

SUPPLEMENTAL APPENDIX

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SUPPLEMENTARY METHODS

Full Eligibility Criteria:

Inclusion criteria for patient enrollment in the study were:

- Patient willing and competent to provide approved informed consent
- Patient must be over 21 years of age.
- Patients must weigh between 45 and 100 kg.
- Patient must have End Stage Renal Disease and currently undergoing maintenance hemodialysis at least three times a week for at least 3 months prior to enrolment.
- Vascular access must be through a functioning double lumen catheter with no thrombolytic therapy or clotting of the catheter within the past 4 weeks.
- Willing to comply with the requirements of experimental treatment with the WAK for up to 24 hours.
- Expected survival of no less than 6 months.
- Consent to allow review of their medical records by the investigators, and monitors.
- Fluency in English
- Hemoglobin level ≥ 9.0 g/dL prior to WAK treatment

Exclusion criteria for the study were:

- Anticipated or scheduled for a living related donor kidney transplant in less than 2 months.
- History (within the 12 weeks prior to the study) of cardiovascular events including;
 - Unstable angina
 - Myocardial Infarction
 - Stroke
 - Clinically significant arrhythmia
- Life threatening arrhythmia within the past 30 days
- Intradialytic hypotension, deemed severe by the investigator, within the past 30 days
- Shock within the past 30 days, as defined by the investigator
- Hemodynamic instability as demonstrated by repeated episodes of hypotension or hypertension requiring intervention by dialysis personnel or representing a present hazard to the patient.
- Seizure disorder requiring active treatment for a seizure episode during the last 6 months.
- Major surgery (excluding vascular access surgery) within the past 30 days.
- Currently receiving intravenous antibiotic therapy for systemic infection.
- Clinical evidence of metastatic malignancy, receiving radiation or chemotherapy, within the past 365 days.
- Active bleeding.
- Hematological diseases such as malignancies, hemolytic anemia, and thrombocytopenia
- Vascular access catheter dysfunction, defined as inability to routinely achieve blood flow rates of at least 300 mL per minute, or requires switching ports (reversing lines), during the past 30 days.

- Current enrolment in another investigational device or drug trial.
- Subject is pregnant (e.g., positive HCG test) or is breast feeding
- Subject has any disorder (excluding illiteracy or visual impairment) that compromises the ability of the subject to give written informed consent and/or to comply with the study procedures.
- Allergy to heparin or ethylene oxide
- Hypertension deemed uncontrolled, at the discretion of the investigator, within the past 30 days.
- Has an implantable electronic device (e.g. pacemaker)

Table S1. Comparison of mean solute clearances (ml/min) calculated using two alternate equations, by study time point

| Solute | Clearance-calculation ^a | Hour | | | | |
|------------------|------------------------------------|-------------|-------------|-------------|------------|------------|
| | | 1 | 8 | 12 | 16 | 24 |
| Urea | Blood-based | 20.7 ± 13.4 | 17.1 ± 8.9 | 15.9 ± 10.0 | 18.7 ± 9.0 | 10.3 ± 8.0 |
| | Dialysate-based | 13.4 ± 8.6 | 18.2 ± 6.9 | 9.1 ± 10.2 | 13.2 ± 3.9 | 12.8 ± 9.6 |
| Creatinine | Blood-based | 20.4 ± 10.8 | 15.6 ± 8.3 | 15.0 ± 8.6 | 16.0 ± 7.3 | 8.5 ± 6.3 |
| | Dialysate-based | N/A | 17.5 ± 12.4 | 13.4 ± 9.4 | 14.3 ± 8.6 | 13.9 ± 8.2 |
| Phosphorus | Blood-based | 22.0 ± 11.9 | 14.4 ± 7.2 | 14.8 ± 8.1 | 15.2 ± 6.1 | 6.3 ± 2.3 |
| | Dialysate-based | 16.4 ± 2.9 | 15.3 ± 6.9 | 14.6 ± 8.8 | 11.5 ± 3.9 | 8.9 ± 4.6 |
| β2-microglobulin | Blood-based | 9.0 ± 3.0 | 4.1 ± 3.4 | N/A | 4.9 ± 3.3 | 1.8 ± 4.4 |
| | Dialysate-based | N/A | 5.4 ± 2.2 | N/A | 4.0 ± 1.4 | 3.5 ± 1.2 |

^a Blood-based clearance calculated as: $(K_B) = \frac{Q_B \times (C_{in} - C_{out}) \times (1 - Hct)}{C_{in}}$, where Q_B is the blood flow rate (mL/min), C_{in} is the blood concentration of solute entering the dialyzer, C_{out} is the blood concentration of solute exiting the dialyzer, and Hct is the blood hematocrit. Dialysate-based clearance calculated as: $(K_D) = \frac{C_{Dialysate} \times Q_D}{C_{Blood}}$, where Q_D is the dialysate flow rate (ml/min), $C_{Dialysate}$ is the dialysate solute concentration, calculated as the difference between the post- and pre-dialyzer dialysate solute measurements, and C_{Blood} is the blood concentration of solute entering the dialyzer.

Table S2. Comparison of mean pre- and post-sorbent dialysate solute concentrations, by study time point

| Solute | Concentration | | | | | | | | | |
|-------------------------|------------------|-------------------|------------------|-------------------|------------------|-------------------|------------------|-------------------|------------------|-------------------|
| | Hour 1 | | Hour 8 | | Hour 12 | | Hour 16 | | Hour 24 | |
| | Pre ^a | Post ^b | Pre ^a | Post ^b | Pre ^a | Post ^b | Pre ^a | Post ^b | Pre ^a | Post ^b |
| Urea (mg/dL) | 8.0 ± 5.3 | 0.7 ± 0.6 | 6.9 ± 2.5 | 0.3 ± 0.5 | 4.1 ± 4.2 | 0.5 ± 1.0 | 5.2 ± 2.9 | 0 | 6.4 ± 5.1 | 0 |
| Creatinine (mg/dL) | - | - | 1.3 ± 0.5 | 0 | 1.1 ± 0.3 | 0 | 1.1 ± 0.3 | 0 | 1.2 ± 0.5 | 0 |
| Phosphorus (mg/dL) | 2.1 ± 0.7 | 0 | 1.8 ± 0.7 | 0.5 ± 0.6 | 1.3 ± 0.4 | 0 | 1.5 ± 0.4 | 0.4 ± 0.4 | 1.8 ± 0.6 | 0.9 ± 0.7 |
| β2-microglobulin (mg/L) | - | - | 3.4 ± 1.5 | 1.0 ± 0.6 | 2.6 ± 2.0 | 1.1 ± 1.0 | 2.7 ± 1.5 | 1.2 ± 0.6 | 2.9 ± 1.9 | 1.5 ± 1.1 |

Results shown are mean values ± the standard deviation. Values are reported if available for ≥ 2 subjects

^a Sample drawn from the post-dialyzer, pre-sorbent dialysate port

^b Sample drawn from the pre-dialyzer, post-sorbent dialysate port

Table S3. Summary of device-related technical issues and corrective actions during treatment phase of study^a

| Issue | Corrective Action Taken | Subject Number | | | | | | |
|---|---------------------------------------|----------------|----|---|---|---|---|----|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Blood Flows <20ml/min | Repositioning tubing and recalibrated | >5 | 0 | 0 | 0 | 2 | 0 | 1 |
| Dialysate Flows <20ml/min | Repositioning tubing and recalibrated | >5 | 5 | 0 | 0 | 2 | 0 | 3 |
| Kinked tubing | Kink removed | >5 | >5 | 0 | 1 | 1 | 0 | 0 |
| Clotting at venous access port | Aspirated and removed clot at port | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| Main pump dysfunction | Replaced pump cartridge | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Excessive bubbles in sorbent cartridges | Replaced sorbent cartridges | 0 | 0 | 0 | 0 | 0 | 0 | 2 |
| Decrease in main pump battery power | Batteries replaced | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| Excessive bubbles in dialysate | Removed via syringe | 1 | 2 | 0 | 1 | 2 | 2 | >5 |
| Bubbles in venous blood circuit | Removed via syringe | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| Cracked bubble trap | Bubble trap replaced | 0 | 0 | 0 | 0 | 0 | 1 | 0 |

^aValues indicate number of instances issue occurred along with corresponding corrective action

Table S4. Detailed description of study adverse events

| Subject Number | Adverse Event | Severity | Serious Event | Relationship to Trial | Corrective Action Taken | Outcome |
|-----------------------|----------------------|-----------------|----------------------|------------------------------|--------------------------------|------------------------|
| 1 | Hand cramping | Mild | No | Related | Decrease UF Rate | Resolved |
| 2 | Leg cramping | Mild | No | Related | None | Spontaneously resolved |
| 2 | Leg cramping | Mild | No | Related | None | Spontaneously resolved |
| 3 | Malaise | Moderate | No | Not related | None | Resolved |
| 5 | Nausea | Mild | No | Not related | None | Spontaneously resolved |
| 7 | Diarrheal | Mild | No | Note related | None | Spontaneously resolved |