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Renoprotective Effects of BX-001N Against Cold Ischemia-Reperfusion Injury in a Murine Model of Kidney Transplantation

JI-JING YAN¹, JOON YOUNG JANG¹, HONGLIN PIAO¹, BOMIN KIM¹, SEUNGHYUN JO², HYUNJIN KIM², DUCKHYANG SHIN², MYUNG L. KIM², JAESEOK YANG¹

¹Department of Internal Medicine-Nephrology, Yonsei University College of Medicine, Korea, Republic of

²Department of Research and Development, BILIX.Co., Ltd, Korea, Republic of

Objectives : Cold ischemia-reperfusion injury (IRI) poses a significant challenge in kidney transplantation, contributing to acute kidney injury and chronic kidney fibrosis. In this study, BX-001N, a synthetic PEGylated bilirubin nanoparticle, demonstrated promising renoprotective effects through its antioxidant and anti-inflammatory properties.

Methods : A syngeneic kidney transplantation cold IRI model was established in mice. BX-001N (30 mg/kg) was administered intravenously at 0 and 2.5 hr post-transplantation. Renal function (BUN, Creatinine), histopathological injury (tubular injury, apoptosis), immune cell infiltration, oxidative stress markers, renal regeneration (Ki67, vascular endothelial growth factor-VEGF), and fibrotic changes (collagen deposition, epithelial-mesenchymal transition (EMT) markers) were assessed at 1 and 7 days post- transplantation.

Results : BX-001N improved renal function and mitigated renal tissue injury and tubular cell apoptosis on day 1 after cold IRI. It significantly reduced neutrophil and macrophage infiltration and suppressed pro-inflammatory cytokines (Tumor Necrosis Factor - α , Interferon - γ) and chemokines (Monocyte Chemoattractant Protein -1, C-X-C motif chemokine ligand 1, 2). Antioxidant defense was enhanced via upregulation of Heme oxygenase-1 and downregulation of Nitrotyrosine and iNOS leading to reduced oxidative stress. Furthermore, on day 7, BX-001N promoted renal regeneration by increasing Ki67 and VEGF expression and inhibited fibrosis by decreasing collagen IV and EMT-associated markers (α - Smooth Muscle Actin, Vimentin) while preserving E-cadherin.

Conclusions : BX-001N effectively attenuates cold IRI-induced renal injury by reducing oxidative stress, inflammation, and fibrosis while promoting renal repair. These findings suggest BX-001N as a promising therapeutic candidate for improving outcomes in renal cold IRI during kidney transplantation.