Protocol Evaluating the Feasibility and Safety of Empagliflozin in Acute Kidney Injury with Residual Renal Function

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Background

Acute kidney injury (AKI) is associated with high morbidity, mortality, and risk of progression to chronic kidney disease (CKD). Despite advances in supportive care, no pharmacologic therapies have consistently demonstrated renal recovery benefits in AKI. Sodium-glucose co-transporter-2 (SGLT2) inhibitors, such as empagliflozin, offer cardio-renal benefits in CKD, even with reduced eGFR. Beyond glucose control, their renoprotective mechanisms—reducing tubular workload, improving oxygenation, modulating inflammation and fibrosis, and enhancing mitochondrial resilience—suggest potential benefit in AKI. However, their safety and feasibility in AKI, particularly in patients with severely reduced eGFR, remain unexplored.

Objectives

This pilot trial aims to evaluate the feasibility and short-term safety of empagliflozin initiation in hospitalized patients with stage 2–3 AKI and residual eGFR from 10-25 mL/min/1.73m². The hypothesis is that early empagliflozin use in select AKI patients may be both safe and tolerable, setting the stage for larger outcome-driven trials.

Materials and Methods

This is a single-center, open-label, randomized pilot trial. Adults aged ≥18 years with KDIGO AKI stage 2-3 and an eGFR 10-25 mL/min/1.73m² (measured within 48 hours of AKI diagnosis) are eligible.

Key exclusion criteria include (1) type 1 diabetes, (2) diabetic ketoacidosis (DKA) or a history of euglycemic DKA, (3) ongoing dialysis, (4) vasopressor-dependent hypotension, (5) terminal illness, (6) anuria, (7) inability to take oral medications, (8) severe metabolic acidosis, defined as serum bicarbonate ≦15 mmol/L or pH ≦7.20. Eligible patients will be randomized 1:1 to receive empagliflozin 10 mg once daily or standard care for up to 14 days.

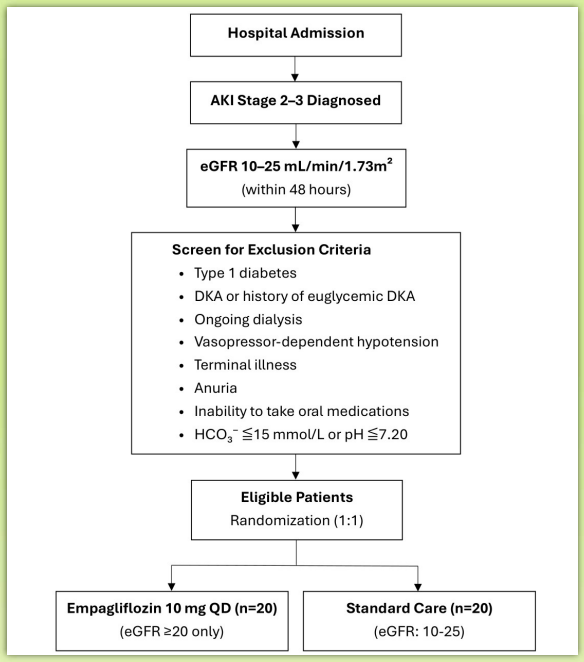

Figure 1. Flowchart of patient enrollment, exclusion, and randomization in the empagliflozin AKI pilot trial.

Empagliflozin will only be administered to those with baseline eGFR ≥20 mL/min/1.73m², per safety guidance. Daily monitoring will include serum creatinine, electrolytes, acid-base status, urine output, and vital signs. Predefined stopping rules will be applied in the event of clinical deterioration, >20% eGFR decline, or serious adverse events.

Table 1. Clinical Monitoring Parameters During the Empagliflozin AKI Pilot Trial

Monitoring Parameter	Frequency	Purpose
BUN, Serum Cr, eGFR	Baseline, BIW and PRN	To monitor renal function and detect progression or recovery of AKI
Urinalysis and sediment	Baseline and PRN	To assess urinary abnormalities suggestive of intrinsic kidney injury
Urine output	Q8H (per shift)	To track real-time kidney function and fluid balance
Intake and output	Q8H (per shift)	To evaluate net fluid balance and guide volume management
Body weight	QD	To assess volume status and detect fluid retention or loss
Vital signs (BP, PR, RR, BT)	QID and PRN	To monitor hemodynamic stability and detect signs of infection or instability
Fingerstick blood glucose	BIDAC and PRN	To ensure glycemic control and detect hypoglycemia
Na, K	Baseline, BIW and PRN	To monitor for electrolyte disturbances associated with AKI or therapy
Serum ketone (β-OHB)	Baseline, QW and PRN	To screen for ketoacidosis, particularly euglycemic DKA
Blood gas (incl. HCO_3^-)	Baseline, QW and PRN	To assess acid-base status and detect metabolic acidosis

Abbreviations: BUN: blood urea nitrogen; Cr: creatinine; eGFR: estimated glomerular filtration rate; BIW: twice weekly; PRN: as needed; AKI: acute kidney injury; Q8H: every 8 hours; QD: once daily; BP: blood pressure; PR: pulse rate; RR: respiratory rate; BT: body temperature; QID: four times daily; BIDAC: twice daily before meals; Na: sodium; K: potassium; β-OHB: β-hydroxybutyrate; QW: once weekly; DKA: diabetic ketoacidosis; incl.: include; HCO_3^-: bicarbonate

The primary endpoint is feasibility, defined as successful initiation and maintenance of empagliflozin in ≥80% of eligible patients.

Secondary endpoints include (1) renal recovery, defined as a ≥30% reduction in peak serum creatinine by day 14, (2) time to renal recovery, (3) in-hospital initiation of dialysis, (4) length of ICU and hospital stay, (5) in-hospital mortality, (6) adverse events e.g., hypotension, acidosis, hypoglycemia.

Results

This abstract describes the protocol of an ongoing pilot trial. Enrollment will begin in late 2025; 40 patients (20 per arm). IRB approval will be obtained prior to study initiation.

Conclusion

This study explores a novel off-label use of empagliflozin in the setting of acute kidney injury with severely impaired renal function. If the intervention proves feasible and safe, it may open the door to larger interventional trials aiming to accelerate renal recovery, reduce dialysis initiation, and improve AKI outcomes. This study addresses an unmet clinical need in AKI therapeutics and may redefine the role of SGLT2 inhibitors in acute care nephrology.

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