IMPROVED METABOLIC CONTROL WITH A FAVORABLE WEIGHT PROFILE IN PATIENTS WITH TYPE 2 DIABETES TREATED WITH INSULIN GLARGINE (LANTUS®) IN CLINICAL PRACTICE

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ABSTRACT

Improving metabolic control without weight gain is a challenge in the management of Type 2 diabetes. In this open label, single center, nine-month study in clinical practice, the effect of insulin glargine (LANTUS®) on metabolic control and body weight was evaluated in 72 patients with Type 2 diabetes. Thirty-two insulin-naïve patients who were previously on oral antidiabetic medication were initiated on once-daily insulin glargine with either glimepiride (Amaryl®) or, in a few cases, glimepiride plus metformin, after participating in an educational program on insulin therapy. Forty patients treated previously with insulin were switched to once-daily insulin glargine plus mealtime regular human insulin or insulin lispro, after an educational program on intensified conventional therapy (ICT). Metabolic control and body weight were monitored for 9 months. In the 32 patients treated previously with oral agents, metabolic control improved significantly from baseline (HbA_{1c} decreased from 9.0% to 7.4%; $p < 0.005$), while body weight was reduced vs baseline. In the 40 patients treated previously with insulin, no statistically significant change in body weight from baseline to endpoint was detected. HbA_{1c} improved significantly in the 13 patients who were previously on mixed insulin (–1.7%; $p < 0.04$ vs baseline) and in the 15 patients on oral agents plus NPH insulin (–1.5%; $p < 0.05$ vs baseline). In patients previously on ICT (n=12), there was a trend towards increased HbA_{1c} (+0.5%). Overall, in the 72 patients examined in this study, there was a significant reduction in HbA_{1c} from baseline to endpoint (8.14% to 7.58%; $p < 0.001$). This was accompanied by slight weight reduction (94.91 kg to 93.79 kg). In conclusion, insulin glargine in combination with glimepiride or prandial insulin improves metabolic control while showing a favorable weight profile, in patients with Type 2 diabetes.

INTRODUCTION

- The advent of insulin analogs is of major clinical significance in the treatment of diabetes[1]
- Patients with Type 2 diabetes often benefit from approaches that aim to improve insulin sensitivity, such as weight reduction through dietary modifications and exercise[2]. However, these approaches often do not lead to satisfactory glycemic control and, consequently, pharmacologic therapy is required
- Improved metabolic control without weight gain is a challenge in the drug treatment of Type 2 diabetes, especially since insulin therapy is often associated with weight gain
- Insulin glargine (LANTUS®) is a novel, long-acting human insulin analog, which has a smooth action profile with no pronounced peak and a prolonged duration of action[2] that makes it appropriate for once-daily use
- Once-daily insulin glargine is as effective as once or twice-daily NPH insulin in improving and maintaining glycemic control in Type 2 diabetes[3]
- Previous studies have demonstrated that insulin glargine improves metabolic control and has a favorable weight profile and reduced incidence of nocturnal hypoglycemia in patients with Type 1 diabetes[4] and Type 2 diabetes[3,5,6]

STUDY OBJECTIVES

- To evaluate the effect of insulin glargine combined with prandial insulin or oral hypoglycemic agents (OHAs) on metabolic control and body weight in patients with Type 2 diabetes who had received pre-treatment with OHAs only, or pre-treatment with conventional insulin therapy or intensified conventional insulin therapy (ICT)
- To determine whether the efficacy variables were influenced by the type of insulin therapy that patients received prior to commencing their insulin glargine regimen
- To improve patient education for self-management of insulin therapy and diet, in order to optimize glycemic control and minimize weight gain

STUDY DESIGN AND METHODS

Study design

- Single center, open-label, 9 month study carried out in a diabetes practice in Germany
- The study design is summarized in Figure 1

Insulin-naïve patients

- Prior to initiating insulin glargine treatment, insulin-naïve patients (n=27) were divided into subgroups and received insulin pre-treatment: 11 were pre-treated with OHAs plus insulin; 16 remained on OHAs only
- After participating in an educational program on insulin therapy and diet, these patients were initiated on once-daily insulin glargine with one of the following therapies:
  – Glimepiride (Amaryl®) (n=21)
  – Glimepiride plus metformin (n=6)

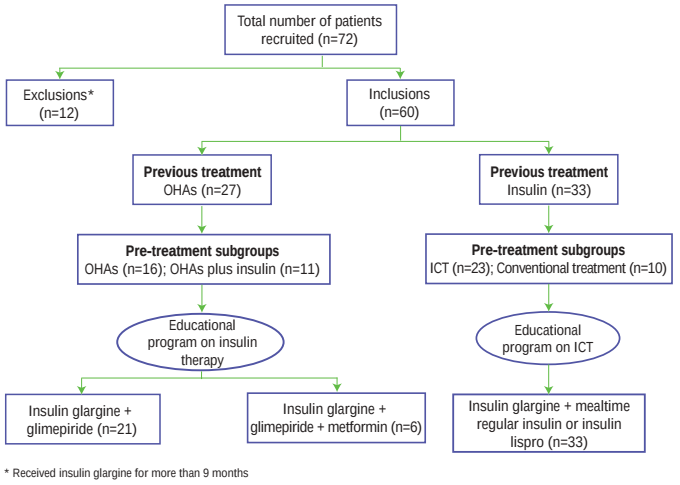
Insulin-experienced patients

- Prior to initiating insulin glargine treatment, insulin-experienced patients (n=33) were divided into subgroups and received pre-treatment with ICT (n=23) or with conventional insulin therapy (n=10)
- After taking part in an educational program on ICT, these patients were switched to once-daily insulin glargine plus mealtime regular human insulin or insulin lispro

Patients

- Patients with Type 2 diabetes (n=72)
- The data presented here refer only to those patients who received insulin glargine for 9 months (n=60)
- Patients who received insulin glargine for longer than nine months (n=12) have been excluded
- The dose of insulin glargine was titrated, whilst the dose of OHAs was kept stable

Figure 1. Flow chart of patient recruitment and group assignment



Efficacy variables

Metabolic control

- Metabolic control was monitored at the start of the study (baseline) and after 9 months (endpoint) through measurement of HbA_{1c}

Body weight

- Changes in body weight were monitored at baseline and endpoint

Safety measurements

- Severe hypoglycemia (requiring the assistance of a third party) was recorded; mild episodes were not recorded

Statistical analysis

- All variables were analyzed using descriptive statistics

RESULTS

Patients

- Baseline characteristics of patients enrolled in the study are summarized in Table 1

Table 1. Baseline characteristics of patients

		Mean ± SD	
Variable	**Total**	**OHA pre-treatment**	**Insulin only pre-treatment**
Patient numbers (male/female)	60 (33/27)	27	33
Age (years)	60.2 ± 8.1	58.0 ± 9.0	62.3 ± 6.8
Body weight (kg)	94.9 ± 19.8*	97.0 ± 19.9	91.4 ± 32.8
HbA_{1c} (%)	8.1 ± 1.6	8.8 ± 1.6	7.0 ± 1.3

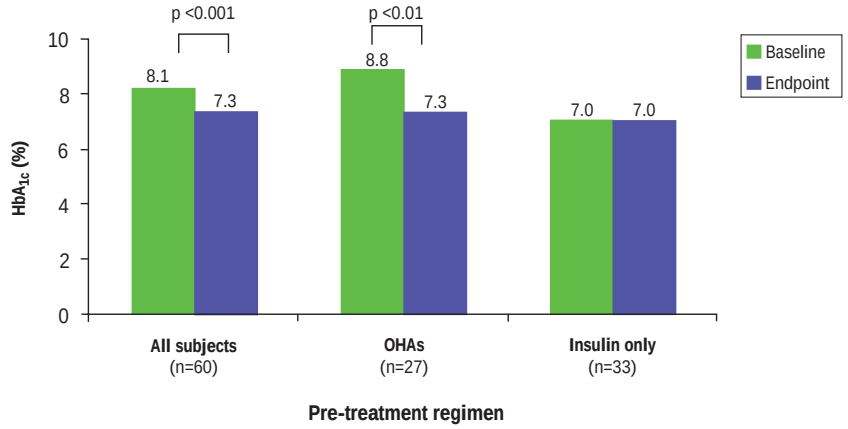
** Male 99.0 kg; Female 88.1 kg*

Efficacy

Metabolic control

- In the 60 patients examined in this study, there was a significant reduction in HbA_{1c} from baseline to endpoint (8.1% to 7.3%; p <0.001) (Figure 2)
- In the 27 patients pre-treated with OHAs, metabolic control improved significantly from baseline, as indicated by a decrease in HbA_{1c} of 1.5% (8.8% to 7.3%; p <0.01) (Figure 2)
- In the 33 patients pre-treated with insulin only, there was no change in HbA_{1c} (Figure 2)

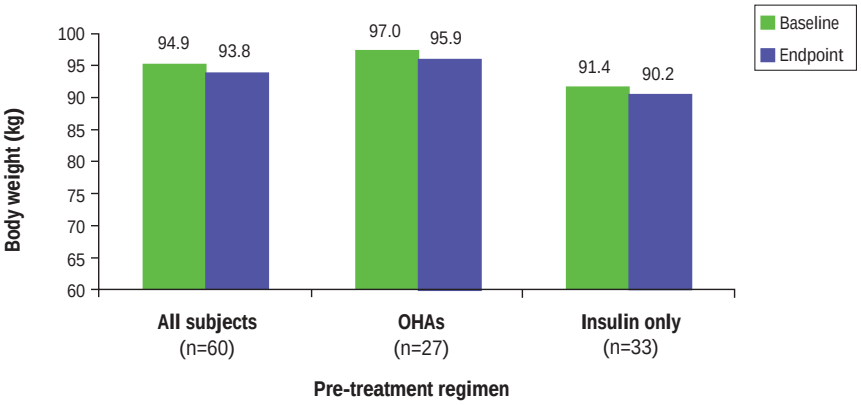
Figure 2. Reduction in mean HbA_{1c} levels in patients with Type 2 diabetes treated with insulin glargine for 9 months



Body weight

- Following 9 months' treatment with insulin glargine, in the 60 patients examined, there was a slight but detectable reduction in body weight (94.9 kg to 93.8 kg) (Figure 3)
- At endpoint, a reduction in body weight was detected in the 27 patients pre-treated with OHAs (mean weight loss 1.1 kg) and in the 33 patients pre-treated with insulin only (mean weight loss 1.2 kg; Figure 3)

Figure 3. Reduction in body weight in patients with Type 2 diabetes treated with insulin glargine for 9 months

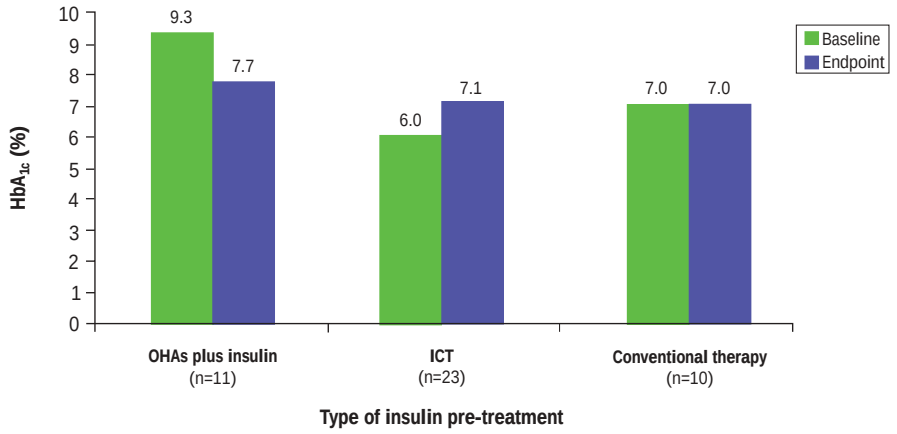


Efficacy

Metabolic control: pre-treatment subgroups

- Following treatment with insulin glargine, HbA_{1c} levels had altered as shown in Figure 4
- A reduction in HbA_{1c} was detected in the subgroup of patients who were pre-treated with OHAs plus insulin (n=11; 1.64% decrease; p <0.05 vs baseline)
- There was no significant change in HbA_{1c} levels in the patients pre-treated with ICT (n=23) or in the patients pre-treated with conventional insulin therapy (n=10)

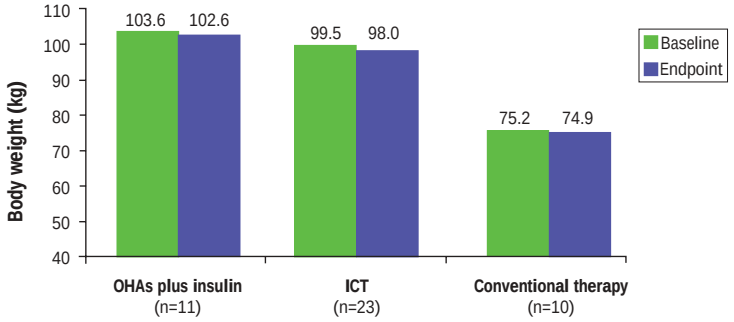
Figure 4. Analysis of HbA_{1c} levels at baseline and endpoint in the pre-treated insulin subgroups following insulin glargine treatment



Body weight: pre-treatment subgroups

- After switching to insulin glargine, there was a clear reduction in body weight in all patients who had received insulin pre-treatment (Figure 5)

Figure 5. Analysis of body weight at baseline and endpoint in the pre-treated insulin subgroups following treatment with insulin glargine



Safety

- No unexpected adverse events or episodes of severe hypoglycemia were reported

CONCLUSIONS

- Overall, over a 9 month period, insulin glargine in combination with glimepiride (and metformin in a small proportion of patients [n=6]), or prandial insulin, significantly improved metabolic control in patients with Type 2 diabetes, without increasing body weight
- The favorable weight outcomes in this study could be attributed to the synergistic approach of providing dietary patient education prior to insulin glargine treatment

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