STUDY PROTOCOL

Document Date: January 20, 2025
Official Title: A Multicenter, Prospective, Observational Study on the Efficacy and Safety of Benidipine in Patients with Hypertension and Stable Angina Pectoris in Turkey (Benidipine-TR)
NCT Number: NCT06808321

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1. BACKGROUND AND RATIONALE

Hypertension and stable angina pectoris are major contributors to cardiovascular morbidity and mortality in Turkey. Benidipine hydrochloride is a triple-acting calcium channel blocker (CCB) that inhibits L, T, and N-type calcium channels, providing renal protection and maintaining heart rate neutrality. While its pharmacological profile is known, "real-world" observational data in the Turkish population is needed to assess clinical performance and treatment persistence.

2. STUDY OBJECTIVES

- **Primary Objective:**
  - To evaluate the clinical effectiveness of Benidipine in achieving target blood pressure levels (<130/85 mmHg) in a real-world cardiology outpatient setting.
  - To assess reduction in angina frequency and severity using the CCS grading scale.
- **Secondary Objectives:**
  - To evaluate treatment persistence and patient compliance over a 3-month period.

3. STUDY DESIGN

- **Type:** Observational, Prospective, Multicenter.
- **Setting:** Cardiology centers across all seven geographical regions of Türkiye.
- **Duration:** 3-month follow-up per participant.

4. ELIGIBILITY CRITERIA

4.1 Inclusion Criteria

- Adult patients aged 18 to 80 years.
- Diagnosis of essential hypertension and/or stable angina.
- Independent clinical decision by a cardiologist to prescribe Benidipine.
- Signed Informed Consent Form (ICF).

4.2 Exclusion Criteria

- Secondary hypertension or hypertensive emergencies.
- Severe renal impairment (creatinine clearance <30 mL/min) or severe hepatic failure.
- Pregnancy, lactation, or women of childbearing potential without contraception.
- Hypersensitivity to dihydropyridine CCBs.

5. STUDY PROCEDURES AND DATA COLLECTION

This is a non-interventional study; all medical decisions (including 4mg or 8mg dosage) are at the investigator's discretion.

1. **Baseline (Visit 1):** Demographics, medical history, BP, HR, CCS grade, and laboratory parameters (LDL-C, Serum Creatinine).
2. **Final Follow-up (Visit 2 - Month 3):** BP and HR measurements, CCS reassessment, medication changes, and adverse event documentation.

6. STATISTICAL ANALYSIS PLAN (SAP)

- **Analysis Populations:** Safety analysis includes all enrolled patients; efficacy analysis is based on the Per-Protocol set.
- **Methods:** Continuous variables will be compared using the Paired-Sample T-test. Categorical data will be analyzed using Chi-square or Wilcoxon Signed-Rank tests.
- **Sample Size:** A minimum of 1,500 participants is required for 90% power (alpha=0.05, SD = 15 mmHg). Aiming for 1,650–1,700 participants to account for a 10% drop-out rate.
- **Significance:** A two-sided p-value < 0.05 is statistically significant.

7. ETHICAL CONSIDERATIONS

The study adheres to the Declaration of Helsinki. The protocol and ICF are approved by the relevant Institutional Ethics Committee. Patient confidentiality is maintained through anonymized coding.