SENIOR STUDY

Sarscov2 immunity **E**valuation post-vaccination i**N** pat**I**entS On **R**enal Replacement Therapy

Version 2.0, 01/06/2021

MAIN SPONSOR: Liverpool University Hospitals NHS Foundation Trust

FUNDERS: Roche Diagnostics International Ltd (materials only)

STUDY COORDINATION CENTRE: Department of Nephrology, Royal Liverpool University Hospital

REC reference: 297083

Sponsor ID: SP0618

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Sponsor

The Liverpool University Hospitals NHS Foundation Trust is the research Sponsor for this Study. For further information regarding the sponsorship conditions, please contact:

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Funder

Roche Diagnostics International Ltd for free of cost materials

STUDY SUMMARY

This protocol describes the SENIOR Study and provides information about procedures for entering participants. Every care was taken in its drafting, but corrections or amendments may be necessary. These will be circulated to investigators in the Study. Problems relating to this Study should be referred, in the first instance, to the Chief Investigator.

This study will adhere to the principles outlined in the NHS Research Governance Framework for Health and Social Care (2nd edition). It will be conducted in compliance with the protocol, the Data Protection Act and other regulatory requirements as appropriate.

GLOSSARY OF ABBREVIATIONS

HRA	Health Research Authority
REC	Research Ethics Committee
LUFT	Liverpool University Hospitals NHS Foundation Trust

KEYWORDS

Sarscov2

Antibody

Polymerase Chain Reaction

TITLE: Sarscov2 immunity **E**valuation post-vaccination i**N** pat**I**ents On **R**enal Replacement Therapy-SENSOR study

DESIGN: Laboratory prospective observational cohort study of the immune response to SARS-CoV-2 vaccination.

AIMS:

Primary Aim:

To determine the scale of antibody-based immune response 21 days after the first and second dose of the SARS-CoV-2 vaccine in dialysis and renal transplant patients.

Secondary Aims:

1. The antibody-based immune response's longevity after 12 months of the SARS-CoV-2 vaccine in dialysis and renal transplant patients.
2. To compare disease rates (SARS CoV-2 infection) in the vaccinated and unvaccinated dialysis and renal transplant patients.
3. To assess HLA sensitisation following the SARS-CoV-2 vaccine in dialysis patients on the renal transplant waiting list and renal transplant patients.

OUTCOME MEASURES:

Primary outcome:

To ascertain the level of antibody-based immune response on day 21 after the second SARS-CoV-2 vaccine with participants classified as responders or non-responders.

Secondary outcome:

1. The longevity of immune response, up to 12 months following the second SARS-CoV-2 vaccine.
2. Disease rates measured by SARS-CoV-2 PCR, including hospitalisation and mortality in the vaccinated and unvaccinated dialysis and renal transplant patients.
3. HLA sensitisation in dialysis patients on the UK renal transplant waiting list and renal transplant patients measured by Luminex solid-phase assay (single antigen beads).

DURATION:

Start date: 15/05/2021

End Date: 30/07/2022

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1. INTRODUCTION

1.1 BACKGROUND

Coronavirus disease 2019 (COVID-19) is caused by a novel coronavirus that has resulted in a global pandemic. (1) Several case reports have identified individuals who have been reinfected with a new and genetically distinct SARS-CoV-2 genome from their initial infection. (2, 3) SARS CoV-2 infection is associated with severely increased morbidity and mortality in patients on Renal Replacement Therapy (RRT). (4-6) One recent study of the antibody prevalence following SARS-CoV-2 infection from three large cross-sectional surveys in England suggested waning antibodies in the population. (7)

Two vaccines now have MHRA Regulation 174 authorisation (Pfizer-BioNTech and AstraZeneca) in the UK.(8, 9). The COVID-19 vaccines currently in use target the spike (S) protein of the coronavirus to produce an immune response. (10)

Phase 3 vaccine trials were undertaken in clearly defined populations that excluded some groups, patients with severe or uncontrolled medical comorbidities, those with immunosuppression, pregnant women, and children. (9, 11) A recently published systematic review by Dorey et al. showed that the inclusion of patients on Renal Replacement Therapy (RRT) (dialysis and renal transplant) in completed and ongoing COVID-19 vaccine studies remains low, with the majority of trials explicitly excluding individuals with “severe” or “chronic” kidney disease and those receiving immunosuppression. (12)

SARS-CoV-2 vaccination commenced in the UK on 8th December 2020. Patients with ESKD were identified nationally and internationally by the kidney associations as a priority group and hence categorised under the risk group 4 (clinically extremely vulnerable) and offered vaccination beginning January 2021. The response to the COVID-19 vaccine to the above groups is unknown. The results from vaccine studies cannot be generalised to these multi-morbid RRT patients. There is variable evidence of immunosuppressed and renal transplant patients’ development of immunity post-COVID 19 infection due to immune dysfunction in the End-Stage Kidney Disease (ESKD). (13) Due to immune dysfunction in the ESKD and the immunosuppressed population, the vaccination efficacy (VE) could be muted. A recent study has shown that in renal transplant patients receiving Moderna and Pfizer vaccine, after the first dose of vaccine (median 20 days (IQR 17-24)), the antibody was detectable in only 17% (95% CI 14%-21%). (14)

Hence there remain many unknowns in this population whether vaccines will significantly contribute to the normalisation of life, in this cohort of patients, for example, renal transplant patients coming out of shielding and for dialysis patients to straddle across different dialysis shifts to mention a few. (15) Currently, strict adherence to specific shifts (Monday/Wednesday/Friday and

Tuesday/Thursday/Saturday) is enforced to ensure Infection prevention and control (IPC) measures.

Emerging evidence shows that cellular immunity is vital in determining the course and outcome of COVID 19 disease. (16) Also, during COVID infection, T cells recognise the viral antigens presented by MHC class I [MHC; Human Leukocyte Antigen (HLA)], which in turn promotes cytokines release and cytotoxic activity of CD8+ T cells. (17, 18). Hence it can be hypothesised that the COVID-19 vaccine could induce HLA-sensitisation.vaccin

1.2 RATIONALE FOR CURRENT STUDY

Based on the foregoing background, the study aim is to

1) Assess the antibody response to the SARS-CoV-2 vaccines in patients on Renal Replacement Therapy.
2) Compare level of antibody response between Pfizer-BioNTech and AstraZeneca SARS-CoV-2 vaccines in patients on Renal Replacement Therapy.
3) Assess the disease rates (symptomatic and asymptomatic) of SARS CoV-2 infection in the vaccinated and unvaccinated RRT patients.
4) Assess if SARS-CoV-2 vaccines induce HLA sensitisation.

2. STUDY OBJECTIVES

Primary Objectives

To determine the scale of antibody-based immune response 21 days after the first and second dose of the SARS-CoV-2 vaccine in dialysis and renal transplant patients using the Roche COVID19 antibody quantitative assay.

Secondary Objectives

1. To assess the antibody-based immune response's longevity over short term periods (reviewed monthly) and 12 months after the SARS-CoV-2 vaccine in dialysis and renal transplant patients, using the Roche COVID19 antibody quantitative assay.
2. To compare the level of antibody response after the Pfizer-BioNTech and AstraZeneca SARS-CoV-2 vaccine in dialysis and renal transplant patients, using the Roche COVID19 antibody quantitative assay.
3. To compare disease rates (symptomatic and asymptomatic SARS CoV-2 infection) using Covid-19 polymerase chain reaction (PCR) test, including hospitalisation and mortality in the vaccinated and unvaccinated dialysis and renal transplant patients.
4. To assess HLA sensitisation following the SARS-CoV-2 vaccine measured by Luminex solid-phase assay (single antigen beads) in dialysis patients on the renal transplant waiting list and renal

transplant patients.

3. STUDY DESIGN

This laboratory prospective observational cohort study evaluates the efficacy, longevity of the antibody-based immune response, and HLA sensitisation from receipt of the MHRA approved SARS-CoV-2 vaccines in dialysis patients and renal transplant recipients.

STUDY POPULATION:
Patients on Renal Replacement Therapy (Dialysis and renal kidney transplant patients at Liverpool University Hospital NHS Foundation Trust).
Cohort 1 Vaccinated dialysis patients on the UK renal transplant waiting list
Cohort 2 Vaccinated dialysis patients not on the UK renal transplant waiting list
Cohort 3: Vaccinated renal transplant patients
Cohort 4: Unvaccinated dialysis and renal transplant patients

METHODS:

ENDPOINT:

Primary Endpoint
1. To ascertain the scale of antibody-based immune response on day 21 after the first and second SARS-CoV-2 vaccine. Participants will be classified as responders or non-responders.

Secondary Endpoint
1. Immune response's longevity up to 12 months following the second SARS-CoV-2 vaccine.
2. Antibody response level between the Pfizer-BioNTech and AstraZeneca SARS-CoV-2 vaccine.
3. Disease rates measured by SARS-CoV-2 PCR, including hospitalisation and mortality in the vaccinated and unvaccinated dialysis and renal transplant patients.
4. HLA sensitisation in dialysis patients on the UK renal transplant waiting list and renal transplant patients measured by Luminex solid-phase assay (single antigen beads) assay.

INTERVENTION:
1. Assessment of immune response
The measurement of SARS-CoV2 specific antibodies will be using the Elecsys Anti-SARS-CoV-2 S assay (Elecsys Anti-SARS-CoV-2 S.09289275500v1.0).

This study is a pragmatic study with the timing of blood samples required for study in the three cohorts centred around the patients routine clinical monitoring, monthly in dialysis patients, and 4 monthly intervals (monthly if logistically possible) for renal transplant patients.

Dialysis patients will have their study samples monthly with their routine monthly blood monitoring on dialysis by nurses. Home dialysis patients will self-obtain the study samples with their routine monthly blood monitoring. Renal transplant patients will have their study samples at 4 monthly intervals (monthly if logistically possible) and bloods taken for their clinic visits by the trust phlebotomy service.

Given that the substantial proportion of participants will have had their first dose of the SARS-CoV2 vaccine, this study intends to utilise stored samples (HLA-specific antibodies and Post-Transplant Save Serum) at Liverpool University Hospitals NHS Foundation Trust pathology department(s) / diagnostic archive(s) for the baseline samples.

The study's blood sampling schedule for assessment of immune response in the four cohorts is detailed below.

Cohort 1 Vaccinated dialysis patients on the UK renal transplant waiting list
Blood/serum for antibody to COVID 19 vaccination
• at baseline (stored sample-transplant listing blood tests)
• 21 days post 1st dose of the SARS-CoV-2 vaccine (stored sample -transplant listing blood tests),
• 21 days post 2nd dose of the SARS-CoV-2 vaccine
• monthly after that for 1 year from the date of the 2nd SARS-CoV-2 vaccine

Cohort 2 Vaccinated dialysis patients not on the UK renal transplant waiting list
Blood/serum for antibody to COVID 19 vaccination
• 21 days post 2nd dose of the SARS-CoV-2 vaccine
• monthly after that for 1 year from the date of the 2nd SARS-CoV-2 vaccine

Cohort 3: Vaccinated renal transplant patients
Blood/serum for antibody to COVID 19 vaccination
• at baseline (stored sample -transplant listing blood tests)
• 21 days post 1st dose of the SARS-CoV-2 vaccine (stored sample -transplant listing blood tests),
• 21 days post 2nd dose of the SARS-CoV-2 vaccine
• 4 monthly after that for 1 year (monthly if logistically possible) from the date of the 2nd SARS-CoV-2 vaccine

Cohort 4: Unvaccinated dialysis and renal transplant patients
• Will have no blood or serum samples taken.

2. Evaluation of other parameters:
a. Incentre haemodialysis dialysis patients (vaccinated and unvaccinated) will have weekly SARS-CoV-2 PCR monitoring as routine standard of clinical care and not a study intervention as per the current trust's policy.
b. Home dialysis and renal transplant patients (vaccinated and unvaccinated) will have COVID-19 PCR, as indicated by symptoms at COVID 19 testing centres. This data will be collected for 12 months after the first vaccine dose.
c. HLA-specific antibodies in dialysis patients on the UK renal transplant waiting list and transplant patients will be assessed for sensitisation by Luminex solid-phase assay (single antigen beads) as routine standard of clinical care. This is routine and done after a clinically significant event such as infection, blood transfusion, pregnancy or vaccination.(19)

3. Data collected as a part of this study will include:

a. Sociodemographics including age, gender, ethnicity, postcode data for deprivation indices
b. Body Mass Index (BMI)
c. Medical history and Comorbidity data (Charlson Co-morbidity Index)
d. Medication data, including immunosuppression
e. Vaccination data (Date and Type of vaccine)
f. COVID-19 infection status (past and during the duration of the study)
g. Survival data (Including date and cause of death)
h. Hospitalisation data
i. Serious Adverse Event

Research Electronic Data Capture (REDCap) database managed by the sponsor will collate the study's data. (20) REDCap supports online and offline data capture.

Table 1.0 below details the SENIOR study schedule.

Table 1: Schedule of events in the SENIOR study

			Screening	Trial Entry	Baseline	21 days post 2nd dose of SARS-CoV-2 vaccine	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12
Eligibility assessment			X															
Consent			X															
Study Entry				X														
Research samples	**Cohort 1**	Blood/Serum for antibody			X[1]	X	X	X	X	X	X	X	X	X	X	X	X	X
		SARS-CoV-2 PCR weekly			X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]
		HLA-specific antibodies			X[2]	X[2]						X						X
	Cohort 2	Blood/Serum for antibody			X[1]	X	X	X	X	X	X	X	X	X	X	X	X	X
		SARS-CoV-2 PCR weekly			X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]
	Cohort 3	Blood/Serum for antibody			X[1]	X	X[3]	X[3]	X[3]	X	X[3]	X[3]	X[3]	X	X[3]	X[3]	X[3]	X
		SARS-CoV-2 PCR			X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]
		HLA-specific antibodies			X[2]	X[2]						X						X
	Cohort 4-HD	SARS-CoV-2 PCR weekly			X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]
	Cohort 4-TX	SARS-CoV-2 PCR			X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]
Data collection					X	X						X						X

Key

1 Stored sample at Liverpool University Hospitals NHS Foundation Trust pathology department(s) / diagnostic archive(s).

2 SARS-CoV-2 PCR monitoring as routine standard of clinical care and not a study intervention as per trust's policy.

3 Collected if logistically possible.

4 SARS-CoV-2 PCR as indicated by symptoms at COVID 19 testing centres.

Table 2.0 details the sample collection and storage in the SENIOR study.

The samples will be stored in the freezer at -80°C in the biochemistry and immunology laboratory at Liverpool University Hospital NHS Foundation Trust. The samples will be accessed and analysed in batches by the laboratory staff at Liverpool University Hospital NHS Trust. The samples will be discarded once they have been analysed and not biobanked.

Table 2: Details of Sample Collection and Storage

Sample Type	Collection Tube	Volume	Laboratory Analysis	Sample Storage
Serum	Serum Gel (Gold)	5ml x 1	Elecsys Anti-SARS-CoV-2 S assay ((Elecsys Anti-SARS-CoV-2 S.09289275500v1.0)	-80°C
Serum	Serum Gel (Gold)	5ml x 2	Luminex solid-phase assay (single antigen beads).	-80°C

3.1 STUDY OUTCOME MEASURES

Primary Outcome

To ascertain the scale of antibody-based immune response on day 21 after the first and second SARS-CoV-2 vaccine with participants classified as responders or non-responders.

Secondary Outcome

1. Immune response's longevity over short term periods (reviewed monthly) and 12 months after the SARS-CoV-2 vaccine.
2. Antibody response between Pfizer-BioNTech and AstraZeneca SARS-CoV-2 vaccines.
3. Disease rates measured by SARS-CoV-2 PCR, including hospitalisation and mortality in the vaccinated and unvaccinated dialysis and renal transplant patients.
4. HLA sensitisation in dialysis patients on the UK transplant waiting list and renal transplant patients.

4. PARTICIPANT ENTRY

4.1 PRE-REGISTRATION EVALUATIONS

Apart from those stated in the exclusion criteria, all RRT patients at the Liverpool University Hospitals NHS Trust will be eligible to participate.

4.2 SCREENING

Patients will be informed of this study by publicity through the CaMKIN (Cheshire and Merseyside

Kidney Information Network) https://kinet.site/camkin/.

Participants will be identified from renal databases (Cyberren), IT systems or specialist clinics lists. They will be identified at the clinical site by the healthcare team members delegated this responsibility on the delegation log by the principal investigator.

4.3 INCLUSION CRITERIA

1. Age of 18 years or older.
2. Renal Replacement Therapy patients (dialysis and renal transplant) who have received the SARS-CoV-2 vaccine
3. A comparative arm of Renal Replacement Therapy patients (dialysis and renal transplant) who have refused the SARS-CoV-2 vaccine.
4. Capable of understanding the purpose and risks of the study, fully informed, and given informed consent.

4.4 EXCLUSION CRITERIA

1. Pregnancy or breastfeeding
2. Active (haematological) malignancy
3. Inherited immune deficiency
4. Infection with Human Immunodeficiency Virus (HIV)

4.5 APPROACH

The initial approach to potential participants will be made by a GCP trained member of the healthcare team or a clinical research nurse on the delegation log. The potential participant will be contacted via telephone or approached face to face during their routine clinical visit to introduce the study. An information sheet will be provided during the face-to-face approach, posted or e-mailed to them from a local healthcare team member. If the participant is agreeable to participate, they will be consented as below.

4.6 WITHDRAWAL CRITERIA

All participants are free to withdraw at any time from the protocol treatment without giving reasons and without prejudicing further treatment. Participants will be offered the choice of investigators using the existing data up to a point in the study.

5. ADVERSE EVENTS

5.1 DEFINITIONS

The potential risk in this study is mainly related to the risk of phlebotomy, which commonly is mainly bruising at the puncture site (hematoma). However, very rarely, phlebotomy can cause nerve injury and arterial puncture or laceration. The blood samples' timing in the three cohorts will be centred around

the patients' routine clinical monitoring. The risk of this is low in dialysis patients who will have blood taken on the machine.

Nasopharyngeal PCR swabs are part of routine clinical care and not a study intervention. However, the risk of nasopharyngeal PCR swab includes a nasal swab break by triggering the swab's breakpoint mechanism and minor complication of epistaxis. This risk is mainly in in-centre haemodialysis patients who have weekly nasopharyngeal PCR swabs per existing trust/ departmental policy.

Adverse Event (AE):

Medical judgement will be exercised in deciding whether an AE is serious in other situations.

- phlebotomy causing nerve injury and arterial puncture or laceration.

Nasopharyngeal PCR swabs are part of routine standard of clinical care and not a study intervention, and hence any complications from this procedure will not be recorded as an adverse event as a part of the study.

Serious Adverse Event (SAE):

- No SAE is anticipated by participating in the study

5.2 REPORTING PROCEDURES

All adverse events will be reported. Depending on the nature of the event, the reporting procedures below should be followed. Any questions concerning adverse event reporting should be directed to the Chief Investigator in the first instance.

5.2.1 Non-serious AEs

All such events, whether expected or not, should be recorded.

5.2.2 Serious AEs

An SAE form should be completed and faxed to the Chief Investigator within 24 hours. However, SARS-CoV-2 infection and death due to SARS-CoV-2 infection and hospitalisations for elective treatment of a pre-existing condition do not need reporting as SAEs.

All SAEs should be reported to the sponsor where in the opinion of the Chief Investigator, the event was:

- 'related', i.e. resulted from the administration of any of the research procedures; and
- 'unexpected', i.e. an event that is not listed in the protocol as an expected occurrence

Reports of related and unexpected SAEs should be submitted within 15 days of the Chief Investigator

becoming aware of the event, using the NRES SAE form for non-IMP studies. The Chief Investigator must also notify the sponsor of all SAEs.

Local investigators should report any SAEs as required by their Local Research Ethics Committee, Sponsor and/or Research & Development Office.

Contact details for reporting SAEs

Please send SAE forms to: RGT@rlbuht.nhs.uk

Tel: 0151 706 3702 (Mon to Fri 09.00 – 17.00)

6. ASSESSMENT AND FOLLOW-UP

Participants will be followed up in accordance with standard clinical practice. Data will be collected retrospectively from clinic records for the participant from the start of the SARS-CoV-2 pandemic (March 2020) until the end of the study (September 2022). The majority of the data will be collected from participant clinical records or general practice (GP) summary care records. Where necessary, it will be acceptable to collect data from face-to-face consultations or telephone follow-up calls.

7. STATISTICS AND DATA ANALYSIS

Sample Size: Given the nature of the research question, there have been no studies to date on this, to inform the sample size calculation. Therefore, convenience sampling has been used.

Sampling Method: Non-Probability Sample. Given that it is a pragmatic, clinical and diagnostic utility study, and antibody testing is likely to be the norm soon, the study aims to recruit a vast majority of vaccinated dialysis (250) and transplant patients (500).

STATISTICS
This study will be analysed using descriptive statistics to measure antibody response and HLA sensitisation rates. Descriptive statistics will also be used to compare SARS-CoV-2 infection rates in the vaccinated and unvaccinated cohorts. Continuous data will be expressed as means ± SD; categorical data expressed as percentages.

Estimates of both cumulative incidences of the vaccine responders and non-responders and magnitude of the antibody-based response will be obtained using mixed-effects models, assuming antibody-positive counts have a negative binomial distribution. An assessment of the role of factors such as age, gender, ethnicity and immunosuppression in immunity will be explored by including interactions within the model.

Time-to-event data will be analysed using Kaplan-Meier methodology and Cox Proportional-Hazards models where appropriate. Comparisons to look at differences in IgG response from vaccination and/or infection across disease groups at specific time points will be carried out using two-sample t-tests.

The standardised incidence ratio (SIR) and the frequency of SARS-CoV-2 infection in the vaccinated dialysis and renal transplant patients will be measured. To compare the risk of SARS-CoV-2 infection between the dialysis and transplant patients, and the general population, the number of person-years at risk of SARS-CoV-2 infection will be first calculated. SIR will be calculated as the number of observed SARS-CoV-2 infection among the dialysis and renal transplant patients divided by the expected number of SARS-CoV-2 infection in the general population. The expected number of cases will be based on the person-years at risk, and the SARS-CoV-2 infection incidence rates in the general population will be obtained from the Office of National Statistics.
(https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases.)

8. REGULATORY ISSUES

8.1 ETHICS APPROVAL

The Chief Investigator has obtained approval from the Research Ethics Committee and Health Research Authority (HRA). The study will be submitted to each proposed research site for Confirmation of Capacity and Capability. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

8.2 CONSENT

It is the responsibility of the investigator or designee (e.g. registrars, Research Nurses if local practice allows, and the Principal Investigator has delegated this responsibility) to obtain written informed consent for each participant before any trial-related procedures. A Participant Information Sheet is provided to facilitate this process. During the consent process, the PI or the person on the delegation log who is consenting will endeavour to inform the participant of the purpose and nature of the research; inform what the research involves, its benefits (or lack of benefits), risks and burdens; explain the alternatives to taking part and able to assess if the participant can retain the information long enough to make an effective decision and provide the opportunity to make a free choice. The participant must be given an opportunity to ask questions which should be answered to their satisfaction. The participant's right to refuse to participate in the trial without giving a reason must be respected.

If the participant agrees to participate in the trial, they should be asked to sign and date the latest version of the Informed Consent Form. The Informed Consent Form should either be wet-ink signed by the participant and the investigator (or designee) or Electronic-Consent (e-Consent) using REDCap. Participants can 'sign' their consent by typing in their name or utilising REDCap's 'Signature' field type.

The REDCap e-Consent Framework provides standardised tools to obtain consent and store consent documentation with a certification screen and a storage function that automatically generates a 'hard-copy' PDF of the signed form. If a wet-ink is signed, the Informed Consent Form could be returned when the participant attends for their first clinic appointment or can be returned in the post, but both parties must sign it before the participant enters the trial. Once the participant is entered into the trial, the participant's registration number should be entered on the Informed Consent Form. A copy of the Informed Consent Form should be given to the participant, a copy should be filed in the hospital notes, and the original placed in the Investigator Site File or in REDCap.

Details of the informed consent discussions should be recorded in the participant's medical notes, including date of and information regarding the initial discussion, the date consent was given, with the name of the trial and the version numbers of the Participant Information Sheet and Informed Consent Form.

Throughout the trial, the participant should have the opportunity to ask questions about the trial, and any new information that may be relevant to the participant's continued participation should be shared with them promptly.

Unvaccinated dialysis and transplant patients will be approached to use their data for the study. If a participant refuses, they will be offered the choice of contributing their data only to the study.

8.3 CONFIDENTIALITY

The Chief Investigator will preserve the confidentiality of participants taking part in the study and will abide by the Data Protection Act 2018 and the UK GDPR as amended from time to time and any successor legislation in the UK and any other directly applicable regulation relating to data protection and privacy. Personal data recorded on all documents will be regarded as strictly confidential and will be handled and stored under the General Data Protection Regulation 2018 and the Data Protection Act 2018.

Access to participants' personal data during the study will be only available to the direct healthcare team. Anonymisation will not be feasible as this study intends to quantify antibody-based immune response after the second SARS-CoV-2 vaccine and classify patients as responders or non-responders. The healthcare team will need access to participants' healthcare data to inform of their antibody results, with the caveat regarding the current uncertainty regarding the antibody response in the short and long term. Patients will also be told that the tests results will not inform decision-making regarding shielding and will be informed by the government guidance on shielding for the duration of the study.

RedCAP is more secure than Microsoft Excel or Microsoft Access and can be accessed from any device with an Internet connection and web browser. It is also Health Insurance Portability and Accountability Act of 1996 (HIPAA) compliant; fields in REDCap can be marked as identifiable; and the user has the option of de-identifying their data during export. REDCap also offers daily backups, basic support, and

an audit trail feature for even more security. REDCap provides easy exports, so users are in control of their data.(20)

Data will be processed under Article 6 (i) (performance of a task carried out in the public interest) and Article 9 (j) (necessary for archiving purposes in the public interest, scientific or historical research purposes, or statistical purposes per Article 89(1)).

- Paper and other manual files will be appropriately filed and stored securely in filing cabinets, cupboards, and/ or rooms which will be locked and will be accessible to only the healthcare team.
- Patient identifiable data held on NHS computers (NHS laptop computers) will be password protected.
- Research folders access will be restricted to those on the delegation log

8.4 INDEMNITY

The Liverpool University Hospitals NHS Foundation Trust holds Indemnity and NHS Indemnity Cover, which apply to this study.

8.5 SPONSOR

The Liverpool University Hospitals NHS Foundation Trust will act as a sponsor for this study. It is recognised that as an employee of the University, the Chief Investigator has been delegated specific duties, as detailed in the Sponsorship Approval letter and And CI Agreement.

8.6 FUNDING

Roche Diagnostics International Ltd is funding the materials for this study.

8.7 AUDITS

The study may be subject to inspection and audit by the Liverpool University Hospitals NHS Foundation Trust under their remit as the sponsor and other regulatory bodies to ensure adherence to GCP and the NHS Research Governance Framework for Health and Social Care (2nd edition).

9. STUDY MANAGEMENT

The day-to-day management of the study will be coordinated through the Chief Investigator and the lead research nurse at Liverpool University Hospitals NHS Foundation Trust.

10. END OF STUDY

The study will be deemed complete when all data collection is completed, and the analyses have been fully performed, and data has been locked, which is anticipated to be after two months from the end date of the study. End of study declaration and final study report will be submitted to HRA/REC and sponsor, notifying them of the conclusion of the study. All data will be held electronically.

All documents will be achieved. Data will be archived for 10 years after the end of the study in line with the sponsor's standard operating procedure on archiving. The serum samples will be destroyed once analysed for SARS-CoV-2 and for HLA sensitisation and will not be bio-banked.

11. ARCHIVING

Data and all appropriate documentation should be stored for a minimum of 10 years after the completion of the study, including the follow-up period unless otherwise directed by the funder/sponsor/regulatory bodies.

12. PUBLICATION POLICY

The study protocol will be published on one of the registries recommended by The International Committee of Medical Journal Editors (ICMJE). The study will be registered on a public registry before the first participant is recruited and no later than six weeks after recruiting the first participant.

Results of this trial will be submitted for publication in peer-reviewed journals. The authors will acknowledge that the trial was performed with the Liverpool University Hospitals NHS Foundation Trust support, and all funding bodies will be appropriately acknowledged per the funder's terms and conditions. Intellectual property rights will be addressed in the agreements between the sponsor, collaborators, and the sites.

Where possible the data will be analysed and published as soon as available rather than waiting until the end of the study. For example, in this study the results of the primary outcome will be analysed and published as soon as possible.

The trial results will be made available on an appropriate study registry and provided to participants in the form of a lay summary.

The study will be submitted for conference presentations of learned societies.

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14. APPENDICES

None