Pharmacy Manual	
GREAT-2 - GRemubamab **E**r**A**dication **T**rial A phase 2 trial of Gremubamab compared to placebo in participants with bronchiectasis and chronic *Pseudomonas aeruginosa* infection	
EudraCT ID: 2022-003215-28	**IRAS ID:** 1005993
Sponsor: University of Dundee & NHS Tayside	Chief Investigator: Prof. James Chalmers

This document describes the process for Investigational Medicinal Product (IMP) and placebo management at site.

Abbreviations / terms used

CTP	Clinical Trial Pharmacy
IMP	Investigational Medicinal Product
IV	Intravenous
PSF	Pharmacy Site File
SOP	Standard Operating Procedure
TM	Trial Manager
TRuST	Tayside Randomisation System

Contents

1. Treatment Overview

Participants will be randomly assigned to receive an intravenous (IV) infusion 4 weekly for a period of 12 weeks of either:

- 1500 mg Gremubamab
- 500 mg Gremubamab
- Placebo

2. IMP/Placebo description

Description	Packaging	Storage conditions	Supplier
Gremubamab 200mg lyophilised product per vial	1 vial per carton	2-8ºC Protect from light	Sharp Clinical Services Ltd
Placebo 4 ml liquid per vial	1 vial per carton	2-8ºC Protect from light	Sharp Clinical Services Ltd

Gremubamab will be supplied in a vial as a 200 mg lyophilised product for concentrate for solution for infusion. The reconstituted solution contains 50 mg/mL Gremubamab with a post-reconstitution volume of 4 mL.

Placebo will be supplied in a vial as a sterile liquid with a volume of 4 mL.

The investigational product (Gremubamab or placebo) is further diluted into 0.9% (weight per volume [w/v]) saline to a total volume of 250 mL for IV infusion.

Each vial is identified by a pack ID number.

See Appendix 1 for IMP vial and carton labels details.

3. Non-IMP

Description	Supplier
Water for injection	Clinical Trial Pharmacy
0.9% Saline for infusion, 250 ml PVC bags	Tayside Clinical Trials Unit
Antihistamine	Clinical Trial Pharmacy

Water for injection is required for reconstitution of the Gremubamab, 4ml per vial.

0.9% Saline, 250ml for infusion is required for dilution of Gremubamab/placebo prior to infusion.

All subjects will be premedicated with IV antihistamine prior to each dose of IMP. The choice of antihistamine will be as per local preference for example, 10 mg chlorpheniramine IV, 50 mg diphenhydramine IV, clemastine 2 mg IV, or dexchlorpheniramine 5 mg IV (or another antihistamine preparation utilised in routine clinical practice for management of acute allergic

reactions). Where a participant is already taking antihistamines then the pre-dose antihistamine should not be given.

4. Investigational Medicinal Product (IMP)/placebo supply

4.1. Initial IMP supply

The Clinical Trial Pharmacy (CTP) will receive an initial supply of 24 vials of Gremubamab and 24 vials of placebo from Sharp Clinical Services. The initial supply may be different with agreement of the CTP. The vials and packaging will be over-labelled with the clinical trial label by Sharp Clinical Services.

4.2. Re-supply

The Trial Manager (TM) will manage stock, contacting Sharp Clinical Services to arrange further shipments as required according to recruitment. The CTP will be informed by email when new supplies are expected.

Pharmacy should contact the Trial Manager ™ if stock levels are causing concern.

5. IMP/placebo storage

Gremubamab and placebo vials should be stored in refrigerated at 2 - 8°C and must not be frozen. Gremubamab and placebo must be kept in original packaging until time of preparation to prevent prolonged light exposure.

Single use only.

Do not use beyond expiry date.

A daily temperature log will be required (paper/electronic); this should be available for review as requested for monitoring purposes. A file note detailing the location of the temperature log should be held in the PSF.

Temperature monitoring is not required when transporting the final infusion bag from the aseptic unit to the ward (unless the ward is on a separate site in which case temperature monitoring is recommended, except where a validated shipper is used).

5.1. Temperature excursions

The IMP will be quarantined by CTP and reported to the TM if exposed to temperatures:

- Below -5°C
- -5°C to 2ºC for more than 30 days
- 8ºC to 25°C for more than 30 days
- Above 25°C

When reporting to the TM the temperature logs from the 4 weeks preceding the excursion should be provided. IMP supplies should be quarantined locally until a response from the Sponsor has been received. Reports of temperature excursions reported to the TM will be discussed with Sharp Clinical Services and/or AstraZeneca, and Sponsor to identify what action is necessary. TM will inform CTP of any action required.

6. Interactive Web-based Randomisation System (IWRS)

The IWRS system used is Tayside Randomisation System (TRuST), see GREAT-2 Pharmacy Training Slides in PSF.

Sites will be expected to use the TRuST to perform the following activities:

- Acknowledge receipt of shipments on arrival - CTP
- Randomise participant – Research Nurse (RN)/CTP
- Completion of IMP request form – RN/Dr
- Dispensing/releasing IMP/placebo – CTP
- Recording discontinuation of treatment - RN
- Recording drug returns - CTP
- Recording expired drugs - CTP
- Recording drug disposals - CTP
- Recording quarantined drugs - CTP
- Drug accountability – CTP
- Recall of IMP/Placebo - CTP

6.1. Acknowledge receipt of shipments on arrival - CTP

The stock control of the IMP/placebo will be managed by TRuST.

The CTP at each site will receive shipments from Sharp Clinical Services via controlled refrigerated shipments. Each shipment will be accompanied by a QP Release Certificate, temperature tracker and an Acknowledgement of Receipt. The Acknowledgement of Receipt will be emailed back to Sharp Clinical Services and copied to the TM to confirm delivery. A copy of the QP Release Certificate and Acknowledgement of Receipt should be filed in the PSF.

The vials of IMP and placebo will be packed separately in individual cartons.

On receipt, each IMP pack number must be entered in TRuST to log IMP stock. This will update the drug accountability on TRuST. If entry is not done on receipt a reminder email will be sent to the CTP after 7 days.

All vials will be referred to as packs on TRuST.

Water for injection for reconstitution of the Gremubamab should be procured by the local CTP.

0.9% (weight per volume [w/v]) saline 250 ml PVC bags for infusion will be provided by Tayside Clinical Trials Unit.

Antihistamine as per local preference should be procured by the local CTP.

6.2. Randomise participant – RN

Randomisation will be carried out by an unblinded member of the trial team using TRuST, see GREAT-2 Randomisation Training Slides in PSF. The participant will be randomised to receive either Gremubamab 1500mg, Gremubamab 500m g or placebo.

Randomisation can also be delegated to the Clinical Trial Pharmacy team, for sites who do not have blinded and unblinded research team members. See Appendix 2 for the randomisation process at sites who have a blinded and unblinded research team. See

Appendix 3 for the randomisation process at sites who do not have a blinded and unblinded research team.

6.3. Completion of IMP request form – RN and Dr

At point of randomisation TRuST will generate a Clinical Trial Request Form. At subsequent visits an unblinded member of the trial team should generate a further Clinical Trial Request Form from TRuST.

The IMP Request form should be completed by adding the participant's name, date of birth and hospital no/CHI. It should then be signed by a doctor delegated this task on the Delegation Log.

6.4. Dispensing/releasing IMP/placebo - CTP

IMP/placebo will be released for each participant as defined by visit schedule, (see Appendix 4) on receipt of a Clinical Trial Request Form generated by TRuST (see Appendix 5). At sites who do not have an unblinded team, a Blinded Clinical Trial Request Form will be signed by a blinded trial doctor prior to randomisation (see Appendix 6). The Blinded or Unblinded Clinical Trial Request Form must be signed by the PI or their delegate named on the Delegation Log.

The Clinical Trial Request Form will detail the dose of Gremubamab/placebo the participant is to receive and the number of vials of Gremubamab/placebo to be released.

Any known allergies to any of the IMP/placebo ingredients will be documented as exclusion therefore the participant will not be randomised.

The packs released will be logged via TRuST by entering the pack ID. A Clinical Trial Release Form (see Appendix 7) will be generated by TRuST. The pharmacist or delegate should print, sign and date the release form. The TRuST system will not allow a release form to be printed where the entered pack IDs do not match the pack IDs on the request form. Visual confirmation of the correct pack ID number on each vial should be checked against the release form.

The Clinical Trial Request and Release Forms should be filed in the PSF.

NB. The participant's name plus hospital number/CHI (if required by local policy) will be handwritten on the Clinical Trial Request Forms by requester to ensure no personal details are evident on TRuST.

The appropriate amount of water for injection, detailed on the Clinical Trial Release Form and one 0.9% saline, 250ml, infusion bag should also be released for making up the infusion.

If an error occurs in completing the Clinical Trial Request or Release Form prior to the release of the IMP a file note should be completed and a copy of erroneous document(s) filed in the PSF. The correct request or release form should be printed from TRuST or if TRuST does not allow this, a blank copy of the form (held in the Investigator Site File and PSF) should be made and completed by hand. The TM should be made aware of any errors to enable an auditable correction on TRuST. Where an error is noticed after dispensing the appropriate action to recall the IMP should be made. The Principal Investigator and TM should be informed, and a Protocol Breach Report completed. The online Breach Reporting Form can be completed here: https://www.dundee.ac.uk/tasc/policies-sops-templates/breach-report-form

6.5. Non-IMP prescribing – RN/Dr/CTP

Pre-dose IV antihistamine should be prescribed as per local procedures.

6.6. Recording discontinuation of treatment – RN

If a participant stops taking their trial drugs for whatever reason this should be entered into TRuST by the trial team.

6.7. Recording drug returns - CTP

If a dose is prepared and not suitable for use or not administered, then this should be recorded as returned on TRuST.

If vials have been released on TRuST but remain unused, vials **must** be unopened and remain in original carton, return to store at 2-8^{o}C and contact the Trial Manager to see if these can be replaced back to stock.

6.8. Recording expired drugs - CTP

All IMP/placebo supplied should have an expiry after trial completion. However, if required expired vials should be recorded on TRuST.

6.9. Recording drug disposals - CTP

Used vials and cartons maybe destroyed as per sites local practice; no approval from sponsor required.

Disposal of any returned or expired IMP/placebo must be recorded on TRuST, disposed of as per local Standard Operating Procedure (SOP), no approval from Sponsor required.

Unused vials at the end of trial should be recorded TRuST and, **after** Sponsor has approved, disposed of as per local SOP

6.10. Recording quarantined drugs - CTP

If requested to by the Sponsor or if the storage conditions are out with the parameters described above (section 5), the IMP must be removed from the stock shelf and placed in a separate area at 2-8^{o}C. The IMP must be clearly marked as in quarantine and not to be dispensed. This should be entered on TRuST. The IMP must remain in quarantine until the Sponsor has notified CTP whether the IMP can be returned to the stock shelf and dispensed as usual or whether the IMP/placebo must be disposed of. When quarantined IMP/placebo is to be either returned to the stock shelf or disposed of this should be entered on TRuST.

6.11. Drug accountability - CTP

Full accountability must be maintained for Gremubamab and placebo. IMP/placebo accountability records will be maintained by TRuST. A drug accountability log can be generated from TRuST if required locally. See GREAT-2 Pharmacy Training Presentation. The use of a paper accountability log is optional and at the discretion of each site, paper accountability logs will not be monitored, TRuST accountability will be used for monitoring purposes.

At the end of the trial CTP will be requested to print out the final Accountability Log and sign, emailing a copy to the TM and filing the original in the PSF.

Drug accountability can be viewed on TRuST for individual participants and also overall for site. Overall CTP stock levels can also be viewed on TRuST.

6.12. Recall of IMP/placebo - CTP

In the event of IMP/placebo recall, which necessitates the return of Gremubamab and/or placebo supplies, sites will be given further information on this as required. Label the stock as ‘quarantined’, record on TRuST and hold in a quarantine area, ideally at 2 to 8°C, until further information is received.

7. IMP/placebo preparation and administration

Individual site decisions to prepare the infusions in the aseptic unit, Clinical Trial Pharmacy or on the Clinical Research Centre/Facility should be based on local procedures and documented within the PSF.

Preparation should always use aseptic technique.

7.1. Supplies required

Description	Supplier
Water for injection	Clinical Trial Pharmacy
0.9% Saline for infusion, 250 ml PVC bag	Tayside Clinical Trials Unit
70% ethanol swab	Clinical Trial Pharmacy
Polypropylene syringes	Clinical Trial Pharmacy
19-, 20-, or 21-gauge × 1.5 inch needle	Clinical Trial Pharmacy
Low protein binding 0.2 µm or 0.22 µm filter	Clinical Trial Pharmacy/clinical area
Infusion bag label	Tayside Clinical Trials Unit
IV bag coloured sleeves	Clinical Trial Pharmacy

7.2. IMP/placebo preparation

Prior to infusion, Gremubamab will be reconstituted with sterile water for injection. Gremubamab and placebo will then be diluted in 0.9% (w/v) saline in an infusion bag and administered as an IV infusion.

The 0.9% (w/v) saline 250 mL infusion bag supplied to sites must be used, this is a PVC bag.

The dose of Gremubamab or placebo for administration must be prepared by the pharmacy staff members delegated by the Investigator (or an appropriate designee trained in study drug preparation), using aseptic technique in compliance with local regulations and site requirements.

The number of vials of Gremubamab or placebo and water for injection required will be detailed on the Clinical Trial Request Form.

Gremubamab/placebo should not be removed from storage at 2 - 8ºC until all other procedures required prior to participant dosing have been completed.

Gremubamab is supplied as a sterile white to off white, lyophilized powder. The reconstituted Gremubamab is a clear to slightly opalescent, colourless to slightly yellow solution, free from or practically free from visible particles.

Placebo is supplied as a sterile, colourless to slightly yellow, clear to slightly opalescent liquid, free from visible particles.

Each vial selected for dose preparation should be inspected. If there are any defects noted with the Gremubamab or placebo, the Principal Investigator and Trial Manager should be notified immediately.

No incompatibilities between Gremubamab and the following component materials of construction have been observed in 0.9% (w/v) saline for injection:

- Polyvinylchloride (PVC) IV bags

7.2.1. Reconstitution procedure for Gremubamab

1) Clean the rubber stopper of the investigational product vial with 70% ethanol or equivalent and allow to air dry.
2) Tilt the vial containing Gremubamab and slowly add 4 mL of sterile water for injection such that the liquid stream is directed along the wall of the vial and not directly upon the lyophilized cake.
3) The solution must be swirled intermittently until all solids have been dissolved. DO NOT SHAKE OR VIGOROUSLY AGITATE THE VIAL. At the end of reconstitution, invert the vial to dissolve any product that might be on the cap.
4) Visually inspect to ensure that the entire content of the lyophilized product is reconstituted. The reconstituted solution should appear clear to opalescent and colourless to slightly yellow. A thin layer of bubbles on the surface of the liquid is normal.
5) If any proteinaceous strands are seen stop infusion preparation and inform the TM.

7.2.2. Infusion bag preparation

1) The IMP/placebo vial rubber stopper should be cleaned with 70% ethanol or equivalent and allowed to air dry. To avoid foaming, the vial should not be shaken.
2) Polyvinyl chloride (PVC) IV bags **only** and polypropylene syringes should be used for dose preparation as no incompatibilities have been observed between Gremubamab and these materials. Do not exceed the manufacturer specified maximum allowable needle sticks into the bag.
3) A volume of 0.9% (w/v) saline equivalent to the required investigational product dose volume (Table 7.2.2.1) must be withdrawn from a pre-filled PVC infusion bag, supplied by Trial Management Team .
4) The required volume of reconstituted Gremubamab or placebo (Table 7.2.2.1) must be withdrawn from the vials using a 19-, 20-, or 21-gauge × 1.5 inch needle and added directly to the saline infusion bag.
5) Mix the bag by gently inverting to ensure homogeneity of the dose in the bag; do not shake the contents.
6) Label the infusion bag with the supplied Infusion bag Label. The following should be added to the infusion bag label

- date and time of initial reconstitution – time of needle puncture of the first vial of Gremubamab or placebo
- Participant name
- Participant trial ID number

7) Gremubamab is sensitive to light. Therefore, plastic IV bag coloured sleeves of appropriate sizes should be used to ensure product quality is not compromised.

7.2.2.1. Investigational Product Dose Preparation;

Treatment Group (Dose Level)	Number of Vials Required	Saline Volume (mL) to be removed	Investigational Product Dose Volume (mL)	Total Filled Bag Volume (mL)	Minimum Dose Administration Time (minutes)
500 mg	3	10	10	250	240
1500 mg	8	30	30	250	240
Placebo	8	30	30	250	240

7.3. Expiry of prepared dose

Total in-use storage time from needle puncture of the first vial of Gremubamab or placebo for investigational product preparation to start of administration must not exceed:

- 4 hours at room temperature or
- 24 hours at 2ºC to 8ºC.

If the final product is stored at both refrigerated and ambient temperatures, the total time must not exceed 24 hours, otherwise a new dose must be prepared from new vials (the individual storage time limits are not additive and the TM must be notified immediately

Gremubamab does not contain preservatives; any unused portion of the vial must be discarded immediately after use.

7.4. Non-IMP administration

IV antihistamine should be administered **prior** to the Gremubamab/placebo infusion following local procedures.

7.5. IMP/Placebo administration

Gremubamab/placebo will be administered as an IV infusion over 4 hours. An IV infusion pump should be used to deliver accurately.

The day of first dosing with Gremubamab/placebo is considered Day 1.

All participants in all 3 dose arm must receive the entire 250-mL volume of Gremubamab/placebo IV unless the infusion is discontinued due to an AE.

Gremubamab/placebo must be infused through a low protein binding 0.2 µm or 0.22 µm filter using an IV infusion pump over a minimum duration of 240 minutes (≤62.5mL/hour). The duration of the infusion must not exceed 8 hours.

Do not co-administer other drugs through the same infusion line.

Gremubamab/placebo must never be administered via IV push or bolus.

The IV tubing should be primed with Gremubamab/placebo from the infusion bag before initiating the investigational product infusion. Once the investigational product infusion bag is empty, the IV tubing should be flushed with 0.9% (w/v) saline via infusion pump at the same rate as dosing.

The start time of the Gremubamab/placebo infusion will be the time the infusion of the Gremubamab/placebo solution from the infusion bag (with IV tubing already primed with Gremubamab/placebo solution) is started. The stop time of the infusion should be the time the IV tubing has been flushed to administer the residual Gremubamab/placebo solution.

7.6. Safety monitoring

Vital signs, blood pressure, pulse, temperature, oxygen saturation, will be recorded during infusion at 5, 30, 60, 120 and 240 mins after the start of the infusion and 30 minutes after end of infusion.

Infusion rate will be slowed in the occurrence of a non-severe (grade 1 or 2) reaction as determined by the local PI (or delegate). Continuation of further doses of Gremubamab/placebo will be decided by the PI in discussion with the participant.

If an allergic reaction ≥ grade 3, including anaphylaxis, assessed as related to the trial drug occurs, the trial drug will be stopped immediately, and treatment will be initiated as appropriate. The participant will be withdrawn from further Gremubamab/placebo treatments.

Site must have drugs/equipment to treat acute anaphylactic reactions plus staff trained to recognise and treat anaphylaxis.

8. Emergency Unblinding

Emergency unblinding will be carried out by the PI or delegate.

Any clinician requiring the emergency unblinding of a participant should, where possible, discuss this with the Principal Investigator, however, this should not stall or delay in any way the unblinding of trial participant treatment in emergency situations. If unblinding is required, the clinician should contact the local PI or delegate. TRuST access will be provided to the local PI which will permit individual participant unblinding in the event of a medical emergency. An unblinding form (see Appendix 8) should be printed and signed by person performing the unblinding. It is the responsibility of the local PI to ensure that adequate training and instructions are given for anyone delegated this role to enable them to access and perform the emergency unblinding procedure. For additional details of the emergency unblinding procedure see GREAT-2 Unblinding Training Presentation.

Signed Shona Carson Date 07/06/2023

Shona Carson

Clinical Trials Pharmacist, Clinical Trial Pharmacy, Ninewells Hospital, Dundee

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Chief Investigator	j.chalmers@dundee.ac.uk	01382 386131

Lead Clinical Trial Pharmacist (Tayside)	shona.carson@nhs.scot	01382 632969
Sharp Clinical Services	SCSUK-ShipmentRequests@sharpclinical.com	

Appendices

Appendix 1 IMP Labels

Outer package of Gremubamab vials	GREAT-2 Trial For Intravenous use only Store refrigerated at 2-8°C. May be stored at room temperature, between -5°C and 25°C for up to 30 days. Protect from light Contains: One single-use vial of: Gremubamab 200mg lyophilized product For reconstitution with 4ml water for injection and further dilution with 0.9% saline to a volume of 250ml Expiry date…… Batch number…… Chief Investigator: Prof James Chalmers, Ninewells Hospital, Dundee DD1 9SY. Tel: 01382 383642 IRAS number 1005993

	Keep out of the sight and reach of children For clinical trial use only
Gremubamab vial labels	GREAT-2 Trial Gremubamab 200mg lyophilized product For intravenous infusion use only. Store refrigerated at 2-8°C. Protect from light Pack ID…….. Expiry date…… Batch number…… IRAS number 1005993 Single use vial Chief Investigator: Prof James Chalmers, University of Dundee
Infusion bag labels	GREAT-2 Trial For Intravenous infusion use only Store at room temperature not exceeding 25°C for a maximum of 4 hours from reconstitution to start of infusion at room temperature or 24 hours at 2-8°C. Protect from light Contains: Gremubamab / Placebo

	250 mls of solution for injection Date and time of reconstitution Date:…… Time:……. Participant Name: …….. Participant Number: …….. Chief Investigator: Prof James Chalmers, Ninewells Hospital, Dundee DD1 9SY. Tel: 01382 383642 IRAS number 1005993 Keep out of the sight and reach of children For clinical trial use only

GREAT-2 Labels Content IMP V2 25-01-23

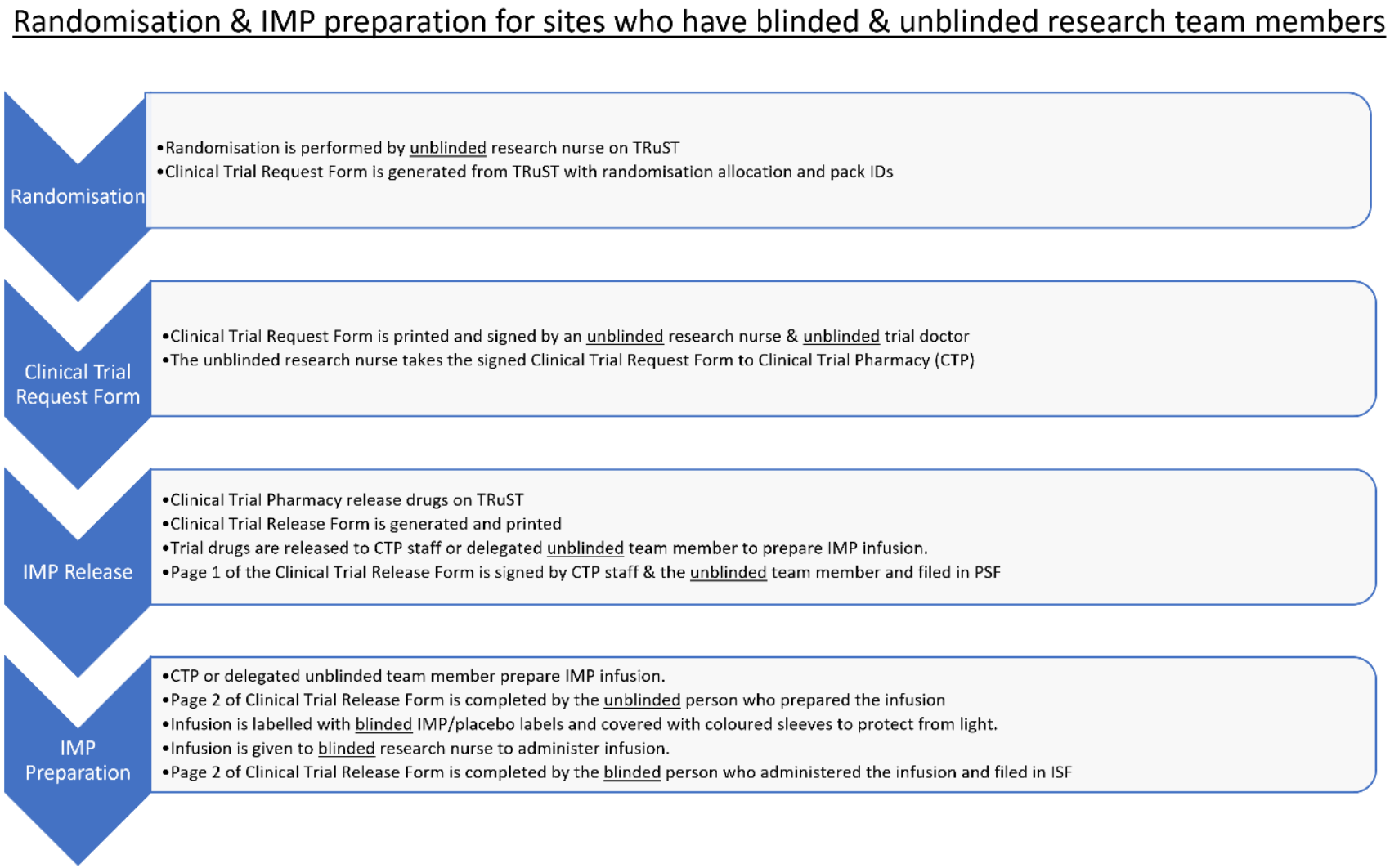
Outer package of Placebo vials	GREAT-2 Trial For Intravenous use only Store refrigerated at 2-8°C. May be stored at room temperature, between -5ºC and 25°C for up to 30 days. Protect from light Contains: One single-use vial of: Placebo 4 ml for dilution with 0.9% saline to a volume of 250ml Expiry date…… Batch number…… Chief Investigator: Prof James Chalmers, Ninewells Hospital, Dundee DD1 9SY. Tel: 01382 383642 IRAS number 1005993 Keep out of the sight and reach of children For clinical trial use only
Placebo vial labels	GREAT-2 Trial Placebo 4ml

	For dilution with 0.9% saline to a volume of 250ml For intravenous infusion use only. Store refrigerated at 2-8°C. Protect from light Pack ID…….. Expiry date…… Batch number…… IRAS number 1005993 Single use vial Chief Investigator: Prof James Chalmers, University of Dundee
Infusion bag labels	GREAT-2 Trial For Intravenous infusion use only Store at room temperature not exceeding 25°C for a maximum of 4 hours from reconstitution to start of infusion at room temperature or 24 hours at 2-8°C. Protect from light Contains: Gremubamab / Placebo 250 mls of solution for injection Date and time of reconstitution

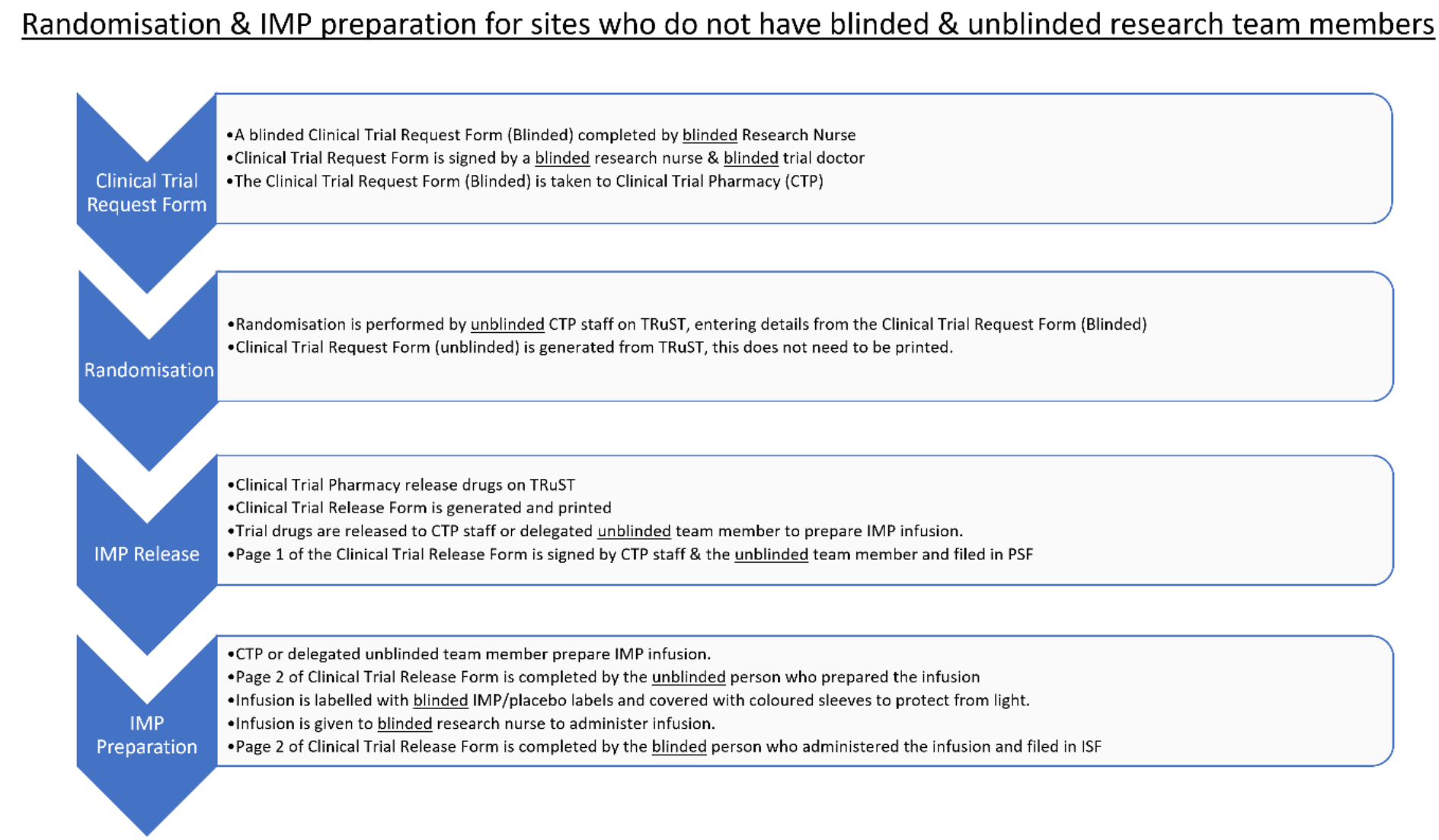
	Date:…… Time:……. Participant Name: …….. Participant Number: …….. Chief Investigator: Prof James Chalmers, Ninewells Hospital, Dundee DD1 9SY. Tel: 01382 383642 IRAS number 1005993 Keep out of the sight and reach of children For clinical trial use only

GREAT-2 Labels Content Placebo V2 25-01-23

Appendix 2 Randomisation Process: Unblinded & Blinded Research Team



Appendix 3 Randomisation Process: Blinded Research Team



Appendix 4 GREAT-2 Visit Schedule

Type of visit	Screening V1	Baseline and randomization V2	Treatment phase V3	Treatment phase V4	Treatment phase V5	Treatment phase V6	End of Treatment Assessments V7	Post treatment assessment 1 V8	Post treatment assessment 2 V9	Unscheduled visit Assessments
Timeline	-35 days prior to baseline	Day 1	Day 7 ±2	Day 14 ±2	Day 28 ±2	Day 56 ±2	Day 84 ±2	Day 112 ±4 Phone call	Day 168 ±4	As Required
Informed Consent	X									
Inclusion/Exclusion Criteria	X	X								
Medical History	X									
Physical Examination	X									X
Record Concomitant Medications	X	X	X	X	X	X	X		X	X
Record Adverse Events		X	X	X	X	X	X	X	X	X
Height & weight	X									
Check Vital Signs	X	X	X	X	X	X	X		X	X
ECG	X									
Pregnancy Test - serum	X									
Pregnancy Test - urine		X			X	X			X	
FBC, U&E, LFT	X				X	X	X		X	
Research bloods	X	X	X	X	X	X	X		X	X
Sputum for P. aeruginosa	X									
Research sputum		X	X	X	X	X	X		X	X
Standard Spirometry	X				X	X	X		X	
Questionnaires	X	X		X	X	X	X		X	X
Exacerbation recording		X	X	X	X	X	X		X	
Randomisation		X								
Trial medication		X			X	X				
Vital signs		X			X	X				

Appendix 5 GREAT-2 IMP Request Form Unblinded

GREAT-2: A phase 2 trial of Gremubamab compared to placebo in participants with bronchiectasis and chronic Pseudomonas aeruginosa infection

CLINICAL TRIAL REQUEST FORM FOR PHARMACY

EudraCT	**2022-003215-28**	Sponsor	**University of Dundee and NHS Tayside**
CTA		Protocol No.	**1-023-22**
IRAS	**1005993**	Local CTP ID	

Chief Investigator	**Prof James Chalmers**	Tel No	**01382 386131**
Principal Investigator		Tel No	

Participant ID:			
Participant Name:			
Date of Birth:		Hospital Number/CHI:	
Visit Number:		Visit Date:	

Randomised to	
Total volume to be infused	**250 ml**
Rate of infusion	**62.5 ml/hour**
Please Supply	
Sodium chloride 0.9% (250ml/500ml)	**1 bag**
Gremubamab 200mg/Placebo 4ml	
Water for injection	

Please Supply	**Gremubamab 1500mg/Gremubamab 500mg/Placebo**					
Dose	**200mg of Gremubamab per pack/4ml of Placebo per pack**					
Pack ID						

Investigator's or delegate's Signature:		Date:
Research Nurse's Signature:		Date:

FOR TRuST Validation:			
Barcodes			

GREAT-2 IMP Request Form V1 04-11-22 Download Date:

Appendix 6 GREAT-2 IMP Request Form Blinded

GREAT-2
GRemubamab ErAdication Trial

GREAT- 2: A phase 2 trial of Gremubamab compared to placebo in participants with bronchiectasis and chronic *Pseudomonas aeruginosa* infection

CLINICAL TRIAL REQUEST FORM FOR PHARMACY BLINDED

EudraCT	**2022-003215-28**	Sponsor	**University of Dundee and NHS Tayside**
IRAS	**1005993**	Protocol No.	**1-023-22**

Chief Investigator	**Prof James Chalmers**	Tel No	**01382 386 131**
Principal Investigator		Tel No	

To be completed by blinded trial team when pharmacy are carrying out randomisation:

Participant trial ID:			
Participant Name:			
Date of Birth:		CHI/hospital number:	
Visit Number:		Visit Date:	

A sputum sample that is culture or PCR positive for *P. aeruginosa* sent at the screening visit and within 35 days of randomization?	YES/NO
FEV1% at screening	
eGFR	
Has the CI/PI signed CRF to confirm eligibility of participant?	YES/NO
Does the participant meet eligibility criteria?	YES/NO

Please Supply	**Gremubamab 1500mg / Gremubamab 500mg / Placebo**
Total volume to be infused:	**250 ml**
Rate of infusion:	**62.5 ml/hour**

Delegate doctor's signature:	Date:
Print name:	

GREAT- 2: A phase 2 trial of Gremubamab compared to placebo in participants with bronchiectasis and chronic *Pseudomonas aeruginosa* infection

Appendix 7 GREAT-2 IMP Release Form

GREAT-2
GRemubamab ErAdication Trial

GREAT-2: A phase 2 trial of Gremubamab compared to placebo in participants with bronchiectasis and chronic Pseudomonas aeruginosa infection

CLINICAL TRIAL RELEASE FORM

EudraCT	**2022-003215-28**	Sponsor	**University of Dundee and NHS Tayside**
CTA		Protocol No.	**1-023-22**
IRAS	**1005993**	Local CTP ID	

Chief Investigator	**Prof James Chalmers**	Tel No	**01382 386131**
Principal Investigator		Tel No	

Participant ID:	

Randomised to	
Total volume to be infused	**250 ml**
Rate of infusion	**62.5 ml/hour**
Please Supply	
Sodium chloride 0.9% (250ml/500ml)	**1 bag**
Gremubamab 200mg/Placebo 4ml	
Water for injection	

Please Supply	**Gremubamab 1500mg/Gremubamab 500mg/Placebo**					
Dose	**200mg of Gremubamab per pack/4ml of Placebo per pack**					
Expiry						
Quantity	**1 vial per pack**					
Pack ID						

Released By:		Date:
Checked By:		Date:
Collected By:		Date:

FOR TRuST Validation:			
Barcodes			

GREAT-2 IMP Release Form V1 04-11-22 Download Date:

GREAT-2: A phase 2 trial of Gremubamab compared to placebo in participants with bronchiectasis and chronic Pseudomonas aeruginosa infection

This sheet ONLY to be given with IMP infusion to blinded Research Nurse

EudraCT	**2022-003215-28**	Sponsor	**University of Dundee and NHS Tayside**
CTA		Protocol No.	**1-023-22**
IRAS	**1005993**	Local CTP ID	

Chief Investigator	**Prof James Chalmers**	Tel No	**01382 386131**
Principal Investigator		Tel No	

Participant ID:			
Participant Name:			
Date of Birth:		Hospital Number/CHI:	
Visit Number:		Visit Date:	

Randomised to	**Gremubamab 1500mg or Gremubamab 500 mg or placebo**
Total volume to be infused	**250 ml**
Rate of infusion	**62.5 ml/hour**
Infusion made up by (signature)	
Date	
Time	
Print name	
Checked by (signature)	
Print name	
Infusion given by (signature)	
Date	
Start time	
Print name	
Checked by (signature)	
Print name	

GREAT-2 Additional Form V1 04-11-22 Download Date:

Appendix 8 Unblinding Form

EMERGENCY UNBLINDING FORM

Unblinding should only occur when patient safety is compromised. Ensure there is a genuine need to perform unblinding

Sponsor	**University of Dundee and NHS Tayside**		
Protocol No.	**1-023-22**	EudraCT	**2022-003215-28**
Chief Investigator	**Prof James Chalmers**	IRAS	**1005993**

Person Performing the Unblinding:	**great2unblinding - Gillian Martin**
Person Requesting the Unblinding:	**Gillian Martin**
Role:	**trial manager**
Contact Number:	**01382 381955**
Email:	**gmartin001@dundee.ac.uk**
Reason for Unblinding Request:	**participant safety**
Date of Request:	**02/05/2023**

Study Participant ID:	**0118**	Site:	**Tayside**		
Pack ID:	**0071**				
Date of birth:	**17/02/2023**	Initials:	**JD**	Gender:	**Male**

Unblinding Result

Gremubamab 1500mg/Gremubamab 500mg/Placebo	**Gremubamab 1500mg**

TRuST Unblinding Performed by:

Name:		Designation:	
Signature:		Date:	

GREAT-2 Additional Form V1 04-11-22 Download Date: 02/05/2023 11:39:25