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Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NCT00489190
		Study Code:	APIDR_L_00041
Generic drug name:	insulin glulisine	**Date:**	19 November 2007

Title of Study:

Local, open, non-randomized phase IV clinical study to evaluate efficacy and tolerability of subcutaneous insulin glulisine (Apidra®) (HMR1964) for the treatment of patients with type I diabetes.

Investigators:

Professor of endocrinology, Almaty Medical University - Rimma Bazarbekova

Co-investigator:

Sholpan Aubakirova (associate professor, Almaty Medical University).

Study centre(s):

Shymkent oblast, endocrinological dispensary

Municipal hospital, Ust-Kamenogorsk city, endocrinological department

Municipal hospital №7, Almaty city, endocrinological department.

Publication (reference):

Bulletin of endocrinology № 1, 2006 (Вестник эндокринологии №1, 2006)

Studied period (years): 2005 (date of first enrolment) 15 July 2005 (date of last completed) 15 November 2005	**Phase of development**: IV

Objectives:

Primary : Efficacy of subcutaneous injections of insulin glulisine (Apidra®) (HMR1964) for the treatment of patients with type I diabetes

Secondary: evolution of fasting and post-prandial glycemia, frequency of hypoglycemia episodes and insulin doses administered to patients with type I diabetes.

Methodology:

Open label non controlled study of 12 weeks duration with evaluation at baseline and at week 12 of clinical and biological parameters:

- Doses of fast-acting insulin glulisine
- Doses of basal insulin
- Glycemia levels (based on the results of glycemic profile
- HbA1C
- Reports of hypoglycemia episodes
- Adverse events

Number of patients (planned and analysed) :

45 patients in three centers were included and received treatment with the drug under trial.

(This number of patients is considered as quite sufficient for approval of protocol of study in Pharmacological Center of Expertise of Kazakhstan for the purpose of approval of registration (marketing authorisation) of Apidra in Kazakhstan.

Diagnosis and main criteria for inclusion :

- Type 1 diabetes mellitus, based on the data of medical history (onset of diabetes before age of 40, necessity in continuous insulin therapy since the time of diagnosis)

- Males and females above 18

- More than 1 year of continuous insulin therapy with basal-bolus regimen.

- Level of HbA1C from 6,5 to 11%

- BMI (body mass index) less than 35 kg/m²

- Ability and wish to carry out self-control of glycemia with the help of glucometer and patient's diary.

Test product, dose and mode of administration:

Drug code: HMR1964 Insulin glulisine

Production form: cartridge, 3 ml (100 IU/ml)

Insulin administration means: syringe-pen Optipen PRO

A syringe-pen was used to inject insulin.

Insulin glulisine was administered as subcutaneous injections

Duration of treatment:

12 week-therapy.

Reference therapy, dose and mode of administration:

No reference therapy

Criteria for evaluation:

Efficacy:

- Change of the level of hemoglobin HbA1c
- Glycemic profiles
- Average total daily dose of rapid and basal insulin
- Patient's body mass evolution

Safety:

- Frequency of hypoglycemia episodes
- Biological monitoring
- Adverse events

Statistical methods:

Quantitative variables were summarized with the following methods of descriptive statistics: number of patients (N), average, standard deviation (SD), median, minimum and maximum.

Categorical variables were summarized with absolute and relative frequencies.

All the statistic tests were two-sided with the significance level ($p < 0,05$).

No interim analysis was performed within the given trial.

SUMMARY

EFFICACY RESULTS:

Glycemia evolution from baseline to week 12:

1. fasting glycemia decreased from 9,61 ± 3,99 mmol/l to 6,92 ± 2,26 mmol/l

2. Glycemia in 2 hours after a breakfast decreased from 10,58±3,94 mmol/l to 7,64±1,63 mmol/l

3. Glycemia before lunch decreased from 8,90±3,70 mmol/l to 6,43±1,36 mmol/l

4. Glycemia post-prandial decreased from 11,43±3,73 mmol/l to 8,29±1,79 mmol/l

5. Glycemia before dinner decreased from 9,27±3,78 mmol/l to 6,45±1,34 mmol/l

6. Glycemia in 2 hours after dinner decreased from 11,22±4,09 mmol/l to 8,65±1,85 mmol/l

7. Glycemia before going to bed decreased from 9,75±3,78 mmol/l to 7,54±1,42 mmol/l

8. Glycemia at 3 o'clock in the morning decreased from 9,67±3,19 mmol/l to 6,75±1,04 mmol/l

(All results non statistically significant)

Change of the level of hemoglobin HbA1c

HbA1c decreased from 9,13±1,64% at baseline to 8,58±1,49% at week 12

(All results non statistically significant)

Average total daily dose of rapid and basal insulin

The average total daily dose of rapid insulin was 23,91 ± 5,87 U at baseline and 23,43 ± 5,54 U at week 12

The average total daily dose of basal insulin was 19,89 ± 5,21 IU at baseline 19,77 ± 5,03 IU at week 12

Patients received insulin glulisine (Apidra) three times a day with basal insulin–glargin (Lantus) once a day or in combination with two injections of any NPH insulin.

(All results non statistically significant)

Patient's body mass evolution

The average body weight was 63,87±9,83 kg, at baseline and 63,74±9,46 kg at the end of the study (week 12)

(All results non statistically significant)

SAFETY RESULTS:

- In total 54 episodes of hypoglycemia occurred during the 12 weeks of application of insulin glulisine in 45 patients: 13 (24 %) cases were not confirmed by definition of glycemia and 41 (76 %) were confirmed.

All hypoglycemia conditions could be managed by patient's intake of carbohydrates, and did not demand the help of the doctor or hospitalization.

- No adverse events were reported

Date of the report: 13. 07. 07