Sponsor

Novartis

Generic Drug Name

Valsartan

Therapeutic Area of Trial

Hypertension

Approved Indication

- Treatment of hypertension either alone or in combination with other antihypertensive agents.
- Treatment of heart failure (NYHA class II –IV)
- To reduce cardiovascular mortality in clinically stable patients with left ventricular failure or left ventricular dysfunction following myocardial infarction.

Study Number

CVAL489AUS52

Title

A Multi-center, Randomized, Placebo Controlled, Double-Blind Study to Evaluate the Effect of the Angiotensin II Antagonist Valsartan on Diastolic Function in Patients with Hypertension and Diastolic Dysfunction.

Phase of Development

Phase IV

Study Start/End Dates

04-Aug-2004 to 19-Jun-2006

Study Design/Methodology

This was a multi-center, randomized, placebo controlled, double-blind trial in patients with hypertension (HTN) and diastolic dysfunction.

Patients with an echocardiographic ejection fraction (EF) > 50% and echocardiographic evidence of diastolic dysfunction were eligible for enrollment. Diastolic dysfunction was defined as:

Age 45-54: Lateral Ea relaxation < 10 cm/s

Age 55-65: Lateral Ea relaxation < 9 cm/s

Age = 66: Lateral Ea relaxation < 8 cm/s

where Ea is defined as early diastolic mitral annular velocity.

Patients were randomized (1:1) to either valsartan or placebo. At the time of randomization, patients were stratified into two groups: those on concomitant antihypertensive therapy and those who were not on concomitant antihypertensive therapy.

Centres

41 centers in the United States and Canada

Publication

Solomon SD, Janardhanan R, Verma A, Bourgoun M, Daley WL, Purkayastha D, Lacourcière Y, Hippler SE, Fields H, Naqvi TZ, Mulvagh SL, Arnold JM, Thomas JD, Zile MR, Aurigemma GP; Valsartan In Diastolic Dysfunction (VALIDD) Investigators. Effect of angiotensin receptor blockade and antihypertensive drugs on diastolic function in patients with hypertension and diastolic dysfunction: a randomised trial. Lancet. 2007 Jun 23;369(9579):2079-87.

http://www.ncbi.nlm.nih.gov/pubmed/17586303?ordinalpos=4&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

Safety Results

Number (%) of patients with AEs by system organ class

	Valsartan N = 185	Placebo N = 197	Overall N = 382
Patients with AE(s) [a,b] – n (%)	152 (82.2)	162 (82.2)	314 (82.2)
AE – n (%)			
Infections and infestations	65 (35.1)	65 (33.0)	130 (34.0)
Gastrointestinal disorders	68 (36.8)	51 (25.9)	119 (31.2)
General disorders and administration site conditions	59 (31.9)	57 (28.9)	116 (30.4)
Nervous system disorders	65 (35.1)	49 (24.9)	114 (29.8)
Musculoskeletal and connective tissue disorders	54 (29.2)	54 (27.4)	108 (28.3)
Respiratory, thoracic and mediastinal disorders	36 (19.5)	40 (20.3)	76 (19.9)
Psychiatric disorders	23 (12.40	21 (10.7)	44 (11.5)
Injury, poisoning and procedural complications	21 (11.4)	19 (9.6)	40 (10.5)
Skin and subcutaneous tissue dosrders	22 (11.9)	17 (8.6)	39 (10.2)
Metabolism and nutrition disorders	20 (10.8)	18 (9.1)	38 (9.9)
Vascular disorders	17 (9.2)	16 (8.1)	33 (8.6)
Cardiac disorders	19 (10.3)	11 (5.6)	30 (7.9)
Renal and urinary disorders	10 (5.4)	11 (5.6)	21 (5.5)
Eye disorders	10 (5.4)	9 (4.6)	19 (5.0)
Ear and labyrinth disorders	8 (4.3)	6 (3.0)	14 (3.7)
Reproductive system and brest disorders	2 (1.1)	10 (5.1)	12 (3.1)
Neoplasms benign, malignant and unspecified	6 (3.2)	3 91.5)	9 (2.4)
Immune system disorders	4 (2.2)	1 (0.5)	5 (1.3)
Endocrine disorders	2 (1.1)	2 (1.0)	4 (1.0)
Hepatobiliary disorders	2 (1.1)	0	2 (0.5)
Congenital, familial and genetic disorders	1 (0.5)	0	1 (0.3)
Other Investigations	7 (3.8)	13 (6.6)	20 (5.2)

AE = adverse event

a AEs were coded using the Medical Dictionary for Regulatory Activities (MedDRA).

b If a patient experienced more that one episode of a particular AE, the patient was counted only once for the event. If a patient had more than one AE in a system organ class, the patient was counted only once for that system organ class.

Note: The denominator for the percentages was the total number of patients in each treatment group.

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

	Valsartan N = 185	Placebo N = 197	Overall N = 382
Patients with AE(s) [a,b] – n (%)	152 (82.2)	162 (82.2)	314 (82.2)
AE Preferred Term – n (%)			
Dizziness	35 (18.9)	19 (9.6)	54 (14.1)
Fatigue	31 (16.8)	20 (10.2)	51 (13.4)
Headache	18 (9.7)	24 (12.2)	42 (11.0)
Nasopharyngitis	26 (14.1)	15 (7.6)	41 (10.7)
Nausea	22 (11.9)	12 (6.1)	34 (8.9)
Edema peripheral	10 (5.4)	22 (11.2)	32 (8.4)
Upper respiratory tract infection	16 (8.6)	16 (8.1)	32 (8.4)
Diarrhea	16 (8.6)	11 (5.6)	27 (7.1)
Back pain	8 (4.3)	12 (6.1)	20 (5.2)
Muscle spasms	12 (6.5)	8 (4.1)	20 (5.2)

AE = adverse event

a AEs were coded using the Medical Dictionary for Regulatory Activities (MedDRA).

b If a patient experienced more that one episode of a particular AE, the patient was counted only once for the event. If a patient had more than one AE in a system organ class, the patient was counted only once for that system organ class.

Note: The denominator for the percentages was the total number of patients in each treatment group.

Serious Adverse Events and Deaths

	Valsartan	Placebo
No. (%) of subjects studied	185	197
No. (%) of subjects with AE(s)	152 (82.2)	162 (82.2)
Number (%) of subjects with serious or other significant events	n (%)	n (%)
Death	0	0
SAE(s)	16 (8.6)	7 (3.6)
Neoplasms benign, malignant and unspecified	5 (2.7)	1 (0.5)
Nervous system disorders	3 (1.6)	2 (1.0)
Vascular disorders	3 (1.6)	2 (1.0)
Cardiac disorders	2 (1.1)	1 (0.5)
Gastrointestinal disorders	1 (0.5)	2 (1.0)
Renal and urinary disorders	3 (1.6)	0
Metabolism and nutrition disorders	2 (1.1)	0
General disorders and administrative site conditions	0	1 (0.5)
Immune system disorders	1 (0.5)	0
Infections and infestations	1 (0.5)	0
Reproductive system and breast disorders	1 (0.5)	0
Respiratory, thoracic and mediastinal disorders	0	1 (0.5)

Discontinued due to clinically significant AEs	8 (4.3)	2 (1.0)

Other Relevant Findings

Not applicable

Date of Clinical Trial Report

08 Jun 2007

Date Inclusion on Novartis Clinical Trial Results Database

17-Oct-2007

Date of Latest Update

04-Mar-2008