NOVARTIS

Full Novartis CTRD Results Template

Sponsor Novartis
Generic Drug Name Vildagliptin Modified Release
Therapeutic Area of Trial Type 2 diabetes mellitus (T2DM)
Approved Indication Vildagliptin has been approved for treatment of type 2 diabetes. Vildagliptin Modified Release is investigational and has not been approved in any country.
Protocol Number CLAF237B2224
Title A multi-center, randomized, double-blind study to evaluate the efficacy and long-term safety of vildagliptin modified release (MR) as add-on therapy to metformin in patients with type 2 diabetes
Phase of Development Phase II /III
Study Start/End Dates 24-Feb-2008 to 31-Mar-2011

Study Design/Methodology

This was a multi-center, randomized, double-blind, parallel group study, with an adaptive element. After a 4-week placebo run-in period, patients were randomized to receive either vildagliptin MR 12.5 mg bid (twice daily), vildagliptin MR 25 mg bid, sitagliptin 50 mg bid, or placebo in a ratio of 1:1:1:1 in addition to their continued metformin treatment for 24 weeks (period 1).

Based on a planned combined assessment of the data of a 12-week interim analysis (IA) from Period 1 of the present study and the 12-week IA results of parallel study CLAF237B2201 with vildagliptin MR as monotherapy, vildagliptin MR 25 mg bid was selected to carry forward to period 2 of this study. Sitagliptin 50 mg bid was continued to be used as an active comparator. The data of period 1 (up to Week 24, considered as the core phase of the study) were analyzed and reported in a 24-week report.

Upon entering period 2 (52 week extension), in addition to their continued metformin treatment, patients who were randomized to the vildagliptin MR 25 mg bid dose (which was carried into period 2) continued on the same dose. Patients who were randomized to the vildagliptin MR 12.5 mg dose were switched to the MR 25 mg bid dose. Patients who were randomized to placebo were also switched to the vildagliptin MR 25 mg bid dose. Those patients who were randomized to sitagliptin 50 mg bid, the active comparator, continued their treatment during period 2. During period 2, patients attended 10 additional visits (Visits 9-18). The final analysis and report at the end of the study extension (Week 76) covered the long-term safety and tolerability of vildagliptin MR 25 mg bid in addition to continued metformin treatment over 76 weeks of treatment.

Centres

A total of 448 centers in 35 countries enrolled 2441 patients (number of centers in brackets): Argentina (6), Austria (5), Belgium (6), Brazil (17), Canada (25), Colombia (8), Denmark (10), Estonia (6), Finland (8), Germany (50), Greece (4), Guatemala (4), Hong-Kong (1), Hungary (12), India (10), Israël (6), Italy (19), Korea (5), Latvia (7), Lithuania (7), Mexico (5), Norway (6), Peru (6), Poland (6), Romania (7), Russia (11), Singapore (2), Slovakia (10), Sweden (5), Turkey (12), United Kingdom (5), United States (148), Venezuela (9).

Publication

None

Outcome measures

Primary outcome measures

Primary objective for 24-week core study:

- To evaluate the efficacy of vildagliptin MR (12.5 mg bid or 25 mg bid) as add-on therapy to metformin in patients with T2DM by testing the hypothesis that the HbA_{1c} reduction with vildagliptin MR added to metformin is superior to that of placebo added to metformin after 24 weeks of treatment.

The primary objective was only defined for the 24-week core study. All other objectives, including those for the 52-week study extension (Week 76, final analysis), were defined as being secondary in the study protocol.

Secondary outcome measures

Secondary objectives of the 24-week core study:

- To evaluate the efficacy of vildagliptin MR (12.5 mg bid or 25 mg bid) as add-on therapy to metformin in patients with T2DM by testing the hypothesis that the HbA_{1c} reduction with vildagliptin MR added to metformin is at least not inferior to that of sitagliptin 50 mg bid added to metformin after 24 weeks of treatment.
- To evaluate the efficacy of vildagliptin MR (12.5 mg bid or 25 mg bid) as add-on therapy to metformin in patients with T2DM by testing the hypothesis that the fasting plasma glucose (FPG) reduction with vildagliptin MR added to metformin is superior to that of placebo added to metformin after 24 weeks of treatment.
- To evaluate the efficacy of vildagliptin MR (12.5 mg bid or 25 mg bid) as add-on therapy to metformin in patients with T2DM by testing the hypothesis that the FPG reduction with vildagliptin MR added to metformin is at least not inferior to that of sitagliptin 50 mg bid added to metformin after 24 weeks of treatment.
- To evaluate the safety and tolerability of vildagliptin MR (12.5 mg bid or 25 mg bid) compared to placebo and sitagliptin over 24 weeks of treatment as add-on therapy to metformin in patients with T2DM.
- To evaluate the body weight change from baseline with vildagliptin MR (12.5 mg bid or 25 mg bid) compared to placebo and sitagliptin after 24 weeks of treatment as add-on therapy to metformin in patients with T2DM.

Secondary objectives defined for the 52-week study extension (76-week analysis):

- To evaluate the long-term safety and tolerability of vildagliptin MR 25 mg (the selected dose for the extension) compared to sitagliptin 50 mg bid over the entire study duration as add-on therapy to metformin in patients with T2DM.
- To evaluate the long-term efficacy of vildagliptin MR 25 mg (the selected dose) compared to sitagliptin (50 mg bid) over the entire study duration as add-on therapy to metformin in patients with T2DM.

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

Period 1: vildagliptin MR 12.5 mg bid + metformin, vildagliptin MR 25 mg bid + metformin, Placebo + metformin, sitagliptin 50 mg bid + metformin

Period 2: vildagliptin MR selected dose (25 mg bid) + metformin, sitagliptin 50 mg bid + metformin

Statistical Methods

For Week 24 efficacy analysis (core analysis):

The primary efficacy variable was change from baseline in HbA_{1c} at Week 24 or at the final visit prior to Week 24 if a patient discontinued during study period 1. Superiority of vildagliptin MR added to metformin in HbA_{1c} reduction after 24 weeks of treatment as compared to placebo added to metformin was the primary objective of the study and was tested based on the following null hypotheses and one-sided alternative hypotheses:

$\delta_{\text{Vilda MR, 12.5 mg bid}} \geq \delta_{\text{Placebo}}$ versus $\delta_{\text{Vilda MR, 12.5 mg bid}} < \delta_{\text{Placebo}}$,

$\delta_{\text{Vilda MR, 25 mg bid}} \geq \delta_{\text{Placebo}}$ versus $\delta_{\text{Vilda MR, 25 mg bid}} < \delta_{\text{Placebo}}$,

where δ_s were the mean change from baseline at Week 24 endpoint in HbA_{1c} in the treatment group indicated.

The primary efficacy variable was analyzed using an analysis of covariance (ANCOVA) model with treatment and pooled center as the classification variables and baseline HbA_{1c} as the covariate. The least squares mean (adjusted mean) change from baseline for each treatment group, the difference in the least squares mean changes between the two treatment groups (vildagliptin MR – placebo), and the two-sided adjusted 95% confidence interval along with the p-value for the difference were obtained from the primary analysis model and presented..

Tests for the non-inferiority of treatment with vildagliptin MR to sitagliptin as add-on therapy to metformin was based on the following null hypotheses and one-sided alternative hypotheses:

$\delta_{\text{Vilda MR, 12,5 mg bid}} \geq \delta_{\text{Sita}} + x\%$ versus $\delta_{\text{Vilda MR, 12.5 mg bid}} < \delta_{\text{Sita}} + x\%$

$\delta_{\text{Vilda MR, 25 mg bid}} \geq \delta_{\text{Sita}} + x\%$ versus $\delta_{\text{Vilda MR, 25 mg bid}} < \delta_{\text{Sita}} + x\%$,

where δ_{Sita} is the mean change from baseline for sitagliptin and x is the non-inferiority margin. Non-inferiority margin 0.4% and 0.3% were used.

The percentage of patients meeting each of the pre-defined responder criteria (categorical changes in HbA_{1c} at Week 24 endpoint $HbA_{1c} < 7\%$, $\leq 6.5\%$, $< 7\%$ in patients with baseline $HbA_{1c} \leq 8\%$ and $\geq 7\%$, HbA_{1c} reduction from baseline at Week 24 endpoint $\geq 0.7\%$) was summarized.

The analysis of the secondary efficacy variables (FPG and body weight) used the same ANCOVA model as specified for the primary efficacy variable HbA_{1c}.

For Week 76 efficacy analysis (final analysis):

The absolute value and change from baseline at each visit over the entire study period and study endpoint for all efficacy variables (HbA_{1c}, FPG, body weight) was presented by treatment group. The efficacy variables were analyzed using an analysis of covariance (ANCOVA) model with treatment and pooled center as the classification variables and baseline HbA_{1c} as the covariate. The percentage of patients meeting each of the pre-defined responder criteria as defined before was summarized.

Safety (for periods 1 and 2):

Demographic and background data as well as safety data were summarized by treatment group. Safety data were summarized based on all data collected during the entire study regardless of rescue medication use. Some safety data of importance (overall adverse events (AEs), serious AEs (SAEs), AEs that lead to discontinuation, pre-defined AEs as potential risks, hypoglycemia, lab abnormality, treatment emergent hepatic enzyme & creatine phosphokinase elevations) collected over the entire study period.

Study Population: Inclusion/Exclusion Criteria and Demographics

Key inclusion:

- Age in the range of 18-78 years inclusive at Visit 1.
- Patients with T2DM treated with metformin for at least 3 months and a stable dose of at least 1500 mg daily for a minimum of 4 weeks prior to Visit 1.
- Agreement to maintain the same dose of metformin throughout the study.
- HbA_{1c} of $\geq$ 7.0 and $\leq$ 9.5% at Visit 1.
- Body Mass Index (BMI) in the range of 22-45 kg/m^2 at Visit 1.
- Male, non-fertile female or female of childbearing potential using a medically approved birth control method based on local regulations.
- Agreement to continue their current diet/exercise regimen throughout the duration of the study unless otherwise instructed by the trial's physician.

Key exclusion:

- Pregnant or nursing (lactating) women, where pregnancy was defined as the state of a female after conception and until the termination of gestation, confirmed by a positive hCG laboratory test (> 5 mIU/mL).
- FPG $\geq$ 270 mg/dL ($\geq$ 15.0 mmol/L).

Other protocol defined inclusion/exclusion criteria applied

Participant Flow

Patient disposition during the entire study period (Randomized population)

Disposition Reason	Vilda MR 12.5mg/25mg bid + Met N=609 n (%)	Vilda MR 25mg bid + Met N=608 n (%)	Sita 50mg bid + Met N=608 n (%)	Placebo/Vilda MR 12.5mg/ 25mg bid + Met N=616 n (%)	Total N=2441 n (%)
Completed	482 (79.1)	489 (80.4)	502 (82.6)	480 (77.9)	1953 (80.0)
Discontinued	125 (20.5)	118 (19.4)	105 (17.3)	135 (21.9)	483 (19.8)
Adverse Event(s)	22 (3.6)	20 (3.3)	21 (3.5)	24 (3.9)	87 (3.6)
Abnormal laboratory value(s)	4 (0.7)	6 (1.0)	5 (0.8)	6 (1.0)	21 (0.9)
Abnormal test procedure result(s)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Unsatisfactory therapeutic effect	17 (2.8)	12 (2.0)	12 (2.0)	21 (3.4)	62 (2.5)
Patient's condition no longer requires study drug	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.1)
Protocol deviation	10 (1.6)	8 (1.3)	5 (0.8)	7 (1.1)	30 (1.2)
Patient withdrew consent	44 (7.2)	48 (7.9)	43 (7.1)	59 (9.6)	194 (7.9)
Lost to follow-up	19 (3.1)	13 (2.1)	17 (2.8)	15 (2.4)	64 (2.6)
Administrative problems	3 (0.5)	9 (1.5)	2 (0.3)	2 (0.3)	16 (0.7)
Death	5 (0.8)	1 (0.2)	0 (0.0)	1 (0.2)	7 (0.3)

Vilda = vildagliptin, Met = metformin, Sita = sitagliptin

Baseline Characteristics

Patient baseline demographic characteristics (Randomized population)

Demographic Variable	Vilda MR 12.5mg/25mg bid + Met N=609 n (%)	Vilda MR 25mg bid + Met N=608 n (%)	Sita 50mg bid + Met N=608 n (%)	Placebo/Vilda MR 12.5mg/ 25mg bid + Met N=616 n (%)	Total N=2441 n (%)
Age (years)					
Mean	56.9	56.7	56.9	57.2	56.9
Standard deviation (SD)	10.50	10.00	9.83	9.76	10.02
Minimum (Min)	21.0	23.0	23.0	26.0	21.0
Median	58.0	57.0	57.0	58.0	58.0
Maximum (max)	78.0	78.0	78.0	78.0	78.0
Age group					
< 65 years	463 (76.0%)	469 (77.1%)	462 (76.0%)	468 (76.0%)	1862 (76.3%)
≥ 65 years	146 (24.0%)	139 (22.9%)	146 (24.0%)	148 (24.0%)	579 (23.7%)
Gender					
Male	310 (50.9)	321 (52.8%)	321 (52.8%)	304 (49.4%)	1256 (51.5%)
Female	299 (49.1%)	287 (47.2%)	287 (47.2%)	12 (50.6%)	1185 (48.5%)
Race					
Caucasian	410 (67.3%)	3 2 (64.5%)	412 (67.8%)	405 (65.7%)	1619 (66.3%)
Black	20 (3.3%)	26 (4.3%)	22 (3.6%)	23 (3.7%)	91 (3.7%)
Asian (non-Indian subcontinent)	19 (3.1%)	20 (3.3%)	17 (2.8%)	20 (3.2%)	76 (3.1%)
Asian (Indian subcontinent)	57 (9.4%)	63 (10.4%)	54 (8.9%)	56 (9.1%)	230 (9.4%)
Hispanic or Latino	85 (14.0%)	91 (15.0%)	82 (13.5%)	84 (13.6%)	342 (14.0%)
Japanese	1 (0.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.0%)
Native American	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.3%)	2 (0.1%)
Pacific Islander	1 (0.2%)	0 (0.0%)	1 (0.2%)	0 (0.0%)	2 (0.1%)
Other	16 (2.6%)	16 (2.6%)	20 (3.3%)	26 (4.2%)	78 (3.2%)

Height (cm)					
Mean	165.8	166.4	166.2	166.0	166.1
SD	10.73	10.75	10.65	10.58	10.67
Min	138.0	120.0	141.0	138.0	120.0
Median	165.0	167.0	167.0	166.0	166.0
Max	200.0	195.0	203.0	195.0	203.0
Body weight (kg)					
Mean	86.7	86.5	86.3	86.9	86.6
SD	18.23	19.09	18.87	19.19	18.84
Min	46.1	44.3	47.2	45.0	44.3
Median	86.0	84.0	85.0	85.2	85.0
Max	162.3	154.0	145.1	148.3	162.3
BMI (kg/m^2)					
Mean	31.4	31.1	31.1	31.3	31.2
SD	5.06	5.24	5.21	5.25	5.19
Min	22.0	18.8	20.7	20.8	18.8
Median	31.0	30.4	30.4	30.6	30.6
Max	44.8	45.4	45.0	44.9	45.4
BMI group					
< 30 kg/m^2	260 (42.7%)	282 (46.4%)	285 (46.9%)	277 (45.0%)	1104 (45.2%)
≥ 30 kg/m^2	349 (57.3%)	326 (53.6%)	323 (53.1%)	339 (55.0%)	1337 (54.8%)
≥ 35 kg/m^2	137 (22.5%)	133 (21.9%)	130 (21.4%)	149 (24.2%)	549 (22.5%)

Demography information is collected on the day of the screening measurement (Week -4, Visit 1).

Patient baseline background characteristics (Randomized population)

ackground Characteristic	Vilda MR 12.5mg/25mg bid + Met N=609 n (%)	Vilda MR 25mg bid + Met N=608 n (%)	Sita 50mg bid + Met N=608 n (%)	Placebo/Vilda MR 12.5mg/ 25mg bid + Met N=616 n (%)	Total N=2441 n (%)
HbA_{1c} (percent)					
n	609	608	608	616	2441
Mean	7.9	7.9	7.8	7.8	7.8
SD	0.81	0.82	0.81	0.81	0.81
Min	6.2	5.9	5.9	5.3	5.3
Median	7.8	7.7	7.7	7.7	7.7
Max	11.2	11.2	12.7	10.3	12.7
HbA_{1c} (percent)					
≤7	68 (11.2%)	86 (14.1%)	87 (14.3%)	96 (15.6%)	337 (13.8%)
>7	541 (88.8%)	522 (85.9%)	521 (85.7%)	520 (84.4%)	2104 (86.2%)
≤8	388 (63.7%)	401 (66.0%)	409 (67.3%)	402 (65.3%)	1600 (65.5%)
>8	221 (36.3%)	207 (34.0%)	199 (32.7%)	214 (34.7%)	841 (34.5%)
≤	550 (90.3%)	553 (91.0%)	565 (92.9%)	565 (91.7%)	2233 (91.5%)
>9	59 (9.7%)	55 (9.0%)	43 (7.1%)	51 (8.3%)	208 (8.5%)
FPG (mmol/L)					
n	609	607	608	616	2440
Mean	9.5	9.3	9.2	9.3	9.3
SD	2.61	2.42	2.52	2.44	2.50
Min	3.1	4.6	4.0	4.6	3.1
Median	9.0	8.8	8.7	8.8	8.8
Max	21.5	20.2	22.1	25.4	25.4

Duration of Type 2 Diabetes (years)					
n	609	608	608	616	2441
Mean	5.9	6.1	5.8	6.2	6.0
SD	4.60	5.12	4.82	5.35	4.98
Min	0.3	0.3	0.3	0.2	0.2
Median	4.8	4.6	4.9	4.8	4.8
Max	32.0	33.7	30.7	38.0	38.0
Duration of diabetes					
< 5 years	320 (52.5%)	322 (53.0%)	319 (52.5%)	321 (52.1%)	1282 (52.5%)
≥ 5 years - <10 years	183 (30.0%)	168 (27.6%)	188 (30.9%)	180 (29.2%)	719 (29.5%)
≥ 10 years	106 (17.4%)	118 (19.4%)	101 (16.6%)	115 (18.7%)	440 (18.0%)
GFR (MDRD) (mL/min/1.73 m^2)					
Normal (>80)	453 (74.4%)	458 (75.3%)	452 (74.3%)	459 (74.5%)	1822 (74.6%)
Mild (≥50 - ≤80)	156 (25.6%)	141 (23.2%)	151 (24.8%)	151 (24.5%)	599 (24.5%)
Moderate (≥30 - <50)	0 (0.0%)	7 (1.2%)	4 (0.7%)	6 (1.0%)	17 (0.7%)
Severe (<30	(0.0%)	1 (0.2%)	1 (0.2%)	0 (0.0%)	2 (0.1%)
Missing	0 (0.0%)	1 (0.2%)	0 (0.0%)	0 (0.0%)	1 (0.0%)
Is subject a current smoker?					
Yes	87 (14.3%)	75 (12.3%)	92 (15.1%)	88 (14.3%)	342 (14.0%)
No	522 (85.7%)	533 (87.7%)	516 (84.9%)	528 (85.7%)	2099 (86.0%)
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Duration of metformin use at screening (months)					
n	609	604	607	616	2436
Mean	22.7	23.6	20.5	22.5	22.3
SD	28.68	30.98	24.79	28.66	28.37
Min	0.0	1.0	1.0	0.2	0.0
Median	11.5	12.3	11.0	11.6	11.7
Max	200.2	236.9	156.9	212.3	236.9
Metformin total daily use at screening (mg)					
n	609	608	608	616	2441
Mean	1880.0	1890.1	1892.4	1893.1	1888.9
SD	378.22	380.15	391.65	366.39	378.97
Min	1500.0	1500.0	1500.0	1500.0	1500.0
Median	1700.0	1700.0	1700.0	1700.0	1700.0
Max	3400.0	3000.0	3000.0	3000.0	3400.0

Duration of type 2 diabetes is collected on the day of the screening visit (Week -4, Visit 1).
For baseline HbA_{1c} measurements, only patients with at least one measurement on or prior to Day 1 are included.
Baseline HbA_{1c} and baseline FPG are the sample obtained on Day 1, or the sample obtained at an earlier visit (scheduled or unscheduled) which was closest to Day 1, if the Day 1 measurement is missing.
GFR (MDRD) = Glomerular filtration rate estimated using the MDRD formula. GFR is calculated using the serum creatinine and body weight value at Day1 measurement, or the sample obtained at an earlier visit (scheduled or unscheduled) which was closest to Day 1, if the Day 1 measurement is missing.

Outcome measures

Primary Outcome Results

Period 1 (Week 24, core analysis)

ANCOVA results for change from baseline in HbA_{1c} (%) to Week 24 endpoint censored at rescue medication (Full analysis set (FAS) population)

Treatment	n	Baseline mean (SE)	Adjusted mean change (SE)	Difference in adjusted mean change between treatment groups mean(SE)	95% CI	p-val(1) (non-inf 0.4 margin)	p-val(2) (non-inf 0.3 margin)	p-val(3) (superiority)
FAS Population								
Vildagliptin MR 12.5 mg bid + Metformin	587	7.89 (0.03)	-0.49 (0.03)					
Vildagliptin MR 25 mg bid + Metformin	581	7.85 (0.03)	-0.58 (0.03)					
Sitagliptin 50 mg bid + Metformin	588	7.80 (0.03)	-0.68 (0.03)					
Placebo + Metformin	591	7.83 (0.03)	-0.09 (0.03)					
Treatment comparison:								
Vilda MR 12.5 mg bid + Met - Placebo + Met				-0.40 (0.05)	(-0.49, -0.31)			<.0001*
Vilda MR 25 mg bid + Met - Placebo + Met				-0.49 (0.05)	(-0.58, -0.41)			<.0001*
Vilda MR 12.5 mg bid + Met - Sita 50 mg bid + Met				0.19 (0.05)	(0.11, 0.28)	<.0001	0.0094*	1.0000
Vilda MR 25 mg bid + Met - Sita 50 mg bid + Met				0.10 (0.05)	(0.01, 0.19)	<.0001	<.0001*	0.9871

Baseline is defined as the Day 1 measurement or the measurement obtained at an earlier visit (scheduled or unscheduled) which was closest to Day 1, if the Day 1 measurement is missing. Week 24 endpoint is the measurement obtained at the last post-baseline study visit prior to or at scheduled Visit 8 (Week 24) and before the start of rescue medication, regardless of whether it was obtained at a scheduled or unscheduled visit.

n is the number of patients with observations at both baseline and Week 24 endpoint.
For Week 24 endpoint (EP), data obtained after the start of rescue medication is imputed with the last available measurement before or at the start of rescue medication.
Adjusted means and the associated standard errors (SE), confidence intervals (CI), and p-values were from an ANCOVA model containing terms for treatment, pooled center and baseline. P-values are for one-sided tests.
(1) non-inferiority test with margin 0.4% (2) non-inferiority test with margin 0.3% (3) superiority test
* indicates statistical significance according to the closed test procedure.

Secondary Outcome Results

Period 1 (Week 24, core analysis)

ANCOVA results for change from baseline in FPG to Week 24 endpoint censored at rescue medication (FAS population)

Treatment	n	Baseline mean(SE)	Adjusted mean change(SE)	Difference in adjusted mean change between treatment groups mean(SE)	95% CI	p-val[(1)] (non-inf 0.6 margin)	p-val[(2)] (superiority)
FAS Population							
Vildagliptin MR 12.5 mg bid + Metformin	599	9.52 (0.11)	-0.84 (0.08)				
Vildagliptin MR 25 mg bid + Metformin	590	9.31 (0.10)	-0.94 (0.08)				
Sitagliptin 50 mg bid + Metformin	593	9.21 (0.10)	-1.01 (0.08)				
Placebo + Metformin	599	9.28 (0.10)	-0.31 (0.08)				
Treatment comparison:							
Vilda MR 12.5 mg bid + Met - Placebo + Met				-0.53 (0.11)	(-0.75, -0.31)		<.0001*
Vilda MR 25 mg bid + Met - Placebo + Met				-0.64 (0.11)	(-0.86, -0.42)		<.0001*
Vilda MR 12.5 mg bid + Met - Sita 50 mg bid + Met				0.17 (0.11)	(-0.05, 0.39)	<.0001*	0.9352
Vilda MR 25 mg bid + Met - Sita 50 mg bid + Met				0.07 (0.11)	(-0.15, 0.290)	<.0001*	0.7208

Baseline is defined as the Day 1 measurement or the measurement obtained at an earlier visit (scheduled or unscheduled) which was closest to Day 1, if the Day 1 measurement is missing. Week 24 endpoint is the measurement obtained at the last post-baseline study visit prior to or at scheduled Visit 8 (Week 24) and before the start of rescue medication, regardless of whether it was obtained at a scheduled or unscheduled visit. n is the number of patients with observations at both baseline and Week 24 endpoint.
For Week 24 EP, data obtained after the start of rescue medication is imputed with the last available measurement before or at the start of rescue medication.
Adjusted means and the associated standard errors (SE), confidence intervals (CI), and p-values were from an ANCOVA model containing terms for treatment, pooled center and baseline. P-values are for one-sided tests.
(1) non-inferiority test with margin 0.6 mmol/L (2) superiority test
* indicates statistical significance of one-sided test at alpha level 0.025.

ANCOVA results for change from baseline in body weight (kg) to Week 24 endpoint (FAS population)

Treatment	n	Baseline mean (SE)	Adjusted mean change (SE)	Difference in adjusted mean change between treatment groups mean(SE)	95% CI	P val[(1)] (two-sided)	P val[(2)] (superiority)
Vildagliptin MR 12.5 mg bid + Metformin	600	86.40 (0.75)	-0.25 (0.12)				
Vildagliptin MR 25 mg bid + Metformin	590	85.99 (0.79)	-0.50 (0.12)				
Sitagliptin 50 mg bid + Metformin	598	86.00 (0.77)	-0.51 (0.12)				

Placebo + Metformin	600	86.69 (0.78)	-0.73 (0.12)			
Treatment comparison						
Vilda MR 12.5 mg bid + Met - Placebo + Met				0.48 (0.16)	(0.17, 0.80)	0.9987
Vilda MR 25 mg bid + Met - Placebo + Met				0.23 (0.16)	(-0.08, 0.55)	0.9271
Vilda MR 12.5 mg bid + Met - Sita 50 mg bid + Met				0.26 (0.16)	(-0.05, 0.58)	0.1042
Vilda MR 25 mg bid + Met - Sita 50 mg bid + Met				0.01 (0.16)	(-0.31, 0.33)	0.9483

Baseline is defined as the Day 1 measurement or the measurement obtained at an earlier visit (scheduled or unscheduled) which was closest to Day 1, if the Day 1 measurement is missing. Week 24 endpoint is the measurement obtained at the last post-baseline study visit prior to or at scheduled Visit 8 (Week 24) and before the start of rescue medication, regardless of whether it was obtained at a scheduled or unscheduled visit.

n is the number of patients with observations at both baseline and Week 24 endpoint.
For Week 24 EP, data obtained after the start of rescue medication is imputed with the last available measurement before or at the start of rescue medication.
Adjusted means and the associated standard errors (SE), confidence intervals (CI), and p-values were from an ANCOVA model containing terms for treatment, pooled center and baseline.

(1) two-sided test (2) superiority test
* indicates statistical significance.

Period 2 (Week 76, final analysis)

ANCOVA results for change from baseline in HbA_{1c} (%) to Week 76 endpoint censored at rescue medication (FAS population)

Treatment	n	Baseline mean(SE)	Adjusted mean change(SE)	Difference in adjusted mean change between treatment groups mean(SE)	95% CI
Vilda MR 12.5mg/25mg bid + Met	587	7.89 (0.03)	-0.50 (0.04)		
Vilda MR 25mg bid + Met	582	7.84 (0.03)	-0.32 (0.04)		
Sita 50mg bid + Met	589	7.80 (0.03)	-0.47 (0.04)		
Treatment comparison					
Vilda MR 12.5mg/25mg bid + Met - Sita 50mg bid + Met				-0.03 (0.06)	(-0.14, 0.09)
Vilda MR 25mg bid + Met - Sita 50mg bid + Met				0.15 (0.06)	(0.03, 0.26)

Baseline is defined as the Day 1 measurement or the measurement obtained at an earlier visit (scheduled or unscheduled) which was closest to Day 1 date, if the Day 1 measurement is missing. Week 76 endpoint is the measurement obtained at the last post-baseline study visit prior to or at scheduled Visit 18 (Week 76) and before the start of rescue medication, regardless of whether it was obtained at a scheduled or unscheduled visit.

n is the number of patients with observation at both baseline and Week 76 endpoint. For Week 76 endpoint, data obtained after the start of rescue medication is imputed with the last available measurement before or at the start of rescue medication. Adjusted means and the associated standard errors (SE), and confidence intervals (CI) were from an ANCOVA model containing terms for treatment, pooled center and baseline.

ANCOVA results for change from baseline in fasting plasma glucose (mmol/L) to Week 76 endpoint censored at rescue medication (FAS population)

Treatment	n	Baseline mean(SE)	Adjusted mean change(SE)	Difference in adjusted mean change between treatment groups mean(SE)	95% CI
Vilda MR 12.5mg/25mg bid + Met	600	9.52 (0.11)	-0.71 (0.10)		
Vilda MR 25mg bid + Met	591	9.32 (0.10)	-0.32 (0.10)		
Sita 50mg bid + Met	597	9.20 (0.10)	-0.59 (0.10)		
Treatment comparison					
Vilda MR 12.5mg/25mg bid + Met - Sita 50mg bid + Met				-0.12 (0.13)	(-0.38, 0.13)
Vilda MR 25mg bid + Met - Sita 50mg bid + Met				0.27 (0.13)	(0.01, 0.53)

Baseline is defined as the Day 1 measurement or the measurement obtained at an earlier visit (scheduled or unscheduled) which was closest to Day 1 date, if the Day 1 measurement is missing. Week 76 endpoint is the measurement obtained at the last post-baseline study visit prior to or at scheduled Visit 18 (Week 76) and before the start of rescue medication, regardless of whether it was obtained at a scheduled or unscheduled visit.

n is the number of patients with observation at both baseline and Week 76 endpoint.

For Week 76 E endpoint , data obtained after the start of rescue medication is imputed with the last available measurement before or at the start of rescue medication.

Adjusted means and the associated standard errors (SE), and confidence intervals (CI) were from an ANCOVA model containing terms for treatment, pooled center and baseline.

ANCOVA results for change from baseline in body weight (kg) to Week 76 endpoint censored at rescue medication (FAS population)

Treatment	n	Baseline mean(SE)	Adjusted mean change(SE)	Difference in adjusted mean change between treatment groups mean(SE)	95% CI.
Vilda MR 12.5mg/25mg bid + Met	600	86.40 (0.75)	-0.40 (0.27)		
Vilda MR 25mg bid + Met	591	86.01 (0.79)	-0.23 (0.27)		
Sita 50mg bid + Met	599	85.97 (0.77)	-0.66 (0.27)		
Treatment comparison					
Vilda MR 12.5mg/25mg bid + Met - Sita 50mg bid + Met				0.26 (0.37)	(-0.46, 0.99)
Vilda MR 25mg bid + Met - Sita 50mg bid + Met				0.43 (0.37)	(-0.30, 1.15)

Baseline is defined as the Day 1 measurement or the measurement obtained at an earlier visit (scheduled or unscheduled) which was closest to Day 1 date, if the Day 1 measurement is missing. Week 76 endpoint is the measurement obtained at the last post-baseline study visit prior to or at scheduled Visit 18 (Week 76) and before the start of rescue medication, regardless of whether it was obtained at a scheduled or unscheduled visit.
n is the number of patients with observation at both baseline and Week 76 endpoint.
For Week 76 endpoint , data obtained after the start of rescue medication is imputed with the last available measurement before or at the start of rescue medication.
Adjusted means and the associated standard errors (SE), and confidence intervals (CI) were from an ANCOVA model containing terms for treatment, pooled center and baseline.

Safety Results

Adverse Events by System Organ Class

Number (%) of patients with AEs during the entire study period (76 weeks) by primary system organ class (Safety population)

Primary system organ class	Vilda MR 12.5mg/25mg bid + Met N=609 n (%)	Vilda MR 25mg bid + Met N=602 n (%)	Sita 50mg bid + Met N=605 n (%)	Placebo/Vilda MR 12.5mg/ 25mg bid + Met N=615 n (%)
Any Primary system organ class	423 (69.5)	435 (72.3)	434 (71.7)	418 (68.0)
Blood and lymphatic system disorders	19 (3.1)	19 (3.2)	23 (3.8)	12 (2.0)
Cardiac disorders	34 (5.6)	34 (5.6)	31 (5.1)	26 (4.2)
Congenital, familial and genetic disorders	2 (0.3)	1 (0.2)	0 (0.0)	1 (0.2)
Ear and labyrinth disorders	19 (3.1)	11 (1.8)	12 (2.0)	23 (3.7)
Endocrine disorders	5 (0.8)	5 (0.8)	3 (0.5)	4 (0.7)
Eye disorders	34 (5.6)	38 (6.3)	20 (3.3)	33 (5.4)
Gastrointestinal disorders	144 (23.6)	125 (20.8)	151 (25.0)	141 (22.9)
General disorders and administration site conditions	75 (12.3)	77 (12.8)	68 (11.2)	69 (11.2)
Hepatobiliary disorders	10 (1.6)	13 (2.2)	11 (1.8)	10 (1.6)
Immune system disorders	10 (1.6)	7 (1.2)	10 (1.7)	8 (1.3)
Infections and infestations	242 (39.7)	223 (37.0)	240 (39.7)	235 (38.2)
Injury, poisoning and procedural complications	51 (8.4)	67 (11.1)	57 (9.4)	66 (10.7)
Investigations	25 (4.1)	33 (5.5)	28 (4.6)	20 (3.3)
Metabolism and nutrition disorders	55 (9.0)	61 (10.1)	60 (9.9)	49 (8.0)
Musculoskeletal and connective tissue disorders	129 (21.2)	134 (22.3)	153 (25.3)	125 (20.3)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	16 (2.6)	9 (1.5)	10 (1.7)	20 (3.3)
Nervous system disorders	120 (19.7)	110 (18.3)	111 (18.3)	109 (17.7)
Psychiatric disorders	33 (5.4)	28 (4.7)	39 (6.4)	25 (4.1)
Renal and urinary disorders	25 (4.1)	28 (4.7)	26 (4.3)	16 (2.6)
Reproductive system and breast disorders	14 (2.3)	28 (4.7)	23 (3.8)	10 (1.6)
Respiratory, thoracic and mediastinal disorders	69 (11.3)	50 (8.3)	54 (8.9)	49 (8.0)
Skin and subcutaneous tissue disorders	56 (9.2)	54 (9.0)	64 (10.6)	67 (10.9)
Social circumstances	2 (0.3)	3 (0.5)	1 (0.2)	0 (0.0)
Vascular disorders	63 (10.3)	59 (9.8)	58 (9.6)	62 (10.1)

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.

A patient with multiple adverse events within a primary system organ class is counted only once in the total row.

10 Most Frequently Reported AEs Overall by Preferred Term n (%)

Number (%) of patients reporting common AEs during the entire study period (76 weeks) by preferred term (Safety population)

Preferred term	Vilda MR 12.5mg/25mg bid + Met N=609 n (%)	Vilda MR 25mg bid + Met N=602 n (%)	Sita 50mg bid + Met N=605 n (%)	Placebo/Vild MR 12.5mg/ 25mg bid + M N=615 n (%)
Nasopharyngitis	65 (10.7)	51 (8.5)	68 (11.2)	68 (11.1)
Back pain	44 (7.2)	26 (4.3)	52 (8.6)	37 (6.0)
Hypertension	44 (7.2)	46 (7.6)	44 (7.3)	46 (7.5)
Headache	42 (6.9)	36 (6.0)	37 (6.1)	24 (3.9)
Upper respiratory tract infection	36 (5.9)	32 (5.3)	29 (4.8)	26 (4.2)
Diarrhoea	33 (5.4)	33 (5.5)	37 (6.1)	30 (4.9)
Influenza	32 (5.3)	36 (6.0)	35 (5.8)	21 (3.4)
Urinary tract infection	32 (5.3)	22 (3.7)	31 (5.1)	27 (4.4)
Arthralgia	27 (4.4)	34 (5.6)	31 (5.1)	27 (4.4)
Bronchitis	21 (3.4)	30 (5.0)	28 (4.6)	29 (4.7)

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

Serious Adverse Events and Deaths

Number (%) of patients with serious or clinically significant AEs over the entire study period of 76 weeks (Safety population)

Preferred term	Vilda MR 12.5mg/25mg bid + Met N=609 n (%)	Vilda MR 25mg bid + Met N=602 n (%)	Sita 50mg bid + Met N=605 n (%)	Placebo/Vilda MR 12.5mg/ 25mg bid + M N=615 n (%)
Deaths	5 (0.8)	1 (0.2	0 (0.0)*	1 (0.2)
SAEs	50 (8.2)	40 (6.6)	48 (7.9)	43 (7.0)

* One death occurred in the sitagliptin group due to bronchial carcinoma 13 days after study completion. That death was reported during safety follow-up in safety database.

Other Relevant Findings

None.

Date of Clinical Trial Report 23-Nov-2011 (content final)
Date Inclusion on Novartis Clinical Trial Results Database 26-Mar-2012
Date of Latest Update 26-Mar-2012

E. Abbreviated Novartis CTRD Results Template

Sponsor

Novartis

Example: *Genentech; Idenix, Schering*

Definition: *Full names of all organizations co-sponsoring and/or providing financial support for the protocol.*

NOTE: *Confirm all collaborator names and permissions to post with Business Development and Licensing before posting this information, if there are collaborators confirmed.*

Generic Drug Name

Example: *Valsartan*

Definition: *Generic name of the drug.*

NOTE: *Do not use trade/commercial names. This information is usually found on the clinical study report (CSR) title page*

Therapeutic Area of Trial

Example: *Hypertension, allergic asthma, malaria, schizophrenia, breast cancer, etc.*

Definition: *Refers to the disease/trial therapeutic area and NOT to the TA/BU.*

Approved Indication

Example:

- *Indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive agents.*
- *Indicated for treatment of heart failure (New York Heart Association Classification II-IV).*
- *Indicated for the management of severely ill schizophrenic patients who fail to respond adequately to standard drug treatment for schizophrenia.*

Definition: *Indication(s) for which the drug was approved.*

- *Include indications as written in the prescribing information insert.*
- *Indicate the country(ies) for which you have provided the indication(s)*
- *If not approved in any country, insert "investigational."*

Protocol Number

Example: *CVAH631B2302*

Definition: *Unique identification assigned to the protocol by Novartis.*

NOTE: *This information is found on the CSR title page. The trial code must match exactly the code in ClinAdmin. Multiple studies conducted under the same grant must each have a unique number.*

Title

Example: *–A multicenter, randomized, double-blind, parallel-group, 24-week study to evaluate the efficacy of the valsartan/hydrochlorothiazide fixed dose combination versus amlodipine on systolic blood pressure in patients with moderate hypertension*

Definition: *Official name of the protocol provided by Novartis.*

NOTE: *Do not use the trade/commercial name even if appearing in official title. Trade/commercial names are considered promotional and will be removed. The study title can be found on the CSR title page.*

Phase of Development

Example: *Phase III*

Definition: *stage of development for the trial*

NOTE: *This template does not apply to investigator-initiated and post-marketing observational studies. Clinical trial phase information can be found on the CSR title page.*

Study Start/End Dates

Example: *01 Jan 2003 to 01 Jan 2005*

Definition: *Study Start: Actual first-patient first-visit; Study End: Actual last-patient last-visit.*

If terminated early: Give reason for early termination.

For Oncology: Primary Completion Date will be listed as an end date (i.e. 10Sep2010 (Primary Completion Date)) if the CTRD is based on the Primary Completion Date to align with publication(s) and/or ClinicalTrials.gov requirements. When the actual LPLV is reached, the CTRD will be updated and the end date will be changed to this date.

NOTE: *This information can be found on the CSR title page.*

Study Design/Methodology

Example: *Multicenter, multinational, randomized, double-blind, parallel-group, efficacy and safety study of valsartan/hydrochlorothiazide (HCTZ) fixed dose combination versus amlodipine in patients with moderate hypertension and at least 1 additional cardiovascular risk factor or concomitant condition. After a 3-week washout and placebo run-in phase, patients were randomized to 4 weeks of once-daily treatment with valsartan 160 mg or amlodipine 5 mg.*

Patients were then treated once daily with valsartan 160 mg/HCTZ 25 mg, valsartan 160 mg/HCTZ 12.5 mg, or amlodipine 10 mg for 20 weeks.

Definition: *Specific information about how the trial was conducted*

NOTE: *This information is found in the CSR synopsis and should, at a minimum, contain the type of study conducted with a description of the treatment periods. Adjust verb tense to past tense as necessary.*

Centres

Example: *57 centers in 11 countries: Argentina (6), Belgium (3), Canada (7), Denmark (6), Finland (1), France (5), Germany (8), Italy (5), Norway (2), Sweden (4), United Kingdom (10)*

Definition: *List of countries and number of centres participating in the trial*

NOTE: *Do not list centre names or cities. This information can be found in the CSR synopsis.*

Publication

Example: *Ridker PM, Danielson E, Rifai N, et al. Valsartan, blood pressure reduction, and C-reactive protein: preliminary findings. Hypertension. 1976;48(1):73-9.*

Definition: *Acceptable publications include manuscripts published in a peer-reviewed journal.*

If a publication has occurred, include the full citation using the sample format and include a publicly accessible link (eg, PubMed) to the abstract if available. If a publication has occurred, the remaining template fields below are not required.

If the publication does not adequately present the efficacy and safety information, the Novartis CTRD template still needs to be completed.

Abstracts are no longer allowed for this field as the sole publication citation.

If posting the results on the CTRD may jeopardize the publication of a manuscript, the clinical team/Medical Communication Leader should contact the CDO. A delayed disclosure form would have to be completed.

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

Example: *Oral tablets of valsartan 160 mg and HCTZ 12.5 mg or 25 mg once each morning*

Definition: *Name, dose, and route of administration of study drug. Do not include preparation instructions of product.*

NOTE: *This information can be found in the CSR synopsis.*

Statistical Methods

Example: Unless otherwise specified, all statistical tests were conducted against a 2-sided alternative hypothesis, employing a significance level of 0.05. Data from all centers were pooled to ensure that adequate subject numbers are available for subgroup analyses. Background and relevant baseline information were summarized with appropriate descriptive statistics (sample size, mean, standard deviation, minimum, 25th percentile, median, 75th percentile, and maximum for continuous variables; frequencies and percentage for discrete variables). Chi-square tests for categorical variables and 2-sample t-test for continuous variables were used to test for homogeneity between the treatment groups. Baseline p-values obtained form these comparison were provided for descriptive purposes, and were not to be considered to define any formal basis for determining factors which should be included in statistical analysis models.

The intent-to-treat (ITT) population, consisting of all randomized subjects for whom at least one valid post-baseline efficacy measurement was obtained, was used for efficacy analyses. The safety population, consisting of all randomized subjects who took at least one dose of study drug, was used for safety analyses. The completers population consisted of all randomized subjects from whom valid measurements of hsCRP were obtained at baseline, Week 6 and Week 12.

The primary efficacy evaluations were performed on the intent-to-treat (ITT) population (defined as all patients with at least one efficacy evaluation after starting valsartan/HCTZ 25). The primary efficacy parameter was the change in MSDBP between Visit 4 (performed at the end of a 4-week treatment period with valsartan 160/HCTZ 12.5 once daily, just before the switch to valsartan 160/HCTZ 25 once daily) and Visit 5 (performed at the end of the 4 week treatment period with valsartan 160/HCTZ 25 once daily) in those patients not controlled by the fixed combination containing the lower HCTZ dose. The mean change was calculated as a point estimate; the statistical significance of the change was assessed by a one-sample t-test with a 2-sided significance level of 5%. Additionally, a 95% confidence interval was calculated. Supportive analyses were conducted for the per protocol (PP) population as a confirmation of the results obtained.

To assess evidence of association of hsCRP, SBP, DBP, pulse and their respective changes with demographic and baseline characteristics, Spearsman correlation coefficients were calculated.

Adverse events were summarized by the number and percentage of subjects who had any adverse event (AE), who had an AE in each body system, and who had each individual AE.

Definition: Statistical methodology applied to the data.

NOTE: This should be a brief description of the statistical methods, which is usually found in the CSR synopsis. The text used in this example is taken from several CSRs and should not be copied and pasted into actual templates to be posted to the CTRD.

Study Population: Inclusion/Exclusion Criteria and Demographics

Example:

Inclusion criteria

- *Male or female patients ≥18 years with essential hypertension defined as MSDBP ≥ 100 mmHg and < 110 mmHg at the end of the wash-out period (Visit 2 or Visit 3) for previously treated patients and at Visit 3 for previously untreated patients.*
- *Female patients: post-menopausal for one year, surgically sterile or using an effective contraceptive method.*
- *Women of Child Bearing Potential (WOCBP) included any female who had experienced menarche and who had not undergone successful surgical sterilization (hysterectomy, bilateral tubal ligation or bilateral oophorectomy) or was not postmenopausal (defined as*

amenorrhea ≥ 12 consecutive months). Even women who were using mechanical products such as an intrauterine device or barrier methods (diaphragm, condoms, spermicides) to prevent pregnancy or practicing abstinence or where partner was sterile (e.g. vasectomy) were considered to be of child bearing potential. WOCBP must have had a negative urine pregnancy test at Visit 1 (week 0).

Exclusion criteria

- *History of secondary hypertension (including primary aldosteronism, renovascular hypertension, pheochromocytoma, etc.)*
- *Mean SBP > 185 mmHg and/or mean DBP > 109 mmHg*
- *Pharmacologic antihypertensive therapy with ACE inhibitors, angiotensin receptor blockers, or aldosterone blockers, within 3 months prior to Visit 1 or with thiazide diuretics within 1 month prior to Visit 1.*
- *Initiation of lipid- lowering pharmacologic therapy or any change in lipid- lowering dose less than 6 weeks prior to Visit 1. The dose could not be modified at any time during the course of the study*
- *Myocardial infarction, stroke, or cardiovascular revascularization/angioplasty, unstable angina pectoris, or onset of congestive heart failure wit hin the last 6 months*
- *History of hospitalization within the last month prior to Visit 1*
- *Uncontrolled treated diabetes mellitus (DM) defined as HbA1C > 11.0 % within the month prior to Visit 1*
- *Diagnosis of cancer, excluding basal cell carcinoma, within 5 years prior to enrollment in the study, or any life threatening illness with expected death within 5 years*
- *Documentation of serum creatinine > 2.0 mg/dl within 3 months prior to Visit 1, serum potassium < 3.5 or >5.5 mEq/L within 3 months prior to Visit 1, any serum aspartate aminotransferase or alanine aminotransferase elevation 2 x the upper limit of normal within 3 months prior to Visit 1*
- *Hypersensitivity to valsartan or other angiotensin II receptor blockers or hydrochlorothiazide*

Definition: *Description of key criteria for including/excluding patients into/from the study.*

- ***NOTE:*** *This information can be found in the CSR synopsis.*

Participant Flow

NOTE: *This information can usually be found in Section 10 of the CSR*

Example. Please paste table from CSR or NLM ClinicalTrials.gov results record.

	Nov drug µg n (%)	Pbo n (%)	Total n (%)
Screenings	-	-	755
Patients			
R ndomized	163 (100.0)	160 (100.0)	323 (100.0)
Expose	163 (100.0)	160 (100.0)	323 (100.0)
Completed	144 (88.3)	1 0 (81.3)	274 (84.8)
Disconti ued	19 11 7)	30 (18.)	49 (15.2)
Primary reason for premature discontinuation			
Adverse event(s)	9 (5.5)	10 (6.3)	19 (5.9)
Subject withdrew consent	4 (2.5)	9 (5.6)	13 (4.0)
Protocol deviation	3 (1.8)	4 (2.5)	7 (2.2)
Abnormal test procedure result(s)	1 (0.6)	0 (0.0)	1 (0.3)
Unsatisfactory therapeutic effect	1 (0.6)	3 (1.9)	4 (1.2)
Lost to follow-up	1 (0.6)	1 (0.6)	2 (0.6)
Abnormal laboratory value(s)	0 (0.0)	1 (0.6)	1 (0.3)
Death	0 (0.0)	2 (1.3)	2 (0.6)

Baseline Characteristics

Definition: *Demographic data serves to provide the characteristics of the population in the study. Include only specific demographic data relevant to your study.*

NOTE: *This information can usually be found in Section 11 of the CSR.*

Example. Please paste table from CSR or NLM ClinicalTrials.gov results record.

		Novartis drug N=163	Pbo N=160	Total N=323
Age (years)	n	163	160	323
	Mean	64.0	64.1	64.0
	SD	8.29	9.43	8.86
	Median	64.0	64.0	64.0
	Min - Max	44 - 85	40 - 90	40 - 90
Age group – n (%)	19–39 years	0 (0.0)	0 (0.0)	0 (0.0)
	40–64 years	85 (52.1)	84 (52.5)	169 52.3)
	≥ 65 years	78 47.9)	76 (47.)	154 47.7)
Sex – (%)	Male	89 (54.6)	87 (54.4)	176 (54.5)
	Female	74 (45.4)	73 (45.6)	147 (45.5)
Race – n (%)	C ucasian	14 (8 .0)	146 (9 .3)	291 (90.1)
	Black	10 (6.1)	10 (6.3)	20 (6.2)
	Asian	5 (3.1)	3 (1.9)	8 (2.5)
	Other	3 (1.8)	1 (0.6)	4 (1.2)

Safety Results

This data can be taken from the NLM ClinicalTrials.gov results record, if available, or from the final CSR.

Note: The AE tables in the NLM ClincalTrials.gov results records differ in the way data is presented due to NLM requirements. NLM has 2 separate AE tables: one is non-serious AEs only; the second is serious AEs only.

NOTE: *This information can usually be found in Section 12 of the CSR*

Adverse Events by System Organ Class

Example. Please paste table from CSR or NLM ClinicalTrials.gov results record.

	Novartis product N (%)	**Comparator N (%)**
Patients studied		
Randomized patients	471	415
Patients with drug-related AE	21 (4.5)	50 (10.8)
Drug-related AEs by primary system organ class		
Respiratory, thoracic and mediastinal disorders	5 (1.1)	37 (8.0)
Nervous system disorders	0 (0.0)	7 (1.5)
Gastrointestinal disorders	6 (1.3)	2 (0.4)
General disorders	2 (0.4)	3 (0.6)
Cardiac disorders	2 (0.4)	2 (0.4)
Vascular disorders	1 (0.2)	3 (0.6)
Skin and subcutaneous tissue disorders	3 (0.6)	0 (0.0)
Ear and labyrinth disorders	2 (0.4)	0 (0.0)
Reproductive system and breast disorders	0 (0.0)	2 (0.4)
Renal and urinary disorders	0 (0.0)	1 (0.2)
Infections and infestations	0 (0.0)	0 (0.0)
Psychiatric disorders	0 (0.0)	0 (0.0)
Immune system disorders	1 (0.2)	0 (0.2)

10 Most Frequently Reported AEs Overall by Preferred Term n (%)

Example. Please paste table from CSR or NLM ClinicalTrials.gov results record.

	Novartis product	Comparator
Nasopharyngitis	7 (1.1)	6 (0.9)
Headache	4 (0.6)	4 (0.6)
Influenza	4 (0.6)	4 (0.6)
Diarrhea	4 (0.6)	4 (0.6)
Depression	3 (0.5)	2 (0.3)
Sinusitis	2 (0.3)	2 (0.3)
Bronchitis	2 (0.3)	2 (0.3)
Hypotension	2 (0.3)	2 (0.3)
Palpitations	2 (0.3)	2 (0.3)
Vertigo	2 (0.3)	2 (0.3)

Serious Adverse Events and Deaths

Example. Please paste table from CSR or NLM ClinicalTrials.gov results record.

	Novartis product	Comparator
No. (%) of subjects studied	836	832
No. (%) of subjects with AE(s)	337 (40.3)	356 (42.8)
Number (%) of subjects with serious or other significant events	n (%)	n (%)
Death	1 (0.1)	0 (0.0)
SAE(s)	14 (1.7)	21 (2.5)
Discontinued due to SAE(s)	2 (0.2)	8 (1.0)

NOTE: *This information can usually be found in Section 11 of the CSR.*

Other Relevant Findings

Definition: *Important finding not meeting the criteria for efficacy/safety results (ie, notable change in laboratory or drug trough values that posed no safety issue, but is of medical interest).*

Example: *Mean (SD) pharmacokinetic parameters of Novartis product*

Parameter	**Arithmetic mean ± SD* (CV%) Novartis Product (N= 96)**
^{t}max (h)*	3.00 (1.00 – 8.00)
^{C}max (ng/mL)	6060 ± 2780 (45.9%)
^{AUC}last (h*ng/mL)	40900 ± 18700 (45.6%)
^{t}½ (h)	12.3 ± 6.07 (49.5%)
AUC∞ (h*ng/mL)	43600 ± 194 0 (44.5%)

*: Me ian (Range) for tmax

Date of Clinical Trial Report ***Definition:*** *CSR finalization date* ***Example:*** *1 June 2004* ***NOTE:*** *This information is usually found on the CSR title page*
Date Inclusion on Novartis Clinical Trial Results Database ***Definition:*** *Date posted to the CTRD* ***Example:*** *1 March 2005* ***NOTE:*** *This field will be completed by the person posting the template.*
Date of Latest Update ***Definition:*** *Date of most recent update (ie, template was modified to include publication information)* ***Example:*** *1 November 2005*