

Supplementary Table 1. Deviations from protocol	
Deviation	Reason
Using propensity-score—weighting as opposed to propensity-score—matching (with propensity-score—matching carried out as an additional analysis)	To obtain average treatment effect as opposed to average treatment effect on treated and increase sample size
Underrepresented group analysis on propensity-score—weighted sample as opposed to propensity-score—matched cohort	This was to increase sample size as comparison between both analyses gave almost identical results
Primary outcome: including both fatal and non-fatal events for stroke and myocardial infarction	Consistency with trial
Included additional outcome- main secondary outcome: composite of cardiovascular-related death, myocardial infarction or stroke	Consistency with trial
Angina inclusion criteria: Removed condition that needed to have previous coronary artery disease diagnosis	Misclassification
CABG Inclusion criteria: Removed condition that could be with angina	Only included events where CABG was within 4 years prior to avoid due to potential of capturing old events
Comparing reason for discontinuation to safety outcomes in trial as opposed to events occurring within 3 months	Consistency with safety outcomes reported in trial
Objective of extending follow-up for safety events	Have not yet addressed this objective due to difficulty replicating safety trial results
Renal function omitted from propensity-score model	Due to large amounts of missingness
Adherence assessed differently and instead reported proportions of patients receiving each drug at different timepoints	Consistency with trial
Additional subgroups studied	To further demonstrate trial replicability and quantify effect modification
On-treatment (per-protocol) analysis for secondary objectives 1 and 2 (extending findings to trial-underrepresented and excluded groups)	Not deemed necessary as on-treatment analysis was sufficiently comparable to ITT for primary outcome
Previously mentioned that patients had to meet inclusion and exclusion criteria prior to start of first exposed period instead trial criteria assessed at start of all exposed periods	Incorrect wording in protocol this reduces bias by assessing at start of follow up
Referred to analysis group as trial-analogous now analysis groups will be labelled as propensity-score—weighted trial-eligible for main analysis and propensity-score—matched trial-eligible for sensitivity analysis	To avoid confusion as only the ACEi trial-eligible cohort is trial-matched
Naming of nephropathy outcomes	Changed from nephropathy 1 and nephropathy 2 to loss of eGFR or ESKD and ESKD
Nephropathy 1 sensitivity analysis requiring 2 measurements at least 3 months apart for both eGFR<15 and 50% reduction in eGFR	Previously stated this is only required for 50% reduction in eGFR which was incorrect