



## Q/ Do ACE inhibitors or ARBs help prevent kidney disease in patients with diabetes and normal BP?

Gregory S. Trietley, PharmD, BCPS; Stephen A. Wilson, MD, MPH; Parul Chaudhri, DO; Nicole Payette, PharmD, BCPS  
UPMC St. Margaret, Pittsburgh, Pa

Ashley Higbee, PharmD, BCPS  
Texas Tech University Health Science Center, Dallas

Joan Nashelsky, MLS  
Family Physician Inquiries Network, Iowa City, Iowa

**DEPUTY EDITOR**

Gary Kelsberg, MD  
Valley Family Medicine Residency, Renton, Wash

### EVIDENCE-BASED ANSWER

**A** YES for angiotensin-converting enzyme (ACE) inhibitors, no for angiotensin receptor blockers (ARBs).

In normotensive patients with type 1 and type 2 diabetes, ACE inhibitor therapy reduces the risk of developing diabetic kidney disease, defined as new-onset microalbuminuria or macroalbuminuria, by 18% (strength of recommendation [SOR]: C, meta-analysis of randomized controlled trials [RCTs], disease-oriented evidence).

ACE inhibitor treatment improves all-cause mortality by 16% in patients with

diabetes, including patients with and without hypertension. Patients on ACE inhibitor therapy are at increased risk of cough (SOR: A, meta-analysis of RCTs).

ARB therapy doesn't lower the risk of developing kidney disease in normotensive patients with type 2 diabetes (SOR: C, meta-analysis of RCTs, disease-oriented evidence); nor does it reduce all-cause mortality in patients with or without hypertension (SOR: A, meta-analysis of RCTs). ARBs aren't associated with significant adverse events (SOR: A, meta-analysis of RCTs).

### Evidence summary

A 2011 meta-analysis of 5 RCTs (total 2975 patients) that compared ACE inhibitor therapy with placebo in diabetic patients without hypertension and albuminuria found that ACE inhibitors reduced the risk of new-onset microalbuminuria or macroalbuminuria by 18% (relative risk [RR]=0.82; 95% confidence interval [CI], 0.73-0.92).<sup>1</sup> Normal albuminuria was defined in all included studies as an albumin excretion rate of <30 mg/d on a timed specimen confirmed with 3 serial measurements.

The RCTs included patients treated with lisinopril, enalapril, and perindopril. All but one examined patients with type 1 diabetes (2781 patients). The study that evaluated type 2 diabetes (194 patients) assessed patients with hypertension who used other antihypertensives to achieve normal blood pressure targets before ACE inhibitor initiation, a potential limitation.

Compared with placebo or no treat-

ment, ACE inhibitor therapy reduced the risk of death from any cause (6 studies; 11,350 patients; RR=0.84; 95% CI, 0.73-0.97).<sup>1</sup> Patient populations across pooled RCTs were heterogeneous, including subjects with type 1 and type 2 diabetes, with or without hypertension, and with or without albuminuria.

#### ACE inhibitors increase risk of cough

Patients taking an ACE inhibitor have an increased risk of cough (6 studies; 11,791 patients; RR=1.84; 95% CI, 1.24-2.72).<sup>1</sup> ACE inhibitor therapy doesn't increase the risk of headache or hyperkalemia.

#### ARBs don't help prevent diabetic kidney disease in normotensive patients

The 2011 meta-analysis also included 5 RCTs (4604 patients, approximately 3000 with type 2 diabetes and more than 1000 with type 1 diabetes) that compared ARBs with placebo in patients without hypertension.<sup>1</sup> Unlike

CONTINUED ON PAGE 263

CONTINUED FROM PAGE 257

ACE inhibitor therapy, ARB treatment didn't significantly affect new-onset microalbuminuria or macroalbuminuria (RR=1.06; 95% CI, 0.67-1.69).

The trials evaluated losartan, candesartan, olmesartan, and valsartan. One study used other antihypertensives to achieve target blood pressure, and another included patients of any albuminuria status.

Compared with placebo or no treatment, ARBs didn't reduce the risk of death (5 studies; 7653 patients; RR=1.12; 95% CI, 0.88-1.41).<sup>1</sup> All 5 RCTs assessed normal-albuminuric patients. Three of the 5 studies

examined normotensive patients; one evaluated only hypertensive patients, and another assessed mostly hypertensive patients.

**ARBs usually don't produce significant adverse effects**

Within the meta-analysis, ARBs didn't increase risk of cough, headache, or hyperkalemia.<sup>1</sup>

JFP

Reference

1. Lv J, Perkovic V, Foote CV, et al. Antihypertensive agents for preventing diabetic kidney disease. *Cochrane Database Syst Rev.* 2012;(12):CD004136.

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