

The results of a recent study favour Toujeo® over degludec and real-world evidence confirms Toujeo®'s value

- Results of studies comparing Sanofi's Toujeo® and insulin degludec
- Clinical implications for people living with diabetes

LAVAL, QC, Dec. 12, 2017 /CNW Telbec/ - Sanofi Canada announces the results of recent studies comparing Sanofi's Toujeo® (insulin glargine 300 Units/mL or Gla-300) to insulin degludec 100 Units/mL (Deg-100). The results show positive data that could lead to a better understanding of optimal treatment for more than 3.4 million Canadians living with diabetes.¹ Each of these co-related studies concludes that Toujeo® is a longer-acting insulin, provides a constant glucose lowering effect over 24 hours with a once-daily administration, low within day variability and clinical benefits.²

The pharmacokinetic/pharmacodynamic (PK/PD) study comparing Sanofi's Toujeo® and insulin degludec



The full results of this first PK/PD study with Toujeo® and Deg-100 were presented on November 11, 2016, during the 16th Annual Diabetes Technology Meeting in Bethesda, Maryland, U.S.³ The results showed that the Toujeo® PK/PD profile was flatter at a clinically relevant dose (0.4 U/kg/day, the average dose used in worldwide clinical practice)⁴ and more evenly distributed over 24 hours than the profile of insulin degludec for patients with type 1 diabetes. The within-day fluctuation of metabolic activity was 20% lower ($p=0.047$) for Toujeo® than insulin degludec. An overall flat PK/PD profile and an evenly distributed exposure over 24 hours were observed for Toujeo® at both dose levels studied (0.4 and 0.6 U/kg/day).

"This is not the first time Toujeo® is compared to other insulins, and consistently showed positive results," said Dr. Hisham A.S. Mahmoud, Medical Director at Sanofi Canada. "Toujeo® has already demonstrated an improved PK/PD profile when compared to insulin glargine 100 Units/mL (Gla-100). In a previous CGM study (continuous glucose monitoring) comparing Gla-300 and Gla-100, Toujeo® showed lower between-day variability and lower within-day fluctuations, associated with a lower risk of nocturnal confirmed (≤ 3 mmol/L) or severe hypoglycemia."⁵

The results observed in the PK/PD study confirm that Toujeo® has the potential to help people with diabetes reach their targets with lower risk of hypoglycemia. Furthermore, these results became the platform for the following ground studies.

The LIGHTNING and Deliver D studies

The findings of two comparative real-world studies, LIGHTNING and Deliver D, show that adults with diabetes who switched their basal insulin therapy to Toujeo® or insulin degludec experienced similar numbers of low blood sugar (hypoglycemia) events. Patients also experienced similar reductions of average blood sugar level (HbA1c) with both insulin treatments. These results were presented on November 30 at the World Congress on Insulin Resistance, Diabetes & Cardiovascular Disease in Los Angeles, California, U.S.^{6,7}

"The LIGHTNING and Deliver D studies extend Sanofi's program of retrospective observational analyses comparing Toujeo® with other basal insulins in a real-world setting and reinforce the consistency of evidence gathered across several patient populations," said Dr. Mahmoud. "In this case, throughout these two studies, we compared Toujeo® and insulin degludec based on two different large U.S. databases of electronic medical records and claims using a statistical technique in order to make the treatment groups comparable. This approach minimizes observed sources of bias typically found in simple observational studies."

The results of this comparison between Toujeo® and insulin degludec from the LIGHTNING and Deliver D studies could be reinforced, and thus, confirmed, with the results of the clinical trial called BRIGHT, intended to be released in 2018.

The BRIGHT study

The BRIGHT study is the first head-to-head randomized clinical trial comparing the efficacy and safety of Toujeo® and insulin degludec 100 Units/mL.⁸

"We are proud to say that Sanofi's Toujeo® met the primary study objective, which was to determine if the effect of Toujeo® on blood sugar levels (HbA1c) was similar to insulin degludec," mentioned Dr. Riccardo Perfetti, Head of Global Diabetes Medical Team, Sanofi.

Secondary objectives included the percentage of patients experiencing adverse events, the total number of participants with low blood sugar events during the study and the rate at which low blood sugar events occurred. The study specifically followed 929 adults whose type 2 diabetes was previously uncontrolled on non-insulin medication.

"Reducing the incidence of hypoglycemic events without compromising blood sugar reduction is an ongoing challenge for HCPs when managing their patients, commented Dr. Alice Y.Y. Cheng, Endocrinologist at Credit Valley Hospital and St. Michael's Hospital and Associate Professor, Department of Medicine, University of Toronto. "The most recently introduced long-acting insulins have demonstrated benefits to adult patients with diabetes. From the perspective of physicians and patients, hypoglycemia remains a major limiting factor in effective blood sugar management in diabetes."

The release of this new data contributes to the body of evidence for positive patient outcomes with Toujeo® in people with diabetes. The findings of the BRIGHT study are consistent with previous pharmacological studies, including the EDITION Phase 3 clinical trial program.^{9,10,11,12}

"All these results demonstrate how Toujeo® can bring value to people living with diabetes," claimed Niven Al-Khoury, President at Sanofi Canada. "With over 100 years of experience of working to understand and support the healthcare needs of Canadians, being able to bring solutions is core to our purpose."

Diabetes in Canada

Diabetes affects approximately 3.4 million Canadians, of which type 2 diabetes accounts for 90% of cases.^{13,14} It is estimated that 5.7 million Canadians have prediabetes; this condition being characterized by blood glucose levels above normal, but not high enough to be diagnosed as diabetes. Fifty percent of individuals with prediabetes will develop type 2 diabetes.¹⁵ Left untreated, diabetes can lead to many serious complications, such as heart disease, kidney disease, loss of vision and amputation of the lower limbs.

About Toujeo®

Toujeo® is a long-acting human insulin analog indicated to improve glycemic control in adults with diabetes mellitus. Toujeo® has been approved by the U.S. Food and Drug Administration (FDA), the European Commission, Health Canada, the Therapeutic Goods Administration in Australia, and the MHLW in Japan (where its approved brand name is Lantus® XR), and is under review by other regulatory authorities around the world.

About Sanofi Diabetes and Cardiovascular

Diabetes and cardiovascular disease affect millions of people worldwide, with many managing the complex challenges of both. Building on its portfolio evolution, heritage and expertise, Sanofi has implemented a focused business unit dedicated to delivering innovative, value-based medicines and integrated solutions in these therapeutic areas. It is committed to a collaborative approach that involves strategic alliances with professional and patient associations, research institutions and leaders in healthcare and other industries, with the goal of advancing scientific knowledge, driving the convergence of science and technology, helping to improve outcomes and inspiring an evolution in care.

About Sanofi www.sanofi.ca

Sanofi, a global healthcare leader, discovers, develops and distributes therapeutic solutions focused on patients' needs. Sanofi is organized into five global business units: Diabetes and Cardiovascular, General Medicines and Emerging Markets, Sanofi Genzyme, Sanofi Pasteur, and Consumer Healthcare. Sanofi is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY).

Together, Sanofi entities in Canada employ close to 1,900 people. In 2016, Sanofi companies invested \$130 million in research and development in Canada, creating jobs, economic activity and opportunities throughout the country.

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¹<http://www.diabetes.ca/how-you-can-help/advocate/why-federal-leadership-is-essential/diabetes-statistics-in-canada>.

²Becker RH, Nowotny I, Teichert L, et al. "Low within- and between-day variability in exposure to new insulin glargine 300 U/ml". *Diabetes Obes Metab*. 2015; 17(3): 261-7.

³Bailey T, et al. "Insulin Glargine 300 U/mL (Gla-300) Provides More Stable and More Evenly Distributed Steady-state PK/PD Profiles Compared with Insulin Degludec in Type 1 Diabetes". Poster presented at Diabetes Technology Meeting, November 11, 2016.

⁴Data on file, Adelphi Real World Diabetes DSP XII, 2015.

⁵Bergenstal RM, et al. *Diabetes Technol Ther* 2015; 17(S1): 16 (Abstract 39).

⁶Zhou LF et al, "Hypoglycemia risk associated with basal insulin use in type 2 diabetes (T2DM): The Lightning study", World Congress on Insulin Resistance, Diabetes & Cardiovascular Disease in Los Angeles, CA, U.S., November 30 – December 2, 2017.

⁷Blonde L et al, "Real-world evidence demonstrates comparable clinical outcomes of switching from insulin glargine 100 U/mL (Gla-100) to insulin glargine 300 U/mL (Gla-300) vs insulin degludec (IDeg) in patients with type 2 diabetes (T2D)", World Congress on Insulin Resistance, Diabetes & Cardiovascular Disease in Los Angeles, CA, U.S., November 30 – December 2, 2017.

⁸Sanofi, data on file: "Insulin glargine 300 U/mL vs insulin degludec in insulin-naïve adults with T2DM: head-to-head trial design and rationale", NCT02738151, November 2017.

⁹Riddle MC et al. *Diabetes Care*. 2014; 37(10): 2755-62, DOI: 10.2337/dc14-0991.

¹⁰Yki-Järvinen H, et al. *Diabetes Care*. 2014; 37(12): 3235-43, DOI: 10.2337/dc14-0990.

¹¹Bolli GB, et al. *Diabetes Obes Metab*. 2015; 17(4): 386-94, DOI: 10.1111/dom.12438.

¹²Ritzel R, et al. *Diabetes Obes Metab*. 2015; 17(9): 859-67, DOI: 10.1111/dom.12485.

¹³Diabetes Canada, "Diabetes statistics in Canada": <http://www.diabetes.ca/how-you-can-help/advocate/why-federal-leadership-is-essential/diabetes-statistics-in-canada>.

¹⁴Diabetes Québec, "Type 2 diabetes": <http://www.diabete.qc.ca/en/understand-diabetes/all-about-diabetes/types-of-diabetes/type-2-diabetes>.

¹⁵Diabetes Canada, "Prediabetes": <https://www.diabetes.ca/about-diabetes/prediabetes>.

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