RECOVERY
Randomised Evaluation of COVID-19 Therapy

NHS
Blood and Transplant

COVID-19 Convalescent Plasma

Training Slides

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Training Outline

NHS Blood and Transplant

- Convalescent Plasma (CP) COVID-19
- RECOVERY Trial overview
- Consent and Randomisation to Recovery trial CP arm
- Convalescent Plasma Dose
- Samples required before administering CP
- Issuing CP
- Transfer and administration of CP
- Assessment of safety of CP

Convalescent Plasma COVID-19

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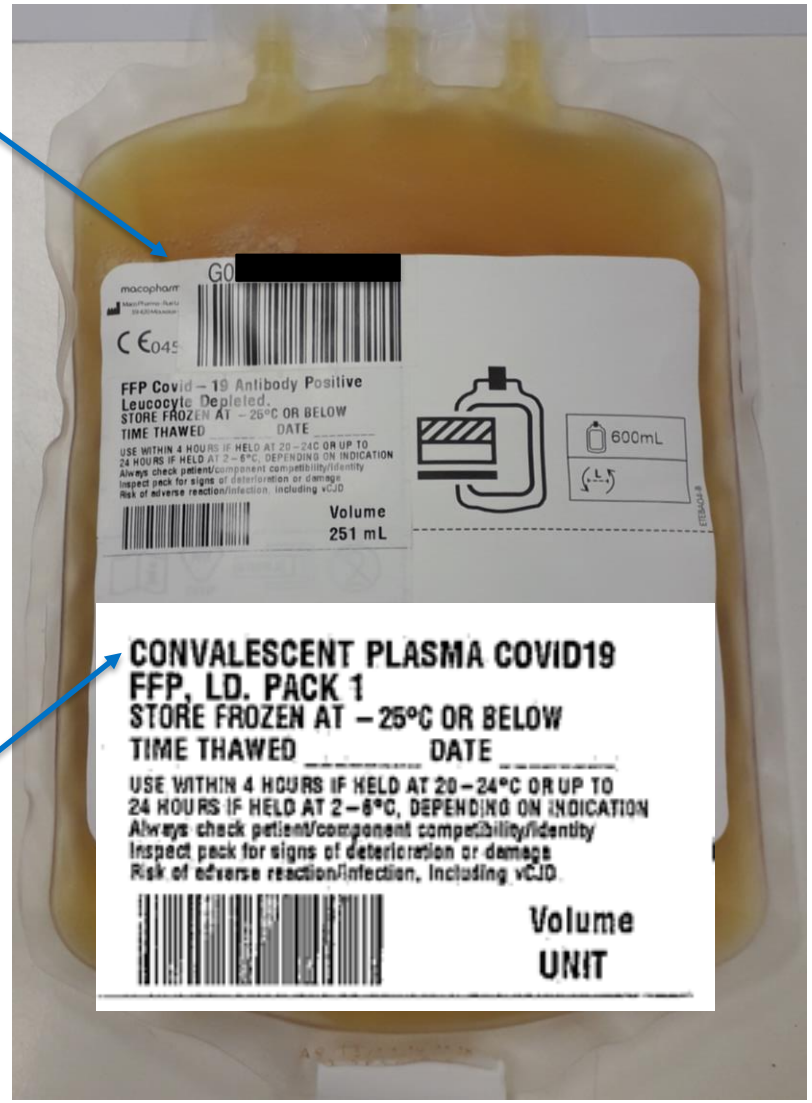
Convalescent plasma COVID-19 FFP (CP) is plasma donated from people who have recovered from COVID-19 and contains antibodies that may help treat COVID-19.

This is a new product and **must ONLY be used for clinical trials.**



RECOVERY
Randomised Evaluation of COVID-19 Therapy

NHS
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RECOVERY Trial:

- A national clinical trial aiming to identify and compare several different treatments that may be beneficial for adults and children hospitalised with confirmed Covid-19.
- The trial commenced with 4 different treatments:
  - Lopinavir-Ritonavir (commonly used to treat HIV) – stopped as shown to be ineffective; hydroxychloroquine – stopped as shown to be ineffective; Dexamethasone- stopped for adults only as **proved to be effective**; azithromycin (commonly-used antibiotic); intravenous immunoglobulin for children only- new
  - Tocilizumab is also an option for those with more severe illness (second randomisation).
- Patients can be randomised (Randomisation A) to the trial treatments, then concurrently randomised (Randomisation B) to CP vs No CP vs Monoclonal Antibody (REGN-COV2) on a 1:1:1 basis.

Consent and Randomisation

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- RECOVERY PIS+ICF V7.0 has information on CP and new sample on consent form:

6. OPTIONAL: Convalescent plasma: I am aware that I may be offered convalescent plasma as one of the treatments I may receive. I am aware that a blood sample will be sent to a central NHS laboratory for measurement of coronavirus and antibodies against it. I have indicated my agreement (or not) to receive this by initialing the appropriate box.	**I agree**	**I do not agree**

NHSBT has produced a CP leaflet, a pdf has been sent to you and is also available through Hospital Services.

Samples required after consent and before randomisation

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1. Group and screen – 1st sample
2. A serum blood sample to be taken for measurement of antibody levels.
   - Details of sample preparation and shipment described in the trial lab SOP.
   - No local sample processing is required.
   - Packaging kits provided by NHSBT for onward transport to central laboratory
   - Sample should be labelled with Randomisation number, date and time.
   - If the lab team is preparing and posting the samples, RECOVERY trial team will provide access to the online randomisation.
   - Once packaged, sample needs to be posted same day – if not possible, keep refrigerated and post next day.
   - Samples taken on Friday/weekend to be kept refrigerated and posted on Monday.
   - Site transfusion and research teams to agree on the process as appropriate – including weekend and out of hours cover plan.

Randomisation

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- Randomisation is performed via RECOVERY trial website
- Patient allocated with unique trial ID (7 digits)
- If a patient is randomised to receive CP the research team must:
  - notify the transfusion laboratory ASAP
  - provide transfusion laboratory with unique patient trial ID number (can be added in the CP request form)
  - Send the second G & S sample if required

Convalescent Plasma – Adult Dose

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Adult patients

- One unit of 275 ml ± 75ml of ABO compatible CP on study days 1 and 2.
- ABO identical plasma is preferred if available.
- Minimum of 12 hour interval between 1st and 2nd units.
- The 2 units should be given with 48 hours after randomisation.
- The second unit of CP should be from a different donor (where possible).
- Two units administered to maximise potential for patients to receive high antibody levels

Convalescent Plasma – Paediatric and Neonatal Dose

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- 5ml/kg of ABO compatible CP intravenous up to standard adult dose of 275 mls per day on study days 1 & 2.
  - Prescription must specify volume of CP to be given according to child's weight.
- Minimum of 12 hour interval between 1st and 2nd units. The 2 units should be given with 48 hours after randomisation
- The second unit should be from a different donor where possible
- CP for neonates and infants up to one year of age needs to be ordered on a named patient basis to ensure the unit meets neonatal requirements – this will be in paediatric packs (barcodes supplied).
  - All the usual testing as for paediatric FFP
  - NB please allow extra time for delivery; available at a few NHSBT units (Colindale, Birmingham, Filton & Manchester)
  - CP for children above one year of age, you will need to use an adult unit – administer the prescribed volume according to child's weight and discard the remainder.

Important information

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- Basic training for Principal Investigators regarding CP is included on the RECOVERY website www.recoverytrial.net
- They have been told:
  - in order for the transfusion laboratory to issue the convalescent plasma (CP) they need to have **2** Group and Screen (G & S) samples on their system. These must have been taken at separate occasions.
  - Collect the 1st Group and Screen sample as soon as the patient has given consent
  - The transfusion lab may have 1 on the system already, if another is required take it after randomisation.
  - These samples are important to avoid transfusion errors.

Issuing CP

- Each unit must be requested and issued as separate events.
- 1 unit of ABO compatible CP defrosted as per normal transfusion laboratory procedures (ABO matched/identical if possible; use standard grouping practice).
- Issue CP via LIMS or other standard systems.
- Laboratory staff must record the patient's trial number in the Convalescent Plasma Log. Versions in *Word* and *Excel* provided; use whichever is more convenient. Send to: CTU@nhsbt.nhs.uk weekly. Logs received from Scotland, Wales and Northern Ireland will be added to those from England for a total UK dataset.

Trial and Patient Trial ID	Donation ID of Issued Convalescent Plasma	Date and Time Issued	Issuer Name	Confirmed Fate of Unit T Transfused W Wasted S Split/Damaged R Re-issued
REMAP-CAP ☐ RECOVERY ☐ Relevant Trial ID:	G_ _ _ _ _ _ _ _ _ _ _ _ _ _ _ Pack No: ___	__/__/____ :		
REMAP-CAP ☐ RECOVERY ☐ Relevant Trial ID:	G_ _ _ _ _ _ _ _ _ _ _ _ _ _ _ Pack No: ___	__/__/____ :		

Hospital Stock - England

NHS Blood and Transplant

- Prior to the green light to start recruiting to RECOVERY-CP
  We will authorise the OBOS team to issue your site:
  - ~6 Units of A
  - ~2 Units of O
  - 2 units of B if required
- Units of AB and B and CP for neonates and infants up to 1 year of age will need to be ordered on a case by case basis
- CP has its own unique product code *(barcodes on next slides)*
- This stock must be stored in the transfusion laboratory **separately from other blood products** at -25°C
- Subsequent stocks can be ordered from the OBOS system: OBOS@nhsbt.nhs.uk
- **Convalescent plasma must be issued for TRIAL USE ONLY**
- Please consider logistics and weekend cover

Barcodes – Adult

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Component description	NHSBT Pulse Code	Start Code	Barcode No.	Stop Code	Barcode
CONVALESCENT PLASMA COVID19, FFP, LD Pack 1	CHP1	a0	37861	3b	a0378613b
CONVALESCENT PLASMA COVID19, FFP, LD Pack 2	CHP2	a0	37862	3b	a0378623b
CONVALESCENT PLASMA COVID19, FFP, LD Pack 3	CHP3	a0	50050	3b	a0500503b
CONVALESCENT PLASMA COVID19, FFP, LD	CHP4	a0	37863	3b	a0378633b

Barcodes – Paediatric

NHS Blood and Transplant

Component description	NHSBT Pulse Code	Start Code	Barcode No.	Stop Code	Barcode
CONVALESCENT PLASMA COVID19. FFP, LD, FOR NEONATAL USE. PACK 1.	CPN1	a0	40081	3b	a0400813b
CONVALESCENT PLASMA COVID19. FFP, LD, FOR NEONATAL USE. PACK 2.	CPN2	a0	40082	3b	a0400823b
CONVALESCENT PLASMA COVID19. FFP, LD, FOR NEONATAL USE. PACK 3.	CPN3	a0	40083	3b	a0400833b
CONVALESCENT PLASMA COVID19. FFP, LD, FOR NEONATAL USE. PACK 4.	CPN4	a0	40084	3b	a0400843b
CONVALESCENT PLASMA COVID19. FFP, LD, FOR NEONATAL USE. PACK 5.	CPN5	a0	40085	3b	a0400853b
CONVALESCENT PLASMA COVID19. FFP, LD, FOR NEONATAL USE. PACK 6.	CPN6	a0	40086	3b	a0400863b
CONVALESCENT PLASMA COVID19. FFP, LD, FOR NEONATAL USE. PACK 7.	CPN7	a0	40087	3b	a0400873b
CONVALESCENT PLASMA COVID19. FFP, LD, FOR NEONATAL USE. PACK 8.	CPN8	a0	40088	3b	a0400883b

Will appear on OBOS as 'CP COVID19,FFP,LD,For Neonatal Use'

Only available in England

Transfer of CP to the ward

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- The Transfusion Laboratory will issue the CP as per normal procedures
- Issuing of CP will be recorded by transfusion Lab on a trial log:
  - Trial number, Unit number, Date & Time …

- Yellow trial bags will be provided for transfer of the unit to the ward.
- Simple Administration guides will be supplied to accompany the CP
- Convalescent plasma is for trial use only

- CP to be transferred to the ward following local procedures.

Administering CP

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- All standard administration transfusion safety checks must be undertaken as per hospital policy.
  - Assess patient for risk of Transfusion Associated Circulatory Overload (TACO)
  - All bedside transfusion safety checks (component integrity & expiry, cross check tag, unit label, prescription, and positive patient identification)
  - Don’t forget adjusted dosing for paediatrics, volume to give rather than 1 unit.
  - The CP should be transfused according to hospital transfusion standard practice.
    - As soon as possible and within 4 hours of defrosting if at room temperature or up to 24 hours if refrigerated between 2 – 6^{o}C
- Date of transfusion and whether the whole unit was given should be documented on the eCRF and all other transfusion observations in patients medical notes as per standard hospital policy.
- Patients can receive other blood products, if required.
- Provided the patient has not had any serious adverse reactions, the research team will request a second unit from the transfusion laboratory.

ASSESSING PATIENTS FOR RISK OF TRANSFUSION ASSOCIATED CIRCULATORY OVERLOAD (TACO) PRIOR TO CONVALESCENT PLASMA TRANSFUSIONS

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SHOT Serious Hazards of Transfusion

Staff should use this checklist, based on the TACO checklist included in the annual SHOT reports, to perform a formal pre-transfusion risk assessment for Transfusion- associated circulatory overload (TACO) in patients receiving convalescent plasma

This should be undertaken, wherever possible for all patients (especially if older than 50 years or weighing less than 50kg) receiving blood transfusion, including transfusion of convalescent plasma for COVID-19

It is important to note that TACO is the most commonly reported cause of transfusion-related mortality and major morbidity

Wherever risks are identified, appropriate mitigating actions need to be taken promptly- this guidance should be used in conjunction with local transfusion policies. Please consult your local transfusion staff for queries and clarifications

TACO can occur in children and neonates as well, mostly due to errors in calculation of blood component volumes. All staff involved in paediatric and neonatal transfusions must be trained and competent to do so and use weight-based dose calculations for convalescent plasma (as ml/kg and not as bags/units of plasma)

TACO risk assessment and suggested mitigating actions
Step 1: Assessing cardiac risk
Does the patient have a diagnosis of “Heart Failure”, congestive cardiac failure (CCF), severe aortic stenosis, or moderate-severe left ventricular dysfunction?
Is the patient on a regular diuretic?
Does the patient have severe anaemia?
Step 2- Assessing pulmonary risk
Is the patient known to have pulmonary oedema?
Does the patient have any respiratory symptoms of undiagnosed cause?
Step 3: Assessing fluid balance
Is the fluid balance clinically significantly positive?
Is the patient on IV fluids (or has been in the past 24 hours)?
Is there any peripheral oedema?
Does the patient have hypoalbuminaemia?
Does the patient have significant renal impairment?
Does the patient need other blood components?
If ‘yes’ to any of the above questions

Consider the following mitigating actions
Step 1:
Can the transfusion of convalescent plasma be safely deferred until the issue can be investigated, treated or resolved?
Step 2:
Review the need for transfusion of additional components (do the benefits outweigh the risks?)
Step 3:
Consider slower transfusion rates. Note that once thawed, CP should be transfused as soon as possible. If delay is unavoidable, the component may be stored and should be used within 4 hours if maintained at 20–24 °C or within 24 hours if stored at 2–6 °C
Measure the fluid balance
Consider giving a prophylactic diuretic
Monitor vital signs closely, including O2 saturations
Consider body weight dosing for other additional blood components needed especially for patients with low body weights
Repeat TACO assessment prior to every transfusion episode in every patient
Please note that these mitigating actions help reduce risk of TACO, but TACO can still occur despite these measures and all patients need to be monitored closely as per national guidelines and local policies

Transfusion Related Serious Adverse Events and Reactions – safety reporting and trial documentation

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- All transfusion-related serious adverse events / reactions are reportable to SHOT / SABRE.
- Other reportable events include wrong component transfused (includes trial patients given standard FFP instead of convalescent plasma or a non-trial patient given CP instead of FFP).
- Ward staff to inform blood bank / transfusion practitioner of any serious reaction immediately.
- Reports to SHOT / SABRE ASAP (preferably within 48 hours) by transfusion teams, with support from ward and research staff supplying all the clinical information.
- Must include trial name and patient's trial number (ID) on the SHOT reporting system in addition to the other details of the reaction.

- SHOT have added CP to their website www.shotuk.org/reporting/covid-19-convalescent-plasma-trial-reporting

Additional assessment of safety of convalescent plasma

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- For **both controls and patients receiving CP or MAb**, the following information will be collected on the following events occurring within the first 72 hours after randomisation:

  ✓ Sudden worsening in respiratory status

  ✓ Severe allergic reaction

  ✓ Temperature >39^{o}C, or at least 2^{o}C temperature rise above baseline

  ✓ Sudden drop in blood pressure of 30 mmHg or more occurring and a systolic blood pressure 80 mm or less requiring urgent medical attention

  ✓ Clinical haemolysis, defined as fall in haemoglobin plus one or more of the following: rise in lactate dehydrogenase (LDH), rise in bilirubin, positive direct antiglobulin test (DAT), positive crossmatch

  ✓ Acute thrombotic event

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RECOVERY-CP

NHS Blood and Transplant Clinical Trials Unit

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Training Attendance

Blood and Transplant

Training can be cascaded – please email **CTU-Recovery@nhsbt.nhs.uk** once new team members have reviewed the slides:

Let us know when you are ready to open for recruitment

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Thank You!

Any Questions

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