How Effective Is the Fixed-Ratio Combination of Insulin Degludec and Liraglutide (IDegLira) in Different Patient Populations, and When Should It Be Used in Clinical Practice?

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The efficacy and safety of the fixed-ratio combination of insulin degludec (degludec) and liraglutide (IDegLira) were confirmed in the DUAL clinical trial program, in which IDegLira demonstrated superior or noninferior glycemic control over comparators in addition to its low risks of hypoglycemia and weight gain. This article identifies the patient types for whom IDegLira is most appropriate by reviewing the DUAL results and subsequent post hoc analyses and presenting real-world cases in which IDegLira has been used effectively in U.S. clinical practice. In the clinic, IDegLira has been used effectively when patients wanted to avoid more complex injectable regimens, particularly those with renal insufficiency for whom treatment options are limited.

IDegLira is a novel, fixed-ratio combination of the basal degludec and the glucagon-like peptide 1 (GLP-1) receptor agonist liraglutide (1). The benefits of combining basal insulin with GLP-1 receptor agonist therapy are well described (2). Importantly, agents from these two drug classes have complementary effects on glycemic control; degludec lowers fasting plasma glucose (FPG), while liraglutide lowers FPG and reduces postprandial glucose (PPG) excursions (3–5). Furthermore, studies have demonstrated that liraglutide has cardioprotective properties (6), improves β-cell function, and restores prandial insulin response (7,8), and evidence is emerging that liraglutide could preserve β-cell function early in the type 2 diabetes disease trajectory (9).

The efficacy and safety of IDegLira in patients with type 2 diabetes were investigated in the DUAL clinical trial program, in which its use provided superior or noninferior glycemic control over comparators, with the added benefit of a lower risk of both hypoglycemia and weight gain compared with other insulin regimens (10–16). The success of this clinical program across a broad patient population has resulted in IDegLira being approved in 55 countries since 2014. In Europe, and—as of February 2019—the United States, IDegLira is indicated for use in adults with insufficiently controlled type 2 diabetes to improve glycemic control as an adjunct to diet and exercise in addition to oral antidiabetic drugs (OADs) (1,17). Current guidelines from the American Diabetes Association and the European Association for the Study of Diabetes for the management of type 2 diabetes recommend intensification to injectable therapies when OADs fail to achieve glycemic control, with GLP-1 receptor agonists being the recommended first choice in most cases (18,19). In patients with an A1C >10% or 2% above their individualized A1C target, a fixed-ratio combination product such as IDegLira may be considered as a first injectable (19).

Outcomes with real-world use of IDegLira are broadly aligned with the findings of the DUAL clinical trial program. Although real-world outcomes of IDegLira use in U.S. patients are not yet published, results from a European study showed that IDegLira treatment resulted in significant reductions in A1C, no mean gain in body weight, and a lower risk of hypoglycemia after 6 months of treatment compared with baseline regimens (20). These results are supported by a survey of primary care physicians and specialists, in which a high percentage of physicians responded that treatment with IDegLira provided greater treatment satisfaction for patients across

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several parameters, including number of injections and avoidance of weight gain when compared with basal-bolus therapy, demonstrating the potential for IDegLira treatment to tackle clinical inertia (21).

This article present cases in which IDegLira has been used effectively in U.S. clinical practice and reviews the efficacy of IDegLira in DUAL trial populations, which are relevant to the case study patients.

Methods

A focused literature review was undertaken and supplemented with studies known to the authors, together with two clinical case studies based on the authors' clinical experience with IDegLira.

Benefits of Combining Basal Insulin and GLP-1 Receptor Agonists

IDegLira combines two agents with complementary modes of action in a once-daily injection. With a half-life of ~25 hours, degludec lowers FPG, while liraglutide, with a half-life of ~13 hours, reduces FPG and PPG excursions (3,4,22). Their respective mechanisms of protraction and stability—formation of multihexamer degludec chains (23) and slowed release of liraglutide from injection site, as well as reduced elimination rate (24)—enable them to be dosed once daily. Liraglutide mimics naturally occurring GLP-1, enhancing insulin secretion and suppressing glucagon secretion in a glucose-dependent manner (25). Because the mechanism of GLP-1 receptor agonist action is glucose-dependent, combining it with degludec helps patients achieve glycemic control with a lower risk of hypoglycemia than treatment with basal insulin alone (11).

The combination of degludec and liraglutide is also a suitable treatment regimen for patients with renal insufficiency because degludec has low pharmacodynamic variability (26), and liraglutide, in contrast to other GLP-1 receptor agonists such as exenatide, is not eliminated predominantly by the kidneys but by total body degradation, which likely involves the endopeptidases dipeptidyl peptidase-4 and neutral endopeptidase (27,28). Furthermore, as a result of the weight-lowering effect of liraglutide, IDegLira is associated with weight loss or weight neutrality, as opposed to weight gain with basal insulin alone (10,14,15).

Cardiovascular outcomes trials (CVOTs) have been conducted to assess the cardiovascular safety of each of the components of IDegLira. Results from the LEADER (Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results) trial demonstrated that the rate of the first occurrence of major adverse cardiovascular events (MACE), defined as death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke, was lower with a 1.8-mg liraglutide daily dose than with placebo among patients with type 2 diabetes and high cardiovascular risk (6). Only patients receiving the maximum dose of IDegLira might expect to benefit from the cardioprotective properties of liraglutide, but a CVOT for another GLP-1 receptor agonist, semaglutide, demonstrated that cardiovascular risk reductions were similar at doses of 0.5 or 1.0 mg once weekly (29).

In the ORIGIN (Outcome Reduction with an Initial Glargine Intervention) trial, insulin glargine 100 units/mL (IGlar U100) was associated with a similar rate of incident cardiovascular outcomes as standard care (30). In the DEVOTE (Trial Comparing Cardiovascular Safety of Insulin Degludec versus Insulin Glargine in Patients with Type 2 Diabetes at High risk of Cardiovascular Events) trial, degludec at 100 units/mL once daily proved noninferior to the same dose of insulin glargine in terms of the incidence of MACE (31). Although a CVOT has not been conducted with IDegLira, results from the DUAL clinical trial program have shown that IDegLira treatment is associated with low risks of weight gain and hypoglycemia (1,10–12,14–17,32,33) and improvements in other cardiovascular risk factors such as lipid profile (34). Additionally, a subanalysis of the DEVOTE trial demonstrated that concomitant use of liraglutide 1.8 mg with basal insulin (degludec or IGlar U100) was associated with a significantly lower risk of MACE and death in patients with type 2 diabetes and high cardiovascular risk using basal insulin (35). Again, it is important to note the average dose of IDegLira in clinical practice is likely to be lower than the equivalent component doses in this subanalysis.

Overview of the DUAL Clinical Trial Program

The DUAL clinical trial program included nine studies in which IDegLira was investigated in a wide range of patients with type 2 diabetes and has shown improved efficacy over a variety of comparators. Three DUAL studies have been excluded from this review because they were not relevant to the patient cases presented here. DUAL II (11), a regulator-requested study investigating the contribution of liraglutide to IDegLira by comparing IDegLira with insulin degludec, was excluded because degludec doses were capped at 50 units, which does not

TABLE 1 Overview of the DUAL I, III, V, VII, VIII, and IX Clinical Trials of IDegLira in Patients With Type 2 Diabetes

Study	Treatment Duration (weeks)	Patients	Comparator	Change in A1C, %: ETD IDegLira – Comparator (95% CI), *P*	Confirmed Hypoglycemia: ERR IDegLira/Comparator (95% CI), *P*	Change in Body Weight, kg:ETD IDegLira – Comparator (95% CI), *P*	EOT Insulin Dose, units: ETD IDegLira – Comparator (95% CI), *P*
DUAL I (10)	26	Uncontrolled on metformin ± pioglitazone (n = 1,663)	Insulin degludec (no dose cap)	−0.47 (−0.58 to −0.36), <0.0001*	0.68 (0.53–0.87), 0.0023	−2.2 (−2.64 to −1.80), <0.0001	−14.9 (−17.14 to −12.66), <0.0001
			Liraglutide 1.8 mg	−0.64 (−0.75 to −0.53), <0.0001†	7.61 (5.17–11.21), <0.0001	2.4 (2.02–2.86), <0.0001	NA
DUAL I extension (37)	52	Uncontrolled on metformin ± pioglitazone (n = 1,311)	Insulin degludec (no dose cap)	−0.46 (−0.57 to −0.34), <0.0001	0.63 (0.50–0.79), <0.0001	−2.8 (NR), <0.0001	−23.4 (−26.4 to −20.3), <0.0001
			Liraglutide 1.8 mg	−0.65 (−0.76 to −0.53), <0.0001	8.52 (6.09– 11.93), <0.0001	2.7 (NR), <0.0001	NA
DUAL III (12)	26	Uncontrolled on GLP-1RA + metformin ± SU ± pioglitazone (n = 438)	GLP-1RA	−0.94 (−1.11 to −0.78), <0.001†	25.36 (10.6–60.5), <0.001	2.9 (2.17–3.62), <0.001	NA
DUAL V (14)	26	Uncontrolled on metformin + IGlar U100 20–50 units (n = 557)	IGlar U100	−0.59 (−0.74 to −0.45), <0.001†	0.43 (0.30–0.61), <0.001	−3.2 (-3.77 to -2.64), <0.001	−25.5 (−28.90 to −22.05), <0.001
DUAL VII (15)	26	Uncontrolled on metformin + IGlar U100 20–50 units (n = 506)	IGlar U100 + insulin aspart	−0.02 (−0.16 to 0.12), <0.0001*	0.39 (0.29–0.51), <0.0001	−3.6 (−4.2 to −2.9), <0.0001	−44.5 (−48.3 to −40.7), <0.0001
DUAL VIII (36)	104	Uncontrolled on metformin, SU, glinide, pioglitazone, or DPP-4i (n = 1,012)	IGlar U100	NA‡	0.44 (0.33–0.60), <0.0001	−1.7 (−2.47 to −0.93), <0.0001	−14.9 (−17.41 to −12.47), <0.0001
DUAL VIII, prespecified 26-week analysis (38)	26	Uncontrolled on metformin, SU, glinide, pioglitazone, or DPP-4i (n = 1,012)	IGlar U100	−0.47 (−0.58 to −0.36), <0.0001	0.56 (0.39–0.82), 0.0023	−1.6 (−2.00 to −1.13), <0.0001	−13.0 (−15.03 to −10.99), <0.0001
DUAL IX (32)	26	Uncontrolled on SGLT2i (n = 420)	IGlar U100	−0.36 (−0.50 to −0.21), <0.0001†	0.42 (0.23–0.75), 0.0035	−1.9 (−2.64 to −1.19), <0.0001	−15.4 (−19.60 to −11.13), <0.0001

*Confirmed noninferiority of IDegLira. †Confirmed superiority of IDegLira. ‡This end point was not analyzed at week 104 in DUALVIII. DPP-4i, DPP-4 inhibitor; ERR, estimated rate ratio; ETD, estimated treatment difference; GLP-1RA, GLP-1 receptor agonist; NA, not applicable; NR, not reported; OR, odds ratio; SGLT2i, SGLT2 inhibitor; SU, sulfonylurea.

accurately reflect real-world clinical practice. DUAL IV (13), a placebo-controlled trial investigating the safety and efficacy of using IDegLira in combination with sulfonylureas, was excluded because the authors recommend that sulfonylureas are discontinued on initiation of basal insulin or GLP-1 receptor agonist therapy. Finally, DUAL VI (16), a trial comparing once-weekly and twice-weekly titration algorithms for IDegLira was excluded because this was not relevant to clinical practice in the United States, where once-weekly titration is not included in the prescribing information.

This review focuses on six studies with relevance to the patient cases presented; these include DUAL I and VIII (post-OAD population), DUAL III (post–GLP-1 receptor agonist population), DUAL V and VII (post–basal insulin population), and DUAL IX (post–sodium–glucose cotransporter 2 [SGLT2] inhibitor population). DUAL I (10) investigated the efficacy and safety of IDegLira compared with that of its monocomponents in patients with type 2 diabetes previously uncontrolled on metformin with or without pioglitazone. DUAL III (12) compared the efficacy and safety of IDegLira to that of unchanged GLP-1 receptor agonist therapy. DUAL V (superiority) (14) and DUAL VII (noninferiority) (15) compared the efficacy and safety of IDegLira with that of continued IGlar U100 up-titration and basal-bolus therapy, respectively, in patients with type 2 diabetes uncontrolled on 20–50 units IGlar U100 and metformin. DUAL VIII (36) investigated the durability of IDegLira compared with IGlar U100. DUAL IX (32) assessed the safety and efficacy of IDegLira as an add-on to SGLT2 inhibitor therapy. An overview of these six studies is presented in Table 1.

These studies all had, or included, a 26-week treatment period, and the sustainability of outcomes in the DUAL I core trial were further investigated in a 26-week extension phase (DUAL I extension) (37). In the 104-week DUAL VIII durability study (which also had prespecified outcomes at week 26), the visit schedule mirrored routine clinical practice (36,38).

In the DUAL clinical trial program, the starting dose of IDegLira was 10 units (10 units insulin degludec/0.36 mg liraglutide) in patients naive to basal insulin or a GLP-1 receptor agonist and 16 units (16 units insulin degludec/0.58 mg liraglutide) in patients with diabetes uncontrolled on basal insulin or a GLP-1 receptor agonist. The maximum dose was 50 units (50 units insulin degludec/1.8 mg liraglutide) regardless of prior therapy (1). In these six studies, IDegLira doses were adjusted twice weekly, aiming for an FPG target of 4.0–5.0 mmol/L (72–90 mg/dL).

The primary end point for the majority of these trials was change in A1C from baseline after 26 weeks of treatment. (In DUAL VIII, the primary end point was time from randomization to inadequate glycemic control and need for treatment intensification, defined as an A1C ≥7.0% at two consecutive visits from week 26 [including week 26 if A1C was ≥7.0% at week 12]).

Reductions in A1C after 26 weeks of treatment were significantly greater with IDegLira compared with comparators in the DUAL III, V, VIII, and IX trials and noninferior to those seen with basal-bolus therapy in DUAL VII. In DUAL I, IDegLira resulted in greater A1C reductions than degludec or liraglutide, meeting the criteria for noninferiority to insulin degludec and superiority to liraglutide (10), and significantly greater A1C reductions with IDegLira were sustained for 52 weeks (37). In DUAL VIII, there was a significantly longer median time to treatment intensification for patients treated with IDegLira compared with IGlar U100 (over 2 years compared with 1 year, respectively), and a significantly greater proportion of patients achieved an A1C <7.0% in the IDegLira group (63%) than in the IGlar U100 group (34%) (36).

In DUAL I, V, VII and VIII, the reductions in A1C with IDegLira were achieved with the added benefits of weight loss and lower rates of hypoglycemia, whereas the comparators of basal insulin alone or basal-bolus therapy were associated with weight gain and higher rates of hypoglycemia, respectively (Table 1). These clinical benefits were achieved with overall lower insulin doses; end-of-trial (EOT) insulin doses in DUAL I (core trial), V, VII, VIII, and IX were 38, 41, 40, 37, and 36 units, respectively, with IDegLira compared with 53, 66, 84, 52, and 54 units, respectively, with insulin therapy (10,14,15,32,36). In DUAL III, IDegLira treatment resulted in higher rates of hypoglycemia and weight gain (+2.0 kg) versus weight loss (–0.8 kg) compared with GLP-1 receptor agonist treatment (12). The hypoglycemia and body weight findings from DUAL I were also more favorable in the liraglutide treatment arm compared with IDegLira (Table 1) (10,37).

Post Hoc Analyses

A number of post hoc analyses of DUAL I, III, V, and VII have demonstrated that the clinical benefits achieved with IDegLira treatment are consistent across a broad patient population. Post hoc analyses of DUAL I, III, and V showed that mean A1C was reduced to a significantly greater extent with IDegLira than with comparators across all baseline BMI categories (<30, ≥30 to <35, and

≥35 kg/m^2) in patients with diabetes previously uncontrolled on a GLP-1 receptor agonist or basal insulin (39,40). The treatment differences among baseline BMI categories were similar, demonstrating that IDegLira is efficacious irrespective of patients' BMI.

In post hoc analyses of DUAL I, III, and V, in which patients were grouped according to baseline A1C level (≤7.5, >7.5% to ≤8.5%, and >8.5%), significantly greater reductions in A1C were achieved with IDegLira than with comparators across all baseline A1C groups. Furthermore, treatment with IDegLira led to the mean A1C being reduced to <7.0% at EOT for all baseline A1C groups. Mean EOT A1C levels were 6.4, 6.4, and 6.6% with IDegLira compared with 6.9 and 7.1% with degludec and liraglutide, respectively, in DUAL I; 7.4% with unchanged GLP-1 receptor agonist therapy in DUAL III; and 7.1% with up-titrated IGlar U100 in DUAL V (33,39). This result was even observed in DUAL V, which included patients with a baseline A1C >9% (mean 9.6%) (33,39).

In DUAL V, significantly greater reductions in A1C from baseline to EOT were also seen with IDegLira compared with basal insulin, regardless of pre-trial insulin dose. These reductions in A1C were also associated with greater reductions in body weight and lower rates of hypoglycemia compared with patients receiving basal insulin (41). Importantly, this finding demonstrates that treatment with IDegLira improved glycemic control even in patients receiving ≥40–50 units of basal insulin before enrollment, despite the reduction in insulin dose to 16 units at initiation. These reductions were achieved secondary to the dose-sparing, complementary action of the two IDegLira components (42,43). For example, in DUAL V and VII, IDegLira was insulin-sparing compared with insulin comparators; IDegLira dose and change in A1C with IDegLira was stable from week 12 to EOT, whereas IGlar U100 and basal-bolus doses continued to increase with limited A1C reductions after week 16 (44).

IDegLira was also efficacious in the DUAL I–V trials in patients with different levels of renal impairment (normal, mild, or moderate with estimated glomerular filtration rates [eGFRs] of ≥90, ≥60 to <90, and ≥30 to <60 mL/min/1.73 m^2, respectively). Reductions in A1C levels from baseline to EOT were significantly greater with IDegLira compared with comparators across all baseline renal function groups (45).

Furthermore, post hoc analyses of DUAL VII confirmed that treatment with IDegLira resulted in reductions in A1C irrespective of baseline characteristics (A1C, BMI, age, diabetes duration, total daily insulin dose, and FPG) that were similar to those seen with basal-bolus therapy (46).

From Clinical Trials to Clinical Practice: Patient Case Studies

The benefits of IDegLira observed in clinical trials have also been observed in real-world patients. Two example cases are discussed below.

Case 1: Use of IDegLira in a Patient With Diabetes Uncontrolled on Basal Insulin

An 80-year-old, retired professional man returned to the clinic for follow-up, having not been seen for 10 months. He retired at the age of 80 years because of progressive spinal stenosis. Besides being diagnosed with type 2 diabetes complicated by peripheral neuropathy, at 60 years of age, he had diagnoses of hypertension and chronic kidney disease. His increased consumption of snacks between meals since retirement led him to suspect that his blood glucose levels were not as well maintained. His weight on presentation was 183 lb, and his BMI was 30.5 kg/m^2.

His diabetes was treated with 22 units of IGlar U100 and the dipeptidyl peptidase 4 (DPP-4) inhibitor linagliptin. His eGFR was maintained near 40 mL/min/1.73 m^2 (having varied from 32 to 47 mL/min/1.73 m^2 over the past 2 years with changes in diuretics), and he did not want to consider metformin therapy. He was also taking a baby aspirin, a statin, and an ACE inhibitor daily for hyperlipidemia and hypertension. He tested his fasting glucose regularly, and it averaged 140 mg/dL. A point-of-care A1C measurement was 9.6%, indicating inadequate glycemic control on his current treatment regimen.

Options for intensification of his diabetes therapy to address spikes in PPG levels were discussed, including the use of multiple-dose insulin. He was very reticent, stating "I am finally retired and do not want to spend all my time consumed by diabetes." He was also cognizant of the increased risk of hypoglycemia associated with prandial insulin and with his renal insufficiency status (47).

The use of a GLP-1 receptor agonist was discussed, and his concerns regarding risks of pancreatic cancer and pancreatitis were addressed. A GLP-1 receptor agonist that could be used in patients with renal insufficiency was chosen. The results from the DUAL VII trial with IDegLira were reviewed, showing similar efficacy in lowering A1C compared with intensification with three injections of prandial insulin added to basal insulin. The patient found the need for only one injection a day appealing.

He stopped linagliptin treatment and began IDegLira at 16 units/day (16 units degludec, 0.58 mg liraglutide). It was explained that there may be some initial

treatment-related nausea. An FPG goal of 130 mg/dL was set, and he was asked to increase his dose of IDegLira by 2 units every 3 days until this goal was attained. There was an increase in FPG when transitioning, but this increase was not clinically significant, and with titration of the IDegLira, his blood glucose improved significantly. He noted mild, tolerable nausea.

After 3 months of treatment with IDegLira, his A1C had decreased to 7.1%, and he noted FPG levels near 130 mg/dL. He had titrated his dose of IDegLira to 22 units. There had been no episodes of hypoglycemia, and the mild nausea had abated.

Case 2: Use of IDegLira to Address a Patient's Fear of Hypoglycemia

A 70-year-old man who was a legal professional came to the clinic having not been clinically assessed for 6 months. He had an 8-year history of type 2 diabetes and was concerned after noting that his FPG had risen to almost 170 mg/dL.

His medications had been carefully chosen because he did not want to risk hypoglycemia at work, particularly if lunch was delayed by a meeting. His medications included liraglutide 1.8 mg/day and an SGLT2 inhibitor at full dose. He was intolerant of metformin. His diabetes was complicated by peripheral neuropathy. He had also had a prior coronary artery bypass surgery, subsequent stents, hypertension, hyperlipidemia, and benign prostatic hyperplasia. Concomitant medications included an ACE inhibitor, a β blocker, clopidogrel, a statin, a bile acid sequestrant, and tamsulosin.

A point-of-care A1C measurement was 8.8%. Options for improving his A1C were reviewed and included adding a sulfonylurea or insulin. The patient expressed concerns about the risk of hypoglycemia with sulfonylureas or basal insulin treatment. The second-generation insulin analog degludec was discussed, particularly the results of the DEVOTE trial, which showed clear evidence of reduced hypoglycemia with degludec compared with IGlar U100, accompanied by a low risk of severe hypoglycemia. Because the patient was happy to try degludec, it was decided that IDegLira would be a suitable medication because it would require him to take only one injection per day.

Liraglutide (1.8 mg/day) was discontinued and IDegLira was initiated at 16 units once daily. His SGLT2 inhibitor was continued. An FPG goal of 130 mg/dL was chosen, and the patient was asked to titrate IDegLira by 2 units every 3 days until this goal was achieved. On return 3 months later, he was taking 34 units of IDegLira and noted an FPG within the desired range. He was pleased that there was no hypoglycemia interfering with his duties at work and that his A1C was now 7.1%.

Discussion of Case Studies

In these real-world cases, switching to IDegLira from their previous regimen provided patients with the clinical benefits of improved A1C and low rates of hypoglycemia while also addressing lifestyle factors that may have otherwise led to clinical inertia. Case 1 highlights the suitability of IDegLira for patients whose diabetes is complicated by chronic kidney disease because liraglutide remains efficacious despite renal insufficiency. For this patient, the possibility of only a once-daily injection with IDegLira made it an attractive option in light of his desire for a regimen that would allow him to enjoy his retirement without being "consumed" by the burden of multiple injections. Case 2 highlights how IDegLira can be used to address a patient's fear of hypoglycemia, which was particularly important for this patient, who has a demanding job and could not guarantee regular meal patterns.

Conclusion

IDegLira is an effective treatment intensification option for patients with type 2 diabetes for whom glucose is uncontrolled on OADs, basal insulin, or GLP-1 receptor agonist therapy. The DUAL clinical trial program and subsequent post hoc analyses have demonstrated that IDegLira is efficacious irrespective of baseline characteristics such as BMI, A1C, and renal insufficiency. As a result of the complementary effects of its components, which target different pathophysiological defects of type 2 diabetes, IDegLira helps patients achieve glycemic control and provides the additional benefits of weight loss or weight neutrality and low rates of hypoglycemia. A post hoc analysis of DUAL V and VII data demonstrated that IDegLira is associated with a general improvement in cardiovascular risk markers compared with insulin comparators, which is likely related to the beneficial effects of liraglutide (34,35).

The benefits associated with IDegLira therapy and highlighted in the DUAL clinical trial program have also been observed in clinical practice. Physicians, particularly those in primary care, often have extremely limited time to make complex treatment decisions. This review illustrates how initiating IDegLira rather than a more complex injectable therapy can benefit health care professionals in terms of time and resources and highlights some of the situations in

which IDegLira can be used effectively. In particular, this review identified patients with renal insufficiency, for whom treatment options are limited by contraindications to therapies such as combination insulin glargine/lixisenatide and SGLT2 inhibitors, as candidates for whom IDegLira therapy could be considered (5,48).

When prescribed and titrated appropriately, IDegLira has the potential to address clinical inertia and improve outcomes for patients with type 2 diabetes who might otherwise languish in poor glycemic control on basal insulin or GLP-1 receptor agonists.

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DUALITY OF INTEREST

J.T. has served as a Novo Nordisk consultant and in speakers' bureaus for AstraZeneca, Merck, and Novo Nordisk. M.E.M. has been an advisory board member for Novo Nordisk. J.S. has served on speakers' bureaus for Abbott, AstraZeneca, Boehringer Ingelheim, Janssen, Merck, Novo Nordisk, and Sanofi; is an American Diabetes Association faculty member and speaker; serves on advisory boards for Novo Nordisk and Sanofi; and has received authorship support from Novo Nordisk and Sanofi.

AUTHOR CONTRIBUTIONS

J.T. contributed to drafting and critically revising the article. M.E.M. and J.S. reviewed and critically revised the article. J.T. is the guarantor of this work and, as such, had full access to all of the studies cited and takes responsibility for the integrity of the data reported and the accuracy of the review.

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