

Irbesartan Improves Survival in Renal Disease

The drug is cost-effective, should be initiated early, and continued long term in diabetic patients with hypertensive kidney disease.

REVIEWED BY ANDREW J. PALMER, BSC, MBBS

Treating type 2 diabetic patients with irbesartan when they first develop microalbuminuria will reduce costs and extend life expectancy, according to researchers.¹ While later use of the angiotensin receptor blocker (ARB) in overt nephropathy is superior to the standard of care, early initiation is recommended.

“This study identified the most efficient time point at which [ARB] treatment with irbesartan for renal disease associated with type 2 diabetes and hypertension should be initiated,” said Andrew J. Palmer, BSc, MBBS, from the CORE-Center for Outcomes Research in Basel, Switzerland. “The study demonstrated the importance of early treatment of patients with type 2 diabetes, hypertension and microalbuminuria,” Dr. Palmer and colleagues reported results in *Diabetes Care*.

DIABETES AND KIDNEY DISEASE

- 10% to 21% of all people with diabetes have nephropathy.
- Approximately 43% of new cases of ESRD are attributed to diabetes.
- ESRD attributed to diabetes is increasing more rapidly than ESRD due to other causes. From 1988 to 1991, diabetes accounted for 33.8% of new ESRD cases, an increase of 23% of new cases in 1982. By 1999, this number reached 43%.
- In the United States, the incidence of reported ESRD in people with diabetes is more than four times as high in African-Americans, four to six times as high in Mexican-Americans and 6 times as high in American-Indians than in the general population of diabetes patients.
- The risk of ESRD is 12 times as high in people with type 1 diabetes as in those with type 2 diabetes.
- In patients with type 1 diabetes who develop persistent proteinuria, ESRD or death usually follows after about 5 to 10 years.

Source: American Diabetes Association

Treating patients with irbesartan when they first develop microalbuminuria extends life and reduces costs.

The investigators used a Markov model to simulate progression from microalbuminuria to overt nephropathy, doubling of serum creatinine, end-stage renal disease (ERSD), and death in hypertensive patients with type 2 diabetes. They created two irbesartan treatment strategies: early irbesartan 300 mg daily and late irbesartan 300 mg daily initiated with overt nephropathy. They compared the strategies with control which consisted of antihypertensive treatment with standard therapy — excluding ACE inhibitors, other ARBs and dihydropyridine calcium-channel antagonists.

COMPARABLE BLOOD PRESSURE MAINTENANCE

The control group had comparable blood pressure maintenance initiated at microalbuminuria. The Irbesartan in Type 2 Diabetes with Microalbuminuria-2 (IRMA-2) Study, the Irbesartan in Diabetic Nephropathy Trial (IDNT) and other published sources were used to calculate transition probabilities, Dr. Palmer said.

The researchers evaluated 1,000 simulated patients, projecting costs and life expectancy over 25 years in a typical American third-party payer system, discounted at 3% yearly. Early and late irbesartan treatment in 1,000 patients were projected to save \$11.9 ±3.3 million and \$3.3 ±2.7 million, respectively.

The early strategy added 1,550 undiscounted life-years in 1,000 patients compared to 71 undiscounted life-years for the late strategy, Dr. Palmer and colleagues said.

“Treating these patients with irbesartan when they first develop microalbuminuria was projected to

IRMA-2² AND IDNT³ AT A GLANCE**IRMA-2**

- IRMA-2 (Irbesartan in Type 2 Diabetes with Microalbuminuria-2) tested the effect of irbesartan on slowing the progression to diabetic nephropathy in hypertensive patients with type 2 diabetes and microalbuminuria.
- The multinational, double-blind, placebo-controlled trial randomized 590 patients to a dose of either 150 mg/day or 300 mg/day irbesartan and followed them for 2 years.
- Researchers evaluated a primary outcome of time to onset of diabetic nephropathy.
- The investigators concluded that, in patients with type 2 diabetes and microalbuminuria, irbesartan is renoprotective independently of its blood-pressure-lowering effects.

IDNT

- IDNT (Irbesartan in Diabetic Nephropathy Trial) compared irbesartan with the calcium-channel antagonist amlodipine on the progression of nephropathy in patients with type 2 diabetes.
- Investigators wanted to see if the two classes of drugs slowed nephropathy independently of blood pressure lowering.
- They randomly assigned 1,715 hypertensive patients with type 2 diabetes and nephropathy to 300 mg/daily irbesartan, 10 mg/daily amlodipine or placebo. A target blood pressure of 135/85 mm Hg was assigned.
- The primary composite endpoint of time to doubling of baseline serum creatinine concentration, development of ESRD or death from any cause.
- They concluded that irbesartan is effective in protecting against the progression of nephropathy in type 2 diabetes, independently of blood pressure reductions.

extend life and reduce costs," Dr. Palmer wrote. "Late use of irbesartan is also better and less costly than standard care, but irbesartan should be started earlier and continued long term to maximize the impact on ESRD, reduction in mortality and cost savings."

The researchers said they were encouraged by the fact that the results were robust under a wide range of plausible assumptions.

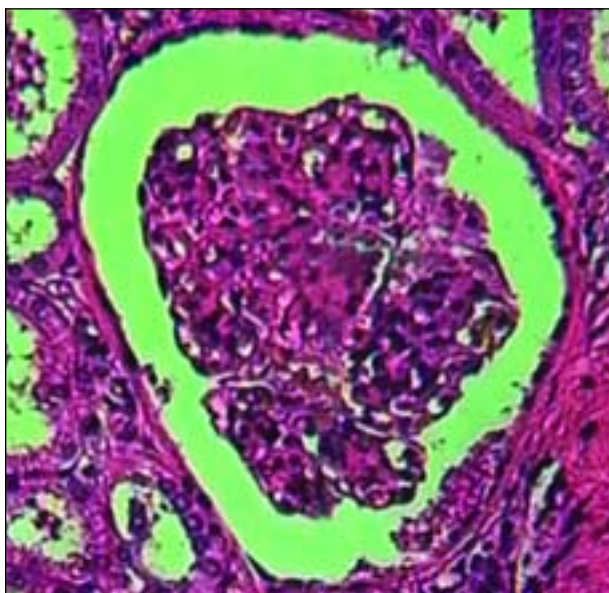


Figure 1. Stage 2 diabetic nephropathy: Histology shows mesangial matrix expansion.

"We need to address the issue of which ARB is best, and the issue of ARB's versus ACE inhibitors," Dr. Palmer said in an interview. "Additionally, further research should address other populations (type 1 diabetes, nondiabetic patients), and should treatment start even before the development of microalbuminuria.

Physicians need to be aware that diabetes patients must be regularly screened for microvascular complications, and that appropriate treatment may lead to substantial improvements in patients' long-term outcomes, Dr. Palmer said. ■

Andrew J. Palmer, BSc, MBBS, is with CORE-Center for Outcomes Research in Basel, Switzerland. He can be reached at 41 (0) 61 383 0756 or ap@thecenter.ch. CORE, Dr. Palmer's company, has received unrestricted research grants and consultation fees from Sanofi-Synthelabo Inc. (New York) and Bristol-Myers Squibb Company (New York).

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