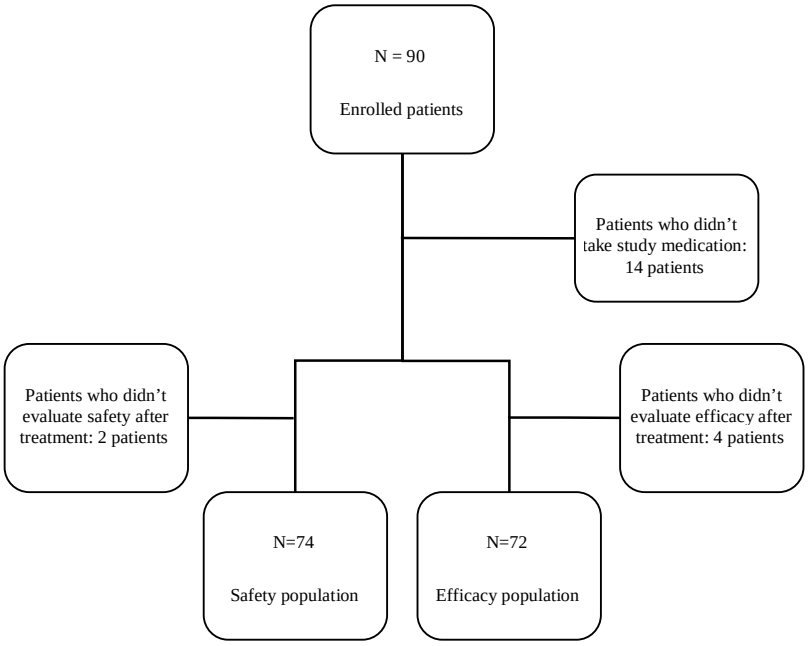
These results are supplied for informational purposes only. *Prescribing decisions should be made based on the approved package insert in the country of prescription*

Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NCT00563225
		Study Code:	HOE901_3506
Generic drug name:	insulin glargine	**Date:**	10 December 07

Title of the study:	A multicenter, non-comparative, one arm, open, phase III study to evaluate the efficacy and safety of insulin glargine on subjects with Type 2 Diabetes Mellitus	
Investigator(s):	Coordinating Investigator : Sung-Koo Kang Department of Endocrinology Catholic University of Korea Holy, Seoul, Korea	
Study center(s):	Multicenter (7sites) study	
Publications (reference):	NA	
Study period: Date of study initiation: 29-Oct-2002 (FPI) Study Completion Date: 02-Apr-2004 (LPO)		**Phase of development:** Phase III study
Objectives:	Primary : ● To evaluate the efficacy of Insulin glargine (injection at bedtime, once a day) on the changes of HbA1c. ● To evaluate the safety of Insulin glargine. Secondary ● To evaluate the efficacy of Insulin glargine (injection at bedtime, once a day) on the changes of FPG.	

Methodology:	The study period consisted of 4-week screening period and 20-week treatment period. During the whole study period, the visits were planned as follows: screening visit, baseline visit(at week 0) , 3 visits during the treatment period (at week 4, week 8, week 20 or last visit). Additional visits were at the discretion of the investigator. 2 telephone contacts were also planned (at week 12, week 16).
Number of patients/subjects:	Total number of planned subjects: 77 Total number of enrolled subjects: 90 Efficacy evaluation subjects: 72 Safety evaluation subjects: 74 Among a total of 90 subjects enrolled, 14 subjects did not take the study medication and there was no safety result for 2 subjects. 4 patients didn't evaluate primary efficacy (HbA1c) after baseline. Among 74 patients, patients of 63 (85.14%) completed this study and patients of 11 (14.86%) were withdrawn. Withdrawals were due to adverse events in 5 patients, informed consent withdrawal in 2 patients and poor blood glucose control in 4 patients 

Diagnosis and criteria for inclusion:	• 40-80 aged male and female • Type 2 Diabetes Mellitus diagnosed at least 3 years ago • Treated concomitantly with insulin once a day and SU over at least 3 months prior to study entry • Treated with OHA monotherapy over at least 1 year • HbA1c ≥ 7.5% and ≤ 12.0%, at visit 1 (screening visit) • BMI < 40 kg/m^2 • No history of ketonemia • Women of childbearing potential using the medically approved contraceptive method • Written informed consent obtained prior to enrollment in the study • Ability and willingness to perform blood glucose monitoring using a blood glucose meter as per the requirement of protocol
Investigational product: Dose: Administration:	Insulin glargine at the discretion of the investigator Subcutaneous, once daily injection (at bedtime)
Duration of treatment: 20-week treatment period.	**Duration of observation:** NA

Reference therapy: Dose: Administration:	NA NA NA
Criteria for evaluation:	
Efficacy:	- Primary efficacy variable : HbA1c Final evaluation on efficacy was based on change of HbA1c level, which was measured in accordance with the standard DCCT method. - Secondary efficacy variable: The changes of FBG from baseline visit to final visit.
Safety:	- Occurrence of hypoglycemia (in particular, serious hypoglycemic incidence, nocturnal hypoglycemia). - Adverse events. - Laboratory test results: hematology, biochemistry, pregnancy test. - Vital signs: weight, blood pressure, heart rate. - Physical examination.
Statistical methods:	The difference of HbA1c between baseline and endpoint was compared using a paired t-test at one-sided significance level of 5%. A 95% one-sided confidence interval was provided. The difference of FPG between baseline and endpoint was compared using a paired t-test. A 95% two-sided confidence interval was provided as well. In case efficacy variables were missed at visit 7, the values were replaced by values measured at visit 4 using LOCF (Last Observation Carried Forward).

Summary:	This study was conducted in order to assess the efficacy and safety of insulin glargine in Korean patients with type 2 diabetes mellitus. Among a total of 90 subjects enrolled, 14 subjects did not take the study medication and there was no safety result for 2 subjects. Among 74 patients, patients of 63 (85.14%) completed this study and patients of 11 (14.86%) were withdrawn. Withdrawals were due to adverse events in 5 patients, informed consent withdrawal in 2 patients and poor blood glucose control in 4 patients The efficacy population was defined by 72 subjects. The safety population was defined by 74 subjects: 27 men (36.49%), 47 women (63.51%). Mean age of 58.73 ± 8.39 years. Among 74 patients, adverse events were reported in 35 patients (47.30%). Adverse events considered to be possibly related to the study medication (ADR) were reported in 2 patients (2.70%) during the course of the study. ADRs were 'injection site oedema' and 'pain NOS'. All the patients from the efficacy and safety populations were previously on NPH + OHA.
Efficacy results:	Primary endpoint: The mean HbA1c level was 9.23 ± 1.53 % at baseline and reached 9.73 ± 2.05 % at endpoint after 20 weeks of treatment. The mean change from baseline to endpoint in HbA1c was + 0.53% (95% one-sided CI: -, 0.84), $p < 0.0001$. Secondary endpoint: The mean FPG level at baseline was 161.50 ± 58.69 mg/dl and 153.31 ± 77.02 mg/dl at endpoint. The mean change from baseline to endpoint in FPG was – 4.73mg/dl, $p = 0.6545$.

Safety results:	Among 74 patients, adverse events were reported in 35 patients (47.30%). Adverse events considered to be possibly related to the study medication (ADR) were reported in 2 patients (2.70%) during the course of the study. The adverse events were mild in 27 patients (36.49%), moderate in 5 patients (6.76%) and severe in 3 patients (4.05%). All adverse events related to treatment were mild. Serious adverse events occurred in 7 patients (9.46%) during the course of the study. Adverse events: The incidence of adverse events related to 'Respiratory, thoracic and mediastinal disorders' was the most frequent (9/74 patients, 12.16%), followed by 'musculoskeletal and connective tissue disorders' (10.81%) and 'infections and infestations' (6.76%). Serious adverse events: Most of the serious adverse events which required hospitalization or prolong existing hospitalization were recovered, except 'intervertebral disc herniation'. The 'intervertebral disc herniation' was not recovered but it didn't have to be followed up. All serious adverse events were not related to treatment. Adverse drug reactions: ADRs were 'injection site oedema' and 'pain NOS'. Five patients discontinued study medication and were withdrawn from the study due to adverse events. From this five patients, six events were reported, consisting of : 'metabolism and nutrition disorders' (2), 'musculoskeletal and connective tissue disorders'(2) and 'nervous system disorders '(2). There was no adverse event leading to death. During the study period, a total of 102 hypoglycemic events occurred in 28 patients (37.84%). Among them, 5 nocturnal hypoglycemias occurred in 4 patients (5.41%) and a severe hypoglycemia occurred in 1 patient (1.35%). There was no clinical significant change in the laboratory tests and no adverse event related to laboratory test abnormality.
Date of report:	20 November 2007