Statistical Analysis Plan (SAP)

OFFICIAL TITLE:

# Fluid Removal With a High Rate Ultrafiltration Protocol in Patients With Intravascular Congestion: the FILTRATE Trial

NCT NUMBER:

NCT Pending

ORGANIZATION'S UNIQUE PROTOCOL ID:

NF26-00006

STUDY START DATE:

04/06/2026

ADDRESS

Monterrey, N.L., México

## 1. Primary Analysis Populating Strategy

- **Intention-to-Treat (ITT) Analysis:** The primary population for all efficacy evaluations will be analyzed according to the randomized treatment group allocation, regardless of subsequent dropouts, protocol deviations, or early session termination. Missing data for the primary endpoint will be handled using multiple imputation techniques or Last Observation Carried Forward (LOCF) as a sensitivity check.
- **Per-Protocol (PP) Analysis:** A secondary safety and efficacy analysis will be conducted restricted to participants who completed their assigned ultrafiltration prescription protocol (10 mL/kg/h vs. >13 mL/kg/h) without early termination or crossing over due to safety triggers.
- **Safety Population:** All safety evaluations (primarily intradialytic hypotension and clinical adverse events) will be evaluated based on the actual ultrafiltration rate received.

## 2. Descriptive Statistics

- **Continuous Variables:** Normality of data will be formally evaluated using the Shapiro-Wilk test. Standard normally distributed variables will be reported as Mean $\pm$ Standard Deviation (SD). Non-normally distributed variables will be reported as Median and Interquartile Range (IQR).
- **Categorical Variables:** Frequencies and percentages (n, %) will be used to describe categorical parameters (e.g., Sex, VExUS grades 0–3, mMRC scale, mMRC changes, presence of intradialytic hypotension).

## 3. Primary Outcomes Analysis

- **Safety Endpoint (Intradialytic Hypotension - IDH):** The incidence of IDH (defined by KDOQI criteria as a drop in SBP >20 mmHg or MAP >10 mmHg with clinical symptoms requiring intervention) will be compared between the two groups using a **Chi-squared test** (or Fisher's Exact test if any expected cell count is <5).
- **Efficacy Endpoints (Decongestion Parameters):**
    - **Continuous parameters:** The absolute and percentage change from baseline to 24 hours post-intervention for the number of lung ultrasound B-lines, E/e' ratio, and Tricuspid Regurgitation Velocity (TRV) will be calculated. Differences between the two groups will be analyzed using an **Independent Samples t-test** (for normally

distributed variables) or a **Mann-Whitney U test** (for non-normal distributions).

- **Categorical parameters:** The proportion of patients achieving a successful reduction of at least 1 grade on the VExUS scale at 24 hours will be compared between groups using a **Chi-squared test**.

**4. Secondary Outcomes Analysis**

- **Predictive Modeling & Threshold Optimization (ROC Curves):** To determine if baseline intravascular congestion scores can predict high-rate ultrafiltration tolerance (>13 mL/kg/h), a **Receiver Operating Characteristic (ROC) Curve** analysis will be conducted. The Area Under the Curve (AUC) will be determined for baseline VExUS grades, lung B-line counts, and E/e' ratios against the binary safety outcome (Presence/Absence of IDH). Optimal clinical cut-off values will be derived using Youden's Index.
- **Clinical Inpatient Metrics:** Differences in total hospital length of stay (days) and total days on supplemental oxygen will be evaluated using the **Mann-Whitney U test**, as hospital length-of-stay metrics are typically right-skewed.
- **Correlation Analyses:** The relationship between quantitative baseline congestion markers, NT-proBNP values, and the net ultrafiltration volume achieved (mL) will be calculated using **Pearson's correlation coefficient (*r*)** or **Spearman's rho (*ρ*)** depending on data normality.
- **Blood Pressure Control Evaluation:** Pre-dialysis vs. 24-hour post-dialysis hemodynamic trends (SBP, DBP, MAP) within each group will be assessed using a **Paired Samples t-test** or **Wilcoxon Signed-Rank test**. Inter-group changes will be compared using an independent analysis.
- **Repeated Measures Dynamic Assessment:** For biomarkers measured across multiple intervals (Baseline vs. Intra-dialytic intervals vs. 24 hours post-dialysis, such as NT-proBNP), changes over time will be examined using a **Repeated Measures ANOVA** (with Mauchly's Test of Sphericity and Greenhouse-Geisser corrections applied if violated) or a non-parametric **Friedman Test**.

**5. Subgroup and Exploratory Analyses**

- **Cardiac Function Interaction:** Stratified subgroup analyses will be executed based on Left Ventricular Ejection Fraction (LVEF) categories (Preserved

[≥50%], Mildly Reduced [41-49%], and Reduced [≤40%]) using **Two-way ANOVA** or **Kruskal-Wallis** tests to establish if underlying systolic or severe diastolic dysfunction significantly alters tolerance or decongestion efficacy when exposed to aggressive ultrafiltration profiles.

## 6. Significance and Software Framework

- All statistical tests will be two-tailed, and a $\mathbf{P \leq 0.05}$ will be considered statistically significant.
- All data computations, processing, and statistical analyses will be performed using **SPSS version 24.0** or above (IBM Corp., Armonk, NY).