

**BARDOXOLONE, A NOVEL ORAL ANTIOXIDANT-INFLAMMATION MODULATOR IMPROVES RENAL FUNCTION IN PATIENTS WITH DIABETES AND CKD**

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Bardoxolone methyl (BARD), an antioxidant inflammation modulator (AIM), potently induces Nrf2, a transcription factor that activates the phase 2 response and induces over 250 antioxidant and detoxification genes. It plays a critical role in suppressing ROS-mediated endothelial dysfunction, thus helping to maintain the structural integrity of the kidney.

Findings from a recent clinical trial in patients with malignancies demonstrated that treatment with BARD resulted in a time-dependent increase in estimated glomerular filtration rate (eGFR). In this current phase 2a, open label, randomized, dose-ranging study, we assessed the efficacy of BARD in patients with Stage 3 or 4 CKD who also had type 2 diabetes. Patients (n=60) were randomized to receive either 25, 75, or 150 mg/day of BARD in addition to standard therapy for 28 days. Primary endpoint was change from baseline in estimated glomerular filtration rate (eGFR) as calculated by the MDRD equation at day 28.

Interim data are available for 25 patients. Mean age was 61 years and average duration of diabetes was 20 years; 75% of patients were concurrently taking an ACE inhibitor and/or ARB. Mean eGFR at baseline was 36 ml/min/1.73m<sup>2</sup> with 36% of patients having Stage 4 CKD. Patients experienced a 20.5% ( $p<0.0001$ ) mean increase in eGFR, with more pronounced effects reported in patients with Stage 4 CKD (mean 36% increase,  $p=0.001$ ). Improvements were also seen in additional markers of renal function, including serum creatinine, cystatin C, creatinine clearance, BUN, phosphorus, and uric acid. Patients also experienced reductions in plasma angiotensin II, circulating endothelial cells and hemoglobin A1c.

Collectively, these data suggest that in patients with CKD and type 2 diabetes, BARD may improve renal function and parameters of diabetes and cardiovascular disease. Larger, longer-term, placebo-controlled studies of BARD in patients with CKD are being initiated to further investigate and confirm these findings.