KSN 2020
FULLY VIRTUAL MEETING

Abstract Type : Oral
Abstract Submission No. : OR-1119

Hypoxia-inducible factor prolyl hydroxylase inhibitor FG-4592 (roxadustat) attenuates tacrolimus-induced renal injury

Sheng Cui[1], Ji Zhe Jin[1], Bum Soon Choi[2], Cheol Whee Park[2], Chul Woo Yang[2], Can Li[1]
[1]Department of Nephrology, Yanbian University Hospital, China
[2]Department of Internal Medicine-Nephrology, The Catholic University of Korea, Seoul St. Mary's Hospital, Korea, Republic of

Objectives: Reducing immunosuppressant-related complication has important therapeutic implication. FG-4592 is an orally active, hypoxia-inducible transcription factor (HIF) prolyl hydroxylases (PHD) inhibitor for the treatment of anemia in patients with chronic kidney disease. The current study aimed to evaluate the renoprotective effects of FG-4592 in a rat model of chronic tacrolimus (TAC) nephropathy.

Methods: Establishment of chronic TAC nephrotoxicity was induced by daily treatment with TAC for 4 weeks, with concurrent FG-4592. The influence of FG-4592 on renal injury (renal function, histopathology, cytokine expressions, oxidative stress, programmed cell death, and PI3K/AKT signaling) was examined.

Results: FG-4592 treatment improved renal function and histopathology; this effect was paralleled by downregulation of proinflammatory and profibrotic cytokine expression. In addition, FG-4592 stimulated the expression of HIF-1a and HIF-2a. TAC-induced oxidative stresses and programmed cell death were significantly decreased by concurrent FG-4592 via interference with HIF-1a/PI3K/AKT pathway.

Conclusions: FG-4592 treatment may protect against chronic TAC nephrotoxicity.