

## Abstract Submission No.: A-0731

### **Protective Effect of Vericiguat, soluble guanylate cyclase (sGC) stimulator, in Attenuating Renal Aging**

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**Objectives :** The progression of renal aging is often accelerated by disruptions in the L-Arginine-NO-sGC-cGMP and Angiotensin-AT-sGC-cGMP pathways, leading to increased oxidative stress, endothelial dysfunction, and altered angiotensin signaling. Vericiguat, a soluble guanylate cyclase (sGC) stimulator, has emerged as a potential agent to modulate these pathways and mitigate renal aging.

**Methods :** Young (2-month-old) and aged (18-month-old) mice were administered 150ppm/kg of vericiguat for six months. Each group consisted of 7 subjects. 8 and 24-month-old mice were assigned to the control group. Urine samples were collected using metabolic cages one week before the end of the experiment. Blood and renal tissue specimens were obtained at the end of the experiment. To confirm the changes in oxidative stress, inflammation, and fibrosis caused by the regulation of sGC, which are key contributors to CKD in the elderly, the protein expression of crucial biomarkers was analyzed.

**Results :** Markers of renal function such as creatinine, BUN, and blood pressure were elevated in aged group. These were ameliorated in the intervention group treated with vericiguat at a dose of 150ppm/kg. Histological analysis revealed increases in mesangial volume and tubulointerstitial fibrosis in the 24-month-old control group, whereas these findings were significantly reduced in the vericiguat group. The expression of arginase 1, arginase 2, and iNOS was upregulated in the 24-month control group but downregulated in the treatment group. Additionally, angiotensin II levels were decreased, and ACE2 and AT2R expressions were increased in the vericiguat-treated group, indicating restorative effects on key inflammatory and fibrotic pathways associated with CKD in aged models.

**Conclusions :** Vericiguat showed promising results in reducing factors associated with renal aging. The downregulation of arginase and the modulation of angiotensin signaling point towards the drug's therapeutic potential in enhancing renal function and vascular health. These findings support further investigation into vericiguat as a viable treatment option for age-related renal impairments.