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Trial record **1 of 1** for: CSPP100AFR01

Previous Study | Return to List | Next Study

Efficacy of Aliskiren Compared to Ramipril in the Treatment of Moderate Systolic Hypertensive Patients (ALIAS)

This study has been completed.

Sponsor:
Novartis

Information provided by (Responsible Party):
Novartis

ClinicalTrials.gov Identifier:
NCT01042392

First received: January 1, 2010
Last updated: March 6, 2012
Last verified: March 2012
History of Changes

Full Text View | Tabular View | Study Results | Disclaimer | How to Read a Study Record

Results First Received: January 12, 2012

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Essential Hypertension
Interventions:	Drug: Aliskiren Drug: Ramipril Drug: Matching placebo to Aliskiren Drug: Matching placebo to Ramipril

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Ramipril	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Ramipril 5 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to Ramipril 10 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).

Placebo to Ramipril	In period III (double-blind withdrawal): At visit 4, part of the patients from Ramipril arm received placebo to Ramipril for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Aliskiren	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Aliskiren 150 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to aliskiren 300 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, part of patients received the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Placebo to Aliskiren	In period III (double-blind withdrawal): At visit 4, part of patients from Aliskiren arm received placebo for 1 day. The study ended at visit 5 (48 hours later than visit 4).

Participant Flow for 2 periods

Period 1: Period II(Randomized,Double Blinded,8wk)

	Ramipril	Placebo to Ramipril	Aliskiren	Placebo to Aliskiren
STARTED	257	0 [1]	249	0 [1]
Intent to Treat (ITT)	222 [2]	0	222	0
COMPLETED	247	0	241	0
NOT COMPLETED	10	0	8	0
Adverse Event	6	0	5	0
Unsatisfactory therapeutic effect	1	0	0	0
Withdrawal by Subject	1	0	2	0
Lost to Follow-up	0	0	1	0
Administrative problems	2	0	0	0

[1] This arm is used only in Period III.
[2] ITT excluded patients from centers where 90% of BP measurements were rounded to 5 or 0

Period 2: Period III (Unblinded,Controlled, 1 Day)

	Ramipril	Placebo to Ramipril	Aliskiren	Placebo to Aliskiren
STARTED	129	118	119	122
Per Protocol Missed-dose (PPMD)	98 [1]	73	93	82
COMPLETED	127	117	115	121
NOT COMPLETED	2	1	4	1
Adverse Event	0	0	1	0
Protocol Violation	2	0	0	0
Withdrawal by Subject	0	0	2	0
Administrative problems	0	1	1	1

[1] PPMD excluded patients violated protocol instructions for period 3 (duration and treatment intake)

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

No text entered.

Reporting Groups

	Description
Ramipril	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Ramipril 5 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to Ramipril 10 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Aliskiren	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Aliskiren 150 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to aliskiren 300 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Total	Total of all reporting groups

Baseline Measures

	Ramipril	Aliskiren	Total
Number of Participants [units: participants]	**257**	**249**	**506**
Age [units: years] Mean (Standard Deviation)	**59.8 (11.6)**	**61.0 (11.4)**	**60.4 (11.5)**
Age, Customized [units: Participants]			
< 50 years	**56**	**39**	**95**
50 - 64 years	**119**	**115**	**234**
65 - 74 years	**56**	**64**	**120**
>= 75 years	**26**	**31**	**57**
Gender [units: participants]			
Female	**142**	**133**	**275**
Male	**115**	**116**	**231**

Outcome Measures

Hide All Outcome Measures

1. Primary: Change From Baseline in Mean Sitting Systolic Blood Pressure (msSBP) [Time Frame: Baseline to 8 weeks]

Measure Type	Primary
Measure Title	Change From Baseline in Mean Sitting Systolic Blood Pressure (msSBP)
Measure Description	The arm in which the highest sitting systolic blood pressure (SBP) was found at study entry was used for all subsequent readings. At each study visit, after leaving the patient to rest 5 minutes in a sitting position, the blood pressure (BP) was measured three times with an oscillometric device. The measurements were performed at 1-2 minute intervals. The mean BP was calculated from the 3 readings. The analysis of covariance included treatment factor and baseline mean sitting SBP as covariable.

Time Frame	Baseline to 8 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent to treat population included all randomized patients who had received at least one dose of study drug. It also excluded all those patients from centers that reported more than 90% of BP measurements rounded to 0 or 5.

Reporting Groups

	Description
Ramipril	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Ramipril 5 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to Ramipril 10 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Aliskiren	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Aliskiren 150 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to aliskiren 300 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).

Measured Values

	Ramipril	Aliskiren
Number of Participants Analyzed [units: participants]	**213**	**213**
Change From Baseline in Mean Sitting Systolic Blood Pressure (msSBP) [units: mmHg] Least Squares Mean (Standard Error)	**-18.80 (0.92)**	**-20.78 (0.92)**

No statistical analysis provided for Change From Baseline in Mean Sitting Systolic Blood Pressure (msSBP)

2. Secondary: Change From Baseline in Mean Sitting Diastolic Blood Pressure (msDBP) [Time Frame: Baseline to 8 weeks]

Measure Type	Secondary
Measure Title	Change From Baseline in Mean Sitting Diastolic Blood Pressure (msDBP)
Measure Description	The arm in which the highest sitting systolic blood pressure (SBP) was found at study entry was used for all subsequent readings. At each study visit, after leaving the patient to rest 5 minutes in a sitting position, the blood pressure (BP) was measured three times with an oscillometric device. The measurements were performed at 1-2 minute intervals. The mean BP was calculated from the 3 readings. The analysis of variance included treatment factor and baseline value of mean sitting DBP as covariable.
Time Frame	Baseline to 8 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent to treat population included all randomized patients who had received at least one dose of study drug. It also excluded all those

patients from centers that reported more than 90% of BP measurements rounded to 0 or 5. Patients with observation at both time points were included in this analysis.

Reporting Groups

	Description
Ramipril	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Ramipril 5 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to Ramipril 10 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Aliskiren	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Aliskiren 150 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to aliskiren 300 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).

Measured Values

	Ramipril	Aliskiren
Number of Participants Analyzed [units: participants]	**213**	**213**
Change From Baseline in Mean Sitting Diastolic Blood Pressure (msDBP) [units: mmHg] Least Squares Mean (Standard Error)	**-5.23 (0.60)**	**-6.39 (0.60)**

No statistical analysis provided for Change From Baseline in Mean Sitting Diastolic Blood Pressure (msDBP)

3. Secondary: Percentage of Patients With Controlled Blood Pressure [Time Frame: At 4 and 8 weeks]

Measure Type	Secondary
Measure Title	Percentage of Patients With Controlled Blood Pressure
Measure Description	The arm in which the highest sitting systolic blood pressure (SBP) was found at study entry was used for all subsequent readings. At each study visit, after leaving the patient to rest 5 minutes in a sitting position, the blood pressure (BP) was measured three times with an oscillometric device. The measurements were performed at 1-2 minute intervals. The mean BP was calculated from the 3 readings. Controlled blood pressure (BP) is defined as mean office systolic BP/ diastolic BP < 140/90 mmHg.
Time Frame	At 4 and 8 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent to treat population included all randomized patients who had received at least one dose of study drug. It also excluded all those patients from centers that reported more than 90% of BP measurements rounded to 0 or 5. Patients with observation at each time point were included in this analysis.

Reporting Groups

	Description
Ramipril	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in.

	In period II (double-blind treatment, randomized): Ramipril 5 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to Ramipril 10 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Aliskiren	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Aliskiren 150 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to aliskiren 300 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).

Measured Values

	Ramipril	Aliskiren
Number of Participants Analyzed [units: participants]	**222**	**222**
Percentage of Patients With Controlled Blood Pressure [units: Percentage]		
At week 4 (N= 218, 217)	**36.7**	**40.1**
At week 8 (N= 213, 213)	**26.8**	**32.4**

No statistical analysis provided for Percentage of Patients With Controlled Blood Pressure

4. Secondary: Number of the Participants With More Than 55 mmHg Difference Between the Mean SBP Measured at the Morning Surge and the Mean Minimal SBP Measured During the Night [Time Frame: After 8 weeks]

Measure Type	Secondary
Measure Title	Number of the Participants With More Than 55 mmHg Difference Between the Mean SBP Measured at the Morning Surge and the Mean Minimal SBP Measured During the Night
Measure Description	Ambulatory blood pressure measurement (ABPM) over 24 hours was performed for all patients on the day before visit 4, the device attached to the ambulatory blood pressure non-dominant arm of the patient. The BP morning surge was defined as the average of the measurements taken during the first 2 hours after waking the patient. The minimal night blood pressure was defined as the average of the two lowest BP measures (the lowest hourly average) recorded during night time.
Time Frame	After 8 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent to treat population included all randomized patients who had received at least one dose of study drug. It also excluded all those patients from centers that reported more than 90% of BP measurements rounded to 0 or 5. Patients with ABPM to evaluate the occurrence or absence of a morning peak were included in this analysis.

Reporting Groups

	Description
Ramipril	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Ramipril 5 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to Ramipril 10 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4.

	In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Aliskiren	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Aliskiren 150 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to aliskiren 300 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).

Measured Values

	Ramipril	Aliskiren
Number of Participants Analyzed [units: participants]	**114**	**112**
Number of the Participants With More Than 55 mmHg Difference Between the Mean SBP Measured at the Morning Surge and the Mean Minimal SBP Measured During the Night [units: Participants]	**3**	**9**

No statistical analysis provided for Number of the Participants With More Than 55 mmHg Difference Between the Mean SBP Measured at the Morning Surge and the Mean Minimal SBP Measured During the Night

5. Secondary: Change in msSBP and msDBP From Visit 2 (Baseline) to Visit 3 (at 4 Weeks) [Time Frame: Baseline to 4 weeks]

Measure Type	Secondary
Measure Title	Change in msSBP and msDBP From Visit 2 (Baseline) to Visit 3 (at 4 Weeks)
Measure Description	The arm in which the highest sitting systolic blood pressure (SBP) was found at study entry was used for all subsequent readings. At each study visit, after leaving the patient to rest 5 minutes in a sitting position, the blood pressure (BP) was measured three times with an oscillometric device. The measurements were performed at 1-2 minute intervals. The mean BP was calculated from the 3 readings. The analysis of covariance included treatment factor and baseline mean sitting SBP and mean sitting DBP as covariables.
Time Frame	Baseline to 4 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent to treat population included all randomized patients who had received at least one dose of study drug. It also excluded all those patients from centers that reported more than 90% of BP measurements rounded to 0 or 5.

Reporting Groups

	Description
Ramipril	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Ramipril 5 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to Ramipril 10 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Aliskiren	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Aliskiren 150 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to aliskiren 300 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week

	period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).

Measured Values

	Ramipril	Aliskiren
Number of Participants Analyzed [units: participants]	**218**	**217**
Change in msSBP and msDBP From Visit 2 (Baseline) to Visit 3 (at 4 Weeks) [units: mmHg] Least Squares Mean (Standard Error)		
Change in msSBP	**-19.42 (0.92)**	**-19.75 (0.92)**
Change in msDBP	**-5.37 (0.56)**	**-5.60 (0.56)**

No statistical analysis provided for Change in msSBP and msDBP From Visit 2 (Baseline) to Visit 3 (at 4 Weeks)

6. Secondary: Difference Between the Maximal and the Minimal Mean-hour SPB Measured Between 1 and 8 am at Week 8 [Time Frame: At week 8]

Measure Type	Secondary
Measure Title	Difference Between the Maximal and the Minimal Mean-hour SPB Measured Between 1 and 8 am at Week 8
Measure Description	Ambulatory blood pressure measurement (ABPM) over 24 hours was performed for all patients on the eve of visit 4 (week 8), the device attached to the ambulatory blood pressure non-dominant arm of the patient. The difference between mean-hour maximum SBP mean-hour minimum SBP between 1 am and 8 am was measured.
Time Frame	At week 8
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent to treat population included all randomized patients who had received at least one dose of study drug. It also excluded all those patients from centers that reported more than 90% of BP measurements rounded to 0 or 5. Patients with ABPM measurements over 24 hours were included in this analysis.

Reporting Groups

	Description
Ramipril	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Ramipril 5 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to Ramipril 10 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Aliskiren	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Aliskiren 150 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to aliskiren 300 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).

Measured Values

	Ramipril	Aliskiren
Number of Participants Analyzed [units: participants]	**175**	**186**
Difference Between the Maximal and the Minimal Mean-hour SPB Measured Between 1 and 8 am at Week 8 [units: mmHg] Mean (Standard Deviation)	**33.6 (14.04)**	**35.5 (15.05)**

No statistical analysis provided for Difference Between the Maximal and the Minimal Mean-hour SPB Measured Between 1 and 8 am at Week 8

7. Secondary: Change in Mean Sitting DBP and SBP in Specified Sub-groups From Visit 2 (Baseline) to Visit 4 (at 8 Weeks) [Time Frame: Baseline to 8 weeks]

Measure Type	Secondary
Measure Title	Change in Mean Sitting DBP and SBP in Specified Sub-groups From Visit 2 (Baseline) to Visit 4 (at 8 Weeks)
Measure Description	The sub-groups were: "Riser" = patients with >= 55 mmHg difference between the mean SPB measured at the morning surge and the mean minimal SBP measured during the night. The "Non-risers" in whom the difference is <55 mmHg. Patients called "dippers" in whom there was a decrease in average nocturnal SBP ≥ 10% compared with average daytime SBP, in contrast to patients "non-dippers " in whom this difference was <10%.
Time Frame	Baseline to 8 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent to treat population included all randomized patients who had received at least one dose of study drug. It also excluded all those patients from centers that reported more than 90% of BP measurements rounded to 0 or 5. Patients with observation at different categories were included in this analysis.

Reporting Groups

	Description
Ramipril	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Ramipril 5 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to Ramipril 10 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Aliskiren	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Aliskiren 150 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to aliskiren 300 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).

Measured Values

	Ramipril	Aliskiren
Number of Participants Analyzed [units: participants]	**222**	**222**
Change in Mean Sitting DBP and SBP in Specified Sub-groups From Visit 2 (Baseline) to Visit 4 (at 8 Weeks) [units: mmHg]		

Mean (Standard Deviation)		
Change in msSBP: Risers (n= 3, 9)	**-19.7 (6.11)**	**-16.9 (10.52)**
Change in msSBP: Non-risers (n=109, 103)	**-19.2 (13.99)**	**-20.5 (14.49)**
Change in msSBP: Dippers (n= 80, 94)	**-18.1 (11.86)**	**-19.8 (12.05)**
Change in msSBP: Non-dippers (n= 93, 92)	**-19.2 (14.93)**	**-21.1 (15.06)**
Change in msDBP: Risers (n= 3, 9)	**-7.3 (10.60)**	**-6.6 (9.11)**
Change in msDBP: Non-risers(n=109, 103)	**-4.2 (9.51)**	**-5.7 (9.61)**
Change in msDBP: Dippers (n= 80, 94)	**-5.5 (9.63)**	**-6.3 (9.81)**
Change in msDBP: Non-dippers (n= 93, 92)	**-5.3 (9.59)**	**-6.5 (9.56)**

No statistical analysis provided for Change in Mean Sitting DBP and SBP in Specified Sub-groups From Visit 2 (Baseline) to Visit 4 (at 8 Weeks)

8. Secondary: Change in Mean Sitting Systolic Blood Pressure (msSBP) and Mean Sitting Diastolic Blood Pressure (msDBP) From Last Active Dose Taken to After a One-day Missed-dose [Time Frame: From 8 weeks to 48 hours after week 8]

Measure Type	Secondary
Measure Title	Change in Mean Sitting Systolic Blood Pressure (msSBP) and Mean Sitting Diastolic Blood Pressure (msDBP) From Last Active Dose Taken to After a One-day Missed-dose
Measure Description	The change in blood pressure was measured between visit 4 (end of the period of double-blind active treatment which was at week 8) and visit 5 (48 hours after the last active dose taken) in the group of patients who received aliskiren or placebo and those who received ramipril or placebo. The analysis of covariance included treatment factor and baseline mean sitting SBP and mean sitting DBP as covariables.
Time Frame	From 8 weeks to 48 hours after week 8
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Per-protocol missed dose population included all per protocol population patients who had received the study treatment for period 3 according to the protocol (duration of period 3 and treatment intake). Patients with observation at both time points were included in this analysis.

Reporting Groups

	Description
Ramipril	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Ramipril 5 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to Ramipril 10 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Placebo to Ramipril	In period III (double-blind withdrawal): At visit 4, part of the patients from Ramipril arm received placebo to Ramipril for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Aliskiren	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Aliskiren 150 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to aliskiren 300 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4.

	In period III (double-blind withdrawal): At visit 4, part of patients received the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Placebo to Aliskiren	In period III (double-blind withdrawal): At visit 4, part of patients from Aliskiren arm received placebo for 1 day. The study ended at visit 5 (48 hours later than visit 4).

Measured Values

	Ramipril	Placebo to Ramipril	Aliskiren	Placebo to Aliskiren
Number of Participants Analyzed [units: participants]	**95**	**73**	**88**	**81**
Change in Mean Sitting Systolic Blood Pressure (msSBP) and Mean Sitting Diastolic Blood Pressure (msDBP) From Last Active Dose Taken to After a One-day Missed-dose [units: mmHg] Least Squares Mean (Standard Error)				
Change in msSBP	**-0.50 (1.05)**	**-1.28 (1.10)**	**0.52 (1.06)**	**3.27 (1.10)**
Change in msDBP	**0.76 (0.69)**	**0.32 (0.79)**	**-0.40 (0.78)**	**0.97 (0.81)**

No statistical analysis provided for Change in Mean Sitting Systolic Blood Pressure (msSBP) and Mean Sitting Diastolic Blood Pressure (msDBP) From Last Active Dose Taken to After a One-day Missed-dose

9. Secondary: Number Patients Reported With Adverse Events (AEs), Serious Adverse Events (SAE) and Death (Period II and Period III) [Time Frame: 8 weeks + 1 day]

Measure Type	Secondary
Measure Title	Number Patients Reported With Adverse Events (AEs), Serious Adverse Events (SAE) and Death (Period II and Period III)
Measure Description	Adverse events are defined as any unfavorable and unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome or disease which either occurs during study, having been absent at baseline, or, if present at baseline, appears to worsen. Serious adverse events are any untoward medical occurrences that result in death, are life threatening, require (or prolong) hospitalization, cause persistent or significant disability/incapacity, result in congenital anomalies or birth defects, or are other conditions which in judgment of investigators represent significant hazards.
Time Frame	8 weeks + 1 day
Safety Issue	Yes

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
All randomized patients except one patient from Aliskiren arm who was lost to follow up after visit 2.

Reporting Groups

	Description
Ramipril	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Ramipril 5 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to Ramipril 10 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at

	visit 5 (48 hours later than visit 4).
Aliskiren	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Aliskiren 150 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to aliskiren 300 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received placebo or the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).

Measured Values

	Ramipril	Aliskiren
Number of Participants Analyzed [units: participants]	**257**	**248**
Number Patients Reported With Adverse Events (AEs), Serious Adverse Events (SAE) and Death (Period II and Period III) [units: Participants]		
Patients with at least 1 AE	**55**	**43**
Patients with at least 1 SAE	**3**	**1**
Death	**0**	**0**

No statistical analysis provided for Number Patients Reported With Adverse Events (AEs), Serious Adverse Events (SAE) and Death (Period II and Period III)

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	8 weeks of period II + 1 day of Period III
Additional Description	The adverse events and serious adverse events are reported on randomized population except one patient who lost to follow up after visit 2.

Reporting Groups

	Description
Ramipril (Period II and III)	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Ramipril 5 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to Ramipril 10 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Placebo to Ramipril (Period III)	In period III (double-blind withdrawal): At visit 4, part of the patients from Ramipril arm received placebo to Ramipril for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Aliskiren (Period II and III)	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Aliskiren 150 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to aliskiren 300 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, part of patients received the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Placebo to Aliskiren (Period III)	In period III (double-blind withdrawal): At visit 4, part of patients from Aliskiren arm received placebo for 1 day. The study ended at visit 5 (48 hours later than visit 4).

Serious Adverse Events

	Ramipril (Period II and III)	Placebo to Ramipril (Period III)	Aliskiren (Period II and III)	Placebo to Aliskiren (Period III)
Total, serious adverse events				
# participants affected / at risk	**3/257 (1.17%)**	**0/118 (0.00%)**	**1/248 (0.40%)**	**0/122 (0.00%)**
Blood and lymphatic system disorders				
normochromic normocytic anemia † 1				
# participants affected / at risk	**0/257 (0.00%)**	**0/118 (0.00%)**	**1/248 (0.40%)**	**0/122 (0.00%)**
Cardiac disorders				
cardiac failure † 1				
# participants affected / at risk	**0/257 (0.00%)**	**0/118 (0.00%)**	**1/248 (0.40%)**	**0/122 (0.00%)**
atrial fibrillation † 1				
# participants affected / at risk	**1/257 (0.39%)**	**0/118 (0.00%)**	**0/248 (0.00%)**	**0/122 (0.00%)**
Gastrointestinal disorders				
abdominal pain † 1				
# participants affected / at risk	**1/257 (0.39%)**	**0/118 (0.00%)**	**0/248 (0.00%)**	**0/122 (0.00%)**
General disorders				
asthenia † 1				
# participants affected / at risk	**1/257 (0.39%)**	**0/118 (0.00%)**	**0/248 (0.00%)**	**0/122 (0.00%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
spine metastasis † 1				
# participants affected / at risk	**0/257 (0.00%)**	**0/118 (0.00%)**	**1/248 (0.40%)**	**0/122 (0.00%)**
bladder cancer † 1				
# participants affected / at risk	**0/257 (0.00%)**	**0/118 (0.00%)**	**1/248 (0.40%)**	**0/122 (0.00%)**
liver metastatis † 1				
# participants affected / at risk	**0/257 (0.00%)**	**0/118 (0.00%)**	**1/248 (0.40%)**	**0/122 (0.00%)**
pancreatic adenocarcinoma † 1				
# participants affected / at risk	**1/257 (0.39%)**	**0/118 (0.00%)**	**0/248 (0.00%)**	**0/122 (0.00%)**
Respiratory, thoracic and mediastinal disorders				
dyspnea † 1				
# participants affected / at risk	**1/257 (0.39%)**	**0/118 (0.00%)**	**0/248 (0.00%)**	**0/122 (0.00%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Other Adverse Events

Hide Other Adverse Events

Time Frame	8 weeks of period II + 1 day of Period III
Additional Description	The adverse events and serious adverse events are reported on randomized population except one patient who lost to follow up after visit 2.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Ramipril (Period II and III)	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Ramipril 5 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to Ramipril 10 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, patients received the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Placebo to Ramipril (Period III)	In period III (double-blind withdrawal): At visit 4, part of the patients from Ramipril arm received placebo to Ramipril for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Aliskiren (Period II and III)	In period I (washout and single-blind): from visit 1 to visit 2, 2 weeks placebo run-in. In period II (double-blind treatment, randomized): Aliskiren 150 mg for 4 weeks (visit 2 - visit 3). At visit 3, medications had to be titrated to aliskiren 300 mg only if BP remained ≥ 140/90 mmHg. Double blind treatment had to be continued for another 4-week period until visit 4. In period III (double-blind withdrawal): At visit 4, part of patients received the active treatment for 1 day. The study ended at visit 5 (48 hours later than visit 4).
Placebo to Aliskiren (Period III)	In period III (double-blind withdrawal): At visit 4, part of patients from Aliskiren arm received placebo for 1 day. The study ended at visit 5 (48 hours later than visit 4).

Other Adverse Events

	Ramipril (Period II and III)	Placebo to Ramipril (Period III)	Aliskiren (Period II and III)	Placebo to Aliskiren (Period III)
Total, other (not including serious) adverse events				
# participants affected / at risk	**0/257 (0.00%)**	**0/118 (0.00%)**	**0/248 (0.00%)**	**0/122 (0.00%)**

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.
The agreement is: ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

Restriction Description: The terms and conditions of Novartis' agreements with its investigators may vary. However, Novartis does not prohibit any investigator from publishing. Any publications from a single-site are postponed until the publication of the pooled data (i.e., data from all sites) in the clinical trial.

Results Point of Contact:

Name/Title: Study Director
Organization: Novartis Pharmaceuticals
phone: 862-778-8300

No publications provided

Responsible Party:	Novartis
ClinicalTrials.gov Identifier:	NCT01042392 History of Changes
Other Study ID Numbers:	**CSPP100AFR01** 2009-011296-80 (EudraCT Number)
Study First Received:	January 1, 2010
Results First Received:	January 12, 2012
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