Title	Observational Cohort Trial -T-cells Antibodies and Vaccine Efficacy in SARS-CoV-2
Trial Design	Multi-centre, multi-disease, prospective observational cohort trial of the immune response to SARS-CoV-2 vaccination.
Aim	To evaluate the immune response to SARS-CoV-2 vaccination in clinically vulnerable groups across the UK.
Objectives	**Primary Objective** • To determine the magnitude of the humoral and T cell immunogenicity of SARS-CoV-2 vaccines in participants with chronic diseases and/or secondary immunodeficiency. **Secondary Objectives** • To determine phenotype and function of SARS-CoV-2 vaccine induced immune responses in participants with chronic diseases and/or secondary immunodeficiency, compared to each other and healthy controls in parallel studies. • To evaluate the impact of distinct immune therapeutic drug classes on the development of humoral and cellular immune responses to SARS-CoV-2 following vaccination.
Outcome Measures	**Primary Outcomes** Vaccine Specific Immunogenicity: • To measure the presence and amount of serum antibodies to discriminate IgG responses to SARS-CoV-2 from vaccination and/or infection. • To measure T cell responses to SARS-CoV-2 peptides following vaccination. **Secondary Outcomes** Clinical Protection • The first symptomatic PCR-proven COVID-19 occurrence from 14 days after first dose of vaccine in participants without evidence of prior infection with SARS-CoV-2. **Exploratory Outcomes** Humoral Immunogenicity • To assess the capacity of vaccine induced SARS-CoV-2 antibodies to neutralise/block SARS-CoV-2 infection. Cellular Immunogenicity • To assess the relative contribution of T cell subsets and T cell function and the recall potential of SARS-CoV-2 memory T cells at later time points.
Patient Population	Vaccine naive participants with end stage kidney disease, liver disease, cancer, immune-mediated rheumatic diseases and haemopoietic stem cell transplant recipients.

Sample Size	Deep Immunophenotyping Group: 150 patients per disease cohort will be recruited for full immune response analysis. Serology Group: up to 850 per disease cohort, for serology analysis.
Inclusion Criteria	• Eligible for vaccination by one of the SARS-CoV-2 approved vaccines and have either: ➢ Not received the first dose of the vaccine or ➢ Have participated in a study where bloods were taken prior to their first dose of vaccine and the blood samples were stored and are available for analysis in OCTAVE trial • Anticipated life expectancy of ≥ 6 months • Fall into one (or more) of the five disease cohorts who will meet disease relevant classification, disease state, and staging according to established international standards (refer to protocol for details)
Exclusion Criteria	Patients being considered for recruitment to the Deep Immunophenotyping Group are excluded from participating in the trial if: • They have already received the first dose of the vaccine and have not participated in a study where blood samples taken prior to their first dose of vaccine were stored and are available for analysis in OCTAVE trial.
Sample Collection	Blood and saliva samples will be collected at the following time points: • Pre-vaccine (baseline) – may have been collected prior to recruitment to OCTAVE • 1 day after first injection (optional) • Pre-boost • 28 days post-boost (ideally within +/- 3 days) • 6 months post-vaccination (as close to time point as possible)
Trial Duration	Patients will be recruited over a 6 month period and followed up for 6 months in accordance with standard clinical practice for the relevant disease cohort.