ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 08/01/2011

Grantor: CDER IND/IDE Number: 61,956 Serial Number:

Insulin Glulisine in Type 2 Diabetic Patients (Basal Plus)

This study has been completed.

Sponsor:	Sanofi
Collaborators:	
Information provided by:	Sanofi
ClinicalTrials.gov Identifier:	NCT00360698

Purpose

To evaluate the efficacy of a single injection of glulisine before the main meal added to insulin glargine plus oral antidiabetic drugs (OADs) compared to insulin glargine plus OADs in Type 2 diabetic patients poorly controlled with basal insulin plus OADs.

Condition	Intervention	Phase
Diabetes Mellitus, Type 2	Drug: Insulin Glargine Drug: Glimepiride Drug: Insulin Glulisine Drug: Metformin	Phase 4

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Open Label, Randomized, Safety/Efficacy Study
Official Title: Comparison of Two Therapeutic Strategies for Treating Type 2 Diabetic Patients Poorly Controlled With Basal Insulin Associated With Oral Antidiabetic Drugs : 6-month Proof of Concept Study.

Further study details as provided by Sanofi:

Primary Outcome Measure:

- Patients With Glycosylated Haemoglobin (HbA1c) Value < 7% [Time Frame: at the end of treatment (week 24)] [Designated as safety issue: No]

Glycosylated Haemoglobin (HbA1c) is a biological parameter that reflects the blood glucose concentration over a long period of time. It is the standard parameter for glycemic control follow -up in diabetic patients. this parameter is expressed in percentage (%) and the target in diabetes management is to reach a HbA1c <7%

Secondary Outcome Measures:

- Glycosylated Haemoglobin (HbA1c) Value [Time Frame: at the end of treatment (week 24)] [Designated as safety issue: No]
- Change in Glycosylated Haemoglobin (HbA1c) Value [Time Frame: from baseline to the end of treatment (week 24)] [Designated as safety issue: No]
- Daily Mean Plasma Glucose [Time Frame: at the end of treatment (week 24)] [Designated as safety issue: No]
- Change in Daily Mean Plasma Glucose [Time Frame: from baseline to the end of treatment (week 24)] [Designated as safety issue: No]
- Change in Weight [Time Frame: from baseline to the end of treatment (week 24)] [Designated as safety issue: No]
- Daily Dose of Insulin Glargine [Time Frame: at the end of treatment (week 24)] [Designated as safety issue: No]
  Mean of 3 daily doses reported during the week prior to the final visit
- Daily Dose of Insulin Glulisine [Time Frame: at the end of treatment (week 24)] [Designated as safety issue: No]
  Mean of 3 daily doses reported during the week prior to the final visit
- Rate of Symptomatic Hypoglycemia With Plasma Glucose < 70mg/dL [Time Frame: during treatment period (12 weeks)] [Designated as safety issue: No]
- Rate of Nocturnal Symptomatic Hypoglycemia With Plasma Glucose < 70mg/dL [Time Frame: during treatment period (12 weeks)] [Designated as safety issue: No]
- Rate of Severe Symptomatic Hypoglycemia [Time Frame: during treatment period (12 weeks)] [Designated as safety issue: No]

Enrollment: 106
Study Start Date: July 2006
Primary Completion Date: August 2008
Study Completion Date: August 2008

Arms	Assigned Interventions
insulin glulisine+insulin glargine+metformin +glimepiride Bolus arm	Drug: Insulin Glargine One daily injection at bedtime Drug: Glimepiride At same dosage as during the run-in period Drug: Insulin Glulisine One bolus given before the main meal Drug: Metformin At same dosage as during the run-in period
insulin glargine+metformin+glimepiride Control arm	Drug: Insulin Glargine One daily injection at bedtime Drug: Glimepiride At same dosage as during the run-in period Drug: Metformin At same dosage as during the run-in period

Eligibility

Ages Eligible for Study: 18 Years to 75 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Diabetes Mellitus, Type 2
- 25 < BMI < 45 kg/m²
- 7,5% < HbA1c < 9%
- Treated with a basal insulin (NPH, Insulin Zinc, Insulin glargine or Insulin detemir), and at least 1g metformin daily, for more than 3 months

Exclusion Criteria:

- Type 1 diabetes mellitus
- Treatment with OADs only
- Treatment with thiazolidinediones, with exenatide or with pramlintide
- Treatment with an insulin other than basal insulin (Premix, rapid insulin, fast-acting insulin analogue)
- Active proliferative diabetic retinopathy,
- Pregnancy (women of childbearing potential must have a negative pregnancy test at study entry and effective contraception)
- Breast-feeding
- History of hypersensitivity to the study drugs or to drugs with a similar chemical structure.
- Treatment with systemic corticosteroids in the 3 months prior to study entry
- Treatment with any investigational product in the 2 months prior to study entry
- Previous treatment with insulin glulisine
- Likelihood of requiring treatment during the study period with drugs not permitted by the clinical study protocol
- Clinically relevant cardiovascular, hepatic, neurological, endocrine, or other major disease making implementation of the protocol or interpretation of the study results difficult
- Impaired hepatic function
- Impaired renal function
- History of drug or alcohol abuse

The above information is not intended to contain all considerations relevant to a patient's potential participation in a clinical trial.

Contacts and Locations

Locations

United States, New Jersey

Sanofi-aventis

Bridgewater, New Jersey, United States, 08807

Bulgaria

sanofi-aventis

Sofia, Bulgaria

Russian Federation
sanofi-aventis
Moscow, Russian Federation
United Kingdom
Sanofi-aventis
Guildford, United Kingdom

Investigators

Study Director:	PILORGET Valérie, MD	Sanofi-aventis

More Information

Responsible Party:	sanofi-aventis (Trial Transparency Team)
Study ID Numbers:	HMR1964A_4002 EUDRACT # : 2005-002614-38
Health Authority:	United States: Institutional Review Board United States: Food and Drug Administration

Study Results

Participant Flow

Pre-Assignment Details	During Run-In period patients were not assigned to a treatment group. They were all treated with Insulin Glargine + Metformin + Glimepiride.

Reporting Groups

	Description
Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glulisine (One daily injection at main meal) + Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)
Insulin Glargine+Metformin +Glimepiride	Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)

Run-In

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
Started	0	135
Completed	0	125 [1]

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
Not Completed	0	10
Physician Decision	0	1
Withdrawal by Subject	0	2
Non compliance with treatment procedure	0	1
Sponsor request	0	2
Patient did not meet inclusion criteria	0	1
Patient personal reasons	0	2
Need of insulin with meals	0	1

[1] 19 patients completed the run-in but were not eligible for randomization in the treatment period

Treatment Period

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
Started	49	57
Completed	48	56
Not Completed	1	1
Non compliance with treatment procedure	1	0
Early termination by error	0	1

Baseline Characteristics

Reporting Groups

	Description
Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glulisine (One daily injection at main meal) + Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)
Insulin Glargine+Metformin +Glimepiride	Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)

Baseline Measures

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride	Total
Number of Participants	49	57	106
Age, Continuous [units: years] Mean (Standard Deviation)	60.6 (6.73)	59.3 (8.84)	59.9 (7.92)
Gender, Male/Female [units: participants]			
Female	29	35	64
Male	20	22	42
Region of Enrollment [units: participants]			
United States	23	27	50
United Kingdom	11	14	25
Russian Federation	15	16	31
Body Mass Index (BMI) [1] [units: kg/m²] Mean (Standard Deviation)	33.2 (5.30)	33.3 (4.39)	33.3 (4.80)
Daily Mean Plasma Glucose [2] [units: mg/dL] Mean (Standard Deviation)	170.2 (27.86)	167.4 (39.41)	169 (34.33)
Duration of diabetes [units: years] Mean (Standard Deviation)	12.1 (7.29)	11.0 (7.02)	11.5 (7.13)
Glycosylated Haemoglobin (HbA1c) [units: percent] Mean (Standard Deviation)	7.8 (0.60)	8.0 (0.67)	7.9 (0.64)
Weight [1] [units: kg] Mean (Standard Deviation)	91.5 (16.60)	92.9 (17.15)	92.3 (16.83)

[1] Total patients analyzed n=105 due to one missing data in the "insulin glulisine+insulin glargine+metformin+glimepiride" group

[2] Patients having a baseline value and a value on treatment:

insulin glulisine+insulin glargine+metformin+glimepiride group n=47 patients, insulin glargine+metformin+glimepiride group n=55 patients

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Patients With Glycosylated Haemoglobin (HbA1c) Value < 7%
Measure Description	Glycosylated Haemoglobin (HbA1c) is a biological parameter that reflects the blood glucose concentration over a long period of time. It is the standard parameter for glycemic control follow -up in diabetic patients. this parameter is expressed in percentage (%) and the target in diabetes management is to reach a HbA1c <7%
Time Frame	at the end of treatment (week 24)
Safety Issue?	No

Analysis Population Description

Modified Intent to treat (ITT) population, LOCF (Last Observation Carried Forward)

Reporting Groups

	Description
Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glulisine (One daily injection at main meal) + Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)
Insulin Glargine+Metformin +Glimepiride	Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)

Measured Values

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
Number of Participants Analyzed	49	57
Patients With Glycosylated Haemoglobin (HbA1c) Value < 7% [units: percentage of participants]	22.4	8.8

Statistical Analysis 1 for Patients With Glycosylated Haemoglobin (HbA1c) Value < 7%

Statistical Analysis Overview	Comparison Groups	Insulin Glulisine+Insulin Glargine+Metformin+Glimepiride, Insulin Glargine+Metformin +Glimepiride

	Comments	The null-hypothesis stated no differences between the 2 treatment groups regarding the percentage of patients with Glycosylated Haemoglobin (HbA1c) level <7%. A sample size of 98 randomized (49/arm) patients would allow to demonstrate with 80% power that 40 % of patients in the Insulin Glulisine+Insulin Glargine+Metformin+Glimepiride group would achieve a HbA1c level < 7 % compared to 15 % of patients in the Insulin Glargine +Metformin+Glimepiride group(5% alpha risk, 2-sided test).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0499
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Risk Difference (RD)
	Estimated Value	13.68
	Confidence Interval	(2-Sided) 95% 0.01 to 28.37
	Estimation Comments	Difference in percentage between groups: Insulin Glulisine+Insulin Glargine+Metformin +Glimepiride group - Insulin Glargine+Metformin+Glimepiride group

2. Secondary Outcome Measure:

Measure Title	Glycosylated Haemoglobin (HbA1c) Value
Measure Description	
Time Frame	at the end of treatment (week 24)
Safety Issue?	No

Analysis Population Description

Modified ITT population, LOCF

Reporting Groups

	Description
Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glulisine (One daily injection at main meal) + Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)
Insulin Glargine+Metformin +Glimepiride	Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)

Measured Values

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
Number of Participants Analyzed	49	57
Glycosylated Haemoglobin (HbA1c) Value [units: percent] Mean (Standard Deviation)	7.5 (0.64)	7.8 (0.85)

3. Secondary Outcome Measure:

Measure Title	Change in Glycosylated Haemoglobin (HbA1c) Value
Measure Description	
Time Frame	from baseline to the end of treatment (week 24)
Safety Issue?	No

Analysis Population Description

Modified ITT population, LOCF

Reporting Groups

	Description
Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glulisine (One daily injection at main meal) + Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)
Insulin Glargine+Metformin +Glimepiride	Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)

Measured Values

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
Number of Participants Analyzed	49	57
Change in Glycosylated Haemoglobin (HbA1c) Value [units: percent] Least Squares Mean (Standard Error)	-0.37 (0.085)	-0.11 (0.078)

Statistical Analysis 1 for Change in Glycosylated Haemoglobin (HbA1c) Value

Statistical Analysis Overview	Comparison Groups	Insulin Glulisine+Insulin Glargine+Metformin+Glimepiride, Insulin Glargine+Metformin +Glimepiride
	Comments	The null-hypothesis stated no difference between the 2 treatment groups regarding the adjusted mean change from baseline in Glycosylated Haemoglobin (HbA1c) at the end of treatment.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.029
	Comments	Threshold for statistical significance (alpha) = 0.05 ; 2 sided-test
	Method	ANCOVA
	Comments	The analysis is an ANCOVA analysis on the change with group as fixed effect and baseline HbA1c as covariate

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	-0.26
	Confidence Interval	(2-Sided) 95% -0.49 to -0.03
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.116
	Estimation Comments	Difference between groups: Insulin Glulisine+Insulin Glargine+Metformin+Glimepiride group - Insulin Glargine+Metformin+Glimepiride group

4. Secondary Outcome Measure:

Measure Title	Daily Mean Plasma Glucose
Measure Description	
Time Frame	at the end of treatment (week 24)
Safety Issue?	No

Analysis Population Description
Modified ITT population, LOCF

Reporting Groups

	Description
Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glulisine (One daily injection at main meal) + Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)
Insulin Glargine+Metformin +Glimepiride	Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)

Measured Values

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
Number of Participants Analyzed	47	55
Daily Mean Plasma Glucose [units: mg/dL] Mean (Standard Deviation)	154.7 (28.62)	165.8 (37.48)

5. Secondary Outcome Measure:

Measure Title	Change in Daily Mean Plasma Glucose
Measure Description	
Time Frame	from baseline to the end of treatment (week 24)
Safety Issue?	No

Analysis Population Description
Modified ITT population, LOCF

Reporting Groups

	Description
Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glulisine (One daily injection at main meal) + Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)
Insulin Glargine+Metformin +Glimepiride	Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)

Measured Values

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
Number of Participants Analyzed	47	55
Change in Daily Mean Plasma Glucose [units: mg/dL] Least Squares Mean (Standard Error)	-15.01 (3.661)	-2.07 (3.384)

Statistical Analysis 1 for Change in Daily Mean Plasma Glucose

Statistical Analysis Overview	Comparison Groups	Insulin Glulisine+Insulin Glargine+Metformin+Glimepiride, Insulin Glargine+Metformin +Glimepiride
	Comments	The null-hypothesis stated no differences between the 2 treatment groups regarding the adjusted mean change from baseline in daily mean plasma glucose at the end of treatment.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0109
	Comments	Threshold for statistical significance (alpha) = 0.05 ; 2 sided-test
	Method	ANCOVA
	Comments	The analysis is an ANCOVA analysis on the change with group as fixed effect and baseline daily mean plasma glucose as covariate

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	-12.94
	Confidence Interval	(2-Sided) 95%

		-22.83 to -3.04
	Parameter Dispersion	Type: Standard Error of the mean Value: 4.987
	Estimation Comments	Difference between groups: Insulin Glulisine+Insulin Glargine+Metformin+Glimepiride group - Insulin Glargine+Metformin+Glimepiride group

6. Secondary Outcome Measure:

Measure Title	Change in Weight
Measure Description	
Time Frame	from baseline to the end of treatment (week 24)
Safety Issue?	No

Analysis Population Description

Modified ITT population, LOCF

Reporting Groups

	Description
Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glulisine (One daily injection at main meal) + Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)
Insulin Glargine+Metformin +Glimepiride	Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)

Measured Values

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
Number of Participants Analyzed	48	56
Change in Weight [units: kg] Least Squares Mean (Standard Error)	0.46 (0.316)	0.22 (0.293)

Statistical Analysis 1 for Change in Weight

Statistical Analysis Overview	Comparison Groups	Insulin Glulisine+Insulin Glargine+Metformin+Glimepiride, Insulin Glargine+Metformin +Glimepiride

	Comments	The null-hypothesis stated no differences between the 2 treatment groups regarding the adjusted mean change from baseline in weight at the end of treatment.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.5762
	Comments	Threshold for statistical significance (alpha) = 0.05 ; 2 sided-test
	Method	ANCOVA
	Comments	The analysis is an ANCOVA analysis on the change with group as fixed effect and baseline weight as covariate

Method of Estimation	Estimation Parameter	Mean Difference (Net)
	Estimated Value	0.24
	Confidence Interval	(2-Sided) 95% -0.61 to 1.1
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.431
	Estimation Comments	Difference between groups: Insulin Glulisine+Insulin Glargine+Metformin+Glimepiride group - Insulin Glargine+Metformin+Glimepiride group

7. Secondary Outcome Measure:

Measure Title	Daily Dose of Insulin Glargine
Measure Description	Mean of 3 daily doses reported during the week prior to the final visit
Time Frame	at the end of treatment (week 24)
Safety Issue?	No

Analysis Population Description
Modified ITT population, LOCF

Reporting Groups

	Description
Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glulisine (One daily injection at main meal) + Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)

	Description
Insulin Glargine+Metformin +Glimepiride	Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)

Measured Values

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
Number of Participants Analyzed	49	57
Daily Dose of Insulin Glargine [units: units of insulin glargine per day] Mean (Standard Deviation)	54.7 (34.84)	62.2 (34.85)

8. Secondary Outcome Measure:

Measure Title	Daily Dose of Insulin Glulisine
Measure Description	Mean of 3 daily doses reported during the week prior to the final visit
Time Frame	at the end of treatment (week 24)
Safety Issue?	No

Analysis Population Description

Modified ITT population, LOCF

Reporting Groups

	Description
Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glulisine (One daily injection at main meal) + Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)
Insulin Glargine+Metformin +Glimepiride	Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)

Measured Values

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
Number of Participants Analyzed	49	0
Daily Dose of Insulin Glulisine [units: units of insulin glulisine per day]	12.8 (6.59)	

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
Mean (Standard Deviation)		

9. Secondary Outcome Measure:

Measure Title	Rate of Symptomatic Hypoglycemia With Plasma Glucose < 70mg/dL
Measure Description	
Time Frame	during treatment period (12 weeks)
Safety Issue?	No

Analysis Population Description
Safety population

Reporting Groups

	Description
Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glulisine (One daily injection at main meal) + Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)
Insulin Glargine+Metformin +Glimepiride	Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)

Measured Values

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
Number of Participants Analyzed	49	57
Rate of Symptomatic Hypoglycemia With Plasma Glucose < 70mg/dL [units: Number of hypoglycemia per patient-year] Mean (Standard Deviation)	8.19 (14.603)	7.68 (13.996)

Statistical Analysis 1 for Rate of Symptomatic Hypoglycemia With Plasma Glucose < 70mg/dL

Statistical Analysis Overview	Comparison Groups	Insulin Glulisine+Insulin Glargine+Metformin+Glimepiride, Insulin Glargine+Metformin +Glimepiride

	Comments	The null-hypothesis stated no difference between the 2 treatment groups regarding the rate of symptomatic hypoglycemia with plasma glucose <70 mg/dL during the treatment period.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.958
	Comments	Threshold for statistical significance (alpha) = 0.05 ; 2 sided-test
	Method	Wilcoxon (Mann-Whitney)
	Comments	[Not specified]

10. Secondary Outcome Measure:

Measure Title	Rate of Nocturnal Symptomatic Hypoglycemia With Plasma Glucose < 70mg/dL
Measure Description	
Time Frame	during treatment period (12 weeks)
Safety Issue?	No

Analysis Population Description

Safety population

Reporting Groups

	Description
Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glulisine (One daily injection at main meal) + Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)
Insulin Glargine+Metformin +Glimepiride	Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)

Measured Values

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
Number of Participants Analyzed	49	57
Rate of Nocturnal Symptomatic Hypoglycemia With Plasma Glucose < 70mg/dL [units: Number of hypoglycemia per patient-year]	1.62 (3.418)	3.95 (9.339)

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
Mean (Standard Deviation)		

Statistical Analysis 1 for Rate of Nocturnal Symptomatic Hypoglycemia With Plasma Glucose < 70mg/dL

Statistical Analysis Overview	Comparison Groups	Insulin Glulisine+Insulin Glargine+Metformin+Glimepiride, Insulin Glargine+Metformin +Glimepiride
	Comments	The null-hypothesis stated no difference between the 2 treatment groups regarding the rate of nocturnal symptomatic hypoglycemia with plasma glucose <70 mg/dL during the treatment period.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.302
	Comments	Threshold for statistical significance (alpha) = 0.05 ; 2 sided-test
	Method	Wilcoxon (Mann-Whitney)
	Comments	[Not specified]

11. Secondary Outcome Measure:

Measure Title	Rate of Severe Symptomatic Hypoglycemia
Measure Description	
Time Frame	during treatment period (12 weeks)
Safety Issue?	No

Analysis Population Description
Safety population

Reporting Groups

	Description
Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glulisine (One daily injection at main meal) + Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)

	Description
Insulin Glargine+Metformin +Glimepiride	Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)

Measured Values

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
Number of Participants Analyzed	49	57
Rate of Severe Symptomatic Hypoglycemia [units: Number of hypoglycemia per patient-year] Mean (Standard Deviation)	0.00 (0.000)	0.20 (1.096)

Statistical Analysis 1 for Rate of Severe Symptomatic Hypoglycemia

Statistical Analysis Overview	Comparison Groups	Insulin Glulisine+Insulin Glargine+Metformin+Glimepiride, Insulin Glargine+Metformin +Glimepiride
	Comments	The null-hypothesis stated no difference between the 2 treatment groups regarding the rate of severe symptomatic hypoglycemia during the treatment period.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.192
	Comments	Threshold for statistical significance (alpha) = 0.05 ; 2 sided-test
	Method	Wilcoxon (Mann-Whitney)
	Comments	[Not specified]

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glulisine (One daily injection at main meal) + Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)
Insulin Glargine+Metformin +Glimepiride	Insulin Glargine (One daily injection at bedtime) + Metformin (At same dosage as during the run-in period) + Glimepiride (At same dosage as during the run-in period)

Serious Adverse Events

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
	Affected/At Risk (%)	Affected/At Risk (%)
Total	1/49 (2.04%)	2/57 (3.51%)
Cardiac disorders		
Angina Pectoris [A] *	1/49 (2.04%)	0/57 (0%)
Atrial Fibrillation [A] *	1/49 (2.04%)	0/57 (0%)
Musculoskeletal and connective tissue disorders		
Scleroderma [A] *	0/49 (0%)	1/57 (1.75%)
Tendon Disorder [A] *	0/49 (0%)	1/57 (1.75%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA 8

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Insulin Glulisine+Insulin Glargine +Metformin+Glimepiride	Insulin Glargine+Metformin+Glimepiride
	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/49 (0%)	0/57 (0%)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

If no publication has occurred within 12 months of the completion of the study, the Investigator shall have the right to publish/present independently the results of the study. The Investigator shall provide the Sponsor with a copy of any such presentation/publication for comment at least 30 days before any presentation/submission for publication. If requested by the Sponsor, any presentation/submission shall be delayed up to 90 days, to allow the Sponsor to preserve its proprietary rights.

Results Point of Contact:

Name/Official Title: Medical Affairs study director
Organization: sanofi-aventis
Phone:
Email: publicregistryGMA@sanofi-aventis.com