ID: TAK-491CLD_307 A Study to Evaluate the Effectiveness and Safety of a Fixed Dose Combination of Azilsartan Medoxomil and Chlorthalidone in Patients With High Blood Pressure Who do Not Achieve Target Blood Pressure Following Treatment With Azilsartan Medoxomil Alone NCT01456169

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Participant Flow

Recruitment Details	A total of 1754 patients were screened at 125 investigative sites in Bulgaria, Estonia, France, Germany, Hungary, Italy, Lithuania, the Netherlands, Poland, Serbia, Slovakia, Spain, Sweden, and the United Kingdom from 31 October 2011 to 24 January 2013.
Pre-Assignment Details	507 participants entered the azilsartan medoxomil 40 mg Single-Blind Monotherapy Treatment Period and 395 participants were eligible to enter the Double-Blind Treatment Period and were randomly assigned to 1 of 3 active treatment arms.

Arm/Group Title	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**	Total (Not public)
Arm/Group Description	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks.	
Period Title: Overall Study				
Started	133 [1]	127 [2]	135 [3]	395
Completed	123	122	123	368
Not Completed	10	5	12	27
Reason Not Completed				
Adverse Event	1	2	7	10
Major Protocol Deviation	3	2	3	8
Voluntary Withdrawal	3	0	2	5
Lack of Efficacy	2	0	0	2
Other	1	1	0	2
NOTE : "Other" is not sufficiently descriptive for "Other" Reason Not Completed. Please provide a more descriptive label. (Not Public)				
	Not Completed = 10 Total from all reasons = 10	Not Completed = 5 Total from all reasons = 5	Not Completed = 12 Total from all reasons = 12	

[1] Indicates participants who were randomized into the double-blind treatment period
[2] Indicates participants who were randomized into the double-blind treatment period
[3] Indicates participants who were randomized into the double-blind treatment period

Baseline Characteristics

Arm/Group Title	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**	**Total**
Arm/Group Description	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks.	

Overall Number of Baseline Participants	133	127	135	**395**
Baseline Analysis Population Description	Participants who were randomized into the double-blind treatment period. Baseline was defined as the last observed value while on monotherapy study drug and before the first dose of double-blind study drug.			
Age, Continuous				
Mean (Standard Deviation)				
Units: years	57.9 (10.18)	59.2 (10.72)	57.7 (10.46)	58.2 (10.45)
Age, Customized				
Measure Type: Number				
Units: participants				
< 45 years	13	10	12	35
45 to < 65 years	87	79	88	254
≥ 65 years	33	38	35	106
Gender, Male/Female				
Measure Type: Number				
Units: participants				
Female	46	54	44	144
Male	87	73	91	251
Race/Ethnicity, Customized [1]				
Measure Type: Number				
Units: participants				
American Indian or Alaska Native	1 NOTE : The sum of participants in all Categories for the Measure does not equal the Overall Number of Baseline Participants in the Arm/Group.	0	1 NOTE : The sum of participants in all Categories for the Measure does not equal the Overall Number of Baseline Participants in the Arm/Group.	2
Asian	0	1	0	1
Black or African American	1	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	1	1
White	132	126	134	392
Multiracial	1	0	1	2
[1] Participants could choose more than 1 category for race and those who indicated more than 1 race category were included in each category and in the Multiracial category. Thus the total number of participants may not generally add up to the total number of each group.				
Region of Enrollment				
Measure Type: Number				
Units: participants				
Bulgaria	11	10	11	32
Estonia	18	16	18	52
France	2	1	2	5
Germany	29	29	28	86
Hungary	10	9	10	29
Italy	6	4	5	15
Lithuania	5	4	6	15
Netherlands	4	6	5	15
Poland	17	18	17	52
Serbia	4	3	4	11
Slovakia	24	24	26	74
Spain	1	1	1	3
Sweden	1	2	1	4
United Kingdom	1	0	1	2
Weight				
Mean (Standard Deviation)				
Units: kg	87.59 (15.794)	86.71 (17.037)	87.39 (14.876)	87.24 (15.868)
Height [1]				
Mean (Standard Deviation)				
Units: cm	171.8 (8.87)	170.6 (9.96)	172.1 (9.74)	171.5 (9.53)
[1] Height data only available for 126 participants in the Azilsartan medoxomil + chlorthalidone 40/12.5 mg treatment group.				

Body Mass Index (BMI) [1]				
Mean (Standard Deviation)				
Units: kg/m^2	29.63 (5.066)	29.78 (5.206)	29.52 (4.572)	29.64 (4.937)

[1] BMI data only available for 126 participants in the Azilsartan medoxomil + chlorthalidone 40/12.5 mg treatment group.

Smoking Classification				
Measure Type: Number				
Units: participants				
Never smoked	77	83	77	237
Current smoker	31	25	30	86
Ex-smoker	25	19	28	72
Diabetes Status				
Measure Type: Number				
Units: participants				
Yes	20	27	20	67
No	113	100	115	328
Estimated Glomerular Filtration Rate (eGFR)				
Mean (Standard Deviation)				
Units: mL/min/1.73 m^2	84.8 (16.41)	81.5 (16.25)	82.4 (16.51)	82.9 (16.41)
Baseline eGFR Categories (mL/min/1.73 m^2)				
Measure Type: Number				
Units: participants				
30 to < 60 ml/min/1.73 m^2	11	10	11	32
60 to < 90 ml/min/1.73 m^2	78	85	80	243
≥ 90 ml/min/1.73 m^2	44	32	44	120
Trough Clinic Systolic Blood Pressure (SBP)				
Mean (Standard Deviation)				
Units: mmHg	150.7 (10.69)	149.6 (11.54)	149.8 (10.95)	150.0 (11.04)
Trough Clinic SBP Category (mmHg)				
Measure Type: Number				
Units: participants				
<140 mmHg	16	17	17	50
≥140 - <160 mmHg	86	87	93	266
≥160 - <180 mmHg	31	23	25	79
≥180 mmHg	0	0	0	0
Trough Clinic Diastolic Blood Pressure (DBP)				
Mean (Standard Deviation)				
Units: mmHg	89.8 (7.76)	87.6 (9.31)	88.8 (7.99)	88.7 (8.39)
Trough Clinic DBP Categories (mmHg)				
Measure Type: Number				
Units: participants				
<90 mmHg	68	72	70	210
≥90 mmHg	65	55	65	185

Outcome Measures

1. Primary Outcome

Title: Change From Baseline to Week 8 in Trough, Sitting, Clinic Systolic Blood Pressure

Description: The change between trough systolic blood pressure measured at final visit or Week 8 relative to baseline. Systolic blood pressure is the arithmetic mean of the 3 trough sitting systolic blood pressure measurements.

Time Frame: Baseline (of the double-blind treatment period) and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set, consisting of all randomized participants who received at least 1 dose of double-blind study drug. A participant was included in the analyses only when there was both a baseline value and at least 1 value during the double-blind treatment period. Last observation carried forward (LOCF) was used.

Arm/Group Title	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**
Arm/Group Description:	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks.
Number of Participants Analyzed	133	126	135
Least Squares Mean (Standard Error) Units: mm Hg			
Baseline	150.7 (0.96)	149.8 (0.98)	149.8 (0.95)
Change from Baseline to Week 8	-6.4 (1.05)	-15.8 (1.08)	-21.1 (1.04)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Groups**	Azilsartan Medoxomil 40 mg, Azilsartan Medoxomil + Chlorthalidone 40/25 mg
	Comments	The type I error was controlled using a 2-step hierarchical testing procedure. In the first step, the high dose (40/25 mg) of Azilsartan medoxomil + chlorthalidone was compared to Azilsartan medoxomil alone. If the comparison in step 1 was statistically significant at a significance level of 5%, then step 2 was performed by comparing the low dose (40/12.5 mg) and monotherapy at the 5% significance level.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	ANCOVA model with treatment as a fixed effect and baseline trough, sitting, clinic SBP as a covariate.
Method of Estimation	**Estimation Parameter**	Other[LS mean difference]
	Estimated Value	-14.7
	Confidence Interval	(2-Sided) 95% -17.6 to -11.8

	Estimation Comments	[Not specified]

Statistical Analysis 2

Statistical Analysis Overview	**Comparison Groups**	Azilsartan Medoxomil 40 mg, Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	**P-Value**	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	ANCOVA model with treatment as a fixed effect and baseline trough, sitting, clinic SBP as a covariate
Method of Estimation	**Estimation Parameter**	Other[LS mean difference]
	Estimated Value	-9.5
	Confidence Interval	(2-Sided) 95% -12.4 to -6.5
	Estimation Comments	[Not specified]

2. Secondary Outcome

Title: Change From Baseline to Week 8 in Trough, Sitting, Clinic Diastolic Blood Pressure

Description: The change between trough diastolic blood pressure measured at final visit or week 8 relative to baseline Diastolic blood pressure is the arithmetic mean of the 3 trough sitting diastolic blood pressure measurements.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set; LOCF was used.

Arm/Group Title	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**
Arm/Group Description:	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks.
Number of Participants Analyzed	133	126	135
Least Squares Mean (Standard Error) Units: mm Hg			
Baseline	89.8 (0.73)	87.7 (0.75)	88.8 (0.72)
Change from Baseline to Week 8	-3.2 (0.65)	-7.7 (0.67)	-10.3 (0.65)

3. Secondary Outcome

Title: Change From Baseline to Week 8 in Trough Systolic Blood Pressure as Measured by Ambulatory Blood Pressure Monitoring

Description: The change in trough systolic blood pressure measured at final visit or week 8 relative to baseline. Ambulatory blood pressure monitoring measures blood pressure at regular intervals throughout the day and night. The trough is the average of all measurements recorded from 22 to 24 hours after dosing.

Time Frame: Baseline and Week 8, 22-24 hours after dosing

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set. Only participants with a baseline and at least 1 post-baseline value of acceptable quality were included.

Arm/Group Title	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**
Arm/Group Description:	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks.
Number of Participants Analyzed	107	98	104
Least Squares Mean (Standard Error) Units: mm Hg			
Baseline	143.1 (1.55)	140.2 (1.62)	142.0 (1.58)
Change from Baseline to Week 8	-2.5 (1.31)	-14.0 (1.36)	-16.6 (1.32)

4. Secondary Outcome

Title: Change From Baseline to Week 8 in Trough Diastolic Blood Pressure as Measured by Ambulatory Blood Pressure Monitoring

Description: The change in trough diastolic blood pressure measured at final visit or week 8 relative to baseline. Ambulatory blood pressure monitoring measures blood pressure at regular intervals throughout the day and night. The trough is the average of all measurements recorded from 22 to 24 hours after dosing.

Time Frame: Baseline and Week 8, 22-24 hours after dosing

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set. Only participants with a Baseline and at least 1 post-baseline value of acceptable quality were included

Arm/Group Title	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**
Arm/Group Description:	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks.
Number of Participants Analyzed	107	98	104
Least Squares Mean (Standard Error) Units: mm Hg			
Baseline	86.4 (1.11)	83.6 (1.16)	86.0 (1.12)
Change from Baseline to Week 8	-2.2 (0.88)	-8.8 (0.92)	-9.4 (0.89)

5. Secondary Outcome

Title: Change From Baseline to Week 8 in the 24-hour Mean Systolic Blood Pressure, as Measured by Ambulatory Blood Pressure Monitoring

Description: The change in 24-hour mean systolic blood pressure measured at final visit or week 8 relative to baseline. Ambulatory blood pressure monitoring measures blood pressure at regular intervals throughout the day and night. The 24-hour mean is the average of all measurements recorded for 24 hours after dosing.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set. Only participants with a Baseline and at least 1 post-baseline value of acceptable quality were included.

Arm/Group Title	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**
Arm/Group Description:	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks.
Number of Participants Analyzed	107	98	104
Least Squares Mean (Standard Error) Units: mm Hg			
Baseline	138.0 (1.21)	137.0 (1.26)	138.2 (1.22)
Change from Baseline to Week 8	-2.3 (1.02)	-14.7 (1.07)	-18.1 (1.03)

6. Secondary Outcome

Title: Change From Baseline to Week 8 in the 24-hour Mean Diastolic Blood Pressure, as Measured by Ambulatory Blood Pressure Monitoring

Description: The change in 24-hour mean diastolic blood pressure measured at final visit or week 8 relative to baseline. Ambulatory blood pressure monitoring measures blood pressure at regular intervals throughout the day and night. The 24-hour mean is the average of all measurements recorded for 24 hours after dosing.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set. Only participants with a Baseline and at least 1 post-baseline value of acceptable quality were included.

Arm/Group Title	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**
Arm/Group Description:	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks.
Number of Participants Analyzed	107	98	104
Least Squares Mean (Standard Error) Units: mm Hg			
Baseline	81.9 (0.89)	80.3 (0.93)	82.5 (0.91)
Change from Baseline to Week 8	-1.6 (0.66)	-8.5 (0.69)	-10.1 (0.67)

7. Secondary Outcome

Title: Change From Baseline to Week 8 in the Mean Daytime Systolic Blood Pressure, as Measured by Ambulatory Blood Pressure Monitoring

Description: The change in daytime (6 am to 10 pm) mean systolic blood pressure measured at final visit or week 8 relative to baseline. Ambulatory blood pressure monitoring measures blood pressure at regular intervals throughout the day and night. Daytime mean is the average of all measurements recorded between the hours of 6 am and 10 pm.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set. Only participants with a Baseline and at least 1 post-baseline value of acceptable quality were included.

Arm/Group Title	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**
Arm/Group Description:	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks.
Number of Participants Analyzed	107	98	104
Least Squares Mean (Standard Error) Units: mm Hg			
Baseline	141.5 (1.24)	141.1 (1.30)	141.9 (1.26)
Change from Baseline to Week 8	-2.4 (1.09)	-15.3 (1.14)	-18.2 (1.11)

8. Secondary Outcome

Title: Change From Baseline to Week 8 in the Mean Daytime Diastolic Blood Pressure, as Measured by Ambulatory Blood Pressure Monitoring

Description: The change in daytime (6 am to 10 pm) mean diastolic blood pressure measured at final visit or week 8 relative to baseline. Ambulatory blood pressure monitoring measures blood pressure at regular intervals throughout the day and night. Daytime mean is the average of all measurements recorded between the hours of 6 am and 10 pm.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set. Only participants with a Baseline and at least 1 post-baseline value of acceptable quality were included.

Arm/Group Title	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**
Arm/Group Description:	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks.
Number of Participants Analyzed	107	98	104
Least Squares Mean (Standard Error) Units: mm Hg			
Baseline	84.9 (0.96)	83.6 (1.01)	85.7 (0.98)
Change from Baseline to Week 8	-1.7 (0.72)	-8.9 (0.75)	-10.1 (0.73)

9. Secondary Outcome

Title: Change From Baseline to Week 8 in the Mean Nighttime Systolic Blood Pressure, as Measured by Ambulatory Blood Pressure Monitoring

Description: The change in nighttime (12 am to 6 am) mean systolic blood pressure measured at final visit or week 8 relative to baseline. Ambulatory blood pressure monitoring measures blood pressure at regular intervals throughout the day and night. Nighttime mean is the average of all measurements recorded between the hours of 12 am and 6 am.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set. Only participants with a Baseline and at least 1 post-baseline value of acceptable quality were included.

Arm/Group Title	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**
Arm/Group Description:	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks.
Number of Participants Analyzed	107	98	104
Least Squares Mean (Standard Error) Units: mm Hg			
Baseline	127.3 (1.50)	124.2 (1.57)	126.3 (1.52)
Change from Baseline to Week 8	-2.2 (1.18)	-12.7 (1.24)	-17.3 (1.20)

10. Secondary Outcome

Title: Change From Baseline to Week 8 in the Mean Nighttime Diastolic Blood Pressure, as Measured by Ambulatory Blood Pressure Monitoring

Description: The change in nighttime (12 am to 6 am) mean diastolic blood pressure measured at final visit or week 8 relative to baseline. Ambulatory blood pressure monitoring measures blood pressure at regular intervals throughout the day and night. Nighttime mean is the average of all measurements recorded between the hours of 12 am and 6 am.

Time Frame: Baseline and Week 8.

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set. Only participants with a Baseline and at least 1 post-baseline value of acceptable quality were included.

Arm/Group Title	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**
Arm/Group Description:	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks.
Number of Participants Analyzed	107	98	104
Least Squares Mean (Standard Error) Units: mm Hg			
Baseline	73.2 (0.95)	70.6 (0.99)	72.9 (0.97)
Change from Baseline to Week 8	-1.6 (0.78)	-7.2 (0.82)	-9.8 (0.79)

11. Secondary Outcome

Title: Change From Baseline to Week 8 in the Mean Systolic Blood Pressure 0 to 12 Hours After Dosing, as Measured by Ambulatory Blood Pressure Monitoring

Description: The change in the 12-hour mean systolic blood pressure measured at final visit or week 8 relative to baseline. Ambulatory blood pressure monitoring measures blood pressure at regular intervals throughout the day and night. The 12-hour mean is the average of all measurements recorded in the first 12 hours after dosing.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set. Only participants with a Baseline and at least 1 post-baseline value of acceptable quality were included.

Arm/Group Title	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**
Arm/Group Description:	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks.
Number of Participants Analyzed	107	98	104
Least Squares Mean (Standard Error) Units: mm Hg			
Baseline	141.6 (1.30)	141.8 (1.36)	142.3 (1.32)
Change from Baseline to Week 8	-2.3 (1.14)	-15.4 (1.19)	-18.2 (1.16)

12. Secondary Outcome

Title: Change From Baseline to Week 8 in the Mean Diastolic Blood Pressure 0 to 12 Hours After Dosing, as Measured by Ambulatory Blood Pressure Monitoring

Description: The change in the 12-hour mean diastolic blood pressure measured at final visit or Week 8 relative to baseline. Ambulatory blood pressure monitoring measures blood pressure at regular intervals throughout the day and night. The 12-hour mean is the average of all measurements recorded in the first 12 hours after dosing.

Time Frame: Baseline and Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set. Only participants with a Baseline and at least 1 post-baseline value of acceptable quality were included.

Arm/Group Title	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**
Arm/Group Description:	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks.
Number of Participants Analyzed	107	98	104
Least Squares Mean (Standard Error) Units: mm Hg			
Baseline	85.2 (1.01)	84.2 (1.05)	86.0 (1.02)
Week 8	-1.6 (0.75)	-8.9 (0.78)	-10.1 (0.76)

13. Secondary Outcome

Title: Percentage of Participants Who Achieve a Target Clinic Systolic Blood Pressure at Week 8

Description: Percentage of participants who achieve a target clinic systolic blood pressure measured at final visit or week 8, defined as less than 140 mm Hg (or less than 130 mm Hg for participants with diabetes or chronic kidney disease). Systolic blood pressure is the arithmetic mean of the 3 trough sitting Systolic blood pressure measurements.

Time Frame: Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set

Arm/Group Title	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**
Arm/Group Description:	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks.
Number of Participants Analyzed	133	126	135
Measure Type: Number Units: percentage of participants	35.3	62.7	77.8

14. Secondary Outcome

Title: Percentage of Participants Who Achieve a Target Clinic Diastolic Blood Pressure at Week 8

Description: Percentage of participants who achieve a target clinic diastolic blood pressure measured at final visit or week 8, defined as less than 90 mm Hg (or less than 80 mm Hg for participants with diabetes or chronic kidney disease). Diastolic blood pressure is based on the arithmetic mean of the 3 trough sitting diastolic blood pressure measurements.

Time Frame: Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set

Arm/Group Title	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**
Arm/Group Description:	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks.
Number of Participants Analyzed	133	126	135
Measure Type: Number Units: percentage of participants	60.2	81.0	85.9

15. Secondary Outcome

Title: Percentage of Participants Who Achieve Both Clinic Systolic and Diastolic Blood Pressure Targets at Week 8

Description: Percentage of participants who achieve both clinic systolic and diastolic blood pressure targets at Week 8, defined as less than 140 mm Hg (or less than 130 mm Hg for participants with diabetes or chronic kidney

disease) for systolic AND less than 90 mm Hg (or less than 80 mm Hg for participants with diabetes or chronic kidney disease) for diastolic blood pressure.

Time Frame: Week 8

Safety Issue? No

Outcome Measure Data

Analysis Population Description

Full analysis set

Arm/Group Title	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**
Arm/Group Description:	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks.
Number of Participants Analyzed	133	126	135
Measure Type: Number Units: percentage of participants	30.8	59.5	74.1

Adverse Events

Time Frame	For 4 weeks during the monotherapy treatment period and from the first dose of double-blind study drug up to 14 days (or 30 days for a Serious AE) after the last dose of study drug in the 8-week double-blind treatment period.
Additional Description	The investigator documented any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of relation to study drug.
Source Vocabulary Name	MedDRA version 15.1
Assessment Type	Systematic Assessment

Arm/Group Title	Monotherapy: Azilsartan Medoxomil 40 mg	Azilsartan Medoxomil 40 mg	Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg	Azilsartan Medoxomil + Chlorthalidone 40/25 mg
Arm/Group Description	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for 4 weeks during the Single-Blind Monotherapy Treatment Period. All enrolled participants, including those who were not randomized to double-blind treatment are included in this group.	Azilsartan medoxomil 40 mg and chlorthalidone placebo combination tablets, orally, once daily for up to 8 weeks during the Double-Blind Treatment Period.	Azilsartan 40 mg and chlorthalidone 12.5 mg combination tablets, orally, once daily for up to 8 weeks during the Double-Blind Treatment Period.	Azilsartan medoxomil 40 mg and chlorthalidone 25 mg combination tablets, orally, once daily for up to 8 weeks during the Double-Blind Treatment Period.

Serious Adverse Events

Monotherapy: Azilsartan Medoxomil 40 mg	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**

	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	3/507 (0.59%)	2/133 (1.5%)	0/127 (0%)	0/135 (0%)
Cardiac disorders				
Acute myocardial infarction † A	1/507 (0.2%)	0/133 (0%)	0/127 (0%)	0/135 (0%)
Myocardial infarction † A	0/507 (0%)	1/133 (0.75%)	0/127 (0%)	0/135 (0%)
Ventricular tachycardia † A	1/507 (0.2%)	0/133 (0%)	0/127 (0%)	0/135 (0%)
Investigations				
Blood pressure increased † A	1/507 (0.2%)	0/133 (0%)	0/127 (0%)	0/135 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Renal cancer † A	1/507 (0.2%)	0/133 (0%)	0/127 (0%)	0/135 (0%)
Nervous system disorders				
Cerebrovascular accident † A	1/507 (0.2%)	1/133 (0.75%)	0/127 (0%)	0/135 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA version 15.1

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	2%

	Monotherapy: Azilsartan Medoxomil 40 mg	**Azilsartan Medoxomil 40 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/12.5 mg**	**Azilsartan Medoxomil + Chlorthalidone 40/25 mg**
	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)	Affected / at Risk (%)
Total	15/507 (2.96%)	15/133 (11.28%)	13/127 (10.24%)	26/135 (19.26%)
Infections and infestations				
Nasopharyngitis † A	6/507 (1.18%)	4/133 (3.01%)	2/127 (1.57%)	4/135 (2.96%)
Viral infection † A	0/507 (0%)	4/133 (3.01%)	0/127 (0%)	0/135 (0%)
Investigations				
Blood creatinine increased † A	2/507 (0.39%)	4/133 (3.01%)	4/127 (3.15%)	11/135 (8.15%)
Nervous system disorders				
Dizziness † A	3/507 (0.59%)	0/133 (0%)	2/127 (1.57%)	6/135 (4.44%)
Headache † A	9/507 (1.78%)	2/133 (1.5%)	3/127 (2.36%)	5/135 (3.7%)
Vascular disorders				
Hypotension † A	0/507 (0%)	1/133 (0.75%)	2/127 (1.57%)	4/135 (2.96%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA version 15.1

Limitations and Caveats

[Not Specified]

More Information

Certain Agreements

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The first study related publication will be a multi-center publication submitted within 24 months after conclusion or termination of a study at all sites. After such multi site publication, all proposed site publications and presentations will be

submitted to sponsor for review 60 days in advance of publication. Site will remove Sponsor confidential information unrelated to study results. Sponsor can delay a proposed publication for another 60 days to preserve intellectual property.

Results Point of Contact

Name/Official Title:	Sr. VP, Clinical Science
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