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-aventis	**ClinicalTrials.gov Identifier:**	NCT00397553
		Study Code:	HMR1964A_3517
Generic drug name:	Insulin Glulisine	**Date:**	29 June 2009

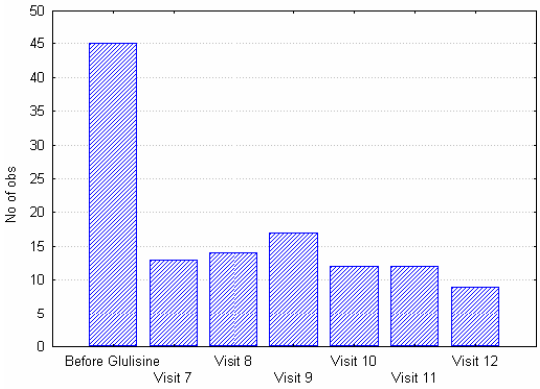
Title of the study:	Multicenter, Open, phase III clinical study of efficacy and safety of Insulin glulisine (HMR1964) injected subcutaneously in patients with type1 diabetes Mellitus using also insulin glargine during 26 weeks of therapy. Extension period up to 52 weeks. Study number: HMR 1964A_3517
Investigator(s):	1. Endocrinology Scientific Center of Russian Academy of Medical Sciences.Dm. Ulianova str..11. Moscow. 117036. Pr. Shestakova M. 2. Moscow Medical Academy named after I.M. Sechenov. Endocrinology Clinic. Pogodinskaya str..1/1.Moscow.19881.Pr. Melnichenko G. 3. Pavlov St-Peterburg State Medical University. Municipal Clinical Hospital-Peterburg. 194354. Dr Zalevskaya A. 4. St-Petersburg Medical Academy for Advanced Medical Studies. St. Elizabeth Municipal Clinical Hospital. Vavilovykh str..14..St-Peterburg.195257, Pr Vorokhobina N. 5. Moscow State Medico-Stomatologic University. City Clinical Hospital № 63 Durovastr,26/3.Moscow.109090,.Pr Mkrtoymyan A. 6. Russian Academy for Advanced Medical Education. Chasovaya 20str. Moscow. 125315., Pr. Ametov A. 7. Moscow Medical Academy named after I.M.Sechenov. Moscow City Hospital № 67. Salyam Adily str.2. Moscow. 123448. , Pr. Balabolkin M.
Study center(s):	7 sites in Russia
Publications (reference):	-

Study period: Date first patient/subject enrolled:22-Sep-2004/Extension: 30-Jan -2005 Date last patient/subject completed:18-Feb-2005/Extension: 27-Dec-2007	Phase of development: Started as phase III translated into the phase IV (post-registration extension)

Objectives: To provide local data on efficacy and safety of insulin glulisine in patients with type 1 DM receiving insulin glargine as basal insulin therapy	Primary - To evaluate changing of HbA1c from baseline to endpoint. Secondary: - To evaluate changing in HbA1c from baseline to 12, 26, 52 weeks, blood glucose parameters - To evaluate changing in dosage of the mealtime and basal insulins		
Methodology:	Open, non- controlled, non-randomization multicenter survey		
Number of patients/subjects:	Planned: 140	Randomized: NA	Treated: 104
	Efficacy: 104	Safety: 104	Pharmacokinetics: NA
Diagnosis and criteria for inclusion:	Inclusion Criteria: - Type 1 diabetes mellitus - ≥ 18 years old - HbA1c 6.5-11.0% - informed consent form to participate in the study - - BMI <35 kg/m²		
Investigational product: Dose: Administration:	Insulin glulisin Insulin glulisin is to be titrated to achieve the titration goals of 2-hour postprandial BG value 6,7 – 8,9 mmol/l Subcutaneous		
Duration of treatment: 26 weeks		Duration of observation: 52 weeks	
Reference therapy:	NA		
Criteria for evaluation:			
Efficacy:	Primary - Change of HbA1c from baseline to endpoint. Secondary: - Change in HbA1c from baseline to 12, 26, 52 weeks, blood glucose parameters - Change in dosage of the mealtime and basal insulins		

Safety:	- Incidence of severe hypoglycemia, - Treatment-emergent adverse event
Statistical methods:	There was no mathematical basis for the sample size definition. All statistical tests were performed as two-sided with alpha level 5%. Efficacy population included all enrolled patients satisfying inclusion/exclusion criteria. Continuous data described as following: number of non-missing values means value standard deviation. Median and extremes. Quality data described by absolute and relative frequencies. Within-group changes evaluated using paired t-test or Wilcoxon sign test. For discrete/quality data. Within-group evaluated using Mc'Nemar test or modifications. Efficacy: Primary: Change Hba1c from the baseline to endpoint (12 ,26, 52 weeks) in the PP population for the Extension period-104 Secondary: Analyses of all secondary variables in the PP population=104 Safety: Treatment-emergent adverse event

Summary: Efficacy results:	Extension period PP population=104 pts 139 patients completed the initial period (142 enrolled), 139-ITT, 142-PP 101- site 1, male, 49 years old, duration of DM-33, "diabetes foot", previous treatment –NPH +human rapid- no assessment data, loss of the follow-up, 116- site 1, no information, loss of the follow-up, 121 – site 1, female 35 y.o, duration of DM-26 years, previous treatment: NPH +human rapid – no assessment data, loss of the follow-up. All 3 patients do not have efficacy assessment. 104- Continued in Extension. 35-refused due to impossibility to come to the site. Mean age of patients - 35±13 years. Duration of diabetes - 25.3±6.1 years. All patients had diabetes type I. • Insulin glulisine injected subcutaneously in patients with Type1 diabetes mellitus using also insulin glargine has a high clinical efficacy in terms of decrease of HbA1c. Mean level of HbA1c was decreased from 8.8±1.3 % at baseline to 7.5±1.16% after 26 weeks. At the endpoint (52 weeks) HbA1c was 6.9±1.1 % with 95 % CI (6.9. 7.3) with p <0.0001. Mean level of fasting blood glucose (FBG) at baseline was 7.1± 2.8mmol/l. After 26 weeks mean level was 6.3±1.6 mmol/l. At the endpoint 52 weeks mean level was 5.9 ± 1.2 mmol/l with p <0.0001 (median=6.1 mmol/l). • For the introduction period (4 weeks), when NPH was switched to Lantus FBG changed from • Post- prandial glycemia decreased from baseline (week1) to the week 26: mean of 2hour glycemia after breakfast decreased from 7.9 to 7.2 mmol/l. At the end of extension period (52 weeks) post- prandial glycemia was 7.7 ±1.9 mmol/l, p<0.05 • At the entry to the introduction period all patients received NPH. 85% of patients received NPH twice daily, daily dosage 24 UI (max 66, min 7); RHI 20 UI (max 52, min 8). At the baseline median of Insulin glargine dose was 21 UI (max 56 UI, min 8 UI). Median of Insulin glulisine dose was 21 UI (max 45, min 4) At the endpoint median of Insulin glargine dose was 22 UI (max 53 IU, min 8). Median of Insulin glulisine dose was 22 IU (max 45, min 4)

Safety results:	No serious adverse event has been registered. No case of severe hypogliycemia hypoglycemia has been registered for 52 weeks of treatment. The number of nocturnal hypoglycemia decreased from 45 (before glulisin initiation) to 9 (week 26). No assessment for nocturnal hypo during the extension period.  Fig. 1: Change of the rate of noctural hypoglycemia during the study treatment
Date of report:	21-Nov-2008