Lilly's tirzepatide led to greater time in range compared to insulin degludec in adults with type 2 diabetes in SURPASS-3 CGM sub-study

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Participants taking highest dose of tirzepatide experienced 91.2% time in range (71-180 mg/dL) and 72.6% time in tight target range (71-140 mg/dL)

CGM sub-study achieved its primary and secondary endpoints

INDIANAPOLIS, Sept. 30, 2021 /PRNewswire/ -- All three tirzepatide doses led to more time in tight target range (71-140 mg/dL), improved glycemic variability and numerically less time in hypoglycemia compared to titrated insulin degludec in adults with type 2 diabetes in a continuous glucose monitoring (CGM) sub-study[1] of Eli Lilly and Company's (NYSE: LLY) phase 3 SURPASS-3 clinical trial. The CGM sub-study was presented today at the 57th European Association for the Study of Diabetes (EASD) Annual Meeting in an EASD-sponsored symposium.

The international consensus for time in range recommends a target of >70% time in range (70-180 mg/dL) for most people with diabetes as well as a target of **<**4% time below range 70 mg/dL and <25% time above range 180 mg/dL.[2] In an exploratory endpoint of this CGM sub-study, participants taking tirzepatide 15 mg experienced 91.2% time in range (71-180 mg/dL) at 52 weeks.

"The CGM data collected through this SURPASS-3 sub-study show that tirzepatide helped participants have less variability in their blood glucose levels throughout the day, including spending less time below target range and more time in a tighter target range reflecting a normal blood glucose range," said Richard Bergenstal, M.D., Executive Director of the International Diabetes Center at Park Nicollet. "Improving glycemic variability, increasing time in range and reducing time below range are important metrics in the management of type 2 diabetes because they reflect glucose control throughout the day, offering context beyond the three-month average of A1C."

Tirzepatide is a novel investigational once-weekly dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist that integrates the actions of both incretins into a single molecule, representing a new class of medicines being studied for the treatment of type 2 diabetes.

SURPASS-3 was a 52-week, multi-center, randomized, phase 3, open-label trial evaluating the efficacy and safety of tirzepatide 5 mg, 10 mg and 15 mg compared to titrated insulin degludec[i] in adults with type 2 diabetes who have inadequate glycemic control on stable doses of metformin with or without an SGLT-2 inhibitor. Study participants were insulin-naïve and had a mean duration of diabetes of 8.4 years, a baseline A1C of 8.17 percent and a baseline weight of 94.3 kg.

In the SURPASS-3 CGM sub-study, a subpopulation of 243 participants wore a CGM for 7 to 10 days at baseline, at 24 weeks and at 52 weeks to evaluate the effect of tirzepatide compared to insulin degludec on time in the hyper- and hypoglycemic range and on glycemic variability. Glycemic variability was measured during 24-hour periods by several measures, including the coefficient of variation (CV).

The CGM sub-study achieved its primary and secondary endpoints. Specifically, at 52 weeks, the primary endpoint showed that participants taking tirzepatide:

- Spent 72.6% of the 24-hour period in tight target range (71-140 mg/dL) for pooled 10 mg and 15 mg arms, an average of approximately six more hours than those taking insulin degludec (48.0%).

Additional exploratory endpoints showed that at 52 weeks, participants taking tirzepatide:

- Spent between 84.9% and 91.2% of the 24-hour period in the target time in range (71-180 mg/dL), compared to 75% for those taking insulin degludec.
- Spent less time in hypoglycemia across all three doses compared to insulin degludec. Time spent ≤70 mg/dL was between 0.6% and 1.0% for tirzepatide and 2.4% for insulin degludec. Time spent **<**54 mg/dL was between 0.11% and 0.14% for tirzepatide and 0.39% for insulin degludec.
- Experienced a significant reduction in the coefficient of variation (CV) during a 24-hour period (between 0.9-3.4%) compared to an increase in CV for those taking insulin degludec.

The overall safety profile of tirzepatide in SURPASS-3 was similar to the well-established GLP-1 receptor agonist class. Gastrointestinal side effects were the most commonly reported adverse events and decreased with continued dosing.

About tirzepatide

Tirzepatide is a once-weekly dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist that integrates the actions of both incretins into a single novel molecule. GIP is a hormone that may complement the effects of GLP-1. In preclinical models, GIP has been shown to decrease food intake and increase energy expenditure therefore resulting in weight reductions, and when combined with a GLP-1 receptor agonist, may result in greater effects on glucose and body weight. Tirzepatide is in phase 3 development for blood glucose management in adults with type 2 diabetes and for chronic weight management. It is also being studied as a potential treatment for non-alcoholic steatohepatitis (NASH) and heart failure with preserved ejection fraction (HFpEF).

About the SURPASS-3 sub-studies and the SURPASS clinical trial program
Lilly developed two sub-studies in order to assess additional glycemic control measures and the effect on liver fat content and abdominal adipose tissue in SURPASS-3, a 52-week randomized, phase 3, open-label trial evaluating the efficacy and safety of tirzepatide compared to titrated insulin degludec in adults with type 2 diabetes who have inadequate glycemic control on stable doses of metformin with or without an SGLT-2 inhibitor. In SURPASS-3, the mean starting dose of insulin degludec was 10 units per day. The insulin dose was titrated following a treat-to-target algorithm with the goal of fasting blood glucose below 90 mg/dL.

The SURPASS-3 CGM sub-study compared the effect of tirzepatide to titrated insulin degludec evaluated by continuous glucose monitoring (CGM) in a subpopulation of participants with type 2 diabetes from the SURPASS-3 trial. In the sub-study, 243 participants wore a CGM for seven to ten days at baseline, at 24 weeks and at 52 weeks and were randomized to receive either tirzepatide 5 mg, 10 mg or 15 mg or titrated insulin degludec. The primary objective of the sub-study was to demonstrate superiority of tirzepatide (pooled 10 mg and 15 mg) once-weekly compared to insulin degludec for the percentage of time in tight target range (71-140 mg/dL) at 52 weeks. Key secondary endpoints included comparing tirzepatide 5 mg, 10 mg and 15 mg versus insulin degludec for the percentage of time per day spent in tight target range (71-140 mg/dL) and for the duration of time (in minutes) per day spent in tight target range (71-140 mg/dL). Exploratory endpoints include time spent in target range (71-180 mg/dL), time spent below target range (≤70 mg/dL and <54 mg/dL) and change in the coefficient of variation.

The SURPASS phase 3 global clinical development program for tirzepatide has enrolled more than 20,000 people with type 2 diabetes across 10 clinical trials, five of which are global registration studies. The program began in late 2018, and all five global registration trials have been completed.

About Diabetes
An estimated 463 million adults worldwide[3] have diabetes. Type 2 diabetes is the most common type, accounting for an estimated 90 to 95 percent of all diabetes cases[4]. 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 and related conditions. We work to deliver breakthrough outcomes through innovative solutions—from medicines and technologies to support programs and more. For the latest updates, visithttp://www.lillydiabetes.com/ or follow us on Twitter: @LillyDiabetes and Facebook: 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 lilly.com and lilly.com/newsroom. P-LLY

Lilly Cautionary Statement Regarding Forward-Looking Statements
This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about tirzepatide as a potential treatment for people with type 2 diabetes and the timeline for future readouts, presentations and other milestones relating to tirzepatide and its clinical trials and reflects Lilly's current belief and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of research, development, and commercialization. Among other things, there can be no guarantee that the studies will be completed as planned, that future study results will be consistent with the results to date or that tirzepatide will receive regulatory approvals. 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.

[1] Battelino, T. Effect of tirzepatide on glycaemic control captured with continuous glucose monitoring in patients with type 2 diabetes (SURPASS-3 CGM). Session S42a. Presented virtually at the 57th European Association for the Study of Diabetes Annual Meeting; September 27- October 1.
[2] Battelino T, Danne T, Bergenstal RM, et al. Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range. Diabetes Care. 2019;42(8):1593-1603.
[3] International Diabetes Federation. IDF Diabetes Atlas, 9th edn. Brussels, Belgium: International Diabetes Federation, 2019. Available at: http://diabetesatlas.org.
[4] Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2020. Atlanta, GA: Centers for Disease Control and Prevention, U.S. Dept. of Health and Human Services; 2020.

[i] The mean starting dose of insulin degludec was 10 units per day. The insulin dose was titrated following a treat-to-target algorithm with the goal of fasting blood glucose below 90 mg/dL.

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