

CHRONIC KIDNEY DISEASE: FACT SHEET

RENIN INHIBITORS FOR THE TREATMENT OF CHRONIC KIDNEY DISEASE

OVERVIEW

Chronic kidney disease (CKD) is a worldwide health problem that is the result of the progressive loss of kidney function over a period of months to years. CKD is significantly under diagnosed at the early stages of the disease especially when there are no overt symptoms. The kidney functions to maintain fluid volume and electrolytes (sodium, potassium, chloride, bicarbonate) and remove wastes and toxins from the body. The progressive damage to the kidney in CKD patients hinders this process, allowing wastes to build up in the blood, leading to complications such as high blood pressure, abnormal heart rhythm, anemia, nerve damage and weak bones.

The National Kidney Foundation has provided guidelines to monitor the progression of kidney damage by determining the ratio of two key protein biomarkers in urine, albumin vs. creatinine (termed the albumin-to-creatinine ratio or ACR). This ratio approximates the amount of albumin that is excreted. Considerable evidence from the past decade indicates that the presence of even small amounts of albumin in the urine is an important early indicator of kidney disease.

The prevalence of CKD has risen more than 25% over the last decade and is currently estimated at 27 million people in the United States. Currently, the Centers for Disease Control and Prevention (CDC) list CKD as the 9th leading cause of death in the United States.

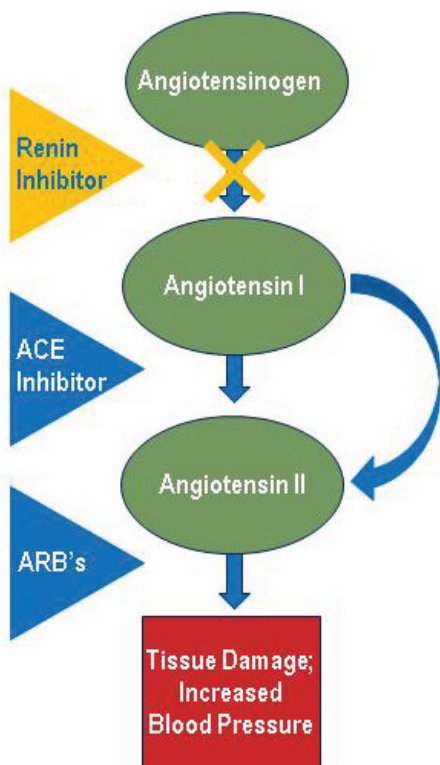
The majority of CKD, ~60% or 14 million people in the United States, is caused by diabetes and hypertension. Most current treatment regimes for CKD are focused on controlling blood pressure by administering anti-hypertension drugs and by controlling diet and glucose levels in diabetic patients with oral drugs or insulin.

THE RENIN ANGIOTENSION SYSTEM

The renin angiotension system (RAS) plays the primary role in regulating blood volume, blood pressure and vascular function in the body. Renin is the first and rate limiting step in the renin-angiotensin system (see illustration below). Tissues (e.g. kidney, heart, eye and brain) also contain RAS that is active independent of the systemic RAS effects on blood pressure. This direct effect of RAS in tissues appears to play a key role in the development of chronic kidney disease.

Protection of the kidney has been demonstrated in studies with the currently marketed RAS inhibitors such as angiotensin-converting enzyme (ACE), angiotensin receptor blockers (ARB) and the renin inhibitor Tekturna® (aliskiren). These studies showed a reduction in the amount of the biomarker albumin excreted in urine, as well as a delay in the progression of chronic kidney disease to end-stage renal disease (ESRD). Significantly, the kidney protection effect of these drugs was independent of any effects the RAS inhibitors had on reducing blood pressure. Although ACE inhibitors and ARBs can slow the progression of chronic kidney disease, many patients still progress to ESRD. There is still a clear need for additional strategies to block RAS more effectively to provide better kidney protection or to even prevent chronic kidney disease.

Renin is synthesized by the kidney in response to a decrease in blood pressure or circulating blood volume. Renin cleaves the plasma protein angiotensinogen, to generate a small protein or peptide angiotensin I. Angiotensin I is then converted to the active hormone, angiotensin II, primarily via angiotensin converting enzyme (ACE). Ultimately, angiotensin II induces vascular constriction and increases renal sodium retention thereby increasing blood pressure.



Damage to Kidney, Heart, Eye, Brain

VITAE'S RENIN INHIBITION PROGRAM

Researchers at Vitae have employed the company's proprietary technology to discovery, in less than 12 months, orally efficacious, small molecule inhibitors of renin. The company's development lead, VTP-27999, is a novel, potent and selective direct renin inhibitor that has demonstrated protection of kidneys and survival benefits in animal models, as well as significant and sustained reductions in blood pressure. In addition, results from a single ascending dose Phase I study in humans have demonstrated VTP-27999 is generally safe and well-tolerated, has good bioavailability and a pharmacokinetic profile supporting once-daily dosing.

Additional Phase I studies are underway and Vitae expects to complete Phase II studies before the end of 2011. This development plan aligns well with the timing of expected results from Novartis's broad, \$1 billion, 35,000-patient post-marketing program of morbidity and mortality trials for Tekturna®, the first marketed renin inhibitor. Results from the Novartis program, which are expected mid-2011 and beyond, will validate the superiority of the renin inhibitor class to protect the kidney and other organs over current treatments. Vitae believes that the clinical profile of VTP-27999 will be superior to Tekturna®, with expected advantages in terms of kidney protection, potency, bioavailability and tolerability.