THE KOREAN SOCIETY OF NEPHROLOGY
APCN & KSN 2024
June 13(Thu) - 16(Sun), 2024 Coex, Seoul, Korea
APSN
Promoting Sustainable Kidney Health: The Asia-Pacific and Beyond

Submission No. : CNEGN-0001
Session Title : Comprehensive Nephrology Education (Glomerular Disease)
Session Topic : -
Date & Time, Place : June 13 (Thu) / 13:30-15:00 / Room 3 (GBR 104-105)

Recent Advance In Management Of Focal Segmental Glomerulosclerosis

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The histologic finding of FSGS in a kidney biopsy is recognized as a pattern of injury, rather than being a manifestation of a disease in itself. FSGS cases can be categorized into four groups: (i) primary FSGS, which result from an immunologic cause; (ii) secondary FSGS, arising from systemic processes; (iii) FSGS attributed to genetic mutations; and (iv) FSGS lacking an identifiable cause. The recently updated guideline recommend high-dose oral glucocorticoids as the initial immunosuppressive therapy for primary FSGS. Despite an improved understanding of pathogenesis, targeted therapies remain uncertain. However, there have been recent advances in novel treatments targeting specific pathogenic signaling pathways. In a phase 2 study, sparsentan, a dual antagonist targeting endothelin type A and angiotensin II type 1 receptors, demonstrated a reduction in proteinuria by 45% from baseline over 8 weeks among patients with FSGS, compared to a 19% reduction observed in patients receiving irbesartan. Atrasentan, an endothelin type A receptor antagonist devoid of angiotensin II type 1 receptor inhibitory effects, is undergoing investigation in a phase 2, open-label basket study. Disturbance in intracellular calcium balance is a pivotal event in podocyte injury. Gain-of-function mutations in TRPC6 are linked to increased intracellular calcium levels. Blocking TRPC6 presents a promising therapeutic target for FSGS, while GFB-887, a TRPC5 inhibitor, is undergoing clinical trials for FSGS. ROBO2 coexists with the podocyte slit diaphragm protein nephrin and serves as a receptor for SLIT2. The efficacy, safety, tolerability, and pharmacokinetics of the ROBO2 fusion protein, which blocks ROBO2/SLIT2 signaling, are under investigation. R3R01 is a small molecule engineered to reduce lipid accumulation in the kidneys. A forthcoming phase 2, multicenter, open-label study is in the planning stages to assess the safety, effectiveness, and pharmacokinetic characteristics of R3R01. Additional investigation is required to discover new biomarkers, subpopulations, and signaling pathways.

Keywords: focal segmental glomeruloscrelosis, emerging treatment