Abbreviated Novartis CTRD Results Template

Sponsor Novartis
Generic Drug Name LFF269
Therapeutic Area of Trial Hypertension
Approved Indication Investigational
Protocol Number CLFF269X2201
Title A multi-center, randomized, double-blind, placebo and active controlled, parallel group, proof-of-concept study to evaluate the efficacy and safety of LFF269 compared to placebo after 4 weeks treatment in subjects with essential hypertension
Phase of Development Phase II
Study Start/End Dates 19 May 2011 to 11 Oct 2011 The study was terminated early due to non-safety related issues.
Study Design/Methodology This was a multi-center, randomized, double-blind, placebo- and active-controlled, parallel group proof-of-concept study in patients with mild-to-moderate, uncomplicated essential hypertension. After a 2-week washout and placebo run-in, patients were randomized equally to 4 weeks of LFF269 low dose, LFF269 high dose, eplerenone 50 mg b.i.d. or placebo, following by a 1-week placebo withdrawal period.
Centres 11 centers in United States, of which 8 randomized patients.
Publication None.

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

LFF269 low dose orally, LFF269 high dose orally, eplerenone 50 mg orally twice daily, or placebo orally.

Statistical Methods

Due to the early termination of the study, none of the planned inferential statistical analyses were performed. Safety data collected were summarized by treatment and visit/time as appropriate.

Study Population: Inclusion/Exclusion Criteria and Demographics

Inclusion criteria:

- Male and female (post-menopausal or surgically sterile).
- Age from 18 to 75 years inclusive.
- Subjects with mild-to-moderate uncomplicated essential hypertension, with (not more than 2 in combination) or without prior treatment.
- Subjects had to weigh at least 50 kg to participate in the study, and must have had a body mass index (BMI) within the range of 18-36 kg/m^2.

Exclusion criteria:

- History or evidence of a secondary form of hypertension.
- History of cardiovascular disease.
- Type 1 or type 2 diabetes mellitus.
- Clinically significant valvular heart disease.

Other protocol-defined inclusion/exclusion criteria applied.

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Participant Flow

	LFF269 Low Dose N=8 n (%)	LFF269 High Dose N=7 n (%)	Eplerenone 50 mg bid N=7 n (%)	Placebo N=8 n (%)	Total N=30 n (%)	Placebo run-in only N=61 n (%)
Patients						
Enrolled	8 (100.0)	7 (100.0)	7 (100.0)	8 (100.0)	30 (100.0)	61 (100.0)
Completed	3 (37.5)	5 (71.4)	5 (71.4)	4 (50.0)	17 (56.7)	0
Discontinued	5 (62.5)	2 (28.6)	2 (28.6)	4 (50.0)	13 (43.3)	61 (100.0)
Main cause of discontinuation						
Abnormal test procedure result(s)	0	1 (14.3)	0	0	1 (3.3)	39 (63.9)
Patient withdrew consent	0	0	0	0	0	6 (9.8)
Administrative problems	5 (62.5)	1 (14.3)	2 (28.6)	4 (50.0)	12 (40.0)	16 (26.2)

Baseline Characteristics

		LFF269 Low Dose N=8	LFF269 High Dose N=7	Eplerenone 50 mg bid N=7	Placebo N=8	Total N=30	Placebo Run-in only N=61
Age (years)	Mean (SD)	57.0 (9.44)	59.9 (8.71)	60.3 (9.74)	55.5 (12.27)	58.0 (9.86)	52.5 (12.05)
	Median	54.5	59.0	60.0	50.5	58.0	54.0
	Range	48-75	52-74	42-74	39-73	39-75	20-74
Gender - n(%)	Male	4 (50.0)	3 (42.9)	3 (42.9)	6 (75.0)	16 (53.3)	38 (62.3)
	Female	4 (50.0)	4 (57.1)	4 (57.1)	2 (25.0)	14 (46.7)	23 (37.7)
Race - n(%)	Caucasian	3 (37.5)	1 (14.3)	4 (57.1)	3 (37.5)	11 (36.7)	25 (41.0)
	Black	1 (12.5)	2 (28.6)	0	2 (25.0)	5 (16.7)	7 (11.5)
	Native american	0	0	0	1 (12.5)	1 (3.3)	1 (1.6)
	Asian	1 (12.5)	0	0	0	1 (3.3)	1 (1.6)
	Other	3 (37.5)	4 (57.1)	3 (42.9)	2 (25.0)	12 (40.0)	27 (44.3)
Ethnicity - n(%)	Hispanic/ Latino	5 (62.5)	6 (85.7)	4 (57.1)	4 (50.0)	19 (63.3)	37 (60.7)
	Japanese	1 (12.5)	0	0	0	1 (3.3)	0
	Mixed Ethnicity	0	0	0	1 (12.5)	1 (3.3)	5 (8.2)
	Other	2 (25.0)	1 (14.3)	3 (42.9)	3 (37.5)	9 (30.0)	19 (31.1)

Weight (kg)	Mean (SD)	76.73 (12.327)	78.97 (10.064)	78.31 (9.158)	77.79 (13.710)	77.90 (11.002)	81.01 (12.976)
	Median	75.20	77.30	79.90	75.25	78.70	82.30
	Range	62.3-93.2	66.3-99.1	60.9-90.0	61.4-97.6	60.9-99.1	52.0-107.0
Height (cm)	Mean (SD)	166.28 (7.432)	163.00 (12.659)	164.70 (6.232)	167.80 (11.227)	165.55 (9.393)	168.31 (9.962)
	Median	167.55	157.00	164.00	165.50	164.30	169.00
	Range	153.5-178.0	148.5-183.0	156.5-174.9	151.3-185.6	148.5-185.6	153.0-191.0
BMI (kg/m2)	Mean (SD)	27.69 (3.613)	29.84 (3.233)	28.83 (2.605)	27.52 (3.100)	28.41 (3.152)	28.49 (3.092)
	Median	27.63	30.06	29.74	28.32	28.87	28.85
	Range	22.2-33.9	23.9-32.7	24.9-31.3	22.2-30.6	22.2-33.9	21.4-35.8
BMI = body mass index							

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Safety Results

Adverse Events by System Organ Class

	LFF269 Low Dose	LFF269 High Dose	Total LFF269	Eplerenone 50 mg bid	Placebo	Run-in
	N=8	N=7	N=15	N=7	N=8	N=91
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Patients with AE(s)	3 (37.5)	2 (28.6)	5 (33.3)	4 (57.1)	4 (50.0)	22 (24.2)
System organ class						
Nervous system disorders	2 (25.0)	1 (14.3)	3 (20.0)	0	3 (37.5)	12 (13.2)
Gastrointestinal disorders	0	1 (14.3)	1 (6.7)	0	0	3 (3.3)
General disorders and administration site conditions	1 (12.5)	0	1 (6.7)	0	0	2 (2.2)
Respiratory, thoracic and mediastinal disorders	0	1 (14.3)	1 (6.7)	0	0	2 (2.2)
Cardiac disorders	0	0	0	0	0	2 (2.2)
Eye disorders	0	0	0	0	0	1 (1.1)
Infections and infestations	0	0	0	1 (14.3)	1 (12.5)	4 (4.4)
Injury, poisoning and procedural complications	0	0	0	1 (14.3)	0	2 (2.2)
Musculoskeletal and connective tissue disorders	0	0	0	1 (14.3)	1 (12.5)	1 (1.1)
Reproductive system and breast disorders	0	0	0	1 (14.3)	0	0
Skin and subcutaneous tissue disorders	0	0	0	0	0	1 (1.1)

AEs by SOC are presented in descending order of frequency in Total LFF269 group.

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

	LFF269 Low Dose	LFF269 High Dose	Total LFF269	Eplerenone 50 mg bid	Placebo	Run-in
	N=8	N=7	N=15	N=7	N=8	N=91
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Patients with AE(s)	3 (37.5)	2 (28.6)	5 (33.3)	4 (57.1)	4 (50.0)	22 (24.2)
Preferred term						
Headache	2 (25.0)	1 (14.3)	3 (20.0)	0	1 (12.5)	9 (9.9)
Cough	0	1 (14.3)	1 (6.7)	0	0	0
Local swelling	1 (12.5)	0	1 (6.7)	0	0	0
Nausea	0	1 (14.3)	1 (6.7)	0	0	0
Arthralgia	0	0	0	0	1 (12.5)	1 (1.1)
Contusion	0	0	0	0	0	2 (2.2)
Diarrhoea	0	0	0	0	0	2 (2.2)
Dizziness	0	0	0	0	2 (25.0)	3 (3.3)
Nasopharyngitis	0	0	0	0	1 (12.5)	4 (4.4)
Palpitations	0	0	0	0	0	2 (2.2)

AEs by preferred terms are presented in descending order of frequency in the Total LFF269 group and then presented alphabetically.

Serious Adverse Events and Deaths

There were no serious adverse events or deaths.

Other Relevant Findings

None

Date of Clinical Trial Report

01 Jun 2012

Date Inclusion on Novartis Clinical Trial Results Database

01 OCT 2012

Date of Latest Update

28 August 2012