



The Newer Ultralong-Acting Insulins



Volume 3 Issue 11

In this Issue...

The currently available ultralong-acting insulins differ from conventional long-acting insulins and their biosimilar equivalents. These newer insulins have altered pharmacodynamics and pharmacokinetics that make them as efficacious but more stable, with longer action profiles and lower rates of hypoglycemia.

In this issue, Dr. Roma Gianchandani from the University of Michigan in Ann Arbor reviews the recent data from both clinical trials and real-world settings that evaluates these newer insulins and identifies which patients might benefit from their use.

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Length of Activity

- 1.0 hour Physicians
- 1.0 hour Nurses

Launch Date

September 07, 2018

Expiration Date

September 06, 2020

LEARNING OBJECTIVES

- Compare the glycemic lowering effectiveness of newer ultralong-acting insulins to conventional basal insulins.
- Describe the hypoglycemia risk profiles of newer ultralong-acting insulins compared to conventional basal insulins.
- Describe the safety and efficacy of faster-acting insulin aspart (FIAsp).

GUEST AUTHOR OF THE MONTH

Commentary & Reviews



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Guest Faculty Disclosure

Dr. Gianchandani has indicated that she has no financial interests or relationships with a commercial entity whose products or services are relevant to the content of this presentation.

Unlabeled/Unapproved uses

Dr. Gianchandani has indicated that there will be no references to unlabeled or unapproved uses of drugs or products.

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COMMENTARY

Within the last decade, a large number of insulins and noninsulin agents (NIA) targeting varied defects in diabetes pathophysiology have been developed with the aim of getting more patients to glycemic goals. The position statement of the American Diabetes Association, the American Diabetes Association, and the European Association for the Study of Diabetes all emphasize individualized diabetes management of both medications and blood glucose (BG) goals.^{1,2} For patients with T2DM with severe hyperglycemia, deterioration of beta cell function and/or intolerance to NIAs, insulin is the recommended agent. For type 1 diabetes (T1DM), insulin remains the mainstay of therapy, either as basal-bolus therapy or continuous subcutaneous infusion. Therefore, basal insulins are widely used and are used at different stages of diabetes management: alone, in combination with NIAs, as part of a multidose insulin regimen, or as premixed preparations.

Until mid-2015, NPH, glargine, and detemir were the three available basal insulins. NPH, the oldest of the basal insulins, has a duration of action of about 12 hours, with a significant peak and trough. The long-acting insulin analogs, glargine and detemir, last 22 hours with a maximum of 24 hours. Although an improvement over NPH, they have significant daily variability, require large injection volumes in insulin-resistant patients, and are expensive. Despite their higher cost and substantial price increases in recent years, they have been increasingly prescribed over NPH in the last two decades, especially since there is a greater risk of hypoglycemia with NPH when treating patients to tight BG targets.³⁻⁵ Unfortunately, in real-life even mild hypoglycemia as seen in the clinical trials limits patient compliance and insulin up-titration by patients and providers, resulting in worse glycemic control and higher incidence of diabetes complications. Hypoglycemia occurs frequently in those with multiple comorbidities, including severe renal insufficiency and cardiovascular disease and is independently linked to patient morbidity and mortality, increased health care utilization, and cost.

To minimize hypoglycemia risk while providing effective glycemic control, the pursuit for

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more physiological insulins has continued, with development of glargine-300 and degludec-100 and -200 (glar-300, deg-100, and deg-200). These ultralong-acting insulins have been bioengineered to address shortcomings of conventional basal insulins. Glar-300 has a duration of action of more than 36 hours, while both formulations of degludec (deg-100 and deg-200) last 48 hours. In several studies, these ultralong-acting insulins have been shown to have lower rates of hypoglycemia (especially nocturnal hypoglycemia) and less daily variability. They are available in more concentrated forms than glargine and detemir (three times for glar-300 and two times for deg-200), so smaller volumes can be injected and prevent insulin lipodystrophy. A recent meta-analysis of all basal insulin analogs, including the newer ultralong-acting insulins, showed no significant differences in their glucose-lowering effect, but a lower risk of nocturnal hypoglycemia with glargine-300 and degludec-100 and -200.⁶

In this issue, we review several key studies regarding the effectiveness and safety of the ultralong-acting insulins. The first two papers are meta-analyses of studies that compare glargine-300 and degludec-100 and -200 to glargine U-100/detemir or NPH. Since insulins are used in a variety of diabetes patients, meta-analyses were selected to provide the reader robust and widely applicable data across several patient groups with varied management.

Post-marketing experiences also add to clinical trial experience. The (reviewed) article by Wei Liu et al explores whether there is any cost-effectiveness of using the ultralong-acting insulins in real-life clinical settings.

With long-acting insulins, we have never had the convenience of a fixed-dose combination. Degludec allows for this possibility, as it can be combined with a rapid-acting insulin. A degludec formulation has been approved as a combination with aspart. The paper by Kalra et al (reviewed herein) evaluates studies and potential uses of this fixed dose combination in a multinational consensus statement.

Finally, for glargine-300 and degludec, data comparing the two insulins in head-to-head clinical trials is just emerging. The first clinical trial currently available in manuscript form by Kawaguchi et al provides comparative data and potential reasons for differences in glycemic profiles with these two insulins. Abstracts comparing these two ultralong-acting insulins are actively being presented at scientific meetings and their publications are underway.

The last paper by Russel-Jones et al discusses a fast-acting insulin aspart formulation now available for use as part of a basal bolus regimen. With the studies discussed in this newsletter, we have tried to empower clinicians to decide when and how these newer insulins may be reasonable choices for their patients. Overall, these newer formulations have been shown to be noninferior to older insulins for glycemic control with a better safety profile. However, these newer agents are expensive, and more studies evaluating their cost-effectiveness are needed. Meanwhile, their ability to provide safe and effective glucose control in several groups of diabetes patients at different stages of disease is a useful addition to the diabetes management toolbox.

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1. American Diabetes Association. [Pharmacologic approaches to glycemic treatment: standards of medical care in diabetes—2018](#). *Diabetes Care*. 2018 Jan;41(Suppl 1):S73-S85.
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3. Bazzano LA, Lee LJ, Shi L, Reynolds K, Jackson JA, Fonseca V. [Safety and efficacy of glargine compared with NPH insulin for the treatment of Type 2 diabetes: a meta-analysis of randomized controlled trials](#). *Diabet Med*. 2008 Aug; 25(8):924-932.
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5. Lipska KJ, Parker MM, Moffet HH, Huang ES, Karter AJ. [Association of initiation of basal insulin analogs vs neutral protamine hagedorn insulin with hypoglycemia-related emergency department visits or hospital admissions and with glycemic control in patients with type 2 diabetes](#). *JAMA*. 2018;320(1):53–62.
6. Madenidou A, Paschos P, Karagiannis T, et al. [Comparative benefits and harms of basal insulin analogues for type 2 diabetes: A systematic review and network meta-analysis](#). *Ann Intern Med*. 2018 Aug 7;169(3):165-174.

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Glar-300 vs Glar-100 in Different Subsets of Patients with T2DM

Ritzel R, Roussel R, Bolli GB, et al. Patient-level meta-analysis of the EDITION 1, 2 and 3 studies: Glycaemic control and hypoglycaemia with new insulin glargine 300 U/ml versus glargine 100 U/ml in people with type 2 diabetes. *Diabetes Obes Metab.* 17: 859–867, 2015.

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The greatest limiting factors in insulin treatment are hypoglycemia and the suboptimal duration of long-acting insulins (< 24 hours). Glargine 300 (glar-300) is an ultralong-acting concentrated formulation of glargine in which 1 ml of insulin contains 300 units of glargine (300 units/ml) instead of 100 units (100 units/ml). Therefore, a smaller, subcutaneously injected volume of insulin is needed to achieve the same total amount of insulin intake. In addition, this higher concentration of insulin alters its pharmacokinetics and pharmacodynamics, increasing the duration of action to 36 hours when compared to glargine U-100 (glar-100).

Data from three trials (EDITION 1,2,3) is combined in this meta-analysis of glar-300 and represents patients at different stages of their disease state, from insulin-naïve to complex basal-bolus therapy. The combined data are complementary and increase the validity of EDITION results, which can then be applied to a varied population of patients with type 2 diabetes (T2DM). Since all three studies were multicenter, randomized, and open label clinical trials with similar endpoints and safety outcomes, this meta-analysis is robust. EDITION 1 evaluated patients with T2DM uncontrolled on basal-bolus insulin of over 42 units/day insulin. EDITION 2 evaluated patients on basal insulin greater than 42 units/day over four weeks. EDITION 3 evaluated patients on six months of oral agents. Data were pooled for 1247 patients on glar-300 and 1239 patients on glar-100. Glar-300 was as effective as glar-100 in reducing HbA1c at six months (-1.02% HbA1c reduction), as was the percentage of patients reaching goal A1c (37.2% on glar-300 vs 35.5% on glar-100) and reduction in fasting plasma glucose (FPG) (36 mg/dL, -40 mg/dL).

Hypoglycemia was significantly lower with glar-300, with a 14% rate reduction in annualized rates of confirmed or severe hypoglycemia at any time of the day (17.73 to 15.22 episodes/patient/year; P = .0116) and a 31% reduction in nocturnal hypoglycemia rates (from 3.06 to 2.1 episodes/patient/year). Lower rates of hypoglycemia were evident very early in the studies, even as insulin doses were being up-titrated to reach glucose goals. Weight gain was slightly lower in glar-300 (0.51 vs 0.79 kg). Adverse events, which were not attributed to study drug, were similar between groups, as was death.

Glar-300 was also evaluated in patients with T1DM in EDITION 4, which showed similar glycaemic control, with lower nocturnal hypoglycemia early in the trial.¹

Thus, an anticipated benefit of using glar-300 is that it is as effective as glar-100 and has a lower hypoglycemia risk, which may make insulin initiation smoother in insulin-naïve patients and intensification easier in patients trying to reach goal BG. As hypoglycemia is a feared limiting factor for insulin adjustment for patients and providers, this benefit should increase compliance and the ability to reach goal HbA1c more effectively.

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1. Home PD, Bergenstal RM, Bolli GB, et al. [New insulin glargine 300 units/ml versus glargine 100 units/ml in people with type 1 diabetes: a randomized, phase 3a, open-label clinical trial \(EDITION 4\)](#). *Diabetes Care.* 2015 Dec;38(12):2217-2225.

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Insulin Degludec vs Glar-100 Among Varied Patient Populations

Wei Liu, Xiaojie Yang, Jing Huang. Efficacy and safety of insulin degludec versus insulin glargine: A systematic review and meta-analysis of fifteen clinical trials. *Int J Endocrinol.* 2018 Mar 12;2018:8726046.

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Degludec is the longest-acting insulin currently available in the market. Its altered pharmacokinetics are based on the addition of phenol and zinc to the formulation, which allows insulin molecules to remain as dihexamers bonded together by zinc. After subcutaneous injection, phenol diffuses out and the dihexamers join to form an insoluble depot of multihexamer chains. Zinc, which binds the multihexamers, then slowly diffuses out from each end of the chain, releasing degludec monomers into the circulation. Insulin degludec thus has a prolonged, flat action profile and a stable glucose lowering effect, which has been shown to have lower patient variability and day-to-day variability than glar-100.

In this meta-analysis, 15 randomized controlled studies were selected to compare the effectiveness and safety of insulin degludec and glar-100 in varied patient populations. Both type 1 diabetes (T1DM) (N = 5) and type 2 diabetes (T2DM) (N = 10) trials were evaluated. To be included in the meta-analysis, all studies had to be multicenter, high-quality randomized controlled trials, at least 12 weeks long, with patients injecting basal insulin daily. Data from a total of 16,328 patients were analyzed.

HbA1c reduction as a measure of glycemic efficacy was similar with degludec and glargine. The proportion of patients who reached a HbA1c goal of less than 7% was also similar (46% in the degludec group and 47% in the glargine group). Therefore, glycemic efficacy of insulin degludec was found to be noninferior compared to glargine.

Rates and episodes of overall hypoglycemia were reported differently among the studies. The overall rates of hypoglycemia were significantly lower with degludec in the patients with T2DM but not in the T1DM studies. Nocturnal hypoglycemia, though, was consistently lower in the degludec group for both patients with T1DM and T2DM ($P < .01$). Weight changes were similar between groups and were consistent in patients with T1DM or T2DM. Other adverse events did not differ in incidence between the two insulins.

This systematic review and meta-analysis found that ultralong-acting insulin degludec is as effective as conventional long-acting insulins in patients with T1DM and T2DM and reduces fasting plasma glucose levels comparably to glargine. With respect to safety, the incidence of hypoglycemia is generally lower with degludec than with glargine. Some studies have suggested that this reduction in hypoglycemia improves mental wellbeing and state.¹ As improved hypoglycemia rates were not attained by compromising glucose control, insulin degludec is both a safe and effective option for basal insulin therapy and may be considered in patients with a history of hypoglycemia or at high risk for hypoglycemia on conventional basal insulin therapy.

References:

1. Freemantle N, Meneghini L, Christensen T, Wolden ML, Jendle J, Ratner R. [Insulin degludec improves health-related quality of life \(SF-36®\) compared with insulin glargine in people with Type 2 diabetes starting on basal insulin: a meta-analysis of phase 3a trials.](#) *Diabet Med.* 2013 Feb;30(2):226-232.

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Can Ultralong-Acting Glar-300 Reduce Health Care Cost?

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Zhou FL, Ye F, Berhanu P, et al. Real-world evidence concerning clinical and economic outcomes of switching to insulin glargine 300 units/mL vs other basal insulins in patients with type 2 diabetes using basal insulin. *Diabetes Obes Metab*. 2018 May;20(5):1293-1297.

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Patients who are uncontrolled on noninsulin agents (NIAs) and cannot reach their HbA1c goal are usually placed on basal or basal bolus insulin as the next step in the treatment paradigm. In recent years, the costs of insulin have increased exponentially, so the patient's financial situation must also be taken into account when selecting antihyperglycemic therapy. In addition, severe hypoglycemic episodes can impact health care resource utilization (HCRU), and that cost can surpass the price of insulin itself. Therefore, developing predictable insulins that provide adequate control of hyperglycemia while reducing the risk of hypoglycemia is an area of active research.

In clinical trials, ultralong-acting analogs have been shown to reduce the risk of hypoglycemia, especially nocturnal hypoglycemia. Real world experience provides supplementary information revealing advantages and adverse events not recognized until the postmarketing stage.

In this 2018 paper, a comparative cost efficacy of ultralong-acting insulins was evaluated from a predictive health intelligence environment (PHIE) database. Subjects who were on basal insulin between March 2015 and May 2016 (when U-300 glargine was made available in US) had to have switched basal insulin during this timeframe. The switch date was considered the index date. HbA1c measurements from six months before and three and six months after the index date were compared between groups.

EMR data from 39 health delivery networks identified patients with T2DM who switched from glar-100 or detemir to glar-300 or "another insulin" (detemir, glar-100 or degludec). Patients were matched for baseline demographics by propensity score matching. HbA1c, hypoglycemia, and hyperglycemia related HCRU of outpatient follow-up visits, ED visits, and admissions were identified and their costs analyzed in 1819 patients in each matched group.

HbA1c decreased similarly between both groups from 8.9% to 8.4%. The proportion of patients who reached a HbA1c of < 7 % was similar (16% vs 18%) and < 8% (44%). Hypoglycemia rates were 19% lower in patients who switched to glar-300 (-0.15 events/patient/year [PPPY]) with 32% fewer hypoglycemia-related patient hospitalizations, and ED and outpatient visits ($P = .037, .007, \text{ and } .011$, respectively), which lowered overall HCRU and costs by \$1,439 PPPY. Regrettably, the prices of insulin preparations were not figured into the cost equations.

These real-world data seem to align with findings from randomized controlled trials and support improved safety with glar-300. Switching to an ultra-long-acting insulin reduced hypoglycemia without impacting or compromising glucose control and reduced HCRU and costs. It should be noted, however, that many patients in this real-world study had HbA1C levels that remained above 8%, which may be expected considering that outcomes were evaluated within six months after the insulin switch. It is therefore possible that more aggressive HbA1C lowering could have increased hypoglycemia rates overall and reduced differences in the incidence of hypoglycemia seen with glar-300 compared to other insulin types. Nonetheless, the findings from this real-world study seem to suggest the possibility of lower health care expenditures resulting from hypoglycemia with glar-300. Further studies that also take into account the price of the insulin formulation itself are needed for a complete cost-effectiveness analysis. Information about overall cost-effectiveness would be useful to providers, patients, payers, and health care systems.

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First Ultralong-Acting Mixed Insulin: Degludec and Aspart (70/30)

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Mixed insulins, which contain a short- or rapid-acting component and an intermediate-acting component have been in use for decades in patients with T2DM to help simplify insulin regimens. Long-acting insulins, glargine and detemir, are unstable when combined with short- or rapid-acting insulins; thus, no mixed insulins are available that contain these combinations.

On the other hand, the ultralong-acting insulin degludec maintains biological stability when combined with the rapid-acting insulin aspart. A 70/30 combination of insulin degludec and aspart has been developed (IDegAsp) that provides both basal insulin coverage from the ultralong-acting insulin component and prandial insulin coverage from the rapid-acting insulin constituent.

Several studies have evaluated the use of DegAsp in patients with both T1DM and T2DM. This consensus paper evaluates several of these studies to guide practitioners on how and in whom to best use this combination insulin. Although approved by the US Food and Drug Administration (FDA), IDegAsp is not yet available in the US but is currently being used clinically in many countries in Europe, Asia, and Africa.

As a mixed insulin, IDegAsp must be injected with a meal to cover postprandial glucose excursions. Suggested usage in this consensus include:

1. In insulin-naïve patients with uncontrolled T2DM on noninsulin agents, the combination can be used as the first insulin for regimen intensification. The injection frequency of once or twice daily would depend on meal patterns, daily glucose profiles, severity of hyperglycemia, and risk for hypoglycemia.
2. For uncontrolled T2DM on basal insulin. Given with the biggest meal of the day as basal plus therapy, the advantage of IDegAsp is that it can be given with a different meal every day as long as injection times are eight hours apart. If lunch is the biggest meal of day today and dinner is largest the next day, it can be safely used at those separate times with adequate basal coverage in between.
3. As a classic biphasic insulin for T2DM management. When used with breakfast and dinner, the combination provides similar A1c control with less hypoglycemia than with other biphasic insulins.
4. Multidose basal bolus regimen. The combination can be one component providing basal insulin and one meal dose of aspart. Other meals can be covered with rapid-acting insulin separately. This regimen can be used in both T1DM and T2DM, and patients may be able to reduce the number of injections. When compared to a basal bolus regimen with detemir plus mealtime aspart, the HbA1c reduction was noninferior, and nocturnal hypoglycemia was reduced by 37%. Total daily insulin dose was also lower by 13%.

The combination IDegAsp is a step toward convenience and reduced injections. It can improve compliance and probably quality of life. In all the comparator studies, IDegAsp showed similar HbA1c but greater FPG reductions. Despite having a rapid-acting insulin component, hypoglycemia rates, especially nocturnal hypoglycemia, were significantly lower with IDegAsp than with BiAsp 30 (biphasic insulin aspart 30/70) formulations. Weight changes were not different between groups.

The consensus specifically identified patient groups for whom IDegAsp would be an ideal insulin type. These include shift workers with erratic meal patterns, people fasting during Ramadan, patients with renal and hepatic impairment, elderly patients, and those with comorbidities where tight control is not desired.

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Glargine U-300 vs Degludec Using CGM

Kawaguchi Y, Sawa J, Sakuma N, Kumeda Y. Efficacy and safety of insulin glargine 300 u/mL versus insulin degludec in patients with type 2 diabetes: A randomized, open-label, crossover study using continuous glucose monitoring profiles. *J Diabetes Investig*. 2018 Jun 26.

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Although several studies compare ultralong-acting insulins glar-300 and degludec to either older insulins (glargine U-100, detemir, or NPH), comparative data between the two ultralong-acting insulins has been lacking. Studies are underway and some are available as abstracts.

This paper presents results of one of the first head-to-head, randomized controlled trials of glar-300 and deg-100. The study enrolled 30 patients with T2DM on varied diabetes regimens (from insulin naive to basal bolus therapy) in a crossover design. Half the group was started on glar-300 and the other half on deg-100. Preenrollment antihyperglycemic regimens included oral agents, biphasic, basal, or basal bolus insulin. Doses of the either the deg-100 or gla-300 were optimized in a 10-day titration period to a moderate goal preprandial blood glucose of 100 mg/dL-130 mg/dL, with the same dose being continued after the insulins were switched.

Patients who achieved three days of stable blood glucose on the first insulin underwent blinded CGM monitoring for five days. They then switched their ultralong-acting insulin. When stability was reestablished with BG checks, a second round of CGM monitoring for five days followed.

The investigators found that the mean percentage of time in target BG range of 70 mg/dL-180 mg/dL was similar between both insulins. Although not statistically significant, patients had slightly lower mean preprandial and overnight BG levels on deg-100. As for safety outcomes, the mean percentage of time with hypoglycemia, defined as BG < 70 mg/dL (1.3% vs 5.5%; $P = .002$) and severe hypoglycemia, defined as a BG < 54 mg/dL (0.04% vs 1.8%; $P = .003$) and nocturnal hypoglycemia (1.1% vs. 4.2%; $P = .009$) were lower with glar-300 than deg, respectively. There was no difference in hypoglycemia among patients whether on basal-bolus insulin or basal insulin plus oral agents. Serum albumin levels were negatively correlated with mean percentage of time with hypoglycemia.

The greatest strength of this study was the use of a blinded continuous glucose monitoring (CGM) system able to identify hypoglycemic episodes not experienced by the patients. It also provided data to calculate 24-hour mean percentage of time in different BG ranges and parameters of variability. Another unique aspect of this study was that it correlated hypoglycemia with albumin status.

Other head-to-head trials of glar-300 and deg should be available for review shortly.

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Uptake and Peak of Fast-Acting Insulin Aspart

Russell-Jones D, Bode BW, De Block C, et al. Fast-acting insulin aspart improves glycemic control in basal-bolus treatment for type 1 diabetes: Results of a 26-week multicenter, active-controlled, treat-to-target, randomized, parallel-group trial (Onset 1). *Diabetes Care*. 2017 Jul;40(7):943-950.

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Rapid-acting insulin analogs — aspart (IAsp), lispro, apidra — are prandial and correction insulins. These insulins are altered by amino acid substitutions that prevent self-association of monomers. For aspart, the amino acid 28 of the beta chain (proline), is replaced by aspartic acid. These aspart hexamers dissociate rapidly to monomers when injected subcutaneously, which makes it more physiologic than regular insulin. Aspart still has a lag time for absorption, which can influence its effectiveness in relation to carbohydrate consumption.

To overcome this lag, a faster-acting aspart has been developed which combines aspart with niacinamide (vitamin B3) to increase its rate of absorption and with L-arginine to act as a stabilizing agent. Faster aspart molecules are biologically identical in function to IAsp. Combining data from several studies, this faster-acting aspart (FIAsp) has an onset of action about five minutes earlier (four vs nine minutes) than conventional aspart (IAsp).

This paper studied the efficacy of mealtime faster aspart (FIAsp) vs IAsp (0-2 minutes before a meal) in 1143 adults with T1DM. Basal detemir dose was optimized during an eight-week run-in period for all groups. The primary outcome was HbA1c at 26 weeks and the effect on postprandial (PP) hyperglycemia. A separate open label trial compared IAsp to faster aspart given after a meal (20 minutes after starting the meal).

There was a modest but significant improvement in HbA1c ($P = .0003$) with mealtime FIAsp vs IAsp at 26 weeks (HbA1c 7.3% vs 7.4%, respectively) and the chance of attaining an HbA1c of $< 7\%$ was higher with mealtime FIAsp than with IAsp or post-meal FIAsp. Comparatively, PP glucose excursions were significantly lower with mealtime FIAsp at one hour (21 mg/dl lower, $P < .0001$) and two hours (12 mg/dL lower, $P = .0375$). When given after a meal, FIAsp was noninferior in HbA1c maintenance but did not affect PP excursions significantly compared to IAsp.

Hypoglycemia rates, including severe and confirmed hypoglycemic events, were not significantly different between groups although the timing varied with higher number of events within one hour of eating for FIAsp. FIAsp performed well even if given after a meal, offering a flexible dosing option without disrupting glucose control. This is important, as patients often forget to take their mealtime insulin and may have unpredictable meal times or altered carbohydrate absorption (eg, postsurgical states and gastroparesis).

Data from trials of patients with T2DM and FIAsp show results similar to those in this study of T1DM patients, although rates of hypoglycemia are lower in T2DM studies (as expected).¹

As postprandial hyperglycemia contributes significantly to overall glucose control, it often limits some patients from reaching their glycemic targets. FIAsp can be of assistance in these select patients.

FIAsp was approved for use in September 2017, indicated to improve glycemic control in adults with type 1 and type 2 diabetes. This insulin is sold in a prefilled pen and in vials. It has yet not been approved for use in insulin pumps.

References:

1. Bowering K, Case C, Harvey J, et al. [Faster aspart versus insulin aspart as part of a basal-bolus regimen in inadequately controlled type 2 diabetes: The Onset 2 Trial](#). *Diabetes Care*. 2017 Jul;40(7):951-957.

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KEY TAKEAWAYS

- Ultralong-acting basal insulin analogs effectively improve glycemic control and are noninferior to long-acting insulins.
- In several clinical trials and meta-analyses, these insulins have been shown to reduce hypoglycemia, especially nocturnal hypoglycemia.
- The combination of an ultralong-acting insulin and a rapid-acting insulin in a single fixed-dose formulation may be an easy step in both therapy initiation and intensification.
- Compared to standard insulin aspart, faster insulin aspart provides similar safety and efficacy, with the benefit of a more flexible dosing option.

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