KHC
The Kidney and Hypertension Center

ZENITH Study

Study drug: **Zilebesiran**
an RNAi therapeutic agent targeting hepatic AGT synthesis

Dose and dose form: **300 mg every 6 months** subcutaneous injection

Study duration: **5 years**
Across 1500 sites, total sponsor enrollment goal of 11,000

Previous studies showed that zilebesiran has an acceptable safety profile across all doses tested in all Phase 1 and Phase 2 studies.

Low rates of hypotension, hyperkalemia, and kidney dysfunction, including in patients on background treatment with ACE-inhibitors or ARBs

INCLUSION/EXCLUSION

Key Inclusion Criteria

- Age: ≥18 yrs
- Established **CVD OR high risk of CVD**
- Treated HTN on stable therapy with 2 or more standard of care HTN medications
  (Must include a **diuretic**)
- Office SBP ≥ 145 and < 180 mmHg at screening

Key Exclusion Criteria

- Secondary HTN
- Serum potassium > 4.8 mEq/L
- ALT or AST >3xULN, total bilirubin > 1.5xULN, INR > 1.5 (unless on anticoagulation)
- HbA1c ≥ 10%
- Weight loss > 10% in 3 mo prior to screening
- eGFR <30 ml/min/1.73 m2
- LVEF < 40%
- CV event within 60 days prior to screening or during the screening perio

PRIMARY OBJECTIVE

To evaluate whether zilebesiran versus placebo **reduces the risk of CV death, nonfatal MI, nonfatal stroke, or HF events**

Primary Endpoint

Time to first occurrence of a composite endpoint of CV death, nonfatal MI, nonfatal stroke, or HF event (hospitalization for HF or urgent HF visit)

Secondary Endpoints

- Change from baseline to 6 mo in mean seated systolic BP (taken in office)
- Time to first occurrence of composite endpoint of CV death, nonfatal MI, nonfatal stroke, or coronary revascularization

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