Overall treatment effect estimates derived from the LEGEND-Hypertension study can be supplemented with risk stratified analyses

**Title:** Evaluation of treatment effect heterogeneity in the LEGEND-Hypertension study.

**Background:** The LEGEND-Hypertension study generated overall effect estimates for all drug classes used in the treatment of hypertension. We supplement these results with evaluation of treatment effect heterogeneity using a new risk-based framework.

Result 1: Results within strata of predicted acute MI risk on the absolute scale in CCAE.

Result 2: Results within strata of predicted acute MI risk on the absolute scale in MDCD.

**Methods**

**Prediction:** We stratify the population on their baseline acute MI risk. We develop prediction models for each database and treatment-comparator pair separately using LASSO logistic regression based on a large pre-defined set of baseline covariates.

**Estimation:** We stratify patients into three risk groups (acute MI risk below 1%, between 1% and 1.5%, and above 1.5%). We use Cox regression to estimate relative effects. We derive absolute risk differences from the differences between the Kaplan-Meier curves on day 730 from treatment initiation.