A tRial Evaluating Mid Cut-Off Value Membrane Clearance of Albumin and Light Chains in Hemodialysis Patients (REMOVAL-HD): A Safety Device Study

Krishnasamy R, Hawley CM, Jardein MJ,. A trial evaluating mid out-off value membrane clearance of albumin and light chains in hemodialysis patients (REMOVAL-HD): a safety device study. *Blood Purif.* 2020; 1-11. doi: 10.1159/000505567.

BACKGROUND

Patients with end-stage kidney disease (ESKD) are often burdened with a myriad of complications including cardiovascular disease, infection, and malnutrition resulting in high rates of hospitalization, reduced quality of life and increased risk of death. Retention of uremic toxins, especially middle molecules that are not well cleared by current dialysis therapies, may contribute to the disease burden in the ESKD cohort.

The clearance of middle molecules has continued to improve with the evolution of dialysis technology over the last 20 years. With the advent of high-flux dialyzers and hemodiafiltration (HDF), the efficiency of middle molecule clearance by chronic hemodialysis (HD) has continually increased; however, the clearance of almost a third of the larger middle molecules (>25kDa) is yet to be optimized. Pore sizes of dialysis membranes are crucial in determining the clearance of larger middle molecules. However, membranes with larger pore sizes such as the high cut-off dialyzer were associated with substantial albumin loss (molecular weight (MW) (65kDa[1]), requiring albumin supplementation following dialysis treatment. This resulted in the view that high cut-off membranes were unsafe and impractical for maintenance HD.

Advancements have led to the development of a new class of dialysis membranes called the mid cut-off dialyzer. This membrane has a pore size between that of a standard high flux and an high cut-off membrane with narrowly distributed pores to enhance membrane permeability and selectivity. However, the safety and efficiency data for the **MCO** dialyzer in a clinical setting are limited.

OBJECTIVE

The primary aim of a tRial Evaluating Mid Cut-Off Value Membrane Clearance of Albumin and Light Chains in Hemodialysis Patients (REMOVAL-HD) study the was to determine the safety of HD using a **MCO** dialyzer (**Theranova** dialyzer; Baxter Healthcare, Sydney, Australia) with regard to its effect on change in serum albumin over 6 months in a prevalent HD cohort.

METHODOLOGY

The study was an investigator initiated, open label, non-randomized, cross over, longitudinal device study conducted across 9 centers in Australia and New Zealand (n=89). Recruitment commenced in January 2017 and the last participant follow-up occurred in April 2018. The criteria for inclusion included >18 years of age, had been on chronic in-center HD for at least 12 weeks.

All visits occurred during participants' mid-week HD session. See Figure 1. Study schema was as follows:

- **Wash-in period (week 0-4)**
  Participants used a 4-week HD wash-in period using a high flux dialyzer (**Revaclear** R400; Baxter Healthcare, Sydney, Australia).
- **Intervention period (week 4-28)**
  Participants then received 24 weeks of treatment with the investigational device, the **MCO** dialyzer (**Theranova** 400 dialyzer; Baxter Healthcare, Sydney, Australia).
- **Wash-out period (week 28-32)**
  Participants then received a 4-week wash-out period using the **Revaclear** high flux dialyzer again.

Centers were advised to maintain the duration (3.0-5.5 hours/session) and frequency of dialysis (3x/week), target blood flow (> 300 mL/minute) and dialysate flow rate (DFR) (500 mL/minute) throughout the study period.

Outcome Measures

Primary Outcomes

The primary outcome was change in centrally measured pre-dialysis serum albumin between baseline (week 4) and 6 months (week 28) during the treatment phase of HD with the **MCO** dialyzer. Other safety outcomes included change in serum albumin across all study visits during the treatment phase monitoring of any large (> 25%) reductions in serum albumin level at every visit. In addition, serious adverse events (SAE) were recorded regardless of whether they were related to the study intervention using standard criteria for clinical trials.

Study Procedures

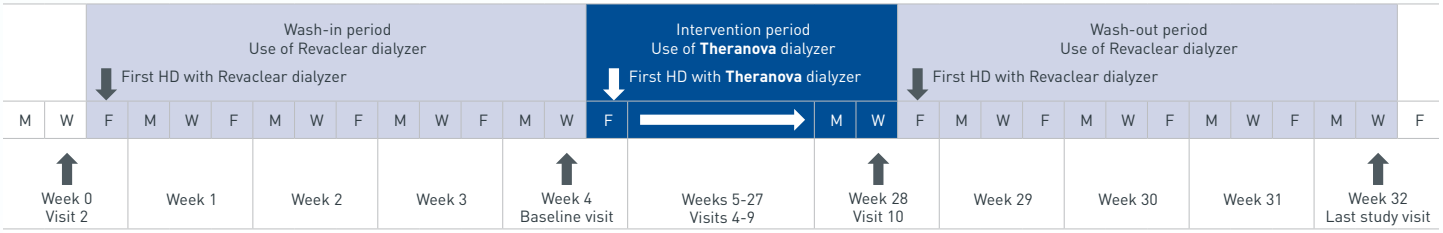

FIGURE 1. REMOVAL-HD study schema. Adapted from Krishnasamy et al. Abbreviations: HD, hemodialysis.