Shaping Tomorrow's Nephrology: Insight-Driven Kidney Care
KSN 2026 SEOUL, KOREA
The 46th Annual Meeting of the Korean Society of Nephrology
THE KOREAN SOCIETY OF NEPHROLOGY
Jun 11 (Thu) – 14 (Sun), 2026
COEX, Seoul, Korea

Lecture Code : IS07-S1
Session Name : Industry Symposium 7 (AstraZeneca)
Session Topic : Industry Symposium 7 (AstraZeneca)
Date & Time, Place : June 13 (Sat) / 11:50-12:30 / Room 1 (GBR 101), 1F

Managing the Ongoing Risk of Hyperkalemia with Sodium Zirconium Cyclosilicate (SZC), LOKELMA

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Hyperkalemia is a frequent, recurrent, and consequential complication in cardiorenal medicine, with prevalence reaching up to 50% in advanced chronic kidney disease (CKD) populations treated with renin-angiotensin-aldosterone system inhibitors (RAASi) and in patients with severe heart failure receiving mineralocorticoid receptor antagonists. Elevated serum potassium is independently associated with all-cause mortality, more than doubles inpatient admissions, increases emergency utilization by approximately 72%, and shortens the interval between successive recurrences. Critically, hyperkalemia remains the dominant barrier to attaining and maintaining guideline-directed RAASi therapy: down-titration or discontinuation following a hyperkalemic event is associated with at least a doubling of mortality and a 50% to 55% increase in the composite risk of progression to end-stage kidney disease and heart-failure hospitalization. This presentation synthesizes contemporary KDIGO, ESC, and ESH guidance, alongside the GUARDIAN-HK and international Delphi consensus recommendations, which together treat hyperkalemia as a predictable, treatable, and manageable complication that should not, by itself, prompt RAASi de-escalation when novel potassium binders are available. The clinical evidence base for sodium zirconium cyclosilicate (SZC, Lokelma) is reviewed, including the HARMONIZE, ZS-004E, and ZS-005 programs, which demonstrate rapid normalization of serum potassium within 48 hours and sustained control through 12 months across CKD, heart failure, diabetes, and RAASi-treated subgroups. Real-world data from OPTIMIZE I and the ZORA multinational meta-analysis show that SZC initiation enables 74% to 89% of patients to maintain RAASi therapy at six months, and the REALIZE-K Phase IV trial documents an approximately 4.4-fold increase in the odds of attaining target spironolactone dosing while maintaining normokalemia in patients with heart failure with reduced ejection fraction.

Safety, tolerability, and drug-interaction considerations are summarized. Patient case studies are reported.

Keywords: hyperkalemia, sodium zirconium cyclosilicate, potassium binder