Statistical Analysis Plan

for

SOW-002 Quanta SC+

Quanta Dialysis Technologies

A Prospective, Multi-Center, Open-Label Assessment of Efficacy and Safety of Quanta SC+ for Home Hemodialysis

Protocol 02-001

NCT04975880

Version 2.0, dated 21JUN2023

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SIGNATURE PAGE

The undersigned hereby jointly declare that they have reviewed the Statistical Analysis Plan and agree to its form and content.

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DOCUMENT HISTORY

Revision Date	Author	Version	Reason for Change
17OCT2022	Taylor Mahoney	1.0	NA – Initial Version
07MAR2023	Taylor Mahoney	1.1	Updating sample size from enrolling 50 to enrolling up to 50. Adding clarification for the term 'evaluable' when discussing study populations by defining additional population called the 'Evaluable' population. Also state that it will be the primary population for analysis. Updating language in section 7.7 regarding data to be excluded from the analysis to match language in protocol. Also updated language for competency achievement by C8, unless otherwise pre-approved by sponsor. Updating section 7.6 to state that the assessment of homogeneity will be on the evaluable population.
03MAY2023	Taylor Mahoney	1.2	Updating text for listing generation to 'listings may be generated', as not all listings are necessary/desired by sponsor. Removing text in section 9.2 regarding summarizing abnormal labs. These summary statistics will not be calculated per sponsor.
30MAY2023	Taylor Mahoney	1.3	Updating section 7.2 to add a statement that a CONSORT diagram may be provided to illustrate flow of the study. Updating section 7.4 to remove text regarding summarizes of protocol deviations due to COVID-19 will be provided.

			Updating discussion of 95% CIs in section 9.2 – these exact confidence intervals will be derived based on a score statistic (not the Clopper-Pearson method), as Clopper-Pearson is only used for exact 95% CI for a single proportion, not a difference in proportions. Updating text in section 10.2 for the special interest adverse events for secondary endpoints to clarify that the post-dialysis blood pressure is within 30 minutes and not strictly at 30 minutes post dialysis Updating text in sections 11.1, 11.3 – 11.5 to add that adverse events will also be presented using a rate per 100 treatments for the in-center, transition, and in-home periods to provide a fairer comparison of adverse events across periods of the study. These rates are in addition to also reporting the number of events and percentage of participants with events.
21JUN2023	Taylor Mahoney	2.0	NA, sponsor has accepted all changes noted in versions 1.1 – 1.3 above. Finalized changes for signatures.

1 ABBREVIATIONS

Abbreviation	Definition
AE	Adverse Event
ADE	Adverse Device Effect
ANOVA	Analysis of Variance
CEC	Clinical Events Committee
CRF	Case Report Forms
CSR	Clinical Study Report
DMC	Data Monitoring Committee
Eq5d	Eq5d Health Questionnaire
ESAS	Edmonton symptom assessment system
FAS	Full Analysis Set
FDA	United States Food and Drug Administration
HHD	Home Hemodialysis
HF	Hemodialysis Facility
IC	Informed Consent
ICH	International Council on Harmonization
I/E	Inclusion/Exclusion Criteria
IRB	Institutional Review Board
ISO	International Standards Organization
MOS	Medical Outcomes Study
n	Number of Patients
NIM	Non-Inferiority Limit
PD	Protocol Deviation
PP	Per-Protocol Population
QDT	Quanta Dialysis Technologies
RTSQ	Renal Treatment Satisfaction Questionnaire
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SC+	Self-Care Plus
SCEC	Safety and Clinical Events Committee
SD	Standard Deviation
spKt/V	Single Pool Kt/V
TTR	Time to Recovery
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect
ZBI-12	Zarit Burden Interview

2 SUMMARY

TITLE	A Prospective, Multi-Center, Open-Label Assessment of Efficacy and Safety of Quanta SC+ for Home Hemodialysis
PREFACE	This Statistical Analysis Plan (SAP) describes the planned analysis and reporting for Quanta Dialysis Technologies protocol 02-001 [A Prospective, Multi-Center, Open-Label Assessment of Efficacy and Safety of Quanta SC+ for Home Hemodialysis]. This study is being completed to assess the safety and efficacy of Quanta SC+ for delivery of self-care home hemodialysis compared to care in a hemodialysis facility. The following documents were reviewed in preparation of this SAP: • Clinical Research Protocol 02-001 Rev. 1.8, issued 09AUG2022 • Case report forms (CRFs) Rev 6.0, issued 15SEP2022 for Protocol 02-001
PURPOSE	The purpose of this SAP is to outline the planned analyses in support of the Clinical Study Report (CSR) for protocol 02-001. Exploratory analyses not necessarily identified in this SAP may be performed to support the clinical development program. Any post-hoc, or unplanned, analyses not identified in this SAP will be clearly identified in the respective CSR.
STUDY OBJECTIVES	The purpose of this study is to determine non-inferiority of efficacy and safety when Quanta SC+ is used for delivery of self-care home hemodialysis, compared to a hemodialysis facility.
STUDY DESIGN	This is a prospective, multi-center, two-period, open-label study. A dialysis prescription for 3 sessions per week, 4 hours per session, or facility standard will be provided during the in-clinic visits. A dialysis prescription for 4 sessions per week, 3.5 hours per session will be provided during home dialysis. This study does not duplicate any current knowledge existing today for the use of the SC+ Hemodialysis System in the United States. The purpose of this study is to determine non-inferiority of efficacy and safety when Quanta SC+ is used for delivery of self-care home hemodialysis, compared to a hemodialysis facility.
ENDPOINTS	**Primary Endpoints:** The study's **primary efficacy endpoint** is the delivery of a mean standardized weekly Kt/V of greater than or equal to 2.1 in each of the in-center period and the in-home period, using hemodialysis prescriptions of 3 sessions per week and 4.0 hours per session during the in-center period and 4 sessions per week and 3.5 hours per session during the home period. The study's **primary safety endpoint** is the adverse event (AE) rate occurring in the in-home phase of the study, compared to the in-clinic phase. All AEs will be collected, summarized by phase of the study, and compared between the in-clinic and in-home phase of the study. Additionally, in accordance with NCT02460263 (Plumb 2020), the rate of pre-specified AEs will be compared

	between study phases with the pre-specified AEs comprising the following components: ○ Serious adverse event: any adverse event that resulted in death, was life-threatening, required hospitalization or prolonged existing hospitalization, required intervention to prevent permanent impairment or damage, or resulted in persistent or significant disability/incapacity. ○ Allergic reaction: type A anaphylactoid or type B dialyzer reactions to dialyzer, blood tubing, or chemical disinfectant. ○ Blood loss: blood loss resulting in hemodynamic compromise that led to death, transfusion, or fluid resuscitation with greater than 1 liter of crystalloid IV fluids. ○ Hemolytic Reaction: hemolytic reactions due to disinfectant exposure, dialysate temperature, mechanical failure, or other device related causes. ○ Infection: any infection related to hemodialysis catheter, its tunnel or exit site, arteriovenous fistula (AVF), or arteriovenous graft (AVG). ○ Intradialytic event: a significant clinical event such as loss of consciousness, cardiac arrest, or seizure caused by device failure. ○ Vascular access complication: defined as AVF or AVG clotting during the dialysis procedure, bleeding for more than 30 minutes post-dialysis for 3 consecutive sessions, difficulty with vascular access resulting in inability to initiate or complete dialysis treatments or complications related to hemodialysis catheters (not including reduced blood flow in catheter or tissue plasminogen activator (TPA) or catheter exchange). ○ Pyrogenic reaction: onset of objective chills (visible rigors) and fever (oral temperature greater than or equal to 37.5 degrees Celsius) in a participant who was afebrile and who had no recorded signs or symptoms of infection before treatment. **Secondary Endpoints:** <u>Safety:</u> • Number of serious adverse events (SAEs) per 100 treatments occurring in the home phase of the study, compared with those occurring in the in-clinic phase. • Number of device-related AEs and SAEs per 100 treatments in the home phase of the study, compared with those occurring in the in-clinic phase. • Additional adverse events of special interest: ○ Individual components of the primary safety endpoint ○ Air in blood tubing that cannot be resolved through usual procedures. ○ Significantly elevated venous (>250 mmHg) or negative arterial (>100 mmHg) pressures during three (3) consecutive treatments. ○ Intradialytic hypotension, as defined by treatments during which hypotensive symptoms led to either lowering the ultrafiltration rate or saline administration.

	○ Post-dialysis (30 minutes) systolic blood pressure <90 mmHg or systolic blood pressure >180 mmHg following two (2) consecutive treatments. The following biochemistry and hematology laboratory values will be collected and compared to target ranges from clinical practice guidelines. <u>Biochemistry:</u> assessments of pre-treatment plasma at visits C1, C2, C4, H2, H4, and H8: • sodium (Na) (target range, 135-145 mEq/L) • urea (BUN) • potassium (K) (target range, 3.5-5.5 mEq/L) • creatinine (Cr) • bicarbonate (HCO3) (target range, ≥22mEq/L) • magnesium (Mg) • phosphate (Phos) (target range, 3.5-5.5 mg/dL) • chloride (Cl) • calcium (Ca) (target range, 8.4-9.5 mg/dL) • albumin (Alb) (target range, ≥4.0 g/dL) • iron (Fe) • transferrin saturation (TS) (target range, >20%) • total protein (TP) • ferritin (Fn) (target range, >200 ng/mL) • alkaline phosphatase (ALP) • parathyroid hormone (PTH) (target range, 150-600 pg/mL) • total iron binding capacity (TIBC) • aspartate transaminase (AST) (target range, 8-33 IU/L) • alanine aminotransferase (ALT) (target range, 7-56 IU/L) <u>Hematology:</u> assessments of pre-treatment blood at visits C1, C2, C4, H2, H4, and H8: • hemoglobin (Hb) (target range, 9-11.1 g/dL) • hematocrit (Hct) • white cell count (WBC) • platelet count (PC) • reticulocyte Count (RC) (target range, 0.5-2.5%) <u>Ultrafiltration (UF):</u> • Ultrafiltration volume (net fluid removal), such that the recorded value from the Quanta SC+ DDS is within 10% of expected net fluid removal per hour, based on the UF prescription <u>Clinical utility:</u> • Number of alarms • Time to resolve alarms • Type of alarms

	Reliability: • Ability to deliver prescribed treatments Training and competence: • Proportion of subjects and caregivers completing training successfully • Attempts required to complete training successfully Device deficiencies: • Descriptive summary of device deficiencies reported Patient reported outcomes: • Time to recovery after dialysis treatment (Lindsay RM, 2006) • EQ-5D-5L (Culleton BF, 2007) • Medical Outcomes Study (MOS) Sleep Index (Hays RD, 2005; Hays R, 1992) • Renal Treatment Satisfaction Questionnaire (RTSQ, Bardense 2005) • Zarit Burden Interview (ZBI12, Bédard 2001, completed by caregiver rather than participant) • Edmonton Symptom Scale (ESAS-r, Davidson SN, 2006)
INTERIM ANALYSES	No interim analyses are planned for this study.
FINAL ANALYSES	All final planned analyses identified in this SAP will be completed after the last participant has completed last treatment.

3 Study Objectives and Endpoints

3.1 Study Objective

The purpose of this study is to determine non-inferiority of efficacy and safety when Quanta SC+ is used for delivery of self-care home hemodialysis, compared to care in a hemodialysis facility.

3.2 Study Endpoints

3.2.1 Primary Endpoint(s)

The study's **primary effectiveness endpoint** is the delivery of a mean standardized weekly Kt/V of greater than or equal to 2.1 in each of the in-center phase and the in-home phase, using hemodialysis prescriptions of 3 sessions per week and 4.0 hours per session during the in-center phase and 4 sessions per week and 3.5 hours per session during the home phase.

The study's **primary safety endpoint** is the rate of adverse events per 100 treatments occurring in the home phase of the study compared with those occurring in the in-clinic phase. Additionally, in accordance with NCT02460263 (Plumb 2020), the rate of pre-specified AEs will be compared descriptively between study phases as a supporting analysis, with the pre-specified AEs comprising the following components:

- Serious adverse event: any adverse event that resulted in death, was life-threatening, required hospitalization or prolonged existing hospitalization, required intervention to prevent permanent impairment or damage, or resulted in persistent or significant disability/incapacity.
- Allergic reaction: type A anaphylactoid or type B dialyzer reactions to dialyzer, blood tubing, or chemical disinfectant.
- Blood loss: blood loss resulting in hemodynamic compromise that led to death, transfusion, or fluid resuscitation with greater than 1 liter of crystalloid IV fluids.
- Hemolytic Reaction: hemolytic reactions due to disinfectant exposure, dialysate temperature, mechanical failure, or other device related causes.
- Infection: any infection related to hemodialysis catheter, its tunnel or exit site, arteriovenous fistula (AVF), or arteriovenous graft (AVG).
- Intradialytic event: a significant clinical event such as loss of consciousness, cardiac arrest, or seizure caused by device failure.
- Vascular access complication: defined as AVF or AVG clotting during the dialysis procedure, bleeding for more than 30 minutes post-dialysis for 3 consecutive sessions, difficulty with vascular access resulting in inability to initiate or complete dialysis treatments or complications related to hemodialysis catheters (not including reduced blood flow in catheter or tissue plasminogen activator (TPA) or catheter exchange).
- Pyrogenic reaction: onset of objective chills (visible rigors) and fever (oral temperature greater than or equal to 37.5 degrees Celsius) in a participant who was afebrile and who had no recorded signs or symptoms of infection before treatment.

3.2.2 SECONDARY ENDPOINT(S)

Secondary safety endpoints include rate of serious adverse events (SAEs), of device-related AEs, and of device-related SAEs per 100 treatments occurring in the home phase of the study compared with those occurring in the in-clinic phase as well as the rate of additional adverse events of special interest:

- Individual components of the primary safety endpoint
- Air in blood tubing that cannot be resolved through usual procedures.
- Significantly elevated venous (>250 mmHg) or negative arterial (>100 mmHg) pressures during three (3) consecutive treatments.
- Intradialytic hypotension, as defined by treatments during which hypotensive symptoms led to either lowering the ultrafiltration rate or saline administration.
- Post-dialysis (30 minutes) systolic blood pressure <90 mmHg or systolic blood pressure >180 mmHg following two (2) consecutive treatments.

Secondary effectiveness endpoints include the following:

Biochemistry and hematology laboratory values will be collected and compared to target ranges from clinical practice guidelines. Values will be measured pre-treatment at visits C1, C2, C4, H2, H4, and H8 and will include: sodium (Na) (target range, 135-145 mEq/L), urea (BUN), potassium (K) (target range, 3.5-5.5 mEq/L), creatinine (Cr), bicarbonate (HCO3) (target range, ≥22 mEq/L), magnesium (Mg), phosphate (Phos) (target range, 3.5-5.5 mg/dL), chloride (Cl), calcium (Ca) (target range, 8.4-9.5 mg/dL), albumin (Alb) (target range, ≥4.0 g/dL), iron (Fe), transferrin saturation (TS) (target range, >20%), total protein (TP), ferritin (Fn) (target range, >200 ng/mL), alkaline phosphatase (ALP),

parathyroid hormone (PTH) (target range, 150-600 pg/mL), total iron binding capacity (TIBC), aspartate transaminase (AST) (target range, 8-33 IU/L), alanine aminotransferase (ALT) (target range, 7-56 IU/L), hemoglobin (Hb) (target range, 9-11.1 g/dL), hematocrit (Hct), white blood cell count (WBC), platelet count (PC), and reticulocyte count (RC) (target range, 0.5-2.5%). To note, not all biochemistry and hematology labs collected will be compared to target ranges – due to the nature of these renal patients, it is expected that they will not fall into the target range for some of these labs.

Other secondary effectiveness endpoints include assessments of ultrafiltration volume, number of alarms triggered during treatment, time to resolve alarms, types of alarms triggered, ability to deliver prescribed treatments, proportion of subjects and caregivers who successfully complete training, number of attempts required to successfully complete training, device deficiencies observed, as well as a number of patient reported outcomes:

- Time to recovery after dialysis treatment (Lindsay RM, 2006)
- EQ-5D-5L (Culleton BF, 2007)
- Medical Outcomes Study (MOS) Sleep Index (Hays RD, 2005; Hays R, 1992)
- Renal Treatment Satisfaction Questionnaire (RTSQ, Bardense 2005)
- Zarit Burden Interview (ZBI12, Bédard 2001, completed by caregiver rather than participant)
- Edmonton Symptom Scale (ESAS-r, Davidson SN, 2006)

4 Sample Size

Sample size for analysis of primary effectiveness endpoint was calculated using a one-sample test. It was determined that a sample of n=11 patients, each measures weekly for 8 weeks of treatment, will have >90% power to detect that the mean weekly standard Kt/V is greater than 2.1. Sample size was calculated under the following assumptions:

- True treatment period mean weekly standard Kt/V is 2.5
- Standard deviation is 0.7
- One-sided α=0.025
- Within patient correlation of ρ=0.50
- AR(1) covariance structure

Sample size for primary safety endpoint was calculated using a two-sample t-test. It was determined that a sample size of n=33 patients, with 4 dialysis intervals per week for 8 weeks, would have >90% power to demonstrate the rate of AEs per 100 treatments is no more than 10% higher in the in-home period compared to the in-center period. Sample size was calculated under the following assumptions:

- μ_{IH} = 0.03, the rate of AEs per dialysis treatment in-Home is 0.03
- μ_{IC} = 0.03, the rate of AEs per dialysis treatment in-Center is 0.03
- $\mu_{IH} - \mu_{IC}$ = 0, the difference in rate of AEs per dialysis treatment is 0
- $\sigma_{IH-IC} \leq 0.17$, the standard deviation of the difference is less than 0.17 AEs per dialysis interval
- Non-inferiority margin of 0.1 AEs per dialysis interval
- One-sided α=0.025

To account for an expected 15% lost to follow-up rate, and an additional 2 expected death or transplant events during the 8 week in-home phase, based on a combined rate of death and transplant of approximately 15 per 100 patient-years in a usual home hemodialysis (HHD) population, up to 50 patients will be enrolled to yield the 33 evaluable patients needed to be sufficiently powered for both the primary efficacy and primary safety endpoints.

5 Sequence of Planned Analyses

5.1 Interim Analyses

There are no planned Interim Analyses for this study.

5.2 Final Analyses and Reporting

All final, planned, analyses identified in the protocol and in this SAP will be performed only after the last participant has completed last treatment. Key statistics and study results will be made available to Quanta Dialysis Technologies following database lock. Any post-hoc, exploratory analyses completed to support planned study analyses, which were not identified in this SAP, will be documented and reported as necessary. Any results from these unplanned analyses will also be clearly identified as post-hoc analyses.

6 Analysis Populations

6.1 Full Analysis Set (FAS)

The full analysis set (FAS) for this study will include all participants who are enrolled in the study. A sensitivity analysis performed on the FAS population with missing value imputation.

Subjects are considered enrolled in the trial after they have signed the informed consent form, met all of the inclusion criteria and none of the exclusion criteria, and who start the first study treatment during the first treatment period.

6.2 Evaluable Population (EVAL)

The evaluable population (EVAL) will include all participants who are enrolled in the study and who have successfully completed at least 75% of their dialysis treatments. A successfully completed dialysis treatment is defined as one completed as prescribed by the physician. The primary analysis population will be the evaluable population with no missing value imputation.

6.3 Per-Protocol Population (PP)

The per-protocol population (PP) will include all participants who are enrolled in the study, who have successfully completed at least 75% of their dialysis treatments, have at least one valid value of the

primary effectiveness variable and have no major protocol deviations while enrolled in the study. A successfully completed dialysis treatment is defined as one completed as prescribed by the physician. A major protocol deviation is defined as any protocol deviation that affects the soundness of the data. Participants to be excluded from the PP analysis set, and the reasons for their exclusion, will be determined and documented prior to statistical analysis. These decisions will not be outcome-data driven.

7 General Issues for Statistical Analysis

The study will use a standard approach to statistical analysis. Descriptive statistics (mean, standard deviation, frequencies, etc.) for baseline participant characteristics, patient disposition and other relevant study parameters will be reported.

7.1 Analysis Software

Analysis data sets, statistical analyses and associated output generated by Avania will be generated using SAS® Software version 9.4 or later.

7.2 Disposition of Subjects and Withdrawals

The number and percent of subjects in each analysis population will be presented, with percentages based on the FAS population.

All subjects who provide written informed consent will be accounted for. The frequency and percent of subjects who completed each scheduled assessment will be presented in a table.

The number and percentage of FAS patients prematurely withdrawing will be presented overall and by reason of discontinuation.

A CONSORT diagram may also be provided to visually illustrate the flow of the study.

7.3 Methods for Withdrawals and Missing Data

Participants are free to withdraw at any time. A participant will be automatically withdrawn if training competency is not achieved after 8 weeks of in-clinic treatment (unless otherwise approved by the sponsor) or if treatments cease with SC+ for a period of more than 7 consecutive days during the course of the study or if 8 or more non-consecutive treatments are missed. Data taken prior to withdrawal will be used for study analysis.

All practical monitoring and follow-up steps will be taken to ensure complete and accurate data collection. However, it is expected that some data may be missing for the primary effectiveness endpoint, Kt/V, in the FAS population. Participants who are missing any Kt/V measurements during the in-center or in-home phases will be considered as “missing data participants” for the primary effectiveness endpoint. As a sensitivity analysis, missing data for the primary effectiveness endpoint will be imputed. The following imputation techniques will be conducted:

- Multiple Imputation (MI) using a fully conditional specification (FCS) method, in which a linear regression model including dry weight for a given week and all previous weekly Kt/V values for a given study phase (in-center or in-home) will be used in order to predict the primary effectiveness endpoint, Kt/V. Kt/V will be imputed for each week for a given study phase. There will be no imputation of missing Kt/V during the transition phase. To be explicit, imputation will occur in the following manner:
    - In-Clinic Weeks
        - Kt/V for C1 will be imputed using only dry weight at C1
        - Kt/V for C2 will be imputed using dry weight at C2 and Kt/V at C1
        - Kt/V for C3 will be imputed using dry weight at C3 and Kt/V at C1 and C2
        - Kt/V for C4 will be imputed using dry weight at C4 and Kt/V at C1 through C3
        - Kt/V for C5 will be imputed using dry weight at C5 and Kt/V at C1 through C4
        - Kt/V for C6 will be imputed using dry weight at C6 and Kt/V at C1 through C5
        - Kt/V for C7 will be imputed using dry weight at C7 and Kt/V at C1 through C6
        - Kt/V for C8 will be imputed using dry weight at C8 and Kt/V at C1 through C7
    - In-Home Weeks
        - Kt/V for H1 will be imputed using only dry weight at H1
        - Kt/V for H2 will be imputed using dry weight at H2 and Kt/V at H1
        - Kt/V for H3 will be imputed using dry weight at H3 and Kt/V at H1 and H2
        - Kt/V for H4 will be imputed using dry weight at H4 and Kt/V at H1 through H3
        - Kt/V for H5 will be imputed using dry weight at H5 and Kt/V at H1 through H4
        - Kt/V for H6 will be imputed using dry weight at H6 and Kt/V at H1 through H5
        - Kt/V for H7 will be imputed using dry weight at H7 and Kt/V at H1 through H6
        - Kt/V for H8 will be imputed using dry weight at H8 and Kt/V at H1 through H7

    The number of imputations will depend on the fraction of missing information (FMI). Initially, a total of 50 imputations will be carried out to create 50 “complete” datasets, which has been demonstrated to produce stable estimates. If the highest FMI percentage is greater than 50, the number of imputations used will be increased to be equal to the highest FMI percentage. The repeated measures analysis of variance (ANOVA) containing terms for participant, treatment phase, and time points (weeks) and using an AR(1) covariance structure will be run on each of the 50 imputed data sets in order to obtain least squares mean (and it’s standard error) for the respective treatment period. Results will be combined across the datasets using standard multiple imputation theory to obtain a single point estimate, 95% confidence interval, and p-value for each of the treatment phases.

The primary efficacy analysis will initially be done on the evaluable population with no missing value imputation and will also be repeated on the PP population with no missing value imputation and on the FAS with missing value imputation as described above.

There will be no imputation for the primary safety endpoint or any secondary endpoints.

7.4 Protocol Deviations

Protocol deviations will be summarized in the CSR. This summary will include the number and percent of participants (overall and by site) with each deviation type. Deviations will be classified as major or minor prior to database lock to determine which patients should be excluded from the PP population. Major protocol deviations are those that affects the soundness of the study data. A data listing of protocol deviations will also be generated.

7.5 Multiple Comparisons and Multiplicity

For the trial to be considered a success, the null hypothesis must be rejected for both co-primary effectiveness endpoints, as well as for the primary safety endpoint. The co-primary effectiveness endpoints will each be tested at the one-sided α=0.025 level of significance, where the one-sided alternative hypothesis represents a mean standardized weekly Kt/V of greater than or equal to 2.1, for both the in-clinic and in-home phases of the study, respectively. The primary safety endpoint will also be tested at the one-sided α=0.025 level of significance, where the one-sided alternative hypothesis represents non-inferiority of the in-home adverse event rate to the in-clinic adverse event rate, under a non-inferiority margin of 10%. No adjustments for multiple comparisons will be made for the primary endpoints.

All secondary effectiveness and safety endpoints will be descriptive in nature and 95% confidence intervals will be presented. No adjustments for multiplicity will be made.

7.6 Assessment of Homogeneity

A test of homogeneity across sites will be done to determine if the study sites have reasonably homogeneous responses of the primary effectiveness endpoint (weekly standardized Kt/V) on the evaluable population. This will be performed using a one-way analysis of variance (ANOVA) for continuous outcomes with site as the independent variable, tested at a 0.15 level of significance. If the responses are not homogenous, the appropriate regression analysis will be done to determine if the lack of homogeneity is due to the site or due to a possible imbalance in baseline characteristics of the subjects across study sites. If the site effect is no longer significant at a 0.15 level of significance after adding the potentially unbalanced baseline covariates, then site will not be considered a source of lack of homogeneity.

The assessment of homogeneity will occur using available data only, and no imputation for missing primary endpoint data will occur.

7.7 Timing of Assessments and Events for Analysis

Patients will be considered enrolled in the study once they or their authorized representative have provided written informed consent and they have been documented to have successfully met all inclusion criteria and no exclusion criteria. In-clinic dialysis should start within 2 weeks of enrollment. Dialysis prescription during the in-clinic phase is 3 times per week, 4 hours per session. The in-clinic phase spans C1 through C4 at a minimum and continues for C5 through C8 until training competency is

established. Clinic visits will occur Monday, Wednesday, and Friday and blood sampling will be performed on Wednesday unless otherwise approved by sponsor. The start of the transition phase will begin the week after competency sign-off and the in-home phase will begin the following week. Dialysis prescription during the transition and in-home phases is 4 times per week, 3.5 hours per session. In-home visits will occur Monday, Wednesday, Friday, and Saturday unless otherwise approved by Sponsor. A participant will be automatically withdrawn if training competency is not achieved by C8, unless otherwise pre-approved by sponsor, or if treatments with SC+ cease for a period of more than 7 consecutive days during the course of the study or if 8 or more (non-consecutive) treatments are missed. Data taken prior to withdrawal will be included in study analyses.

C1 will be considered baseline for standard weekly Kt/V, as well as for biochemistry and hematology labs.

The baseline values for vital signs are the pre-dialysis measurements taken during the first treatment of C1.

8 Demographics and Other Baseline Characteristics

8.1 Demographics

Baseline demographics and patient characteristics will be summarized in the evaluable, FAS, and PP populations including, age, sex, ethnicity, race, height, weight, and BMI. Categorical demographics will be summarized as frequency and percentage. Continuous demographics will be summarized by reporting n, mean, standard deviation, median, minimum, and maximum. A listing may also be generated.

8.2 Prior and Concomitant Medications

Prior and concurrent medications use will be summarized as frequency and percent in the evaluable population. Prior and concomitant medication collection will be limited to erythropoiesis-stimulating agents (ESAs), intravenous iron, phosphate binders, calcimimetics, and anti-hypertensive medications (ACE inhibitors, ARBs, beta blockers, calcium channel blockers, central alpha agonists, and vasodilators [specifically, hydralazine and minoxidil]). A data listing may also be generated.

8.3 Baseline Medical and Surgical History

Baseline medical and surgical history will be summarized in the evaluable population. The frequency and percent of patients will be summarized for each medical and surgical history attribute as either a current or past/resolved condition. Data listings will also be generated.

8.4 Baseline Physical Exam

Baseline physical exam will be summarized in the evaluable population. The frequency and percent of patients with a normal and abnormal results for each body system will be displayed. A data listing may also be generated.

8.5 Dialysis Treatment History

Baseline dialysis treatment history will be summarized in the evaluable population. The frequency and percent of patients will be summarized for each type of dialysis (hemodialysis – in facility, hemodialysis – home, peritoneal dialysis) they have received. A data listing may also be generated.

8.6 Baseline Vital Signs

Baseline vital signs, including blood pressure, pulse, and temperature (oral, tympanic, temporal), will be summarized in a table using n, mean, standard deviation, median, minimum, and maximum in the evaluable population. A data listing may also be generated.

8.7 Baseline Biochemistry Labs

Baseline biochemistry labs including, sodium, blood urea nitrogen, potassium, creatinine, bicarbonate, magnesium, phosphate, chloride, calcium, albumin, iron, transferrin saturation, total protein, ferritin, alkaline phosphate, parathyroid hormone, total iron binding capacity, AST (SGOT), and ALT (SGPT), will be summarized in a table using n, mean, standard deviation, median, minimum, and maximum in the evaluable population. A data listing may also be generated.

8.8 Baseline Hematology Labs

Baseline hematology labs including hemoglobin, hematocrit, white blood cell count, platelet count, and reticulocyte count, will be summarized in a table using n, mean, standard deviation, median, minimum, and maximum in the evaluable population. A data listing may also be generated.

9 Effectiveness Analyses

9.1 Primary Effectiveness Variable

The primary effectiveness endpoint is the delivery of a mean standardized weekly Kt/V of greater than or equal to 2.1 in each of the in-center period and the in-home period, using hemodialysis prescriptions of 3 sessions per week and 4.0 hours per session during the in-center period and 4 sessions per week and 3.5 hours per session during the home period.

The primary effectiveness hypotheses are:

$$HH_{aa0}: \mu\mu_{IIII} \leq 2.1 \; vvvv. \; HH_{aa1}: \mu\mu_{IIII} > 2.1$$

and

$$HH_{bb0}: \mu\mu_{IIII} \leq 2.1 \; vvvv. \; HH_{bb1}: \mu\mu_{IIII} > 2.1$$

where μ_{IC} is the mean weekly standardized Kt/V for the in-center period and μ_{IH} is the mean weekly standardized Kt/V for the in-home period. These hypotheses will be tested at a one-sided α=0.025 level of significance using the least squares mean for the respective treatment period from a repeated

measures analysis of variance (ANOVA) containing terms for participant, treatment period, and time points (weeks) and using an AR(1) covariance structure.

The weekly standardized Kt/V value will be calculated using the Leypoldt chain (2004):

$$UUUU = BBUUBB_{pppppppp}/BBUUBB_{pppppp}$$

$$vvssssss/VV = (-1 \times \log(UUUU - 0.008) * (ss_{ppppppaappttppttpp}/60))) + ((4 - 3.5 \times UUUU) \times (UUUUVV/wwwwwwwwhss))$$

$$qq = (0.924 \times vvssssss/VV) - \text{\textdiamond}0.395 * (vvssssss/VV/(ss_{ppppppaappttppttpp}/60))\text{\textdiamond} + 0.056$$

$$wwssss/VV = \min(vvssssss/VV, qq)$$

$$SSssSSSSSSSSSSS\ ssss/vv = 168 \times (1 - e^{-eKt/V})/ss/((1 - ww^{-pp/VV})/(ssss/VV) + 168/(BB \times ss) - 1)$$

Where BUN_{pre} = blood urea nitrogen concentration before treatment, BUN_{post} = blood urea nitrogen concentration after treatment, $t_{treatment}$ = treatment duration (in hours), UFV = ultrafiltration volume (in liters), weight = dry weight, and N = number of treatments during the week (7-day period).

Summary statistics (mean, sample size, standard deviation, minimum, maximum, and median) will be computed on the weekly standardized Kt/V values for each treatment period.

All analyses of the primary effectiveness variable will be performed on the evaluable population with no missing value imputation, the FAS population with missing value imputation, and the PP population without missing value imputation. Analysis of both primary endpoints will exclude the transition phase treatment sessions due to the supervision of study staff, as it is believed these treatment sessions will not represent a true in-home treatment session.

The number of prescription changes occurring during the study is expected to be low. A summary table will be provided of all prescription changes by treatment period (in-center and in-home).

The study will be considered a success from a statistical standpoint if:

1. Both primary effectiveness variables pass their respective hypotheses, i.e., Ha0 and Hb0 above are rejected in favor of Ha1 and Hb1, respectively, and
2. The rate of adverse events per 100 treatments is not worse during the In-Home period as compared to the In-Center period. (see Section 10.1)

9.2 Secondary Effectiveness Variables

Summary statistics (n, mean, standard deviation, median, minimum, and maximum) on the raw data as well as changes from baseline will be presented by timepoint for all endpoints shown below in the evaluable population for continuous variables. Categorical variables will be displayed as frequencies and percent. If multiple labs were performed at a given timepoint, the lab results from the date the site is basing clinical care from will be used and summarized in the analysis tables. All laboratory analysis will be performed by the local labs affiliated with the hemodialysis facility. Missing endpoints will not be imputed. Endpoints (with timepoint) include:

- Post-dialysis systolic blood pressure <90 mmHg or systolic blood pressure >180 mmHg following two consecutive treatments (C1, C2, C3, C4, C5, C6, C7, C8, T, H1, H2, H3, H4, H5, H6, H7, H8)
- Sodium (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Urea (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal; measured both immediately before and after each treatment)
- Potassium (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Creatinine (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Bicarbonate (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Magnesium (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Phosphate (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Chloride (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Calcium (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Albumin (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Iron (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Transferring saturation (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Total protein (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Ferritin (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Alkaline phosphatase (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Parathyroid hormone (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Total iron binding capacity (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Aspartate transaminase (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Alanine aminotransferase (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Hemoglobin (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Hematocrit (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- White blood cell count (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Platelet count (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Reticulocyte count (C1, C2, C4, C6, C8, H2, H4, H6, H8, Withdrawal)
- Ultrafiltration volume (net fluid removal) (All treatments)
- Number of alarms (All treatments)
- Time to resolve alarms (All treatments)
- Types of alarms (All treatments)
- Ability to deliver prescribed treatment
- Successful training of participant and caregiver (C4, C5, C6, C7, C8)
- Attempts required to complete training successfully (C4, C5, C6, C7, C8)
- Device deficiency assessment (All treatments and Withdrawal)
- Time to recovery after dialysis (TTR) (C1, H1, H4, H8, Withdrawal)
- EQ-5D-5L (C1, H1, H8, Withdrawal)
- Medical Outcomes Study (MOS) Sleep Index (C1, H1, H8, Withdrawal)
- Renal Treatment Satisfaction Questionnaire (C1, H1, H8, Withdrawal)
- Zarit Burden Interview (ZBI-12) (H8, Withdrawal)
- Edmonton Symptom Scale (ESAS-r) (C1, H1, H8, Withdrawal)

Estimates of secondary endpoints and differences measured between the last measurement (H8 or withdrawal) and the first measurement (C1) will be reported along with their two-sided 95% confidence intervals, as applicable. For continuous endpoints, we will derive the estimate of the difference in means and it's 95% CI from a paired t-test for dependent samples. For dichotomous endpoints, we will derive the estimate of the difference in proportions and it's exact 95% CI based on a score statistic. In terms of the PRO secondary endpoints, the total scores for EQ-5D-5L, MOS, and RTQS, as well as the per symptom scores on the ESAS-r will be descriptively analyzed. Finally, for TTR, the difference in rate and corresponding exact 95% CI (derived from a score statistic) between last measurement minus first measurement for each category (0-2 hours, 2-6 hours, 6-12 hours, 12-24 hours and >24 hours) will be shown. As these endpoints are not intended for labeling, the analysis will be descriptive in nature and therefore no type I error adjustment is required.

The analysis of the primary and secondary endpoints will exclude the data collected from the extended treatment phase (described in section 12.2).

10 SAFETY ANALYSES

Safety endpoints will be assessed from C1 until participant withdrawal. The analysis of the safety endpoints will exclude the data collected from the extended treatment phase. Safety endpoints will be presented using descriptive statistics and will be completed in the evaluable population.

10.1 PRIMARY SAFETY ENDPOINT

The primary safety endpoint is the adverse event rate: the number of adverse events per 100 treatments occurring in the in-clinic portion of the study compared with those occurring in the home portion.

For each treatment period, a 95% confidence interval will be computed on the AE rate per 100 treatments. This confidence interval will be computed using the least squares mean for the respective treatment period from a repeated measures GEE model containing terms for participant, treatment period and time points using a Poisson link function and AR(1) covariance structure. Additionally, to compare the AE rate between treatment periods, the difference in number of AEs between treatment periods and the associated 95% CI of the difference will be computed using the least squares means from the above GEE model. The difference in LS means will be used to test the following hypothesis at a one-sided α=0.025 level of significance:

$$HH_{cc0}: \mu\mu_{IIII} - \mu\mu_{IIII} \geq 0.1 \; vvvv. \; HH_{cc1}: \mu\mu_{IIII} - \mu\mu_{IIII} < 0.1$$

If the upper bound of the 95% CI for the difference between number of AEs between treatment periods is below 10%, the AE rate for the In-Home treatment period will be considered not worse than the AE rate for the In-Center treatment period.

Additionally, in accordance with NCT02460263 (Plumb 2020), the rate of pre-specified AEs will be compared between study phases, with the pre-specified AEs comprising the following components:

- Serious adverse event: any adverse event that resulted in death, was life-threatening, required hospitalization or prolonged existing hospitalization, required intervention to prevent permanent impairment or damage, or resulted in persistent or significant disability/incapacity.
- Allergic reaction: type A anaphylactoid or type B dialyzer reactions to dialyzer, blood tubing, or chemical disinfectant.
- Blood loss: blood loss resulting in hemodynamic compromise that led to death, transfusion, or fluid resuscitation with greater than 1 liter of crystalloid IV fluids.
- Hemolytic Reaction: hemolytic reactions due to disinfectant exposure, dialysate temperature, mechanical failure, or other device related causes.
- Infection: any infection related to hemodialysis catheter, its tunnel or exit site, arteriovenous fistula (AVF), or arteriovenous graft (AVG).
- Intradialytic event: a significant clinical event such as loss of consciousness, cardiac arrest, or seizure caused by device failure.
- Vascular access complication: defined as AVF or AVG clotting during the dialysis procedure, bleeding for more than 30 minutes post-dialysis for 3 consecutive sessions, difficulty with vascular access resulting in inability to initiate or complete dialysis treatments or complications related to hemodialysis catheters (not including reduced blood flow in catheter or tissue plasminogen activator (TPA) or catheter exchange).
- Pyrogenic reaction: onset of objective chills (visible rigors) and fever (oral temperature greater than or equal to 37.5 degrees Celsius in a participant who was afebrile and who had no recorded signs or symptoms of infection before treatment.

No formal testing will be done on the rate of pre-specified AEs in accordance with NCT02460263. The estimate of the difference in rates between study phases and it's 95% CI will be generated using the repeated measures GEE model as described above for the primary safety endpoint. The analysis of these pre-specified AEs will be descriptive in nature, and do not require an adjustment to be made to the type I error rate.

10.2 Secondary Safety Endpoints

Secondary safety endpoints will be analyzed in the same manner as the primary safety endpoint, as described above. These shall include:

- Number of serious adverse events (SAEs) per 100 treatments occurring in the home phase of the study, compared with those occurring in the in-clinic phase
- Number of device-related AEs and SAEs per 100 treatments in the home phase of the study, compared with those occurring in the in-clinic phase
- Adverse events of special interest:
    - Individual components of the primary safety endpoint
    - Air in blood tubing that cannot be resolved through usual procedures
    - Significantly elevated venous (>250 mmHg) or negative arterial (>100 mmHg) pressures during three (3) consecutive treatments
    - Intradialytic hypotension, as defined by treatments during which hypotensive symptoms led to either lowering the ultrafiltration rate or saline administration

- Post-dialysis (within 30 minutes) systolic blood pressure <90 mmHg or systolic blood pressure >180 mmHg following two (2) consecutive treatments

Additionally, a table will be provided to show the number and percentage of the evaluable population subjects with at least one pre-specified AE by treatment period, and overall, for each dialysis treatment period (in-center and in-home), by MedDRA system organ class (SOC) and preferred term (PT). All AEs, all SAEs, and all device-related AEs will be summarized in a similar manner.

11 Adverse Events

All adverse events (AEs) will be coded using the standardized Medical Dictionary for Regulatory Activities (MedDRA) central coding dictionary, version 24.0 or greater. All adverse event related tables and listings described below will be based on the FAS population.

11.1 All Adverse Events

Summaries of incidence rates of individual AEs by System Organ Class (SOC) and Preferred Term (PT) will be presented for the FAS population. Because a patient may experience more than one AE, summaries will provide both the number of patients experiencing at least one event and the number of events within a reporting period. Percentages provided will be the percent of patients experiencing one or more adverse events. Additionally, raw adverse event rates per 100 treatments will be presented by SOC/PT for the in-clinic, transition, and in-home phases of the study to allow for fair comparison of adverse event occurrence across study periods. Due to the granularity of reporting by SOC/PT, the rates per 100 events will be raw and not computed via GEE models as in the primary safety endpoint.

A listing of all adverse events will include the subject number, AE number, start date, stop date, AE SOC and PT, severity, seriousness, action taken, outcome, and adjudication status as well as relationship to investigational device, non-investigational device, procedure, concomitant medications, pre-existing condition, intercurrent condition, intercurrent intervention, or other.

11.2 Adverse Events Leading to Withdrawal

A data listing of AEs leading to withdrawal in the FAS population will be provided, displaying details of the event(s) captured on the CRF.

11.3 Serious Adverse Events

Summaries of incidence rates of individual SAEs by SOC and PT will be prepared for the FAS population. Summaries will provide both the number of subjects and the number of events within a reporting period. Percentages provided will be the percent of subjects experiencing one or more serious adverse events. Additionally, raw adverse event rates per 100 treatments will be presented by SOC/PT for the in-clinic, transition, and in-home phases of the study to allow for fair comparison of adverse event occurrence across study periods. Due to the granularity of reporting by SOC/PT, the rates per 100 events will be raw and not computed via GEE models as in the primary safety endpoint.

A data listing of SAEs may also be provided, displaying details of the event(s) captured on the CRF.

11.4 Device or Procedure Related Adverse Events

Summaries of incidence rates of device (investigational and non-investigational) and procedure related AEs by SOC and PT will be prepared for the FAS population. Summaries will provide both the number of subjects and the number of events within a reporting period. Percentages provided will be the percent of subjects experiencing one or more device or procedure related adverse events. Additionally, raw adverse event rates per 100 treatments will be presented by SOC/PT for the in-clinic, transition, and in-home phases of the study to allow for fair comparison of adverse event occurrence across study periods. Due to the granularity of reporting by SOC/PT, the rates per 100 events will be raw and not computed via GEE models as in the primary safety endpoint.

Data listings of device and procedure related AEs may also be provided, displaying details of the event(s) captured on the CRF.

11.5 Unanticipated Adverse Events

Summaries of incidence rates of unanticipated AEs by SOC and PT will be prepared for the FAS population. Summaries will provide both the number of subjects and the number of events within a reporting period. Percentages provided will be the percent of subjects experiencing one or more unanticipated adverse events. Additionally, raw adverse event rates per 100 treatments will be presented by SOC/PT for the in-clinic, transition, and in-home phases of the study to allow for fair comparison of adverse event occurrence across study periods. Due to the granularity of reporting by SOC/PT, the rates per 100 events will be raw and not computed via GEE models as in the primary safety endpoint.

A data listing of unanticipated AEs will also be provided, displaying details of the event(s) captured on the CRF.

11.6 Deaths

Should any subjects die during the course of the Quanta SC+ trial, relevant information will be supplied in a data listing.

12 Other Planned Analyses

12.1 Planned Subgroup Analyses

Subgroups will be performed on both co-primary effectiveness endpoints (the delivery of a mean standardized weekly Kt/V of greater than or equal to 2.1 in each of the in-center period and the in-home period), as well as the primary safety endpoint (the number of adverse events per 100 treatments occurring in the in-clinic portion of the study compared with those occurring in the home portion). The Quanta SC+ Clinical Trial is not powered for these subgroup analyses and therefore, there will be no formal hypothesis testing for the primary endpoints within subgroups. These analyses will be performed on the evaluable Population.

12.1.1 Age

The analyses of the primary endpoints will be summarized descriptively in the following age categories: 18-50 years, 50-70 years, and 70-80 years.

12.1.2 Sex

In accordance with FDA guidance, the analyses of the primary endpoints will be summarized descriptively separately within each sex.

12.1.3 Race

In accordance with FDA guidance, the analyses of the primary endpoints will be summarized descriptively separately within each race.

12.1.4 Dry Weight at C1

The analyses of the primary endpoints will be summarized descriptively in the following dry weight at C1 categories: 50-70 kg, 70-100 kg, and >100 kg.

12.1.5 Diabetes Status

The analyses of the primary endpoints will be summarized descriptively separately in patients who have diabetes and patients who do not have diabetes.

12.1.6 Cardiovascular Disease History

The analyses of the primary endpoints will be summarized descriptively separately in patients who have a history of cardiovascular disease and patients who do not have a history of cardiovascular disease.

12.1.7 Dialysis Access Method Used For the Majority of the Duration of the Study

The analyses of the primary endpoints will be summarized descriptively separately in patients who use the following methods for dialysis access for the majority of the duration of the study: fistula, central line, and graft.

12.2 Planned Analyses for the Extension Phase

Patients who complete the HOME RUN Trial protocol will be permitted via new informed consent to remain on the SC+ in the home setting for a period not exceeding 18 months or until FDA clearance is granted for home use. Subjects will be instructed to report any device-related medical events or deficiencies throughout the extended treatment phase.

The analysis of the primary and secondary endpoints will exclude the data collected from this extended treatment phase. At the conclusion of the extended treatment phase, data collected during extended treatment will be summarized in tables and/or data listings.

13 Summary of Changes from the Protocol

The following table provides a list of changes from the protocol to the SAP, and the justification for each change. Any changes from the protocol made in the SAP will override the protocol.

Section	Description	Justification
Protocol Section 10.2.2 / SAP Section 4	Changing the number of subjects enrolled from 50 to up to 50	Clarifying that the trial will enroll up to 50 patients to obtain an evaluable sample size of 33 patients.
Protocol Section 10.3.1 / SAP Section 6.2	Updating primary analysis population to be the evaluable population rather than FAS	This decision ensures that patients will have data in both the in-clinic and in-home phases of the study which was an assumption of the power/SS calculations. The FAS does not ensure that patients will have data in both study phases.
Protocol Section 6.5 / SAP Section 7.7	Added 'unless otherwise pre-approved by sponsor' to the withdrawal if competency not achieved by C8	Sponsor will consider approving additional clinic time for participants that are competent on the SC+ but have not been deemed competent with another component of home training or whose homes were not prepared for device installation by the end of C8.
Protocol Section 10.6 / SAP Section 10.2	Changing methodology used to derive exact 95% CIs for difference in proportions from Clopper-Pearson to based on a score statistic	Clopper-Pearson is only used for exact 95% CI for a single proportion, not a difference in proportions. Exact 95% CIs based on a score statistic are more appropriate here.
Protocol Section 8.2 / SAP Section 7.7	Removing text regarding to be included in the data analysis, scheduled visits occurring after competency sign off must occur within +/- 3 days of the expected time point	This statement is not applicable to the statistical analysis due to the nature of the data collection and the frequency of visits in this study.

14 Reporting Conventions

All reporting will meet the standards of SOP-68 AS Data Analysis Reporting and SOP-83 AS Programming Standards.

15 References

Bardense S, Speight J, Bradley C. The Renal Treatment Satisfaction Questionnaire (RTSQ): A Measure of Satisfaction with Treatment for Chronic Kidney Failure. Am J Kidney Dis. 2005;45(3):572-579.

Bédard M, Molloy DW, Squire L, Dubois S, Lever JA, O'Donnell M. The Zarit Burden Interview: a new short version and screening version. Gerontologist. 2001;41(5):652-657.

EQ5D-L user guide: https://euroqol.org/publications/user-guides/