INSIGHT Trial Overview and Design

- Data from the Implementing **N**ew **S**trategies with **I**nsulin **G**largine for **H**yperglycemia **T**reatment (**INSIGHT**) trial confirmed that Lantus® (insulin glargine [rDNA origin] injection) added to oral antidiabetic drugs (OADs) helped many patients reach blood glucose goal compared with the adjustment of OADs alone[1]

- **INSIGHT** was a 24-week trial involving patients with type 2 diabetes mellitus who were randomized to starting Lantus® with 10 units + self-titration (n=206) by 1 unit/day if the fasting plasma glucose (FPG) was >100 mg/dL, or conventional therapy with physician adjustment of oral glucose-lowering agents (n=199)[1]

- Patients had to be taking 0, 1, or 2 OADs, with at least 1 of the OADs taken at half or below half-maximal dose at study start. Patients could not have any substantial change in oral dose for at least 3 months before randomization. Primary endpoint was first achievement of 2 consecutive A1C levels ≤6.5%[1]

INSIGHT Trial Results

Percentage of patients achieving 2 consecutive A1C levels of ≤6.5% or ≤7% at 24 weeks[1]

- Patients treated with Lantus® were significantly more likely (1.68 times) to achieve 2 consecutive A1C values ≤6.5% vs patients treated with adjustments of OADs alone (*P*=0.049), and achieved it significantly earlier (*P*=0.041)

From Gerstein.[1]

Reductions in A1C from baseline at 24 weeks[1]

- 58.3% of patients treated with Lantus® + OADs achieved an A1C ≤7% compared with 44.2% of those on adjustment of OADs alone (*P*=0.005)

- Mean A1C at endpoint was 6.96% for Lantus® + OADs and 7.24% for adjustment of OADs alone after adjustment for baseline levels, site, and stratum; *P*=0.0007 difference between groups

FPG reductions at 24 weeks[1]

- Fixing FPGs first with once-daily Lantus® helped many patients achieve glycemic goals

- 24% of patients in the adjustment of OADs alone group were taking 3 OADs by the end of the study

- The mean (standard deviation) Lantus® dose reached by the last visit was 38.1 (28.5) units or 0.41 (0.28) units/kg body weight

Safety Results[1,2]

From Gerstein[1] and data on file.[2]
[a]Severe hypoglycemia was defined as an event requiring assistance and at least 1 of either promptly responding to therapy with oral carbohydrate, intravenous glucose or parenteral glucagon, or a documented capillary glucose ≤36 mg/dL.
[b]By system organ class.

Registration Trial: Lantus® + OADs vs NPH + OADs in Patients With Type 2 Diabetes Mellitus

- In a 52-week study, 570 patients with type 2 diabetes poorly controlled by OADs were randomized to either Lantus® (n=289) or NPH (n=281) at bedtime to reach a target FPG of <120 mg/dL. OADs were continued, and the initial insulin dose and titration schedule was left to the discretion of the individual investigators. Primary endpoint was change in A1C[2-4]

Mean A1C levels[2]

- 0.5% mean A1C reduction at 52 weeks[2]

From data on file,[2] Lantus® Prescribing Information,[3] and Yki-Järvinen.[4]

FPG reductions during the 52-week study (N=570)[2-4]

- Study designed to compared efficacy and safety of Lantus® and NPH[2]
- Lantus® dose at 52 weeks: 26 Units (range 3-120 Units)

From data on file.[2]

Safety Results[2,3]

From data on file.[2]
[c]Severe symptomatic hypoglycemia was defined as an event with symptoms consistent with hypoglycemia in which the subjects required the assistance of another person and which was associated with a plasma glucose level <50 mg/dL or prompt recovery after oral carbohydrate, intravenous glucose, or glucagon administration.
[d]Nocturnal hypoglycemia was defined as hypoglycemia occurring while subject was asleep, between bedtime after the evening injection and before getting up in the morning, ie, before the morning determination of FPG and before the morning injection.
[e]Plasma glucose level <50 mg/dL.
[f]By system organ class.

Indications and Usage for Lantus® (insulin glargine [rDNA origin] injection)

Lantus® is a long-acting insulin analog indicated to improve glycemic control in adults and children (6 years and older) with type 1 diabetes mellitus and in adults with type 2 diabetes mellitus. Lantus® should be administered once a day at the same time every day.

Important Limitations of Use: Lantus® is not recommended for the treatment of diabetic ketoacidosis. Use intravenous short-acting insulin instead.

Important Safety Information for Lantus® (insulin glargine [rDNA origin] injection)

Contraindications
Lantus® is contraindicated in patients hypersensitive to insulin glargine or one of its excipients.

Warnings and Precautions
Monitor blood glucose in all patients treated with insulin. Insulin regimens should be modified cautiously and only under medical supervision. Changes in insulin strength, manufacturer, type, or method of administration may result in the need for a change in insulin dose or an adjustment in concomitant oral antidiabetic treatment.

Do not dilute or mix Lantus® with any other insulin or solution. If mixed or diluted, the solution may become cloudy, and the onset of action/time to peak effect may be altered in an unpredictable manner. Do not administer Lantus® via an insulin pump or intravenously because severe hypoglycemia can occur. Insulin devices and needles must not be shared between patients.

Hypoglycemia is the most common adverse reaction of insulin therapy, including Lantus®, and may be life-threatening.

Severe life-threatening, generalized allergy, including anaphylaxis, can occur.

A reduction in the Lantus® dose may be required in patients with renal or hepatic impairment.

Drug Interactions
Certain drugs may affect glucose metabolism, requiring insulin dose adjustment and close

monitoring of blood glucose. The signs of hypoglycemia may be reduced in patients taking anti-adrenergic drugs (e.g., beta-blockers, clonidine, guanethidine, and reserpine).

Adverse Reactions
Other adverse reactions commonly associated with Lantus® are injection site reaction, lipodystrophy, pruritus, and rash.

In clinical studies in adult patients there was a higher incidence of treatment-emergent injection-site pain (2.7% Lantus® vs. 0.7% NPH). The reports of pain at the injection site were usually mild and did not result in discontinuation of therapy.

Important Safety Information for Lantus® SoloSTAR®

Lantus® SoloSTAR® is a disposable prefilled insulin pen. To help ensure an accurate dose each time, patients should follow all steps in the Instruction Leaflet accompanying the pen; otherwise they may not get the correct amount of insulin, which may affect their blood glucose.

Click here to view the full Prescribing Information for Lantus®.

References

1. Gerstein HC, Yale J-F, Harris SB, Issa M, Stewart JA, Dempsey E. A randomized trial of adding insulin glargine vs. avoidance of insulin in people with Type 2 diabetes on either no oral glucose-lowering agents or submaximal doses of metformin and/or sulphonylureas. The Canadian INSIGHT (Implementing New Strategies with Insulin Glargine for Hyperglycaemia Treatment) Study. *Diabet Med.* 2006;23(7):736–742.
2. Data on file, Sanofi US.
3. Lantus® Prescribing Information, April 2010.
4. Yki-Järvinen H, Dressler A, Ziemen M; HOE 901/3002 Study Group. Less nocturnal hypoglycemia and better post-dinner glucose control with bedtime insulin glargine compared with bedtime NPH insulin during insulin combination therapy in type 2 diabetes. HOE 901/3002 Study Group. *Diabetes Care.* 2000;23(8):1130–1136.

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