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INSULIN GLARGINE IN TYPE 2 DIABETES: AN OBSERVATIONAL STUDY OF EVERYDAY PRACTICE

STEPHAN A SCHREIBER[1], KERSTIN SCHNEIDER[2], MATTHIAS AXEL SCHWEITZER[2]

[1]QUICKBORN, GERMANY; [2]BAD SODEN AM TAUNUS, GERMANY

ABSTRACT

Insulin glargine (LANTUS®) is a long-acting basal insulin analog. The aim of this observational study was to investigate the effect of adding insulin glargine basal therapy to support oral antidiabetic treatment in patients with type 2 diabetes in everyday practice. In this 9-month, uncontrolled observational study, 12,216 patients with type 2 diabetes not adequately controlled on oral antidiabetic drugs (OADs) received add-on insulin glargine treatment. Dosing decisions, including any changes to OADs, were made at the physician's discretion, reflecting everyday practice. Efficacy outcomes included baseline, 3-month and 9-month changes in A1c, fasting blood glucose (FBG), body weight and body mass index (BMI). At baseline, the mean (± SD) age of patients was 64 (± 11.3) years. Duration of diabetes was >5 years in 47% of patients, 1–5 years in 39% of patients and <1 year in 10% of patients. The remaining 4% of patients were newly diagnosed. After 3 months of treatment, reductions in FBG and A1c were observed (Table). Improvements in metabolic control were maintained for at least 9 months. The mean starting dose of insulin glargine was 13.7 ± 7.0 IU. By 9 months, the mean dose was 20.3 ± 9.6 IU. Adverse drug reactions were documented in a total of 26 patients (0.21%). Of 47 adverse events documented, 19 were due to hypoglycemia. These data suggest that, in daily clinical practice, insulin glargine in combination with OADs is effective in patients with type 2 diabetes inadequately controlled on OADs alone, and is consistent with results seen in other clinical trials.

	A1c (%)	FBG (mmol/L)	BMI (kg/m²)
Baseline	8.7 ± 1.4 (n=11,511)	11.2 ± 3.1 (n=12,100)	29.0 ± 4.7 (n=11,090)
3 months' insulin glargine	7.2 ± 0.9 (n=11,296)	7.4 ± 1.8 (n=11,872)	28.7 ± 4.5 (n=10,692)
9 months' insulin glargine	7.0 ± 1.0 (n=6,031)	7.3 ± 1.9 (n=6,335)	28.5 ± 4.8 (n=5,324)

INTRODUCTION

- In newly diagnosed patients with type 2 diabetes, diet and exercise are initially recommended to improve glycemic control
- Over time, this strategy is usually insufficient to maintain glycemic control, necessitating the introduction of oral antidiabetic agents (OADs)[1]
- However, as the disease progresses, management becomes increasingly difficult and the addition of insulin therapy is required[2]
- NPH insulin is an intermediate-acting insulin, which has traditionally been used in patients with type 2 diabetes
- However, NPH insulin often requires twice-daily injections to provide 24-hour insulin coverage
- Furthermore, NPH insulin demonstrates a peak of activity at 4–6 hours following administration, which often leads to a sharp fall in fasting blood glucose (FBG) levels, resulting in an increased risk of hypoglycemia, particularly nocturnal hypoglycemia, following bedtime administration
- Insulin glargine (LANTUS®), a long-acting human insulin analog, mimics the action of endogenous basal insulin, providing control close to 24 hours with a once-daily dose[3]
- A large body of data obtained from clinical trials has shown the benefit of insulin glargine in patients with type 2 diabetes; however, this is the first large scale observational study to be completed in everyday practice

STUDY OBJECTIVE

- To investigate the effect of adding insulin glargine basal therapy to support OAD treatment in patients with type 2 diabetes in everyday practice

STUDY DESIGN AND METHODS

- This was an open-label, multicenter, observational study assessing the efficacy and safety of insulin glargine in patients with type 2 diabetes in everyday practice in Germany

Study population

- Patients with type 2 diabetes who were not adequately controlled on current oral therapy were eligible for participation in the study

Treatment regimen

- Patients were treated with insulin glargine (100 IU/mL), which was administered using OptiSet®, a disposable pen
- Patients continued on OADs
- During the study period, the decision regarding treatment and dosing was made at the physician's discretion, based on individual blood glucose (BG) levels, to reflect everyday practice

Outcome measures

- The following measures were documented at baseline and after 12 weeks and 9 months of therapy (endpoint):
  - Glycosylated hemoglobin (A1c)
  - Fasting blood glucose (FBG)
  - Daily insulin dose
  - Body mass index (BMI)

Safety

- All adverse events occurring during the course of the observational period were documented, whether thought related to the study treatment or not

Table 1. Baseline characteristics

Characteristic	n=12,216
Age (years)*	63.9 ± 11.3
Patients >66 years (%)	46.2
Male/female (%)	50.2/49.8
BMI (kg/m²)*	29.0 ± 4.7
A1c (%)	8.7 ± 1.4
FBG, mg/dL (mmol/L)	202 ± 55.8 (11.2 ± 3.1)
Previous OAD taken (%)†:	
Metformin	58.2
Sulfonylurea	72.1
Alpha-glucosidase inhibitors	10.2
Thiazolidinones	1.5
Others	7.6

*Presented as mean ± standard deviation; †Some people were taking multiple OAD therapy;
BMI=body mass index; OAD=oral antidiabetic agent; A1c=glycosylated haemoglobin; FBG=fasting blood glucose

Statistical analysis

- Descriptive analyses only were performed

Study population

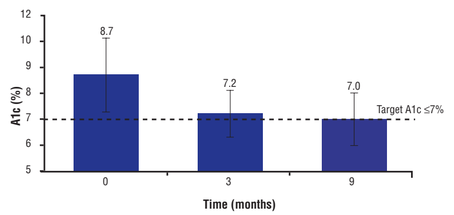
- A total of 12,216 patients with type 2 diabetes entered the study at baseline
- A total of 6,576 patients were treated with insulin glargine could be followed for a period of 9 months
- Baseline characteristics, metabolic control measures and previous treatment regimens of the total population are presented in Table 1

RESULTS

Metabolic control

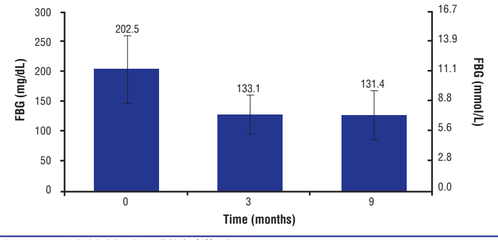
- There was a decrease in A1c from baseline to 9 months (endpoint) (8.7 ± 1.4% vs 7.0 ± 1.0%), which was evident at 3 months (7.2 ± 0.9%) (n=5729; Figure 1)
- A total of 3,223 patients (49%) reached A1c level <7%
- Mean FBG levels decreased over the study period from 202.5 ± 56.1 mg/dL (11.3 ± 3.1 mmol/L) at baseline to 133.1 ± 33.0 mg/dL (7.4 ± 1.8 mmol/L) at 12 weeks and 131.4 ± 34.5 mg/dL (7.3 ± 1.9 mmol/L) at endpoint (n=6180; Figure 2)

Figure 1. Change in A1c levels over 9 months*



*Error bars represent standard deviation; data available for 5729 patients

Figure 2. Change in FBG over 9 months*



*Error bars represent standard deviation; data available for 6180 patients

Body mass index

- There was little change in BMI throughout the study period, with values at baseline and endpoint (n=4800; 9 months) being 29.0 ± 4.7 kg/m² and 28.5 ± 4.8 kg/m², respectively

Daily insulin dose

- The mean daily dose of insulin glargine increased during the study period from 13.8 ± 6.9 IU at baseline to 18.1 ± 8.3 at 3 months and 20.3 ± 9.5 at study endpoint (n=6303)

Safety

- A total of 142 adverse events were reported in 12,216 patients (1.16%)
- A total of 26 patients (0.21%) experienced 47 adverse drug reactions, of which 19 events were due to hypoglycemia; none of the reactions were unexpected
- Treatment discontinuations were observed in 0.3% of treated patients due to adverse events

CONCLUSION

- This observational study in everyday practice supports data obtained in a number of clinical trials[4,5], demonstrating that in patients with type 2 diabetes inadequately controlled on OAD regimens, the introduction of insulin glargine greatly improves glycemic control with a neutral effect on weight over 9 months
- An increase in daily insulin glargine dose was noted in this cohort of treated patients due to therapy adjustment at the physician's discretion
- Improved disease control was achieved safely; few patients experienced adverse events during the 9-month study
- In conclusion, in everyday clinical practice, patients with type 2 diabetes who are inadequately controlled on OADs can benefit from the initiation of basal insulin therapy with insulin glargine, which can facilitate reaching the target of A1c ≤7%

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[1]Diabetologe DDG, Quickborn, Germany; Email: stephan.schreiber@diabetes-hamburg.de