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Trial record **1 of 1** for: CSPP100G2301

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A Randomized Controlled Trial of Aliskiren in the Prevention of Major Cardiovascular Events in Elderly People (APOLLO)

This study has been terminated.

(Terminated early in agreement with Health Authorities for feasibility reasons)

Sponsor:
Novartis Pharmaceuticals

Information provided by (Responsible Party):
Novartis (Novartis Pharmaceuticals)

ClinicalTrials.gov Identifier:
NCT01259297

First received: December 10, 2010
Last updated: February 27, 2014
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History of Changes

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Results First Received: December 18, 2013

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Factorial Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Cardiovascular Events
Interventions:	Drug: Aliskiren Drug: Amlodipine Drug: Hydrochlorothiazide (HCTZ) Drug: Placebo for Aliskiren Drug: Placebo for Amlodipine Drug: Placebo for Hydrochlorothiazide (HCTZ)

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
Aliskiren + Hydrochlorothiazide (HCTZ)	In run-in period (4-5 weeks) , patients on CCB background therapy and approximately 50% of patients on neither thiazide nor CCB background therapy: received hydrochlorothiazide 12.5/25 mg and Aliskiren 150/300 mg daily in a titrated manner as per protocol. In double blind period, all patients who successfully completed run-in with HCTZ plus aliskiren were randomized equally to the 4 arms of the HCTZ add-on stratum. Patients randomized to this arm received Aliskiren 300 mg + HCTZ 25 mg once daily.
Aliskiren + Placebo for HCTZ	In double blind period, all patients who successfully completed run-in with HCTZ plus Aliskiren were randomized equally to the 4 arms of the HCTZ add-on stratum. In double blind period, randomized patients to this arm received Aliskiren 300 mg + placebo for HCTZ 25 mg once daily
Aliskiren + Amlodipine	In run-in period (4-5 weeks) , patients on thiazide background therapy and approximately 50% of

	patients on neither CCB nor thiazide background therapy received Amlodipine 5 mg and Aliskiren 150/300 mg daily in a titrated manner as per protocol. In double blind period, patients who successfully completed run-in with Amlodipine plus Aliskiren were randomized equally to the 4 arms of the Amlodipine add-on stratum. Patients randomized to this arm received Aliskiren 300 mg + Amlodipine 5 mg once daily during the double blind period.
Aliskiren + Placebo for Amlodipine	In double blind period, all patients who successfully completed run-in with Amlodipine plus aliskiren were randomized equally to the 4 arms of the Amlodipine add-on stratum. In double blind period, randomized patients to this arm received Aliskiren 300 mg + placebo for Amlodipine 5 mg
HCTZ + Placebo for Aliskiren	In double blind period, all patients who successfully completed run-in with HCTZ plus Aliskiren were randomized equally to the 4 arms of the HCTZ add-on stratum. In double blind period, randomized patients to this arm received HCTZ 25 mg + placebo for Aliskiren 300 mg once daily
Placebo for Aliskiren + Placebo for HCTZ	In double blind period, all patients who successfully completed run-in with HCTZ plus aliskiren were randomized equally to the 4 arms of the HCTZ add-on stratum. In double blind period, randomized patients to this arm received placebo for Aliskiren 300 mg + placebo for HCTZ 25 mg once daily
Amlodipine + Placebo for Aliskiren	In double blind period, all patients who successfully completed run-in with Amlodipine plus Aliskiren were randomized equally to the 4 arms of the Amlodipine add-on stratum. In double blind period, randomized patients to this arm received Amlodipine 5 mg + placebo for Aliskiren 300 mg once daily
Placebo for Aliskiren + Placebo for Amlodipine	In double blind period, all patients who successfully completed run-in with Amlodipine plus Aliskiren were randomized equally to the 4 arms of the Amlodipine add-on stratum. In double blind period, randomized patients to this arm received placebo for Aliskiren 300 mg + placebo for Amlodipine 5 mg once daily

Participant Flow for 2 periods

Period 1: Run-in Open Label Period (4-5 Weeks)

	Aliskiren + Hydrochlorothiazide (HCTZ)	Aliskiren + Placebo for HCTZ	Aliskiren + Amlodipine	Aliskiren + Placebo for Amlodipine	HCTZ + Placebo for Aliskiren	Placebo for Aliskiren + Placebo for HCTZ	Amlodipine + Placebo for Aliskiren	Placebo for Aliskiren + Placebo for Amlodipine
STARTED	1335	0	1001	0	0	0	0	0
COMPLETED	980	0	779	0	0	0	0	0
NOT COMPLETED	355	0	222	0	0	0	0	0

Period 2: Double Blind Randomized Period

	Aliskiren + Hydrochlorothiazide (HCTZ)	Aliskiren + Placebo for HCTZ	Aliskiren + Amlodipine	Aliskiren + Placebo for Amlodipine	HCTZ + Placebo for Aliskiren	Placebo for Aliskiren + Placebo for HCTZ	Amlodipine + Placebo for Aliskiren	Placebo for Aliskiren + Placebo for Amlodipine
STARTED	244	232	189	195	251	253	196	199
COMPLETED	242	229	188	191	247	245	190	196
NOT COMPLETED	2	3	1	4	4	8	6	3
Death	1	1	1	2	1	5	2	1
Withdrew informed consent/ refused visit	1	1	0	2	2	1	1	1
Other reasons	0	1	0	0	1	2	3	1

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.
Full analysis Set (FAS): All randomized patients, regardless of receiving study medication.

Reporting Groups

	Description
Aliskiren + Hydrochlorothiazide (HCTZ)	In double blind period, all patients who successfully completed run-in with HCTZ plus Aliskiren were randomized equally to the 4 arms of the HCTZ add-on stratum. Patients randomized to this arm received Aliskiren 300 mg + HCTZ 25 mg once daily.
Aliskiren + Placebo for HCTZ	In double blind period, all patients who successfully completed run-in with HCTZ plus Aliskiren were randomized equally to the 4 arms of the HCTZ add-on stratum. In double blind period, randomized patients to this arm received Aliskiren 300 mg + placebo for HCTZ 25 mg once daily
Aliskiren + Amlodipine	In double blind period, all patients who successfully completed run-in with Amlodipine plus Aliskiren were randomized equally to the 4 arms of the Amlodipine add-on stratum. Patients randomized to this arm received Aliskiren 300 mg + Amlodipine 5 mg once daily during the double blind period.
Aliskiren + Placebo for Amlodipine	In double blind period, all patients who successfully completed run-in with Amlodipine plus Aliskiren were randomized equally to the 4 arms of the Amlodipine add-on stratum. In double blind period, randomized patients to this arm received Aliskiren 300 mg + placebo for Amlodipine 5 mg
HCTZ + Placebo for Aliskiren	In double blind period, all patients who successfully completed run-in with HCTZ plus Aliskiren were randomized equally to the 4 arms of the HCTZ add-on stratum. In double blind period, randomized patients to this arm received HCTZ 25 mg + placebo for Aliskiren 300 mg once daily
Placebo for Aliskiren + Placebo for HCTZ	In double blind period, all patients who successfully completed run-in with HCTZ plus Aliskiren were randomized equally to the 4 arms of the HCTZ add-on stratum. In double blind period, randomized patients to this arm received placebo for Aliskiren 300 mg + placebo for HCTZ 25 mg once daily
Amlodipine + Placebo for Aliskiren	In double blind period, all patients who successfully completed run-in with Amlodipine plus Aliskiren were run-in stratum randomized equally to the 4 arms of the Amlodipine add-on stratum. In double blind period, randomized patients to this arm received Amlodipine 5 mg + placebo for Aliskiren 300 mg once daily
Placebo for Aliskiren + Placebo for Amlodipine	In double blind period, all patients who successfully completed run-in with Amlodipine plus Aliskiren were randomized equally to the 4 arms of the Amlodipine add-on stratum. In double blind period, randomized patients to this arm received placebo for Aliskiren 300 mg + placebo for Amlodipine 5 mg once daily
Total	Total of all reporting groups

Baseline Measures

	Aliskiren + Hydrochlorothiazide (HCTZ)	Aliskiren + Placebo for HCTZ	Aliskiren + Amlodipine	Aliskiren + Placebo for Amlodipine	HCTZ + Placebo for Aliskiren	Placebo for Aliskiren + Placebo for HCTZ	Amlodipine + Placebo for Aliskiren	Placebo for Aliskiren + Placebo for Amlodipine	Total
Number of Participants [units: participants]	**244**	**232**	**189**	**195**	**251**	**253**	**196**	**199**	**1759**
Age, Customized [units: participants]									
>=65 to <75 years	**165**	**174**	**127**	**125**	**180**	**189**	**135**	**134**	**1229**

>=75 years	79	58	62	70	71	64	61	65	530
Gender [units: participants]									
Female	119	109	91	89	122	108	87	88	813
Male	125	123	98	106	129	145	109	111	946

Outcome Measures

Hide All Outcome Measures

1. Primary: Number of Participants With Composite Cardiovascular Endpoints in Aliskiren Based Regimen Versus Non-Aliskiren Based Regimen [Time Frame: End of study (209 days (median))]

Measure Type	Primary
Measure Title	Number of Participants With Composite Cardiovascular Endpoints in Aliskiren Based Regimen Versus Non-Aliskiren Based Regimen
Measure Description	The composite CV endpoint is based on the following first adjudicated events: CV death, non-fatal MI,non-fatal stroke, significant heart failure
Time Frame	End of study (209 days (median))
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.
Full Analysis set. 1759 patients were randomized as against the originally planned 11,000. A total of 25 primary CV composite endpoints had accrued during median follow-up of 209 days versus planned 2000 primary endpoints during planned follow-up of average 5 years. These low numbers significantly limit interpretation of the results.

Reporting Groups

	Description
Aliskiren Based Regimen	This regimen includes all the patients who were randomized to the treatment arms that included Aliskiren such as Aliskiren + hydrochlorothiazide (HCTZ), Aliskiren + placebo for HCTZ, Aliskiren + Amlodipine, Aliskiren + placebo for Amlodipine.
Non-Aliskiren Based Regimen	This regimen includes all the patients who were randomized to the treatment arms that did not include Aliskiren such as HCTZ + Placebo for Aliskiren, Placebo for Aliskiren + Placebo for HCTZ, Amlodipine + Placebo for Aliskiren, Placebo for Aliskiren + Placebo for Amlodipine

Measured Values

	Aliskiren Based Regimen	Non-Aliskiren Based Regimen
Number of Participants Analyzed [units: participants]	**860**	**899**
Number of Participants With Composite Cardiovascular Endpoints in Aliskiren Based Regimen Versus Non-Aliskiren Based Regimen [units: participants]	**11**	**14**

No statistical analysis provided for Number of Participants With Composite Cardiovascular Endpoints in Aliskiren Based Regimen Versus Non-Aliskiren Based Regimen

2. Primary: Number of Participants With Composite Cardiovascular Endpoints in Aliskiren+Amlodipine/HCTZ Group Versus All Placebo Group [Time Frame: End of study (209 days (median))]

Measure Type	Primary
Measure Title	Number of Participants With Composite Cardiovascular Endpoints in Aliskiren+Amlodipine/HCTZ Group Versus All Placebo Group
Measure Description	The composite CV endpoint is based on the following first adjudicated events: CV death, non-fatal MI,non-fatal stroke, significant

	heart failure
Time Frame	End of study (209 days (median))
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.
Full Analysis set. 1759 patients were randomized as against the originally planned 11,000. A total of 25 primary CV composite endpoints had accrued during median follow-up of 209 days versus planned 2000 primary endpoints during planned follow-up of average 5 years. These low numbers significantly limit interpretation of the results.

Reporting Groups

	Description
Aliskiren+Amlodipine/HCTZ Group	This reporting group includes all the patients who has received Aliskiren plus an additional BP lowering drug (Amlodipine or Hydrochlorothiazide). This reporting group includes patients from arms such as Aliskiren + Hydrochlorothiazide (HCTZ) and Aliskiren + Amlodipine.
Placebo	This reporting group includes all the patients who has received placebo of aliskiren plus placebo of an additional BP lowering drug (amlodipine or hydrochlorothiazide). This reporting group includes patients from arms such as Placebo for Aliskiren + Placebo for HCTZ and Placebo for aliskiren + Placebo for Amlodipine .

Measured Values

	Aliskiren+Amlodipine/HCTZ Group	**Placebo**
Number of Participants Analyzed [units: participants]	**433**	**452**
Number of Participants With Composite Cardiovascular Endpoints in Aliskiren+Amlodipine/HCTZ Group Versus All Placebo Group [units: participants]	**2**	**8**

No statistical analysis provided for Number of Participants With Composite Cardiovascular Endpoints in Aliskiren+Amlodipine/HCTZ Group Versus All Placebo Group

3. Secondary: Change From Baseline to End of Study in Standard Assessment of Global Activities in the Elderly (SAGE) Dimensions (Part I) [Time Frame: Baseline, End of study (209 days [median])]

Measure Type	Secondary
Measure Title	Change From Baseline to End of Study in Standard Assessment of Global Activities in the Elderly (SAGE) Dimensions (Part I)
Measure Description	Decline in ability to perform everyday activities independently was measured primarily by using the Standard Assessment of Global Activities in the Elderly (SAGE) scale. The SAGE comprised of 15 questions, each describing an activity. Patient had to indicate how much difficulty he/she had encountered in performing the activity in last month. Each question's score ranges from 0 (No difficulty) to 3 (difficulty levels were mild (score = 1), moderate (score =2) and severe (score=3)). Part I of SAGE included 4 dimensions: • Community Cognition (maximum of scores of questions 1 to 6); • Instrumental Activities of daily Living (IADL) (maximum of scores of questions 7 to 10); • Mobility (maximum of scores of questions 11 and 12);. • Basic Activities of daily Living (ADL) (maximum of scores of questions 13 to 15) Each dimension's total score ranged from 0 to 3. 0=best, 3=worst A negative change in value from baseline means improvement in the ability to perform everyday activities.
Time Frame	Baseline, End of study (209 days [median])
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.
Full Analysis Set: Due to the sparse post-baseline data following early termination of the study, this analysis was not performed as planned in protocol.Hence, no meaningful conclusion could be drawn. Patients who completed both baseline and post-baseline SAGE questionnaires (Part II) were included in this analysis.

Reporting Groups

	Description
Aliskiren Based Regimen	This regimen includes all the patients who were randomized to the treatment arms that included Aliskiren such as Aliskiren + Hydrochlorothiazide (HCTZ), Aliskiren + placebo for HCTZ, Aliskiren + Amlodipine, Aliskiren + placebo for Amlodipine.
Non-Aliskiren Based Regimen	This regimen includes all the patients who were randomized to the treatment arms that did not include Aliskiren such as HCTZ + Placebo for Aliskiren, Placebo for Aliskiren + Placebo for HCTZ, Amlodipine + Placebo for Aliskiren, Placebo for Aliskiren + Placebo for Amlodipine

Measured Values

	Aliskiren Based Regimen	Non-Aliskiren Based Regimen
Number of Participants Analyzed [units: participants]	**592**	**618**
Change From Baseline to End of Study in Standard Assessment of Global Activities in the Elderly (SAGE) Dimensions (Part I) [units: units on a scale] Mean (Standard Deviation)		
Community Cognition	**-0.04 (0.768)**	**-0.05 (0.741)**
Instrumental Activities of daily Living (IADL)	**-0.06 (0.562)**	**-0.04 (0.505)**
Mobility	**0.01 (0.791)**	**0.00 (0.779)**
ADL	**-0.09 (0.525)**	**-0.08 (0.520)**

No statistical analysis provided for Change From Baseline to End of Study in Standard Assessment of Global Activities in the Elderly (SAGE) Dimensions (Part I)

4. Secondary: Percentage of Participants With Standard Assessment of Global Activities in the Elderly (SAGE) Dimensions (Part II) [Time Frame: End of study (209 days [median])]

Measure Type	Secondary
Measure Title	Percentage of Participants With Standard Assessment of Global Activities in the Elderly (SAGE) Dimensions (Part II)
Measure Description	Decline in ability to perform everyday activities independently was measured primarily by using the Standard Assessment of Global Activities in the Elderly (SAGE) scale. The SAGE was comprised of 15 questions, each describing an activity. Patient had to indicate how much difficulty he/she had encountered in performing the activity in the last month. Each question's score ranges from 0 (No difficulty) to 3 (difficulty levels were mild (score = 1), moderate (score =2) and severe (score=3)). Part II of SAGE included 2 dimensions: • "Normal" if the scores of all SAGE questions is 0 (i.e., No difficulty) • "Mobility Only" if scores of both SAGE questions 11 and 12 are 0
Time Frame	End of study (209 days [median])
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.
Full Analysis Set. Number of patients with all SAGE questions non-missing for the specific visit are included in this population. Due to the sparse post-baseline data following early termination of the study, this analysis was not performed as planned in protocol.Hence, no meaningful conclusion could be drawn.

Reporting Groups

	Description
Aliskiren Based Regimen	This regimen includes all the patients who were randomized to the treatment arms that included Aliskiren such as Aliskiren + hydrochlorothiazide (HCTZ), Aliskiren + placebo for HCTZ, Aliskiren + Amlodipine, Aliskiren + placebo for Amlodipine.
Non-Aliskiren Based Regimen	This regimen includes all the patients who were randomized to the treatment arms that did not include Aliskiren such as HCTZ + Placebo for Aliskiren, Placebo for Aliskiren + Placebo for HCTZ, Amlodipine + Placebo for Aliskiren, Placebo for Aliskiren + Placebo for Amlodipine

Measured Values

	Aliskiren Based	Non-Aliskiren Based

	Regimen	Regimen
Number of Participants Analyzed [units: participants]	**608**	**641**
Percentage of Participants With Standard Assessment of Global Activities in the Elderly (SAGE) Dimensions (Part II) [units: percentage of participants]		
Normal	**44.2**	**46.5**
Mobility Only	**66.8**	**68.6**

No statistical analysis provided for Percentage of Participants With Standard Assessment of Global Activities in the Elderly (SAGE) Dimensions (Part II)

5. Secondary: Number of Participants With Renal Dysfunction in Aliskiren Based Regimen Versus Non-Aliskiren Based Regimen [Time Frame: End of study (209 days (median))]

Measure Type	Secondary
Measure Title	Number of Participants With Renal Dysfunction in Aliskiren Based Regimen Versus Non-Aliskiren Based Regimen
Measure Description	The renal dysfunction (composite endpoint) was defined as the first occurrence of either of the following: • End-stage renal disease [ESRD] requiring dialysis or transplantation • Doubling of serum creatinine and reaching an eGFR < 45 ml/min/1.73 m^2.
Time Frame	End of study (209 days (median))
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.
Full Analysis set. 1759 patients were randomized as against the originally planned 11,000. The duration of study follow-up was 209 days (median) as against the planned follow-up of average 5 years. These low numbers significantly limit interpretation of the results.

Reporting Groups

	Description
Aliskiren Based Regimen	This regimen includes all the patients who were randomized to the treatment arms that included Aliskiren such as Aliskiren + Hydrochlorothiazide (HCTZ), Aliskiren + placebo for HCTZ, Aliskiren + Amlodipine, Aliskiren + placebo for Amlodipine.
Non-Aliskiren Based Regimen	This regimen includes all the patients who were randomized to the treatment arms that did not include Aliskiren such as HCTZ + Placebo for Aliskiren, Placebo for Aliskiren + Placebo for HCTZ, Amlodipine + Placebo for Aliskiren, Placebo for Aliskiren + Placebo for Amlodipine

Measured Values

	Aliskiren Based Regimen	Non-Aliskiren Based Regimen
Number of Participants Analyzed [units: participants]	**860**	**899**
Number of Participants With Renal Dysfunction in Aliskiren Based Regimen Versus Non-Aliskiren Based Regimen [units: participants]		
ESRD requiring dialysis or transplantation	**0**	**0**
Doubling of creatinine & eGFR<45 ml/min/1.73 m^2	**7**	**1**

No statistical analysis provided for Number of Participants With Renal Dysfunction in Aliskiren Based Regimen Versus Non-Aliskiren Based Regimen

6. Secondary: Number of Participants With Total Mortality in Aliskiren Based Regimen Versus Non-aliskiren Based Regimen [Time Frame: End of study (209 days (median))]

Measure Type	Secondary
Measure Title	Number of Participants With Total Mortality in Aliskiren Based Regimen Versus Non-aliskiren Based Regimen

Measure Description	The total mortality endpoint was defined as time to death from any cause. Total mortality analysis used the date of last follow-up including the washout period as the censoring date.
Time Frame	End of study (209 days (median))
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.
Full Analysis set. 1759 patients were randomized as against the originally planned 11,000. The duration of study follow-up was 209 days (median) as against the planned follow-up of average 5 years. These low numbers significantly limit interpretation of the results.

Reporting Groups

	Description
Aliskiren Based Regimen	This regimen includes all the patients who were randomized to the treatment arms that included Aliskiren such as Aliskiren + Hydrochlorothiazide (HCTZ), Aliskiren + placebo for HCTZ, Aliskiren + Amlodipine, Aliskiren + placebo for Amlodipine.
Non-Aliskiren Based Regimen	This regimen includes all the patients who were randomized to the treatment arms that did not include Aliskiren such as HCTZ + Placebo for Aliskiren, Placebo for Aliskiren + Placebo for HCTZ, Amlodipine + Placebo for Aliskiren, Placebo for Aliskiren + Placebo for Amlodipine

Measured Values

	Aliskiren Based Regimen	**Non-Aliskiren Based Regimen**
Number of Participants Analyzed [units: participants]	**860**	**899**
Number of Participants With Total Mortality in Aliskiren Based Regimen Versus Non-aliskiren Based Regimen [units: Participants]	**5**	**9**

No statistical analysis provided for Number of Participants With Total Mortality in Aliskiren Based Regimen Versus Non-aliskiren Based Regimen

7. Other Pre-specified: Change From Baseline in Mean Sitting Systolic Blood Pressure (msSBP) [Time Frame: Baseline (BL), 6 week, 6 month and 12 month]

Measure Type	Other Pre-specified
Measure Title	Change From Baseline in Mean Sitting Systolic Blood Pressure (msSBP)
Measure Description	Mean sitting systolic blood pressure (msSBP) is the average of 2 sitting SBP measurements (2 minutes apart). Since each patient had their final follow-up visit at a different time in the trial, these measurements were classified as falling into the 6 week, 6 month, or 12 month measurement period. All available blood pressures were sorted within these periods and the last value within each time range used for analysis. At each timepoint, a patient must have both baseline and postbaseline values to be included in the analysis.
Time Frame	Baseline (BL), 6 week, 6 month and 12 month
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.
Full analysis Set : All randomized patients, regardless of receiving study medication. n=number of patients with non-missing assessments at baseline and each post-baseline visit.

Reporting Groups

	Description
Aliskiren Based Regimen	This regimen includes all the patients who were randomized to the treatment arms that included Aliskiren such as Aliskiren + Hydrochlorothiazide (HCTZ), Aliskiren + placebo for HCTZ, Aliskiren + Amlodipine, Aliskiren + placebo for Amlodipine.
Non-Aliskiren Based Regimen	This regimen includes all the patients who were randomized to the treatment arms that did not include Aliskiren such as HCTZ + Placebo for Aliskiren, Placebo for Aliskiren + Placebo for HCTZ, Amlodipine + Placebo for Aliskiren, Placebo for Aliskiren + Placebo for Amlodipine

Measured Values

	Aliskiren Based Regimen	Non-Aliskiren Based Regimen
Number of Participants Analyzed [units: participants]	**860**	**899**
Change From Baseline in Mean Sitting Systolic Blood Pressure (msSBP) [units: mmHg] Least Squares Mean (Standard Error)		
change from Baseline to 6 week (n=821,867)	**-11.9 (0.50)**	**-8.02 (0.48)**
change from baseline to 6 month (n=730,775)	**-10.1 (0.52)**	**-6.8 (0.50)**
change from baseline to 12 month (n=397,399)	**-7.7 (0.68)**	**-5.8 (0.68)**

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

8. Other Pre-specified: Change From Baseline in Mean Sitting Diastolic Blood Pressure (msDBP) [Time Frame: Baseline (BL), 6 week, 6 month and 12 month]

Measure Type	Other Pre-specified
Measure Title	Change From Baseline in Mean Sitting Diastolic Blood Pressure (msDBP)
Measure Description	Mean sitting diastolic blood pressure (msDBP) is the average of 2 sitting DBP measurements (2 minutes apart). Since each patient had their final follow-up visit at a different time in the trial, these measurements were classified as falling into the 6 week, 6 month, or 12 month measurement period. All available blood pressures were sorted within these periods and the last value within each time range used for analysis. At each timepoint, a patient must have both baseline and postbaseline values to be included in the analysis.
Time Frame	Baseline (BL), 6 week, 6 month and 12 month
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.
Full analysis Set : All randomized patients, regardless of receiving study medication. n=number of patients with non-missing assessments at baseline and each post-baseline visit.

Reporting Groups

	Description
Aliskiren Based Regimen	This regimen includes all the patients who were randomized to the treatment arms that included Aliskiren such as Aliskiren + Hydrochlorothiazide (HCTZ), Aliskiren + placebo for HCTZ, Aliskiren + Amlodipine, Aliskiren + placebo for Amlodipine.
Non-Aliskiren Based Regimen	This regimen includes all the patients who were randomized to the treatment arms that did not include Aliskiren such as HCTZ + Placebo for Aliskiren, Placebo for Aliskiren + Placebo for HCTZ, Amlodipine + Placebo for Aliskiren, Placebo for Aliskiren + Placebo for Amlodipine

Measured Values

	Aliskiren Based Regimen	Non-Aliskiren Based Regimen
Number of Participants Analyzed [units: participants]	**860**	**899**
Change From Baseline in Mean Sitting Diastolic Blood Pressure (msDBP) [units: mmHg] Least Squares Mean (Standard Error)		
change from Baseline to 6 week (n=821,867)	**-5.6 (0.31)**	**-3.6 (0.30)**
change from baseline to 6 month (n=730,775)	**-4.9 (0.33)**	**-3.5 (0.32)**
change from baseline to 12 month (n=397,399)	**-4.3 (0.43)**	**-3.9 (0.43)**

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

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	Safety Set (SAF): The safety set consists of all randomized patients who took at least one dose of study medication. Patients were analyzed according to treatment received.

Reporting Groups

	Description
Run-in Period: Aliskiren + Hydrochlorothiazide (HCTZ)	In run-in period (4-5 weeks) , patients on CCB background therapy and approximately 50% of patients on neither thiazide nor CCB background therapy: received Hydrochlorothiazide 12.5/25 mg and Aliskiren 150/300 mg daily in a titrated manner as per protocol. Patients randomized to this arm received Aliskiren 300 mg + HCTZ 25 mg once daily.
Run-in Period: Aliskiren + Amlodipine	In run-in period (4-5 weeks) , patients on thiazide background therapy and approximately 50% of patients on neither CCB nor thiazide background therapy received Amlodipine 5 mg and Aliskiren 150/300 mg daily in a titrated manner as per protocol. Patients randomized to this arm received Aliskiren 300 mg + Amlodipine 5 mg once daily during the double blind period.
Double Blind Period: Aliskiren + Hydrochlorothiazide (HCTZ)	In double blind period, all patients who successfully completed run-in with HCTZ plus Aliskiren were randomized equally to the 4 arms of the HCTZ add-on stratum. Patients randomized to this arm received Aliskiren 300 mg + HCTZ 25 mg once daily.
Double Blind Period: Aliskiren + Placebo for HCTZ	In double blind period, all patients who successfully completed run-in with HCTZ plus Aliskiren were randomized equally to the 4 arms of the HCTZ add-on stratum. In double blind period, randomized patients to this arm received Aliskiren 300 mg + placebo for HCTZ 25 mg once daily
Double Blind Period: Aliskiren + Amlodipine	In double blind period, patients who successfully completed run-in with Amlodipine plus Aliskiren were randomized equally to the 4 arms of the Amlodipine add-on stratum. Patients randomized to this arm received Aliskiren 300 mg + Amlodipine 5 mg once daily during the double blind period.
Double Blind Period: Aliskiren + Placebo for Amlodipine	In double blind period, all patients who successfully completed run-in with Amlodipine plus Aliskiren were randomized equally to the 4 arms of the Amlodipine add-on stratum. In double blind period, randomized patients to this arm received Aliskiren 300 mg + placebo for Amlodipine 5 mg
Double Blind Period: HCTZ + Placebo for Aliskiren	In double blind period, all patients who successfully completed run-in with HCTZ plus Aliskiren were randomized equally to the 4 arms of the HCTZ add-on stratum. In double blind period, randomized patients to this arm received HCTZ 25 mg + placebo for Aliskiren 300 mg once daily
Double Blind Period: Placebo for Aliskiren + Placebo for HCTZ	In double blind period, all patients who successfully completed run-in with HCTZ plus Aliskiren were randomized equally to the 4 arms of the HCTZ add-on stratum. In double blind period, randomized patients to this arm received placebo for Aliskiren 300 mg + placebo for HCTZ 25 mg once daily
Double Blind Period: Amlodipine + Placebo for Aliskiren	In double blind period, all patients who successfully completed run-in with Amlodipine plus Aliskiren were randomized equally to the 4 arms of the Amlodipine add-on stratum. In double blind period, randomized patients to this arm received Amlodipine 5 mg + placebo for Aliskiren 300 mg once daily
Double Blind Period: Placebo for Aliskiren + Placebo for Amlod	In double blind period, all patients who successfully completed run-in with Amlodipine plus Aliskiren were randomized equally to the 4 arms of the Amlodipine add-on stratum. In double blind period, randomized patients to this arm received placebo for Aliskiren 300 mg + placebo for Amlodipine 5 mg once daily

Serious Adverse Events

	Run-in Period: Aliskiren +	**Run-in Period:**	**Double Blind Period: Aliskiren +**	**Double Blind Period:**	**Double Blind**	**Double Blind Period:**	**Double Blind Period:**	**Double Blind Period:**

	Hydrochlorothiazide (HCTZ)	Aliskiren + Amlodipine	Hydrochlorothiazide (HCTZ)	Aliskiren + Placebo for HCTZ	Period: Aliskiren + Amlodipine	Aliskiren + Placebo for Amlodipine	HCTZ + Placebo for Aliskiren	Placebo for Aliskiren + Placebo for HCTZ
Total, serious adverse events								
# participants affected / at risk	10/1335 (0.75%)	10/1001 (1.00%)	8/244 (3.28%)	5/232 (2.16%)	7/189 (3.70%)	8/195 (4.10%)	4/251 (1.59%)	6/253 (2.37%)
Blood and lymphatic system disorders								
Anaemia † [1]								
# participants affected / at risk	0/1335 (0.00%)	1/1001 (0.10%)	1/244 (0.41%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Cardiac disorders								
Angina pectoris † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	1/244 (0.41%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Atrial fibrillation † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	1/253 (0.40%)
Cardiac arrest † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	1/253 (0.40%)
Ventricular fibrillation † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	1/251 (0.40%)	0/253 (0.00%)
Gastrointestinal disorders								
Abdominal hernia † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	1/253 (0.40%)
Diarrhoea † [1]								
# participants affected / at risk	1/1335 (0.07%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	1/251 (0.40%)	0/253 (0.00%)
Gastrointestinal haemorrhage † [1]								
# participants affected / at risk	0/1335 (0.00%)	1/1001 (0.10%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Haematochezia † [1]								
# participants affected / at	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)

risk								
Intestinal perforation † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Pancreatitis acute † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
General disorders								
Chest pain † [1]								
# participants affected / at risk	0/1335 (0.00%)	1/1001 (0.10%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Drug interaction † [1]								
# participants affected / at risk	1/1335 (0.07%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Drug intolerance † [1]								
# participants affected / at risk	1/1335 (0.07%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Hepatobiliary disorders								
Cholecystitis † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	1/195 (0.51%)	0/251 (0.00%)	0/253 (0.00%)
Cholecystitis acute † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	1/253 (0.40%)
Infections and infestations								
Bronchitis † [1]								
# participants affected / at risk	0/1335 (0.00%)	1/1001 (0.10%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Cellulitis † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	1/195 (0.51%)	1/251 (0.40%)	0/253 (0.00%)
Gastroenteritis † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	1/232 (0.43%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Herpes zoster †								

[1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	1/251 (0.40%)	0/253 (0.00%)
Pneumonia † [1]								
# participants affected / at risk	1/1335 (0.07%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	1/253 (0.40%)
Urinary tract infection † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	1/195 (0.51%)	1/251 (0.40%)	0/253 (0.00%)
Viral infection † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	1/244 (0.41%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Injury, poisoning and procedural complications								
Femur fracture † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	1/232 (0.43%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Subdural haematoma † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Investigations								
Blood creatinine increased † [1]								
# participants affected / at risk	1/1335 (0.07%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Blood urea increased † [1]								
# participants affected / at risk	1/1335 (0.07%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Metabolism and nutrition disorders								
Diabetes mellitus † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	1/251 (0.40%)	0/253 (0.00%)
Electrolyte imbalance † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	1/189 (0.53%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)

Hyperkalaemia † [1]								
# participants affected / at risk	2/1335 (0.15%)	1/1001 (0.10%)	1/244 (0.41%)	0/232 (0.00%)	3/189 (1.59%)	1/195 (0.51%)	0/251 (0.00%)	0/253 (0.00%)
Hypokalaemia † [1]								
# participants affected / at risk	2/1335 (0.15%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Hyponatraemia † [1]								
# participants affected / at risk	1/1335 (0.07%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)								
Basal cell carcinoma † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	1/244 (0.41%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Colon cancer † [1]								
# participants affected / at risk	0/1335 (0.00%)	1/1001 (0.10%)	0/244 (0.00%)	0/232 (0.00%)	1/189 (0.53%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Colon cancer metastatic † [1]								
# participants affected / at risk	0/1335 (0.00%)	1/1001 (0.10%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Small intestine carcinoma † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	1/232 (0.43%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Nervous system disorders								
Cerebral hypoperfusion † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Cerebrovascular accident † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	1/253 (0.40%)
Coma † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	1/253 (0.40%)

Hemiparesis † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	1/189 (0.53%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Loss of consciousness † [1]								
# participants affected / at risk	0/1335 (0.00%)	1/1001 (0.10%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Paraesthesia † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	1/189 (0.53%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Syncope † [1]								
# participants affected / at risk	0/1335 (0.00%)	1/1001 (0.10%)	3/244 (1.23%)	0/232 (0.00%)	1/189 (0.53%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Psychiatric disorders								
Psychotic disorder † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	1/189 (0.53%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Renal and urinary disorders								
Azotaemia † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	1/195 (0.51%)	0/251 (0.00%)	0/253 (0.00%)
Renal disorder † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	1/195 (0.51%)	0/251 (0.00%)	0/253 (0.00%)
Renal failure † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	2/244 (0.82%)	1/232 (0.43%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Renal failure acute † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	1/232 (0.43%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Renal impairment † [1]								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	1/232 (0.43%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)
Respiratory, thoracic and mediastinal disorders								
Pulmonary								

oedema † 1								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	1/195 (0.51%)	0/251 (0.00%)	0/253 (0.00%)
Skin and subcutaneous tissue disorders								
Angioedema † 1								
# participants affected / at risk	0/1335 (0.00%)	2/1001 (0.20%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	1/195 (0.51%)	0/251 (0.00%)	0/253 (0.00%)
Vascular disorders								
Arterial occlusive disease † 1								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	1/195 (0.51%)	0/251 (0.00%)	0/253 (0.00%)
Hypertensive crisis † 1								
# participants affected / at risk	0/1335 (0.00%)	0/1001 (0.00%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	1/195 (0.51%)	0/251 (0.00%)	0/253 (0.00%)
Hypotension † 1								
# participants affected / at risk	0/1335 (0.00%)	2/1001 (0.20%)	0/244 (0.00%)	0/232 (0.00%)	0/189 (0.00%)	0/195 (0.00%)	0/251 (0.00%)	0/253 (0.00%)

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

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	Safety Set (SAF): The safety set consists of all randomized patients who took at least one dose of study medication. Patients were analyzed according to treatment received.

Frequency Threshold

Threshold above which other adverse events are reported	1%

Reporting Groups

	Description
Run-in Period: Aliskiren + Hydrochlorothiazide (HCTZ)	In run-in period (4-5 weeks) , patients on CCB background therapy and approximately 50% of patients on neither thiazide nor CCB background therapy: received Hydrochlorothiazide 12.5/25 mg and Aliskiren 150/300 mg daily in a titrated manner as per protocol. Patients randomized to this arm received Aliskiren 300 mg + HCTZ 25 mg once daily.
Run-in Period: Aliskiren + Amlodipine	In run-in period (4-5 weeks) , patients on thiazide background therapy and approximately 50% of patients on neither CCB nor thiazide background therapy received Amlodipine 5 mg and Aliskiren 150/300 mg daily in a titrated manner as per protocol. Patients randomized to this arm received Aliskiren 300 mg + Amlodipine 5 mg once daily during the double blind period.
Double Blind Period: Aliskiren + Hydrochlorothiazide (HCTZ)	In double blind period, all patients who successfully completed run-in with HCTZ plus Aliskiren were randomized equally to the 4 arms of the HCTZ add-on stratum.

	Patients randomized to this arm received Aliskiren 300 mg + HCTZ 25 mg once daily.
Double Blind Period: Aliskiren + Placebo for HCTZ	In double blind period, all patients who successfully completed run-in with HCTZ plus Aliskiren were randomized equally to the 4 arms of the HCTZ add-on stratum. In double blind period, randomized patients to this arm received Aliskiren 300 mg + placebo for HCTZ 25 mg once daily
Double Blind Period: Aliskiren + Amlodipine	In double blind period, patients who successfully completed run-in with Amlodipine plus Aliskiren were randomized equally to the 4 arms of the Amlodipine add-on stratum. Patients randomized to this arm received Aliskiren 300 mg + Amlodipine 5 mg once daily during the double blind period.
Double Blind Period: Aliskiren + Placebo for Amlodipine	In double blind period, all patients who successfully completed run-in with Amlodipine plus Aliskiren were randomized equally to the 4 arms of the Amlodipine add-on stratum. In double blind period, randomized patients to this arm received Aliskiren 300 mg + placebo for Amlodipine 5 mg
Double Blind Period: HCTZ + Placebo for Aliskiren	In double blind period, all patients who successfully completed run-in with HCTZ plus Aliskiren were randomized equally to the 4 arms of the HCTZ add-on stratum. In double blind period, randomized patients to this arm received HCTZ 25 mg + placebo for Aliskiren 300 mg once daily
Double Blind Period: Placebo for Aliskiren + Placebo for HCTZ	In double blind period, all patients who successfully completed run-in with HCTZ plus Aliskiren were randomized equally to the 4 arms of the HCTZ add-on stratum. In double blind period, randomized patients to this arm received placebo for Aliskiren 300 mg + placebo for HCTZ 25 mg once daily
Double Blind Period: Amlodipine + Placebo for Aliskiren	In double blind period, all patients who successfully completed run-in with Amlodipine plus Aliskiren were randomized equally to the 4 arms of the Amlodipine add-on stratum. In double blind period, randomized patients to this arm received Amlodipine 5 mg + placebo for Aliskiren 300 mg once daily
Double Blind Period: Placebo for Aliskiren + Placebo for Amlod	In double blind period, all patients who successfully completed run-in with Amlodipine plus Aliskiren were randomized equally to the 4 arms of the Amlodipine add-on stratum. In double blind period, randomized patients to this arm received placebo for Aliskiren 300 mg + placebo for Amlodipine 5 mg once daily

Other Adverse Events

	Run-in Period: Aliskiren + Hydrochlorothiazide (HCTZ)	Run-in Period: Aliskiren + Amlodipine	Double Blind Period: Aliskiren + Hydrochlorothiazide (HCTZ)	Double Blind Period: Aliskiren + Placebo for HCTZ	Double Blind Period: Aliskiren + Amlodipine	Double Blind Period: Aliskiren + Placebo for Amlodipine	Double Blind Period: HCTZ + Placebo for Aliskiren	Double Blind Period: Placebo for Aliskiren + Placebo for HCTZ
Total, other (not including serious) adverse events								
# participants affected / at risk	**7/1335 (0.52%)**	**19/1001 (1.90%)**	**6/244 (2.46%)**	**5/232 (2.16%)**	**9/189 (4.76%)**	**8/195 (4.10%)**	**6/251 (2.39%)**	**5/253 (1.98%)**
Gastrointestinal disorders								
Gastritis † [1]								
# participants affected / at risk	**0/1335 (0.00%)**	**0/1001 (0.00%)**	**0/244 (0.00%)**	**0/232 (0.00%)**	**0/189 (0.00%)**	**2/195 (1.03%)**	**0/251 (0.00%)**	**0/253 (0.00%)**
General disorders								
Oedema peripheral † [1]								

# participants affected / at risk	0/1335 (0.00%)	7/1001 (0.70%)	0/244 (0.00%)	1/232 (0.43%)	4/189 (2.12%)	0/195 (0.00%)	0/251 (0.00%)	2/253 (0.79%)
Metabolism and nutrition disorders								
Hyperkalaemia † 1								
# participants affected / at risk	1/1335 (0.07%)	0/1001 (0.00%)	1/244 (0.41%)	1/232 (0.43%)	0/189 (0.00%)	2/195 (1.03%)	1/251 (0.40%)	1/253 (0.40%)
Nervous system disorders								
Dizziness † 1								
# participants affected / at risk	3/1335 (0.22%)	7/1001 (0.70%)	1/244 (0.41%)	0/232 (0.00%)	0/189 (0.00%)	2/195 (1.03%)	1/251 (0.40%)	1/253 (0.40%)
Vascular disorders								
Hypotension † 1								
# participants affected / at risk	3/1335 (0.22%)	5/1001 (0.50%)	4/244 (1.64%)	3/232 (1.29%)	6/189 (3.17%)	2/195 (1.03%)	4/251 (1.59%)	1/253 (0.40%)

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

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
Due to early termination, 1759 patients were randomized as against 11,000. Only 25 primary endpoints had accrued during median follow-up of 209 days as against planned 2000 in 5 years. These low numbers significantly limit interpretation of results.

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 or disclosure of trial results in their entirety.

Results Point of Contact:

Name/Title: Study Director

Organization: Novartis Pharmaceuticals
phone: 862-778-8300
e-mail: trialandresults.registries@novartis.com

No publications provided by Novartis

Publications automatically indexed to this study:

Teo KK, Pfeffer M, Mancia G, O'Donnell M, Dagenais G, Diaz R, Dans A, Liu L, Bosch J, Joseph P, Copland I, Jung H, Pogue J, Yusuf S; Aliskiren Prevention of Later Life Outcomes trial Investigators. Aliskiren alone or with other antihypertensives in the elderly with borderline and stage 1 hypertension: the APOLLO trial. Eur Heart J. 2014 Jul;35(26):1743-51. doi: 10.1093/eurheartj/ehu079. Epub 2014 Mar 9.

Responsible Party:	Novartis (Novartis Pharmaceuticals)
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