Supplementary Methods

Study design and participants

The study was an investigator-initiated, prospective pilot study. Eligible participants were children (aged 6-18 years) with proteinuria who were diagnosed with inherited kidney disease. All the participants were required to have been receiving a stable dose of an ACE inhibitor or ARB for at least 1 month before study drug administration, and estimated glomerular filtration rate (eGFR) were more than 60 mL/min per 1.73 m^2 calculated by the Schwartz formula[1]. Patients were excluded if they were with diabetes, orthotic proteinuria, untreated urinary tract infection, current treatment with systemic corticosteroids/calcineurin inhibitors/other immunosuppressant medications, or with evidence of hepatic disease. The full inclusion and exclusion criteria were described in Supplementary Table S1.

After enrolment, patients were prescribed dapagliflozin 5 mg per day (bodyweight ≤30 kg) or 10 mg per day (bodyweight > 30 kg) for 12 weeks. The efficacy of dapagliflozin in lowering the proteinuria was accessed by the percentage change in daily protein excretion over 12 weeks treatment relative to baseline; Safety was monitored throughout the study by assessing adverse events, laboratory data, vital sign measurements, physical examinations, and self-monitoring of blood glucose. Reported adverse events were recorded during the study. This pilot study was registered at clinicaltrials.gov (NCT 04534270) and was approved by the ethical committee of Children's Hospital of Fudan University. All patients or their legal guardians provided written informed consent before study related procedure commenced.

Statistical Analysis

All statistical analyses were conducted using SPSS 25.0. Descriptive statistics were expressed as mean (SD) or median (interquartile range). Paired t-tests or nonparametric equivalents were performed to analyse endpoints. P values < 0.05 were considered statistically significant.

Supplementary References

1. Schwartz GJ, Munoz A, Schneider MF, et al. New equations to estimate GFR in children with CKD. *Journal of the American Society of Nephrology : JASN.* 2009;20(3):629-637.

Supplementary Figure S1

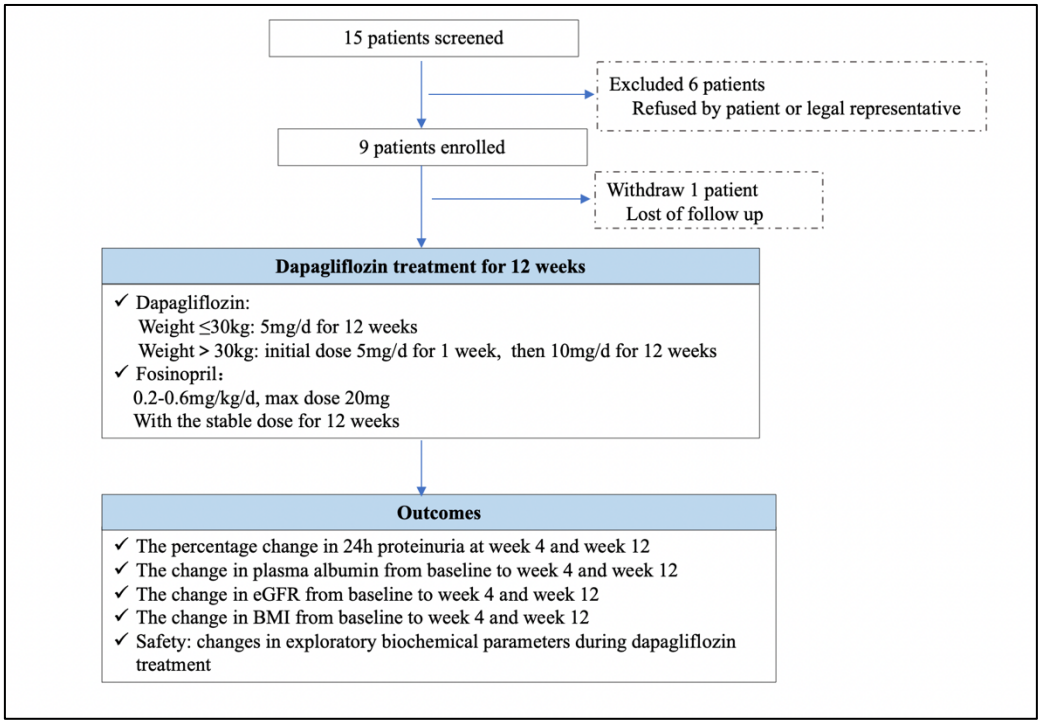

Figure S1. Study flow chart

Supplementary Table S1.

Table S1. The full inclusion and exclusion criteria

Inclusion Criteria

- ✓ Age 6 to 18 years
- ✓ Urinary protein excretion > 0.2g in a 24-hr urine collection
- ✓ eGFR≥60ml/min/1.73m^2 (estimated by Schwartz formula)
- ✓ On stable doses of ACE inhibitors for > 1 month
- ✓ Not receiving immunosuppressive therapy (including systemic corticosteroids, calcineurin inhibitors, or other immunosuppressant medications) within three months prior to enrolment
- ✓ No history of diabetes
- ✓ Willing to sign informed consent

Exclusion Criteria

- ✓ Uncontrolled urinary tract infection at screening
- ✓ Blood pressure is less than the 5th percentile of the same gender, age, height
- ✓ At risk for dehydration or volume depletion
- ✓ History of organ transplantation, cancer, liver disease
- ✓ Bariatric surgery or other gastrointestinal surgeries that induce chronic malabsorption within the past 2 years
- ✓ With the evidence of liver disease: defined by serum levels of alanine transaminase, aspartate transaminase, or alkaline phosphatase >2 times the upper limit of normal during screening
- ✓ Participation in another therapeutic trial with an investigational drug within 30 days prior to informed consent
- ✓ History of noncompliance to medical regimens or unwillingness to comply with the study protocol

Table S2. Changes in exploratory biochemical parameters during dapagliflozin treatment

Safety parameters	Baseline	12 weeks	P value
FBG, mean (SD), mmol/L	5.1 (0.3)	5.3 (0.4)	0.98
Uric acid, mean (SD), μmol/L	420.1 (149.7)	322.1 (91.3)	0.45
Hb, mean (SD), g/L	139.9 (12.2)	145.0 (13.3)	0.68
Hct, median (IQR), %	39.3 (37.8 to 44.8)	41.9 (39.8 to 45.8)	0.17
ALT, mean (SD), IU/L	13.0 (1.2)	12.4 (2.4)	0.57
AST, mean (SD), IU/L	24.4 (4.1)	22.5 (3.8)	0.36
TCH, mean (SD), IU/L	5.9 (1.7)	6.2 (1.3)	0.82
TG, mean (SD), IU/L	2.2 (1.0)	1.7 (0.9)	0.62
Potassium, mean (SD), mmol/L	4.5 (0.4)	4.4 (0.3)	0.88
Sodium, mean (SD), mmol/L	139.0 (2.2)	138.6 (1.5)	0.78
Calcium, mean (SD), mmol/L	2.3 (0.1)	2.4 (0.2)	0.59
Phosphate, mean (SD), mmol/L	1.5 (0.2)	1.4 (0.2)	0.83

FBG, fasting blood glucose; Hb, haemoglobin; Hct, haematocrit ratio; ALT, aspartate aminotransferase; AST, alanine aminotransferase; TCH, total cholesterol; TG, triglycerides.