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Full Novartis CTRD Results Template

Sponsor Novartis
Generic Drug Name vildagliptin
Therapeutic Area of Trial Type 2 diabetes
Approved Indication Type 2 diabetes
Protocol Number CLAF237A23138E1
Title A 28 week extension to a 24 week multi-center, randomized, double-blind, active-controlled clinical trial to evaluate the safety and tolerability of vildagliptin 50mg qd versus sitagliptin 25mg qd in patients with type 2 diabetes and severe renal insufficiency
Phase of Development IIIB
Study Start/End Dates 24 Jan 2008 (core) / 19 Apr-2011
Study Design/Methodology 28-week extension to a 24-week multicenter, randomized, double-blind, active-controlled study (CLAF237A23138). Patients maintained their current therapy and blinded treatment regimen assigned during the core trial (either vildagliptin 50 mg qd or sitagliptin 25mg qd) throughout the extension.

Centres

Brazil (6), USA (81) (number of centers that recruited patients in the core study)

Publication

Not Applicable

Outcome measures

Primary outcome measures(s)

- to evaluate the long term safety and tolerability of vildagliptin 50 mg qd versus sitagliptin 25 mg qd in patients with T2DM and severe renal insufficiency over 52 weeks of treatment.

Secondary outcome measures(s)

- There were no secondary objectives for this study.

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

Oral tablet (once daily)

- vildagliptin 50 mg tablets
- sitagliptin 25 mg capsules
- vildagliptin 50 mg matching placebo tablets
- sitagliptin 25 mg matching placebo capsules

Statistical Methods

The number and percentage of patients with adverse events (AEs), serious adverse events (SAEs), AEs leading to discontinuation, program-wise predefined events of special interest and hypoglycemic events occurring during the combined core and extension treatment period were summarized by treatment. Hematology and biochemistry data and changes in GFR MDRD from study entry value to endpoint value were also summarized by treatment. Vital signs, body weight and ECG findings by category were evaluated descriptively.

Safety results were reported regardless of rescue medication use, i.e. whether or not data occurred during rescue insulin use (new use, new type, ≥20% dose increase). Selected safety data (e.g. predefined risks and hypoglycemic events) were also summarized for the rescue free data.

Study Population: Inclusion/Exclusion Criteria and Demographics

Inclusion

- Completion of the core study.
- Written informed consent to participate in the extension study
- Ability to comply with all study requirements

Exclusion:

- Premature discontinuation from the core study
- Concomitant medical conditions that interfered with the interpretation of the study results as defined in the core protocol

- Failure to comply with the core study protocol per the judgment of the investigator.
- Potentially unreliable patients, and those judged by the investigator to be unsuitable for the study

Other protocol defined inclusion/exclusion criteria applied.

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Participant Flow(Extension set)

Disposition Reason	Vilda 50mg qd N=46 n (%)	Sita 25mg qd N=38 n (%)	Total N=84 n (%)
Completed	35 (76.1)	34 (89.5)	69 (82.1)
Discontinued	11 (23.9)	4 (10.5)	15 (17.9)
Adverse event (s)	6 (13.0)	4 (10.5)	10 (11.9)
Patient's condition no longer requires study drug	1 (2.2)	0 (0.0)	1 (1.2)
Patient withdrew consent	2 (4.3)	0 (0.0)	2 (2.4)
Protocol deviation	2 (4.3)	0 (0.0)	2 (2.4)

Baseline Characteristics (Extension set)

Demographic variable	Vilda 50mg qd N=46	Sita 25mg qd N=38	Total N=84
Age (years)			
N	46	38	84
Mean	66.4	66.7	66.5
SD	9.44	9.90	9.60
Min	48.0	46.0	46.0
Median	68.0	68.5	68.5
Max	83.0	85.0	85.0
Age group			
< 65 yrs	20 (43.5%)	13 (34.2%)	33 (39.3%)
≥ 65 yrs	26 (56.5%)	25 (65.8%)	51 (60.7%)
< 75 yrs	35 (76.1%)	30 (78.9%)	65 (77.4%)
≥ 75 yrs	11 (23.9%)	8 (21.1%)	19 (22.6%)
Sex			
Male	22 (47.8)	15 (39.5%)	37 (44.0%)
Female	24 (52.2%)	23 (60.5%)	47 (56.0%)
Age/Gender			
≥ 65 yrs female	13 (28.3)	14 (36.8%)	27 (32. %)
Others	33 (71.7%)	24 (63.2%)	57 (67.9%)
Race			
Asian (Non Indian Subcontinent)	1 (2.2%)	0 (0.0%)	1 (1.2%)

Black	10 (21.7)	9 (23.7%)	19 (22.6%)
Caucasian	31 (67.4%)	26 (68.4%)	57 (67.9%)
Hispanic or Latino	3 (6.5%)	1 (2.6%)	4 (4.8%)
Other	0 (0.0%)	1 (2.6%)	1 (1.2%)
Pacific islander	1 (2.2%)	1 (2.6%)	2 (2.4%)
Height (cm)			
N	46	38	84
Mean	165.7	164.9	165.3
SD	9.42	9.90	9.59
Min	143.0	152.0	143.0
Median	165.0	163.0	165.0
Max	188.0	189.0	189.0
Body weight (kg)			
N	46	38	84
Mean	90.8	93.1	91.8
SD	14.70	18.39	16.41
Min	59.3	55.0	55.0
Median	86.7	95.3	91.0
Max	140.9	147.5	147.5
BMI (kg/m^2)			
N	46	38	84
Mean	33.1	34.1	33.6
SD	4.83	5.08	4.94
Min	25.3	23.2	23.2
Median	32.3	36.3	33.8
Max	41.7	41.8	41.8
BMI group			
<30 (kg/m^2)	16 (34.8%)	9 (23.7%)	25 (29.8%)
≥ 30 (kg/m^2)	30 (65.2%)	29 (76.3%)	59 (70.2%)
≥ 35 (kg/m^2)	15 (32.6%)	20 (52.6%)	35 (41.7%)

Outcome measures

Not Applicable

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Primary Outcome Result(s) --- Safety Results

The reported frequencies for adverse events in extension safety set were influenced by a lower number of patients included in the extension protocol (84 patients), compared to the core study (148 patients). In addition, 28% of patients who completed the core study decided not to continue in the extension protocol (reasons were not collected) creating an imbalance at the beginning of the extension study because events occurring during the first 24 weeks of the core study contributed to the overall AE rates.

The impact of random patient discontinuation after the completion of the core study should be considered when assessing incidences of adverse events reported in the overall relatively small extension study.

Number (%) of patients with AEs during the combined core and extension study period by primary system organ class and treatment (Extension safety set)

Primary system organ class	Vilda 50mg qd N=46 n (%)	Sita 25mg qd N=38 n (%)
- Any primary system organ class	44 (95.7)	36 (94.7)
Blood and lymphatic system disorders	7 (15.2)	3 (7.9)
Cardiac disorders	10 (21.7)	8 (21.1)
Ear and labyrinth disorders	1 (2.2)	3 (7.9)
Endocrine disorders	0 (0.0)	1 (2.6)
Eye disorders	2 (4.3)	8 (21.1)
Gastrointestinal disorders	14 (30.4)	17 (44.7)
General disorders and administration site conditions	22 (47.8)	21 (55.3)
Hepatobiliary disorders	1 (2.2)	1 (2.6)
Immune system disorders	1 (2.2)	0 (0.0)
Infections and infestations	24 (52.2)	21 (55.3)
Injury, poisoning and procedural complications	15 (32.6)	5 (13.2)
Investigations	9 (19.6)	11 (28.9)
Metabolism and nutrition disorders	28 (60.9)	16 (42.1)
Musculoskeletal and connective tissue disorders	16 (34.8)	14 (36.8)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2 (4.3)	2 (5.3)
Nervous system disorders	22 (47.8)	20 (52.6)
Psychiatric disorders	6 (13.0)	8 (21.1)
Renal and urinary disorders	12 (26.1)	8 (21.1)
Reproductive system and breast disorders	2 (4.3)	2 (5.3)
Respiratory, thoracic and mediastinal disorders	14 (30.4)	7 (18.4)
Skin and subcutaneous tissue disorders	22 (47.8)	17 (44.7)
Vascular disorders	12 (26.1)	6 (15.8)

Primary system organ classes are presented alphabetically.

A patient with multiple occurrences of an AE under one treatment is counted only once in the AE category for that treatment.

Coded using MedDRA version 14.0.

Serious Adverse Events and Deaths

Number (%) of patients with SAEs during the combined core and extension study period by preferred term (Extension safety set).

Event category	Vilda 50mg qd N=46 n (%)	Sita 25mg qd N=38 n (%)
Deaths*	0 (0.0)	0 (0.0)
SAEs	15 (32.6)	10 (26.3)
Discontinuation due to AEs	6 (13.0)	4 (10.5)
AEs causing dose adjustment or study drug interruption	5 (10.9)	3 (7.9)
Clinically significant CCV AEs**	6 (13.0)	6 (15.8)
Clinically significant hepatic AEs***	2 (4.3)	1 (2.6)
Clinically significant SVEM AEs****	2 (4.3)	1 (2.6)
Clinically significant breast cancer AEs*****	0 (0.0)	0 (0.0)

* One death happened 20 days after discontinuation from treatment and thus is not shown as it was adjudicated by the CCV committee.

** Patients with events confirmed by the Cardiovascular and Cerebrovascular adjudication committee

*** Patients with events confirmed by the Hepatic adjudication committee

**** Patients with events confirmed by the Skin, Vascular, Edema and Muscle adjudication committee

***** Patients with events confirmed by the Breast Cancer adjudication committee

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Number (%) of patients with SAEs during the combined core and extension study period by preferred term and treatment (Extension Safety set)

Preferred term	Vilda 50mg qd N=46 n (%)	Sita 25mg qd N=38 n (%)
- Any SAE	15 (32.6)	10 (26.3)
Abdominal pain upper	0 (0.0)	1 (2.6)
Acute coronary syndrome	1 (2.2)	0 (0.0)
Acute myocardial infarction	1 (2.2)	1 (2.6)
Acute pulmonary edema	0 (0.0)	1 (2.6)
Anemia	0 (0.0)	1 (2.6)
Angina pectoris	2 (4.3)	0 (0.0)
Angina unstable	0 (0.0)	1 (2.6)
Arteriovenous fistula thrombosis	1 (2.2)	0 (0.0)
Arthralgia	1 (2.2)	0 (0.0)
Atrial fibrillation	2 (4.3)	0 (0.0)
Benign renal neoplasm	1 (2.2)	0 (0.0)
Cardiac failure congestive	3 (6.5)	2 (5.3)
Cellulitis	0 (0.0)	1 (2.6)
Cerebrovascular accident	0 (0.0)	1 (2.6)
Coronary artery disease	3 (6.5)	1 (2.6)
Coronary artery occlusion	0 (0.0)	1 (2.6)
Deep vein thrombosis	1 (2.2)	0 (0.0)
Dehydration	0 (0.0)	1 (2.6)
Dermal cyst	0 (0.0)	1 (2.6)
Diabetes mellitus	1 (2.2)	0 (0.0)
Diabetic ketoacidosis	1 (2.2)	0 (0.0)
Dyspnea	2 (4.3)	0 (0.0)
Femoral neck fracture	0 (0.0)	1 (2.6)
Fluid overload	0 (0.0)	1 (2.6)
Gastritis	0 (0.0)	1 (2.6)
Gastroenteritis viral	1 (2.2)	0 (0.0)
Hyperkalemia	1 (2.2)	0 (0.0)
Hypertension	0 (0.0)	1 (2.6)
Hypoglycemia	0 (0.0)	2 (5.3)
Hypoxia	1 (2.2)	0 (0.0)
Impaired gastric emptying	1 (2.2)	0 (0.0)
Loss of consciousness	0 (0.0)	1 (2.6)
Malignant hypertension	1 (2.2)	0 (0.0)
Metabolic acidosis	1 (2.2)	0 (0.0)
Muscular weakness	1 (2.2)	0 (0.0)
Non-cardiac chest pain	1 (2.2)	1 (2.6)
Pleural effusion	0 (0.0)	1 (2.6)
Pneumonia	0 (0.0)	1 (2.6)
Pulmonary hemorrhage	1 (2.2)	0 (0.0)
Pulmonary hypertension	1 (2.2)	0 (0.0)
Pulmonary edema	0 (0.0)	1 (2.6)
Pyelonephritis	1 (2.2)	0 (0.0)

A patient with multiple occurrences of an SAE under one treatment is counted only once in the SAE category
Date of Clinical Trial Report 8 Nov 2011
Date Inclusion on Novartis Clinical Trial Results Database 19 APR 2012
Date of Latest Update