



Lilly's ultra rapid lispro provided similar A1C reductions compared to Humalog® (insulin lispro), with superior post-meal blood glucose reductions

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Pivotal phase 3 data in people with type 1 and type 2 diabetes presented at the American Diabetes Association's® 79th Scientific Sessions®

INDIANAPOLIS, June 9, 2019 /PRNewswire/ -- Two phase 3 studies show that Eli Lilly and Company's (NYSE: LLY) ultra rapid lispro (URLi) provided non-inferior A1C reductions compared to Humalog® (insulin lispro) at 26 weeks in people with type 1 and type 2 diabetes. The data from these treat-to-target studies showed URLi also significantly reduced the rise in blood glucose one hour and two hours after a test meal compared to Humalog.^{1,2} Additional data from the study in people with type 1 diabetes demonstrated URLi significantly improved glucose time in range during the day.³ URLi is an investigational novel mealtime insulin formulation being developed to better manage blood glucose levels. These data and several other studies were presented at the American Diabetes Association's® 79th Scientific Sessions®.

The two phase 3 studies, PRONTO-T1D and PRONTO-T2D, evaluated the safety and efficacy of URLi compared to Humalog in adults with type 1 and type 2 diabetes, respectively. Both studies met the primary endpoint of non-inferior A1C reduction from baseline compared to Humalog at 26 weeks, when the insulins were dosed at mealtime. Further, URLi demonstrated superior reduction in blood glucose spikes at both one hour (-27.9 mg/dL [T1D], -11.8 mg/dL [T2D]) and two hours (-31.2 mg/dL [T1D] and -17.4 mg/dL [T2D]) after a test meal compared to Humalog.^{1,2}

Hypoglycemia is the most common adverse reaction associated with insulin. The studies showed no significant difference in severe, nocturnal or overall hypoglycemia rates reported by study participants.^{1,2}

"Many people taking mealtime insulin are not meeting their A1C goals while also experiencing high blood glucose levels after eating. This may create worry about their ability to achieve good control," said Bruce Bode, MD, FACE, diabetes specialist at Atlanta Diabetes Associates.⁴ "The results from these two studies suggest that URLi may help control blood glucose after meals, as well as help people reach A1C goals."

The PRONTO studies were designed as treat-to-target, which enables clinicians to determine differences in other important treatment effects – such as rates of hypoglycemia, post-meal glucose control and glucose time in range – at the same level of glycemic control. A sub-set of participants in PRONTO-T1D were evaluated using blinded continuous glucose monitoring to provide more complete information on daily blood glucose patterns. At 26 weeks, URLi demonstrated a significantly better blood glucose profile up to four hours after breakfast compared to Humalog. The study further showed that URLi had significantly longer (+43.6 minutes) time in range (71-180 mg/dL) during the day and similar time in range during the night compared to Humalog.³

Data from a phase 1 clinical pharmacology study in people with type 1 diabetes also demonstrated URLi's effect on post-meal blood glucose control. Results showed URLi was absorbed significantly faster into the blood stream compared to Humalog, insulin aspart and fast-acting insulin aspart. URLi also showed lower blood glucose spikes after a test meal compared to the insulins tested, which was significant compared to Humalog and insulin aspart. Additionally, the early blood glucose profile with URLi closely matched that of participants without diabetes.⁵

"We're developing URLi to provide a mealtime insulin option that more closely mirrors the way insulin works in people without diabetes," said Tom Hardy, MD, PhD, senior medical director at Lilly. "If approved, URLi will offer a new mealtime insulin option that, in clinical trials, showed similar A1C reductions to Humalog with significant improvements in post-meal blood glucose after a test meal."

Lilly submitted applications for URLi with regulatory authorities in Europe and Japan and plans to submit in the U.S. later this year.

About the PRONTO Studies

PRONTO-T1D and PRONTO-T2D were randomized, double-blind, controlled, treat-to-target comparisons of ultra rapid lispro (URLi) and Humalog (insulin lispro), both in combination with either insulin glargine or insulin degludec in adults with type 1 and type 2 diabetes, respectively. The primary objective of each study, conducted in 1,222 and 673 participants, respectively, was to evaluate whether URLi is non-inferior to Humalog in reducing A1C from baseline after 26 weeks of treatment. Key endpoints were adjusted for multiple testing, including the comparisons of one and two hour post-prandial glucose and A1C superiority.

Important Safety Information for Humalog

What is the most important information I should know about Humalog?

- **Do not share your Humalog KwikPen, Humalog Junior KwikPen, cartridges, reusable pen compatible with Lilly 3 mL cartridges, or syringes with other people, even if the needle has been changed. You may give other people a serious infection or get a serious infection from them.**
- Do not change the insulin you use without talking to your healthcare provider. Changes may make you more likely to

experience low or high blood glucose. Changes should be made cautiously under the supervision of your healthcare provider.

- Test your blood glucose levels as your healthcare provider instructs.
- Your insulin dose may need to change because of illness, stress, other medicines you take, change in diet, or change in physical activity or exercise.
- When used in a pump, do not mix or dilute Humalog with any other insulin or liquid.

Who should not take Humalog?

- Do not take Humalog if your blood glucose is too low (hypoglycemia) or if you are allergic to insulin lispro or any of the ingredients in Humalog.

Before using Humalog, what should I tell my healthcare providers?

- About all of your medical conditions, including liver, kidney, or heart failure or other heart problems.
- If you are pregnant, planning to become pregnant, or are breastfeeding.
- About all the medicines you take, including prescription (especially ones commonly called TZDs [thiazolidinediones]) and nonprescription medicines, vitamins, and herbal supplements.

How should I use Humalog?

- Humalog is a rapid-acting insulin. Take Humalog within fifteen minutes before eating or right after eating a meal.
- Always make sure you receive the correct type of Humalog from the pharmacy.
- Do not use Humalog if it is cloudy, colored, or has solid particles or clumps in it.
- Inject Humalog under your skin (subcutaneously). Never inject into a vein or muscle. Change (rotate) your injection site with each dose. Make sure you inject the correct insulin and dose.
- Do not re-use needles. Always use a new needle for each injection. Re-use of needles can cause you to receive the wrong dose of Humalog and result in infection.
- Do not drive or operate heavy machinery until you know how Humalog affects you. Do not use alcohol while using Humalog.

What are the possible side effects of Humalog?

- Severe low blood glucose can cause unconsciousness (passing out), seizures, and death. Low blood glucose is the most common side effect. There are many causes of low blood glucose, including taking too much Humalog. It is important to treat it quickly. You can treat mild to moderate low blood glucose by drinking or eating a quick source of glucose right away. Symptoms may be different for each person. Be sure to talk to your healthcare provider about low blood glucose symptoms and treatment.
- Severe life-threatening allergic reactions (whole-body reactions) can happen. Get medical help right away if you develop a rash over your whole body, have trouble breathing, have a fast heartbeat, or are sweating.
- Humalog can cause life-threatening low potassium in your blood (hypokalemia), which can cause severe breathing problems, irregular heartbeat, and death.
- Serious side effects can include swelling of your hands and feet and heart failure when taking certain pills called thiazolidinediones or "TZDs" with Humalog. This may occur in some people even if they have not had heart problems before. Tell your healthcare provider if you have shortness of breath, swelling of your ankles or feet, or sudden weight gain, which may be symptoms of heart failure. Your healthcare provider may need to adjust or stop your treatment with TZDs or Humalog.
- Failure of your insulin pump or infusion set or degradation of the insulin in the pump can cause hyperglycemia and ketoacidosis. Always carry an alternate form of insulin administration in case of pump failure.
- The most common side effects of Humalog include low blood glucose, allergic reactions, including reactions at your injection site, skin thickening or pits at the injection site (lipodystrophy), itching, and rash. These are not all of the possible side effects. Ask your healthcare provider for more information or for medical advice about side effects.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Humalog is available by prescription only.

For additional information, talk to your healthcare providers and please [click to access](#) Full Prescribing Information and Patient Prescribing Information.

Please see Instructions for Use included with the Humalog KwikPen.

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About Diabetes

Approximately 30 million Americans⁶ and an estimated 425 million adults worldwide have diabetes.⁷ Type 2 diabetes is the most common type internationally, accounting for an estimated 90 to 95 percent of all diabetes cases in the United States alone.⁶ Diabetes is a chronic disease that occurs when the body does not properly produce or use the hormone insulin.

About Lilly Diabetes

Lilly has been a global leader in diabetes care since 1923, when we introduced the world's first commercial insulin. Today we are building upon this heritage by working to meet the diverse needs of people with diabetes and those who care for them. Through research, collaboration and quality manufacturing we strive to make life better for people affected by diabetes. We offer a wide range of therapies and a continued determination to provide real solutions—from medicines and technologies to support programs and more. For the latest updates, visit <http://www.lillydiabetes.com/> or follow us on Twitter: [@LillyDiabetes](https://twitter.com/LillyDiabetes) and Facebook: [LillyDiabetesUS](https://www.facebook.com/LillyDiabetesUS).

About Eli Lilly and Company

Lilly is a global healthcare leader that unites caring with discovery to make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at www.lilly.com and www.lilly.com/newsroom/social-channels. P-LLY

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Ultra Rapid Lispro as a treatment of type 1 and type 2 diabetes, and Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. Among other things, there can be no guarantee that future study results will be consistent with study findings to date, that Ultra Rapid Lispro will receive regulatory approvals or that Ultra Rapid Lispro will prove to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's most recent Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

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