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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 CLAF237A23137E1
Title A 28 week extension to a 24 week multi-center, randomized, double-blind clinical trial to evaluate the safety and tolerability of vildagliptin (50mg qd) versus placebo in patients with type 2 diabetes and moderate or severe renal insufficiency
Phase of Development IIIB
Study Start/End Dates 11-Nov-2010 / 20 Apr 2011 (Last Patient Last Visit) ; 04-May-2011 (last data received)
Study Design/Methodology 28-week extension to a 24-week multicenter, randomized, double-blind, placebo-controlled study (CLAF237A23137). Patients maintained current therapy and treatment regimen assigned during the core trial (either vildagliptin 50 mg qd or placebo) throughout the extension.

Centers

Argentina (6), Australia (4), Canada (5), Costa Rica (4), Finland (2), France (6), Germany (20), Guatemala (3), India (5), Norway (1), Russia (14), Spain (11), Sweden (5)

Publication

Not Applicable

Outcome measures

Primary outcome measures(s)

The safety and tolerability of vildagliptin (50 mg qd) versus placebo in patients with T2DM and moderate or 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 tablets of vildagliptin 50mg qd or matching placebo tablets

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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 and renal impairment. Hematology and biochemistry data and changes in GFR MDRD from study entry value to endpoint value were also summarized by treatment and renal impairment. 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 criteria:
Completion of the core, CLAF237A23137 study.

Exclusion criteria:

1. Premature discontinuation from the core study

2. Concomitant medical conditions that interfere with the interpretation of the study results as defined in the core protocol
3. Failure to comply with the core study protocol per the judgment of the investigator
4. Potentially unreliable patients, and those judged by the investigator to be unsuitable for the study

Other protocol defined inclusion/exclusion criteria applied.

Participant Flow

Patient disposition by renal impairment severity and treatment (Extension set)

Renal impairment: Moderate			
Disposition **Reason for discontinuation**	**Vilda 50mg qd N=122 n (%)**	**Placebo N=89 n (%)**	**Total N=211 n (%)**
Completed	113 (92.6)	81 (91.0)	194 (91.9)
Discontinued, total	9 (7.4)	8 (9.0)	17 (8.1)
Abnormal test procedure result(s)	1 (0.8)	1 (1.1)	2 (0.9)
Adverse event(s)	5 (4.1)	4 (4.5)	9 (4.3)
Death	1 (0.8)	0 (0.0)	1 (0.5)
Lost to follow-up	2 (1.6)	1 (1.1)	3 (1.4)
Patient withdrew consent	0 (0.0)	1 (1.1)	1 (0.5)
Unsatisfactory therapeutic effect	0 (0.0)	1 (1.1)	1 (0.5)
Renal impairment: Severe			
Disposition **Reason for discontinuation**	**Vilda 50mg qd N=94 n (%)**	**Placebo N=64 n (%)**	**Total N=158 n (%)**
Completed	83 (88.3)	56 (87.5)	139 (88.0)
Discontinued, total	11(11.7)	8(12.5)	19(12.0)
Abnormal laboratory value(s)	0 (0.0)	1 (1.6)	1 (0.6)
Administrative problems	1 (1.1)	0 (0.0)	1 (0.6)
Adverse event(s)	6 (6.4)	3 (4.7)	9 (5.7)
Death	3 (3.2)	1 (1.6)	4 (2.5)
Lost to follow-up	1 (1.1)	1 (1.6)	2 (1.3)
Patient withdrew consent	0 (0.0)	1 (1.6)	1 (0.6)
Unsatisfactory therapeutic effect	0 (0.0)	1 (1.6)	1 (0.6)

Baseline Characteristics

Patient baseline demographic characteristics by renal impairment severity and treatment (Extension set)

Renal impairment: Moderate			
Demographic variable	**Vilda 50mg qd N=122**	**Placebo N=89**	**Total N=211**
Age (years)			
N	122	89	211

Mean	67.1	69.3	68.0
SD	9.00	7.22	8.35
Min	40.0	51.0	40.0
Median	69.0	70.0	69.0
Max	84.0	85.0	85.0
Age group – n (%)			
< 65 yrs	41 (33.6)	19 (21.3)	60 (28.4)
>=65 yrs	81 (66.4)	70 (78.7)	151 (71.6)
< 75 yrs	98 (80.3)	69 (77.5)	167 (79.1)
>=75 yrs	24 (19.7)	20 (22.5)	44 (20.9)
Sex – n (%)			
Male	70 (57.4)	55 (61.8)	125 (59.2)
Female	52 (42.6)	34 (38.2)	86 (40.8)
Age/Gender – n (%)			
>=65 yrs female	33 (27.0)	28 (31.5)	61 (28.9)
Others	89 (73.0)	61 (68.5)	150 (71.1)
Race – n (%)			
Asian (Indian Subcontinent)	15 (12.3)	12 (13.5)	27 (12.8)
Black	2 (1.6)	0 (0.0)	2 (0.9)
Caucasian	83 (68.0)	62 (69.7)	145 (68.7)
Hispanic or Latino	21 (17.2)	12 (13.5)	33 (15.6)
Other	1 (0.8)	3 (3.4)	4 (1.9)
Body weight (kg)			
N	122	89	211
Mean	83.4	81.6	82.6
SD	18.78	15.36	17.40
Min	41.2	50.1	41.2
Median	79.2	80.0	79.5
Max	138.1	127.0	138.1
BMI (kg/m^2)			
N	122	89	211
Mean	30.3	30.1	30.2
SD	5.17	4.97	5.08
Min	18.8	18.2	18.2
Median	30.2	29.9	30.0
Max	41.8	45.0	45.0
BMI group – n (%)			
<30 kg/m^2	59 (48.4)	45 (50.6)	104 (49.3)
>=30 kg/m^2	63 (51.6)	44 (49.4)	107 (50.7)
>=35 kg/m^2	23 (18.9)	12 (13.5)	35 (16.6)

Renal impairment: Severe			
Demographic variable	**Vilda 50mg qd N=94**	**Placebo N=64**	**Total N=158**
Age (years)			
N	94	64	158
Mean	63.7	65.4	64.4
SD	9.08	10.52	9.69
Min	40.0	43.0	40.0
Median	63.0	66.5	64.5
Max	83.0	82.0	83.0
Age group – n (%)			
< 65 yrs	49 (52.1)	30 (46.9)	79 (50.0)
>=65 yrs	45 (47.9)	34 (53.1)	79 (50.0)
< 75 yrs	83 (88.3)	50 (78.1)	133 (84.2)
>=75 yrs	11 (11.7)	14 (21.9)	25 (15.8)
Sex – n (%)			
Male	49 (52.1)	33 (51.6)	82 (51.9)
Female	45 (47.9)	31 (48.4)	76 (48.1)
Age/Gender – n (%)			
>=65 yrs female	25 (26.6)	18 (28.1)	43 (27.2)
Others	69 (73.4)	46 (71.9)	115 (72.8)
Race – n (%)			
Asian (Indian Subcontinent)	15 (16.0)	11 (17.2)	26 (16.5)
Asian (Non Indian Subcontinent)	2 (2.1)	0 (0.0)	2 (1.3)
Black	2 (2.1)	0 (0.0)	2 (1.3)
Caucasian	45 (47.9)	36 (56.3)	81 (51.3)
Hispanic or Latino	29 (30.9)	17 (26.6)	46 (29.1)
Other	1 (1.1)	0 (0.0)	1 (0.6)
Body weight (kg)			
N	94	64	158
Mean	81.9	80.9	81.5
SD	18.07	15.41	17.00
Min	43.0	54.3	43.0
Median	81.0	82.1	81.3
Max	135.9	117.0	135.9
BMI (kg/m^2)			
N	94	64	158
Mean	30.8	30.0	30.5
SD	5.77	4.74	5.37
Min	19.6	20.0	19.6
Median	29.8	29.6	29.8
Max	41.8	41.5	41.8
BMI group – n (%)			
<30 kg/m^2	50 (53.2)	33 (51.6)	83 (52.5)
>=30 kg/m^2	44 (46.8)	31 (48.4)	75 (47.5)
>=35 kg/m^2	25 (26.6)	9 (14.1)	34 (21.5)

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Outcome Measure:

Please see "Safety Results" below.

Safety Results

Primary Outcome Result(s) – Safety Results

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

Renal impairment: Moderate **Primary system organ class**	**Vilda 50mg qd N=122 n (%)**	**Placebo N=89 n (%)**
- Any primary system organ class	103 (84.4)	76 (85.4)
Blood and lymphatic system disorders	5 (4.1)	4 (4.5)
Cardiac disorders	12 (9.8)	11 (12.4)
Congenital, familial and genetic disorders	1 (0.8)	0 (0.0)
Ear and labyrinth disorders	5 (4.1)	4 (4.5)
Endocrine disorders	2 (1.6)	0 (0.0)
Eye disorders	16 (13.1)	9 (10.1)
Gastrointestinal disorders	30 (24.6)	21 (23.6)
General disorders and administration site conditions	43 (35.2)	29 (32.6)
Hepatobiliary disorders	3 (2.5)	0 (0.0)
Infections and infestations	45 (36.9)	38 (42.7)
Injury, poisoning and procedural complications	15 (12.3)	11 (12.4)
Investigations	23 (18.9)	8 (9.0)
Metabolism and nutrition disorders	44 (36.1)	22 (24.7)
Musculoskeletal and connective tissue disorders	35 (28.7)	22 (24.7)
Neoplasms benign, malignant & unspecified (incl cysts & polyps)	2 (1.6)	1 (1.1)
Nervous system disorders	39 (32.0)	27 (30.3)
Psychiatric disorders	10 (8.2)	11 (12.4)
Renal and urinary disorders	7 (5.7)	6 (6.7)
Reproductive system and breast disorders	4 (3.3)	1 (1.1)
Respiratory, thoracic and mediastinal disorders	13 (10.7)	13 (14.6)
Skin and subcutaneous tissue disorders	27 (22.1)	24 (27.0)
Vascular disorders	16 (13.1)	7 (7.9)

Renal impairment: Severe **Primary system organ class**	**Vilda 50mg qd N=94 n (%)**	**Placebo N=64 n (%)**
- Any primary system organ class	80 (85.1)	56 (87.5)

Blood and lymphatic system disorders	11 (11.7)	7 (10.9)
Cardiac disorders	18 (19.1)	7 (10.9)
Ear and labyrinth disorders	6 (6.4)	0 (0.0)
Endocrine disorders	1 (1.1)	1 (1.6)
Eye disorders	14 (14.9)	8 (12.5)
Gastrointestinal disorders	25 (26.6)	20 (31.3)
General disorders and administration site conditions	34 (36.2)	25 (39.1)
Hepatobiliary disorders	1 (1.1)	1 (1.6)
Immune system disorders	1 (1.1)	0 (0.0)
Infections and infestations	43 (45.7)	21 (32.8)
Injury, poisoning and procedural complications	11 (11.7)	2 (3.1)
Investigations	17 (18.1)	7 (10.9)
Metabolism and nutrition disorders	30 (31.9)	29 (45.3)
Musculoskeletal and connective tissue disorders	19 (20.2)	10 (15.6)
Nervous system disorders	33 (35.1)	16 (25.0)
Psychiatric disorders	9 (9.6)	5 (7.8)
Renal and urinary disorders	13 (13.8)	9 (14.1)
Reproductive system and breast disorders	2 (2.1)	1 (1.6)
Respiratory, thoracic and mediastinal disorders	13 (13.8)	14 (21.9)
Skin and subcutaneous tissue disorders	29 (30.9)	21 (32.8)
Vascular disorders	17 (18.1)	14 (21.9)

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

Number (%) of patients with serious or clinically significant AEs during the combined core and extension period (Extension safety set)

Renal impairment: Moderate **Event category**	**Vilda 50mg qd N=122** **n (%)**	**Placebo N=89** **n (%)**
Deaths (during extension period only)	1 (0.8)	0 (0.0)
SAEs	26 (21.3)	17 (19.1)
Discontinuation due to an AE	6 (4.9)	5 (5.6)
AEs causing study drug interruption	7 (5.7)	8 (9.0)
Renal impairment: Severe **Event category**	**Vilda 50mg qd N=94** **n (%)**	**Placebo N=64** **n (%)**
Deaths (during extension period only)	3 (3.2)	1 (1.6)
SAEs	23 (24.5)	16 (25.0)
Discontinuation due to an AE	9 (9.6)	4 (6.3)
AEs causing study drug interruption	11 (11.7)	7 (10.9)

* 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

Deaths during the extension study period by primary system organ class, preferred term, renal impairment severity and treatment (Extension safety set)

Renal impairment: Moderate		
Primary system organ class Principal cause of death	**Vilda 50mg qd N=122 n (%)**	**Placebo N=89 n (%)**
Any primary system organ class	1 (0.8)	0 (0.0)
General disorders and administration site conditions	1 (0.8)	0 (0.0)
Death	1 (0.8)	0 (0.0)
Renal impairment: Severe		
Primary system organ class Principal cause of death	**Vilda 50mg qd N=94 n (%)**	**Placebo N=64 n (%)**
Any primary system organ class	3 (3.2)	1 (1.6)
Infections and infestations	1 (1.1)	0 (0.0)
Septic shock	1 (1.1)	0 (0.0)
Renal and urinary disorders	1 (1.1)	1 (1.6)
Renal failure	1 (1.1)	0 (0.0)
Renal impairment	0 (0.0)	1 (1.6)
Vascular disorders	1 (1.1)	0 (0.0)
Aortic dissection	1 (1.1)	0 (0.0)

Primary system organ classes are presented alphabetically; preferred terms are sorted within primary system organ class alphabetically

Other Relevant Findings

None

Date of Clinical Trial Report:

3-Oc-2011 (content final)

Date Inclusion on Novartis Clinical Trial Results Database

19 APR 2012

Date of Latest Update