Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

Antihypertensive Medication Washout Guidance Provided to Sites

Short-acting antihypertensive (2-week washout)	Long-acting antihypertensive (4-week washout)
ACE-Is: Lisinopril Enalapril Captopril Benazepril **ARBs:** Losartan Irbesartan Valsartan Candesartan Telmisartan Olmesartan Azilsartan **Aldosterone antagonists:** Eplerenone Spironolactone Finerenone **Beta blockers:** Atenolol Carvedilol Metoprolol Bisoprolol Nebivolol **Thiazide diuretics:** Hydrochlorothiazide Indapamide **Potassium-sparing diuretics:** Triamterene **Calcium channel blockers:** Nifedipine	**ACE-Is:** Ramipril **Thiazide diuretics:** Chlorthalidone **Calcium channel blockers:** Amlodipine Felodipine **Direct renin inhibitors:** Aliskiren

Abbreviations: ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

Notes:

For combination pills, the recommended duration of washout is 4 weeks if one of the ingredients in the combination is in the 4-week washout list.

Please reach out to your Medical Monitor if an antihypertensive is not on the list and you have questions about the duration of washout.

Determination of antihypertensives as short or long acting was based on their circulating half-life.

Automated BP Measurement Methods

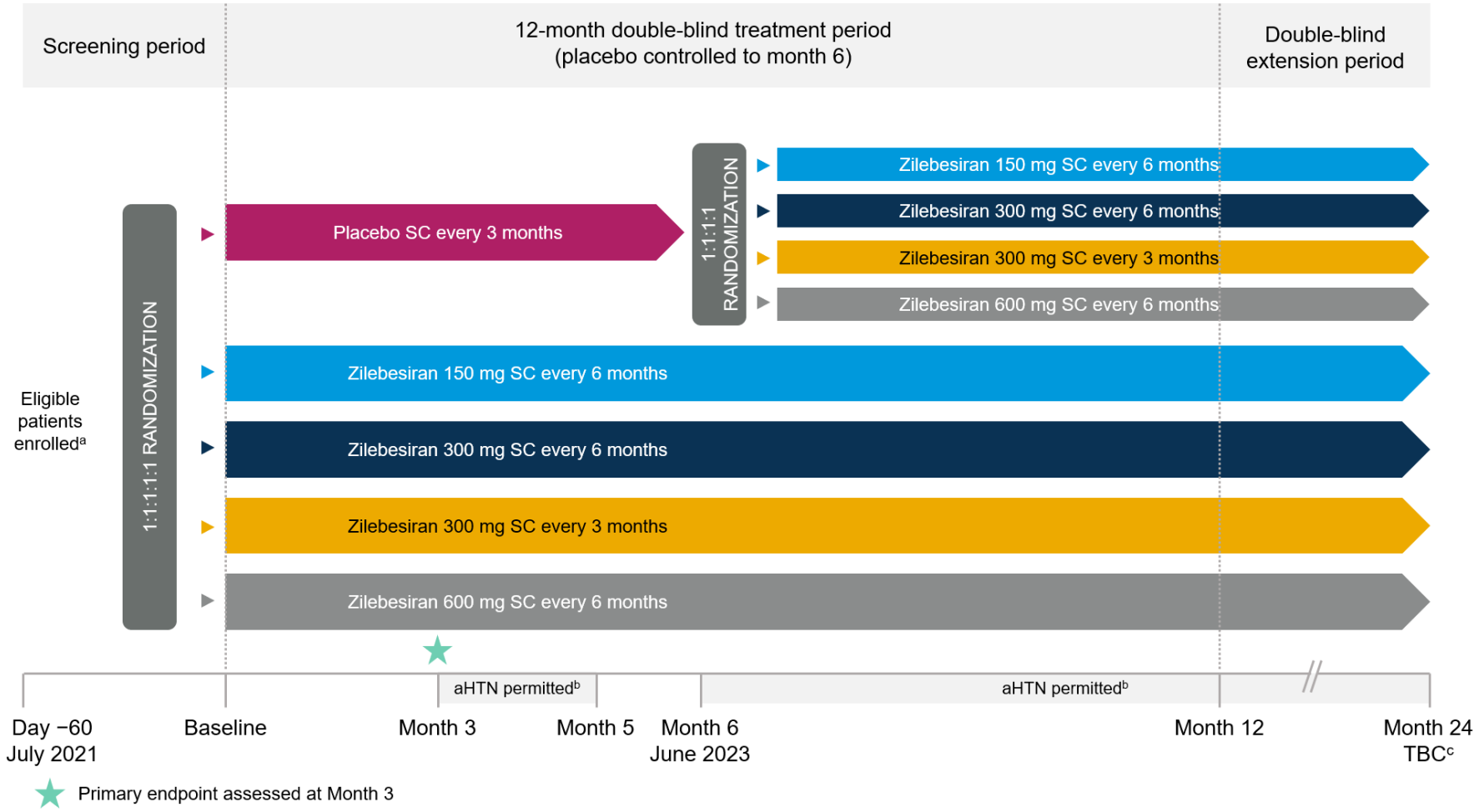
All blood pressure (BP) measurements were taken using the standardized equipment provided by the sponsor, according to the methods described in the relevant user manuals.

Ambulatory BP assessment (Suntech Oscar 2M250)
Ambulatory BP was measured using the patient's nondominant arm. All ambulatory BP collections were taken in the outpatient/ambulatory state. During the 24-hour monitoring period, patients were asked to avoid strenuous exercise but otherwise maintain their usual level of physical activity. The automated device was programmed to take readings every 20 minutes during the day (6AM to 9:59PM) and every 30 minutes during the night (10PM to 5:59AM). The ambulatory BP assessment was considered valid if: (1) the number of successful daytime readings was 33 or more; (2) the number of successful nighttime readings was 11 or more; and (3) no more than 3 hours were not represented (i.e. 3 sections of 60 minutes where no valid readings were obtained).

Office BP assessment (Microlife WBP Office 2G)
At the first screening visit, office BP was measured in both arms to select the appropriate arm to use for office BP measurements. Unless a concomitant condition favored the use of a specific arm, the arm with the higher office SBP was used for all subsequent office BP readings. Office BP was measured early in the visit before the morning dose of antihypertensive medication, before phlebotomy or other potentially stressful assessments. Before BP assessment, patients were asked to confirm that there had been no exercise or consumption of caffeine, nicotine, or tobacco in the past 30 minutes. If necessary, BP assessment was delayed to meet these requirements. Because a full bladder can impact BP measurements, patients were asked to use the bathroom before the assessment.
Measurement procedure:

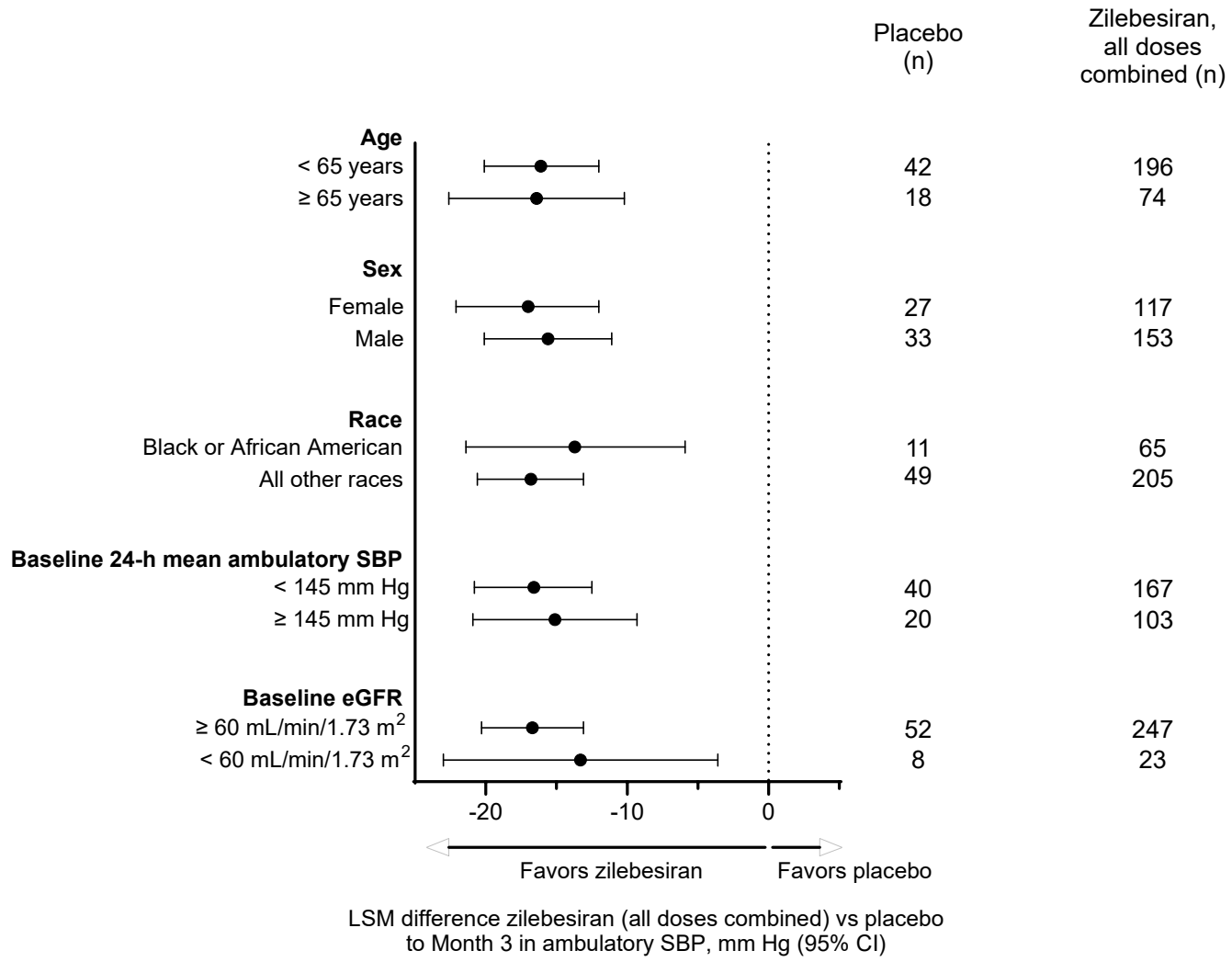
- The patient was in a comfortable resting position in a chair with their back supported and their feet flat on the floor.
- An appropriately sized cuff was placed on the correct arm with no clothing between the patient's arm and the cuff and with the midpoint of the bladder length positioned over the brachial artery (located by palpation). The arm was supported on an armrest or table with mid-cuff at heart level and the palm facing the ceiling.
- The automated BP device's seated measurement protocol includes a 5-minute period of rest, followed by four sequential BP measurements at 1-minute intervals. The seated BP for the visit was defined by the average of the last three individual measurements.
- Staff members left the room for the duration of the automated measurement protocol.

eFigure 1. Study Design



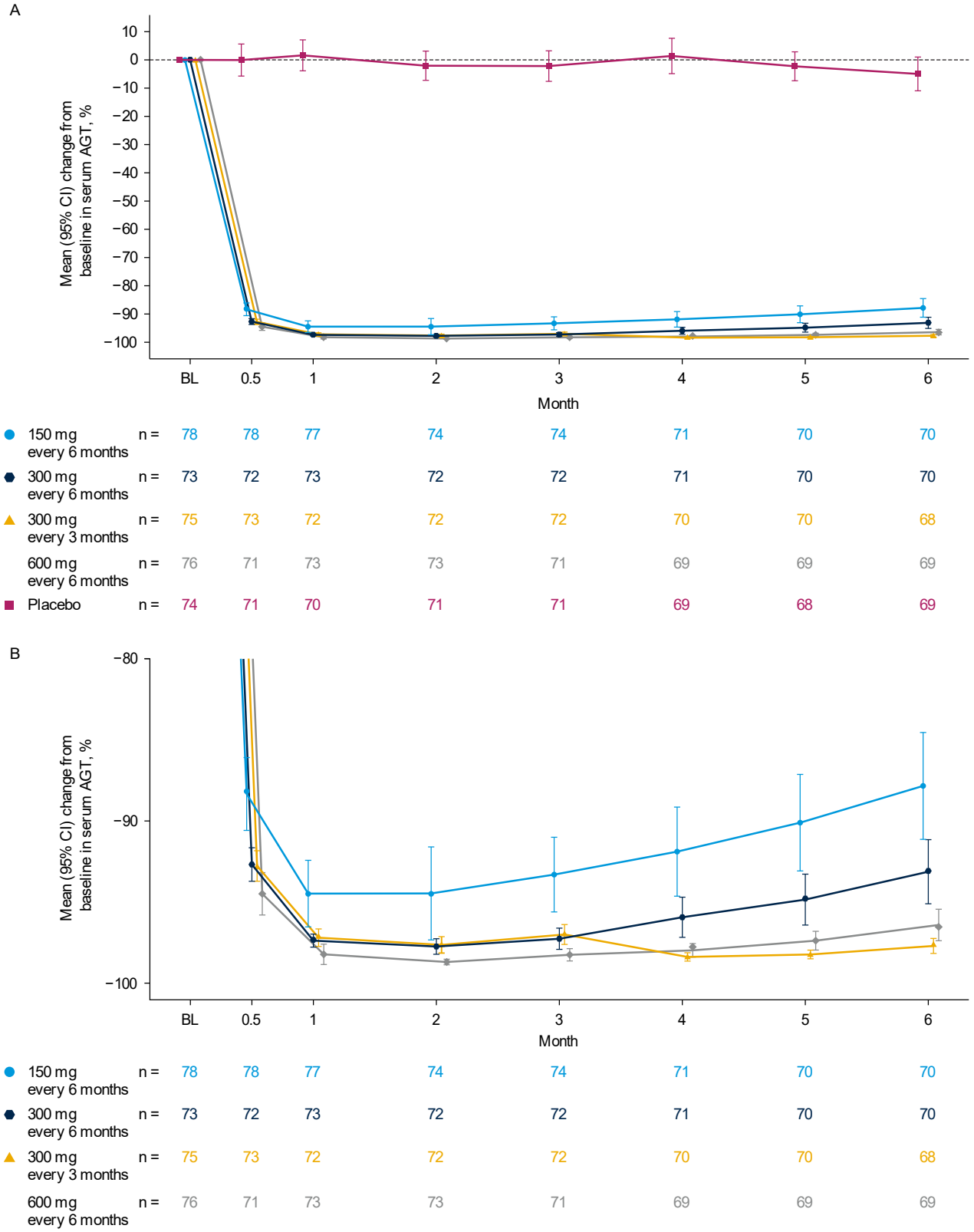
Abbreviations: aHTN, antihypertensive medication; SC, subcutaneous.
[a]Patients who were taking aHTN at screening underwent a washout of these medications of at least 2 weeks. [b]Patients could receive aHTN as rescue agents at the discretion of the Investigator between Months 3 and 5 and after Month 6. Washout of aHTN was required between Months 5 and 6. Blood pressure measurements were censored if recorded while patients were on or within 2 weeks after stopping aHTN. [c]The study is ongoing as of February 2024.

eFigure 2. Subgroup Analysis (Full Analysis Set [a])



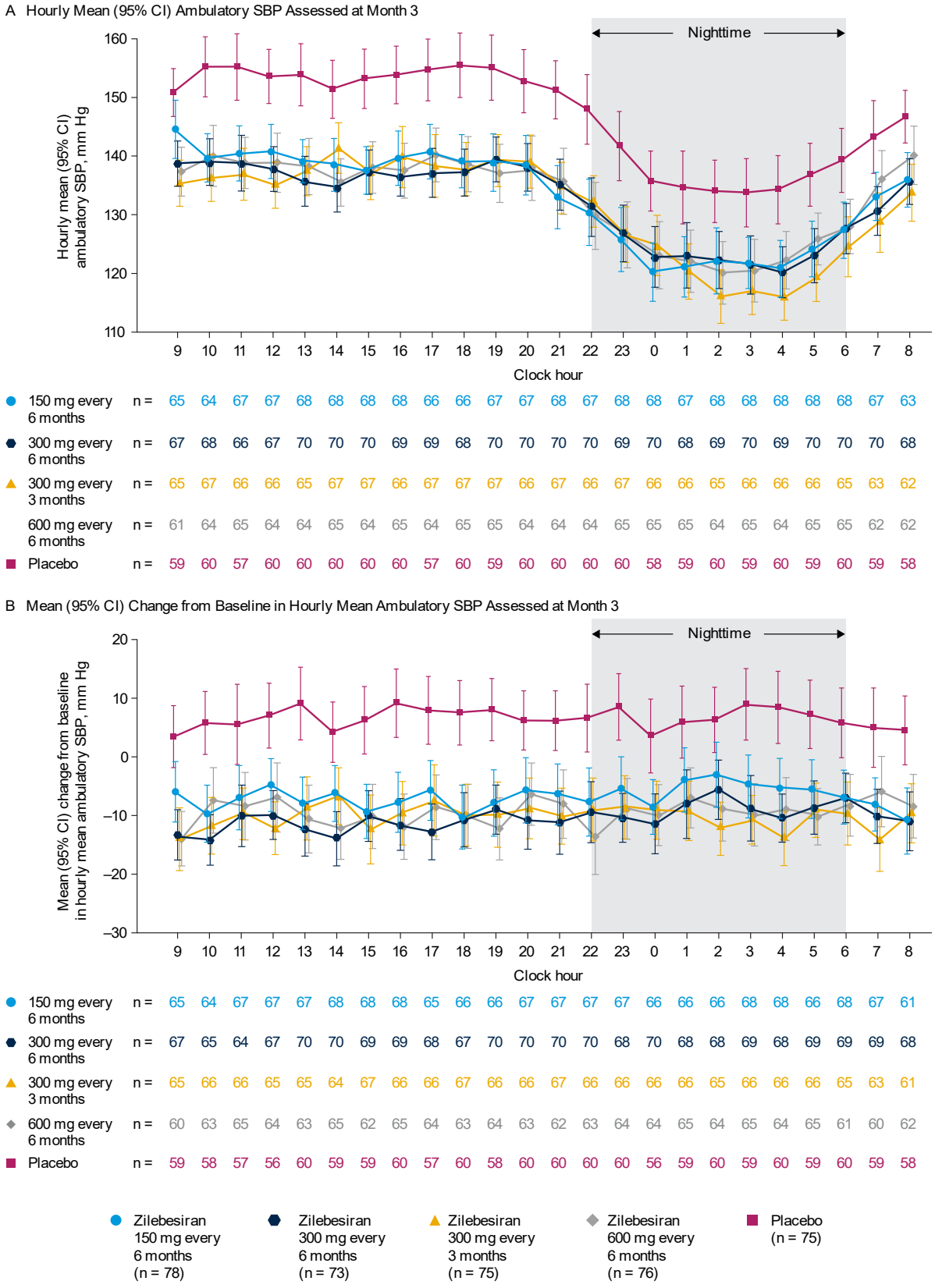
Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; LSM, least-squares mean; SBP, systolic blood pressure. [a]All randomized patients who received any amount of study drug, analyzed according to randomized treatment. All subgroups were predefined.

eFigure 3. Percentage Change (95% CI) in Serum Angiotensinogen Concentration from Baseline (A) and Detail (B)



Abbreviations: AGT, angiotensinogen; BL, baseline; CI, confidence interval.

eFigure 4. Hourly Mean Ambulatory SBP Assessments at Month 3



Abbreviations: CI, confidence interval; SBP, systolic blood pressure. Plots show a single 24-hour period collection at Month 3. Patients are measured multiple times during the 24-hour period (every 20 minutes during the day, every 30 minutes during the night). For each clock hour the measurements are averaged to calculate the hourly mean.

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eTable 1. Blood Pressure Response at Month 6 (Full Analysis Set[a])

Response criteria[b] assessment at Month 6	Zilebesiran				Placebo (N = 75)
	150 mg every 6 mo (N = 78)	300 mg every 6 mo (N = 73)	300 mg every 3 mo (N = 75)	600 mg every 6 mo (N = 76)	
Met response criteria, n (%)	24 (30.8)	37 (50.7)	29 (38.7)	36 (47.4)	5 (6.7)
Zilebesiran vs placebo odds ratio estimate (95% CI)	6.8 (2.4 to 19.4)	19.7 (6.8 to 56.9)	10.7 (3.8 to 30.6)	17.9 (6.2 to 51.5)	–

Abbreviations: CI, confidence interval; SBP, systolic blood pressure. [a]All randomized patients who received any amount of study drug, analyzed according to randomized treatment. [b]Response defined as 24-hour mean SBP < 130 mm Hg and/or reduction ≥ 20 mm Hg without additional antihypertensive medication.

eTable 2. Change From Baseline to Month 3 or Month 6 in 24-Hour Mean Ambulatory and Office DBP (Full Analysis Set[a])

	Zilebesiran 150 mg every 6 mo	Zilebesiran 300 mg every 6 mo	Zilebesiran 300 mg every 3 mo	Zilebesiran 300 mg every 3 mo or every 6 mo	Zilebesiran 600 mg every 6 mo	Placebo
Ambulatory DBP at baseline, patients with data	n = 78	n = 73	n = 75	n = 148	n = 76	n = 75
Mean DBP, mm Hg (SD)	81.7 (8.3)	82.3 (8.7)	82.0 (8.6)	82.2 (8.6)	81.4 (8.3)	81.7 (7.8)
Office DBP at baseline, patients with data	n = 78	n = 73	n = 74	n = 147	n = 76	n = 75
Mean DBP, mm Hg (SD)	87.4 (9.6)	88.8 (8.8)	85.3 (9.1)	87.0 (9.1)	85.6 (8.8)	87.9 (10.5)
Ambulatory DBP at Month 3, patients with data	n = 68	–	–	n = 137	n = 65	n = 60
Mean DBP, mm Hg (SD)	76.7 (10.6)	–	–	76.1 (9.3)	75.4 (8.2)	84.8 (9.3)
LSM change from baseline, mm Hg (95% CI)	−4.5 (−6.1 to −2.9)	–	–	−5.7 (−6.8 to −4.5)	−5.8 (−7.4 to −4.1)	3.5 (1.8 to 5.2)
LSM difference vs placebo, mm Hg (95% CI)	−8.0 (−10.3 to −5.6)	–	–	−9.2 (−11.2 to −7.1)	−9.2 (−11.6 to −6.8)	–
Office DBP at Month 3, patients with data	n = 68	–	–	n = 134	n = 64	n = 60
Mean DBP, mm Hg (SD)	81.6 (10.0)	–	–	79.8 (9.5)	80.0 (9.6)	86.8 (8.5)
LSM change from baseline, mm Hg (95% CI)	−5.3 (−7.2 to −3.4)	–	–	−7.0[b] (−8.4 to −5.7)	−5.4 (−7.3 to −3.5)	−0.6 (−2.6 to 1.3)
LSM difference vs placebo, mm Hg (95% CI)	−4.7 (−7.4 to −2.0)	–	–	−6.4[b] (−8.8 to −4.0)	−4.7 (−7.5 to −2.0)	–
Ambulatory DBP at Month 6, patients with data	n = 62	n = 68	n = 60	–	n = 63	n = 54
Mean DBP, mm Hg (SD)	76.8 (11.5)	75.9 (8.9)	75.6 (9.4)	–	74.2 (9.5)	83.1 (10.9)
LSM change from baseline, mm Hg (95% CI)	−4.8 (−6.6 to −3.0)	−6.1 (−7.9 to −4.4)	−6.3 (−8.1 to −4.5)	–	−6.3 (−8.0 to −4.5)	2.2 (0.3 to 4.1)
LSM difference vs placebo, mm Hg (95% CI)	−7.0 (−9.6 to −4.3)	−8.3 (−10.9 to −5.7)	−8.5 (−11.1 to −5.8)	–	−8.4 (−11.0 to −5.8)	–

	Zilebesiran 150 mg every 6 mo	Zilebesiran 300 mg every 6 mo	Zilebesiran 300 mg every 3 mo	Zilebesiran 300 mg every 3 mo or every 6 mo	Zilebesiran 600 mg every 6 mo	Placebo
Office DBP at Month 6, patients with data	n = 65	n = 68	n = 58	–	n = 62	n = 57
Mean DBP, mm Hg (SD)	83.2 (11.0)	81.3 (11.3)	77.6 (10.1)	–	79.8 (12.1)	86.1 (11.1)
LSM change from baseline, mm Hg (95%CI)	−4.1 (−6.3 to −1.8)	−6.8 (−9.0 to −4.6)	−8.2[c] (−10.5 to −5.8)	–	−5.0 (−7.3 to −2.8)	−1.2 (−3.6 to 1.2)
LSM difference vs placebo, mm Hg (95% CI)	−2.9 (−6.1 to 0.4)	−5.6 (−8.8 to −2.4)	−7.0[c] (−10.3 to −3.6)	–	−3.8 (−7.1 to −0.6)	–

Abbreviations: CI, confidence interval; DBP, diastolic blood pressure; LSM, least-squares mean; SD, standard deviation. [a]All randomized patients who received any amount of study drug, analyzed according to randomized treatment. [b]Data available for 133 patients. [c]Data available for 57 patients.

eTable 3. Change from Baseline to Month 3 in Mean Daytime and Nighttime Ambulatory SBP (Full Analysis Set[a])

	Zilebesiran 150 mg every 6 mo	Zilebesiran 300 mg every 3 mo or every 6 mo	Zilebesiran 600 mg every 6 mo	Placebo
Daytime (6AM to 9:59PM)				
Baseline, patients with data	n = 78	n = 148	n = 76	n = 75
Mean SBP, mm Hg (SD)	146.1 (7.9)	147.0 (8.1)	147.3 (7.4)	146.1 (7.2)
Month 3, patients with data	n = 68	n = 137	n = 65	n = 60
Mean SBP, mm Hg (SD)	138.1 (14.6)	136.2 (12.8)	137.6 (14.5)	151.9 (15.3)
LSM change from baseline, mm Hg (95% CI)	−7.6 (−10.7 to −4.6)	−10.3 (−12.5 to −8.2)	−8.9 (−12.0 to −5.8)	6.4 (3.2 to 9.6)
LSM difference vs placebo, mm Hg (95% CI)	−14.1 (−18.5 to −9.7)	−16.8 (−20.6 to −12.9)	−15.4 (−19.8 to −10.9)	–
Nighttime (10PM to 5:59AM)				
Baseline, patients with data	n = 78	n = 148	n = 76	n = 75
Mean SBP, mm Hg (SD)	129.2 (12.5)	131.9 (12.4)	134.6 (15.7)	131.1 (12.9)
Month 3, patients with data	n = 68	n = 137	n = 65	n = 60
Mean SBP, mm Hg (SD)	123.4 (18.1)	122.7 (16.0)	124.0 (17.7)	137.5 (18.6)
LSM change from baseline, mm Hg (95% CI)	−6.6 (−10.1 to −3.2)	−9.0 (−11.5 to −6.6)	−8.6 (−12.1 to −5.1)	6.6 (3.0 to 10.3)
LSM difference vs placebo, mm Hg (95% CI)	−13.3 (−18.3 to −8.2)	−15.7 (−20.1 to −11.3)	−15.2 (−20.3 to −10.2)	–

Abbreviations: CI, confidence interval; LSM, least-squares mean; SBP, systolic blood pressure; SD, standard deviation.
[a]All randomized patients who received any amount of study drug, analyzed according to randomized treatment.

eTable 4. Change from Baseline to Month 6 in Mean Daytime and Nighttime Ambulatory SBP (Full Analysis Set[a])

	Zilebesiran 150 mg every 6 mo	Zilebesiran 300 mg every 6 mo	Zilebesiran 300 mg every 3 mo	Zilebesiran 600 mg every 6 mo	Placebo
Daytime (6AM to 9:59PM)					
Baseline, patients with data	n = 78	n = 73	n = 75	n = 76	n = 75
Mean SBP, mm Hg (SD)	146.1 (7.9)	147.4 (8.0)	146.7 (8.3)	147.3 (7.4)	146.1 (7.2)
Month 6, patients with data	n = 62	n = 68	n = 60	n = 63	n = 54
Mean SBP, mm Hg (SD)	139.1 (15.8)	136.6 (13.0)	136.6 (12.1)	137.0 (17.2)	149.5 (15.3)
LSM change from baseline, mm Hg (95% CI)	−6.9 (−10.3 to −3.6)	−10.4 (−13.6 to −7.1)	−9.3 (−12.7 to −5.8)	−8.8 (−12.2 to −5.5)	4.5 (0.9 to 8.1)
LSM difference vs placebo, mm Hg (95% CI)	−11.4 (−16.4 to −6.5)	−14.8 (−19.7 to −10.0)	−13.8 (−18.7 to −8.8)	−13.3 (−18.3 to −8.4)	–
Nighttime (10PM to 5:59AM)					
Baseline, patients with data	n = 78	n = 73	n = 75	n = 76	n = 75
Mean SBP, mm Hg (SD)	129.2 (12.5)	132.5 (13.9)	131.2 (10.8)	134.6 (15.7)	131.1 (12.9)
Month 6, patients with data	n = 62	n = 68	n = 60	n = 63	n = 54
Mean SBP, mm Hg (SD)	124.7 (15.8)	123.3 (18.2)	121.5 (14.7)	120.7 (18.4)	134.9 (16.7)
LSM change from baseline, mm Hg (95% CI)	−5.8 (−9.3 to −2.4)	−8.9 (−12.2 to −5.5)	−10.2 (−13.7 to −6.7)	−11.1 (−14.5 to −7.6)	4.7 (1.0 to 8.3)
LSM difference vs placebo, mm Hg (95% CI)	−10.5 (−15.5 to −5.5)	−13.5 (−18.5 to −8.6)	−14.9 (−19.9 to −9.8)	−15.7 (−20.7 to −10.7)	–

Abbreviations: CI, confidence interval; LSM, least-squares mean; SBP, systolic blood pressure; SD, standard deviation.
[a]All randomized patients who received any amount of study drug, analyzed according to randomized treatment.

eTable 5. Add-on Antihypertensive Use During the Double-Blind Treatment Period (Safety Analysis Set[a])

	Zilebesiran 150 mg every 6 mo (N = 78)	Zilebesiran 300 mg every 6 mo (N = 73)	Zilebesiran 300 mg every 3 mo (N = 75)	Zilebesiran 600 mg every 6 mo (N = 76)	Zilebesiran total (N = 302)	Placebo (N = 75)
At least 1 medication	25 (32.1)	15 (20.5)	20 (26.7)	21 (27.6)	81 (26.8)	39 (52.0)
Selective calcium channel blockers with mainly vascular effects	13 (16.7)	10 (13.7)	14 (18.7)	14 (18.4)	51 (16.9)	26 (34.7)
Amlodipine	10 (12.8)	6 (8.2)	12 (16.0)	9 (11.8)	37 (12.3)	19 (25.3)
Amlodipine besilate	2 (2.6)	3 (4.1)	1 (1.3)	3 (3.9)	9 (3.0)	3 (4.0)
Nifedipine	1 (1.3)	1 (1.4)	1 (1.3)	1 (1.3)	4 (1.3)	4 (5.3)
Citicoline; nimodipine	0	0	0	1 (1.3)	1 (0.3)	0
Low-ceiling diuretics, thiazides	11 (14.1)	3 (4.1)	4 (5.3)	4 (5.3)	22 (7.3)	8 (10.7)
Hydrochlorothiazide	11 (14.1)	3 (4.1)	4 (5.3)	4 (5.3)	22 (7.3)	8 (10.7)
Low-ceiling diuretics, excluding thiazides	1 (1.3)	0	1 (1.3)	1 (1.3)	3 (1.0)	4 (5.3)
Indapamide	1 (1.3)	0	0	1 (1.3)	2 (0.7)	1 (1.3)
Chlorthalidone	0	0	1 (1.3)	0	1 (0.3)	3 (4.0)
Angiotensin II receptor blockers, plain	0	0	0	1 (1.3)	1 (0.3)	2 (2.7)
Irbesartan	0	0	0	1 (1.3)	1 (0.3)	0
Losartan	0	0	0	0	0	2 (2.7)
Agents acting on arteriolar smooth muscle	0	0	0	0	0	1 (1.3)
Hydralazine	0	0	0	0	0	1 (1.3)
ACE inhibitors, combinations	0	2 (2.7)	0	0	2 (0.7)	1 (1.3)
Hydrochlorothiazide; lisinopril	0	2 (2.7)	0	0	2 (0.7)	0
Amlodipine besilate; benazepril hydrochloride	0	0	0	0	0	1 (1.3)
ACE inhibitors, plain	1 (1.3)	0	0	3 (3.9)	4 (1.3)	0
Lisinopril	1 (1.3)	0	0	2 (2.6)	3 (1.0)	0
Perindopril	0	0	0	1 (1.3)	1 (0.3)	0
Perindopril erbumine	0	0	0	1 (1.3)	1 (0.3)	0
Beta-blocking agents	0	0	1 (1.3)	3 (3.9)	4 (1.3)	0
Metoprolol	0	0	1 (1.3)	2 (2.6)	3 (1.0)	0
Bisoprolol	0	0	0	2 (2.6)	2 (0.7)	0
Metoprolol succinate	0	0	0	1 (1.3)	1 (0.3)	0
Beta-blocking agents and other diuretics	0	0	0	1 (1.3)	1 (0.3)	0
Atenolol; chlortalidone	0	0	0	1 (1.3)	1 (0.3)	0

	Zilebesiran 150 mg every 6 mo (N = 78)	Zilebesiran 300 mg every 6 mo (N = 73)	Zilebesiran 300 mg every 3 mo (N = 75)	Zilebesiran 600 mg every 6 mo (N = 76)	Zilebesiran total (N = 302)	Placebo (N = 75)
High-ceiling diuretics	1 (1.3)	0	0	1 (1.3)	2 (0.7)	0
Furosemide sodium	1 (1.3)	0	0	0	1 (0.3)	0
Furosemide	0	0	0	1 (1.3)	1 (0.3)	0
Selective calcium channel blockers with direct cardiac effects	1 (1.3)	0	0	1 (1.3)	2 (0.7)	0
Diltiazem hydrochloride	1 (1.3)	0	0	1 (1.3)	2 (0.7)	0

Abbreviations: ACE, angiotensin-converting enzyme. [a]All patients who received any amount of study drug, grouped according to the treatment actually received. Each patient was counted once for each applicable anatomical therapeutic class or preferred term. Medications were coded using the WHO Drug Dictionary (March 2023).

eTable 6. Change from Baseline to Month 6 in Serum Creatinine, eGFR, and Serum Glucose (Safety Analysis Set[a])

	Zilebesiran 150 mg every 6 mo (N = 78)	Zilebesiran 300 mg every 6 mo (N = 73)	Zilebesiran 300 mg every 3 mo (N = 75)	Zilebesiran 600 mg every 6 mo (N = 76)	Placebo (N = 75)
Serum creatinine (µmol/L)					
Baseline, n Mean (SD)	78 81.1 (18.6)	73 81.4 (15.7)	75 84.1 (18.8)	76 82.7 (19.0)	75 85.0 (25.3)
Week 2, n Mean (SD)	74 82.6 (19.1)	72 83.8 (15.3)	73 84.2 (20.7)	73 84.1 (21.2)	71 86.5 (27.2)
Percentage change from BL, mean (SD)	2.2 (8.7)	3.8 (11.7)	0.3 (8.9)	1.9 (8.7)	1.2 (8.6)
Month 1, n Mean (SD)	77 82.3 (17.5)	73 83.3 (15.3)	70 86.6 (20.2)	73 86.0 (20.9)	71 85.6 (26.9)
Percentage change from BL, mean (SD)	1.9 (9.7)	3.2 (13.6)	2.7 (10.8)	4.6 (12.4)	1.6 (19.4)
Month 2, n Mean (SD)	73 83.7 (19.1)	72 83.3 (16.2)	70 86.8 (20.1)	72 86.3 (21.3)	72 86.6 (22.2)
Percentage change from BL, mean (SD)	2.6 (10.1)	3.4 (12.4)	2.8 (8.4)	4.4 (8.5)	4.8 (17.7)
Month 3, n Mean (SD)	73 82.0 (18.8)	71 82.4 (14.6)	72 86.1 (21.6)	71 85.3 (19.5)	72 86.4 (23.5)
Percentage change from BL, mean (SD)	1.8 (9.4)	2.0 (9.5)	1.8 (9.5)	3.9 (10.2)	3.9 (22.4)
Month 4, n Mean (SD)	69 84.3 (19.9)	70 84.2 (15.7)	70 87.6 (21.0)	69 86.6 (20.1)	70 86.4 (23.9)
Percentage change from BL, mean (SD)	3.5 (9.7)	4.5 (10.7)	3.5 (10.6)	4.7 (9.9)	4.4 (21.7)
Month 6, n Mean (SD)	69 82.8 (20.7)	69 83.8 (16.0)	68 87.0 (19.3)	67 85.3 (19.7)	69 86.2 (23.0)
Percentage change from BL, mean (SD)	2.4 (11.0)	4.0 (11.6)	3.4 (10.0)	3.8 (11.0)	3.7 (14.6)
eGFR (mL/min/1.73 m^2)					
Baseline, n Mean (SD)	78 81.7 (16.5)	73 82.0 (14.5)	75 80.2 (18.3)	76 81.9 (19.4)	75 78.7 (21.0)
Week 2, n Mean (SD)	74 79.9 (17.3)	72 79.3 (15.0)	73 80.8 (20.0)	73 80.8 (21.5)	71 77.2 (20.7)

	Zilebesiran 150 mg every 6 mo (N = 78)	Zilebesiran 300 mg every 6 mo (N = 73)	Zilebesiran 300 mg every 3 mo (N = 75)	Zilebesiran 600 mg every 6 mo (N = 76)	Placebo (N = 75)
Percentage change from BL, mean (SD)	−1.6 (9.3)	−2.8 (11.6)	0.6 (10.1)	−1.3 (9.5)	−0.5 (9.5)
Month 1, n Mean (SD)	77 80.1 (16.5)	73 79.9 (14.9)	70 78.6 (19.4)	73 78.4 (19.8)	71 78.0 (21.4)
Percentage change from BL, mean (SD)	−1.1 (10.2)	−1.7 (13.8)	−1.8 (11.3)	−3.6 (11.9)	0.5 (12.7)
Month 2, n Mean (SD)	73 79.9 (17.2)	72 80.0 (16.7)	70 77.4 (17.9)	72 78.3 (20.5)	72 76.0 (20.5)
Percentage change from BL, mean (SD)	−1.9 (10.1)	−2.1 (13.5)	−2.3 (9.9)	−4.1 (8.6)	−2.8 (14.6)
Month 3, n Mean (SD)	73 80.8 (17.8)	71 80.7 (14.9)	72 78.9 (19.4)	71 79.2 (20.7)	72 76.6 (21.2)
Percentage change from BL, mean (SD)	−1.0 (10.2)	−1.2 (11.2)	−1.0 (11.2)	−3.2 (11.0)	−1.5 (13.6)
Month 4, n Mean (SD)	69 78.5 (16.7)	70 78.7 (15.7)	70 77.0 (18.5)	69 77.8 (20.2)	70 76.2 (20.1)
Percentage change from BL, mean (SD)	−2.9 (9.5)	−3.7 (12.1)	−2.6 (11.8)	−4.1 (10.9)	−2.1 (13.6)
Month 6, n Mean (SD)	69 80.2 (17.5)	69 79.7 (16.5)	68 77.1 (18.4)	67 78.3 (17.8)	69 76.1 (18.9)
Percentage change from BL, mean (SD)	−1.5 (10.5)	−2.9 (12.9)	−2.7 (10.7)	−3.0 (11.4)	−2.4 (12.0)
Serum glucose (mmol/L)					
Baseline, n Mean (SD)	78 5.6 (1.5)	73 5.5 (1.1)	75 5.8 (1.4)	76 5.7 (1.2)	75 5.6 (1.8)
Week 2, n Mean (SD)	73 6.2 (1.8)	70 6.1 (1.9)	73 6.2 (2.0)	73 6.0 (1.4)	67 6.1 (2.7)
Percentage change from BL, mean (SD)	8.9 (18.0)	10.8 (23.5)	6.9 (18.9)	7.2 (22.9)	7.1 (20.7)
Month 1, n Mean (SD)	77 6.1 (2.0)	73 5.7 (1.0)	69 6.1 (1.2)	72 5.9 (1.3)	70 6.0 (2.0)
Percentage change from BL, mean (SD)	8.2 (18.4)	4.9 (17.6)	5.8 (18.9)	6.1 (24.7)	9.8 (31.2)
Month 2, n Mean (SD)	72 6.0 (1.7)	70 5.7 (1.2)	70 5.9 (1.3)	72 6.0 (1.2)	72 6.2 (3.2)

	Zilebesiran 150 mg every 6 mo (N = 78)	Zilebesiran 300 mg every 6 mo (N = 73)	Zilebesiran 300 mg every 3 mo (N = 75)	Zilebesiran 600 mg every 6 mo (N = 76)	Placebo (N = 75)
Percentage change from BL, mean (SD)	6.3 (15.0)	5.6 (18.1)	3.5 (17.1)	7.8 (20.4)	10.6 (34.5)
Month 3, n Mean (SD)	73 5.9 (2.0)	71 5.5 (1.0)	71 5.7 (1.0)	71 5.8 (1.5)	72 5.8 (2.0)
Percentage change from BL, mean (SD)	3.6 (13.9)	1.2 (11.2)	0.9 (16.2)	4.9 (25.5)	4.9 (30.6)
Month 4, n Mean (SD)	68 6.2 (1.8)	69 5.8 (1.1)	70 6.3 (1.8)	69 6.1 (1.6)	70 6.1 (2.6)
Percentage change from BL, mean (SD)	9.2 (20.5)	5.7 (17.9)	8.7 (18.8)	10.8 (26.7)	7.7 (23.0)
Month 6, n Mean (SD)	68 5.8 (2.3)	69 5.6 (1.3)	68 5.9 (1.6)	67 5.9 (1.8)	68 6.0 (3.7)
Percentage change from BL, mean (SD)	3.1 (18.4)	3.0 (17.6)	2.4 (19.1)	3.5 (25.3)	9.3 (82.7)

Abbreviations: BL, baseline; eGFR, estimated glomerular filtration rate; SD, standard deviation. [a]All patients who received any amount of study drug, grouped according to the treatment actually received.