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Real-world study on the effectiveness and safety of basal insulin IDegLira in type 2 diabetic patients previously treated with multi-injective insulin therapy

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Abstract. – OBJECTIVE: Achieving glycemic target is paramount to control diabetes mellitus (DM) and reduce micro-vascular and macro-vascular complications. Despite the mostly recent-developed drugs, most patients still show an above desired glycated hemoglobin (HbA1c) level due to DM complex pathophysiology, therapeutic and dietary compliance and clinical inertia in introducing or intensifying insulin therapy. To support the promising results of clinical trials on the effectiveness and safety of the degludec/liraglutide combination (IDegLira) in type 2 DM patients with C-peptide values >1 ng/ml who were previously treated with basal-bolus multiple daily-dose insulin injections.

PATIENTS AND METHODS: This observational, prospective and non-randomized trial enrolled type 2 DM patients referred to our outpatient clinic between January 2019 and December 2019, who were shifted from multiple daily-dose insulin injection therapy to degludec/liraglutide combination as per the physician's decision. The main assessment was HbA1c variation at 6 months from baseline. Secondary assessments included variation in fasting glycemia, routine anthropometric assessments, blood chemistry, blood pressure and patients' quality of life (measured by the Diabetes Treatment Satisfaction Questionnaire [DTSQ]), from baseline to 6 months.

RESULTS: HbA1c (8.4 *vs.* 7.4%; $p<0.0001$) and body weight (94.1 *vs.* 93 kg; $p<0.0001$) were significantly lower after 6 months for patients on the degludec/liraglutide combination. A similar trend was observed in fasting glycemia levels (159 *vs.* 125 mg/dl; $p<0.0001$). An improved glycemic control was achieved with degludec/liraglutide despite a reduction in total daily insulin units (42 U at 6 months *vs.* 22 U at baseline; $p<0.0001$). In addition, higher scores in the DTSQ were registered after 6 months on degludec/liraglutide (mean score: 27 *vs.* 20; $p<0.0001$). The combination therapy also proved more convenient than basal-bolus therapy in terms of costs, with an average per-patient cost difference of €-0.41±0.59/die ($p<0.0001$).

CONCLUSIONS: These real-world findings show that degludec/liraglutide seems to be more effective than basal-bolus insulin in achieving glycemic control, allowing cost sustainability and improving patient satisfaction.

Key Words:
Type 2 diabetes mellitus, Degludec/liraglutide, Real-world, Basal-bolus insulin, HbA1c, Glycemic control, Healthcare costs.

Introduction

Diabetes mellitus (DM) is a global, widespread, chronic disease associated with multi-organ complications[1]. The natural history of type 2 DM (T2DM) is characterized by a progressive reduction in the function of b-cells (with approximately 50% loss at the time of diagnosis followed by an estimated 4-6% subsequent loss per year), which causes a progressive decrease in insulin secretion and reserve[2].

The key goal of T2DM treatment is to achieve and maintain a tight glycemic control to reduce the risk of micro- and macro-vascular complications, and its associated morbidity and mortality[3]. However, despite the current availability of multiple drugs and combined therapies, most diabetic patients still do not achieve their glycemic target[1,4]. Current Italian guidelines for T2DM management, recommend an add-on therapy for patients who do not achieve their glycemic target by means of metformin intake alone[6]. The

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second-line therapy should be chosen with an individual approach, taking into consideration the patient's needs, age, time since T2DM onset, severity of metabolic impairment and presence of comorbidities, such as kidney disease, obesity or cardiovascular (CV) risk[6].

During their therapeutic course, most patients with T2DM would need insulin replacement therapy (basal or basal-bolus) to correct the gluco-toxicity and lipo-toxicity, which also have a negative impact on the function of b-cells[7,8]. Despite the effectiveness of insulin therapy in glycemic control, this approach can be associated with weight gain and increased hypoglycemic risk, besides being a complex treatment regimen. These contraindications potentially result in reduced patients' therapeutic adherence, which negatively affects the maintenance of a tight glycemic control[9].

In addition to insulin, other treatment options, such as dipeptidyl peptidase-4 inhibitor (DPP4-i) and glucagon-like peptide 1 receptor agonist (GLP-1-RA), can positively affect the function of b-cells by promoting cell proliferation and regeneration[10-12]. Unlike insulin therapy, such drugs present the advantage of having a neutral (DPP4-i) or positive (GLP1-RA) effect on weight loss; moreover, GLP-1-RAs are particularly useful in obese patients and those with high CV risk[13].

Despite the benefits associated with GLP-1-RA, insulin is still the most used injectable therapy, especially in patients with uncontrolled disease[14,15]. However, the combination of GLP-1-RA with insulin may represent a valuable alternative to GLP-1-RA or insulin alone, as it requires a reduced number of subcutaneous injections, thus favoring treatment compliance. Moreover, it can help reduce fasting and postprandial glucose levels without the common side effects of increased basal insulin and prandial bolus introduction, namely higher hypoglycemic risk and weight gain[16-19].

IDegLira is a once daily, titratable, fixed-ratio combination therapy of basal insulin, degludec and GLP-1-RA, liraglutide[20]. Each unit dose of degludec/liraglutide contains insulin 1 U and liraglutide 0.036 mg. Notably, degludec basal insulin seems to have a more stable hypoglycemic effect with low intraday variability compared to glargine, a long-acting insulin, thus reducing total and nocturnal hypoglycemic risk[21].

The DUAL clinical trial program aimed at demonstrating the higher effectiveness and safety of degludec/liraglutide compared to basal insulin therapy or to its combination with oral anti-diabetic drugs[22,23].

The DUAL V study enrolled T2DM patients with a 7-9% baseline glycated hemoglobin ($HbA1_c$) on basal insulin + metformin, who were randomized to degludec/liraglutide treatment or to a more aggressive basal insulin titration with glargine. Patients treated with degludec/liraglutide showed a higher $HbA1_c$ improvement compared with the control group (-0.59%), as well as a concomitant reduction in postprandial blood glucose levels and fewer hypoglycemic episodes. Furthermore, patients in degludec/liraglutide arm achieved a weight loss (-1.4 kg) *vs.* a weight gain observed in the glargine group (+1.8 kg). No differences in fasting glycemia values were observed, although the degludec/liraglutide final dose was significantly lower than the basal insulin dose (41 U *vs.* 66 U)[24].

The phase IIIb randomized study, DUAL VII, further supported the beneficial effects of degludec/liraglutide *vs.* basal-bolus therapy (glargine) in T2DM patients with an uncontrolled disease while on basal insulin. After 26 weeks of treatment, patients from the two groups presented almost the same $HbA1_c$ reduction (-1.48% with degludec/liraglutide *vs.* -1.46% with glargine); however, degludec/liraglutide was associated with fewer hypoglycemic episodes and a more significant change in body weight (-0.35 kg/m^2 *vs.* + 0.96 kg/m^2)[25].

A real-world evidence (RWE) study (EXTRA) conducted in different European diabetes centers, showed a significant reduction in $HbA1_c$ (-0.7%) and in body weight (-2.4 kg) in patients who switched from multiple daily-dose insulin injections (MDI) to degludec/liraglutide for at least 6 months[26]. These findings were further supported by a small RWE study conducted in relatively well-controlled ($HbA1_c$ baseline 7.5%) subjects with T2DM who switched from low-dose MDI to degludec/liraglutide, achieving similar or better glycemic control, benefiting from weight loss and reaching a substantial reduction in their insulin requirement[27]. Finally, a cost-minimization analysis based on data from the DUAL VII trial showed that, although degludec/liraglutide is more expensive than glargine + aspart (IGlar+IAsp), when other cost items are taken into consideration, such as needles, blood glucose self-monitoring and hypoglycemia costs, degludec/liraglutide is associated with a significant reduction in overall healthcare costs[28].

Our study aimed at supporting the promising results of DUAL VII with evidence from real practice experience on the effectiveness and safety of degludec/liraglutide in T2DM patients previously treated with basal-bolus MDI. In particular, we investigated whether degludec/liraglutide can be successfully used in clinical practice instead of MDI to achieve an adequate Hb1Ac target, increase patients' adherence to treatment thanks to a lower number of daily injections and decrease healthcare costs.

Patients and Methods

Study Design and Population

This was an observational, prospective, single-arm, cohort study conducted in a real-world setting at the Servizio di Diabetologia e Nutrizione Clinica, Ospedale Cà Foncello, Treviso, Italy. All study procedures were performed in compliance with ethical standards for human clinical trials (institutional and national) and with the Helsinki Declaration of 1964, as revised in 2013. Informed consent was obtained from all patients before they were included in the study. The study was approved by the Local Ethics Committee of Treviso.

The study enrolled patients with T2DM, >18 years, with C-peptide >1 ng/ml, who had been referred to our outpatient clinic between January 2019 and December 2019 and were switched from insulin basal-bolus schedule with or without oral antidiabetic drugs (sodium-glucose cotransporter-2 (SGLT2)-inhibitors, metformin, pioglitazone or sulfonylureas) to degludec/liraglutide therapy by their reference physician based on clinical judgement. Notably, patients enrolled in the study had been treated for at least 1 year with bolus insulin therapy due to poor glycemic control with previous hypoglycemic drugs. They were, therefore, switched to degludec/liraglutide, as this was considered the best therapeutic option given the unlikelihood of positive response with other hypoglycemic strategies.

Patients with type 1 DM, those aged >75 years, patients naïve to insulin therapies, pregnant women, patients with diabetic kidney disease and glomerular filtration rate <15 ml/min, patients with chronic heart failure (New York Heart Association class III-IV), previous or current thyroid disease and known hepatic disease were excluded. Exclusion from the study also included contraindications to degludec/liraglutide administration (personal or family history of medullary thyroid carcinoma, patients with multiple endocrine neoplasia syndrome type 2 or history of pancreatitis) or therapeutic strategies not allowed in the degludec/liraglutide summary of product characteristics[29].

Patients who were switched to degludec/liraglutide stopped their ongoing basal-bolus insulin therapy and started with 16 step units (SU) starting dose degludec/liraglutide (baseline) following to the approved national indications for prescriptions. Each patient was trained to titrate the degludec/liraglutide dose at home twice weekly in order to reach a 90-130 mg/dl fasting glycemic target (130-160 mg/dl for weak elderly patients); adjustments were made in increments of 2 SU at a time.

Variables Analyzed

The main assessment was $HbA1_c$ variation at 6 months from baseline. Secondary assessments included fasting glycemic variation, routine anthropometric measurements (BMI, body weight), changes in blood chemistry (cholesterol and triglycerides) and blood pressure, type and quantity of insulin and oral therapy taken, and occurrence of adverse events. All patients were also asked to respond to a validated Italian version of Diabetes Treatment Satisfaction Questionnaire (DTSQ)[30] at baseline and after 6 months to assess their level of satisfaction with the ongoing antidiabetic therapy schedule. We also performed a comparative subgroup analysis of patients with different characteristics to identify those who would benefit more from switching to degludec/liraglutide.

Finally, we performed a simple cost analysis to evaluate whether degludec/liraglutide therapy was competitive with the previous basal-bolus therapy in terms of costs. We only considered direct costs and patient-related costs; indirect costs were excluded. Costs accounted for in the analysis, as provided by the local pharmacy service, included the cost of various types of insulin therapy used (cost per unit administered), and glycemic self-control tools (lancing devices, strips for self-monitoring of blood glucose). We considered that insulin therapy with a basal-bolus scheme would require, on average, 3 controls/die and 4 injections/die, while degludec/liraglutide therapy would consist of 1 control/die and 1 injection/die. Furthermore, we carried out an estimate analysis of the costs for the two therapeutic options in a 6-month timeframe projection, considering the

last available data for patients before switching and after 6 months of therapy with degludec/liraglutide.

Statistical Analysis

Continuous variables are expressed as mean ± standard deviation (SD) or median and interquartile range (IQR); categorical variables are presented as frequencies (%). Continuous variables measured before and after switching therapy were compared using *t*-student test for paired data if normally distributed and Wilcoxon signed-rank test if not. Significance was set at $p<0.05$. Statistical analysis on all priorly collected and tabulated patient data was performed using SPSS (version 20.0 SPSS Inc., Armonk, NY, USA).

Results

Overall, we enrolled 45 patients (31 males and 14 females) with median age of 62 (IQR: 57-73) years and median duration of the disease of 11 (7.5-13) years (Table I). The main reasons why physicians recommended to switch from basal-bolus insulin therapy to degludec/liraglutide were patient's lack of compliance with treatment, occurrence of hypoglycemia events, high CV risk and increase in body weight due to MDI therapy.

Table I. Baseline patients' characteristics.

Characteristics	Median (IQR) or mean ± SD
N	45
Male (%)	68.9%
Age (years)	62 (57-73)
Duration of DM (years)	11 (7.5-13)
Weight (kg)	94.1 (84.3-102)
BMI (kg/m^2)	33 (30-36.8)
ACR (mg/g)	15.4 ± 23.2
Total cholesterol (mg/dl)	162 (141.5-189)
LDL (mg/dl)	83.5 (70-118.5)
HDL (mg/dl)	44 (39-49)
Triglycerides (mg/dl)	138 (99.8-191)
SBP (mmHg)	140 (130-150)
DBP (mmHg)	80 (80-90)
HbA1c (%)	8.4 (7.7-9.6)
HbA1c mean 2 previous years	8.6 ± 1.2
FPG (mg/dl)	159 (128-220)
Total daily insulin units	42 U (30-59)

ACR: albumin-to-creatinine ratio; BMI: body mass index; DBP: diastolic blood pressure; DM: diabetes mellitus; FPG: fasting plasma glucose; HbA1c: glycated hemoglobin; HDL: high-density lipoprotein; IQR: interquartile range; LDL: low-density lipoprotein; M: male; SD: standard deviation; SPB: systolic blood pressure.

After 6 months of treatment with degludec/liraglutide, we observed a significant reduction in $HbA1_c$ levels (from 8.4% [7.7-9.6] to 7.4% [6.7-8]; -0.67%; $p<0.0001$) (Figure 1) and fasting plasma glucose (FPG; from 159 mg/dl [range 128-220] to 125 mg/dl [111.5-154]; -35.3 mg/dl; $p<0.0001$) compared with baseline. The biochemical improvement was supported by a significant decrease in average weight (from 94.1 kg [84.3-102] to 93 kg [81.5-101]; -2.4±4.3 kg; $p<0.0001$; n=41) and BMI (-0.7±1.5 kg/m^2; $p=0.006$; n=41). Patients also achieved a statistically significant decrease in LDL cholesterol (-13.3±34.2 mg/dl; $p=0.002$; n=40), triglycerides (-24±65.9 mg/dl; $p=0.026$; n=39) and total cholesterol (-20.9±36.8 mg/dl; $p=0.02$; n=39) without modifying their lipid-lowering therapy. A non-significant increase in HDL was also observed (+0.38±6 mg/dl; n=39). We also noted a non-significant improvement in systolic blood pressure and diastolic blood pressure (-1.8±14.8 and -1.2±6.3, respectively; n=38), regardless of blood pressure lowering therapies, which were unchanged during the study.

The type and quantity of insulin and oral antidiabetic therapy (OAD) taken by patients prior to degludec/liraglutide are shown in Table II. Before switching to degludec/liraglutide, 46.3% of the patients only took basal-bolus insulin therapy, 48.8% took basal-bolus plus metformin and 4.9% combined basal-bolus and others, such as OAD. Metformin therapy was maintained without changes after the switch to degludec/liraglutide. Mean basal insulin (glargine, detemir, degludec/liraglutide, HI) intake was 17.1±7.84, whereas median rapid insulin (aspart, lispro, glulisine) intake was 28.1±11.9, for a total daily

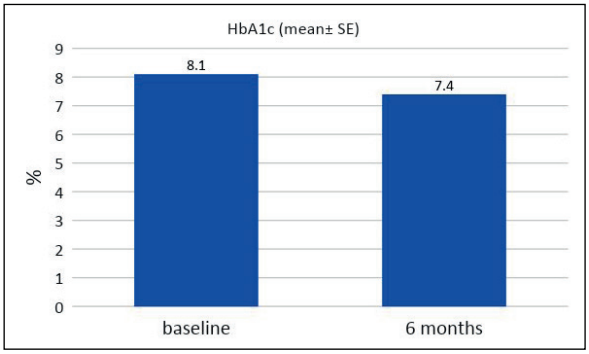

Figure 1. Variation of HbA1c from baseline to 6 months (n = 40). *$p<0.0001$.

Table II. Type and quantity of insulin therapy and OAD taken by patients before switching to degludec/liraglutide.

	Mean ± SD or %
U/die of previous basal bolus insulin therapy	17.1 ± 7.84
Type of previous basal bolus insulin therapy	Glar U-100 = 79.5% Det = 6.82% Degludec/liraglutide = 11.36% NPH = 0% Glar U-300 = 2.27%
U/die previous rapid insulin	28.1 ± 11.9
Type of previous rapid insulin	Aspart = 31.82% Lispro = 54.5% Glulisin = 13.64% HI = 0%
OAD	BB = 46.3% BB+Met = 48.8% BB+other OAD = 4.9%
Concomitant OHA at baseline	Met = 90.5% Met+SU = 2.4% Met+PIO = 2.4% No OHA = 4.8%

BB: basal bolus; Det: Detemir; Glar U-100: glargine 100 units/ml; Glar U-300: glargine 300 units/ml; Met: metformin; OAD: oral antidiabetic; OHA: oral hypoglycemic agents; PIO: pioglitazone; SU: sulfonylurea.

insulin units' intake equal to 42 UI/die (30-59). Degludec/liraglutide starting dose was 16 SU, while insulin intake at 6 months was 22 SU/die (18.5-30), thus showing a significant reduction in total insulin units compared with baseline (p<0.0001).

The DTSQ test results, which were available only for a subset of patients, also showed an important and significant increase in patient satisfaction after switching from basal bolus therapy to degludec/liraglutide, with mean score from 20.1 (14.5-26.5) to 27.6 (25-29; +7.5±5.8; p<0.0001) (Figure 2).

To identify which patients would benefit most from switching to degludec/liraglutide, we conducted a comparative analysis between 13 patients with specific characteristics (C-peptide >1 ng/ml, BMI >30 kg/m^2, total daily insulin units >40, 8-10% $HbA1_c$ at baseline) and 32 patients without such characteristics. The former group showed a higher decrease in $HbA1_c$ (-0.86±0.91% *vs.* -0.58±1.08% p=not significant), FPG (-64.29±78.81 mg/dl *vs.* -24.44±42.16 mg/dl; p=0.046), body weight (-3.95±3.73 kg *vs.* -1.62±4.64 kg; p=not significant) and systolic blood pressure, SBP (-6.15±13.09 mmHg *vs.* +2.61±11.76 mmHg; p=0.047) compared to the latter.

Similarly, patients on total insulin units >40 UI/die before switching to degludec/liraglutide showed higher decrease of $HbA1_c$ (-0.76±1.02% *vs.* -0.33±1.39%), FPG (-27.92±48.01 mg/dl *vs.* -0.86±50.07 mg/dl), body weight (-2.2±4.82 kg *vs.* -1.29±1.11 kg) and SBP (-2.39±11.86 mmHg *vs.* +5.83±3.76 mmHg) compared to those who required less than 40 UI/die of insulin.

In terms of costs, the average daily cost per patient on basal bolus therapy accounted for €3.13±0.54 (€115.74 for 37 patients), whereas the average daily costs per patient on degludec/liraglutide was €2.72±0.7 (€100.46 for 37

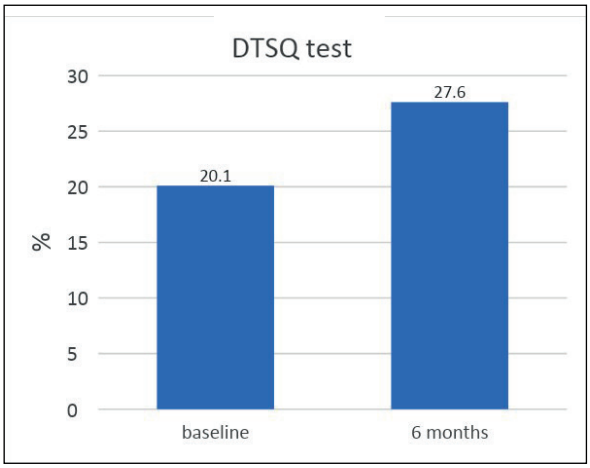

Figure 2. Variation of Diabetes Treatment Satisfaction Questionnaire score from baseline to 6 months (n=21). *p<0.0001. DTSQ: Diabetes Treatment Satisfaction Questionnaire.

patients), thus representing a significant decrease of €-0.41±0.59 (€-15.17/die for 37 patients; $p<0.001$) with degludec/liraglutide compared to basal bolus.

Estimation of total expenses in 6 months would account for €21,123.03 for basal bolus *vs.* €18,334.41 for degludec/liraglutide, with an average cost difference in favor of degludec/liraglutide of approximately €2,788 in 6 months.

Notably, the cost of OAD associated with insulin therapy were excluded from the analysis as they did not vary between baseline and the end of the study.

Discussion

According to current international diabetes guidelines, MDI therapy should be initiated in symptomatic T2DM patients with $HbA1_c$ >10% (86 mmol/mol), random blood sugar levels >300 mg/dl (16.7 mmol/l) or with hyperglycemia symptoms (i.e., polyuria and polydipsia). Guidelines also provide useful recommendations on how to escalate to injection therapy (GLP-1-RA, basal insulin, rapid insulin) based on the achievement of a target $Hb1A_c$, but do not give many indications on how to manage inappropriate therapies in basal-bolus, for example, in case of patients with strong insulin resistance[31].

Based on the encouraging results of DUAL VII trial, in this observational real-world study, we aimed at verifying whether degludec/liraglutide would be safe and effective in patients not controlled with basal-bolus therapy, reducing the number of insulin injections per day, improving their glycemic control, increasing patient's compliance and satisfaction with treatment.

Patients enrolled in our study had C-peptide values >1 ng/ml, an index of preserved b-cell function that allowed us to change their treatment from multiple insulin injections per day to one basal degludec/liraglutide injection. The positive and relatively quick results obtained both in terms of glycemic control and weight loss confirm the effectiveness and rapid action of the liraglutide/degludec fixed combination. Since $HbA1_c$ and FPG reductions were observed after a short follow-up period, it is possible that further amelioration of both parameters could be obtained during long-term treatment, and that similar results could be achieved also for weight loss and BMI reduction in the long run. Noteworthy, clinical and biochemical improvements were remarkable even on suboptimal liraglutide dose (data not shown); it is likely that a closer follow-up might allow a more effective and prompter degludec/liraglutide up-titration to liraglutide full dose. Moreover, since other concomitant antidiabetic mediations were not modified during the follow-up period, we can assume that the results observed were entirely due to degludec/liraglutide therapy.

We also observed some changes in lipids profile that were comparable with those already reported in literature[32], thus suggesting that besides its effects on glycemic control, degludec/liraglutide may be beneficial in reducing CV risk factors, as already shown in LEADER and DEVOTE trials[13,25,33]. Moreover degludec/liraglutide allowed for a reduction in insulin daily requirement, with a significant decrease in insulin total daily dose (from 42 IU/die to 22 SU/die), thus confirming its pleiotropic actions on T2DM patients[34].

The reduced number of injections (from 4 to 1) and of glucose capillary controls was associated with a higher patients' satisfaction and possibly with a greater long-term treatment adherence, as demonstrated by the significant improvement of the DTSQ score observed in our study (Figure 2).

Finally, from the safety point of view, we recorded no severe adverse events; only mild gastrointestinal side effects were self-reported by few patients, as expected (data not shown)[24].

Although hypoglycemic events were not recorded, we can speculate that the overall reduction of daily insulin units could have lowered the number of these events; in fact, despite being an efficacious glucose-lowering therapy, basal-bolus treatment is associated with a higher rate of hypoglycemia *vs.* other anti-diabetes therapies[35].

It should be noted that the reduction in $HbA1_c$ (-0.7%) observed in our study was slightly higher than that obtained in the RWE by Taybani et al[27] (-0.30%) and Melzer-Cohen et al[36] (-0.39%) and was similar to that obtained in the RWE study by Price et al[26] (-0.7%). This is probably due to the differences in study design (prospective *vs.* retrospective), inclusion/exclusion criteria, $HbA1_c$ values at baseline and dose escalation[26,27,36]. Notably the Taybani's prospective RWE study included only patients with detectable random non-fasting serum C-peptide levels ≥1.1 ng/mL, $HbA1_c$ <7.5%, and previous MDI treatment (stable daily doses of insulin ± metformin 70 IU/day) for at least 90 days prior to enrollment[27]. Conversely, our study included patients with T2DM, C-pep-

tide ≥1 ng/ml and previous basal bolus therapy who also showed sign of metabolic failure at baseline (median HbA1c levels of 8.4%).

The analysis of a subset of patients who achieved optimal results with degludec/liraglutide suggest that C-peptide levels >1.1 ng/mL, BMI >30 kg/m^2 and a high amount (>40 UI/die) of total insulin in basal-bolus are the main predictive criteria for obtaining clinically relevant results after switching to degludec/liraglutide. In particular, the concomitant presence of these features and HbA1$_c$ between 8 and 10% at baseline was associated with higher biochemical and clinical improvements, although the results did not reach statistical significance probably due to the small sample size and the number disparity between the two groups. Since degludec/liraglutide is a fixed combination of insulin degludec and liraglutide, patients taking higher doses of insulin at baseline also reached higher levels of liraglutide during the titration phase, which probably explains why patients with >40 UI/die at baseline achieved better results.

Therapy simplification positively affected both patients' satisfaction and sustainability. Data at 6 month of treatment highlighted a lower cost of degludec/liraglutide therapy compared to basal-bolus schedule in terms of medical supplies, further supporting the use of degludec/liraglutide as a valid alternative to basal bolus therapy also in terms of economics advantages, as previously reported[37,38]. Interestingly, a more comprehensive analysis of direct and indirect costs derived from the DUAL VII trial, showed that the total annual cost of degludec/liraglutide was €434 higher than basal-bolus at the dosage of 40.4 U; the two treatments had equal costs with a 34% dose reduction in degludec/liraglutide (26.7 U), while below this value degludec/liraglutide became less expensive, with approximately €215 gain at 50% dose reduction (20.2 U)[30]. Although we could not make a detailed analysis of all the costs, as some data (e.g., hypoglycemic data) were not available, we still observed that the switch to degludec/liraglutide from previous basal bolus therapy is economically competitive in terms of direct costs and in daily clinical practice.

We acknowledge some limitations of our study, such as its observational nature, the low sample size, the absence of a control group and of a treat-to-target titration process, the lack of data on the incidence of hypoglycemia, and the fact that the cost analysis does not take into account also indirect costs.

Conclusions

Our study shows the DUAL VII study data, suggesting that degludec/liraglutide may be a valid alternative to prandial bolus introduction or to an already set basal bolus regimen in clinical practice, as it helps reduce daily injections, capillary controls and body weight, thus improving patients' therapy adherence and satisfaction.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Authors' Contribution

MP: patient enrollment, data collection and drafting and revision of the article. LN, MS, MR, IN and SM: statistical data elaboration and revision of the article. AP: data interpretation and critical revision of the article. All authors read and approved the final version of the manuscript.

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