



Clinical trial results:

A Randomized, Double-blind, Placebo-Controlled, Dose-Ranging Multicenter Study to Evaluate the Efficacy and Safety of ALN-AGT01 in Patients with Mild-to-Moderate Hypertension

Summary

EudraCT number	2021-001248-82
Trial protocol	DE
Global end of trial date	05 December 2024

Results information

Result version number	v1 (current)
This version publication date	21 December 2025
First version publication date	21 December 2025

Trial information

Trial identification

Sponsor protocol code	ALN-AGT01-002
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04936035
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alnylam Pharmaceuticals, Inc.
Sponsor organisation address	300 Third Street, Cambridge, MA, United States,
Public contact	Clinical Trial Information Line, Alnylam Pharmaceuticals, Inc., +1 8772569526, clinicaltrials@alnylam.com
Scientific contact	Clinical Trial Information Line, Alnylam Pharmaceuticals, Inc., +1 8772569526, clinicaltrials@alnylam.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 December 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	05 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to evaluate the effect of ALN-AGT01 on systolic blood pressure (SBP) as assessed by ambulatory blood pressure monitoring (ABPM) at Month 3.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy:

NA

Evidence for comparator:

NA

Actual start date of recruitment	21 July 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 68
Country: Number of subjects enrolled	Puerto Rico: 8
Country: Number of subjects enrolled	United Kingdom: 16
Country: Number of subjects enrolled	United States: 286
Worldwide total number of subjects	378
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	275
From 65 to 84 years	103
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 394 subjects were enrolled across 111 sites-86 in North America (76 US, 10 Canada) and 25 in Europe (5 UK, 20 Ukraine). Due to geopolitical instability 16 subjects enrolled in Ukraine were unable to continue participation. Challenges in data collection led to their exclusion from analysis, so results reflect 378 randomized subjects.

Pre-assignment

Screening details:

As pre-specified in SAP, data collected for the participant flow after the '6-Month Placebo-controlled DB Period' (i.e., Months 6 to 12 DB period + DB Extension Period) was to be reported together as 'Post-6-Month DB Period' per treatment sequence (Pbo/Zil & Zil/Zil).

Period 1

Period 1 title	6-Month Placebo-controlled DB Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received zilebesiran matching placebo, as subcutaneous (SC) injection, once every 3 months (Q3M) during the 6-month placebo-controlled DB period.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Zilebesiran matching placebo, as SC injection, Q3M during the 6-month placebo-controlled DB period.

Arm title	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)
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Arm description:

Subjects received zilebesiran, 150 mg, as SC injection on Day 1 of the 6-month placebo-controlled DB period. They received placebo at Month 3 of the 6-month placebo-controlled DB period to maintain the blind.

Arm type	Experimental
Investigational medicinal product name	Zilebesiran
Investigational medicinal product code	ALN-AGT01
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Zilebesiran, 150 mg, as SC injection on Day 1 of the 6-month placebo-controlled DB period.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Zilebesiran matching placebo at Month 3 of the 6-month placebo-controlled DB period to maintain the blind.

Arm title	Zilebesiran 300 mg Q6M
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Arm description:

Subjects received zilebesiran, 300 mg, as SC injection on Day 1 of the 6-month placebo-controlled DB period. They received placebo at Month 3 of the 6-month placebo-controlled DB period to maintain the blind.

Arm type	Experimental
Investigational medicinal product name	Zilebesiran
Investigational medicinal product code	ALN-AGT01
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Zilebesiran, 300 mg, as SC injection on Day 1 of the 6-month placebo-controlled DB period.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Zilebesiran matching placebo at Month 3 of the 6-month placebo-controlled DB period.

Arm title	Zilebesiran 300 mg Q3M
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Arm description:

Subjects received zilebesiran, 300 mg, as SC injection, Q3M, during the 6-month placebo-controlled DB period.

Arm type	Experimental
Investigational medicinal product name	Zilebesiran
Investigational medicinal product code	ALN-AGT01
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Zilebesiran, 300 mg, as SC injection, Q3M, during the 6-month placebo-controlled DB period.

Arm title	Zilebesiran 600 mg Q6M
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Arm description:

Subjects received zilebesiran, 600 mg, as SC injection, on Day 1 of the 6-month placebo-controlled DB period. They received placebo at Month 3 of the 6-month placebo-controlled DB period to maintain the blind.

Arm type	Experimental
Investigational medicinal product name	Zilebesiran
Investigational medicinal product code	ALN-AGT01
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Zilebesiran, 600 mg, as SC injection, on Day 1 of the 6-month placebo-controlled DB period.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Zilebesiran matching placebo at Month 3 of the 6-month placebo-controlled DB period.

Number of subjects in period 1	Placebo	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)	Zilebesiran 300 mg Q6M
Started	76	78	73
Completed	70	70	70
Not completed	6	8	3
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	1	-	-
Physician decision	-	1	-
Adverse event, non-fatal	-	1	-
Reason Not Specified	-	-	-
Lost to follow-up	-	1	1
Subject Stopped Participation in the Study	5	5	1
Protocol deviation	-	-	1

Number of subjects in period 1	Zilebesiran 300 mg Q3M	Zilebesiran 600 mg Q6M
Started	75	76
Completed	70	71
Not completed	5	5
Adverse event, serious fatal	1	-
Consent withdrawn by subject	-	-
Physician decision	-	-
Adverse event, non-fatal	-	-
Reason Not Specified	-	1
Lost to follow-up	2	1
Subject Stopped Participation in the Study	2	3
Protocol deviation	-	-

Period 2

Period 2 title	Post 6 months DB Period (30months)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo/Zilebesiran 150 mg Q6M

Arm description:

Subjects receiving placebo during 6-month placebo-controlled DB period were re-randomized at Month 6 to 1 of the 4 initial zilebesiran regimens. This arm received zilebesiran, 150 mg, SC, Q6M after re-randomization. Placebo was administered at visits without zilebesiran dosing to maintain blind between Q3M & Q6M regimens.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo was administered at visits without zilebesiran dosing to maintain blind between Q3M & Q6M regimens.

Investigational medicinal product name	Zilebesiran
Investigational medicinal product code	ALN-AGT01
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Zilebesiran, 150 mg, as SC injection Q6M after re-randomization.

Arm title	Placebo/Zilebesiran 300 mg Q6M
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Arm description:

Subjects receiving placebo during 6-month placebo-controlled DB period were re-randomized at Month 6 to 1 of the 4 initial zilebesiran regimens. This arm received zilebesiran, 300 mg, SC, Q6M after re-randomization. Placebo was administered at visits without zilebesiran dosing to maintain blind between Q3M & Q6M regimens.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Arm type	Experimental
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Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo was administered at visits without zilebesiran dosing to maintain blind between Q3M & Q6M regimens.

Investigational medicinal product name	Zilebesiran
Investigational medicinal product code	ALN-AGT01
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Zilebesiran, 300 mg, as SC injection Q6M after re-randomization.

Arm title	Placebo/Zilebesiran 300 mg Q3M
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Arm description:

Subjects receiving placebo during 6-month placebo-controlled DB period were re-randomized at Month 6 to 1 of the 4 initial zilebesiran regimens. This arm received zilebesiran, 300 mg, SC, Q3M after re-randomization.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Arm type	Experimental
Investigational medicinal product name	Zilebesiran
Investigational medicinal product code	ALN-AGT01
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Zilebesiran, 300 mg, as SC injection Q3M after re-randomization.

Arm title	Placebo/Zilebesiran 600 mg Q6M
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Arm description:

Subjects receiving placebo during 6-month placebo-controlled DB period were re-randomized at Month 6 to 1 of the 4 initial zilebesiran regimens. This arm received zilebesiran, 600 mg, SC, Q6M after re-randomization. Placebo was administered at visits without zilebesiran dosing to maintain blind between Q3M & Q6M regimens.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo was administered at visits without zilebesiran dosing to maintain blind between Q3M & Q6M regimens.

Investigational medicinal product name	Zilebesiran
Investigational medicinal product code	ALN-AGT01
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Zilebesiran, 600 mg, as SC injection Q6M after re-randomization.

Arm title	Zilebesiran/Zilebesiran 150 mg Q6M
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Arm description:

Subjects who received zilebesiran 150 mg Q6M during the 6-month placebo-controlled DB period remained on the same regimen throughout the study. Subjects received placebo at the visit where no zilebesiran dose was planned to maintain blinding between the Q3M and Q6M regimens.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo was administered at visits without zilebesiran dosing to maintain blind between Q3M & Q6M regimens.

Investigational medicinal product name	Zilebesiran
Investigational medicinal product code	ALN-AGT01
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Zilebesiran 150 mg Q6M, as SC injection after re-randomization.

Arm title	Zilebesiran/Zilebesiran 300 mg Q6M
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Arm description:

Subjects who received zilebesiran 300 mg Q6M during the 6-month placebo-controlled DB period remained on the same regimen throughout the study. Subjects received placebo at the visit where no zilebesiran dose was planned to maintain blinding between the Q3M and Q6M regimens.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Arm type	Experimental
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Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo was administered at visits without zilebesiran dosing to maintain blind between Q3M & Q6M regimens.

Investigational medicinal product name	Zilebesiran
Investigational medicinal product code	ALN-AGT01
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Zilebesiran 300 mg Q6M, as SC injection after re-randomization.

Arm title	Zilebesiran/Zilebesiran 300 mg Q3M
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Arm description:

Subjects who received zilebesiran 300 mg Q3M during the 6-month placebo-controlled DB period remained on the same regimen throughout the study.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Arm type	Experimental
Investigational medicinal product name	Zilebesiran
Investigational medicinal product code	ALN-AGT01
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Zilebesiran 300 mg Q3M, as SC injection after re-randomization.

Arm title	Zilebesiran/Zilebesiran 600 mg Q6M
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Arm description:

Subjects who received zilebesiran 600 mg Q6M during the 6-month placebo-controlled DB period remained on the same regimen throughout the study. Subjects received placebo at the visit where no zilebesiran dose was planned to maintain blinding between the Q3M and Q6M regimens.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo was administered at visits without zilebesiran dosing to maintain blind between Q3M & Q6M regimens.

Investigational medicinal product name	Zilebesiran
Investigational medicinal product code	ALN-AGT01
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Zilebesiran 600 mg Q6M, as SC injection after re-randomization.

Number of subjects in period 2^[1]	Placebo/Zilebesiran 150 mg Q6M	Placebo/Zilebesiran 300 mg Q6M	Placebo/Zilebesiran 300 mg Q3M
Started	17	17	16
Completed Month 12 Visit	13	16	16
Completed	12	15	15
Not completed	5	2	1
Adverse event, serious fatal	-	-	-
Physician decision	-	-	-
Adverse event, non-fatal	1	-	1
Reason Not Specified	1	-	-
Lost to follow-up	1	1	-
Subject Stopped Participation in the Study	2	1	-

Number of subjects in period 2^[1]	Placebo/Zilebesiran 600 mg Q6M	Zilebesiran/Zilebesiran 150 mg Q6M	Zilebesiran/Zilebesiran 300 mg Q6M
Started	18	69	67
Completed Month 12 Visit	18	65	62
Completed	18	60	57
Not completed	0	9	10
Adverse event, serious fatal	-	1	-
Physician decision	-	2	-
Adverse event, non-fatal	-	-	-
Reason Not Specified	-	1	2
Lost to follow-up	-	3	1
Subject Stopped Participation in the Study	-	2	7

Number of subjects in period 2^[1]	Zilebesiran/Zilebesiran 300 mg Q3M	Zilebesiran/Zilebesiran 600 mg Q6M
Started	66	65
Completed Month 12 Visit	65	61
Completed	59	58
Not completed	7	7
Adverse event, serious fatal	-	-
Physician decision	1	-

Adverse event, non-fatal	-	-
Reason Not Specified	-	-
Lost to follow-up	1	4
Subject Stopped Participation in the Study	5	3

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all participants who completed the 6-Month Placebo-controlled DB Period chose to continue to the next period.

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: Subjects received zilebesiran matching placebo, as subcutaneous (SC) injection, once every 3 months (Q3M) during the 6-month placebo-controlled DB period.	
Reporting group title	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)
Reporting group description: Subjects received zilebesiran, 150 mg, as SC injection on Day 1 of the 6-month placebo-controlled DB period. They received placebo at Month 3 of the 6-month placebo-controlled DB period to maintain the blind.	
Reporting group title	Zilebesiran 300 mg Q6M
Reporting group description: Subjects received zilebesiran, 300 mg, as SC injection on Day 1 of the 6-month placebo-controlled DB period. They received placebo at Month 3 of the 6-month placebo-controlled DB period to maintain the blind.	
Reporting group title	Zilebesiran 300 mg Q3M
Reporting group description: Subjects received zilebesiran, 300 mg, as SC injection, Q3M, during the 6-month placebo-controlled DB period.	
Reporting group title	Zilebesiran 600 mg Q6M
Reporting group description: Subjects received zilebesiran, 600 mg, as SC injection, on Day 1 of the 6-month placebo-controlled DB period. They received placebo at Month 3 of the 6-month placebo-controlled DB period to maintain the blind.	

Reporting group values	Placebo	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)	Zilebesiran 300 mg Q6M
Number of subjects	76	78	73
Age categorical Units: Subjects			
In Utero	0	0	0
Preterm newborn infants (gestional age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days - 23 months)	0	0	0
Children (2 - 11 years)	0	0	0
12 - 17 years	0	0	0
Adults (18 - 64 years)	55	61	55
From 65 - 84 years	21	17	18
85 years and over	0	0	0
Gender categorical Units: Subjects			
Male	37	39	44
Female	39	39	29
Ethnicity Units: Subjects			
Hispanic or Latino	9	19	16
Not Hispanic or Latino	67	59	57

Unknown or Not Reported	0	0	0
Race			
Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	5	4	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	19	20	17
White	52	53	54
More than one race	0	0	0
Unknown or Not Reported	0	0	0
24-hour Mean Systolic Blood Pressure (SBP) Assessed by Ambulatory Blood Pressure Monitoring (ABPM)			
24-hour ABPM was programmed to take readings every 20 minutes during day (6 am-9:59 pm) & every 30 minutes during night (10 pm-5:59 am).ABPM was considered adequate if: number of successful daytime readings were ≥33, number of successful nighttime readings were ≥11, no more than 3 hours were not represented (3 sections of 60 minutes where 0 valid readings were obtained).To summarize 24 hour ABPM, hourly adjusted mean was calculated. Hourly mean= average of BP by each hour of day. 24 hour mean=average of hourly mean. Data has presented for only 75 subjects in placebo arm.			
Units: millimeter of mercury (mmHg)			
arithmetic mean	141.1	140.6	142.5
standard deviation	± 7.9	± 8.5	± 8.8

Reporting group values	Zilebesiran 300 mg Q3M	Zilebesiran 600 mg Q6M	Total
Number of subjects	75	76	378
Age categorical			
Units: Subjects			
In Utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days - 23 months)	0	0	0
Children (2 - 11 years)	0	0	0
12 - 17 years	0	0	0
Adults (18 - 64 years)	51	53	275
From 65 - 84 years	24	23	103
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Male	45	45	210
Female	30	31	168
Ethnicity			
Units: Subjects			
Hispanic or Latino	10	20	74
Not Hispanic or Latino	65	56	304
Unknown or Not Reported	0	0	0
Race			
Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	7	5	23
Native Hawaiian or Other Pacific Islander	1	0	1

Black or African American	19	19	94
White	48	52	259
More than one race	0	0	0
Unknown or Not Reported	0	0	0
24-hour Mean Systolic Blood Pressure (SBP) Assessed by Ambulatory Blood Pressure Monitoring (ABPM)			
24-hour ABPM was programmed to take readings every 20 minutes during day (6 am-9:59 pm) & every 30 minutes during night (10 pm-5:59 am).ABPM was considered adequate if: number of successful daytime readings were ≥ 33 , number of successful nighttime readings were ≥ 11 , no more than 3 hours were not represented (3 sections of 60 minutes where 0 valid readings were obtained).To summarize 24 hour ABPM, hourly adjusted mean was calculated. Hourly mean= average of BP by each hour of day. 24 hour mean=average of hourly mean. Data has presented for only 75 subjects in placebo arm.			
Units: millimeter of mercury (mmHg)			
arithmetic mean	141.6	143.1	
standard deviation	± 7.7	± 9.0	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Subjects received zilebesiran matching placebo, as subcutaneous (SC) injection, once every 3 months (Q3M) during the 6-month placebo-controlled DB period.	
Reporting group title	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)
Reporting group description: Subjects received zilebesiran, 150 mg, as SC injection on Day 1 of the 6-month placebo-controlled DB period. They received placebo at Month 3 of the 6-month placebo-controlled DB period to maintain the blind.	
Reporting group title	Zilebesiran 300 mg Q6M
Reporting group description: Subjects received zilebesiran, 300 mg, as SC injection on Day 1 of the 6-month placebo-controlled DB period. They received placebo at Month 3 of the 6-month placebo-controlled DB period to maintain the blind.	
Reporting group title	Zilebesiran 300 mg Q3M
Reporting group description: Subjects received zilebesiran, 300 mg, as SC injection, Q3M, during the 6-month placebo-controlled DB period.	
Reporting group title	Zilebesiran 600 mg Q6M
Reporting group description: Subjects received zilebesiran, 600 mg, as SC injection, on Day 1 of the 6-month placebo-controlled DB period. They received placebo at Month 3 of the 6-month placebo-controlled DB period to maintain the blind.	
Reporting group title	Placebo/Zilebesiran 150 mg Q6M
Reporting group description: Subjects receiving placebo during 6-month placebo-controlled DB period were re-randomized at Month 6 to 1 of the 4 initial zilebesiran regimens. This arm received zilebesiran, 150 mg, SC, Q6M after re-randomization. Placebo was administered at visits without zilebesiran dosing to maintain blind between Q3M & Q6M regimens. Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.	
Reporting group title	Placebo/Zilebesiran 300 mg Q6M
Reporting group description: Subjects receiving placebo during 6-month placebo-controlled DB period were re-randomized at Month 6 to 1 of the 4 initial zilebesiran regimens. This arm received zilebesiran, 300 mg, SC, Q6M after re-randomization. Placebo was administered at visits without zilebesiran dosing to maintain blind between Q3M & Q6M regimens. Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.	
Reporting group title	Placebo/Zilebesiran 300 mg Q3M
Reporting group description: Subjects receiving placebo during 6-month placebo-controlled DB period were re-randomized at Month 6 to 1 of the 4 initial zilebesiran regimens. This arm received zilebesiran, 300 mg, SC, Q3M after re-randomization.	

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Reporting group title	Placebo/Zilebesiran 600 mg Q6M
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Reporting group description:

Subjects receiving placebo during 6-month placebo-controlled DB period were re-randomized at Month 6 to 1 of the 4 initial zilebesiran regimens. This arm received zilebesiran, 600 mg, SC, Q6M after re-randomization. Placebo was administered at visits without zilebesiran dosing to maintain blind between Q3M & Q6M regimens.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Reporting group title	Zilebesiran/Zilebesiran 150 mg Q6M
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Reporting group description:

Subjects who received zilebesiran 150 mg Q6M during the 6-month placebo-controlled DB period remained on the same regimen throughout the study. Subjects received placebo at the visit where no zilebesiran dose was planned to maintain blinding between the Q3M and Q6M regimens.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Reporting group title	Zilebesiran/Zilebesiran 300 mg Q6M
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Reporting group description:

Subjects who received zilebesiran 300 mg Q6M during the 6-month placebo-controlled DB period remained on the same regimen throughout the study. Subjects received placebo at the visit where no zilebesiran dose was planned to maintain blinding between the Q3M and Q6M regimens.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Reporting group title	Zilebesiran/Zilebesiran 300 mg Q3M
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Reporting group description:

Subjects who received zilebesiran 300 mg Q3M during the 6-month placebo-controlled DB period remained on the same regimen throughout the study.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Reporting group title	Zilebesiran/Zilebesiran 600 mg Q6M
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Reporting group description:

Subjects who received zilebesiran 600 mg Q6M during the 6-month placebo-controlled DB period remained on the same regimen throughout the study. Subjects received placebo at the visit where no zilebesiran dose was planned to maintain blinding between the Q3M and Q6M regimens.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Subject analysis set title	Zilebesiran 300 mg Q6M and Q3M
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received zilebesiran, 300 mg, as SC injection, Q6M or Q3M during the 6-month placebo-controlled DB period. Subjects assigned to the Q6M regimen received placebo at Month 3 of the 6-month placebo-controlled DB period to maintain the blind. As specified in the SAP, 'Zilebesiran 300 mg Q6M' and 'Zilebesiran 300 mg Q3M' arms were pooled together to report Month 3 analysis.

Primary: Change from Baseline at Month 3 in 24-hour Mean SBP Assessed by ABPM

End point title	Change from Baseline at Month 3 in 24-hour Mean SBP Assessed by ABPM ^[1]
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End point description:

24-hour ABPM was programmed to take readings every 20 minutes during the day (6 am to 9:59 pm) and every 30 minutes during the night (10 pm to 5:59 am). An ABPM was considered adequate if: 1. number of successful daytime readings were ≥ 33 , 2. number of successful nighttime readings were ≥ 11 , 3. no more than 3 hours are not represented (i.e., 3 sections of 60 minutes where 0 valid readings were obtained). To summarize the 24-hour ABPM, the hourly adjusted mean was calculated. Hourly mean was the average of BP by each hour of the day. The 24-hour mean was average of the hourly means. Least squares (LS) mean & standard error (SE) were calculated using a mixed model repeated measures (MMRM) approach. Full Analysis Set included all randomized subjects who received any amount of the study drug. Subjects analysed is the number of subjects with data available for analyses. As pre-specified in the SAP, for assessment of Month 3 endpoint, zilebesiran 300mg Q3M & 300mg Q6M were pooled together.

End point type	Primary
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End point timeframe:

Baseline and Month 3

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As specified in the SAP, 'Zilebesiran 300 mg Q6M' and 'Zilebesiran 300 mg Q3M' arms were pooled together to report Month 3 analysis. Hence, the endpoint reports data for 4 arms only.

End point values	Placebo	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)	Zilebesiran 600 mg Q6M	Zilebesiran 300 mg Q6M and Q3M
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	60	68	65	137
Units: millimeters of mercury (mmHg)				
least squares mean (standard error)	6.8 (\pm 1.58)	-7.3 (\pm 1.49)	-8.9 (\pm 1.52)	-10.0 (\pm 1.05)

Statistical analyses

Statistical analysis title	Mean SBP Assessed by ABPM (Analysis 2)
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Statistical analysis description:

The adjusted 95% CI and p-value are based on Dunnett's test. LS Mean Difference between zilebesiran 600 mg Q6M and placebo, 95% CI was calculated using Dunnett's procedure.

Comparison groups	Placebo v Zilebesiran 600 mg Q6M
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Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[2]
Method	MMRM
Parameter estimate	Difference in LS Mean
Point estimate	-15.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.8
upper limit	-10.6
Variability estimate	Standard error of the mean
Dispersion value	2.19

Notes:

[2] - The MMRM model included treatment, visit, treatment-by-visit interaction, and race (categorized as Black and all other races) as fixed factors, with baseline 24-hour mean SBP assessed by ABPM as a covariate.

Statistical analysis title	Mean SBP Assessed by ABPM (Analysis 1)
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Statistical analysis description:

LS Mean Difference between zilebesiran 300 mg Q6M and placebo, 95% CI was calculated using Dunnett's procedure.

Comparison groups	Placebo v Zilebesiran 600 mg Q6M
Number of subjects included in analysis	125
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[3]
Method	MMRM
Parameter estimate	Difference in LS Mean
Point estimate	-16.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.2
upper limit	-12.3
Variability estimate	Standard error of the mean
Dispersion value	1.9

Notes:

[3] - MMRM model included treatment, visit, treatment-by-visit interaction, and race (categorized as Black and all other races) as fixed factors, with baseline 24-hour mean SBP assessed by ABPM as a covariate.

Secondary: Change From Baseline at Month 3 in Mean Sitting Office SBP

End point title	Change From Baseline at Month 3 in Mean Sitting Office SBP ^[4]
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End point description:

The mean office BP in the sitting position was used for the analysis. Office BP in the sitting position was collected with a set of 4 replicates. The average of the last 3 replicates was calculated and used for analysis. LS mean and SE were calculated using a MMRM approach. Full Analysis Set included all randomized subjects who received any amount of the study drug. Subjects analysed is the number of subjects with data available for analyses. As pre-specified in the SAP, for assessment of Month 3 endpoint, zilebesiran 300mg Q3M and 300mg Q6M were pooled together.

End point type	Secondary
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End point timeframe:

Baseline and Month 3

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As specified in the SAP, 'Zilebesiran 300 mg Q6M' and 'Zilebesiran 300 mg Q3M' arms were pooled together to report Month 3 analysis. Hence, the endpoint reports data for 4 arms only.

End point values	Placebo	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)	Zilebesiran 600 mg Q6M	Zilebesiran 300 mg Q6M and Q3M
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	60	68	64	133
Units: mmHg				
least squares mean (standard error)	-0.1 (\pm 1.57)	-9.7 (\pm 1.49)	-9.2 (\pm 1.52)	-12.1 (\pm 1.06)

Statistical analyses

Statistical analysis title	Mean Sitting Office SBP at Month 3 (Analysis 2)
Statistical analysis description:	
Tested in hierarchical order with success criterion of nominal p-value <0.05.	
Comparison groups	Placebo v Zilebesiran 600 mg Q6M
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[5]
Method	MMRM
Parameter estimate	Difference in LS Mean
Point estimate	-9.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.4
upper limit	-4.8
Variability estimate	Standard error of the mean
Dispersion value	2.19

Notes:

[5] - The MMRM model included treatment, visit, treatment-by-visit interaction, and race (categorized as Black and all other races) as fixed factors, with office SBP as a covariate.

Statistical analysis title	Mean Sitting Office SBP at Month 3 (Analysis 1)
Comparison groups	Placebo v Zilebesiran 300 mg Q6M and Q3M
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority ^[6]
P-value	< 0.0001 ^[7]
Method	MMRM
Parameter estimate	Difference in LS Mean
Point estimate	-12

Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.7
upper limit	-8.3
Variability estimate	Standard error of the mean
Dispersion value	1.89

Notes:

[6] - Tested in hierarchical order with success criterion of nominal p-value <0.05.

[7] - The MMRM model included treatment, visit, treatment-by-visit interaction, and race (categorized as Black and all other races) as fixed factors, with office SBP as a covariate.

Secondary: Change From Baseline at Month 6 in 24-hour Mean SBP Assessed by ABPM

End point title	Change From Baseline at Month 6 in 24-hour Mean SBP Assessed by ABPM
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End point description:

24-hour ABPM was programmed to take readings every 20 minutes during the day (6 am to 9:59 pm) and every 30 minutes during the night (10 pm to 5:59 am). An ABPM was considered adequate if: 1. the number of successful daytime readings were ≥ 33 , 2. the number of successful nighttime readings were ≥ 11 , 3. no more than 3 hours are not represented (i.e., 3 sections of 60 minutes where 0 valid readings were obtained). To summarize the 24-hour ABPM, the hourly adjusted mean was calculated. Hourly mean was the average of blood pressure (BP) by each hour of the day. The 24-hour mean was the average of the hourly means. LS mean and SE were calculated using a MMRM approach. Full Analysis Set included all randomized subjects who received any amount of the study drug. Subjects analysed is the number of subjects with data available for analyses.

End point type	Secondary
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End point timeframe:

Baseline and Month 6

End point values	Placebo	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)	Zilebesiran 300 mg Q6M	Zilebesiran 300 mg Q3M
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	62	68	60
Units: mmHg				
least squares mean (standard error)	4.6 (\pm 1.73)	-6.5 (\pm 1.63)	-9.9 (\pm 1.58)	-9.5 (\pm 1.65)

End point values	Zilebesiran 600 mg Q6M			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: mmHg				
least squares mean (standard error)	-9.6 (\pm 1.62)			

Statistical analyses

Statistical analysis title	24-hour Mean SBP Assessed by ABPM (Analysis 2)
Statistical analysis description:	
Tested in hierarchical order with success criterion of nominal p-value <0.05.	
Comparison groups	Placebo v Zilebesiran 600 mg Q6M
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[8]
Method	MMRM
Parameter estimate	Difference in LS Mean
Point estimate	-14.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.9
upper limit	-9.5
Variability estimate	Standard error of the mean
Dispersion value	2.38

Notes:

[8] - The MMRM model included treatment, visit, treatment-by-visit interaction, and race (categorized as Black and all other races) as fixed factors, with baseline 24-hour mean SBP assessed by ABPM as a covariate.

Statistical analysis title	24-hour Mean SBP Assessed by ABPM (Analysis 1)
Statistical analysis description:	
Tested in hierarchical order with success criterion of nominal p-value <0.05.	
Comparison groups	Placebo v Zilebesiran 300 mg Q3M
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[9]
Method	MMRM
Parameter estimate	Difference in LS Mean
Point estimate	-14.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.9
upper limit	-9.4
Variability estimate	Standard error of the mean
Dispersion value	2.4

Notes:

[9] - The MMRM model included treatment, visit, treatment-by-visit interaction, and race (categorized as Black and all other races) as fixed factors, with baseline 24-hour mean SBP assessed by ABPM as a covariate.

Secondary: Change From Baseline at Month 6 in Mean Sitting Office SBP

End point title	Change From Baseline at Month 6 in Mean Sitting Office SBP
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End point description:

The mean office BP in the sitting position was used for the analysis. Office BP in the sitting position was collected with a set of 4 replicates. The average of the last 3 replicates was calculated and used for analysis. LS mean and SE were calculated using a MMRM approach. Full Analysis Set included all randomized subjects who received any amount of the study drug. Subjects analysed is the number of subjects with data available for analyses.

End point type	Secondary
End point timeframe:	
Baseline and Month 6	

End point values	Placebo	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)	Zilebesiran 300 mg Q6M	Zilebesiran 300 mg Q3M
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	65	68	57
Units: mmHg				
least squares mean (standard error)	-0.6 (± 1.80)	-8.2 (± 1.70)	-11.1 (± 1.67)	-12.8 (± 1.80)

End point values	Zilebesiran 600 mg Q6M			
Subject group type	Reporting group			
Number of subjects analysed	62			
Units: mmHg				
least squares mean (standard error)	-10.8 (± 1.73)			

Statistical analyses

Statistical analysis title	Mean Sitting Office SBP at Month 6 (Analysis 1)
Statistical analysis description:	
Tested in hierarchical order with success criterion of nominal p-value <0.05.	
Comparison groups	Placebo v Zilebesiran 300 mg Q3M
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[10]
Method	MMRM
Parameter estimate	Difference in LS Mean
Point estimate	-12.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.2
upper limit	-7.1
Variability estimate	Standard error of the mean
Dispersion value	2.55

Notes:

[10] - The MMRM model included treatment, visit, treatment-by-visit interaction, and race (categorized as Black and all other races) as fixed factors, with office SBP as a covariate.

Statistical analysis title	Mean Sitting Office SBP at Month 6 (Analysis 2)
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Statistical analysis description:

Tested in hierarchical order with success criterion of nominal p-value <0.05.

Comparison groups	Placebo v Zilebesiran 600 mg Q6M
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[11]
Method	MMRM
Parameter estimate	Difference in LS Mean
Point estimate	-10.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.1
upper limit	-5.3
Variability estimate	Standard error of the mean
Dispersion value	2.5

Notes:

[11] - The MMRM model included treatment, visit, treatment-by-visit interaction, and race (categorized as Black and all other races) as fixed factors, with office SBP as a covariate.

Secondary: Percentage of Participants With 24-hour Mean SBP Assessed by ABPM <130 mmHg and/or Reduction ≥20 mmHg From Baseline Without Additional Antihypertensive Medications at Month 6

End point title	Percentage of Participants With 24-hour Mean SBP Assessed by ABPM <130 mmHg and/or Reduction ≥20 mmHg From Baseline Without Additional Antihypertensive Medications at Month 6
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End point description:

24-hour ABPM was programmed to take readings every 20 minutes during the day (6 am to 9:59 pm) and every 30 minutes during the night (10 pm to 5:59 am). An ABPM was considered adequate if: 1. the number of successful daytime readings were ≥33, 2. the number of successful nighttime readings were ≥11, 3. no more than 3 hours are not represented (i.e., 3 sections of 60 minutes where 0 valid readings were obtained). To summarize the 24-hour ABPM, the hourly adjusted mean was calculated. Hourly mean was the average of BP by each hour of the day. The 24-hour mean was the average of the hourly means. Full Analysis Set included all randomized subjects who received any amount of the study drug.

End point type	Secondary
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End point timeframe:

Month 6

End point values	Placebo	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)	Zilebesiran 300 mg Q6M	Zilebesiran 300 mg Q3M
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	75	78	73	75
Units: percentage of subjects				
number (not applicable)	6.7	30.8	50.7	38.7

End point values	Zilebesiran 600 mg Q6M			
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Subject group type	Reporting group			
Number of subjects analysed	76			
Units: percentage of subjects				
number (not applicable)	47.4			

Statistical analyses

Statistical analysis title	Percentage of Participants With 24-hour Mean SBP 2
Statistical analysis description:	
Tested in hierarchical order with success criterion of nominal p-value <0.05.	
Comparison groups	Placebo v Zilebesiran 600 mg Q6M
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[12]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	17.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.24
upper limit	51.52

Notes:

[12] - Logistic regression model included treatment and race (black; all other races) as factors and baseline 24-hour mean SBP as a covariate.

Statistical analysis title	Percentage of Participants With 24-hour Mean SBP 1
Statistical analysis description:	
Tested in hierarchical order with success criterion of nominal p-value <0.05.	
Comparison groups	Placebo v Zilebesiran 300 mg Q3M
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 ^[13]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	10.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.76
upper limit	30.64

Notes:

[13] - Logistic regression model included treatment and race (black; all other races) as factors and baseline 24-hour mean SBP as a covariate.

Secondary: Change From Baseline at Month 3 in 24-hour Mean DBP Assessed by ABPM

End point title	Change From Baseline at Month 3 in 24-hour Mean DBP
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End point description:

24-hour ABPM was programmed to take readings every 20 minutes during the day (6 am to 9:59 pm) and every 30 minutes during the night (10 pm to 5:59 am). An ABPM was considered adequate if: 1. the number of successful daytime readings were ≥ 33 , 2. the number of successful nighttime readings were ≥ 11 , 3. no more than 3 hours are not represented (i.e., 3 sections of 60 minutes where 0 valid readings were obtained). To summarize the 24-hour ABPM, the hourly adjusted mean was calculated. Hourly mean was the average of BP by each hour of the day. The 24-hour mean was the average of the hourly means. LS mean and SE were calculated using a MMRM approach. Full Analysis Set included all randomized subjects who received any amount of the study drug. Subjects analysed is the number of subjects with data available for analyses. As pre-specified in the SAP, for assessment of Month 3 endpoints, zilebesiran 300mg Q3M and 300mg Q6M were pooled together.

End point type	Secondary
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End point timeframe:

Baseline and Month 3

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As specified in the SAP, 'Zilebesiran 300 mg Q6M' and 'Zilebesiran 300 mg Q3M' arms were pooled together to report Month 3 analysis. Hence, the endpoint reports data for 4 arms only.

End point values	Placebo	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)	Zilebesiran 600 mg Q6M	Zilebesiran 300 mg Q6M and Q3M
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	60	68	65	137
Units: mmHg				
least squares mean (standard error)	3.5 (\pm 0.87)	-4.5 (\pm 0.82)	-5.8 (\pm 0.84)	-5.7 (\pm 0.58)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Month 6 in 24-hour Mean DBP Assessed by ABPM

End point title	Change From Baseline at Month 6 in 24-hour Mean DBP Assessed by ABPM
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End point description:

24-hour ABPM was programmed to take readings every 20 minutes during the day (6 am to 9:59 pm) and every 30 minutes during the night (10 pm to 5:59 am). An ABPM was considered adequate if: 1. the number of successful daytime readings were ≥ 33 , 2. the number of successful nighttime readings were ≥ 11 , 3. no more than 3 hours are not represented (i.e., 3 sections of 60 minutes where 0 valid readings were obtained). To summarize the 24-hour ABPM, the hourly adjusted mean was calculated. Hourly mean was the average of BP by each hour of the day. The 24-hour mean was the average of the hourly means. LS mean and SE were calculated using a MMRM approach. Full Analysis Set included all randomized subjects who received any amount of the study drug. Subjects analysed is the number of subjects with data available for analyses.

End point type	Secondary
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End point timeframe:

Baseline and Month 6

End point values	Placebo	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)	Zilebesiran 300 mg Q6M	Zilebesiran 300 mg Q3M
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	62	68	60
Units: mmHg				
least squares mean (standard error)	2.2 (± 0.97)	-4.8 (± 0.91)	-6.1 (± 0.89)	-6.3 (± 0.93)

End point values	Zilebesiran 600 mg Q6M			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: mmHg				
least squares mean (standard error)	-6.3 (± 0.91)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Month 3 in Mean Sitting Office DBP

End point title	Change From Baseline at Month 3 in Mean Sitting Office DBP ^[15]
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End point description:

The mean office BP in the sitting position was used for the analysis. Office BP in the sitting position was collected with a set of 4 replicates. The average of the last 3 replicates was calculated and used for analysis. LS mean and SE were calculated using a MMRM approach. Full Analysis Set included all randomized subjects who received any amount of the study drug. Subjects analysed is the number of subjects with data available for analyses. As pre-specified in the SAP, for assessment of Month 3 endpoints, zilebesiran 300mg Q3M and 300mg Q6M were pooled together.

End point type	Secondary
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End point timeframe:

Baseline and Month 3

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As specified in the SAP, 'Zilebesiran 300 mg Q6M' and 'Zilebesiran 300 mg Q3M' arms were pooled together to report Month 3 analysis. Hence, the endpoint reports data for 4 arms only.

End point values	Placebo	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)	Zilebesiran 600 mg Q6M	Zilebesiran 300 mg Q6M and Q3M
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	60	68	64	133
Units: mmHg				
least squares mean (standard error)	-0.6 (± 1.00)	-5.3 (± 0.94)	-5.4 (± 0.97)	-7.0 (± 0.67)

Statistical analyses

No statistical analyses for this end point

Secondary: Time Adjusted Change From Baseline Through Month 3 in Mean Sitting Office SBP and DBP

End point title	Time Adjusted Change From Baseline Through Month 3 in Mean Sitting Office SBP and DBP ^[16]
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End point description:

Time adjusted change from baseline in mean sitting office SBP and DBP was the area under the curve (AUC) between Month 1 and 3 visits divided by the duration of time period. Full Analysis Set included all randomized subjects who received any amount of the study drug. Subjects analysed is the number of subjects with data available for analyses. As pre-specified in the SAP, for assessment of Month 3 endpoints, zilebesiran 300mg Q3M and 300mg Q6M were pooled together.

End point type	Secondary
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End point timeframe:

Baseline and Month 3

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As specified in the SAP, 'Zilebesiran 300 mg Q6M' and 'Zilebesiran 300 mg Q3M' arms were pooled together to report Month 3 analysis. Hence, the endpoint reports data for 4 arms only.

End point values	Placebo	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)	Zilebesiran 600 mg Q6M	Zilebesiran 300 mg Q6M and Q3M
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	60	68	64	133
Units: mmHg				
least squares mean (standard error)				
Office SBP	-0.6 (± 1.29)	-9.1 (± 1.24)	-10.1 (± 1.26)	-10.9 (± 0.89)
Office DBP	-0.0 (± 0.80)	-4.8 (± 0.77)	-6.0 (± 0.78)	-6.5 (± 0.55)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Month 6 in Mean Sitting Office DBP

End point title	Change From Baseline at Month 6 in Mean Sitting Office DBP
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End point description:

The mean office BP in the sitting position was used for the analysis. Office BP in the sitting position was collected with a set of 4 replicates. The average of the last 3 replicates was calculated and used for analysis. LS mean and SE were calculated using a MMRM approach. Full Analysis Set included all randomized subjects who received any amount of the study drug. Subjects analysed is the number of

subjects with data available for analyses.

End point type	Secondary
End point timeframe:	
Baseline and Month 6	

End point values	Placebo	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)	Zilebesiran 300 mg Q6M	Zilebesiran 300 mg Q3M
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	65	68	57
Units: mmHg				
least squares mean (standard error)	-1.2 (\pm 1.20)	-4.1 (\pm 1.13)	-6.8 (\pm 1.12)	-8.2 (\pm 1.20)

End point values	Zilebesiran 600 mg Q6M			
Subject group type	Reporting group			
Number of subjects analysed	62			
Units: mmHg				
least squares mean (standard error)	5.0 (\pm 1.16)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time Adjusted Change From Baseline Through Month 6 in 24-hour Mean SBP and DBP Assessed by ABPM

End point title	Time Adjusted Change From Baseline Through Month 6 in 24-hour Mean SBP and DBP Assessed by ABPM
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End point description:

Time adjusted change from baseline through Month 6 in 24-hour mean SBP and DBP was determined as the AUC between Month 1 and 6 visits divided by the duration of the time period. Full Analysis Set included all randomized subjects who received any amount of the study drug. Subjects analysed is the number of subjects with data available for analyses.

End point type	Secondary
End point timeframe:	
Baseline and Month 6	

End point values	Placebo	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)	Zilebesiran 300 mg Q6M	Zilebesiran 300 mg Q3M
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	62	68	60
Units: mmHg				
least squares mean (standard error)				
24-hour Mean SBP	5.8 (± 1.26)	-6.3 (± 1.20)	-9.2 (± 1.20)	-9.6 (± 1.22)
24-hour Mean DBP	3.1 (± 0.72)	-4.2 (± 0.69)	-5.5 (± 0.69)	-5.8 (± 0.70)

End point values	Zilebesiran 600 mg Q6M			
Subject group type	Reporting group			
Number of subjects analysed	63			
Units: mmHg				
least squares mean (standard error)				
24-hour Mean SBP	-9.1 (± 1.22)			
24-hour Mean DBP	-5.9 (± 0.70)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time Adjusted Change From Baseline Through Month 6 in Mean Sitting Office SBP and DBP

End point title	Time Adjusted Change From Baseline Through Month 6 in Mean Sitting Office SBP and DBP
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End point description:

Time adjusted change is the AUC between Month 1 and 6 visits divided by the duration of time period. Full Analysis Set included all randomized subjects who received any amount of the study drug. Subjects analyzed is the number of subjects with data available for analyses.

End point type	Secondary
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End point timeframe:

Baseline and Month 6

End point values	Placebo	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)	Zilebesiran 300 mg Q6M	Zilebesiran 300 mg Q3M
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	65	68	57
Units: mmHg				
least squares mean (standard error)				
Office SBP	-0.5 (± 1.25)	-9.0 (± 1.20)	-12.1 (± 1.21)	-11.0 (± 1.24)

Office DBP	-0.6 (± 0.80)	-4.7 (± 0.76)	-7.2 (± 0.77)	-6.7 (± 0.79)
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End point values	Zilebesiran 600 mg Q6M			
Subject group type	Reporting group			
Number of subjects analysed	62			
Units: mmHg				
least squares mean (standard error)				
Office SBP	-10.0 (± 1.22)			
Office DBP	-5.5 (± 0.78)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Daytime/Nighttime Mean SBP and DBP Assessed by ABPM at each Visit

End point title	Change From Baseline in Daytime/Nighttime Mean SBP and DBP Assessed by ABPM at each Visit
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End point description:

ABPM was programmed to take readings every 20 minutes during the day (6 am to 9:59 pm) and every 30 minutes during the night (10 pm to 5:59 am). An ABPM was considered adequate if: 1. the number of successful daytime readings were ≥33, 2. the number of successful nighttime readings were ≥11, and 3. no more than 3 hours are not represented (i.e., 3 sections of 60 minutes where 0 valid readings were obtained). Baseline was defined as the last assessment prior to receiving the first dose of study drug. LS mean and SE were calculated using a MMRM approach. Full Analysis Set included all randomized subjects who received any amount of the study drug. Subjects analysed is the number of subjects with data available for analyses. 'n' is the number of subjects with data available for analyses at specified timepoints. Daytime is denoted as DT and Nighttime as NT in the data table.

End point type	Secondary
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End point timeframe:

Baseline, and Months (M) 1, 3 and 6

End point values	Placebo	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)	Zilebesiran 300 mg Q6M	Zilebesiran 300 mg Q3M
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	72	70	71
Units: mmHg				
least squares mean (standard error)				
Change in DT Mean SBP at M 1 (n=67,72,66,71,69)	4.3 (± 1.50)	-3.6 (± 1.45)	-6.4 (± 1.51)	-9.6 (± 1.46)
Change in DT Mean SBP at M 3 (n=60,68,70,67,65)	6.7 (± 1.62)	-7.6 (± 1.53)	-10.7 (± 1.52)	-9.8 (± 1.54)
Change in DT Mean SBP at M 6 (n=54,62,68,60,63)	4.5 (± 1.83)	-6.9 (± 1.72)	-10.4 (± 1.66)	-9.3 (± 1.74)

Change in NT Mean SBP at M 1 (n=67,72,66,71,69)	4.7 (± 1.64)	-3.4 (± 1.59)	-5.1 (± 1.64)	-9.5 (± 1.60)
Change in NT Mean SBP at M 3 (n=60,68,70,67,65)	7.0 (± 1.85)	-6.4 (± 1.76)	-8.2 (± 1.74)	-9.7 (± 1.77)
Change in NT Mean SBP at M 6 (n=54,62,68,60,63)	4.7 (± 1.86)	-5.8 (± 1.75)	-8.9 (± 1.69)	-10.2 (± 1.78)
Change in DT Mean DBP at M 1 (n=67,72,70,71,69)	2.9 (± 0.91)	-2.7 (± 0.88)	-4.0 (± 0.91)	-5.9 (± 0.89)
Change in DT Mean DBP at M 3 (n=60,68,70,67,65)	3.5 (± 0.94)	-4.8 (± 0.89)	-6.1 (± 0.88)	-5.7 (± 0.90)
Change in DT Mean DBP at M 6 (n=54,62,68,60,63)	2.1 (± 1.07)	-4.8 (± 1.01)	-6.2 (± 0.98)	-6.1 (± 1.02)
Change in NT Mean DBP at M 1 (n=67,72,66,71,69)	3.2 (± 1.01)	-2.4 (± 0.98)	-3.5 (± 1.02)	-5.9 (± 0.99)
Change in NT Mean DBP at M 3 (n=60,68,70,67,65)	3.7 (± 1.08)	-3.6 (± 1.02)	-5.1 (± 1.01)	-4.8 (± 1.03)
Change in NT Mean DBP at M 6 (n=54,62,68,60,63)	2.2 (± 1.09)	-4.3 (± 1.03)	-5.9 (± 1.00)	-6.7 (± 1.05)

End point values	Zilebesiran 600 mg Q6M			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: mmHg				
least squares mean (standard error)				
Change in DT Mean SBP at M 1 (n=67,72,66,71,69)	-9.1 (± 1.48)			
Change in DT Mean SBP at M 3 (n=60,68,70,67,65)	-8.9 (± 1.56)			
Change in DT Mean SBP at M 6 (n=54,62,68,60,63)	-8.8 (± 1.71)			
Change in NT Mean SBP at M 1 (n=67,72,66,71,69)	-8.0 (± 1.62)			
Change in NT Mean SBP at M 3 (n=60,68,70,67,65)	-8.5 (± 1.79)			
Change in NT Mean SBP at M 6 (n=54,62,68,60,63)	-11.1 (± 1.74)			
Change in DT Mean DBP at M 1 (n=67,72,70,71,69)	-5.8 (± 0.89)			
Change in DT Mean DBP at M 3 (n=60,68,70,67,65)	-5.6 (± 0.90)			
Change in DT Mean DBP at M 6 (n=54,62,68,60,63)	-5.7 (± 1.00)			
Change in NT Mean DBP at M 1 (n=67,72,66,71,69)	-5.4 (± 1.00)			
Change in NT Mean DBP at M 3 (n=60,68,70,67,65)	-5.8 (± 1.04)			
Change in NT Mean DBP at M 6 (n=54,62,68,60,63)	-7.6 (± 1.03)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline in Serum Angiotensinogen (AGT) Through Month 6

End point title	Percentage Change From Baseline in Serum Angiotensinogen (AGT) Through Month 6
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End point description:

Pharmacodynamic (PD) Analysis Set included all subjects who received at least 1 full dose of study drug. All by-treatment analyses based on the PD Analysis Set were grouped according to the treatment actually received. Subjects analysed is the number of subjects with data available for analyses. 'n' analyzed is the number of subjects with data available for analyses at specified timepoints. Percent Change is denoted as PC and Baseline as BL in the data table.

End point type	Secondary
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End point timeframe:

Baseline, Week 2 and Months 1, 2, 3, 4, 5 and 6

End point values	Placebo	Zilebesiran 150 milligrams (mg) once every 6 months (Q6M)	Zilebesiran 300 mg Q6M	Zilebesiran 300 mg Q3M
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	78	73	75
Units: percent change				
arithmetic mean (standard deviation)				
PC from BL at Week 2 (n=71,78,72,73,71)	-0.05 (± 23.99)	-88.34 (± 9.96)	-92.68 (± 4.40)	-92.77 (± 4.03)
PC from BL at Month 1 (n=70,77,73,72,73)	1.61 (± 22.96)	-94.48 (± 9.04)	-97.38 (± 1.72)	-97.20 (± 2.30)
PC from BL at Month 2 (n=71,74,72,72,73)	-2.06 (± 21.87)	-94.47 (± 12.38)	-97.74 (± 2.04)	-97.64 (± 2.15)
PC from BL at Month 3 (n=71,74,72,72,71)	-2.19 (± 22.86)	-93.31 (± 9.94)	-97.26 (± 2.78)	-97.00 (± 2.61)
PC from BL at Month 4 (n=69,71,71,70,69)	1.39 (± 26.06)	-91.89 (± 11.61)	-95.94 (± 5.23)	-98.38 (± 1.08)
PC from BL at Month 5 (n=68,70,70,70,69)	-2.27 (± 21.18)	-90.10 (± 12.48)	-94.85 (± 6.58)	-98.23 (± 1.13)
PC from BL at Month 6 (n=69,70,70,68,69)	-4.97 (± 24.90)	-87.84 (± 13.82)	-93.13 (± 8.29)	-97.71 (± 1.91)

End point values	Zilebesiran 600 mg Q6M			
Subject group type	Reporting group			
Number of subjects analysed	76			
Units: percent change				
arithmetic mean (standard deviation)				
PC from BL at Week 2 (n=71,78,72,73,71)	-94.49 (± 5.52)			
PC from BL at Month 1 (n=70,77,73,72,73)	-98.22 (± 2.69)			
PC from BL at Month 2 (n=71,74,72,72,73)	-98.70 (± 0.74)			
PC from BL at Month 3 (n=71,74,72,72,71)	-98.25 (± 1.60)			

PC from BL at Month 4 (n=69,71,71,70,69)	-97.98 (± 1.74)			
PC from BL at Month 5 (n=68,70,70,70,69)	-97.38 (± 2.41)			
PC from BL at Month 6 (n=69,70,70,68,69)	-96.41 (± 4.04)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Placebo-controlled (PC) DB Period: Day 1 up to Month 6; Post-6-Month DB Period: Placebo/Zilebesiran (Zil) arms: From first zil dose (Month 6) up to Month 36; Zil/ Zil: From first zilebesiran dose (Day 1) up to Month 36

Adverse event reporting additional description:

PC DB: Safety Analysis Set=subjects who received any amount of study drug, grouped per actual treatment. Final AEs=Zilebesiran Treatment Period using All Zilebesiran Treated Set [all subjects receiving any of the 4 zil regimens: those taking zil during 6-month placebo-controlled DB(Zil/Zil) & those switching from pbo to zil after Month 6(Pbo/Zil)].

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Subjects received zilebesiran matching placebo, as subcutaneous (SC) injection, once every 3 months (Q3M) during the 6-month placebo-controlled DB period.

Reporting group title	Zilebesiran 300 mg Q6M
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Reporting group description:

Subjects received zilebesiran, 300 mg, as SC injection on Day 1 of the 6-month placebo-controlled DB period. They received placebo at Month 3 of the 6-month placebo-controlled DB period to maintain the blind.

Reporting group title	Zilebesiran 300 mg Q3M
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Reporting group description:

Subjects received zilebesiran, 300 mg, as SC injection, Q3M, during the 6-month placebo-controlled DB period.

Reporting group title	Zilebesiran 600 mg Q6M
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Reporting group description:

Subjects received zilebesiran, 600 mg, as SC injection, on Day 1 of the 6-month placebo-controlled DB period. They received placebo at Month 3 of the 6-month placebo-controlled DB period to maintain the blind.

Reporting group title	Placebo/Zilebesiran 150 mg Q6M
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Reporting group description:

Subjects receiving placebo during 6-month placebo-controlled DB period were re-randomized at Month 6 to 1 of the 4 initial zilebesiran regimens. This arm received zilebesiran, 150 mg, SC, Q6M after re-randomization. Placebo was administered at visits without zilebesiran dosing to maintain blind between Q3M & Q6M regimens.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Reporting group title	Zilebesiran 150 mg Q6M
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Reporting group description:

Subjects received zilebesiran, 150 mg, as SC injection on Day 1 of the 6-month placebo-controlled DB period. They received placebo at Month 3 of the 6-month placebo-controlled DB period to maintain the blind.

Reporting group title	Placebo/Zilebesiran 300 mg Q6M
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Reporting group description:

Subjects receiving placebo during 6-month placebo-controlled DB period were re-randomized at Month 6

to 1 of the 4 initial zilebesiran regimens. This arm received zilebesiran, 300 mg, SC, Q6M after re-randomization. Placebo was administered at visits without zilebesiran dosing to maintain blind between Q3M & Q6M regimens.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visits at Months 18/24/30/36 did not receive further study drug.

Reporting group title	Placebo/Zilebesiran 600 mg Q6M
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Reporting group description:

Subjects receiving placebo during 6-month placebo-controlled DB period were re-randomized at Month 6 to 1 of the 4 initial zilebesiran regimens. This arm received zilebesiran, 600 mg, SC, Q6M after re-randomization. Placebo was administered at visits without zilebesiran dosing to maintain blind between Q3M & Q6M regimens.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Reporting group title	Placebo/Zilebesiran 300 mg Q3M
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Reporting group description:

Subjects receiving placebo during 6-month placebo-controlled DB period were re-randomized at Month 6 to 1 of the 4 initial zilebesiran regimens. This arm received zilebesiran, 300 mg, SC, Q3M after re-randomization.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Reporting group title	Zilebesiran/Zilebesiran 150 mg Q6M
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Reporting group description:

Subjects who received zilebesiran 150 mg Q6M during the 6-month placebo-controlled DB period remained on the same regimen throughout the study. Subjects received placebo at the visit where no zilebesiran dose was planned to maintain blinding between the Q3M and Q6M regimens.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Reporting group title	Zilebesiran/Zilebesiran 300 mg Q3M
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Reporting group description:

Subjects who received zilebesiran 300 mg Q3M during the 6-month placebo-controlled DB period remained on the same regimen throughout the study.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Reporting group title	Zilebesiran/Zilebesiran 300 mg Q6M
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Reporting group description:

Subjects who received zilebesiran 300 mg Q6M during the 6-month placebo-controlled DB period remained on the same regimen throughout the study. Subjects received placebo at the visit where no zilebesiran dose was planned to maintain blinding between the Q3M and Q6M regimens.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Reporting group title	Zilebesiran/Zilebesiran 600 mg Q6M
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Reporting group description:

Subjects who received zilebesiran 600 mg Q6M during the 6-month placebo-controlled DB period remained on the same regimen throughout the study. Subjects received placebo at the visit where no zilebesiran dose was planned to maintain blinding between the Q3M and Q6M regimens.

Prior to PA6, subjects completing Months 6 to 12 of treatment & assessment at Month 12, before availability of separate OLE study, could continue receiving blinded zilebesiran treatment up to 24 months in DB Extension Period. Following PA6, DB Extension was discontinued. Subjects who had not completed Month 12 visit at time of PA6 implementation received their last dose of study drug at Month 9. For subjects already in DB Extension at time of PA6 implementation, dosing depended on scheduled visits: those with next visit at Months 15/21/27/33 received their planned study drug, while those with next visit at Months 18/24/30/36 did not receive further study drug.

Serious adverse events	Placebo	Zilebesiran 300 mg Q6M	Zilebesiran 300 mg Q3M
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 75 (6.67%)	1 / 73 (1.37%)	4 / 75 (5.33%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer stage II			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign salivary gland neoplasm			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma stage III			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraganglion neoplasm			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive urgency			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic aneurysm			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary infarction			

subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary bypass stenosis			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 75 (1.33%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Colitis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 75 (0.00%)	1 / 73 (1.37%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive pancreatitis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Endocarditis			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Zilebesiran 600 mg Q6M	Placebo/Zilebesiran 150 mg Q6M	Zilebesiran 150 mg Q6M
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 76 (7.89%)	1 / 16 (6.25%)	0 / 78 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer stage II			

subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign salivary gland neoplasm			
subjects affected / exposed	1 / 76 (1.32%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma stage III			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraganglion neoplasm			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive urgency			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic aneurysm			
subjects affected / exposed	1 / 76 (1.32%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	1 / 76 (1.32%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			

subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary infarction			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 76 (1.32%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 76 (0.00%)	1 / 16 (6.25%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 76 (0.00%)	1 / 16 (6.25%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Meniscus injury			

subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary bypass stenosis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 76 (1.32%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive pancreatitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Osteoarthritis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Endocarditis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Serious adverse events	Placebo/Zilebesiran 300 mg Q6M	Placebo/Zilebesiran 600 mg Q6M	Placebo/Zilebesiran 300 mg Q3M
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)

number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer stage II			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign salivary gland neoplasm			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma stage III			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraganglion neoplasm			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive urgency			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic aneurysm			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary infarction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary bypass stenosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive pancreatitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Endocarditis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			

subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Zilebesiran/Zilebesiran 150 mg Q6M	Zilebesiran/Zilebesiran 300 mg Q3M	Zilebesiran/Zilebesiran 300 mg Q6M
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 78 (6.41%)	7 / 75 (9.33%)	5 / 73 (6.85%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer stage II			
subjects affected / exposed	0 / 78 (0.00%)	1 / 75 (1.33%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign salivary gland neoplasm			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma stage III			
subjects affected / exposed	0 / 78 (0.00%)	1 / 75 (1.33%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraganglion neoplasm			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 78 (0.00%)	1 / 75 (1.33%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive urgency			

subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic aneurysm			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	1 / 78 (1.28%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary infarction			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Abnormal behaviour			

subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 78 (1.28%)	0 / 75 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary bypass stenosis			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 78 (0.00%)	1 / 75 (1.33%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			

subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 78 (0.00%)	1 / 75 (1.33%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 78 (1.28%)	1 / 75 (1.33%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 78 (1.28%)	0 / 75 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			

subjects affected / exposed	1 / 78 (1.28%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive pancreatitis			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 78 (1.28%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Endocarditis			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 78 (1.28%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 78 (0.00%)	1 / 75 (1.33%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Urosepsis			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 78 (1.28%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Zilebesiran/Zilebesiran 600 mg Q6M		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 76 (11.84%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer stage II			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Benign salivary gland neoplasm			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma stage III			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Paraganglion neoplasm			

subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertensive urgency			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aortic aneurysm			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Orthostatic hypotension			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary infarction			

subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary bypass stenosis			

subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Colitis			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Obstructive pancreatitis			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal haemorrhage			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Endocarditis			

subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	Zilebesiran 300 mg Q6M	Zilebesiran 300 mg Q3M
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 75 (24.00%)	24 / 73 (32.88%)	23 / 75 (30.67%)
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 75 (6.67%)	0 / 73 (0.00%)	3 / 75 (4.00%)
occurrences (all)	7	0	3

Hypotension subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Orthostatic hypotension subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
General disorders and administration site conditions			
Discomfort subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Injection site reaction subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	4 / 73 (5.48%) 5	8 / 75 (10.67%) 9
Fatigue subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Malaise subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Immune system disorders			
Seasonal allergy subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Nasal discomfort subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Sinus congestion			

subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Psychiatric disorders			
Depression			
subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Investigations			
Blood cholesterol increased			
subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Blood creatine increased			
subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Blood creatinine increased			
subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Blood uric acid increased			
subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Glomerular filtration rate decreased			
subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Glycosylated haemoglobin increased			
subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Transaminases increased			
subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Brain contusion			
subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Fall			

subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Muscle injury			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Post-traumatic neck syndrome			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 75 (5.33%)	2 / 73 (2.74%)	3 / 75 (4.00%)
occurrences (all)	4	2	3
Dizziness postural			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	7 / 75 (9.33%)	4 / 73 (5.48%)	2 / 75 (2.67%)
occurrences (all)	8	4	2
Sciatica			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Eye disorders			

Conjunctival haemorrhage subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Glaucoma subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 2
Vomiting subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Umbilical hernia subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 2	0 / 75 (0.00%) 0
Hepatobiliary disorders			
Hepatic steatosis subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Skin hyperpigmentation			

subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Renal and urinary disorders			
Renal cyst			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	2 / 75 (2.67%)	4 / 73 (5.48%)	2 / 75 (2.67%)
occurrences (all)	3	4	2
Intervertebral disc degeneration			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			

subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Infections and infestations			
Bronchitis subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 1	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Acute sinusitis subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 2
Coronavirus Disease of 2019 (COVID-19) subjects affected / exposed occurrences (all)	3 / 75 (4.00%) 3	6 / 73 (8.22%) 6	6 / 75 (8.00%) 6
Diverticulitis subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Herpes zoster subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Gastroenteritis viral subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Onychomycosis subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Paronychia subjects affected / exposed occurrences (all)	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0	0 / 75 (0.00%) 0
Upper respiratory tract infection			

subjects affected / exposed	1 / 75 (1.33%)	4 / 73 (5.48%)	2 / 75 (2.67%)
occurrences (all)	1	5	3
Sinusitis			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 75 (1.33%)	4 / 73 (5.48%)	5 / 75 (6.67%)
occurrences (all)	2	4	5
Diabetes mellitus			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Dyslipidaemia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 75 (0.00%)	0 / 73 (0.00%)	0 / 75 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Zilebesiran 600 mg Q6M	Placebo/Zilebesiran 150 mg Q6M	Zilebesiran 150 mg Q6M
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 76 (26.32%)	9 / 16 (56.25%)	21 / 78 (26.92%)
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 76 (6.58%)	1 / 16 (6.25%)	4 / 78 (5.13%)
occurrences (all)	5	1	4
Hypotension			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Discomfort			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	4 / 76 (5.26%)	0 / 16 (0.00%)	3 / 78 (3.85%)
occurrences (all)	4	0	3
Fatigue			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			

subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Nasal discomfort subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Sinus congestion subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Investigations Blood cholesterol increased subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Blood creatine increased subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Blood uric acid increased subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Glomerular filtration rate decreased subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Glycosylated haemoglobin increased subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Transaminases increased subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Injury, poisoning and procedural complications			

Arthropod sting			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Brain contusion			
subjects affected / exposed	0 / 76 (0.00%)	1 / 16 (6.25%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Muscle injury			
subjects affected / exposed	0 / 76 (0.00%)	1 / 16 (6.25%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Post-traumatic neck syndrome			
subjects affected / exposed	0 / 76 (0.00%)	1 / 16 (6.25%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 76 (3.95%)	0 / 16 (0.00%)	2 / 78 (2.56%)
occurrences (all)	3	0	2
Dizziness postural			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 76 (1.32%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	0 / 76 (0.00%)	1 / 16 (6.25%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Syncope			

subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Ear and labyrinth disorders Vertigo positional subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	1 / 16 (6.25%) 1	0 / 78 (0.00%) 0
Eye disorders Conjunctival haemorrhage subjects affected / exposed occurrences (all) Glaucoma subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0 0 / 76 (0.00%) 0	0 / 16 (0.00%) 0 1 / 16 (6.25%) 1	0 / 78 (0.00%) 0 0 / 78 (0.00%) 0
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Umbilical hernia subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0 0 / 76 (0.00%) 1 0 / 76 (0.00%) 0 0 / 76 (0.00%) 0 0 / 76 (0.00%) 0 0 / 76 (0.00%) 0 0 / 76 (0.00%) 0	1 / 16 (6.25%) 1 0 / 16 (0.00%) 0 2 / 16 (12.50%) 2 0 / 16 (0.00%) 0 0 / 16 (0.00%) 0 0 / 16 (0.00%) 0 1 / 16 (6.25%) 1	0 / 78 (0.00%) 0 0 / 78 (0.00%) 0 0 / 78 (0.00%) 0 0 / 78 (0.00%) 0 0 / 78 (0.00%) 3 0 / 78 (0.00%) 0
Hepatobiliary disorders			

Hepatic steatosis subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Skin hyperpigmentation subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Renal and urinary disorders Renal cyst subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Urinary retention subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Endocrine disorders Thyroid mass subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	1 / 16 (6.25%) 1	0 / 78 (0.00%) 0
Musculoskeletal and connective tissue disorders Bursitis subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Arthralgia subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	2 / 78 (2.56%) 2
Intervertebral disc degeneration subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Osteoarthritis			

subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 16 (6.25%)	0 / 78 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal pain			
subjects affected / exposed	0 / 76 (0.00%)	1 / 16 (6.25%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Acute sinusitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Coronavirus Disease of 2019 (COVID-19)			
subjects affected / exposed	4 / 76 (5.26%)	0 / 16 (0.00%)	3 / 78 (3.85%)
occurrences (all)	4	0	3
Diverticulitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			

subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 76 (1.32%)	2 / 16 (12.50%)	3 / 78 (3.85%)
occurrences (all)	1	2	3
Sinusitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 76 (0.00%)	1 / 16 (6.25%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 76 (0.00%)	1 / 16 (6.25%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 76 (0.00%)	1 / 16 (6.25%)	0 / 78 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	5 / 76 (6.58%)	0 / 16 (0.00%)	5 / 78 (6.41%)
occurrences (all)	11	0	5
Diabetes mellitus			
subjects affected / exposed	0 / 76 (0.00%)	0 / 16 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Dyslipidaemia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 16 (6.25%)	0 / 78 (0.00%)
occurrences (all)	0	1	0

Vitamin D deficiency subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	0 / 16 (0.00%) 0	0 / 78 (0.00%) 0
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0	1 / 16 (6.25%) 1	0 / 78 (0.00%) 0

Non-serious adverse events	Placebo/Zilebesiran 300 mg Q6M	Placebo/Zilebesiran 600 mg Q6M	Placebo/Zilebesiran 300 mg Q3M
Total subjects affected by non-serious adverse events subjects affected / exposed	12 / 16 (75.00%)	8 / 18 (44.44%)	9 / 16 (56.25%)
Vascular disorders			
Hypertension subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 18 (0.00%) 0	1 / 16 (6.25%) 1
Hypotension subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 18 (0.00%) 0	2 / 16 (12.50%) 2
Orthostatic hypotension subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 18 (0.00%) 0	0 / 16 (0.00%) 0
General disorders and administration site conditions			
Discomfort subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 18 (0.00%) 0	1 / 16 (6.25%) 2
Injection site reaction subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 4	1 / 18 (5.56%) 1	1 / 16 (6.25%) 1
Fatigue subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 18 (5.56%) 1	1 / 16 (6.25%) 2
Malaise subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 18 (5.56%) 1	0 / 16 (0.00%) 0

Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Nasal discomfort			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Sinus congestion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Investigations			
Blood cholesterol increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Blood creatine increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood uric acid increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Glomerular filtration rate decreased			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 18 (0.00%) 0	1 / 16 (6.25%) 1
Glycosylated haemoglobin increased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 18 (5.56%) 1	0 / 16 (0.00%) 0
Transaminases increased subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 18 (0.00%) 0	0 / 16 (0.00%) 0
Injury, poisoning and procedural complications			
Arthropod sting subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 18 (0.00%) 0	0 / 16 (0.00%) 0
Brain contusion subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 18 (0.00%) 0	0 / 16 (0.00%) 0
Fall subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 18 (5.56%) 1	0 / 16 (0.00%) 0
Foot fracture subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 18 (5.56%) 1	0 / 16 (0.00%) 0
Ligament sprain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 18 (5.56%) 1	0 / 16 (0.00%) 0
Muscle injury subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 18 (0.00%) 0	0 / 16 (0.00%) 0
Post-traumatic neck syndrome subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 18 (0.00%) 0	0 / 16 (0.00%) 0
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 18 (5.56%) 1	0 / 16 (0.00%) 0
Dizziness postural			

subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Glaucoma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	2
Vomiting			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 18 (5.56%) 1	0 / 16 (0.00%) 0
Umbilical hernia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 18 (0.00%) 0	0 / 16 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 18 (0.00%) 0	0 / 16 (0.00%) 0
Hepatobiliary disorders Hepatic steatosis subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 18 (0.00%) 0	0 / 16 (0.00%) 0
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 18 (0.00%) 0	1 / 16 (6.25%) 2
Skin hyperpigmentation subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 18 (0.00%) 0	1 / 16 (6.25%) 1
Renal and urinary disorders Renal cyst subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 18 (0.00%) 0	0 / 16 (0.00%) 0
Urinary retention subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 18 (0.00%) 0	1 / 16 (6.25%) 1
Endocrine disorders Thyroid mass subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 18 (0.00%) 0	0 / 16 (0.00%) 0
Musculoskeletal and connective tissue disorders Bursitis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 18 (5.56%) 1	0 / 16 (0.00%) 0
Back pain			

subjects affected / exposed	2 / 16 (12.50%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Arthralgia			
subjects affected / exposed	0 / 16 (0.00%)	2 / 18 (11.11%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Osteoarthritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Acute sinusitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Coronavirus Disease of 2019 (COVID-19)			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Diverticulitis			

subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	1
Gastroenteritis viral			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Onychomycosis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Paronychia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Sinusitis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	1	2	0
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	3 / 16 (18.75%)
occurrences (all)	0	2	3
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Hyperkalaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	3	0	0
Diabetes mellitus			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Dyslipidaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Vitamin D deficiency			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 16 (6.25%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Zilebesiran/Zilebesiran 150 mg Q6M	Zilebesiran/Zilebesiran 300 mg Q3M	Zilebesiran/Zilebesiran 300 mg Q6M
Total subjects affected by non-serious adverse events			
subjects affected / exposed	53 / 78 (67.95%)	49 / 75 (65.33%)	47 / 73 (64.38%)
Vascular disorders			
Hypertension			
subjects affected / exposed	9 / 78 (11.54%)	4 / 75 (5.33%)	3 / 73 (4.11%)
occurrences (all)	10	6	3
Hypotension			
subjects affected / exposed	2 / 78 (2.56%)	2 / 75 (2.67%)	1 / 73 (1.37%)
occurrences (all)	3	2	1
Orthostatic hypotension			
subjects affected / exposed	4 / 78 (5.13%)	0 / 75 (0.00%)	4 / 73 (5.48%)
occurrences (all)	5	0	4
General disorders and administration site conditions			
Discomfort			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences (all)	0	3	0

Injection site reaction subjects affected / exposed occurrences (all)	5 / 78 (6.41%) 5	13 / 75 (17.33%) 30	8 / 73 (10.96%) 16
Fatigue subjects affected / exposed occurrences (all)	2 / 78 (2.56%) 2	2 / 75 (2.67%) 2	1 / 73 (1.37%) 1
Malaise subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	1 / 75 (1.33%) 1	0 / 73 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Chronic obstructive pulmonary disease subjects affected / exposed occurrences (all)	1 / 78 (1.28%) 1	1 / 75 (1.33%) 1	0 / 73 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	1 / 78 (1.28%) 1	2 / 75 (2.67%) 2	0 / 73 (0.00%) 0
Nasal discomfort subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	0 / 73 (0.00%) 2
Sinus congestion subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	1 / 75 (1.33%) 1	0 / 73 (0.00%) 0
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	1 / 78 (1.28%) 1	0 / 75 (0.00%) 0	1 / 73 (1.37%) 1
Investigations Blood cholesterol increased subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0
Blood creatine increased			

subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	3 / 78 (3.85%)	0 / 75 (0.00%)	2 / 73 (2.74%)
occurrences (all)	4	0	2
Blood uric acid increased			
subjects affected / exposed	1 / 78 (1.28%)	1 / 75 (1.33%)	1 / 73 (1.37%)
occurrences (all)	1	1	1
Glomerular filtration rate decreased			
subjects affected / exposed	2 / 78 (2.56%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences (all)	2	0	0
Glycosylated haemoglobin increased			
subjects affected / exposed	2 / 78 (2.56%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences (all)	2	0	0
Transaminases increased			
subjects affected / exposed	1 / 78 (1.28%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	0 / 78 (0.00%)	1 / 75 (1.33%)	0 / 73 (0.00%)
occurrences (all)	0	1	0
Brain contusion			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	1 / 78 (1.28%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences (all)	1	0	0
Foot fracture			
subjects affected / exposed	0 / 78 (0.00%)	1 / 75 (1.33%)	1 / 73 (1.37%)
occurrences (all)	0	2	1
Ligament sprain			
subjects affected / exposed	4 / 78 (5.13%)	0 / 75 (0.00%)	1 / 73 (1.37%)
occurrences (all)	4	0	1
Muscle injury			

subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0
Post-traumatic neck syndrome subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0
Nervous system disorders			
Dizziness subjects affected / exposed occurrences (all)	3 / 78 (3.85%) 3	4 / 75 (5.33%) 4	3 / 73 (4.11%) 4
Dizziness postural subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	1 / 73 (1.37%) 1
Headache subjects affected / exposed occurrences (all)	2 / 78 (2.56%) 2	5 / 75 (6.67%) 6	6 / 73 (8.22%) 7
Sciatica subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0
Syncope subjects affected / exposed occurrences (all)	2 / 78 (2.56%) 2	1 / 75 (1.33%) 1	0 / 73 (0.00%) 0
Ear and labyrinth disorders			
Vertigo positional subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	1 / 75 (1.33%) 1	0 / 73 (0.00%) 0
Eye disorders			
Conjunctival haemorrhage subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	1 / 75 (1.33%) 1	0 / 73 (0.00%) 0
Glaucoma subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	2 / 73 (2.74%) 2
Constipation			

subjects affected / exposed occurrences (all)	4 / 78 (5.13%) 5	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	1 / 78 (1.28%) 2	3 / 75 (4.00%) 3	2 / 73 (2.74%) 3
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	2 / 75 (2.67%) 2	3 / 73 (4.11%) 3
Vomiting subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	2 / 75 (2.67%) 2	1 / 73 (1.37%) 1
Umbilical hernia subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	1 / 78 (1.28%) 1	0 / 75 (0.00%) 0	3 / 73 (4.11%) 3
Hepatobiliary disorders Hepatic steatosis subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	1 / 73 (1.37%) 1
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	2 / 78 (2.56%) 2	0 / 75 (0.00%) 0	2 / 73 (2.74%) 2
Skin hyperpigmentation subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0
Renal and urinary disorders Renal cyst subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0
Urinary retention subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	1 / 75 (1.33%) 1	0 / 73 (0.00%) 0
Endocrine disorders			

Thyroid mass subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Bursitis subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	2 / 78 (2.56%) 2	3 / 75 (4.00%) 3	3 / 73 (4.11%) 3
Arthralgia subjects affected / exposed occurrences (all)	3 / 78 (3.85%) 3	4 / 75 (5.33%) 5	6 / 73 (8.22%) 6
Intervertebral disc degeneration subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0
Osteoarthritis subjects affected / exposed occurrences (all)	4 / 78 (5.13%) 4	3 / 75 (4.00%) 3	0 / 73 (0.00%) 0
Myalgia subjects affected / exposed occurrences (all)	1 / 78 (1.28%) 1	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0
Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0
Muscle spasms subjects affected / exposed occurrences (all)	2 / 78 (2.56%) 2	3 / 75 (4.00%) 5	1 / 73 (1.37%) 1
Pain in extremity subjects affected / exposed occurrences (all)	1 / 78 (1.28%) 1	3 / 75 (4.00%) 3	1 / 73 (1.37%) 1
Infections and infestations			
Bronchitis subjects affected / exposed occurrences (all)	2 / 78 (2.56%) 2	1 / 75 (1.33%) 1	2 / 73 (2.74%) 2
Acute sinusitis			

subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences (all)	3	0	0
Coronavirus Disease of 2019 (COVID-19)			
subjects affected / exposed	7 / 78 (8.97%)	9 / 75 (12.00%)	7 / 73 (9.59%)
occurrences (all)	8	10	8
Diverticulitis			
subjects affected / exposed	1 / 78 (1.28%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 78 (1.28%)	5 / 75 (6.67%)	4 / 73 (5.48%)
occurrences (all)	1	6	6
Herpes zoster			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	1 / 78 (1.28%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences (all)	1	0	0
Onychomycosis			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	6 / 78 (7.69%)	6 / 75 (8.00%)	5 / 73 (6.85%)
occurrences (all)	7	9	6
Sinusitis			
subjects affected / exposed	2 / 78 (2.56%)	4 / 75 (5.33%)	0 / 73 (0.00%)
occurrences (all)	2	4	0
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	0 / 73 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	3 / 78 (3.85%)	9 / 75 (12.00%)	5 / 73 (6.85%)
occurrences (all)	4	10	5

Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	2 / 75 (2.67%) 2	0 / 73 (0.00%) 0
Metabolism and nutrition disorders			
Gout subjects affected / exposed occurrences (all)	1 / 78 (1.28%) 1	2 / 75 (2.67%) 2	0 / 73 (0.00%) 0
Hyperkalaemia subjects affected / exposed occurrences (all)	6 / 78 (7.69%) 10	7 / 75 (9.33%) 9	5 / 73 (6.85%) 6
Diabetes mellitus subjects affected / exposed occurrences (all)	2 / 78 (2.56%) 2	2 / 75 (2.67%) 2	1 / 73 (1.37%) 1
Dyslipidaemia subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	1 / 73 (1.37%) 1
Vitamin D deficiency subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 75 (0.00%) 0	1 / 73 (1.37%) 1
Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	1 / 78 (1.28%) 1	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0
Hypokalaemia subjects affected / exposed occurrences (all)	1 / 78 (1.28%) 1	0 / 75 (0.00%) 0	0 / 73 (0.00%) 0

Non-serious adverse events	Zilebesiran/Zilebesiran 600 mg Q6M		
Total subjects affected by non-serious adverse events subjects affected / exposed	49 / 76 (64.47%)		
Vascular disorders			
Hypertension subjects affected / exposed occurrences (all)	9 / 76 (11.84%) 11		
Hypotension subjects affected / exposed occurrences (all)	2 / 76 (2.63%) 2		
Orthostatic hypotension			

subjects affected / exposed occurrences (all)	4 / 76 (5.26%) 4		
General disorders and administration site conditions			
Discomfort			
subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Injection site reaction			
subjects affected / exposed occurrences (all)	9 / 76 (11.84%) 18		
Fatigue			
subjects affected / exposed occurrences (all)	3 / 76 (3.95%) 3		
Malaise			
subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Dyspnoea			
subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1		
Nasal discomfort			
subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Sinus congestion			
subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1		
Psychiatric disorders			
Depression			

subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Investigations			
Blood cholesterol increased subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Blood creatine increased subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Blood creatinine increased subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1		
Blood uric acid increased subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1		
Glomerular filtration rate decreased subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1		
Glycosylated haemoglobin increased subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1		
Transaminases increased subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Injury, poisoning and procedural complications			
Arthropod sting subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Brain contusion subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Fall subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 2		
Foot fracture			

subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Ligament sprain			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Muscle injury			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Post-traumatic neck syndrome			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	8 / 76 (10.53%)		
occurrences (all)	8		
Dizziness postural			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	3 / 76 (3.95%)		
occurrences (all)	5		
Sciatica			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Glaucoma			

subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 76 (2.63%)		
occurrences (all)	2		
Umbilical hernia			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	2 / 76 (2.63%)		
occurrences (all)	2		
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	1		
Skin hyperpigmentation			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			

Renal cyst subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Urinary retention subjects affected / exposed occurrences (all)	1 / 76 (1.32%) 1		
Endocrine disorders Thyroid mass subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Musculoskeletal and connective tissue disorders Bursitis subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Back pain subjects affected / exposed occurrences (all)	2 / 76 (2.63%) 2		
Arthralgia subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Intervertebral disc degeneration subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Osteoarthritis subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Myalgia subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Muscle spasms subjects affected / exposed occurrences (all)	0 / 76 (0.00%) 0		
Pain in extremity			

subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 76 (2.63%)		
occurrences (all)	2		
Acute sinusitis			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	1		
Coronavirus Disease of 2019 (COVID-19)			
subjects affected / exposed	8 / 76 (10.53%)		
occurrences (all)	8		
Diverticulitis			
subjects affected / exposed	2 / 76 (2.63%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	2 / 76 (2.63%)		
occurrences (all)	4		
Herpes zoster			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Gastroenteritis viral			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Onychomycosis			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Paronychia			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	4 / 76 (5.26%)		
occurrences (all)	4		
Sinusitis			

subjects affected / exposed	3 / 76 (3.95%)		
occurrences (all)	5		
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	3 / 76 (3.95%)		
occurrences (all)	3		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	5 / 76 (6.58%)		
occurrences (all)	14		
Diabetes mellitus			
subjects affected / exposed	3 / 76 (3.95%)		
occurrences (all)	3		
Dyslipidaemia			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Vitamin D deficiency			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 76 (1.32%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	0 / 76 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 April 2021	The following change was made as per Amendment 1: 1. Corrected the inclusion criterion of systolic blood pressure assessed by ABPM to daytime mean instead of 24-hour mean.
09 June 2021	The following changes were made as per Amendment 2: 1. Added neurological examination to symptom-directed physical examinations. 2. Added treatment discontinuation criteria based on neurological adverse effects.
09 December 2021	The following changes were made as per Amendment 3: 1. Removed limitations on the allowable classes of prior antihypertensive medication. 2. Revised washout period of beta blockers to 2 weeks. 3. Amended Washout period of prior antihypertensive medications.
22 March 2022	The following changes were made as per Amendment 4: 1. Removed 24-hour urine sample collection and decreased the number of fasting laboratory samples to reduce the subject burden. 2. Removed 24-hour ABPM during the DB Extension period and Safety Follow-up period. 3. Revised and simplified the exclusion criterion for diabetes mellitus. 4. Removed exclusion criterion for known change in body weight >10% in last 6 months prior to screening. 5. Removed the exclusion criterion for being unable or unwilling to perform HBPM as it is redundant with inclusion criterion. 6. Revised the period in which patients should avoid nonsteroidal anti-inflammatory drugs (NSAIDs) before office blood pressure and ABPM assessments to 2 days as the effects of these medications are expected to be washed out within 2 days.
04 November 2022	The following changes were made as per Amendment 5: 1. Extended the duration of the DB Extension period of the study from 12 to 24 months to allow patients to continue to receive zilebesiran until a separate open-label extension study is initiated. 2. Revised the timing of repeat ABPM measurements in case of an invalid assessment from 4 days to 7 days to allow more time to complete this assessment.
20 July 2023	The following changes were made as per Amendment 6: 1. Removed the 12-month DB Extension period as a separate OLE study would not be conducted. 2. Removed an exploratory endpoint related to comparing blood pressure measurements obtained with an optional wearable, noninvasive, cuffless device to those obtained by standard cuff-based methods due to low subject participation.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported