Sponsor

Novartis

Generic Drug Name

Vildagliptin

Therapeutic Area of Trial

Type 2 diabetes

Approved Indication

Vildagliptin is indicated in the treatment of type 2 diabetes mellitus:
- in the treatment of adult patients who are unable to achieve sufficient glycaemic control at their maximally tolerated dose of oral metformin alone.

Protocol Number

CLAF237AFR03

Title

Prospective, randomized, open-label study comparing over 6 months the clinical benefit on hypoglycemia of vildagliptin versus another oral antidiabetic drugs as add-on therapy in elderly patients with type 2 diabetes insufficiently controlled with metformin alone. (GLYCEMIA)

Phase of Development

Phase IV

Study Start/End Dates

First-patient first-visit: 22-Oct-2010

Last-patient last-visit: 02-Dec-2011

Study terminated early due to futility, after authorization by the local French regulatory authorities following major recruitment difficulties, and could not proceed with the planned objectives.

Study Design/Methodology

This was a prospective, national, multicenter, out-patient, randomized, open-label, parallel 2 arm study respecting the product marketing prescription recommendations (vildagliptin) and current recommendations in France in elderly patients (over 65 years) with DT2 insufficiently controlled with metformin alone (HbA1c > 6.5% or > 7% depending on their individualized HbA1c target). Eligible patients were centrally randomized into 2 balanced groups: vildagliptin (50 mg twice a day) or « Usual treatment » (all other oral antidiabetic drugs (OAD) prescribed within the scope of the French label) in addition to continuing their regular background treatment by metformin unchanged (commercialized form, dose, number of daily intakes) throughout the study.

Centres

33 active centers in France

Publication

None

Test Product (s), Dose(s), and Mode(s) of Administration

Study Treatment- Oral tablets of vildagliptin 50 mg twice daily.

Reference therapy (« Usual treatment »): includes all other oral antidiabetic treatments of another therapeutic class usually prescribed in bitherapy with metformin. The choice of another OAD class, molecule, posology and administration frequency etc. was determined by the physician strictly within the scope of the French label.

Statistical Methods

Due to the study being prematurely stopped, the inclusion of only a very small portion of the required number of patients and the limited amount of data collected for these patients due to the significantly shortened length of the study, statistical analysis was confined to patient demography at inclusion, treatments, analysis of AEs reported at the follow-up visit, together with individual patient data listings.
Descriptive statistics, including mean, standard deviation (SD), minimum, maximum and median for quantitative variables and frequency tables for qualitative variables, are presented overall for the selection, inclusion and end-of-study visits.
Safety was assessed from AE frequency and the number of abnormal laboratory results and vital signs.

Study Population: Key inclusion/Exclusion Criteria and Demographics

Inclusion criteria

- Male or female out-patients aged ≥ 65 and ≤ 80 years old
- Patients with T2DM insufficiently controlled with metformin alone since at least 3 months and for whom treatment modification has been decided (escalation to bitherapy) to achieve their individualized HbA1c target.
- Patients had to have
    - a BMI between 22 and 45 kg/m^2,
    - an HbA1c level > 6.5% or > 7% (depending on their individualized HbA1c target)
    - a fasting blood glucose level of <15 mmol/l.

Exclusion criteria

Patients with

- any other type of diabetes,
- acute metabolic complications within last 6 months,
- acute infections likely to affect glycemic control within last 4 weeks,
- serious CV history,
- ALAT or ASAT values > 3 times normal upper limit,
- creatinine clearance < 50 ml/min or insufficiently treated dysthyroidism

Participant Flow

	Total
Total number of patients – n (%) *	
Screened	59
Randomized	46 (78.0%)
Safety	46 (78.0%)
ITT	42 (71.2%)
Per Protocol	30 (50.8%)
Premature discontinuation – n (%)	31 (67.4%)
Reason #	
Adverse event(s)	3 (9.7%)
Unsatisfactory therapeutic effect	1 (3.2%)
Administrative reasons	27 (87.1%)

* Percent is calculated on the number of randomized patients.
# Percent is calculated on the number of patients with premature discontinuation.
There was no death during the study.

Baseline Characteristics

Demographic characteristics of the population in the study (randomized population)

		Randomized Population (N = 46)
Age (years)	N	46
	Mean	70.4
	SD	4.91
	Median	69.0
	Min;Max	65.0 ; 80.0
Sex n (%)	N	46
	Male	23 (50.0%)
	Female	23 (50.0%)
Weight (kg)	N	46
	Mean	79.1
	SD	14.04
	Median	75.3
	Min;Max	52.0 ; 110.0
BMI (kg/m^2)	N	46
	Mean	29.3
	SD	4.87
	Median	29.0
	Min;Max	20.8 ; 39.7
Disease duration (years)	N	46
	Mean	8.8
	SD	6.23
	Median	7.0
	Min;Max	0.3 ; 22.0
Duration of metformin use (years)	N	45
	Mean	4.7

	SD	4.51
	Median	4.0
	Min;Max	0.2 ; 20.0
Metformin dose	N	46
(mg/day)	Mean (SD)	2078.3 (648.30)
HbA1c (%)	N	46
	Mean (SD)	7.2 (0.41)

Safety Results

Summary of significant Adverse Events (AEs) by treatment group

Event (Preferred term)	Type: AE / SAE	Relationship: NS / S	Treatment stopped
Patients taking Galvus® + metformin			
Folliculitis	AE	S	YES
Nausea	AE	NS	YES
Epilepsy	SAE	NS	YES
Femoral neck fracture	SAE	NS	NO
Patients taking another OAD + metformin			
Hypoglycaemia	SAE	S	NO
Haematuria	SAE	NS	NO
Concomitant disease progression	SAE	NS	NO

S : suspected ; NS : Not suspected ; SAE = Serious AE

Adverse Events by System Organ Class - n (%) of patients – Safety Population

	Vildagliptin (N = 24)	Other OAD (N = 22)	Total (N = 46)
Patients with at least one Adverse Event	7 (29.2%)	7 (31.8%)	14 (30.4%)
Patients with at least one Serious Adverse Event	2 (8.3%)	3 (13.6%)	5 (10.9%)
System Organ Class			
Metabolism and nutrition disorders	0 (0.0%)	5 (22.7%)	5 (10.9%)
Gastrointestinal disorders	3 (12.5%)	1 (4.5%)	4 (8.7%)
General disorders and administration site conditions	1 (4.2%)	2 (9.1%)	3 (6.5%)
Infections and infestations	2 (8.3%)	1 (4.5%)	3 (6.5%)
Injury, poisoning and procedural complications	1 (4.2%)	0 (0.0%)	1 (2.2%)
Musculoskeletal and connective tissue disorders	1 (4.2%)	0 (0.0%)	1 (2.2%)
Nervous system disorders	1 (4.2%)	0 (0.0%)	1 (2.2%)
Renal and urinary disorders	0 (0.0%)	1 (4.5%)	1 (2.2%)
Skin and subcutaneous tissue disorders	1 (4.2%)	0 (0.0%)	1 (2.2%)
Surgical and medical procedures	0 (0.0%)	1 (4.5%)	1 (2.2%)

By order of decreasing frequency for the Total column

Most Frequently Reported AEs Overall by Preferred Term n (%) - Safety Population

	Vildagliptin (N = 24)	OtherOAD (N = 22)	Total (N = 46)
Patients with at least one AE	7 (29.2%)	7 (31.8%)	14 (30.4%)
Preferred term			
Hypoglycaemia	0 (0.0%)	5 (22.7%)	5 (10.9%)
Nausea	2 (8.3%)	0 (0.0%)	2 (4.3%)
Bronchitis	1 (4.2%)	1 (4.5%)	2 (4.3%)
Constipation	1 (4.2%)	0 (0.0%)	1 (2.2%)
Diarrhoea	0 (0.0%)	1 (4.5%)	1 (2.2%)
Concomitant disease progression	0 (0.0%)	1 (4.5%)	1 (2.2%)

Irritability	1 (4.2%)	0 (0.0%)	1 (2.2%)
Oedema peripheral	0 (0.0%)	1 (4.5%)	1 (2.2%)
Folliculitis	1 (4.2%)	0 (0.0%)	1 (2.2%)
Femoral neck fracture	1 (4.2%)	0 (0.0%)	1 (2.2%)
Muscle spasms	1 (4.2%)	0 (0.0%)	1 (2.2%)
Epilepsy	1 (4.2%)	0 (0.0%)	1 (2.2%)
Haematuria	0 (0.0%)	1 (4.5%)	1 (2.2%)
Sweat gland disorder	1 (4.2%)	0 (0.0%)	1 (2.2%)
Polypectomy	0 (0.0%)	1 (4.5%)	1 (2.2%)

By order of decreasing frequency for the Total column

Serious Adverse Events and Deaths

	Total (N = 46)
Patients	
Number of patients with at least one SAE	5 (10.9%)
Death	0
Other SAE	5
SAE leading to discontinuation	0
Premature discontinuation for safety reason	3

Date of Clinical Trial Report

15-OCT-2012

Date Inclusion on Novartis Clinical Trial Results Database

17-OCT-2012

Date of Latest Update

20-SEP-2012