Clinical Protocol

A pK study comparing the clearance of Vancomycin during haemodialysis using Medium cut-off membrane (Theranova) and High-Flux membranes (Revaclear)

**UPDATED FOR –**

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**PROTOCOL Synopsis**

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|  |
| **Tile:**   * A pK study comparing the Clearance of vancomycin during haemodialysis using the Medium cut-off membrane (Theranova) and High-Flux membranes (Revaclear)   **Study Site**:   * Hastings Hospital, Hawke’s Bay, New Zealand   **Objectives:**   * To evaluate the drug clearance profile of vancomycin on haemodialysis with Medium cut-off membrane (Theranova) dialyser compared with high-flux dialysers (Revaclear) in haemodialysis patients   **Design:**   * This is an observational study comparing the clearance of vancomycin on two standard dialysis therapies: Medium cut-off membrane (Theranova) dialyser and high-flux dialysis (Revaclear) * Drug clearance will be studied in patients receiving vancomycin for standard clinical indications in the dialysis unit (e.g. line sepsis). * Patients will receive vancomycin as per standard treatment procedures for a 2 week treatment period. * Eligible subjects will receive vancomycin as a loading dose followed by maintenance dose at the next dialysis sessions following standard treatment pathways for a total of six haemodialysis sessions. * At each visit, blood samples for drug concentration will be collected at the start of dialysis session, then at 5, 15, 30, 45, 120, and 30 minutes post dialysis session. Subjects will be discharged from the dialysis unit after each dialysis session. * During the study period patients will receive alternative dialysis sessions on Revaclear and Theranova dialysers   **Sample Size:**   * A total of 6 volunteers on haemodialysis   **Method of Subject Assignment**:   * Open label   **Primary Outcome Measures:**   * Vancomycin drug clearance   **Secondary Outcome Measures:**   * Obtaining Adverse Events: All volunteered, elicited and observed adverse events (AEs) will be documented. | |  |

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# **Introduction:**

Vancomycin is an antibiotic produced by *Streptomyces orientalis*, an actinomycete isolated from soil samples in Indonesia and India. Vancomycin is a glycopeptide with bactericidal action that acts by inhibiting peptidoglycan synthesis in the cell wall. It is poorly absorbed by the oral route and is excreted in large amounts in faeces. Following intravenous (IV) administration to subjects with normal kidney function, plasma protein binding is 10%-55%. Eighty percent of the drug is excreted unchanged by glomerular filtration, with a half-life of 6-8 hours. In patients with advanced renal failure (RF), half-life may be up to 150-250 hours, and plasma protein binding is 18%. Despite its low molecular weight (1,449 D), vancomycin is not removed by conventional haemodialysis (HD) with low flux membranes, but its removal is increased when high permeability filters, such as polysulphone, polyacrylonitrile, or polymethylmethacrylate, are used. Monitoring of vancomycin plasma levels allows for ensuring therapeutic levels (15-20 mg/L) and avoiding toxic levels. [1-4]

Because of the high rate of infections by Staphylococcus aureus, sometimes methicillin-resistant, and frequently related to the vascular access, vancomycin is widely used in patients on HD. Moreover, dosing is simple according to the conventional administration regimen since the drug is infused at the end of the dialysis session and no dose is required in the period between dialyses. Current guidelines and dosing recommendations are based on assuming that high flux haemodialysis removes about 20% of vancomycin per 3-hour session. [5]

End-stage renal disease (ESRD) results in the retention of uremic toxins, which is associated with high mortality. Uremic toxins are classified into small (<500 Da) and middle molecular (500 Da–60 kDa) water-soluble solutes and protein bound substances. While conventional hemodialysis (HD)modalities remove small solutes and smaller-sized middle molecules, clearance of larger middle molecules and protein bound substances is poor. Studies have associated middle molecules to pathological features of uremia, such as immune dysfunction and inflammation, as well as adverse outcomes in dialysis patients. [6]

The medium cut-off membrane dialyser has been shown to remove a wide range of middle molecules more effectively than high-ﬂux HD and even exceeds the performance of high-volume hemodiaﬁltration for large solutes, particularly Kappa Free light chains. The theory is that removing these molecules will potentially reduce the risk of cardiovascular disease and secondary immune deficiency and make it better for the patient. [7]

Currently, there is limited data on the clearance of drugs on the medium cut-off dialyser

### **1.1. Rational**

Vancomycin has been used successfully for the treatment of gram positive septicemia in haemodialysis patients. Current guidelines and dosing recommendations are based on assuming that high flux haemodialysis removes about 20% of vancomycin per 3-hour session.

To our knowledge, there have been no studies looking at vancomycin clearance and pharmacokinetics using medium cut-off membrane dialyser. This is the first study that will compare the Drug Clearance of vancomycin when administered during the use of Medium cut-off membrane (Theranova) and high-flux (Revaclear) dialysers in haemodialysis patients.

### **1.2. Summary of non-clinical and clinical studies**

None

# **Objectives**

### **2.1. Primary**

To compare the drug clearance profile of vancomycin when administered during the use of Medium cut-off membrane (Theranova) with high flux dialysers (Revaclear) in haemodialysis patients.

### **2.2. Secondary**

Obtaining Adverse Events: All volunteered, elicited and observed adverse events (AEs) will be documented.

# **Study design**

### **3.1. Design**

This is an observational study comparing the clearance of Vancomycin during haemodialysis sessions on the Medium cut-off membrane (Theranova) and High-Flux membranes (Revaclear) in patients treated with vancomycin for standard clinical indications.

The subjects meeting the entry criteria will receive intravenous vancomycin as per treatment nature.

The screening day will be day 0 when subject is receiving the loading dose of vancomycin. The duration of the study for each subject will be the next six haemodialysis sessions (approximately 14 days, i.e. the 6 HD sessions following the loading dose of vancomycin). The study procedures for each visit are presented in the study flow chart (Appendix 1). (Note that standard weekly dialysis is 4 to 5 hours per session three times per week)

The treatment will consist of a single loading dose of 30mg/kg (rounded to the nearest 50mg) to the maximum of 2000mg will be administered in an intravenous infusion (IV). All subjects will receive vancomycin in the last 60-120 minutes of a dialysis session.

|  |  |
| --- | --- |
| **Loading dose** | **Infusion rate** |
| 750mg | 60 minutes |
| 1000mg | 60 minutes |
| 1250mg | 90 minutes |
| 1500mg | 90 minutes |
| 1750mg | 120 minutes |
| 2000mg | 120 minutes |

The infusion rate will vary depending on the dose administered as per table above. [8]

A maintenance dose of 10 – 15 mg/kg will be administered at each session when pre-dialysis concentration is less than or equal to 20 mg/L in infections. The dose will be delivered in the last 60-120 minutes of a dialysis session. The maximum dose delivered would be 2000mg.

The vital signs for each subject will be monitored before and during infusion as per standard care. Subjects will be monitored over the infusion period up to 30 minutes after the infusion is completed.

At each visit, blood samples for drug concentration will be collected at the start of dialysis session, then at 5, 15, 30, 45, 120 minutes after starting dialysis, and 30 minutes post dialysis session. Subjects will remain at the dialysis unit for up to 30 minutes post-infusion and will be discharged if no adverse events (AEs) are observed. Subjects will return to the unit at their next arranged haemodialysis session.

The Principle Investigator will review all test results and AEs reported prior to the next dose. The dose will be adjusted based on review of pre-dialysis vancomycin concentration by the Principle investigator. Dose adjustments will be made in an approximately linear fashion in accordance with trough plasma levels. For example, an increase in dose by 50% would result in an increase in trough level by approximately 50% and vice versa. [9]

Vancomycin drug concentration will provide a pharmacokinetic profile, including AUC0-inf, Tmax, Cmax, and Cmin, and will be calculated for each subject.

All PK samples of vancomycin will be analysed during the study for all subjects. This will be done at the local hospital laboratory. This data will be used as adjunct information for a safety review, which will include a review of adverse events and changes in vital signs. Unexpectedly high plasma concentrations will be reviewed for dose adjustment and correlation to related adverse events.

### **3.2. Indication:**

Therapeutic use of vancomycin i.e. prophylactic or therapeutic

### **3.3. Blinding**

Not applicable

### **3.4. Controls**

Not applicable

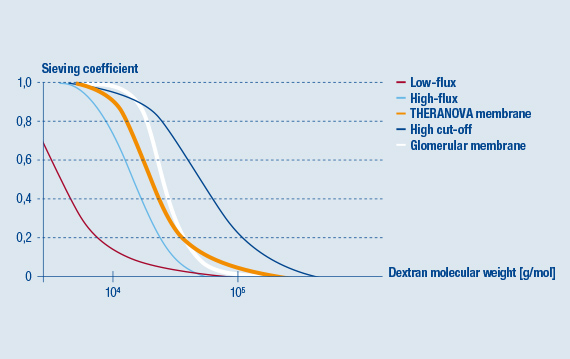
### **3.5. Randomization**

No randomization

### **3.6. Dose Rationale**

Following the administration of intravenous (IV) vancomycin to subjects with normal kidney function, plasma protein binding is 10%-55%. Eighty percent of the drug is excreted unchanged by glomerular filtration, with a half-life of 6-8 hours. In patients with advanced renal failure (RF), half-life may be up to 150-250 hours, and plasma protein binding is 18%. Its removal is increased when high permeability filters are used. [10]

With an increased nominal pore size along the membrane, the THERANOVA dialyser has a significantly higher permeability for large middle molecules than conventional high-flux membranes. The sieving coefficient is higher for the medium cut-off membrane. Therefore, the exact drug clearance is unknown. We are postulating that there be will similar or higher clearance of vancomycin when compared to using high-flux dialyser. Hence using similar guidelines (figure one). [11]



*Figure 1: Dextran Sieving Curves for Blood Purification Membranes [11]*

### **3.7. Stopping Criteria**

If any subject experiences a serious adverse event, that in the judgment of the Principle Investigator is life-threatening and definitely related to study medication (see Section 7.2), the study will be stopped

### **3.8. Study Flow Chart**

See Appendix 1

# **SUBJECT POPULATION**

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### **4.1. Inclusion Criteria**

The following are the inclusion criteria:

1. Male or female over the age of 18.
2. Be an In-centre haemodialysis subject using a middle cut-off dialyser (Theranova)
3. Female subjects of child bearing age must have a negative serum pregnancy test at baseline
4. Females of child-bearing potential must be non-pregnant and not lactating at the time of the study
5. Not allergic or have had an adverse reaction to vancomycin previously
6. Provide written informed consent
7. Have the ability to understand the requirements of the study and to comply with the study protocol and dosing regimen

### **4.2. Exclusion Criteria**

Subjects will be excluded from the study if they:

1. Have clinical evidence of any active significant disease that could potentially compromise the ability of the investigator to evaluate or interpret the effects of the study treatment on safety assessment and thus increase the risk to the subject to unacceptable levels
2. Are on other concomitant antibiotics at the time of the study
3. Are pregnant or nursing
4. Have a history of allergy to vancomycin
5. Are considered by the Investigator to be an unsuitable candidate for this study
6. Are on hemodiafiltration (HDF)
7. Have sensitivity (allergic reaction) to Revaclear or Theranova membranes

# **STUDY PROCEDURES AND VISIT SCHEDULE**

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### **5.1. Pre-Screening**

In-centre haemodialysis patients at Hastings dialysis unit presenting with an indication requiring treatment with vancomycin will be screened and approached to be enrolled in the study.

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### **5.2. Screening day (Day 0), day of the event leading to the use of vancomycin**

1. Investigator will review all inclusion and exclusion criteria and determine subject's ongoing eligibility to be enrolled in the study.
2. Investigator will approach the subject for inclusion in the study and provide patient information sheet and when required use a suitable interpreter from the District Health Board (DHB)

### **5.3. Study day 1: i.e. next haemodialysis session**

1. Prior to commencement of dialysis, written consent will be taken from the patients wishing to participate in the study
2. The following data will be captured:
   1. Demographics (date of birth, gender, ethnic origin)
   2. Medical history (including concomitant medication use, allergies, and medical conditions)
   3. Complete physical examination, including vital signs (temperature, oxygen saturation, respiratory rate, blood pressure and heart rate), dry weight (kg), and weight on day of study
   4. Haemodialysis access type, blood flow, dialyser flow rate, dialyser surface area, and monthly URR will be recorded
   5. Therapeutic dose of vancomycin, i.e. prophylactic or therapeutic, will be given as per criteria above (section 3.1)
3. Dialysis will be performed on the medium cut-off dialyser
4. Blood samples (5ml) will be taken for pK samples at the following time points:
   1. prior to starting haemodialysis
   2. then at 5, 15, 30, 45, and 120 minutes after starting dialysis.
5. The next Vancomycin dose will be infused in the last 60-120 minutes of dialysis based on the pre-dialysis vancomycin concentration
6. Withdrawal of 5ml blood for plasma vancomycin concertation at 30 min post dialysis
7. Adverse events will be recorded in Data sheet

### **5.4. Study day 2: i.e. next haemodialysis session**

1. Body weight and vital signs will be recorded
2. Dialysis will be performed on the High-Flux dialyser (Revaclear)
3. Blood samples (5ml) will be taken for pK samples at the following time points:
   1. prior to starting haemodialysis
   2. then at 5, 15, 30, 45, and 120, minutes after starting dialysis
4. Vancomycin will be infused in the last 60-120 minutes of dialysis based on the pre-dialysis vancomycin concentration
5. Withdrawal of 5ml blood for plasma vancomycin concentration at 30 min post dialysis
6. Adverse events will be recorded

### **5.5. Study days 3-6**

1. Dialysis sessions will continue to alternate between the high-flux and medium cut-off dialysers
2. Blood samples (5ml) will be taken for pK samples at the following time points (each session):
   1. prior to starting haemodialysis
   2. then at 5, 15, 30, 45 and 120 minutes after starting dialysis.
3. Vancomycin will be infused in the last 60-120 minutes of dialysis based on the pre-dialysis vancomycin concentration
4. Withdrawal of 5ml blood for plasma vancomycin concentration at 30 min post dialysis
5. Adverse events will be recorded

|  |
| --- |
| ***Labelling of blood tubes***  *Please ensure that blood tubes and laboratory forms are clearly labelled with the study ID, date, and the time*  ***Recording sample times***  *Record the exact time of each blood sample (nearest minute) on the data entry sheet* |

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### **5.6. Observations and Measurements**

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#### **5.6.1. Blood Tests**

Only serum vancomycin concentrations are required. This will be processed locally at the hospital.

#### **5.6.2. PK Analysis**

AUC, Tmax, Cmax and Cmin will be calculated for each subject.

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#### **5.6.3. Adverse Events**

All adverse events (AEs) observed by the Principle Investigator and/or health professional managing the dialysis session, or self-reported by the patient, will be documented with respect to onset, severity, relationship to study treatment, and resolution.

# **STUDY MEDICATION**

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### **6.1. Dosage and Formulation**

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#### **6.1.1. Dosage**

* A single loading dose of 30mg/kg (rounded to the nearest 50mg, ) to the maximum 2000mg) of vancomycin, will be administered in an intravenous infusion (IV).
* A maintenance dose of 10 – 15 mg/kg of vancomycin to the maximum of 2000mg will be administered at each session when pre-dialysis concentration is less than or equal 20 mg/L.

#### **6.1.2. Formulation**

Standard vancomycin available in New Zealand will be used.

Each vial will contain:

* Vancomycin 500mg vial: white to almost white lyophilised powder which has been prepared in a sterile fashion. Each vial contains vancomycin hydrochloride equivalent to 500mg vancomycin base.
* Vancomycin 1000mg vial: white to almost white lyophilised powder which has been prepared in a sterile fashion. Each vial contains vancomycin hydrochloride equivalent to 1000mg vancomycin base.

### 

### **6.2. Study Drug Administration**

Vancomycin will be administered as an intravenous infusion (IV) delivered during the last 60 to 120 minutes of dialysis session depending on the dose being administered. Red man syndrome may occur if the vancomycin infusion is too rapid. It is not an allergic reaction but may be characterized by hypotension and/or a maculopapular rash appearing on the face, neck, trunk, and/or upper extremities. If this occurs, the infusion rate will be slowed to 1.5 to 2 hours and the dilution volume increased. Treatment with anti-histamines and steroids may be provided for suspected Red man syndrome.

Subjects will be monitored for 30 minutes at the local dialysis unit post infusion completion.

### **6.3. Blinding**

Not applicable

### **6.4. Preparation and labelling**

At the time of use, the 500 milligrams vial will be reconstituted with 10 mL of Water for Injections. The resulting solution contains vancomycin 50 milligrams/mL. The 1g vial will be reconstituted with 20 mL of Water for Injections. The resulting solution contains vancomycin 50 milligrams/mL. The reconstituted solution containing 500 milligrams of vancomycin must be further diluted with at least 250 mL of Sodium Chloride Intravenous Infusion 0.9%. The reconstituted solution containing 1 g of vancomycin must be further diluted with at least 500 mL of Sodium Chloride Intravenous Infusion 0.9%.

The extra intravenous fluid needed for the drug will be ultrafiltrated during dialysis.

Standard fluid, drug labelling, and handling protocols at the local unit will be followed during preparation.

### **6.5. Storage**

Drug will be stored between 2-8oC. To reduce microbiological hazard, the infusion will be commenced as soon as practicable after reconstitution/preparation.

### **6.6. Overdosage:**

Supportive care will be provided in the event of an overdosage. We would consider the possibility of interaction with other drugs, and unusual drug kinetics in our subjects in suspected overdosage.

# **ADVERSE EVENTS**

An adverse event is an undesirable or unintentional event that occurs during the usage of the study drug, whether or not it is related to the drug. This includes clinically significant changes in laboratory values. Regardless of the severity or relationship to the drug, all adverse events occurring during the study period are to be recorded in the subject's data sheet.

# **SUBJECT WITHDRAWAL**

Subjects will be discontinued from the study prematurely if:

* An intercurrent illness occurs which precludes further treatment
* A serious adverse event occurs, which in the judgment of the principle investigator or managing physicians, is probably related to the drug and cannot be acceptably managed
* The subject requests to be withdrawn from the study
* The investigator decides that it is in the subject's best interest
* The subject is noncompliant with the protocol
* The study is discontinued

All subjects prematurely discontinued from the trial, regardless of cause, will be followed up to assess that they are well and other form of antibiotics are provided if needed.

# **DATA ANALYSIS AND STATISTICS**

### 

### **9.1. Study Design**

This is an observational study of the drug clearance (pK) of Vancomycin on Medium cut-off membrane (Theranova) dialyser compared with high-flux dialysis (Revaclear).

### **9.2. Primary Endpoint**

To compare the drug clearance profile of vancomycin when administered during the use of Medium cut-off membrane (Theranova) with High-Flux (Revaclear) dialyser in haemodialysis patients. Vancomycin drug concentrations will provide a pharmacokinetic profile, including AUC0-inf, Tmax, Cmax and Cmin and will be calculated for each subject when given on this type of dialyser. This will allow establishment of a vancomycin administration protocol or guidelines for patients on this type of dialyser.

### **9.****3. Secondary Endpoint**

Obtaining Adverse Events: All volunteered, elicited and observed adverse events (AEs) will be documented.

### **9.4. Statistical Methods and Sample Size Justification**

#### 

#### **9.4.1. Baseline Measurements**

Baseline characteristics of subjects will be summarised by descriptive statistics.

#### 

#### **9.4.2. Safety Assessments**

Safety parameters at each follow-up assessment, as well as changes from baseline, will be examined. Safety will also be assessed through the recording of adverse events, monitoring of vital signs and vascular access.

#### 

#### **9.4.3. Pharmacokinetics**

AUC, Tmax, Cmax and Cmin will be calculated for each subject.

#### 

#### **9.4.4. Sample Size**

No formal power or sample size calculations were made. The data collected will be used to estimate possible effect size and variability of measures and allow us to assess drug clearance. A total of 6 volunteers on haemodialysis presenting with an acute infection/indication requiring vancomycin will participate. This will allow us a maximum of 36 sessions to obtain data.

In general, all the analyses described above are considered exploratory and are designed to give some insight into the relationship between the treatment and potential outcomes.

# **Ethics**

Ethics approval will be obtained. It is the responsibility of the investigator to obtain informed consent in written form from each subject participating in this study. All subjects are to be informed of the aims, methods, anticipated benefits, potential side effects, and confidentiality of data. Candidates will also be told that they are free to refuse participation at any time and choosing not to participate will not affect their standard care.

### **10.1.** **Protocol Amendments and Emergency Deviations**

It is not anticipated that during the study period any protocol amendments will be required.

### **10.2. Informed Consent**

Upon identification as suitable for the study, the participant will be approached by the investigator or another member of the study team to provide the patient information sheet and consent form. The participant will then have 48 hours to the start of the next dialysis session to consider inclusion in the study.

At the start of the next dialysis session the patient will be approached to confirm their inclusion in the study and written consent will be taken.

### **10.3.** **Confidentiality, case reports and study records**

All information provided to the investigator (or designates) will be kept strictly confidential and confined to the clinical personnel involved in conducting the study as part of the participant’s permanent patient record. All data and medical information gathered for each subject will be identified only by a unique subject study number.

# **Publication**

The investigator shall have the right to publish the results of this study.

All information, basic scientific data, and formulation information provided to the investigator, the methodologies used in this study, as well as information obtained during the course of the study, are confidential. Individual subject data obtained during this study is confidential and will not be disclosed except:

* When the data are needed by a subject’s personal physician or other medical personnel responsible for the subject’s welfare.

Individual subject identity must not and will not be divulged in any publication.

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# **Abbreviations:**

* AEs Adverse events
* AUC0-inf Area under curve
* C Celsius
* Cmax maximum (or peak) serum concentration that a drug achieves
* after dosing
* Cmin minimum (or trough) concentration that a drug achieves after

dosing

* D Daltons
* ESRF End stage renal failure
* ESRD End stage renal disease
* HD haemodialysis
* HDF hemodiafiltration
* IV Intravenous
* kg kilogram
* MCO Medium Cut-off dialyser
* mg milligram
* pK pharmacokinetics
* Tmax time after administration of a drug when the maximum

plasma concentration is reached

* URR Urea reduction ratio

# **Appendix 1**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Pre-Screening | Screening (study day 0, vancomycin loading day) | Study day 1, next HD | Study day 2, next HD | Study day 3, next HD | Study day 4, next HD | Study day 5, next HD | Study day 6, next HD |
| **Date** |  |  |  |  |  |  |  |  |
| Informed consent | x | X | x |  |  |  |  |  |
| Inclusion/exclusion criteria |  | X |  |  |  |  |  |  |
| Provide patient information sheet |  | X |  |  |  |  |  |  |
| Dialyser type (medium cut-off dialyser (MCO)/ High-Flux) |  | X | MCO | High-Flux | MCO | High-Flux | MCO | High-Flux |
| Demographics (DOB, gender, ethnic origin) |  |  | x |  |  |  |  |  |
| Medical history |  |  | x |  |  |  |  |  |
| Concomitant medications |  |  | x | x | x | x | x | x |
| Vital Signs |  |  | x | x | x | x | x | X |
| Temperature |  |  | x | x | x | x | x | x |
| Body Weight (actual) |  | X | x | x | x | x | x | x |
| Dry weight (target weight) |  |  | x | x | x | x | x | x |
| Physical examination |  |  | x |  |  |  |  |  |
| Dialysis access type |  |  | x |  |  |  |  |  |
| Blood flow |  |  | x | x | x | x | x | X |
| Dialysate flow |  |  | x | x | x | X | x | x |
| Dialysate surface area |  |  | x |  |  |  |  |  |
| Monthly URR (from recent results) |  |  | x |  |  |  |  |  |

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Blood samples and Vancomycin dosing** | | | | | | | | | | |
|  | Vancomycin indication | Vancomycin loading dose (mg) | Vancomycin concentration before starting HD (time hrs) | 5 min from start of dialysis (hrs) | 15 min from start of HD (hrs) | 30 min from start of HD (hrs) | 45 min from start of HD (hrs) | 120 min from start of HD (hrs) | Vancomycin dose based on pre-HD concentration (mg) | 30 Minutes after dialysis has completed |
| Pre-screening |  |  |  |  |  |  |  |  |  |  |
| Screening Study day 0, vancomycin loading day) | X | x |  |  |  |  |  |  |  |  |
| Study day 1, next HD) | X |  | x | x | x | x | x | x | x | x |
| Study day 2, next HD) | X |  | x | x | x | x | x | x | x | x |
| Study day 3, next HD) | X |  | x | x | x | x | x | x | x | x |
| Study day 4, next HD | X |  | x | x | x | x | x | x | x | x |
| Study day 5, next HD | X |  | x | x | x | x | x | x | x | x |
| Study day 6, next HD | X |  | x | x | x | x | x | x | x | x |

**APPENDIX 2: Patient data sheet**

Patient unique number: ­­­­­­­­­­­­­­­­­­­­­­\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

***Study day 1:***

Written Consent: Y/N

DOB: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Gender: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Ethnic origin: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Indication for vancomycin: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Vancomycin loading dose on day 0: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Medical history:

Medications:

Allergies/Adverse drug reactions:

**Physical examination:**

Temp: RR: BP: Saturation: HR:

Dry weight:

Current weight:

CVS exam

Respiratory exam:

Abdominal exam:

Neurological exam:

Haemodialysis access type:

Arterio-venous fistula if applicable:

Tunnelled line and exit site if applicable

blood flow rate: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

dialysate flow rate: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

dialyser surface area: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

monthly URR: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Vancomycin concentration and dose:

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Pre HD trough | 5 min | 15 min | 30 min | 45 min | 120 min | Dose (mg) | 30 min post HD level |
|  |  |  |  |  |  |  |  |  |

Adverse reaction during or after completion of vancomycin infusion: \_\_\_\_\_\_\_\_\_\_\_\_

If yes, any treatment

Investigator: Signature:

Date:

***Study day 2:***

Temp: RR: BP: Saturation: HR:

Dry weight: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Current weight: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Dialysis blood flow rate: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Dialysate flow rate; \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Vancomycin concentration and dose:

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Pre HD trough | 5 min | 15 min | 30 min | 45 min | 120 min | Dose (mg) | 30 min post HD level |
|  |  |  |  |  |  |  |  |  |

Adverse reaction during or after completion of vancomycin infusion: \_\_\_\_\_\_\_\_\_\_\_\_

If yes, any treatment

Investigator: Signature:

Date:

***Study day 3:***

Temp: RR: BP: Saturation: HR:

Dry weight: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Current weight: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Dialysis blood flow rate: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Dialysate flow rate; \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Vancomycin concentration and dose:

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Pre HD trough | 5 min | 15 min | 30min | 45 min | 120 min | Dose (mg) | 30 min post HD level |
|  |  |  |  |  |  |  |  |  |

Adverse reaction during or after completion of vancomycin infusion: \_\_\_\_\_\_\_\_\_\_\_\_

If yes, any treatment

Investigator: Signature:

Date:

***Study day 4:***

Temp: RR: BP: Saturation: HR:

Dry weight: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Current weight: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Dialysis blood flow rate: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Dialysate flow rate; \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Vancomycin concentration and dose:

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Pre HD trough | 5 min | 15 min | 30 min | 45 min | 120 min | Dose (mg) | 30 min post HD level |
|  |  |  |  |  |  |  |  |  |

Adverse reaction during or after completion of vancomycin infusion: \_\_\_\_\_\_\_\_\_\_\_\_

If yes, any treatment

Investigator: Signature:

Date:

***Study day 5:***

Temp: RR: BP: Saturation: HR:

Dry weight: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Current weight: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Dialysis blood flow rate: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Dialysate flow rate; \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Vancomycin concentration and dose:

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Pre HD trough | 5 min | 15 min | 30 min | 45 min | 120 min | Dose (mg) | 30 min post HD level |
|  |  |  |  |  |  |  |  |  |

Adverse reaction during or after completion of vancomycin infusion: \_\_\_\_\_\_\_\_\_\_\_\_

If yes, any treatment

Investigator: Signature:

Date:

***Study day 6:***

Temp: RR: BP: Saturation: HR:

Dry weight: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Current weight: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Dialysis blood flow rate: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Dialysate flow rate; \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Vancomycin concentration and dose:

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Pre HD trough | 5 min | 15 min | 30 min | 45 min | 120 min | Dose (mg) | 30 min post HD level |
|  |  |  |  |  |  |  |  |  |

Adverse reaction during or after completion of vancomycin infusion: \_\_\_\_\_\_\_\_\_\_\_\_

If yes, any treatment

Investigator: Signature: