLira can be prescribed in Italy under the Italian Drug Agency rules in patients with specific characteristics, and with a net clinical benefit.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Authors' Contribution

Chiara Di Loreto was the principal investigator and designed the study. All the authors collected the data, revised the manuscript and approved the final version. .

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