GREAT-2
GRemubamab ErAdication Trial

IMP/Placebo Preparation

Non-IMP Materials Required

Pharmacy/clinical site should procure:

- Water for injection
- Antihistamine
- Polypropylene syringes to be used for dose preparation.
- Low protein binding 0.2 µm or 0.22 µm filter
- Plastic IV bag coloured sleeves

Tayside Clinical Trials Unit will provide:

- 0.9% Saline 250 ml for infusion, these are PVC, other saline bags should **not** be used

IMP/Placebo preparation

- IMP & Placebo vials are to be stored at 2 – 8°C in clinical trial pharmacy
- Each vial contains:
  - Gremubamab 200mg lyophilised powder

  or
  - Placebo 4ml liquid
- Prior to infusion, Gremubamab 1500 mg and Gremubamab 500 mg will be reconstituted with sterile water for injection.
- Placebo does not require reconstitution
- Both Gremubamab will be diluted to a volume of 250ml 0.9% saline
- Preparation should always use aseptic technique.
- Gremubamab/placebo should not be removed from 2 - 8°C storage until all other procedures required prior to participant dosing have been completed.

Clinical Trial Request Form – to be completed by Research Nurse

- Person randomising participant – unblinded – will print Clinical Trial Request Form

- Clinical Trial Request Form details:
  - Participant ID
  - Participant date of birth
  - Visit number
  - Visit date
  - Randomisation arm - Gremubamab 1500mg / Gremubamab 500mg / Placebo
  - Total volume to be infused – 250ml
  - Rate of infusion – 62.5 ml/hr (4 hours)
  - Number of Gremubamab/placebo vials required – 8 / 3 / 8
  - Amount of Saline 0.9% - 250 ml
  - Amount of water for injection required - 32ml / 12ml / 0ml
  - Allocated pack ID numbers

- Details to be added:
  - Participant's name
  - CHI/hospital number
  - Research nurse & doctor signature

Clinical Trial Request Form – Clinical Trial Pharmacy Actions

- When a Clinical Trial Request Form for Pharmacy is received, the clinical trial pharmacist must check the treatment allocation, check that the number of packs allocated is correct and ensure that the request form is signed before pack IDs can be released.

- The Clinical Trial Request Form must be filed in the pharmacy site file

Example Clinical Trial Request Form

- This must be reviewed and signed by a doctor delegated this task on the Delegation Log
- This must be an unblinded doctor and cannot be the PI

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

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	**Prof James Chalmers**	Tel No	**01382 386131**

Participant ID:	**0110**		
Participant Name:			
Date of Birth:	**21/08/2023**	Hospital Number/CHI:	
Visit Number:	**2**	Visit Date:	**04/04/2023**

Randomised to	**Gremubamab 1500mg**
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	**8 vials**
Water for injection	**40 ml**

Please Supply	**Gremubamab 1500mg/Gremubamab 500mg/Placebo**					
Dose	**200mg for Gremubamab per pack/4ml for Placebo per pack**					
Pack ID						
0103	**0104**	**0106**	**0107**	**0109**	**0110**	**0112**
0113						

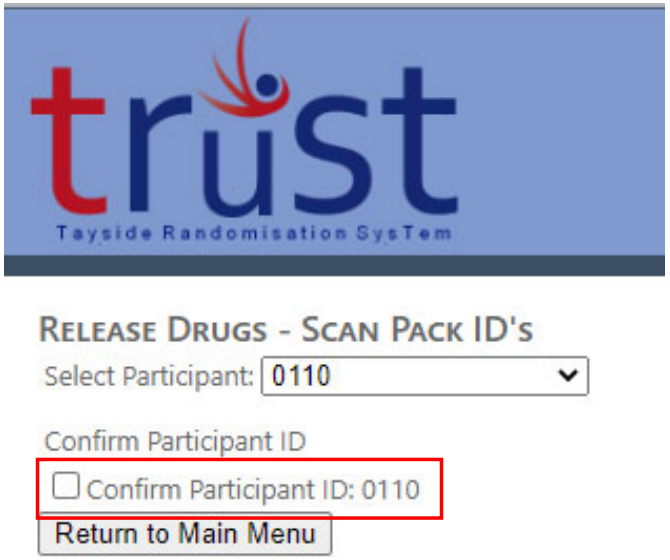
Investigator's or delegate's Signature:		Date:
Research Nurse's Signature:		Date:

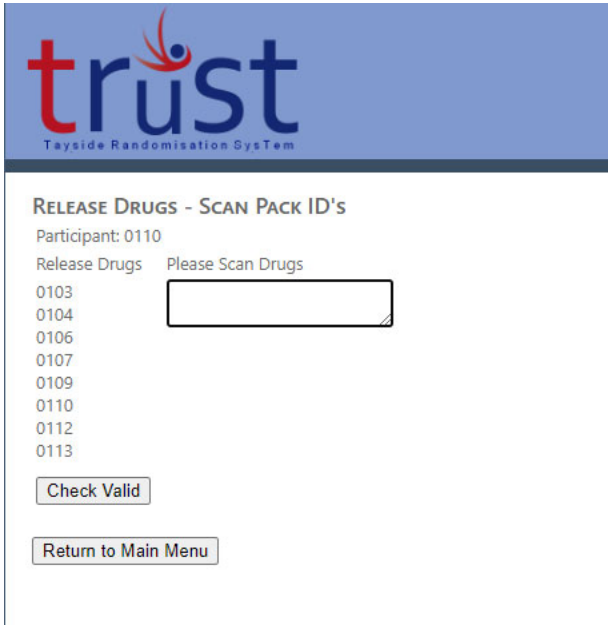
FOR TRuST Validation:			
Barcodes			
0103	**0104**	**0106**	**0107**
0109	**0110**	**0112**	**0113**

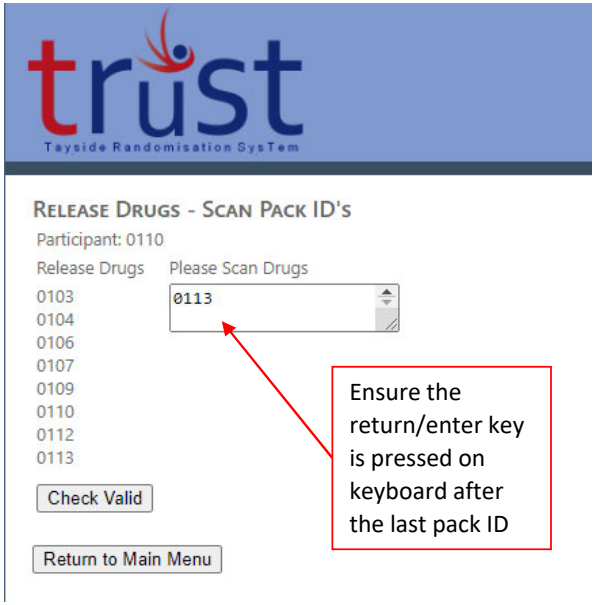
TRuST IMP Release by Pharmacy

- Must be completed on TRuST Randomisation and Drug Accountability system
- Login
- Click “Release Drugs”
- Select and confirm the participant ID listed on the Clinical Trial Request Form
- Check that the pack IDs listed on TRuST match the pack IDs listed on the Clinical Trial Request Form
- Enter the pack IDs listed on the Request Form in the box that says “Please Scan Drugs”.
- Pack IDs should be listed as one ID number per line
- Press return/enter key on keyboard after the last pack ID on the list (see screenshot on next slide)
- Click “check valid”
- Click “Release Drugs”.
- This will generate a Clinical Trial Release Form

TRuST IMP Release by Pharmacy







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	**Prof James Chalmers**	Tel No	**01382 386131**

Participant ID:	**0110**

Randomised to	**Gremubamab 1500mg**
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	**8 vials**
Water for injection	**40 ml**

Please Supply	**Gremubamab 1500mg/Gremubamab 500mg/Placebo**					
Dose	**200mg for Gremubamab per pack/4ml for Placebo per pack**					
Expiry	**20/03/2024**					
Quantity	**1 vial per pack**					
Pack ID						
0103	**0104**	**0106**	**0107**	**0109**	**0110**	**0112**
0113						

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

FOR TRuST Validation:			
Barcodes			
0103	**0104**	**0106**	**0107**
0109	**0110**	**0112**	**0113**

Clinical Trial Release Form – page 1

- Page 1 of the Clinical Trial Release Form shows the treatment allocation & pack IDs
- This should only be viewed by the **unblinded** pharmacy team.
- Page 1 must be signed by the person releasing the packs, this must be checked and signed by another person in the pharmacy
- The person who collects the packs must also sign this form.
- An unblinded team member will prepare the IV bag with the IMP or placebo vials, according to the IMP management plan.
- IV bags should be prepared as close as possible to when the treatment will be given.
- **Important: page 1 of the Clinical Trial Release Form contains unblinded information and should only be viewed by unblinded team members.**
- **Ensure that the Clinical Trial Release Form is printed on 2 separate pages.**

Reconstitution of Gremubamab

- IMP preparation can be performed by a pharmacist or a study team member trained in drug preparation – individuals performing this role must be recorded on the delegation log

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.

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 below) 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 below) 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.

Infusion Bag Preparation continued

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.

Volume of Gremubamab/Placebo to add to each dose

	Dose per vial	Final dose required	Number of vials required	Volume of sterile water to add to each vial	Volume of saline to remove from IV bag	Number of vials added to IV bag	Total Filled Bag Volume (mL)
Gremubamab 500 mg	200 mg	500 mg	3	4 ml	10 ml	2.5 vials = 10 ml	250 ml
Gremubamab 1500 mg	200 mg	1500 mg	8	4 ml	30 ml	7.5 vials = 30 ml	250 ml
Placebo	N/A	N/A	8	N/A placebo comes as 4 ml vial	30 ml	7.5 vials = 30 ml	250 ml

- Each dose preparation will have a remaining 2 ml that is not used (from the remaining unused ½ vial)
- Unused Gremubamab/ placebo should be disposed of and recorded by pharmacy as per local policy

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 should not exceed 4 hours at room temperature or 24 hours at 2°C to 8°C.
- If storage time exceeds these limits, a new dose must be prepared from new vials and the TM must be notified immediately.
- Any unused portion must be disposed of as per local policy.

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**
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Participant ID:	**0110**		
Participant Name:			
Date of Birth:	**21/08/2023**	Hospital Number/CHI:	
Visit Number:	**2**	Visit Date:	**04/04/2023**

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	

Clinical Trial Release Form – page 2

- Clinical Trial Release Form Page 2 must be signed by the person who made up the IV infusion
- Add date & time of infusion preparation.
- To be checked & signed by another team member (blue bracket)
- **Only page 2 of the Clinical Trial Release Form should be given to the blinded team member who will administer the infusion.**
- Clinical Trial Release Form Page 2 must be signed by the person who is administering the IV infusion
- Add start time of the infusion.
- To be checked & signed by another team member (orange bracket)
- After the infusion has been completed, the signed Clinical Trial Release Form Page 2 must be filed in the Investigator Site File