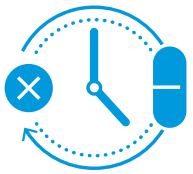


KARDIA-3 Study Design: Zilebesiran as Add-On Therapy in Patients with High Cardiovascular Risk and Hypertension Inadequately Controlled by Standard of Care Antihypertensives

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Nonadherence to SoC daily oral regimens contributes to inadequate BP control



Zilebesiran is an investigational RNA interference therapeutic targeting hepatic AGT synthesis with potential for biannual SC dosing

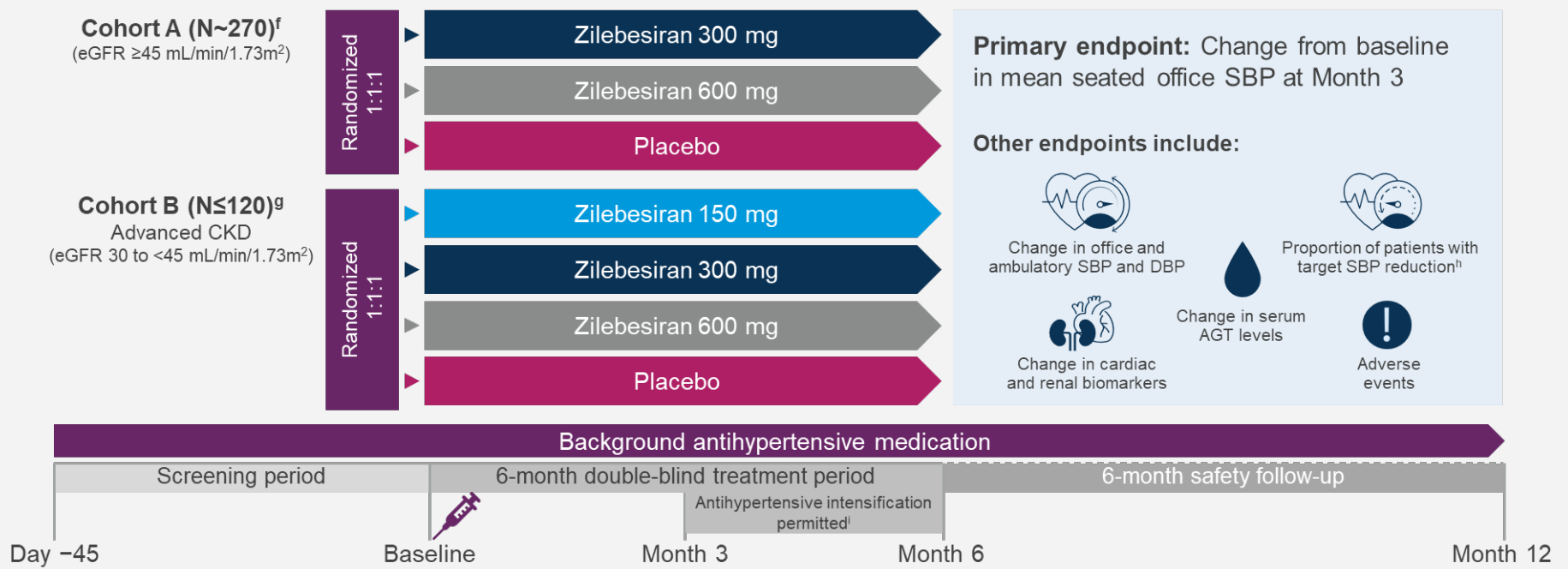


A single SC dose of zilebesiran significantly reduced 24-hour mean ambulatory and office SBP from baseline to Month 3, with effects largely sustained to Month 6, compared with placebo when used as:

- monotherapy in KARDIA-1^{1,a}
- add-on to SoC therapy in KARDIA-2^{2,b}

KARDIA-3^c is evaluating a single SC dose of zilebesiran in adults with CVD or at high CV risk

- History of CVD and/or 10-year ASCVD risk >15% and/or eGFR 30<60 mL/min/1.73 m²
- Inadequate BP control with two to four antihypertensives:
 - office SBP^d 140–170 mmHg at screening
 - ambulatory SBP^e 130–170 mmHg before randomization



Trial status: ongoing/enrolling as of May 2024

^aNCT04936035. ^bNCT05103332. ^cNCT06272487. ^dSeated automated office SBP. ^e24-hour mean ambulatory SBP. ^fCohort A will be analyzed based on statistical modeling, and summarized descriptively. ^gCohort B will be summarized descriptively by treatment group. ^hMean SBP <140 mmHg (seated office SBP) or <130 mmHg (24-hr mean ambulatory SBP), or ≥10 mmHg reduction, and no intensification of antihypertensives. ⁱAntihypertensives may be intensified per investigator judgment. AGT, angiotensinogen; ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; hr, hour; Q6M, every 6 months; SBP, systolic blood pressure; SC, subcutaneous; SoC, standard of care. 1. Bakris GL *et al.* JAMA 2024;331:740–9. 2. Desai AS *et al.* Oral presentation 21475 presented at the American College of Cardiology Annual Scientific Session & Expo, April 7, 2024, Atlanta, GA, USA.