These results are supplied for informational purposes only.
Prescribing decisions should be made based on the approved package insert in the country of prescription.

Sponsor / Company: Sanofi **Drug substance(s):** Insulin Glulisine (HMR1964) Insulin Glargine (HOE901)	**Study Identifiers:** NCT01079364, EudraCT 2009-015742-34 **Study code:** APIDR_L_04717
Title of the study: Better Acceptance of a Single injection Apidra (insulin glulisine) Added to once daily Lantus (insulin glargine) versus twice daily Premixed insulin in a real Life Use Setting (BASAAL PLUS)	
Study center(s): Study conducted in The Netherlands: 27 active sites	
Study period: Date first patient enrolled: 26/01/10 Date last patient completed: 10/07/12	
Phase of development: Phase 4	
Objectives: Primary: To demonstrate non-inferiority of once daily injection of insulin glargine (Lantus®) plus one injection of mealtime insulin glulisine (Apidra®) at the main meal versus twice daily premixed insulin (NovoMix® 30/70) based on the reduction of HbA1c percentage from baseline to endpoint. Secondary: - To determine treatment satisfaction (DTSQs, DTSQc and ITSQ) - To determine the mean HbA1c, Fasting Blood Glucose (FBG), prandial BG and proportion of patients with a HbA1c <7%. - To determine the effect on adverse events (e.g. symptomatic hypoglycemic events, weight gain and injection site reactions). - To determine the total insulin dose, average insulin glargine, insulin glulisine and premixed insulin dosages.	
Methodology: National, open, multi-center, prospective (26 weeks), randomized, parallel phase IV clinical study	
Number of patients: Planned: 220 Randomized: 52 (26 per treatment arm) Treated: 52 Evaluated: 3 months: 45; 6 months: 44. Efficacy: 44 Safety : 45	
Diagnosis and criteria for inclusion: - Patients with type 2 diabetes mellitus treated with insulin glargine once daily and oral blood glucose lowering - medication - Patients with a HbA1c > 53 mmol/mol (7%) - Patients for which the physician indicates that the best possible FBG value, with insulin glargine and oral blood glucose lowering medication only, has been reached. - Aged 18 years and above - Obtained written informed consent	

Study treatments

Investigational medicinal product(s):

Formulation:

- insulin glargine (Lantus®)
- insulin glulisine (Apidra®)
- biphasic insulin aspart/insulin aspart protamine (NovoMix 30/70®)

Route(s) of administration: Subcutaneously

Duration of treatment: 24 weeks

Duration of observation: 26 weeks

Criteria for evaluation:

- HbA1C
- treatment satisfaction (DTSQs, DTSQc and ITSQ)
- changes from baseline in HbA1c, FBG, prandial BG and proportion of patients with a HbA1c < 53 mmol/mol (7%)
- adverse events (symptomatic hypoglycemic events, weight gain and injection site reactions)
- total insulin dose, average insulin glargine, insulin glulisine and premixed insulin dosages

Statistical methods:

Sample size calculation:

It was calculated that 109 patients per treatment arm would be necessary. Eventually, this was not reached and no more than 52 patients were randomized.

Regarding the statistics, baseline values were compared between groups using Student's t-test for unpaired samples. Effects of treatment were compared using ANOVA or ANCOVA for repeated measurements.

Summary:

This was an aborted study, because it took 2 years to include 52 patients and it was deemed improbable that recruitment would proceed any faster (most likely even slower) for the next 168 patients required per protocol. A lot of actions were taken to increase the recruitment (mailings, phone-calls, meetings), but due to the fact that there were less eligible patients than expected (better HbA1C than allowed according to protocol) and less patients willing to participate (due to randomization). Finally, it was decided that it would take too long to conduct the study and the study was aborted.

Both interventions similarly reduced HbA1C in the course of 24 weeks of treatment. There was no significant difference between interventions in terms of glucose control (i.e. HbA1C, blood glucose levels at several standard time points during 4 clusters of 2 consecutive days) or total insulin dose. Both treatment strategies appeared safe: although approximately one half of patients in both groups had experienced one or more episodes of symptomatic hypoglycemia by 24 weeks of intervention, there were no serious hypoglycemic events reported. Other adverse events were similar in both groups as well, and very unlikely to be related to the study drugs. Finally, there were no significant differences between groups in terms of satisfaction with treatment, as evaluated by validated and internationally well-accepted specific questionnaires.

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