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Treatment Satisfaction with a Basal Insulin added to Oral Agents versus Twice-daily Premixed Insulin Alone in Patients With Type 2 Diabetes

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ABSTRACT

In type 2 diabetes, if good glycemic control is not maintained with oral antidiabetic agents (OADs), physicians often stop OADs and introduce twice-daily premixed insulins. In this 24-week, multicenter, open, parallel group study, 364 patients with type 2 diabetes and poor glycemic control using OADs were treated with once-daily insulin glargine (GLAR) with continued OADs (GLAR+OAD; glimepiride + metformin) or premixed 30% regular/70% human NPH insulin twice daily (70/30) alone. Insulin dosage was titrated to target fasting blood glucose (FBG) ≤100 mg/dL (≤5.6 mmol/L) with GLAR+OAD and to both FBG ≤100 mg/dL and pre-dinner BG ≤100 mg/dL with 70/30, using a weekly forced-titration algorithm. To measure treatment satisfaction and change in treatment satisfaction, patients completed the Diabetes Treatment Satisfaction Questionnaire (DTSQs; status version) at baseline and endpoint and DTSQc (change version) at endpoint; 323 and 253 patients were included in the analysis of DTSQs and DTSQc scores, respectively. Maximum scores of 36.00 (DTSQs) and 18.00 (DTSQc) indicated optimal treatment satisfaction and improvement in treatment satisfaction. Mean HbA_{1c} decrease was significantly greater (−1.64 vs −1.31%; p=0.0003) and more patients reached HbA_{1c} ≤7.0% without nocturnal hypoglycemia (45.5 vs 28.6%; p=0.0013) in the GLAR+OAD versus 70/30 group. At baseline, there was no difference in treatment satisfaction scores between the groups (GLAR+OAD: 26.91 vs 70/30: 26.26; p=0.3603). At study end, scores increased in both groups but changes were significantly greater in the GLAR+OAD vs the 70/30 group (+3.95 vs +2.32; p=0.0022). For DTSQc, the treatment satisfaction score at study end was higher in GLAR+OAD- versus 70/30-treated patients (mean score 14.00 vs 11.54; p=0.0012). Initiating insulin therapy with the GLAR+OAD regimen is associated with a greater improvement in treatment satisfaction versus switching to twice-daily 70/30 alone.

INTRODUCTION

- In type 2 diabetes, many patients treated with oral antidiabetic agents (OADs) require supplemental insulin therapy to achieve good glycemic control (HbA_{1c} ≤7%)[1]
- In these patients, physicians often stop OADs and introduce twice-daily premixed insulins; nearly 40% of insulin-treated patients with diabetes worldwide receive premixed insulin[2]
- However, there is no consensus on how or when to initiate insulin in patients with type 2 diabetes
- Once-daily insulin glargine (LANTUS®) plus OADs has recently been shown to provide better glycemic control with fewer hypoglycemic episodes than twice-daily premixed human 70/30 insulin (Insulin Actraphane HM 30/70®; premixed insulin) alone[3]
- Presented here are additional findings from this study[3] concerning patients' treatment satisfaction

STUDY OBJECTIVE

- To assess the effect of initiating insulin therapy with insulin glargine while continuing OADs versus switching to premixed insulin alone in patients with type 2 diabetes regarding:
  - Glycemic control (as assessed by HbA_{1c} levels)
  - Treatment satisfaction (as assessed by the Diabetes Treatment Satisfaction Questionnaire [DTSQ])

STUDY DESIGN AND METHODS

Patients

- Patients aged 35–75 years with type 2 diabetes treated with OADs (stable dose of sulfonylureas [glimepiride; Amaryl® 3 or 4 mg] and metformin [≥850 mg]) for ≥1 month prior to the study, and no prior insulin use
- HbA_{1c} levels were 7.5–10.5%, fasting blood glucose (FBG) levels were ≥120 mg/dL (≥6.7 mmol/L) and body mass index (BMI) values were ≤35 kg/m² at screening

Study design

- The study was an open-label, randomized, parallel group, multicenter (n=66), multinational (n=10 European countries), 24-week study, with an additional 1–4-week screening phase (Figure 1)
- The forced titration schedule is shown in Table 1
- Patients completed the status version of the DTSQ (DTSQs) during the screening period and at endpoint and the change version (DTSQc) at endpoint (Table 2)
- Maximum scores of 36.00 (DTSQs) and 18.00 (DTSQc) indicate optimal treatment satisfaction and improvement in treatment satisfaction
- The DTSQ was developed as a status measure of satisfaction with treatment and perceptions of glycemic control in patients with diabetes[4,5] and is recommended by the World Health Organization and the International Diabetes Federation as a measure of psychological outcomes of diabetes care[6]

Figure 1. Study design

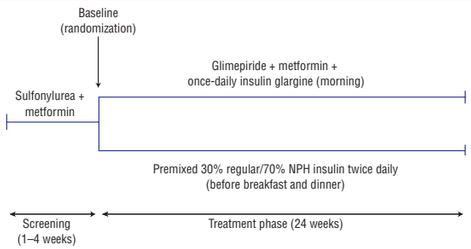


Table 1. Forced insulin titration schedule

Start with 10 IU/Day (Insulin Glargine) or 20 IU/Day (Premixed Insulin) Dose and Adjust Weekly	
Self-monitored FBG (GLAR + OAD group) (mg/dL) or fasting and pre-dinner blood glucose levels (PREMIX) for 2 consecutive days with no hypoglycemia	Increase in insulin dose (IU/day)
≥180	8
140–180	6
120–140	4
100–120	2
Treat to target FBG ≤100 mg/dL	

GLAR + OAD=insulin glargine plus oral antidiabetic agents (OADs); PREMIX=premixed insulin; FBG=fasting blood glucose

Table 2. Diabetes Treatment Satisfaction Questionnaire (DTSQ)

1	How satisfied are you with your current treatment?	very satisfied	6	5	4	3	2	1	0 very dissatisfied
2	How often have you felt that your blood sugars have been unacceptably high recently?	most of the time	6	5	4	3	2	1	0 none of the time
3	How often have you felt that your blood sugars have been unacceptably low recently?	most of the time	6	5	4	3	2	1	0 none of the time
4	How convenient have you been finding your treatment recently?	very convenient	6	5	4	3	2	1	0 very inconvenient
5	How flexible have you been finding your treatment recently?	very flexible	6	5	4	3	2	1	0 very inflexible
6	How satisfied are you with your understanding of your diabetes?	very satisfied	6	5	4	3	2	1	0 very dissatisfied
7	Would you recommend this form of treatment to someone else with your kind of diabetes?	yes, I would definitely recommend the treatment	6	5	4	3	2	1	0 no, I would definitely not recommend the treatment
8	How satisfied would you be to continue with your present form of treatment?	very satisfied	6	5	4	3	2	1	0 very dissatisfied

Outcome measures

Primary measure

- Change in HbA_{1c} level from baseline to endpoint

Secondary measures

- HbA_{1c} level (≤7.0% with no nocturnal hypoglycemia)
- Treatment satisfaction and change in treatment satisfaction scores:
  - Treatment satisfaction (sum of items 1, 4, 5, 6, 7 and 8)

Definition of nocturnal hypoglycemia

- Symptomatic or asymptomatic (blood glucose level <60 mg/dL [<3.3 mmol/L]) occurring between bedtime and getting up in the morning

Statistical analyses

- The intent-to-treat (ITT) population (all randomized patients who received at least one dose of study medication) was used for all efficacy and safety analyses
- Analysis of covariance was performed to compare changes in HbA_{1c} and secondary continuous variables between the treatment groups

RESULTS

Patients

- All 364 patients included in the ITT population were included in the HbA_{1c} analysis[3]
- A total of 323 patients were included in the analysis of the DTSQs:
  - 159 randomized to the insulin glargine plus OADs group
  - 164 randomized to the premixed insulin group
- The DTSQc was only administered to patients if a validated version in the local language was available; a total of 253 patients were included in the analysis of the DTSQc:
  - 128 randomized to the insulin glargine plus OADs group
  - 125 randomized to the premixed insulin group
- Baseline characteristics were similar in both groups (Table 3)

Table 3. Baseline characteristics[3]

Characteristic	Insulin glargine + OADs	Premixed insulin
Patients (n)	177	187
Male/female (%*)	61/39	57/43
Age (years)	60.9 ± 8.7	60.4 ± 9.1
Weight (kg)	85.1 ± 14.7	84.6 ± 14.2
BMI (kg/m²)	29.5 ± 3.6	29.6 ± 3.6
Duration of diabetes (years)	9.9 ± 7.3	9.9 ± 6.4
Duration of OADs treatment (years)	7.0 ± 5.8	7.3 ± 5.5
C-peptide (ng/mL)	3.5 ± 2.1	3.5 ± 2.1
HbA_{1c} (%)	8.85 ± 0.98	8.83 ± 0.87
FBG, mg/dL (mmol/L)	171 ± 35 (9.5 ± 1.9)	172 ± 38 (9.6 ± 2.1)
Patients scoring maximum on DTSQs at screening (%)	9.4	9.7

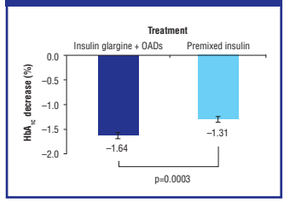
*Data are mean ± standard deviation, except where specified; BMI=body mass index; OADs=oral antidiabetic agents (sulfonylurea plus metformin); FBG=fasting blood glucose; DTSQs=Diabetes Treatment Satifaction Questionnaire status

Glycemic control[3]

HbA_{1c} levels

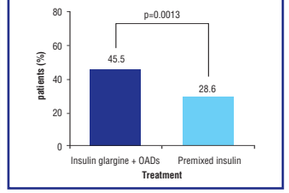
- Adjusted mean between-treatment difference in HbA_{1c} levels and proportion of patients achieving HbA_{1c} ≤7% without an episode of confirmed nocturnal hypoglycemia are illustrated for both treatment groups in Figures 2 and 3
- The adjusted mean decrease in HbA_{1c} levels and the percentage of patients achieving HbA_{1c} ≤7.0% without nocturnal hypoglycemia was significantly greater in the insulin glargine plus OADs group versus the premixed insulin group (p=0.0003 and p=0.0013, respectively)

Figure 2. Improvement in HbA_{1c} (adjusted mean decrease from baseline to endpoint[3])



OAD=oral antidiabetic agents

Figure 3. Proportion of all patients reaching HbA_{1c} ≤7%, without experiencing nocturnal hypoglycemia[3]

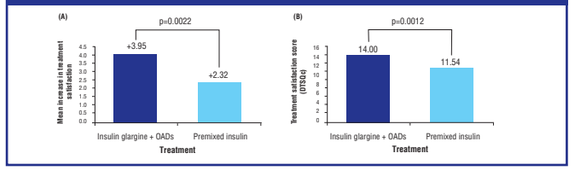


OAD=oral antidiabetic agents

Treatment satisfaction

- At baseline, there was no difference in treatment satisfaction scores between the groups (26.91 vs 26.26: insulin glargine plus OADs versus premixed insulin; p=0.3603)
- At study end, the scores improved in both groups (to 30.86 vs 28.58: insulin glargine plus OADs versus premixed insulin); however, the changes from the screening period were significantly greater in the insulin glargine plus OADs versus the premixed group (Figure 4A)
- For DTSQc, the treatment satisfaction score at study end was higher in insulin glargine plus OADs versus premixed insulin-treated patients showing a significantly greater improvement in treatment satisfaction with insulin glargine plus OADs (Figure 4B)

Figure 4. Overall mean increase in Diabetes Treatment Satisfaction as assessed by (A) endpoint minus screening DTSQ scores and (B) DTSQc scores at endpoint



CONCLUSIONS

- These results show that as previously reported[3], adding a single injection of insulin glargine to prior OADs is superior to the premixed insulin alone regimen in achieving appropriate glycemic control in terms of:
  - Significantly better HbA_{1c} improvements over the treatment period
  - Significantly more patients achieving HbA_{1c} ≤7%, without experiencing nocturnal hypoglycemia
- The insulin glargine plus OADs regimen was also associated with a greater improvement in patients' treatment satisfaction versus switching to twice-daily premixed insulin alone
- When patients made direct comparisons between treatment at endpoint and treatment prior to the study using the DTSQc, their scores revealed an even more positive assessment of treatment satisfaction for the insulin glargine plus OADs versus the premixed insulin group
- In conclusion, this study demonstrates that for patients with type 2 diabetes who are inadequately controlled with OADs, adding a once-daily injection of insulin glargine is more effective and results in less nocturnal hypoglycemia and greater treatment satisfaction than switching to twice-daily injections of premixed insulin

REFERENCES

1. ADA Position Statement. Standards of medical care for patients with diabetes mellitus. *Diabetes Care* 2002; **25**: S33–S49.
2. Koivisto V, Tuominen J, Ebeling P. Lispro Mix25 insulin as premeal therapy in type 2 diabetic patients. *Diabetes Care* 1999; **22**: 459–462.
3. Janka HU, Plewe G, Riddle MC, et al. Comparison of basal insulin added to oral agents versus twice-daily premixed insulin as initial insulin therapy for type 2 diabetes. *Diabetes Care* 2005; **28**(2): 254–259.
4. Bradley C, Lewis KS. Measures of psychological well–being and treatment satisfaction developed from the responses of people with tablet-treated diabetes. *Diabetic Med* 1990; **7**(5): 445–451.
5. Bradley C. The Diabetes Treatment Satisfaction Questionnaire: DTSQ. In: Bradley C, ed. Handbook of Psychology and Diabetes: a Guide to Psychological Measurement in Diabetes Research and Practice. Switzerland: Harwood Academic Publishers, 1994.
6. Bradley C, Gamsu DS. Guidelines for encouraging psychological well-being: Report of a Working Group of the World Health Organization Regional Office for Europe and International Diabetes Federation European Region St. Vincent Declaration Action Programme for Diabetes. *Diabet Med* 1994; **11**(5): 510–516.

For access to the Diabetes Treatment Satisfaction Questionnaire, contact c.bradley@rhul.ac.uk

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