Supplementary Table 1: Formulas and equations that will be used during the study

- **Residual Renal Urea Clearance, $K_r$urea (mL/min)** = [[urine urea conc. (mmol/L) x urine volume (mL)]/((BUN1+BUN2)/2) (mmol/L) X period of urine collection (min)]

where BUN1 is the BUN concentration in a blood sample collected immediately after the HD session that preceded the collection interval, BUN2 is the BUN concentration in a sample collected before the next HD session.

- **Weekly Residual Renal Urea Clearance (K_rt/Vurea):**
  a) Calculate $K_r$urea in liters/week = $K_r$urea in mL/min X 10.08 (to convert mL/min to liters/week)
  b) t = 1 week
  c) V (total body water): calculate from the Watson formula:

For men: V(L) = 2.447 + (0.3362 x Weight [kg]) + (0.1074 x Height [cm]) – (0.09516 x Age)

For women: V(L) = -2.097 + (0.2466 x Weight [kg]) + (0.1069 x Height [cm])

- **Residual Renal Creatinine Clearance (mL/min)** = [[urine creatinine conc. (mmol/L) x urine volume (mL)]/((Scr1+Scr2)/2) (mmol/L) X period of urine collection (min)]

where Scr1 is the serum creatinine concentration in a blood sample collected immediately after the HD session that preceded the collection interval, SCr2 is the serum creatinine concentration in a sample collected before the next HD session

- **Residual Renal Urea Clearance (mL/min/1.73m2)** = $K_r$urea (mL/min) x 1.73/BSA

- **Residual Renal Creatinine Clearance (mL/min/1.73m2)** = $K_r$creatinine (mL/min) x 1.73/BSA

- **Residual Kidney Function (RKF) (mL/min/1.73m2)** = (Residual Renal Urea Clearance (mL/min/1.73m2) + Residual Renal Creatinine Clearance (mL/min/1.73m2))/2

- **Renal B2MG Clearance (mL/min)** = ((Urine B2MG concentration [mg/L] x Urine volume [mL])/(serum2 B2MG + serum1 B2MG [mg/L])/2) x period of urine collection (min)

  where serum1 B2MG is the B2MG concentration in a blood sample collected immediately after the HD session that preceded the collection interval, serum2 B2MG is the B2MG concentration in a sample collected before the next HD session

- **Renal B2MG Clearance at baseline (mL/min)** based on 24-hour urine collection, prior to HD initiation = ((Urine B2MG concentration [mg/L] x Urine volume [mL])/serum B2MG [mg/L]) x 1440

  where serum B2MG is the solute concentration in the blood collected at baseline, before HD initiation

- **Normalized protein catabolic rate (nPCR**) will be calculated using formula[33]:

nPCR (g/kg/day) = 149.7 x G/V + 0.17, where G/V = [BUN2(V+W)/V − BUN1 + (Uv x Uc/V)]/idi

where BUN1 is the post-dialysis BUN concentration (mmol/L), BUN2 is the pre-dialysis blood urea concentration (mmol/L), W is the interdialytic weight gain (grams), V is the total body water (L), Uv is the volume of interdialytic urine collection (mL), Uc is the urea concentration in interdialytic urine collection (mmol/L), and idi is the interdialytic interval (minutes).

Pre-dialysis blood samples will be drawn before injecting saline, heparin, or other potential diluents. Post-dialysis blood samples will be drawn from the dialyzer inflow port using a slow-flow method (100 mL/min for 15 seconds)[1].

Abbreviations: BUN, blood urea nitrogen; B2MG, beta-2 microglobulin; BSA, body surface area; SCr, serum creatinine; UCC, urine creatinine concentration; UUC, urine urea concentration.

Supplementary Table 2. Secondary outcomes measurements

Outcome	Measurements
Change in RKF	Difference in changes in RKF from baseline to set time points post-randomization.
Volume management	Inter-dialytic weight gain (expressed as percentage [%] of estimated dry weight), residual weight (post-dialysis weight – estimated dry weight; expressed as % of estimated dry weight), ultrafiltration rate (mL/kg/hour), and intra-dialytic peak and nadir systolic blood pressure.
Hospitalization	All hospitalizations, cause of hospitalization, hospital length of stay, time to first hospitalization and 30-day readmission rate.
Solute clearance	spKdt/Vurea, stdKdt/Vurea, weekly Krt/Vurea, total weekly Kt/Vurea, and renal clearance for beta 2 microglobulin.
Electrolyte and acid-base homeostasis	Average levels of serum potassium, serum sodium and serum bicarbonate levels.
Nutrition	Average levels of serum albumin and normalized protein catabolic rate (nPCR)[33].
Anemia and erythropoietin requirements	Average levels of hemoglobin, ferritin and transferrin saturation. The erythropoietin resistance index (units/week/kg/g/dl) will be calculated from average weekly erythropoietin dose (IU/week) divided by weight (kg) and then by hemoglobin level (g/dl).
Bone-mineral metabolism	Average levels of serum phosphorus, calcium and intact PTH levels; and average of weekly doses of active vitamin D and calcimimetic agents.
Vascular access	Arteriovenous access (AVA) infiltration/hematoma, requirement of dialysis catheter in those who initiated HD with an AVA, AVA revision, AVA thrombosis, change of vascular access, and vascular access infection (bacteremia/sepsis related to vascular access, AVA cellulitis, catheter exit site or tunnel infection).
Patient reported outcomes	Health-related quality of life (HRQoL) will be measured using the Kidney Disease Quality of Life Short Form (KDQOL-SF) version 1.. and the Dialysis Symptom Index (DSI)[34,35]. Depression will be screened using the PHQ-9 instrument[36,37]. Anxiety will be assessed using the GAD-7[37,38].

Supplementary Table 3. Participant Feedback Questionnaire					
Dimensions and individual items within each dimension	Use the Scale to Rate the Answers				
Information and communication					
Overall study explained to my full understanding	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know
Risks/benefits of joining the study explained	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know
Study details were included in the informed consent docs	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know
Informed consent document was understandable	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know
Coordination of care					
Something happened that I was not well prepared for, which was related to the study	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know
Understood which tests were for research	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know
After the participant provides the answer, the interviewer will assess whether the participant had correct understanding urine collections were for research purposes only	*Definitely Yes*	*Probably Yes*	*Probably No*	*Definitely No*	*I don't know*
Did you feel that your healthcare was compromised during the study?	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know
Do you think the patients will need to be reminded every day about collecting the urine, during the period of urine collection, if the collection is longer than 1 day	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know
Perception on study-related assessments: urine collections					
During the study, did you feel that the urine collections were burdensome?	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know
What do you think is the chance that a person might accidentally flush (or forget to collect) some of the urine voids when they need to collect the urine?	Very high	High	Low	Very Low	I don't know
Do you think the patients will disclose if they brought an incomplete urine collection?	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know
Do you think that collecting the urine every 2-3 months, for 1 or 2 years, would be manageable for most people on dialysis?	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know
Motivation					
Why did you choose to participate in this study?					
To contribute important information to medical science	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know
To potentially help other people with similar conditions	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know
I hoped that the research study would improve my medical condition	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know
To gain insights into my own health	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know
To benefit from the additional medical attention and testing that the study provided	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know

Because of the financial incentives of the study	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know
Future studies					
Do you think researchers should study *if* and *when* twice-a-week dialysis is safe?	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know
[If answer was 'Definitely Yes' or 'Probably Yes' to the above question] What do you think that the researchers should focus on when they study twice-a-week vs three-times a week dialysis? *[Rate in order of preference, from 1 being most preferred to be studied, to 5 being least preferred to be studied. Numbers 1 through 5 cannot be use more than twice]*					
How long the patient survives	1	2	3	4	5
How often the patient gets sick (e.g., feels short of breath, goes to ED, is admitted to the hospital)	1	2	3	4	5
How long the patient makes more than a cup of urine per day	1	2	3	4	5
How satisfied the patients are with their quality of life	1	2	3	4	5
Would you recommend joining a research study to other patients who are started on dialysis if they are eligible for such a study?	Definitely Yes	Probably Yes	Probably No	Definitely No	I don't know