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Media Update

New Soliqua®* data shows improved blood sugar control without weight gain versus premixed insulin

- Study also shows more people on Soliqua had improved blood sugar control without weight gain and without low blood sugar events (hypoglycemia) in first head-to-head comparison with premixed insulin

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A new study of Soliqua (insulin glargine 100 Units/mL and lixisenatide, iGlarLixi) met its two primary endpoints and all key secondary endpoints in a head-to-head comparison against premixed insulin (biphasic insulin aspart 30, BIAsp 30) in adults living with type 2 diabetes, the most common form of diabetes, uncontrolled on insulin and one or two oral anti-diabetic medicines. The findings were presented today at the American Diabetes Association (ADA) 81st Scientific Sessions[1] and simultaneously published in Diabetes Care.[2]

The study met both primary endpoints with Soliqua demonstrating noninferiority of blood sugar (HbA_{1c}) reduction and superiority on body weight change from baseline compared to premixed insulin. The study also met its key secondary endpoints with Soliqua achieving a greater proportion of people reaching a HbA_{1c} target of <7% without weight gain, a greater proportion of people reaching a HbA_{1c} target of <7% without weight gain and without hypoglycemia, and superiority in reduction of HbA_{1c} compared with those using premixed insulin.

> *"Concerns about hypoglycemia and weight gain are known barriers when advancing basal insulin therapy, especially with complex insulin regimens,"* says Julio Rosenstock, Director of the Dallas Diabetes Research Center at Medical City, Dallas, TX, and main author of the study. *"These results show improved outcomes with iGlarLixi over BIAsp 30, demonstrating better glucose control without body weight gain and less hypoglycemia. This combined benefit could help clinicians consider advancing basal insulin therapy by switching to a once-daily fixed-ratio combination of basal insulin plus a GLP-1 receptor agonist rather than switching to a twice-daily premixed insulin regimen."*

A secondary analysis also found study participants using Soliqua reported greater improvements in patient-reported outcomes compared to premixed insulin as measured by Treatment-Related Impact Measure Diabetes (TRIM-D) and patient- and physician-rated Global Treatment Effectiveness Evaluation (GTEE) scores.[3] These tools include measurements of treatment burden, daily life, diabetes management, compliance, psychological health, and treatment effectiveness.

"While premixed is used by around 40% of people taking insulin globally to manage their type 2 diabetes today, recent real-world evidence suggests only 18.2% of people using it reach their blood sugar goal,"[4,5] said Sandra Silvestri, M.D., Ph.D., Global Medical Head of General Medicines at Sanofi. "*Today's results provide further information on Soliqua's impact and patient-reported outcomes that could be considered by healthcare providers in regions such as India, China, the Middle East and North Africa, where premix is widely used."*

Safety findings were in line with the established profiles of Soliqua and premixed insulin.

About the SoliMix study

The SoliMix study was a 26-week, randomized controlled trial of 887 adults living with type 2 diabetes who were uncontrolled on insulin plus metformin with or without a sodium-glucose cotransporter-2 inhibitor (SGLT-2i). The study compared the efficacy and safety of Soliqua compared to a commonly used premixed insulin (BIAsp 30). Participants were randomized to switch from their prior insulin to either Soliqua once daily or premixed insulin twice daily, with starting doses determined and adjusted weekly. Any metformin or SGLT-2i treatment was maintained through the study period.

The study met its two primary endpoints and all three of its key secondary endpoints.

SoliMix Data Summary			
		Soliqua (n=443)	Premixed Insulin (n=444)
HbA1c, %	Baseline	8.61 ± 0.67	8.57 ± 0.65
	LS mean change from baseline to Week 26 ± SE	-1.30 ± 0.06	-1.05 ± 0.06
	LS mean difference (97.5% CI)*	-0.24 (-0.41, -0.08)	
	p-value for non-inferiority†	p<0.001	
	LS mean difference (95% CI)‡	-0.24 (-0.39, -0.10)	
	p-value for superiority§	p<0.001	
HbA1c, mmol/mol	Baseline	70.6 ± 7.3	70.2 ± 7.1
	LS mean change from baseline to Week 26 ± SE	-14.2 ± 0.7	-11.5 ± 0.7
	LS mean difference (97.5% CI)*	-2.6 (-4.5, -0.9)	
	p-value for non-inferiority†	p<0.001	
	LS mean difference (95% CI)‡	-2.6 (-4.3, -1.1)	
	p-value for superiority§	p<0.001	
	Baseline	80.7 ± 16.5	82.2 ± 18.5

Bodyweight, kg	LS mean change from baseline to Week 26 ± SE	-0.70 ± 0.20	+1.15 ± 0.20
	LS mean difference (95% CI) p-value for superiority*	-1.86 (-2.28, -1.43) p<0.001	
HbA1c <7 % without weight gain, n (%)		122 (27.5)	55 (12.4)
Odds ratio (95% CI)‡		2.83 (1.98, 4.04); p<0.001	
HbA1c <7 % without weight gain and without hypoglycemia (plasma glucose <70 mg/dL [<3.9 mmol/L]), n (%)		86 (19.4)	31 (7.0)
Odds ratio (95% CI)‡		3.40 (2.19, 5.28); p<0.001	
HbA1c <7 %, n (%)*§*		187 (42.2)	141 (31.8)
Odds ratio (95% CI)		1.65 (1.25, 2.19)	
Incidence and rates of hypoglycemia (safety population)		**n=442 223.15 PY**	**n=441 217.85 PY**
Level 1 (ADA definition: <70 mg/dL [<3.9 mmol/L] and ≥54 mg/dL [≥3.0 mmol/L])			
n (%)		114 (25.8)	170 (38.5)
Odds ratio (95% CI)		0.55 (0.42, 0.74)	
PPY (events)		2.03 (453)	2.83 (616)
Rate ratio (95% CI)		0.71 (0.52, 0.99)	
Level 2 (ADA definition: <54 mg/dL [<3.0 mmol/L])			
n (%)		28 (6.3)	57 (12.9)
Odds ratio (95% CI)		0.45 (0.28, 0.73)	
PPY (events)		0.25 (56)	0.56 (121)
Rate ratio (95% CI)		0.40 (0.23, 0.71)	
Level 3 (ADA definition: severe hypoglycemia)¶			
n (%)		1 (0.2)	2 (0.5)
Odds ratio (95% CI)		0.50 (0.04, 5.56)	
PPY (events)		0 (1)	0.01 (2)
Rate ratio (95% CI)		0.49 (0.04, 5.40)	

*Data shown are mean ± SD unless otherwise specified. *Primary endpoint was assessed at 0.025 for non-inferiority on HbA1c change from baseline then 0.05 for other endpoints, as the alpha was distributed to subsequent tests. †Two primary efficacy endpoints, non-inferiority of HbA1c reduction assessed using a margin of 0.3 %; ‡Secondary endpoint was assessed at the alpha 0.05 level. §Secondary endpoint. ¶A hypoglycemic event with severe cognitive impairment (hypoglycemic unconsciousness) requiring external assistance for recovery.*

ADA, American Diabetes Association; AE, adverse event; BiAsp, biphasic aspart insulin; BMI, body mass index; CI, confidence interval; iGlarLixi, a fixed-ratio combination of insulin glargine 100 U/mL and the glucagon-like peptide-1 receptor agonist, lixisenatide; ITT, intent to treat population; LS, least squares; PPY, per participant-year; PY, participant-year; SD, standard deviation; SE, standard error; T2D, type 2 diabetes.

In a secondary analysis, participants using Soliqua also reported greater improvements in patient-reported outcomes as measured by TRIM-D and patient- and physician-rated GTEE scores at 26 weeks.

- TRIM-D results demonstrated greater improvements for participants using Soliqua compared to those using premixed insulin, across domains including compliance, diabetes management, and psychological health, among others.[3]
- GTEE findings showed that nearly twice as many patients reported complete control of their diabetes with Soliqua compared to premixed insulin (27.5% vs 15%). Similarly, nearly twice as many physicians also reported treatment effectiveness (i.e., complete control of diabetes) with Soliqua compared to premixed insulin (29.9% vs 15.3%).[3]

Safety findings were in line with the established profiles of both treatments. The most commonly reported adverse events in the study were hypoglycemia (31.2% Soliqua, 42.4% premixed insulin), nausea (7.7% Soliqua, 0% premixed insulin), headache (2.5% Soliqua, 0.5% premixed insulin), dizziness (1.4% Soliqua, 0.5% premixed insulin), and vomiting (1.1% Soliqua, 0.2% premixed insulin).

** Soliqua® is an injectable prescription medicine that contains two diabetes medicines, insulin glargine and lixisenatide. Soliqua® is marketed in the EU as Suliqua®, where it is indicated in combination with metformin for the treatment of adults with type 2 diabetes mellitus to improve glycemic control when this has not been provided by metformin alone or metformin combined with another oral glucose lowering medicinal product or with basal insulin. It is marketed in the U.S. as Soliqua® 100/33, where it is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. It is marketed as Soliqua® in other geographies where it is approved.*

References

1. Rosenstock, J., et al. "Advancing Therapy in Uncontrolled Basal Insulin-Treated Type 2 Diabetes (T2D): Better Clinical Outcomes with iGlarLixi vs Premix 70/30 in the SoliMix Trial", Presentation 234-OR, American Diabetes Association (ADA) 81st Scientific Sessions (virtual event), June 28, 2021.
2. Rosenstock, J., et al. Advancing therapy in suboptimally controlled basal insulin-treated type 2 diabetes: Clinical outcomes with iGlarLixi versus premix BIAsp 30 in the SoliMix randomized controlled trial. *Diabetes Care*. 2021 Jun 28.
3. Polonsky, W., et al. "Improved Treatment Perceptions with iGlarLixi vs Premix Insulin in Type 2 Diabetes (T2D) Uncontrolled on Basal Insulin (BI) + Oral Antihyperglycemic Drugs (OADs): Patient-reported Outcomes (PROs) of the SoliMix Trial", Presentation 747-P, American Diabetes Association (ADA) 81st Scientific Sessions (virtual event), June 28, 2021.
4. Source: Market sales data, IQVIA
5. Jude E., et al. Effectiveness of premix insulin in type 2 diabetes: a retrospective UK cohort study. *Diabetes Obes Metab*. 2021;23:929-937.

About Sanofi

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions.

With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe.

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