New Study results support the “Basal Plus” Strategy with LANTUS® and APIDRA® to Improve Blood Sugar control In Patients with Type 2 Diabetes

Paris, France, September 10, 2008: Sanofi-aventis, a world leader in diabetes care, announced results from two randomized clinical studies presented at the European Association for the Study of Diabetes (EASD) 44th Annual Meeting demonstrating that the “basal plus” insulin strategy with LANTUS® (insulin glargine [rDNA origin] injection) once daily (basal insulin) and APIDRA® once daily (prandial insulin) (insulin glulisine [rDNA origin] injection) administered at the main meal (defined by the highest postprandial blood glucose level) improve blood glucose levels in patients with type 2 diabetes after basal insulin optimisation.

In the ELEONOR (Optimising basal plus insulin therapy in type 2 diabetes by telecare assistance for self-monitoring of blood glucose) and OPAL (Adding a single dose of insulin glulisine at breakfast or main meal to basal insulin and oral antidiabetic therapy) clinical studies, patients previously treated with LANTUS® and oral diabetes medications achieved significantly improved glycaemic control by implementing a “basal plus” regimen - adding one injection of APIDRA® at the main meal of the day. In the ELEONOR study, the addition of one APIDRA® injection resulted in a further A1C drop of 0.7-0.8%. In the OPAL study, A1C scores improved, significantly dropping 0.4% from baseline to endpoint in both patients that were administered APIDRA® at breakfast and patients who were administered APIDRA® at main meal.

“With so many people living with diabetes not reaching their A1C goals, we’re always looking for new ways to help manage blood glucose levels,” said Dr. Del Prato, Professor of Endocrinology and Metabolism and Chief of the Section of Diabetes at the School of Medicine, University of Pisa, Italy. “The results from ELEONOR and OPAL show us that a basal plus strategy is an option for insulin intensification for Type 2 Diabetes insufficiently controlled despite optimized titration of LANTUS® combined with oral antidiabetic drug therapy.”

The ELEONOR study also confirmed that in a large proportion of patients with secondary failure to oral antidiabetic agents, both Telecare and standard blood glucose monitoring can be used for initiation and titration of the “basal/basal plus” strategy. In the Telecare arm of the study, 50.6% of patients reached an A1C score of less than or equal to 7%, whereas in the standard blood glucose monitoring arm, 54.6% of patients similarly achieved an A1C score of less than or equal to 7%.
About the ELEONOR Study

ELEONOR was an open-label, multicentre, randomised, controlled, parallel-group study of 200 patients (54% male, 46% female) with poor glycaemic control (A1C 8.9±0.9%) on one or more oral hypoglycaemic agents. Following a 4-week run-in period, all patients began treatment with LANTUS® (Visit 2) and titrated to achieve blood glucose ≤5.5 mmol/L. At LANTUS® initiation (baseline), patients were randomised to either Telecare (allowing electronic transfer of blood glucose readings,) or standard blood glucose monitoring to identify the highest postprandial peak and APIDRA® dose adjustment by phone, as deemed necessary by the investigators, or dose adjustment at each visit, respectively. After 8-16 weeks of LANTUS®, patients with blood glucose ≤7.0 mmol/L in both groups added one dose of APIDRA® at the meal with the highest postprandial blood glucose; this treatment was maintained for 24 weeks. The primary objective was to compare Telecare with standard blood glucose in terms of A1C change. Secondary endpoints included blood glucose profiles, weight change, size of insulin dose and safety (including hypoglycaemia). Preliminary results are reported without lifting the study blinding.

Additional study findings showed that during LANTUS® titration, A1C improved with both blood glucose monitoring approaches by 1%. One APIDRA® injection was added to 88% of patients reaching target blood glucose (Breakfast 7%; Lunch 43%; Supper 50%), resulting in a further 0.7-0.8% A1C drop in both groups (endpoint A1C: 7.1±0.7 versus 7.0±0.7%; both p<0.0001 versus LANTUS® alone) with 50.6% and 54.6% of patients, respectively, reaching A1C ≤7.0% at endpoint. With LANTUS®, fasting blood glucose decreased in both groups (from 11.7±3.1 to 6.0±1.0 and from 11.6±3.3 to 6.1±1.1 mmol/L, respectively; both p<0.0001) with no further change after APIDRA® initiation (6.4±1.6 versus 6.3±1.6 mmol/L). There was no difference in weight changes (+0.4±3.0 versus +0.1±5.0 kg) in LANTUS® (29±16 versus 28±17 U/d) or APIDRA® (8.3±7.1 versus 8.1±8.1 U/d) dose. Five episodes of severe hypoglycaemia were experienced by 4 patients.

About the OPAL Study

OPAL was a 26-week, randomized, multicentre study conducted in 316 patients with type 2 diabetes, who were poorly controlled (A1C >6.5-9.0%) on previous treatment with LANTUS®+ oral hypoglycaemic agents. Patients (blood glucose ≤6.7 mmol/L [≤120 mg/dL]) were stratified by the main meal (breakfast, lunch or dinner), determined by the highest postprandial blood glucose level, and randomised to APIDRA® once daily + LANTUS® once daily + oral hypoglycaemic agents (LANTUS® as basal insulin) with APIDRA® given at breakfast (n=162) or main meal (n=154). The primary aim was to demonstrate equivalence in baseline to endpoint A1C change between both arms.

Baseline demographics for the overall, breakfast and main meal groups were similar. Patients had an average age >60 years, obese (>30 kg/m²) and had suboptimally controlled type 2 diabetes management (blood glucose ~6 mmol/L and A1C ~7.3%). Additional study findings showed that overall A1C significantly improved from baseline to endpoint (p<0.0001), while both arms were equivalent in terms of A1C change (equivalence margin=0.4%). Blood glucose values improved significantly within each arm for most pre- and post-meal timepoints. Overall, 30.7% of patients achieved A1C ≤6.5% (27.8% breakfast and 33.8% main meal arms; p=0.21). For those patients with baseline A1C>7.0%, 44.1% achieved A1C ≤7.0% at endpoint (36.5% breakfast and 52.2% main meal arms; p=0.028). Mean LANTUS® dose was unchanged (baseline versus endpoint: 31 versus 32 U/day breakfast and 27 versus 27 U/day main meal arms), whereas APIDRA® dose increased (starting dose of 5 U/day versus 11 and 12 U/day, respectively). The rate of on-treatment hypoglycaemia (blood glucose ≤3.3 mmol/L [≤60 mg/dL]) was 3.21 events/patient year for the overall group (2.72 and 3.69 events/patient year for the breakfast and main meal arms, respectively).

Additional details about the ELEONOR and OPAL data are included in the study abstracts, available at EASD.org.
About LANTUS® (insulin glargine [rDNA origin])

LANTUS® is indicated for once-daily subcutaneous administration in the treatment of adult patients with type 2 diabetes mellitus who require basal (long-acting) insulin for the control of hyperglycemia and for adult and pediatric patients (6 years and older) with type 1 diabetes mellitus. LANTUS® demonstrates a peakless and sustained concentration/time profile over 24 hours thus reducing the risk of hypoglycemia and allowing a constant and high efficacy over 24h with one single daily injection. LANTUS® is the number one prescribed insulin worldwide.

About APIDRA® (insulin glulisine [rDNA origin])

APIDRA® is a rapid-acting insulin analog with a unique zinc-free molecular structure that maintains a rapid onset and a short duration of action, indicated for adults and for adolescents and children (6 years and older) with diabetes in the EU. APIDRA® offers patients mealtime dosing flexibility—it can be taken shortly (0-15 min) before or soon after the meal. APIDRA® is also flexible for use in a wide range of patients from lean to obese. APIDRA® is the logical partner to LANTUS® once prandial insulin is required.

About Diabetes

Diabetes is a chronic, progressive widespread disease in which the body reduces or does not produce or properly use insulin – the hormone needed to convert glucose (sugar) into energy. In 2008 over 250 million people worldwide are living with diabetes. This number would dramatically increase up to 380 million by 2025. It is estimated more than 24 million Americans have diabetes. At the same time, more than 40% of those diagnosed are not achieving the general blood sugar control standard of A1C <7% recommended by the American Diabetes Association and the European Association for the Study of Diabetes (ADA/EASD). The A1C test reflects average blood glucose levels over a two- to three-month period. Without proper insulin production and action, glucose remains in the blood, leading to chronic hyperglycaemia (raised blood sugar). This can result in short and long-term complications, many of which, if not prevented and left untreated, can be fatal. All have the potential to reduce the quality of life of people with diabetes and their families.

The most common long-term complications are:

- Diabetic nephropathy (kidney disease), which may result in total kidney failure and in the need for dialysis or kidney transplant.
- Diabetic eye disease (retinopathy and macular oedema), damage to the retina of the eye which can lead to vision loss.
- Diabetic neuropathy (nerve disease), which can ultimately lead to ulceration and amputation of the feet and lower limbs.
- Cardiovascular disease, which affects the heart and blood vessels and may cause fatal complications such as coronary heart disease (leading to a heart attack) and stroke.

Diabetes is the fourth leading cause of death by disease globally. Every year, 3.8 million people die from diabetes-related causes.

About sanofi-aventis

Sanofi-aventis, a leading global pharmaceutical company, discovers, develops and distributes therapeutic solutions to improve the lives of everyone. Sanofi-aventis is listed in Paris (EURONEXT : SAN) and in New York (NYSE : SNY).

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