

Supplementary Table 8: Safety outcomes assessed among non-switchers using trial criteria and propensity-score—weighting for ARB vs ACEi (sensitivity analysis)

Safety outcome	CPRD			ONTARGET
	Reason for treatment cessation			telmisartan vs ramipril
	ARB (N=11,856)	ACEi (N=90,597)	ARB vs ACEi	
	<i>Number (percent)</i>		<i>Relative risk (95% CI)</i>	<i>Relative risk (P value)</i>
Cough	178 (1.5)	1455 (1.6)	0.84 (0.70, 1.01)	0.26 (<0.001)
Angioedema	10 (0.08)	77 (0.08)	0.72 (0.35, 1.48)	0.4 (0.01)
Hyperkalaemia ¹	685 (7.7)	5473 (7.4)	1.06 (0.97, 1.16)	
≥30% increase in serum creatinine	1730 (18.8)	11781 (15.5)	1.25 (1.18, 1.31)	1.14 (0.01) ²

Notes: In CPRD, treatment cessation is defined as the end date of the trial-eligible exposed period included in analysis (i.e., the date prior to a prescription gap of >90 days) and the latest event occurring prior to end of trial-eligible period is counted as the reason for treatment cessation. Multiple reasons that occur on the same day are both counted.

Reason for treatment cessation represents the main analysis which is compared to ONTARGET and events occurring within 3 months represents the additional analysis exploring safety events which occur within 3 months of the start of eligible period.

Non-switchers include first trial-eligible period per patient and excludes patients with previous exposure to opposing drug at any time prior to start of included trial-eligible period.

Both analyses are adjusted for number of previous GP appointments within 6 months prior.

¹Defined as potassium >5.5 mmol/l. Analysis out of number of people with non-missing potassium.

Definition of kidney impairment in ONTARGET is not stated so results are not directly comparable to CPRD

Kidney outcomes are adjusted for baseline serum creatinine and are out of the number of people with non-missing eGFR in CPRD.

ONTARGET did not present 95% CI.