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Statistical Analysis Plan for

RAPID PROTECT: Multi-centre, interventional, open label, trial with cohorts of immunocompromised participants treated with AZD7442. Patients will then be randomised to receive an approved vaccine booster 28 days after initiation of AZD7442 treatment.

Eudract/ISRCTN No:	2021-006703-15	Version Number:	1.0

Final Plan V2.0 dated 22nd January 2024

Based on protocol version: 5 dated 09/05/2023

SAP Revision History				
Protocol version	Updated Sap version no.	Section number changed	Description and reason for change	Date changed
5	2	3.6 Timing of final analysis; Table A Schedule of assessments; All instances of day 273 and 364 were removed from	Recruitment to the trial was suspended in April 2024 since the percentage of circulating Evusheld resistant SARS-CoV-2 variants had exceeded a pre-specified 90 % threshold. The trial had not reached the target recruitment. The analysis of serology outcomes vs PROVENT trial data was therefore no longer required	22/01/2024

		the text and tables. Sections 6.3.1.2, 6.3.1.3 and 6.3.1.4- removed analysis vs PROVENT data and all associated tables were removed from the Appendix. Appendix 3 was removed (data from healthy age and gender matched controls from PROVENT III trial	as this was to enable a sample size recalculation once 280 complete day 28 datasets had been received. The decision was also made to reduce the follow up period from 12 months to 6 months for all patients.	
		6.1.1.2 and 6.3.1.2. Figures were added for this analysis	Analysis of humoral outcomes using Meso Scale Discovery assays was added as this had not previously been specified in the SAP	22/01/2024
		6.1.1.2 and 6.3.1.2. Figures were amended for this analysis	Changes were made to the analysis of neutralisation assays from % neutralisation to IC50.	22/01/2024
		Figures	Many of the figures were combined into one figure or panel of figures to show the results overall and for each cohort	22/01/2024
		Tables	Table 12 was combined into one table to show the results overall and for each cohort	22/01/2024

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		Section 6.5.3	Additional exploratory analyses to be performed in Ellie Barnes Oxford lab were added	22/01/2024

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Short title:	ISAP / SAP Template

1. INTRODUCTION

This statistical analysis plan provides guidelines for the final presentation and analysis for the RAPID-PROTECTION trial. This plan, along with all other documents relating to the analysis of this trial, will be stored in the Statistical Analysis Master File electronically and/or in hard signed copy formats.

2. BACKGROUND

2.1 RATIONALE AND RESEARCH QUESTION

This is an adaptive trial to assess the safety and immunogenicity of the AZD7442 and SARS-CoV-2 vaccines in patients that are highly immunocompromised against SARS-CoV-2 infection. Adaptation will occur to drive continued recruitment in particular sub-cohorts to distinguish between the patients who benefit from AZD7442 and those who do not. Improvement in immune responses seen 28 days after administration of AZD7442 will be compared to healthy volunteers in other trials such as the PROVENT clinical trial, and other trials of AZD7442 and SARS-CoV-2 vaccines. Where there is increased variability in the response than the healthy population, analysis will be divided into cohorts to plan extending recruitment.

All participants who consent will be randomised to receive one of the UK approved vaccines currently in deployment to assess the impact of the MAB on response to the vaccine.

Hypotheses to be tested

1) That treatment with AZD7442 in combination with a SARS-CoV-2 vaccine is safe and well tolerated,
2) That vaccination with a SARS-CoV-2 vaccine does not reduce AZD7442 titres in humans and
3) That AZD7442 in combination with a SARS-CoV-2 vaccine enhances immune responses to SARS-CoV-2.

Short title:	ISAP / SAP Template

2.2 OBJECTIVES

The following table lists the objectives of the study.

	Objectives
Co-Primary	To assess the pharmacokinetics of AZD7442 administered as a single dose of 300 mg IM in immunosuppressed patients
	To assess the safety and tolerability of a single IM dose of AZD7442, followed by SARS-CoV2 vaccine booster 28 days later with reference to serious adverse events (SAEs) in highly vulnerable patients.
	To assess the SARS-CoV-2 specific humoral and cellular immune response against SARS-CoV-2 variants when a SARS-CoV-2 vaccine is administered 28 days after AZD7442 in patients who are immune suppressed.
	To assess the effect of a SARS-CoV-2 vaccine on AZD7442 monoclonal antibody titres.
	To assess neutralizing antibodies to SARS-CoV-2 using validated wild-type neutralization assay or pseudo-neutralization assays over time
Secondary	The incidence of participants who have a post-treatment response (negative/low at baseline to positive at any time post-baseline) for SARS-CoV-2 nucleocapsid antibodies.
	The incidence of SARS-CoV-2 infection in trial participants.
	Sequencing of confirmed SARS-CoV2 infections to identify SARS-CoV2 variant and potential AZD7442 escape variants.
	To assess the behaviour of the trial participants before and after trial treatment and vaccination.
	To assess if different SARS-CoV-2 vaccines will preferentially enhance humoral and/or T cell responses in immune suppressed patients receiving AZD7442
	To assess the severity of SARS-CoV-2 infection contracting COVID within the duration of the trial.
Exploratory	To investigate the mechanism of immunogenicity across disorder/disease treatment across the cohorts.
	To identify markers that predict loss/maintenance of AZD7422 titres, response to SARS-CoV-2 vaccines, and adverse events across the cohort.

3. STUDY MATERIALS

3.1 TRIAL DESIGN

The trial is a multicentre, open-label, phase II trial with a randomised comparison of vaccine booster type at 28 days following AZD7442 treatment. Up to 350 patients will be recruited and treated at NHS sites including those already participating in the studies of candidate SARS-COV-2 vaccines and other interested sites in the UK. Participants will be recruited from groups known to be highly vulnerable to SARS-CoV-2 and therefore likely to benefit from AZD7442 as defined by those recommended as high priority for a third vaccine doses by the Joint Committee on Vaccination and Immunisation (JCVi). Patients will be stratified by cohort into 4 groups: Haematological malignancies, Solid tumours, Renal and Hepatic disorders and inflammatory disorders.

All participants will receive AZD7442 treatment followed by vaccination with SARS-CoV2 vaccine booster 28 days later. Immunogenic response will be measured at baseline, throughout treatment and at follow up. The design of the prospective cohort will be initially observational with all participants receiving AZD7442 treatment followed by randomisation to a vaccination with SARS-CoV2 vaccine booster. The cohorts will be sub divided into sub cohorts for comparison to healthy volunteers. The study schema is shown in Figure A below.

Participants will be subdivided into 4 cohorts (see figure A); up to 120 of these patients enrolled at Oxford University Hospitals NHS site will have additional translational bloods for the additional immunological studies described within the protocol. The Oxford site will decide in conduction with the trial management team on which patients from each cohort at the Oxford site will have standard study bloods or translational bloods tests.

Where subjects have conditions that allow entry into more than one cohort of the study then the subject will be allocated into the cohort for the condition that they have had the longest, should that cohort be full, then the subject will be allowed to enter the other cohort for their other condition.

Short title:	ISAP / SAP Template

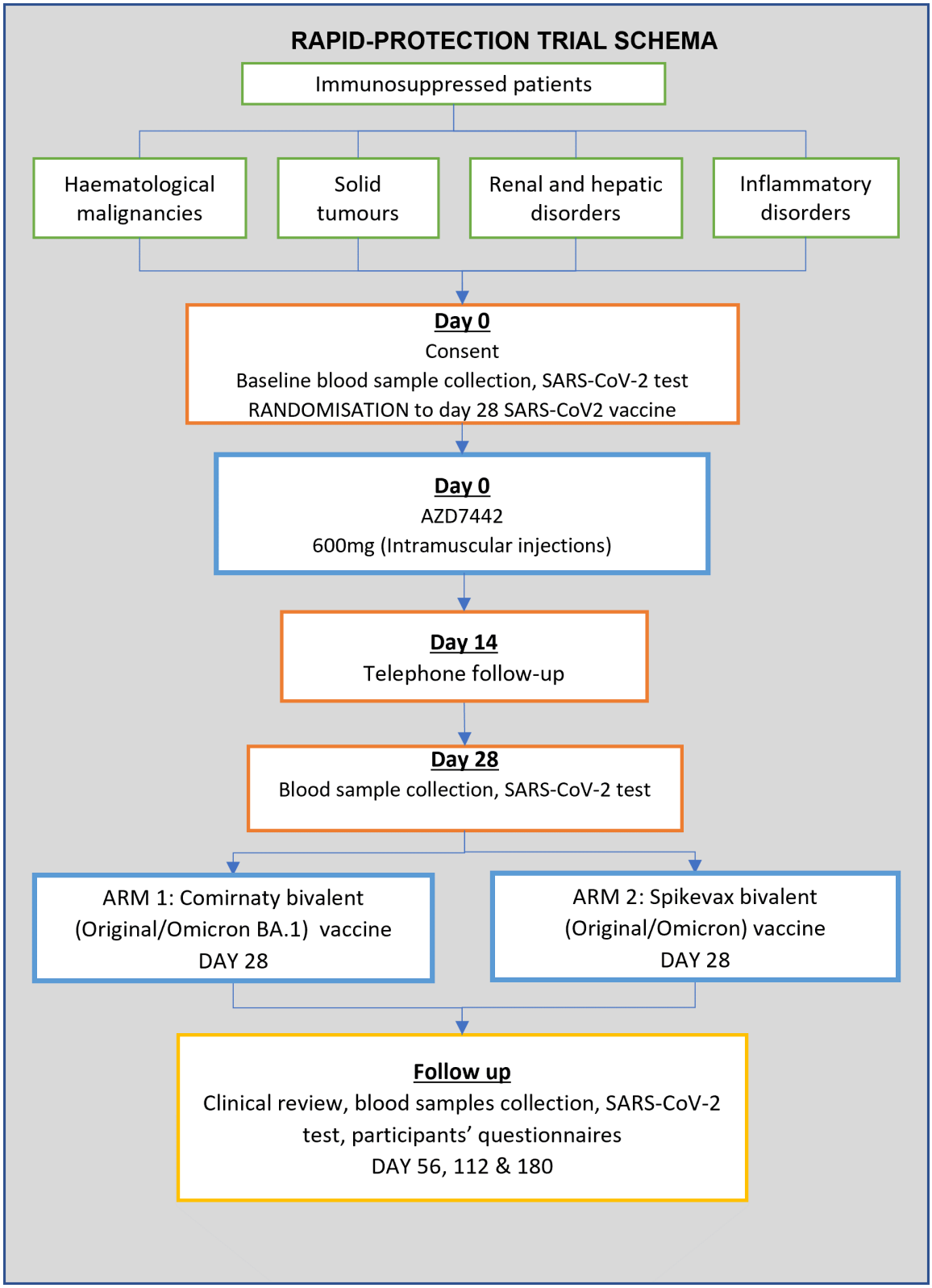
RAPID-PROTECTION TRIAL SCHEMA
Immunosuppressed patients
Haematological malignancies
Solid tumours
Renal and hepatic disorders
Inflammatory disorders
Day 0
Consent
Baseline blood sample collection, SARS-CoV-2 test
RANDOMISATION to day 28 SARS-CoV2 vaccine
Day 0
AZD7442
600mg (Intramuscular injections)
Day 14
Telephone follow-up
Day 28
Blood sample collection, SARS-CoV-2 test
ARM 1: Comirnaty bivalent (Original/Omicron BA.1) vaccine DAY 28
ARM 2: Spikevax bivalent (Original/Omicron) vaccine DAY 28
Follow up
Clinical review, blood samples collection, SARS-CoV-2 test, participants' questionnaires
DAY 56, 112 & 180

Figure A: Study schema

Description of Study Cohorts

1. Haematological malignancies (anticipated 70 participants)

Patients with haematological malignancies and haemopoietic stem cell transplantation will be subdivided into patients receiving active therapy with immunosuppressive or immunomodulating agents and patients receiving aggressive therapy expected to cause temporary ablation of immune.

2. Solid tumours (anticipated 70 participants)

The cancer cohorts will be subdivided into the following sub cohorts for comparison to healthy volunteers:

- Early cancer on systemic treatment
- Advanced cancer on systemic treatment

3. Renal and Hepatic disorders (anticipated 70 participants)

Patients with renal and hepatic disorders will be divided into those receiving immunosuppression as part of their treatment, patients with advanced disease for example kidney disease on dialysis, or liver cirrhosis and liver and renal transplantation.

4. Inflammatory disorders (anticipated 70 participants)

Patients' inflammatory disorders will be divided into those receiving rituximab or not and those receiving other forms of immunosuppressants.

Each treatment group will then be compared to age-matched healthy volunteers from the mid-2021 phase 1 and 3 trials of AZD7442 and SARS-CoV2 vaccine booster for both point estimator and variance, and across all patient cohorts.

This was originally an adaptive trial that would extend recruitment in any sub-cohort where more information is required in order to come to a reliable estimator. The immunological assessments would be analysed to allow cohorts to be expanded in case of poor immunogenicity to SARS-COV-2 or closed if good immunogenicity against SARS-COV-2 is seen. Recruitment of patients from each group was limited to ensure the trial captured a representative group of patients from all major immunosuppressive groups most at risk of SARS-CoV-2 mortality. The group sizes were calculated based on the expected heterogeneity of the group and the degree of variability in the general population.

This may have included subdividing groups by disease type to gain more homogenous responses. The anticipated 70 participants per cohort was based on expected attrition. Allowing for an assumed attrition rate of 20% recruitment of 350 participants was anticipated to take 3 months. However, the trial was suspended early, in April 2024, since the percentage of circulating Evusheld resistant SARS-CoV-2 variants had exceeded a pre-specified 90 % threshold. 148 participants had been entered before the trial was suspended.

3.2 RANDOMISATION

Once participants are identified, consented, and deemed eligible, they will be assigned a unique trial ID and randomised by the treating team via the same portal. Participants will be randomised to receive one of two boosters in a 1:1 ratio:

- Arm 1: Comirnaty bivalent (Original/Omicron BA.1)
- Arm 2: Spikevax bivalent (Original/Omicron)

For reporting, Comirnaty bivalent (Original/Omicron BA.1) vaccine will be abbreviated to Comirnaty; and Spikevax bivalent (Original/Omicron) will be abbreviated to Spikevax.

Randomisation will be performed using random permuted blocks of sizes 2, 4 and 6 which will be chosen at random to aid in allocation concealment. The randomisation will be automated using the TMS2 system with a manual randomisation list if there are technical issues with the automated process.

3.3 SAMPLE SIZE

We aim to recruit a total of 350 patients with immunosuppressive conditions. Samples sizes required for analysis of the various cohorts and outcomes have been based on SARS-COVID-2 Ig responses taken from the analysis of the PROVENT trial and other similar trials.

To compare Cohorts 1 + 2 + 3 + 4 with healthy volunteers to show a reduction in Ig levels at 90% power with a 5% significance of 0.5 (log domain) and SD of 1 we need 70 patients. We expect this consideration to show that the variance in Ig levels is larger than healthy volunteers and have therefore powered to allow for the same comparison in each of the four cohorts (1, 2, 3, 4) – 70 per cohort to give a total of 280 required. Allowing for loss to follow-up of 20% we will aim to recruit 350 patients stratified across the selected cohorts. To maximise heterogeneity at the cohort level and improve branching decisions, we will target even recruitment numbers in the sub-cohorts of each cohort (level 3 in figure B below). We

originally planned to analyse the identified cohorts 1+2+3+4 once 280 completed datasets at 28 days have been achieved. If the variance in Ig levels had been shown to be significantly different to age and gender matched controls or more variable, then the analysis would progress to cohorts 1+2+3+4 individually and recruitment targets re-estimated. This analysis will no longer take place.

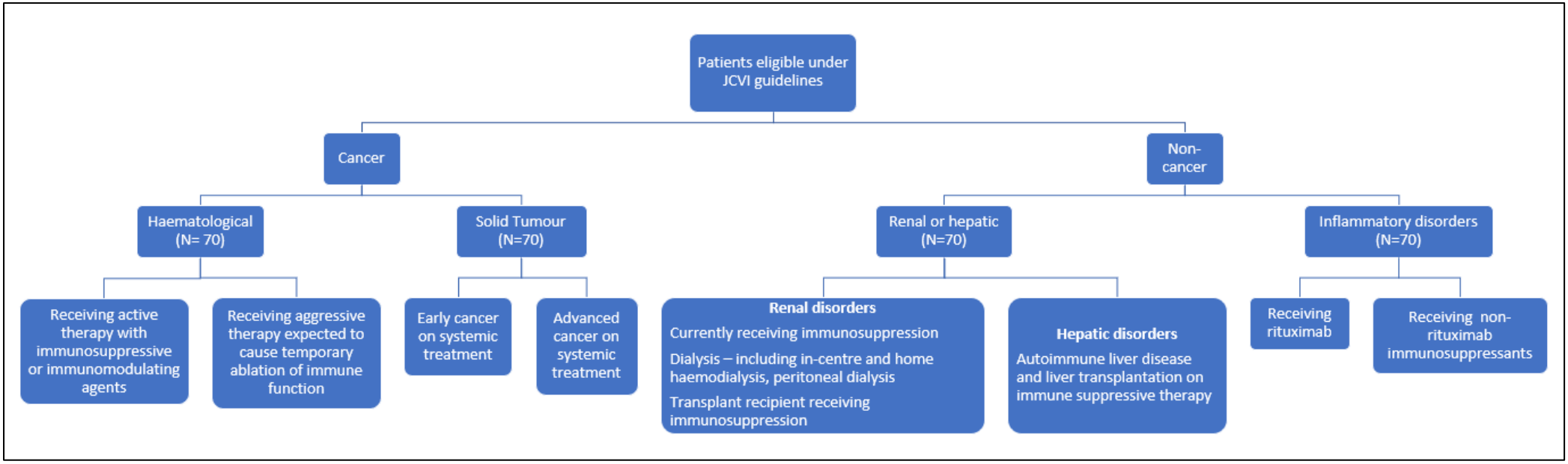

Figure B: Cohorts and further sub-grouping of immunocompromised participants

3.4 FRAMEWORK

The RAPID-PROTECTION trial is an adaptive observational single arm study of the attributes of the AZD7442 monoclonal antibody in specified immunocompromised patients. The adaptive nature of the study was a planned analysis to identify potential recruitment enrichment candidate patient cohorts (see section 3.5.1). Embedded in the observational study is a randomised study of two SARS-CoV-2 vaccines. In general, a treatment policy approach to estimands will be used to deal with intercurrent events.

3.5 INTERIM ANALYSES

The data will first be reviewed by the IDMC when one-third of patients (116) have been recruited and data at 28 days post AZD7442 administration has been returned. This will consist of recruitment, data collection and safety data. Subsequent meetings will be held at the end of recruitment and if a potential adaptation to extend recruitment in any sub-cohort where more information is required in order to come to a reliable estimator.

3.5.1 PLANNED SAMPLE SIZE ADJUSTMENT

This is an adaptive trial originally with a planned sample size enrichment. Analysis of the identified cohorts 1+2+3+4 would be undertaken once 280 completed datasets at 28 days have been achieved. The outcome measure will be the concentration of anti-SARS-CoV-2 anti-S total Ig (U/ml) at day 28 post immunisation with AZD7442. The concentrations will be transformed using a log base 10 transformation. For each patient the concentration at baseline will also be log transformed.

The ratio of the variances in the log transformed domain would be tested to assess if it is significantly different from 1. All tests would be be one sided and focussed on if the trial patients perform less well than the healthy volunteers in terms of response to vaccine. Results would be reported as the ratio of variances, 95% confidence intervals and p values. If the hypothesis test of the ratio of variances is not statistically significant at the 5% level, then no further enrichment would be undertaken as this would indicate insufficient evidence to reject the null hypothesis of no difference in variances amongst the cohorts.

If the hypothesis test was significant at the 5% level those cohorts would be identified as candidates for enrichment. A further division into sub-cohorts would occur and recruitment targets re-estimated to allow more detailed investigation. A separate statistical analysis plan would be produced for this.

3.5.2 STOPPING RULES

There are no formal statistical stopping rules for termination of the trial. The IDMC will assess safety and efficacy data on an ongoing basis and will report to the TSC any concerns that would merit investigating the potential termination of the trial.

3.6 TIMING OF FINAL ANALYSIS

Final analysis will take place once all participants have had 6 months of follow up, completely withdrawn or died.

3.7 TIMING OF OUTCOME ASSESSMENT

Outcome assessments will be collected at fixed time points through the study. Table A shows the timing of the outcome assessments.

Short title:	ISAP / SAP Template

Table A: Schedule of assessments

Procedures	**Visits**						
	Baseline†	**Treatment Phase**			**Follow Up**		
		Day 0	Day 14	Day 28	Day 56	Day 112	Day 180
Informed consent	x						
Medical history	x						
Clinical review				x	x		
Inclusion/Exclusion criteria	x						
Physical examination		x					
Vital signs (including height and weight)		x		x	x		
Concomitant Medications Review	x			x	x	x	x
Toxicity assessment		x	x***	x	x		
Urine pregnancy test	x						
Blood sample collection		x*		x	x	x	x
Safety blood sample (FBC, LFT, bone profile and U&E)		x*		x	x		x

AZD7442 administration		x					
SARS-CoV-2 vaccine administration				x			
Routine (asymptomatic) lateral flow testing for SARS-CoV-2 infection**		x		x	x	x	x
COVID-19 infection severity (where applicable)			x	x	x	x	x
Participant questionnaires (risk behaviour changes, PROMIS 10, EQ-5D-5L)	x					x	x

† Within 28 days prior to AZD7442 administration

* Sample collected prior to AZD7442

** Lateral flow testing for SARS-CoV-2 infection to be performed for sub-set of participants. If the lateral flow test is positive for SARS-CoV-2, a nasal PCR swab will be taken to be sent for testing.

*** Toxicity assessment can be done via telephone call with the participant

4. STATISTICAL PRINCIPLES

4.1 LEVELS OF CONFIDENCE AND P-VALUES

Results will be presented as point estimates and two-sided 95% confidence intervals. P values will be two sided.

4.2 ADJUSTMENT FOR MULTIPLICITY

There is no adjustment for multiplicity.

4.3 ADHERENCE AND PROTOCOL DEVIATIONS

4.3.1 DEFINITION AND ASSESSSMENT OF ADHERENCE

The study intervention is a single dose of AZD7442 followed by a SARS-CoV-2 vaccination at 28 days. Adherence up to 28 days is defined as having received a single dose of AZD7442. Adherence after 28 days is defined as a patient having received both of those interventions. Partial adherence can only be defined as a patient who has been in the study longer than 28 days not having a vaccination at 28 days after receiving the initial treatment of AZD7442. A sub-group of partial adherence will be those who have the vaccine late (after day 28).

4.3.2 PRESENTATION OF ADHERENCE

6 will report the number of patients and the proportion fully and partially adhering. Any protocol deviations, e.g., receiving a different vaccine than the one randomised, will also be shown.

4.3.3 DEFINITION OF PROTOCOL DEVIATION

A protocol deviation is defined as a failure to adhere to the protocol. A protocol deviation should be defined as major or minor, and their impact will be assessed on patient safety, rights and welfare as well as on data integrity. A deviation may be considered a serious breach if it affects efficacy, the safety, physical or mental integrity of the participants in the trial, or

the scientific value of the trial. For this study protocol deviations will be defined as deviations from the treatment schedule as per the protocol.

4.3.4 PRESENTATION OF PROTOCOL DEVIATIONS

A line listing of protocol deviations likely to affect data integrity will be presented inTable 6.

4.4 ANALYSIS POPULATION

The analysis population will consist of all patients who are registered and enter the study (intention to treat (ITT) population). The safety population will consist of all patients who are registered and enter the study and have the single dose of AZD7442. The analysis population for the examination of the effects of the different SARS-CoV-2 vaccines will be the ITT population. The per protocol population will be those patients who have the single dose of AZD7442 followed by their randomised SARS-CoV-2 vaccine at day 28.

5. STUDY POPULATION

5.1 SCREENING DATA

A screening log of all ineligible and eligible but not consented will be kept at each site so that any biases from differential recruitment will be detected. Separate screening logs will be used for each cohort at each site.

5.2 ELIGIBILITY

Eligibility will be confirmed as part of the necessary enrolment and randomisation process at each timepoint. Participating centres should take every care to ensure the required information is accurate and to hand. A full description of the inclusion and exclusion criteria is given in the protocol, section 8.

5.3 RECRUITMENT

Recruitment figures will be presented as the number of patients recruited in each of the study cohorts and sub-cohorts. Recruitment will also be presented by randomised vaccine group. These will be shown in the baseline summary tables (Table 1, Table 2, Table 3, Table 4,

Baseline characteristic	Inflammatory disorders		
	4A (n=)	4B (n=)	Overall (n=)
Age (median (IQR; range; n)			
Gender (n (%))			
Male			
Female			
WHO Performance status (n (%))			

Baseline characteristic	Inflammatory disorders		
	4A (n=)	4B (n=)	Overall (n=)
0			
1			
2			
3			
4			
Household composition (living continuously in the household in the past month)(median (IQR;n)			
Total number of household members			
Household members who….			
Attended school/college in person or outside the home			
Attended childcare/nursery in person or worked outside of home			
Work in health and social care e.g. nurse, doctor, healthcare assistant, social worker			
Number of previous COVID vaccinations			
0			
1			
2			
3			
4			
Previous COVID infection (n (%))			
Yes			
No			
If yes, severity			
Asymptomatic			
Symptomatic - Not hospitalised for COVID-19			
Hospitalised for COVID-19 with no Oxygen			
Hospitalised for COVID-19 with Oxygen			
ITU for COVID-19			
Full blood count (median (IQR; range; n))			
White blood cells ($x10^9$/L)			
Lymphocytes ($x10^9$/L)			
Absolute neutrophil count ($x10^9$/L)			

Baseline characteristic	Inflammatory disorders		
	4A (n=)	4B (n=)	Overall (n=)
Platelets (x10^9/L)			
Haemoglobin (g/L)			
Eosinophils (x10^9/L)			
Basophils (x10^9/L)			
Monocytes (x10^9/L)			
Liver function tests			
INR			
APTT ratio			
Albumin (g/L)			
Serum bilirubin (µmol/L)			
AST (IU/L)			
ALT (IU/L)			
ALP (IU/L)			
Urea and electrolytes			
Sodium			
Potassium (mmol/L)			
Urea (mmol/L)			
Serum creatinine (µmol/L)			
Calculated GFR (ml/min)			
Bone profile			
Albumin (g/L)			
Alkaline phosphatase (g/L)			
Total protein (g/L)			
Calcium (mmol/L)			
INFLAMMATORY DISORDERS			
Receiving T-cell co-stimulation modulators, B-cell targeted therapies (including rituximab), tumour necrosis factor inhibitors (TNFi), soluble TNF receptors, interleukin (IL)-6 receptor inhibitors, IL-17 inhibitors, IL 12/23 inhibitors, IL 23 inhibitors or JAK inhibitors (n(%))			
Yes			
No			

Baseline characteristic	Inflammatory disorders		
	4A (n=)	4B (n=)	Overall (n=)
Received any immunotherapies listed above in the previous 3 months for autoimmune diseases, except in the case of rituximab treatment within the previous 6-month period.			
Yes			
No			
Receiving or had received in the previous 6 months immunosuppressive chemotherapy.			
Yes			
No			
Receiving systemic immunosuppression for a chronic inflammatory disorders.			
Yes			
No			
Rituxumab status (n (%))			
Receiving rituxumab			
Receiving non-rituximab immunosuppressants			
Treatment (n (%))			
T-cell co-stimulation modulators			
B-cell targeted therapies			
Tumour necrosis factor inhibitors (TNFi			
Belimumab			
Interleukin (IL)-6 receptor inhibitors			
IL-17 inhibitors			
IL 12/23 inhibitors			
IL 23 inhibitors			
JAK inhibitors			
Concomitant medication (n (%))			
Mycophenolate mofetil			
Methotrexate			
Disease type (n (%))			
Inflammatory Bowel Disease			
Inflammatory rheumatic diseases			
If primary inflammatory bowel disease (IBD), disease type (n (%))			
Ulcerative Colitis			

Baseline characteristic	Inflammatory disorders		
	4A (n=)	4B (n=)	Overall (n=)
Crohn's disease			
IBD Unclassified			
Not Known			
If Ulcerative Colitis, Primary sclerosing cholangitis (PSC)? (n (%))			
Yes			
No			
If inflammatory rheumatic diseases, Condition (n (%))			
ANCA-associated vasculitis (AAV)			
Axial Spondyloarthritis (axSpA)			
Psoriatic arthritis (PsA)			
Rheumatoid arthritis (RA)			
Systemic lupus erythematosus (SLE)			
SeroNegative Inflammatory Arthritis			
Generic disease activity assessment numerical rating scale (mean/median, SD/IQR)			
Physician-reported			
Patient-reported			
SEROLOGICAL STATUS			
Cyclic Citrullinated Peptide (CCP) (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Rheumatoid factor (RF) (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Myeloperoxidase (MPO) (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Proteinase 3 (PR3) (n (%))			
Negative			

Baseline characteristic	Inflammatory disorders		
	4A (n=)	4B (n=)	Overall (n=)
Positive			
Not known			
Not applicable			
Anti-nuclear antibody (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Anti-double stranded DNA antibody (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Anti-extractable nuclear antigen antibody (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Erythrocyte sedimentation rate at baseline (ESR) (mm/hr) (mean/median, SD/IQR)			

Inflammatory disorders
4A=Receiving rituximab
4B=Receiving non-rituximab immunosuppressants

Table 5).

In addition, CONSORT flow diagrams (Figure 1, Figure 2, Figure 3, Figure 4) will be used to summarise the number of patients who were:

1. Registered or randomised by cohort and vaccine allocation.
2. Received the treatment as per protocol.
3. Did not receive the treatment as per protocol with reasons provided.
4. Withdrawn completely with reasons provided
5. Included in the primary endpoint analysis (ITT population).
6. Included in the PP population.

5.4 WITHDRAWAL/FOLLOW UP

Patients remain free not to complete study treatment at any time without giving reasons and without prejudicing any further treatment. All patients who come off protocol therapy, for whatever reason, will remain within the study for the purposes of follow-up and data analysis. If a patient withdraws consent originally given; this means that they no longer wish to be involved in the trial. In this case the patient will not be followed up.

5.4.1 LEVEL OF WITHDRAWAL

Note that as patients may withdraw from several of the below options, the total numbers may be greater than number of withdrawals. The level of consent or treatment withdrawal will be tabulated and will be classified as:

1. Withdrawal from AZD7442
2. Withdrawal from booster
3. Withdrawal from further trial assessments
4. Withdrawal from future research using excess participant samples.
5. Withdrawal from future research using data.
6. Withdraw trial data collected up to the date of withdrawal
7. Destroy trial samples collected up to the date of withdrawal

5.4.2 TIMING OF WITHDRAWAL

Withdrawn patient numbers and reasons for withdrawals will be shown at days 28, 56 and 180 after study entry (Table 7,

Table 8 and

	Cohort/sub-cohort							
	1		2		3		4	
	1A	1B	2A	2B	3A	3B	4A	4B
Level of withdrawal (n (%))								
Withdrawal from AZD7442								
Withdrawal from booster								
Withdrawal from further trial assessments Data and samples collected from trial visits that have taken place up until the withdrawal date can still be sent but participant will not attend any further visits.								
Withdrawal from future research using excess participant samples.								
Withdrawal from future research using data. Participants have the option to remove their consent to sharing of their de-identified data outside of the trial for future research.								
Withdraw trial data collected up to the date of withdrawal								
Destroy trial samples collected up to the date of withdrawal								
Reason for withdrawal (n (%))								
Intolerance to medication								
Withdrawal of consent for treatment by participant								
Non-compliance								
Any alteration in the participants condition which justifies the discontinuation of the treatment in the Investigator's opinion								
Other (specify)								

Table 9).

5.4.3 REASONS FOR WITHDRAWAL

The numbers (with reasons) of withdrawal by cohort at each of the specified time points above will be summarised in a table format and will include the following reasons:

1. Intolerance to trial medication
2. Withdrawal of consent for treatment by participant
3. Non-compliance
4. Any alteration in the participants condition which justifies the discontinuation of the treatment in the Investigator's opinion
5. Other (specified)

5.4.4 PRESENTATION OF WITHDRAWAL/LOSS TO FOLLOW-UP

Patient withdrawals from the trial (by level of withdrawal) and reasons for withdrawal by cohort and sub-cohort will be presented in Table 7,

Table 8 and

	Cohort/sub-cohort							
	1		2		3		4	
	1A	1B	2A	2B	3A	3B	4A	4B
Level of withdrawal (n (%))								
Withdrawal from AZD7442								
Withdrawal from booster								
Withdrawal from further trial assessments Data and samples collected from trial visits that have taken place up until the withdrawal date can still be sent but participant will not attend any further visits.								
Withdrawal from future research using excess participant samples.								
Withdrawal from future research using data. Participants have the option to remove their consent to sharing of their de-identified data outside of the trial for future research.								
Withdraw trial data collected up to the date of withdrawal								
Destroy trial samples collected up to the date of withdrawal								
Reason for withdrawal (n (%))								
Intolerance to medication								
Withdrawal of consent for treatment by participant								
Non-compliance								
Any alteration in the participants condition which justifies the discontinuation of the treatment in the Investigator's opinion								
Other (specify)								

Table 9.

5.5 PRESENTATION OF DEATHS

The numbers and percentages of deaths will be presented by cohort and sub-cohort, including cause of death (

Table 10). This will include death due to COVID infection.

5.6 BASELINE PARTICIPANT CHARACTERISTICS

5.6.1 LIST OF BASELINE DATA

The different study cohorts reflect a heterogeneous group of patients and hence will have a different set of baseline variables captured for presentation. In general, the baseline data will consist of:

- Demographic data common to all cohorts
- Physical examination
- Prior COVID-19 infection history
- Prior COVID-19 vaccination history
- Full blood count
- Liver function test
- Urea and electrolytes
- Bone profile
- Pre-study medical history
- Pre-study concomitant medications
- Household composition from patient questionnaires

The baseline data will be presented for each study cohort and vaccine randomisation group (Table 1, Table 2, Table 3, Table 4, Table 5).

5.6.2 DESCRIPTIVE STATISTICS

Baseline data will be shown separately for each study cohort and by vaccine randomisation group. For the latter, tests of statistical significance will not be undertaken for baseline characteristics; rather the clinical importance of any imbalance will be noted.

Histograms and boxplots will be used to check the distribution and possible outliers for continuous variables. Continuous variables that follow a normal distribution will be summarised using means and standard deviations. Skewed continuous variables will be summarised using medians and inter-quartile ranges. Categorical variables will be summarised using frequencies and percentages.

6. ANALYSIS

6.1 OUTCOME DEFINITIONS

6.1.1.1 Pharmacokinetics (primary outcome)

AZD7442 serum concentrations (µg/mL) will be measured at baseline and days 28 and 180.

6.1.1.2 Humoral and cellular response (primary and secondary outcomes)

Humoral and cellular response will be measured using serology and T-cell assays.

- Serology: the outcome measure will be the anti-SARS-CoV2 anti-S-RBD total Ig antibody concentration measured at baseline and days 28, 56, 112, and 180 post treatment with AZD7442. The concentrations are assessed using the Roche assay and measured as ELISA units per ml. For the Oxford patients, samples will be assayed for IgG concentrations (AU/ml) in response to multiple COVID-19 antigens at baseline and days 28, 56, 112 and 180 (SARS-CoV-2 N, SARS-CoV-2 Spike, SARS-CoV-2 Spike (B.1.1.529; BA.1), SARS-CoV-2 Spike (BA.5), SARS-CoV-2 Spike (BQ.1.1), SARS-CoV-2 Spike (XBB.1), SARS-CoV-2 Spike (XBB.1.5), SARS-CoV-2 Spike (XBB.1.16), SARS-CoV-2 Spike (XBB.1.16.1), SARS-CoV-2 Spike (XBB.2.3))using Meso Scale Discovery assays. For all patients, samples will be assayed for IgG concentrations (AU/ml) in response to different ancestral SARS-COV-2 antigens (SARS-CoV-2 Spike, S1 RBD, S1 NTD, and S1 N and SARS-CoV-1 Spike) at baseline and days 28 and 56 only using Meso Scale Discovery assays.
- T-cells: the outcome measure is the concentration of antigen specific T-cells recognising the SARS-CoV-2 S antigen, specifically the ex vivo IFGn ELISPOT assay. The outcome is measured as spot forming cells per million peripheral blood mononuclear cells (PBMC). These will be measured at baseline and days 28, 56, 112, and 180 post treatment with AZD7442 for the Oxford patients only.

6.1.1.3 Neutralising antibodies to SARS-CoV-2 (primary outcome)

Neutralising antibodies will be measured at baseline, and day 28, day 56, 112 and 180post administration of AZD7442 in the Oxford patients. A specific neutralising antibody assay against three variants of the COVID-19 virus will be used to measure IC50 (IC50 is the reciprocal dilution of serum that neutralises 50% of the virus).

6.1.1.4 Adverse events and serious adverse events (primary outcome)

Adverse events (AEs) and severity (using CTCAE version 5.0) will be assessed at baseline, and days 14, 28 and 56. Serious adverse events (SAEs) will be assessed for severity (using CTCAE

version 5.0), expectedness, seriousness and relationship to each cohort and sub-cohort at baseline.

6.1.1.5 Dynamics of nucleocapsid antibodies over time in patients during the course of the study

The incidence of participants who have a post-treatment increase (negative/low at baseline to positive at any time post-baseline) in SARS-CoV-2 nucleocapsid antibodies (anti-SARS-CoV-2 nucleocapsid total IgG (results provided as cut-off index (COI)). This will be assessed at baseline and days 28, 56, 112 and 180. Infection naïve participants at study entry who become positive during the course of the study. (negative to low/high), and those participants with low nucleocapsid antibodies at study entry that become high, will be presented.

6.1.1.6 Incidence of SARS-CoV-2 infection

Incidence of SARS-CoV-2 infection will be ascertained by lateral flow test and (if positive) PCR swab test. The assessment of SARS-CoV-2 severity will be measured by the WHO Clinical Progression Scale.

6.1.1.7 Genomic Sequencing

For participants who are PCR swab test positive and confirmed SARS-CoV-2 cases, genomic RNA sequencing will be used to identify the SARS-CoV-2 variant.

6.1.1.8 Patient behaviour

Patient behaviour before and after treatment will be measured using a standard questionnaire consisting of the following instruments:

- Household composition (only at baseline)
- COVID-19 Risk Behaviour Changes
- EQ5D-DL quality of life
- PROMIS v1.2

6.2 PRIMARY OUTCOME(S)

Most primary outcome measures are taken directly or derived from bioanalytical assays. These are described in detail in the associated laboratory manual, protocol section 13.1 and section 6.1 above.

The following are considered primary outcomes:

Pharmacokinetics of serum concentrations of AZD7442

Effect of a SARS-CoV-2 vaccination on serum concentration titres of AZD7442

Humoral and cellular response measured by anti-SARS-CoV2 anti-S RBD total Ig, and antigen specific T-cells recognising the SARS-CoV-2 S antigen.

Levels of neutralising antibodies to SARS-CoV-2

Adverse events and serious adverse events

6.2.1 SECONDARY OUTCOMES

The following are secondary outcomes:

- To assess if different SARS-CoV-2 vaccines will preferentially enhance humoral and/or T cell responses in immune suppressed patients receiving AZD7442.
- The incidence of SARS-CoV-2 infection in trial participants
- The severity of SARS-CoV-2 infection in trial participants
- The incidence of participants who have an increase in SARS-CoV-2 nucleocapsid antibodies (from negative/low at baseline to low/high at any time post-baseline).
- Sequencing of confirmed SARS-CoV2 infections to identify SARS-CoV2 variants and potential AZD7442 escape variants.
- To assess the behaviour of the trial participants before and after trial treatment

6.2.2 TIMING, UNITS AND DERIVATION OF PRIMARY AND SECONDARY OUTCOMES

The timing and units of study outcomes are described in section 6.1 above. Derivation of the primary outcomes is described in section 6.1 and the bioanalytical details in the Laboratory manual. Transformations of outcome measures are detailed in the relevant analysis methods described in section 0 below.

6.2.3 ORDER OF TESTING

There is no prespecified order of testing.

6.3 ANALYSIS METHODS

6.3.1 LIST OF METHODS AND PRESENTATION

6.3.1.1 Pharmacokinetics

Serum concentrations and titres of AZD7442 will be calculated at each time point and summarised using descriptive statistics (mean, medium, standard deviation, interquartile range and range) (

Baseline characteristic	Solid tumours		
	2A (n=)	2B (n=)	Overall (n=)
Age (median (IQR; range; n)			
Gender (n (%))			

Baseline characteristic	Solid tumours		
	2A (n=)	2B (n=)	Overall (n=)
Male			
Female			
WHO Performance status (n (%))			
0			
1			
2			
3			
4			
Household composition (living continuously in the household in the past month)(mean/median (SD/IQR;n)			
Total number of household members			
Household members who….			
Attended school/college in person or outside the home			
Attended childcare/nursery in person or worked outside of home			
Work in health and social care e.g. nurse, doctor, healthcare assistant, social worker			
Number of previous COVID vaccinations			
0			
1			
2			
3			
4			
Previous COVID infection (n (%))			
Yes			
No			
If yes, severity			
Asymptomatic			
Symptomatic - Not hospitalised for COVID-19			
Hospitalised for COVID-19 with no Oxygen			
Hospitalised for COVID-19 with Oxygen			
ITU for COVID-19			
Full blood count (mean/median (SD/IQR; range; n))			

Baseline characteristic	Solid tumours		
	2A (n=)	2B (n=)	Overall (n=)
White blood cells (x10^9/L)			
Lymphocytes (x10^9/L)			
Absolute neutrophil count (x10^9/L)			
Platelets (x10^9/L)			
Haemoglobin (g/L)			
Eosinophils (x10^9/L)			
Basophils (x10^9/L)			
Monocytes (x10^9/L)			
Liver function tests			
INR			
APTT ratio			
Albumin (g/L)			
Serum bilirubin (µmol/L)			
AST (IU/L)			
ALT (IU/L)			
ALP (IU/L)			
Urea and electrolytes			
Sodium			
Potassium (mmol/L)			
Urea (mmol/L)			
Serum creatinine (µmol/L)			
Calculated GFR (ml/min)			
Bone profile			
Albumin (g/L)			
Alkaline phosphatase (g/L)			
Total protein (g/L)			
Calcium (mmol/L)			
Cancer type (n (%))			
Breast			
Lung			
Colorectal			
Bladder			
Kidney (Renal Cell and Renal Pelvis)			
Endometrial			
Liver and Intrahepatic Bile Duct			
Melanoma			
Pancreatic			

Baseline characteristic	Solid tumours		
	2A (n=)	2B (n=)	Overall (n=)
Prostate			
Thyroid			
Head and Neck			
Brain cancer and other CNS cancer types			
Ovarian			
Stomach			
Other sites (specify)			
Disease status (n (%))			
First Diagnosed			
Relapsed			
Relapsed refractory disease			
Stage of breast cancer (n (%))			
1			
2			
3			
4			
Not known			
If stage 4 breast cancer, volume of disease (n (%))			
High			
Low			
Not known			
Stage of lung cancer (n (%))			
1			
2			
3A			
3B			
4			
Not known			
Stage of colorectal cancer (n (%))			
1			
2			
3			
4			
Not known			
Stage of bladder cancer (n (%))			
1			
2			

Baseline characteristic	Solid tumours		
	2A (n=)	2B (n=)	Overall (n=)
3			
4			
Not known			
Stage of kidney cancer (n (%))			
1			
2			
3A			
3B			
4			
Not known			
Stage of endometrial cancer (n (%))			
1			
2			
3			
4			
Not known			
Stage of Liver and Intrahepatic Bile Duct cancer (n (%))			
1			
2			
3			
4			
Not known			
Stage of Melanoma (n (%))			
1			
2			
3A			
3B			
4			
Not known			
Stage of pancreatic cancer (n (%))			
1			
2			
3			
4			
Not known			
Stage of prostate cancer (n (%))			
1			

Baseline characteristic	Solid tumours		
	2A (n=)	2B (n=)	Overall (n=)
2			
3			
4			
Not known			
Stage of thyroid cancer (n (%))			
1			
2			
3			
4			
Not known			
Stage of head and neck cancer (n (%))			
1			
2			
3A			
3B			
4			
Not known			
Stage of Brain cancer and other CNS cancer types (n (%))			
1			
2			
3			
4			
Not known			
Stage of ovarian cancer (n (%))			
1			
2			
3			
4			
Not known			
Stage of Stomach Cancer (n (%))			
1			
2			
3A			
3B			
4			
Not known			
Stage of other cancer (n (%))			

Short title:	ISAP / SAP Template

Baseline characteristic	Solid tumours		
	2A (n=)	2B (n=)	Overall (n=)
1			
2			
3			
4			
Not known			
Solid tumour 2A=Early cancer on systemic treatment 2B=Advanced cancer on systemic treatment			

Table 3: Baseline characteristics and medical history of participants in cohort 3 (renal and hepatic disorders), by sub-cohort and overall

Baseline characteristic	Renal and hepatic disorders		
	3A (n=)	3B (n=)	Overall (n=)
Age (median (IQR; range; n)			
Gender (n (%))			
Male			
Female			
WHO Performance status (n (%))			
0			
1			
2			
3			
4			
Household composition (living continuously in the household in the past month)(mean/median (SD/IQR;n)			
Total number of household members			
Household members who….			
Attended school/college in person or outside the home			
Attended childcare/nursery in person or worked outside of home			
Work in health and social care e.g. nurse, doctor, healthcare assistant, social worker			
Number of previous COVID vaccinations			
0			
1			
2			
3			
4			
Previous COVID infection (n (%))			
Yes			
No			
If yes, severity			
Asymptomatic			
Symptomatic - Not hospitalised for COVID-19			
Hospitalised for COVID-19 with no Oxygen			

Baseline characteristic	Renal and hepatic disorders		
	3A (n=)	3B (n=)	Overall (n=)
Hospitalised for COVID-19 with Oxygen			
ITU for COVID-19			
Full blood count (median (IQR; range; n))			
White blood cells (x10^9/L)			
Lymphocytes (x10^9/L)			
Absolute neutrophil count (x10^9/L)			
Platelets (x10^9/L)			
Haemoglobin (g/L)			
Eosinophils (x10^9/L)			
Basophils (x10^9/L)			
Monocytes (x10^9/L)			
Liver function tests			
INR			
APTT ratio			
Albumin (g/L)			
Serum bilirubin (µmol/L)			
AST (IU/L)			
ALT (IU/L)			
ALP (IU/L)			
Urea and electrolytes			
Sodium			
Potassium (mmol/L)			
Urea (mmol/L)			
Serum creatinine (µmol/L)			
Calculated GFR (ml/min)			
Bone profile			
Albumin (g/L)			
Alkaline phosphatase (g/L)			
Total protein (g/L)			
Calcium (mmol/L)			
RENAL DISORDERS			
If renal disorder (n (%))			
Currently receiving immunosuppression			
Dialysis – including in-centre and home haemodialysis, peritoneal dialysis			
Transplant recipient receiving immunosuppression			

Baseline characteristic	Renal and hepatic disorders		
	3A (n=)	3B (n=)	Overall (n=)
Renal diagnosis (n (%))			
Autosomal dominant polycystic kidney disease			
Diabetes			
Glomerulonephritis			
Urological			
Other (specify)			
Not Known			
Current treatment (n (%))			
Currently receiving immunosuppression			
In-centre haemodialysis			
Home haemodialysis			
Peritoneal dialysis			
Transplant recipient			
Has the transplant failed (n (%))			
Yes			
No			
HEPATIC DISORDERS			
Category of liver disease recruited to (n (%))			
Liver Transplant			
Autoimmune Hepatitis on immunosuppression			
Cirrhosis not on immunosuppression			
Type of liver disease (n (%))			
Non-alcoholic fatty liver disease (NAFLD)			
Alcohol-related liver disease (ALD)			
Hepatitis C virus (HCV)			
Hepatitis B virus (HBV)			
Autoimmune hepatitis (AIH)			
IgG4-related disease			
Primary biliary cholangitis (PBC)			
Primary sclerosing cholangitis (PSC)			
Hemochromatosis			
Wilson's disease			
Other (specify)			
Assessment of ascites (n (%))			
Absent			

Baseline characteristic	Renal and hepatic disorders		
	3A (n=)	3B (n=)	Overall (n=)
Mild to Moderate (diuretic responsive)			
Moderate to Severe (diuretic refractory)			
Assessment of encephalopathy (n (%))			
Absent			
Mild to Moderate (grades I-II)			
Moderate to Severe (grades III-IV)			
Cirrhosis (n (%))			
Yes			
No			
If yes, what is the Child Pugh grade?			
A			
B			
C			
Not known			
Has the participant received dialysis at least twice or CVVHD for more than 24 hours in the past week? (n (%))			
Yes			
No			
Is the participant positive for Hepatitis B surface antigen (HBsAg)? (n (%))			
Yes			
No			
Did the participant have detectable hepatitis C virus (HCV) RNA at the time of trial entry? (n (%))			
Yes			
No			
If HCV RNA present, specify HCV genotype (n (%))			
1			
2			
3			
4			
5			
6			
7			
8			

Baseline characteristic	Renal and hepatic disorders		
	3A (n=)	3B (n=)	Overall (n=)
Not Known			
Has the participant had a liver transplant? (n (%))			
Yes			
No			
Indication for the liver transplant (n (%))			
Decompensation cirrhosis			
Hepatocellular carcinoma			
Acute Liver failure			
Other			

Renal and hepatic disorders
3A=Renal disorders (currently receiving immunosuppression; dialysis; transplant recipient receiving immunosuppression)
3B=Hepatic disorders (autoimmune liver disease and liver transplantation on immune suppressive therapy)

Table 4: Baseline characteristics and medical history of participants in cohort 4 (inflammatory disorders), by sub-cohort and overall

Baseline characteristic	Inflammatory disorders		
	4A (n=)	4B (n=)	Overall (n=)
Age (median (IQR; range; n)			
Gender (n (%))			
Male			
Female			
WHO Performance status (n (%))			
0			
1			
2			
3			
4			
Household composition (living continuously in the household in the past month)(median (IQR;n)			
Total number of household members			
Household members who….			
Attended school/college in person or outside the home			
Attended childcare/nursery in person or worked outside of home			
Work in health and social care e.g. nurse, doctor, healthcare assistant, social worker			
Number of previous COVID vaccinations			
0			
1			
2			
3			
4			
Previous COVID infection (n (%))			
Yes			
No			
If yes, severity			
Asymptomatic			
Symptomatic - Not hospitalised for COVID-19			

Baseline characteristic	Inflammatory disorders		
	4A (n=)	4B (n=)	Overall (n=)
Hospitalised for COVID-19 with no Oxygen			
Hospitalised for COVID-19 with Oxygen			
ITU for COVID-19			
Full blood count (median (IQR; range; n))			
White blood cells ($x10^9$/L)			
Lymphocytes ($x10^9$/L)			
Absolute neutrophil count ($x10^9$/L)			
Platelets ($x10^9$/L)			
Haemoglobin (g/L)			
Eosinophils ($x10^9$/L)			
Basophils ($x10^9$/L)			
Monocytes ($x10^9$/L)			
Liver function tests			
INR			
APTT ratio			
Albumin (g/L)			
Serum bilirubin (µmol/L)			
AST (IU/L)			
ALT (IU/L)			
ALP (IU/L)			
Urea and electrolytes			
Sodium			
Potassium (mmol/L)			
Urea (mmol/L)			
Serum creatinine (µmol/L)			
Calculated GFR (ml/min)			
Bone profile			
Albumin (g/L)			
Alkaline phosphatase (g/L)			
Total protein (g/L)			
Calcium (mmol/L)			
INFLAMMATORY DISORDERS			

Baseline characteristic	Inflammatory disorders		
	4A (n=)	4B (n=)	Overall (n=)
Receiving T-cell co-stimulation modulators, B-cell targeted therapies (including rituximab), tumour necrosis factor inhibitors (TNFi), soluble TNF receptors, interleukin (IL)-6 receptor inhibitors, IL-17 inhibitors, IL 12/23 inhibitors, IL 23 inhibitors or JAK inhibitors (n(%))			
Yes			
No			
Received any immunotherapies listed above in the previous 3 months for autoimmune diseases, except in the case of rituximab treatment within the previous 6-month period.			
Yes			
No			
Receiving or had received in the previous 6 months immunosuppressive chemotherapy.			
Yes			
No			
Receiving systemic immunosuppression for a chronic inflammatory disorders.			
Yes			
No			
Rituximab status (n (%))			
Receiving rituximab			
Receiving non-rituximab immunosuppressants			
Treatment (n (%))			
T-cell co-stimulation modulators			
B-cell targeted therapies			
Tumour necrosis factor inhibitors (TNFi			
Belimumab			
Interleukin (IL)-6 receptor inhibitors			
IL-17 inhibitors			
IL 12/23 inhibitors			
IL 23 inhibitors			

Baseline characteristic	Inflammatory disorders		
	4A (n=)	4B (n=)	Overall (n=)
JAK inhibitors			
Concomitant medication (n (%))			
Mycophenolate mofetil			
Methotrexate			
Disease type (n (%))			
Inflammatory Bowel Disease			
Inflammatory rheumatic diseases			
If primary inflammatory bowel disease (IBD), disease type (n (%))			
Ulcerative Colitis			
Crohn's disease			
IBD Unclassified			
Not Known			
If Ulcerative Colitis, Primary sclerosing cholangitis (PSC)? (n (%))			
Yes			
No			
If inflammatory rheumatic diseases, Condition (n (%))			
ANCA-associated vasculitis (AAV)			
Axial Spondyloarthritis (axSpA)			
Psoriatic arthritis (PsA)			
Rheumatoid arthritis (RA)			
Systemic lupus erythematosus (SLE)			
SeroNegative Inflammatory Arthritis			
Generic disease activity assessment numerical rating scale (mean/median, SD/IQR)			
Physician-reported			
Patient-reported			
SEROLOGICAL STATUS			
Cyclic Citrullinated Peptide (CCP) (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Rheumatoid factor (RF) (n (%))			
Negative			

Baseline characteristic	Inflammatory disorders		
	4A (n=)	4B (n=)	Overall (n=)
Positive			
Not known			
Not applicable			
Myeloperoxidase (MPO) (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Proteinase 3 (PR3) (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Anti-nuclear antibody (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Anti-double stranded DNA antibody (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Anti-extractable nuclear antigen antibody (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Erythrocyte sedimentation rate at baseline (ESR) (mm/hr) (mean/median, SD/IQR)			

Inflammatory disorders
4A=Receiving rituximab
4B=Receiving non-rituximab immunosuppressants

Short title:	ISAP / SAP Template

Table 5: Baseline characteristics and medical history of participants by vaccine allocation

Baseline characteristic	Vaccine	
	Comirnaty (n=)	Spikevax (n=)
Age (median (IQR; range; n)		
Gender (n (%))		
Male		
Female		
WHO Performance status (n (%))		
0		
1		
2		
3		
4		
Household composition (living continuously in the household in the past month)(mean/median (SD/IQR;n)		
Total number of household members		
Household members who….		
Attended school/college in person or outside the home		
Attended childcare/nursery in person or worked outside of home		
Work in health and social care e.g. nurse, doctor, healthcare assistant, social worker		
Number of previous COVID vaccinations		
0		
1		
2		
3		
4		
Previous COVID infection (n (%))		
Yes		
No		
If yes, severity		
Asymptomatic		
Symptomatic - Not hospitalised for COVID-19		
Hospitalised for COVID-19 with no Oxygen		

Baseline characteristic	Vaccine	
	Comirnaty (n=)	Spikevax (n=)
Hospitalised for COVID-19 with Oxygen		
ITU for COVID-19		
Full blood count (mean/median (SD/IQR; range; n))		
White blood cells ($x10^9$/L)		
Lymphocytes ($x10^9$/L)		
Absolute neutrophil count ($x10^9$/L)		
Platelets ($x10^9$/L)		
Haemoglobin (g/L)		
Eosinophils ($x10^9$/L)		
Basophils ($x10^9$/L)		
Monocytes ($x10^9$/L)		
Liver function tests		
INR		
APTT ratio		
Albumin (g/L)		
Serum bilirubin (µmol/L)		
AST (IU/L)		
ALT (IU/L)		
ALP (IU/L)		
Urea and electrolytes		
Sodium		
Potassium (mmol/L)		
Urea (mmol/L)		
Serum creatinine (µmol/L)		
Calculated GFR (ml/min)		
Bone profile		
Albumin (g/L)		
Alkaline phosphatase (g/L)		
Total protein (g/L)		
Calcium (mmol/L)		
COHORT		
Haematological malignancies (n (%))		
1A		
1B		
Solid tumours (n (%))		
2A		

Short title:	ISAP / SAP Template

Baseline characteristic	Vaccine	
	Comirnaty (n=)	Spikevax (n=)
2B		
Renal and hepatic disorders (n (%))		
3A		
3B		
Inflammatory disorders (n (%))		
4A		
4B		

Table 6: Treatment adherence by cohort and sub-cohort

	Cohort						
	Haematological malignancies (n=)		Solid tumours (n=)		Renal and hepatic disorders (n=)		Inflamm disorder
	1A (n=)	1B (n=)	2A (n=)	2B (n=)	3A (n=)	3B (n=)	4A (n=)
AZD7442 administration at day 0 (n (%))							
Booster vaccine at day 28 (n (%))							
Full adherence (n (%))*							
Partial adherence (n (%))**							
Partial adherence, had vaccine late (n (%))							
Non-adherence (n (%))							
Received allocated vaccine (n (%))							

* Full adherence is defined as a patient having had both theAZD7442 injection and the booster vaccine at day 28.

** Partial adherence can only be defined as a patient who has been in the study longer than 28 days not having a vaccination at 28 days after receiving the initial treatment of AZD7442. A sub-group of partial adherence is having th vaccine after day 28.

Table 7: Withdrawal levels and reasons by cohort and sub-cohort (day 28)

	Cohort/sub-cohort							
	1		2		3		4	
	1A	1B	2A	2B	3A	3B	4A	4B
Level of withdrawal (n (%))								
Withdrawal from AZD7442								
Withdrawal from booster								
Withdrawal from further trial assessments Data and samples collected from trial visits that have taken place up until the withdrawal date can still be sent but participant will not attend any further visits.								
Withdrawal from future research using excess participant samples.								
Withdrawal from future research using data. Participants have the option to remove their consent to sharing of their de-identified data outside of the trial for future research.								
Withdraw trial data collected up to the date of withdrawal								
Destroy trial samples collected up to the date of withdrawal								
Reason for withdrawal (n (%))								
Intolerance to medication								
Withdrawal of consent for treatment by participant								
Non-compliance								
Any alteration in the participants condition which justifies the discontinuation of the treatment in the Investigator's opinion								
Other (specify)								

Short title:	ISAP / SAP Template

Table 8: Withdrawal levels and reasons by cohort and sub-cohort (day 56)

	Cohort/sub-cohort							
	1		2		3		4	
	1A	1B	2A	2B	3A	3B	4A	4B
Level of withdrawal (n (%))								
Withdrawal from AZD7442								
Withdrawal from booster								
Withdrawal from further trial assessments Data and samples collected from trial visits that have taken place up until the withdrawal date can still be sent but participant will not attend any further visits.								
Withdrawal from future research using excess participant samples.								
Withdrawal from future research using data. Participants have the option to remove their consent to sharing of their de-identified data outside of the trial for future research.								
Withdraw trial data collected up to the date of withdrawal								
Destroy trial samples collected up to the date of withdrawal								
Reason for withdrawal (n (%))								
Intolerance to medication								
Withdrawal of consent for treatment by participant								
Non-compliance								
Any alteration in the participants condition which justifies the discontinuation of the treatment in the Investigator's opinion								
Other (specify)								

Table 9: Withdrawal levels and reasons by cohort and sub-cohort (day 180)

	Cohort/sub-cohort							
	1		2		3		4	
	1A	1B	2A	2B	3A	3B	4A	4B
Level of withdrawal (n (%))								
Withdrawal from AZD7442								
Withdrawal from booster								
Withdrawal from further trial assessments Data and samples collected from trial visits that have taken place up until the withdrawal date can still be sent but participant will not attend any further visits.								
Withdrawal from future research using excess participant samples.								
Withdrawal from future research using data. Participants have the option to remove their consent to sharing of their de-identified data outside of the trial for future research.								
Withdraw trial data collected up to the date of withdrawal								
Destroy trial samples collected up to the date of withdrawal								
Reason for withdrawal (n (%))								
Intolerance to medication								
Withdrawal of consent for treatment by participant								
Non-compliance								
Any alteration in the participants condition which justifies the discontinuation of the treatment in the Investigator's opinion								
Other (specify)								

Short title:	ISAP / SAP Template

Table 10: Deaths and causes of death by cohort and sub-cohort

	Cohort and sub-cohort								
	1		2		3		4		Overa
	1A (n=)	1B (n=)	2A (n=)	2B (n=)	3A (n=)	3B (n=)	4A (n=)	4B (n=)	
Deaths (n (%))									
Cause of death (n (%))									
Covid-19 related									
Disease cohort related									
Other (specify)									
Not known									

Table 11). Means and two-sided 95% confidence intervals will be calculated and plotted over time, overall and for each cohort (Figure 5). PK parameters T_{max} and C_{max} will be calculated and summarised using means and standard deviation (C_{max}) or medians and IQR (T_{max}) (Table 11). Comparisons of Cmax between cohorts will be made using ANCOVA models adjusted for age and gender. Comparison of Cmax for age groups and gender will also be performed. Mann-Whitney U tests will be used to compare Tmax between cohorts, age groups and gender. Exploratory analysis of specific sub-groups of interest (e.g. haemodialysis in cohort 3) will also be performed dependent on numbers in each sub-group.

6.3.1.2 Analysis of immunogenicity outcomes: general considerations

Immunogenicity measurements are i) humoral and cellular response measured by anti-SARS-CoV2 anti-S-RBD total Ig and antigen specific T-cells recognising the SARS-CoV-2 S antigen ii) IgG concentrations (AU/ml) in response to selected COVID-19 antigens at baseline and days 28, 56, 112 and 180, using Meso Scale Discovery assays, and iii) Levels of neutralising antibodies to SARS-CoV-2 (reported as IC50).

Immunogenicity data will be presented as means or medians, and standard deviations or interquartile range/range at each timepoint overall and for each cohort and sub-cohort. Anti-SARS-CoV2 anti-S-RBD total Ig will be presented in Table 12. IgG concentrations (AU/ml) in response to multiple COVID-19 antigens overall and for each cohort and sub-cohort will be presented for Oxford patients in Table 13 and all patients in Table 14. T cell responses for each cohort at each timepoint overall and for each cohort and sub-cohort will be shown in

	All cohorts (all patients)				
	SARS-CoV-2 Spike	SARS-CoV-2 S1 RBD	SARS-CoV-2 S1 NTD	SARS-CoV-2 S1 N	SA 1
Median/mean (IQR/SD; range; n) log-transformed IgG concentration (AU/ml)					
Day 0					
All cohorts					
Cohort 1					
Cohort 2					
Cohort 3					
Cohort 4					
Day 28					
All cohorts					
Cohort 1					
Cohort 2					
Cohort 3					

Cohort 4					
Day 56					
All cohorts					
Cohort 1					
Cohort 2					
Cohort 3					
Cohort 4					

Cohort 1 Haematological malignancies
Cohort 2 Solid tumours
Cohort 3 Renal and hepatic disorders
Cohort 4 Inflammatory disorders

Table 15; neutralising antibodies levels will be presented by cohort and sub-cohort at each timepoint (Table 16). T cell response and neutralising antibodies will be for an estimated 80 selected Oxford patients only.

Data will be shown as dot plots using a logarithmic scale, overall and for each cohort at each timepoint, including means:

- anti-SARS-CoV2 anti-S-RBD total Ig will be shown in Figure 6.
- IgG concentrations (AU/ml) in response to 10 COVID-19 antigens at baseline and days 28, 56, 112 and 180 will be shown in Figure 8.
- IgG concentrations (AU/ml) in response to ancestral SARS-CoV-2 antigens (N, S1 NTD, S1 RBD, Spike) and SARS-CoV-1 Spike at baseline and days 28, and 56 for all patients will be shown in Figure 10
- SARS-CoV-2 S antigen specific T-cells (spot forming cells per million peripheral blood mononuclear cells (PBMC)) will be shown in Figure 12.
- Neutralising antibodies (IC50) against three COVID-19 variants (Figure 14)).

Data will also be shown as a time series with the mean and 95% confidence interval at each time using a logarithmic scale (overall and for each cohort):

- anti-SARS-CoV2 anti-S-RBD total Ig overall and for each cohort will be shown in Figure 7.
- IgG concentrations (AU/ml) in response to multiple COVID-19 antigens at baseline and days 28, 56, 112 and 180 will be shown in Figure 9.
- IgG concentrations (AU/ml) in response to 4 ancestral SARS-CoV-2 antigens (N, S1 NTD, S1 RBD, Spike) and SARS-CoV-1 Spike at baseline and days 28, and 56 for all patients will be shown in Figure 11.
- SARS-CoV-2 S antigen specific T-cells (spot forming cells per million peripheral blood mononuclear cells (PBMC)) will be shown in Figure 13
- Neutralising antibodies (IC50) against three COVID-19 variants will be shown in Figure 15.

6.3.1.3 Comparison of immunogenicity outcomes between the two vaccines (secondary outcome)

Comparisons will be made between each of the vaccines using an ANCOVA model with baseline value as a covariate. Difference in mean outcomes between the two vaccine arms will be presented, with 95% confidence intervals and p-values (Table 17). An exploratory analysis will be conducted to examine differences between the vaccine types and patient cohorts (see section 6.5 below) (Table 42).

6.3.1.4 Adverse events and serious adverse events

The frequency of adverse events (AEs) and severity (using CTCAE version 5.0) will be assessed at baseline, and days 14, 28 and 56 in the safety population. Serious adverse events (SAEs) will be assessed for severity (using CTCAE version 5.0), expectedness, seriousness and relationship to each cohort and sub-cohort at baseline. In addition, all AEs and SAEs will be summarised by toxicity type using the Medical Dictionary for Regulatory Activities (MedDRA) System Organ Class (SOC), preferred term (PT) at baseline (Table 18, Table 19, Table 20, Table 21 and Table 22) and worst reported excluding baseline (Table 23, Table 24Table 24, Table 25, Table 26 and Table 27), for each cohort and over all cohorts up to day 28 and up to day 56 (Table 28, Table 29, Table 30, Table 31 and Table 32

Table 32

When calculating the incidence of AEs, or any sub-classification thereof by cohort, time, severity, etc., each subject will only be counted once, and any repetitions will be ignored with only the maximum severity experienced of each type of AE displayed; the denominator will be the total number of patients with toxicity forms returned. The number percentage and 95% confidence interval of patients experiencing each AE/SAE, categorised by severity will be tabulated. 95% confidence intervals will be calculated using the Clopper-Pearson method as it is likely AEs will be relatively uncommon. No formal statistical testing will be undertaken. Summary statistics will be produced in accordance with Section 5.6.2. A line listing of SAEs will be presented (Table 33) and numbers (percentages) of SAEs, SARs and SUSARs by cohort, sub-cohort and overall (Table 34).

6.3.1.1 Dynamics of nucleocapsid antibodies over time in patients during the course of the study

The incidence of participants who have a post-treatment increase (negative/low at baseline to positive at any time post-baseline) in SARS-CoV-2 nucleocapsid antibodies (anti-SARS-CoV-2 nucleocapsid total IgG) will be shown in Table 35 by cohort, sub-cohort and overall (results provided as cut-off index (COI)). This will be assessed at baseline and days 28, 56, 112 and 180. Infection naïve participants at study entry, who become positive during the course of the study (negative to low/high), and those participants with low nucleocapsid antibodies at study entry that become high, will be presented.

6.3.1.2 Analysis of SARS-CoV-2 infections

Incidence of SARS-CoV-2 infection will be a descriptive analysis and summarised by incidence rates and 95% confidence intervals; this will include data on SARS-CoV-2 strain. This will be performed overall and over specified periods of time up to day 28, day 56, day 84, day 112 day 180. Comparison of incidence rates between cohorts will be performed using Poisson

regression and summarised as Incidence rate ratios, risk differences, 95% confidence intervals and p values (Table 36).

6.3.1.3 Analysis of SARS-CoV-2 severity

Assessment of SARS-CoV-2 severity will be measured by the WHO Clinical Progression Scale, shown below in Table C.

Table C: WHO Clinical Progression Scale

Patient state	Descriptor	Score
Uninfected	Uninfected; no viral RNA detected	0
Ambulatory mild disease	Asymtomatic; viral RNA detected Symptomatic; independent Symptomatic; assistance needed	1 2 3
Hospitalised: moderate disease	Hospitalised; no oxygen therapy Hospitalised; oxygen by mask or nasal prongs	4 5
Hospitalised: severe diseases	Hospitalised; oxygen by NIV or high flow Intubation and mechanical ventilation, pO_2/FIO_2, ≥150 or SpO_2/FIO_2, ≥200 Mechanical ventilation SpO_2/FIO_2, <150 (SpO_2/FIO_2, <200) or vasopressors Mechanical ventilation SpO_2/FIO_2, <150 and vasopressors, dialysis, or ECMO	6 7 8 9
Dead	**Dead**	**10**

The frequency and percentage of patients in each score category will be tabulated overall and in each study cohort (Table 36).

6.3.1.4 Genomic Sequencing

For participants who are lateral flow test/PCR swab test positive and confirmed SARS-CoV-2 cases genomic RNA sequencing will be used to identify the SARS-CoV-2 variant. Results will be reported in Table 36.

6.3.1.5 Analysis of Patient Questionnaires

Household composition at baseline will be summarised using medians and IQR and presented in baseline tables.

Patient COVID-19 risk behaviour questionnaires will be summarised using frequencies and proportions over time (Table 37). PROMIS® Scale v1.2—Global Health will be scored as described in the Scoring Manual[1]. For continuous measures, e.g., EQD visual analogue scale

(VAS) responses will be summarised using means and standard deviations, or medians and interquartile ranges dependent on the distribution of the baseline data. Differences in responses for questions between cohorts will be assessed using the Wilcoxon-Mann-Whitney test. Changes in responses over time will be examined using multilevel models accounting for the longitudinal nature of the data. Results for COVID risk behaviour will be presented in Table 37 and Table 38;EQ5D-5L in Table 39 and Table 40; and PROMIS Global Health in Table 41.

6.3.2 COVARIATE ADJUSTMENT

There will be no covariate adjustment of the primary endpoint analysis as this is based on comparison of group level data.

6.3.3 ASSUMPTION CHECKING

Distributional assumptions of the main analytical methods will be checked using histograms, normal quantile plots and residual plots.

6.3.4 ALTERNATIVE METHODS IF DISTRIBUTIONAL ASSUMPTIONS NOT MET

If the main distributional assumptions of the main analysis are not met, then an appropriate non-parametric analysis will be performed.

6.3.5 SENSITIVITY ANALYSES

Since it is possible that patients entered into the study may be eligible for more than one cohort or sub-cohort we shall conduct a sensitivity analysis of the primary analysis by reassigning these patients to the alternative cohort and examining the impact on the adaptive portion of the study (section **Error! Reference source not found.**) and the impact of the vaccine types (section 6.3.1.3). These analyses will be added to the relevant analysis tables if required.

6.3.6 SUBGROUP ANALYSES

There are no prespecified subgroup analyses.

6.4 MISSING DATA

Missing data patterns will be examined and described for each participant cohort. After examination of the missing data patterns and extent of missing data multiple imputation using full conditional specification (chained equations) may be considered (van Buuren (2018).

In the specific case where bioanalytical assay values are below the level of detection (LOD) or lower level of quantification (LLOQ) then the value will be replaced by 0.5 x LOD or 0.5 x LLOQ.

In the case where values are greater than the upper limit of quantification (ULOQ) then the value will be replaced by the ULOQ.

6.5 ADDITIONAL ANALYSES

EXPLORATORY OUTCOMES

6.5.1 Immunogenicity across disorder/disease treatment across the cohorts

We will examine the Covid-19 vaccine type used as a booster at 28 days post treatment with AZD7442. This will be assessed at day 56, that is 28 days after the booster vaccine is administered. This analysis will examine the differences in immunogenicity outcomes for each vaccine type with each study cohort. This will proceed with a linear regression ANCOVA model of the log 10 transformed humoral or cellular assay including the baseline value in the model. The ANCOVA model will include categorical variables indicating the cohort and vaccine type for that participant. To measure the effect of that cohort and vaccine type an interaction term will be included between the cohort and vaccine types. Results will be presented as cohort and vaccine specific GMRs and 95% two-sided confidence intervals. A likelihood ratio test will be conducted to evaluate the cohort and vaccine type interaction term. The p value from the likelihood ratio test will be reported as the overall test of interaction (Table 42 and Figure 16).

6.5.2 Predictive biomarkers for primary and secondary endpoints

Where sufficient data is available, linear or logistic regression models will be constructed to examine factors associated with immunogenicity response. These factors will be peak IgG response; durability of IgG response; peak T-cell response; durability of T cell response; high, mid and low PK dynamics. In addition, should infections undergo an increase during the study then this may allow an analysis of any link between immunogenicity response and infection; as well as an analysis of the SARS-CoV-2 severity using the WHO Clinical Progression Scale comparing differences in the study cohorts. For this analysis to be feasible we would require approximately 50 confirmed infections and a reduction in the WHO scale to 5 categories. Additional tables will be produced to present this data if this analysis is possible.

6.5.3 Regulation of immune memory responses after monoclonal therapy followed by vaccination

We will examine how passive administration of monoclonal antibodies (AZD7442) might influence development of memory B cells in response to vaccination. We will measure frequency and affinity of antigen (SARS-CoV-2) specific memory B cells via flow cytometry in select patients from the Oxford cohort. Patients will be selected based on the difference in total anti-Spike Ig response between before and after vaccination. Additional tables and

figures will be produced to present this data. This analysis will be performed at the Oxford laboratory under the supervision of Ellie Barnes.

6.6 HARMS

See Section 6.1.1.4

6.7 STATISTICAL SOFTWARE

Analyses will be conducted using Stata statistical software from version 17.

7. REFERENCES

1) PROMIS_Global_Health_Scoring_Manual.pdf (healthmeasures.net) last accessed 23/09/2022

2) Van Buuren, S., 2018. Flexible imputation of missing data. CRC press.

7.1 NON STANDARD STATISTICAL METHODS

7.2 DATA MANAGEMENT PLAN

7.3 TRIAL MASTER FILE AND STATISTICAL MASTER FILE

7.4 OTHER SOPS OR GUIDANCE DOCUMENTS

Short title:	ISAP / SAP Template

SAP/ISAP DEVIATION LOG

Document number:		**Document version:**	
Reason for deviation:			

APPENDIX 1: FIGURES

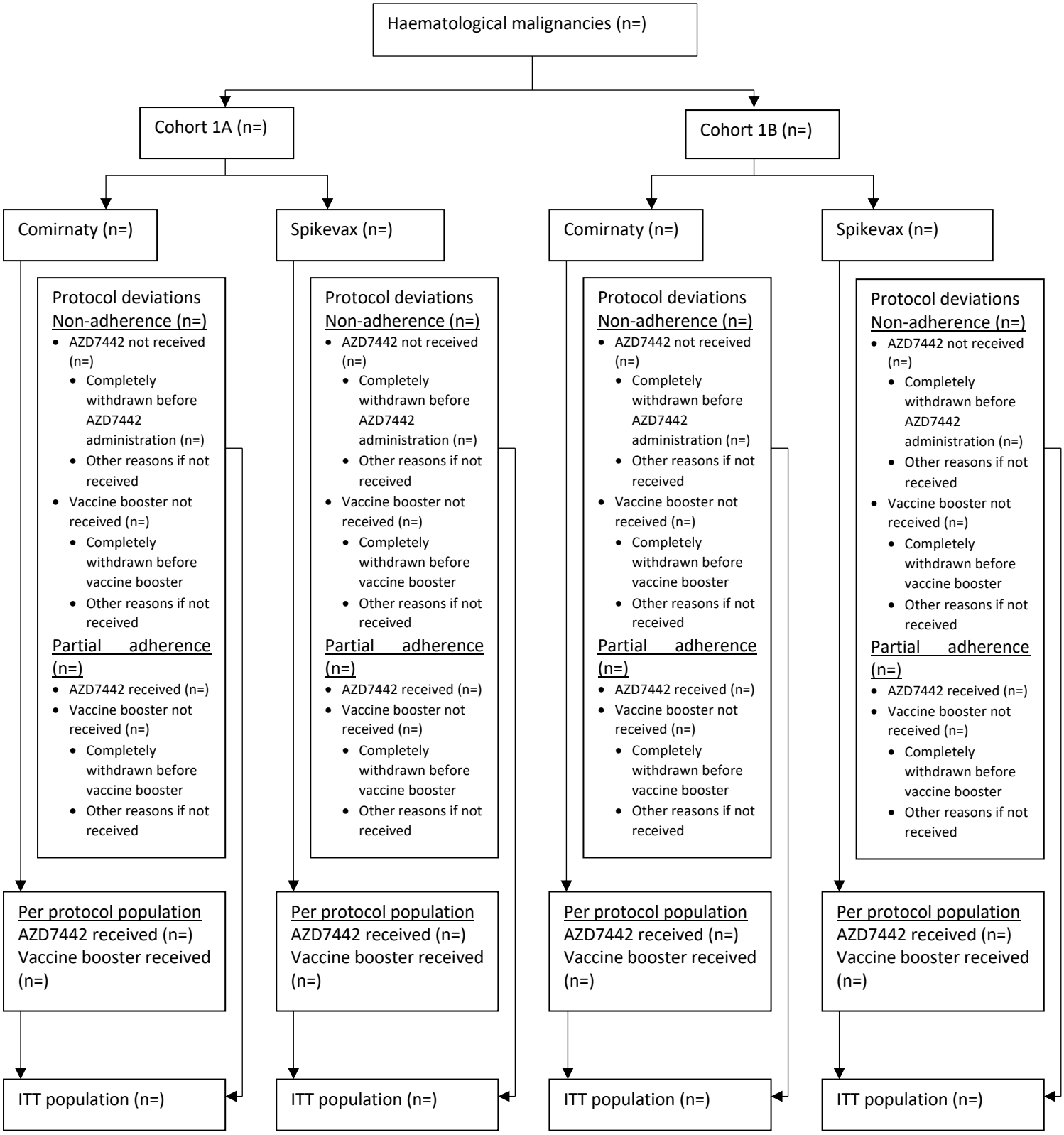

Figure 1: CONSORT flow diagram (haematological malignancies cohort)

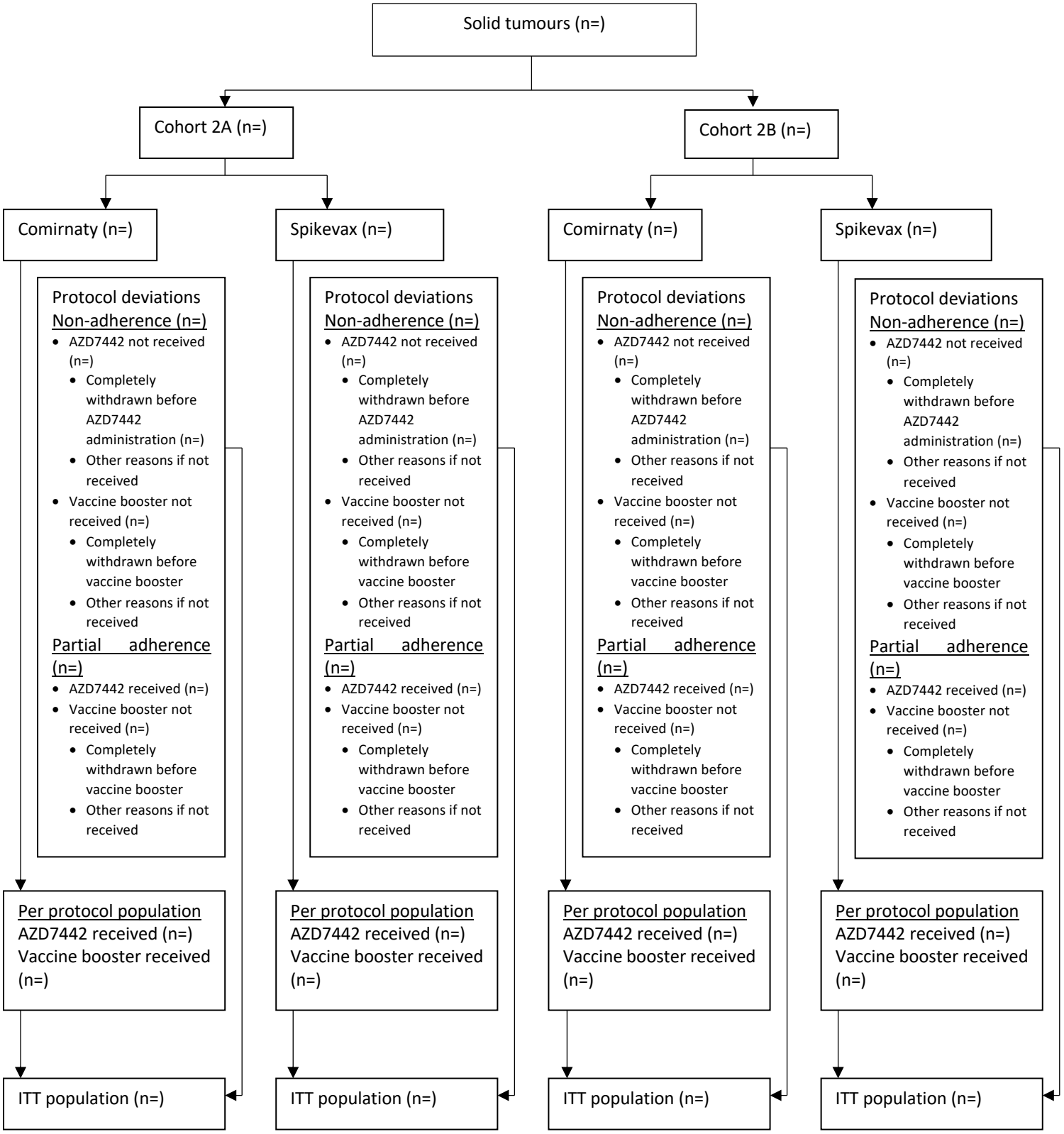

Figure 2: CONSORT flow diagram (solid tumours cohort)

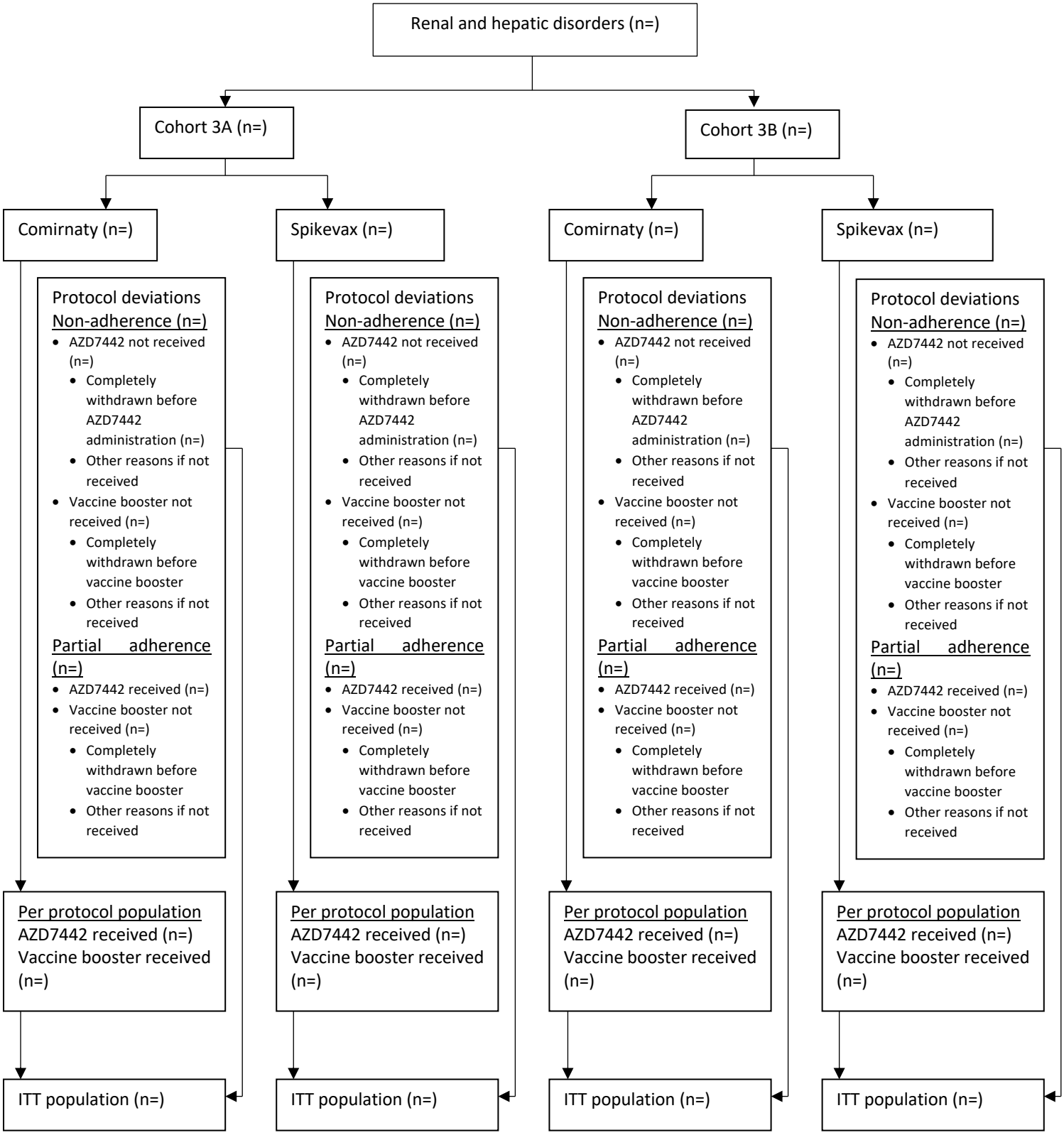

Figure 3: CONSORT flow diagram (renal and hepatic disorders cohort)

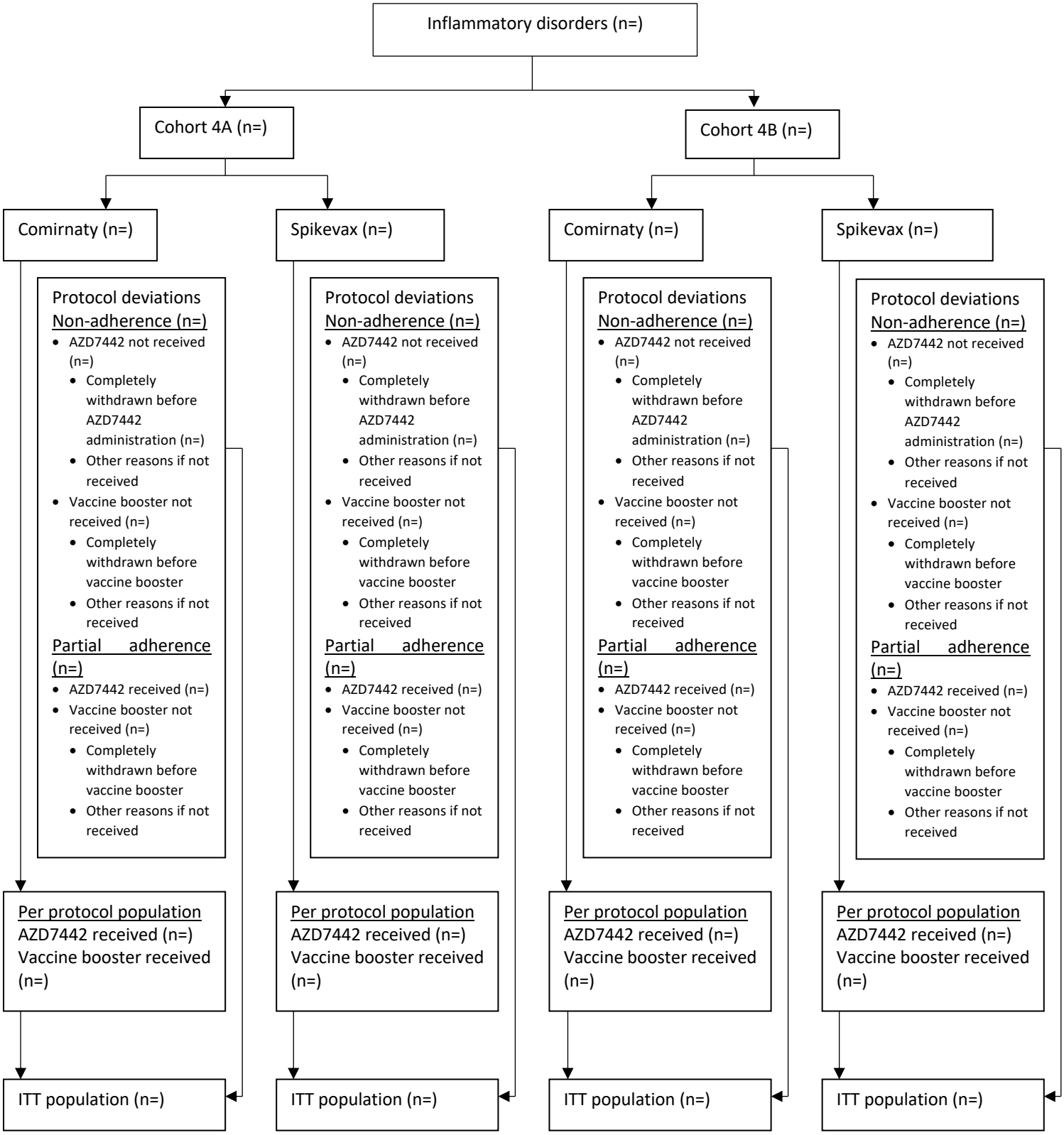

Figure 4: CONSORT flow diagram (inflammatory disorders cohort)

Figure 5: Plot of mean AZD7442 serum concentration over time (tixagevimab and cilgavimab), including 95% confidence intervals overall and for each disease cohort

Figure 6: Dot plots showing log-transformed anti-SARS-CoV-2 anti S-RBD Ig concentration (U/ml) over time (all cohorts), including mean (shown overall and for each cohort on combined graph)

Figure 7: Mean (95% CI) log-transformed anti-SARS CoV-2 anti S-RBD Ig concentration (U/ml) over time (overall and each cohort on a combined graph panel)

Figure 8: Dot plots showing log-transformed IgG concentrations (AU/ml) against selected COVID antigens over time (all cohorts; Oxford patients only) , including mean (shown overall and for each cohort on combined graph)

Figure 9: Mean (95% CI) log-transformed IgG concentrations (AU/ml) against selected COVID antigens over time over time (overall and all cohorts on a combined graph panel; Oxford patients only)

Figure 10: Dot plots showing log-transformed IgG concentrations (AU/ml) against selected ancestral COVID antigens over time (all cohorts; all cohorts) , including mean (shown overall and for each cohort on combined graph; all patients)

Figure 11: Mean (95% CI) log-transformed IgG concentrations (AU/ml) against selected ancestral COVID antigens over time (overall and all cohorts on a combined graph panel; all patients)

Figure 12: Dot plot showing log-transformed SARS-CoV-2 antigen specific T cell concentration (spot forming cells per million peripheral blood mononuclear cells) over time (all cohorts) , including mean (shown overall and for each cohort on combined graph)

Figure 13: Mean (95% CI) log-transformed SARS-CoV-2 antigen specific T cell concentration (spot forming cells per million peripheral blood mononuclear cells) over time (overall and all cohorts on a combined graph panel)

Figure 14: Dot plots showing log-transformed neutralising antibodies against three COVID-19 variants (IC50) over time (all cohorts) , including mean (shown overall and for each cohort on combined graph)

Figure 15: Mean (95% CI) log-transformed neutralising antibodies against three COVID-19 variants (IC50) over time (overall and all cohorts on a combined graph panel)

Figure 16: Mean anti SARS-CoV-2 anti S-RBD Ig levels between vaccine types and cohorts over time (overall and all cohorts on a combined graph)

Short title:	ISAP / SAP Template

Short title:	ISAP / SAP Template

APPENDIX 2: TABLES

Table 1: Baseline characteristics and medical history of participants in cohort 1 (haematological malignancies), by sub-cohort and overall

Baseline characteristic	Haematological malignancies		
	1A (n=)	1B (n=)	Overall (n=)
Age (median (IQR; range; n)			
Gender (n (%))			
Male			
Female			
WHO Performance status (n (%))			
0			
1			
2			
3			
4			
Household composition (living continuously in the household in the past month)(mean/median (SD/IQR;n)			
Total number of household members			
Household members who….			
Attended school/college in person or outside the home			
Attended childcare/nursery in person or worked outside of home			
Work in health and social care e.g. nurse, doctor, healthcare assistant, social worker			
Number of previous COVID vaccinations			
0			
1			
2			
3			
4			
Previous COVID infection (n (%))			
Yes			
No			
If yes, severity			
Asymptomatic			
Symptomatic - Not hospitalised for COVID-19			

Short title:	ISAP / SAP Template

Baseline characteristic	Haematological malignancies		
	1A (n=)	1B (n=)	Overall (n=)
Hospitalised for COVID-19 with no Oxygen			
Hospitalised for COVID-19 with Oxygen			
ITU for COVID-19			
Full blood count (mean/median (SD/IQR; range; n))			
White blood cells ($x10^9$/L)			
Lymphocytes ($x10^9$/L)			
Absolute neutrophil count ($x10^9$/L)			
Platelets ($x10^9$/L)			
Haemoglobin (g/L)			
Eosinophils ($x10^9$/L)			
Basophils ($x10^9$/L)			
Monocytes ($x10^9$/L)			
Liver function tests			
INR			
APTT ratio			
Albumin (g/L)			
Serum bilirubin (µmol/L)			
AST (IU/L)			
ALT (IU/L)			
ALP (IU/L)			
Urea and electrolytes			
Sodium			
Potassium (mmol/L)			
Urea (mmol/L)			
Serum creatinine (µmol/L)			
Calculated GFR (ml/min)			
Bone profile			
Albumin (g/L)			
Alkaline phosphatase (g/L)			
Total protein (g/L)			
Calcium (mmol/L)			
Acute leukaemia (AML or ALL) being treated with curative intent (n (%))			
Yes			
No			
If AML/ALL			

Short title:	ISAP / SAP Template

Baseline characteristic	Haematological malignancies		
	1A (n=)	1B (n=)	Overall (n=)
Remission status at trial entry (n (%))			
1st complete remission			
2nd complete remission			
1st relapse			
Refractory disease			
Complete remission with failure to recover counts			
Partial remission			
Resistant disease			
Other (specify)			
Stage of current cycle (n (%))			
Induction			
Consolidation			
Maintenance			
Current treatment (n (%))			
..list of treatments as specified in the metadata			
Within 12 months of allograft (n (%))			
Yes			
No			
If within 12 months of allograft			
On immunosuppressive medication (n (%))			
Yes			
No			
GvHD (n (%))			
Yes			
No			
If yes, is the GvHD..			
Acute			
Chronic			
Conditioning intensity (n (%))			
Myeloablative			
Reduced intensity			
Other (specify)			
Receiving anti B-cell antibody therapy (rituximab or equivalent) (n (%))			
Yes			
No			

Short title:	ISAP / SAP Template

Baseline characteristic	Haematological malignancies		
	1A (n=)	1B (n=)	Overall (n=)
MPN and receiving JAK inhibitors (n (%))			
Yes			
No			
Myeloma and on IMiD drugs (n (%))			
Yes			
No			
Chronic lymphocytic leukaemia (CLL) / lymphoproliferative disorders and on ibrutinib (or other BTKi) (n (%))			
Yes			
No			
Aggressive B-cell Non Hodgkin Lymphoma (NHL) (n (%))			
Yes			
No			
If NHL			
Remission status at trial entry (N (%))			
1st Complete remission			
2nd Complete remission			
1st relapse			
Refractory disease			
Complete remission with failure to recover counts			
Partial remission			
Resistant disease			
Other (specify)			
If on active treatment, what line of therapy? (n (%))			
R-CHOP			
R-GDP			
ESHAP			
Not applicable			
Other (specify)			
Chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL) (n (%))			
Yes			
No			

Short title:	ISAP / SAP Template

Baseline characteristic	Haematological malignancies		
	1A (n=)	1B (n=)	Overall (n=)
If CLL, what line of therapy is the patient receiving (n (%))			
First			
Second			
Third			
Fourth			
Fifth			
Hodgkin Lymphoma (n (%))			
Yes			
No			
Indolent B NHL (n (%))			
Yes			
No			
Multiple Myeloma (n (%))			
Yes			
No			
If myeloma, what line of therapy is the patient receiving? (n (%))			
First			
Second			
Third			
Fourth			
Fifth			

Haematological malignancies
1A=Active therapy with immuno-suppressive or modulating agents
1B=Aggressive therapy expected to cause temporary ablation of immune function

Table 2: Baseline characteristics and medical history of participants in cohort 2 (solid tumours), by sub-cohort and overall

Baseline characteristic	Solid tumours		
	2A (n=)	2B (n=)	Overall (n=)
Age (median (IQR; range; n)			
Gender (n (%))			
Male			
Female			
WHO Performance status (n (%))			
0			
1			
2			
3			
4			
Household composition (living continuously in the household in the past month)(mean/median (SD/IQR;n)			
Total number of household members			
Household members who….			
Attended school/college in person or outside the home			
Attended childcare/nursery in person or worked outside of home			
Work in health and social care e.g. nurse, doctor, healthcare assistant, social worker			
Number of previous COVID vaccinations			
0			
1			
2			
3			
4			
Previous COVID infection (n (%))			
Yes			
No			
If yes, severity			
Asymptomatic			
Symptomatic - Not hospitalised for COVID-19			

Short title:	ISAP / SAP Template

Baseline characteristic	Solid tumours		
	2A (n=)	2B (n=)	Overall (n=)
Hospitalised for COVID-19 with no Oxygen			
Hospitalised for COVID-19 with Oxygen			
ITU for COVID-19			
Full blood count (mean/median (SD/IQR; range; n))			
White blood cells ($x10^9$/L)			
Lymphocytes ($x10^9$/L)			
Absolute neutrophil count ($x10^9$/L)			
Platelets ($x10^9$/L)			
Haemoglobin (g/L)			
Eosinophils ($x10^9$/L)			
Basophils ($x10^9$/L)			
Monocytes ($x10^9$/L)			
Liver function tests			
INR			
APTT ratio			
Albumin (g/L)			
Serum bilirubin (µmol/L)			
AST (IU/L)			
ALT (IU/L)			
ALP (IU/L)			
Urea and electrolytes			
Sodium			
Potassium (mmol/L)			
Urea (mmol/L)			
Serum creatinine (µmol/L)			
Calculated GFR (ml/min)			
Bone profile			
Albumin (g/L)			
Alkaline phosphatase (g/L)			
Total protein (g/L)			
Calcium (mmol/L)			
Cancer type (n (%))			
Breast			
Lung			
Colorectal			
Bladder			

Short title:	ISAP / SAP Template

Baseline characteristic	Solid tumours		
	2A (n=)	2B (n=)	Overall (n=)
Kidney (Renal Cell and Renal Pelvis)			
Endometrial			
Liver and Intrahepatic Bile Duct			
Melanoma			
Pancreatic			
Prostate			
Thyroid			
Head and Neck			
Brain cancer and other CNS cancer types			
Ovarian			
Stomach			
Other sites (specify)			
Disease status (n (%))			
First Diagnosed			
Relapsed			
Relapsed refractory disease			
Stage of breast cancer (n (%))			
1			
2			
3			
4			
Not known			
If stage 4 breast cancer, volume of disease (n (%))			
High			
Low			
Not known			
Stage of lung cancer (n (%))			
1			
2			
3A			
3B			
4			
Not known			
Stage of colorectal cancer (n (%))			
1			
2			
3			

Short title:	ISAP / SAP Template

Baseline characteristic	Solid tumours		
	2A (n=)	2B (n=)	Overall (n=)
4			
Not known			
Stage of bladder cancer (n (%))			
1			
2			
3			
4			
Not known			
Stage of kidney cancer (n (%))			
1			
2			
3A			
3B			
4			
Not known			
Stage of endometrial cancer (n (%))			
1			
2			
3			
4			
Not known			
Stage of Liver and Intrahepatic Bile Duct cancer (n (%))			
1			
2			
3			
4			
Not known			
Stage of Melanoma (n (%))			
1			
2			
3A			
3B			
4			
Not known			
Stage of pancreatic cancer (n (%))			
1			
2			

Short title:	ISAP / SAP Template

Baseline characteristic	Solid tumours		
	2A (n=)	2B (n=)	Overall (n=)
3			
4			
Not known			
Stage of prostate cancer (n (%))			
1			
2			
3			
4			
Not known			
Stage of thyroid cancer (n (%))			
1			
2			
3			
4			
Not known			
Stage of head and neck cancer (n (%))			
1			
2			
3A			
3B			
4			
Not known			
Stage of Brain cancer and other CNS cancer types (n (%))			
1			
2			
3			
4			
Not known			
Stage of ovarian cancer (n (%))			
1			
2			
3			
4			
Not known			
Stage of Stomach Cancer (n (%))			
1			
2			

Short title:	ISAP / SAP Template

Baseline characteristic	Solid tumours		
	2A (n=)	2B (n=)	Overall (n=)
3A			
3B			
4			
Not known			
Stage of other cancer (n (%))			
1			
2			
3			
4			
Not known			

Solid tumour
2A=Early cancer on systemic treatment
2B=Advanced cancer on systemic treatment

Short title:	ISAP / SAP Template

Table 3: Baseline characteristics and medical history of participants in cohort 3 (renal and hepatic disorders), by sub-cohort and overall

Baseline characteristic	Renal and hepatic disorders		
	3A (n=)	3B (n=)	Overall (n=)
Age (median (IQR; range; n)			
Gender (n (%))			
Male			
Female			
WHO Performance status (n (%))			
0			
1			
2			
3			
4			
Household composition (living continuously in the household in the past month)(mean/median (SD/IQR;n)			
Total number of household members			
Household members who….			
Attended school/college in person or outside the home			
Attended childcare/nursery in person or worked outside of home			
Work in health and social care e.g. nurse, doctor, healthcare assistant, social worker			
Number of previous COVID vaccinations			
0			
1			
2			
3			
4			
Previous COVID infection (n (%))			
Yes			
No			
If yes, severity			
Asymptomatic			
Symptomatic - Not hospitalised for COVID-19			
Hospitalised for COVID-19 with no Oxygen			

Baseline characteristic	Renal and hepatic disorders		
	3A (n=)	3B (n=)	Overall (n=)
Hospitalised for COVID-19 with Oxygen			
ITU for COVID-19			
Full blood count (median (IQR; range; n))			
White blood cells ($x10^9$/L)			
Lymphocytes ($x10^9$/L)			
Absolute neutrophil count ($x10^9$/L)			
Platelets ($x10^9$/L)			
Haemoglobin (g/L)			
Eosinophils ($x10^9$/L)			
Basophils ($x10^9$/L)			
Monocytes ($x10^9$/L)			
Liver function tests			
INR			
APTT ratio			
Albumin (g/L)			
Serum bilirubin (µmol/L)			
AST (IU/L)			
ALT (IU/L)			
ALP (IU/L)			
Urea and electrolytes			
Sodium			
Potassium (mmol/L)			
Urea (mmol/L)			
Serum creatinine (µmol/L)			
Calculated GFR (ml/min)			
Bone profile			
Albumin (g/L)			
Alkaline phosphatase (g/L)			
Total protein (g/L)			
Calcium (mmol/L)			
RENAL DISORDERS			
If renal disorder (n (%))			
Currently receiving immunosuppression			
Dialysis – including in-centre and home haemodialysis, peritoneal dialysis			
Transplant recipient receiving immunosuppression			

Baseline characteristic	Renal and hepatic disorders		
	3A (n=)	3B (n=)	Overall (n=)
Renal diagnosis (n (%))			
Autosomal dominant polycystic kidney disease			
Diabetes			
Glomerulonephritis			
Urological			
Other (specify)			
Not Known			
Current treatment (n (%))			
Currently receiving immunosuppression			
In-centre haemodialysis			
Home haemodialysis			
Peritoneal dialysis			
Transplant recipient			
Has the transplant failed (n (%))			
Yes			
No			
HEPATIC DISORDERS			
Category of liver disease recruited to (n (%))			
Liver Transplant			
Autoimmune Hepatitis on immunosuppression			
Cirrhosis not on immunosuppression			
Type of liver disease (n (%))			
Non-alcoholic fatty liver disease (NAFLD)			
Alcohol-related liver disease (ALD)			
Hepatitis C virus (HCV)			
Hepatitis B virus (HBV)			
Autoimmune hepatitis (AIH)			
IgG4-related disease			
Primary biliary cholangitis (PBC)			
Primary sclerosing cholangitis (PSC)			
Hemochromatosis			
Wilson's disease			
Other (specify)			
Assessment of ascites (n (%))			
Absent			

Baseline characteristic	Renal and hepatic disorders		
	3A (n=)	3B (n=)	Overall (n=)
Mild to Moderate (diuretic responsive)			
Moderate to Severe (diuretic refractory)			
Assessment of encephalopathy (n (%))			
Absent			
Mild to Moderate (grades I-II)			
Moderate to Severe (grades III-IV)			
Cirrhosis (n (%))			
Yes			
No			
If yes, what is the Child Pugh grade?			
A			
B			
C			
Not known			
Has the participant received dialysis at least twice or CVVHD for more than 24 hours in the past week? (n (%))			
Yes			
No			
Is the participant positive for Hepatitis B surface antigen (HBsAg)? (n (%))			
Yes			
No			
Did the participant have detectable hepatitis C virus (HCV) RNA at the time of trial entry? (n (%))			
Yes			
No			
If HCV RNA present, specify HCV genotype (n (%))			
1			
2			
3			
4			
5			
6			
7			
8			

Short title:	ISAP / SAP Template

Baseline characteristic	Renal and hepatic disorders		
	3A (n=)	3B (n=)	Overall (n=)
Not Known			
Has the participant had a liver transplant? (n (%))			
Yes			
No			
Indication for the liver transplant (n (%))			
Decompensation cirrhosis			
Hepatocellular carcinoma			
Acute Liver failure			
Other			

Renal and hepatic disorders
3A=Renal disorders (currently receiving immunosuppression; dialysis; transplant recipient receiving immunosuppression)
3B=Hepatic disorders (autoimmune liver disease and liver transplantation on immune suppressive therapy)

Short title:	ISAP / SAP Template

Table 4: Baseline characteristics and medical history of participants in cohort 4 (inflammatory disorders), by sub-cohort and overall

Baseline characteristic	Inflammatory disorders		
	4A (n=)	4B (n=)	Overall (n=)
Age (median (IQR; range; n)			
Gender (n (%))			
Male			
Female			
WHO Performance status (n (%))			
0			
1			
2			
3			
4			
Household composition (living continuously in the household in the past month)(median (IQR;n)			
Total number of household members			
Household members who….			
Attended school/college in person or outside the home			
Attended childcare/nursery in person or worked outside of home			
Work in health and social care e.g. nurse, doctor, healthcare assistant, social worker			
Number of previous COVID vaccinations			
0			
1			
2			
3			
4			
Previous COVID infection (n (%))			
Yes			
No			
If yes, severity			
Asymptomatic			
Symptomatic - Not hospitalised for COVID-19			

Short title:	ISAP / SAP Template

Baseline characteristic	Inflammatory disorders		
	4A (n=)	4B (n=)	Overall (n=)
Hospitalised for COVID-19 with no Oxygen			
Hospitalised for COVID-19 with Oxygen			
ITU for COVID-19			
Full blood count (median (IQR; range; n))			
White blood cells (x10^9/L)			
Lymphocytes (x10^9/L)			
Absolute neutrophil count (x10^9/L)			
Platelets (x10^9/L)			
Haemoglobin (g/L)			
Eosinophils (x10^9/L)			
Basophils (x10^9/L)			
Monocytes (x10^9/L)			
Liver function tests			
INR			
APTT ratio			
Albumin (g/L)			
Serum bilirubin (µmol/L)			
AST (IU/L)			
ALT (IU/L)			
ALP (IU/L)			
Urea and electrolytes			
Sodium			
Potassium (mmol/L)			
Urea (mmol/L)			
Serum creatinine (µmol/L)			
Calculated GFR (ml/min)			
Bone profile			
Albumin (g/L)			
Alkaline phosphatase (g/L)			
Total protein (g/L)			
Calcium (mmol/L)			
INFLAMMATORY DISORDERS			

Baseline characteristic	Inflammatory disorders		
	4A (n=)	4B (n=)	Overall (n=)
Receiving T-cell co-stimulation modulators, B-cell targeted therapies (including rituximab), tumour necrosis factor inhibitors (TNFi), soluble TNF receptors, interleukin (IL)-6 receptor inhibitors, IL-17 inhibitors, IL 12/23 inhibitors, IL 23 inhibitors or JAK inhibitors (n(%))			
Yes			
No			
Received any immunotherapies listed above in the previous 3 months for autoimmune diseases, except in the case of rituximab treatment within the previous 6-month period.			
Yes			
No			
Receiving or had received in the previous 6 months immunosuppressive chemotherapy.			
Yes			
No			
Receiving systemic immunosuppression for a chronic inflammatory disorders.			
Yes			
No			
Rituxumab status (n (%))			
Receiving rituxumab			
Receiving non-rituximab immunosuppressants			
Treatment (n (%))			
T-cell co-stimulation modulators			
B-cell targeted therapies			
Tumour necrosis factor inhibitors (TNFi			
Belimumab			
Interleukin (IL)-6 receptor inhibitors			
IL-17 inhibitors			
IL 12/23 inhibitors			
IL 23 inhibitors			

Baseline characteristic	Inflammatory disorders		
	4A (n=)	4B (n=)	Overall (n=)
JAK inhibitors			
Concomitant medication (n (%))			
Mycophenolate mofetil			
Methotrexate			
Disease type (n (%))			
Inflammatory Bowel Disease			
Inflammatory rheumatic diseases			
If primary inflammatory bowel disease (IBD), disease type (n (%))			
Ulcerative Colitis			
Crohn's disease			
IBD Unclassified			
Not Known			
If Ulcerative Colitis, Primary sclerosing cholangitis (PSC)? (n (%))			
Yes			
No			
If inflammatory rheumatic diseases, Condition (n (%))			
ANCA-associated vasculitis (AAV)			
Axial Spondyloarthritis (axSpA)			
Psoriatic arthritis (PsA)			
Rheumatoid arthritis (RA)			
Systemic lupus erythematosus (SLE)			
SeroNegative Inflammatory Arthritis			
Generic disease activity assessment numerical rating scale (mean/median, SD/IQR)			
Physician-reported			
Patient-reported			
SEROLOGICAL STATUS			
Cyclic Citrullinated Peptide (CCP) (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Rheumatoid factor (RF) (n (%))			
Negative			

Short title:	ISAP / SAP Template

Baseline characteristic	Inflammatory disorders		
	4A (n=)	4B (n=)	Overall (n=)
Positive			
Not known			
Not applicable			
Myeloperoxidase (MPO) (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Proteinase 3 (PR3) (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Anti-nuclear antibody (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Anti-double stranded DNA antibody (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Anti-extractable nuclear antigen antibody (n (%))			
Negative			
Positive			
Not known			
Not applicable			
Erythrocyte sedimentation rate at baseline (ESR) (mm/hr) (mean/median, SD/IQR)			

Inflammatory disorders
4A=Receiving rituximab
4B=Receiving non-rituximab immunosuppressants

Short title:	ISAP / SAP Template

Short title:	ISAP / SAP Template

Table 5: Baseline characteristics and medical history of participants by vaccine allocation

Baseline characteristic	Vaccine	
	Comirnaty (n=)	Spikevax (n=)
Age (median (IQR; range; n)		
Gender (n (%))		
Male		
Female		
WHO Performance status (n (%))		
0		
1		
2		
3		
4		
Household composition (living continuously in the household in the past month)(mean/median (SD/IQR;n)		
Total number of household members		
Household members who….		
Attended school/college in person or outside the home		
Attended childcare/nursery in person or worked outside of home		
Work in health and social care e.g. nurse, doctor, healthcare assistant, social worker		
Number of previous COVID vaccinations		
0		
1		
2		
3		
4		
Previous COVID infection (n (%))		
Yes		
No		
If yes, severity		
Asymptomatic		
Symptomatic - Not hospitalised for COVID-19		
Hospitalised for COVID-19 with no Oxygen		

Baseline characteristic	Vaccine	
	Comirnaty (n=)	Spikevax (n=)
Hospitalised for COVID-19 with Oxygen		
ITU for COVID-19		
Full blood count (mean/median (SD/IQR; range; n))		
White blood cells ($x10^9$/L)		
Lymphocytes ($x10^9$/L)		
Absolute neutrophil count ($x10^9$/L)		
Platelets ($x10^9$/L)		
Haemoglobin (g/L)		
Eosinophils ($x10^9$/L)		
Basophils ($x10^9$/L)		
Monocytes ($x10^9$/L)		
Liver function tests		
INR		
APTT ratio		
Albumin (g/L)		
Serum bilirubin (µmol/L)		
AST (IU/L)		
ALT (IU/L)		
ALP (IU/L)		
Urea and electrolytes		
Sodium		
Potassium (mmol/L)		
Urea (mmol/L)		
Serum creatinine (µmol/L)		
Calculated GFR (ml/min)		
Bone profile		
Albumin (g/L)		
Alkaline phosphatase (g/L)		
Total protein (g/L)		
Calcium (mmol/L)		
COHORT		
Haematological malignancies (n (%))		
1A		
1B		
Solid tumours (n (%))		
2A		

Short title:	ISAP / SAP Template

Baseline characteristic	Vaccine	
	Comirnaty (n=)	Spikevax (n=)
2B		
Renal and hepatic disorders (n (%))		
3A		
3B		
Inflammatory disorders (n (%))		
4A		
4B		

Short title:	ISAP / SAP Template

Table 6: Treatment adherence by cohort and sub-cohort

	Cohort								
	Haematological malignancies (n=)		Solid tumours (n=)		Renal and hepatic disorders (n=)		Inflammatory disorders (n=)		Overall
	1A (n=)	1B (n=)	2A (n=)	2B (n=)	3A (n=)	3B (n=)	4A (n=)	4B (n=)	
AZD7442 administration at day 0 (n (%))									
Booster vaccine at day 28 (n (%))									
Full adherence (n (%))*									
Partial adherence (n (%))**									
Partial adherence, had vaccine late (n (%))									
Non-adherence (n (%))									
Received allocated vaccine (n (%))									

* Full adherence is defined as a patient having had both theAZD7442 injection and the booster vaccine at day 28.

** Partial adherence can only be defined as a patient who has been in the study longer than 28 days not having a vaccination at 28 days after receiving the initial treatment of AZD7442. A sub-group of partial adherence is having the vaccine after day 28.

Short title:	ISAP / SAP Template

Table 7: Withdrawal levels and reasons by cohort and sub-cohort (day 28)

	Cohort/sub-cohort								
	1		2		3		4		
	1A	1B	2A	2B	3A	3B	4A	4B	Overall
Level of withdrawal (n (%))									
Withdrawal from AZD7442									
Withdrawal from booster									
Withdrawal from further trial assessments Data and samples collected from trial visits that have taken place up until the withdrawal date can still be sent but participant will not attend any further visits.									
Withdrawal from future research using excess participant samples.									
Withdrawal from future research using data. Participants have the option to remove their consent to sharing of their de-identified data outside of the trial for future research.									

Short title:	ISAP / SAP Template

	Cohort/sub-cohort								
	1		2		3		4		
	1A	1B	2A	2B	3A	3B	4A	4B	Overall
Withdraw trial data collected up to the date of withdrawal									
Destroy trial samples collected up to the date of withdrawal									
Reason for withdrawal (n (%))									
Intolerance to medication									
Withdrawal of consent for treatment by participant									
Non-compliance									
Any alteration in the participants condition which justifies the discontinuation of the treatment in the Investigator's opinion									
Other (specify)									

Short title:	ISAP / SAP Template

Table 8: Withdrawal levels and reasons by cohort and sub-cohort (day 56)

	Cohort/sub-cohort								
	1		2		3		4		
	1A	1B	2A	2B	3A	3B	4A	4B	Overall
Level of withdrawal (n (%))									
Withdrawal from AZD7442									
Withdrawal from booster									
Withdrawal from further trial assessments Data and samples collected from trial visits that have taken place up until the withdrawal date can still be sent but participant will not attend any further visits.									
Withdrawal from future research using excess participant samples.									
Withdrawal from future research using data. Participants have the option to remove their consent to sharing of their de-identified data outside of the trial for future research.									

Short title:	ISAP / SAP Template

	Cohort/sub-cohort								
	1		2		3		4		
	1A	1B	2A	2B	3A	3B	4A	4B	Overall
Withdraw trial data collected up to the date of withdrawal									
Destroy trial samples collected up to the date of withdrawal									
Reason for withdrawal (n (%))									
Intolerance to medication									
Withdrawal of consent for treatment by participant									
Non-compliance									
Any alteration in the participants condition which justifies the discontinuation of the treatment in the Investigator's opinion									
Other (specify)									

Short title:	ISAP / SAP Template

Table 9: Withdrawal levels and reasons by cohort and sub-cohort (day 180)

	Cohort/sub-cohort								
	1		2		3		4		
	1A	1B	2A	2B	3A	3B	4A	4B	Overall
Level of withdrawal (n (%))									
Withdrawal from AZD7442									
Withdrawal from booster									
Withdrawal from further trial assessments Data and samples collected from trial visits that have taken place up until the withdrawal date can still be sent but participant will not attend any further visits.									
Withdrawal from future research using excess participant samples.									
Withdrawal from future research using data. Participants have the option to remove their consent to sharing of their de-identified data outside of the trial for future research.									

Short title:	ISAP / SAP Template

	Cohort/sub-cohort								
	1		2		3		4		
	1A	1B	2A	2B	3A	3B	4A	4B	Overall
Withdraw trial data collected up to the date of withdrawal									
Destroy trial samples collected up to the date of withdrawal									
Reason for withdrawal (n (%))									
Intolerance to medication									
Withdrawal of consent for treatment by participant									
Non-compliance									
Any alteration in the participants condition which justifies the discontinuation of the treatment in the Investigator's opinion									
Other (specify)									

Short title:	ISAP / SAP Template

Table 10: Deaths and causes of death by cohort and sub-cohort

	Cohort and sub-cohort								
	1		2		3		4		Overall
	1A (n=)	1B (n=)	2A (n=)	2B (n=)	3A (n=)	3B (n=)	4A (n=)	4B (n=)	
Deaths (n (%))									
Cause of death (n (%))									
Covid-19 related									
Disease cohort related									
Other (specify)									
Not known									

Short title:	ISAP / SAP Template

Table 11: Pharmacokinetic analysis of serum AZD7442 concentrations over time, by cohort, sub-cohort and overall

	Cohort/sub-cohort									Age-group or gender	ANCOVA or Mann-Whitney U test p-value
	1		2		3		4				
	1A	1B	2A	2B	3A	3B	4A	4B	Overall		
Median/mean (IQR/SD; range) AZD7442 serum concentration (µg/ml)											
Day											
0											
28											
180											
Median/mean (IQR/SD; range) C_{max} (µg/ml)											
Cohort 1 vs Cohort 2											
Cohort 1 vs Cohort 3											
Cohort 1 vs Cohort 4											
Cohort 2 vs Cohort 3											
Cohort 2 vs Cohort 4											
Cohort 3 vs Cohort 4											
Age-groups (specify)*											
Gender											

Short title:	ISAP / SAP Template

	Cohort/sub-cohort									Age-group or gender	ANCOVA or Mann-Whitney U test p-value
	1		2		3		4				
	1A	1B	2A	2B	3A	3B	4A	4B	Overall		
Male											
Female											
Median/mean (IQR/SD; range) T_{max} (µg/ml)											
Cohort 1 vs Cohort 2											
Cohort 1 vs Cohort 3											
Cohort 1 vs Cohort 4											
Cohort 2 vs Cohort 3											
Cohort 2 vs Cohort 4											
Cohort 3 vs Cohort 4											
Age-groups (specify)*											
Gender											
Male											
Female											

Cohorts and sub-cohorts
1=Haematological malignancies

Short title:	ISAP / SAP Template

1A=Active therapy with immuno-suppressive or modulating agents
1B=Aggressive therapy expected to cause temporary ablation of immune function
2=Solid tumour
2A=Early cancer on systemic
treatment
2B=Advanced cancer on systemic treatment
3=Renal and hepatic
disorders
3A=Renal disorders (currently receiving immunosuppression; dialysis; transplant recipient receiving immunosuppression)
3B=Hepatic disorders (autoimmune liver disease and liver transplantation on immune suppressive therapy)
4=Inflammatory disorders
4A=Receiving
rituximab
4B=Receiving non-rituximab immunosuppressants
* Age groups to be defined dependent on numbers in each group

Table 12: Average anti-SARS-CoV2 anti S-RBD Ig concentration over time (all cohorts)

	All cohorts	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
		1A	1B	Overall	2A	2B	Overall	3A	3B	Overall	4A	4B	Overall
Median/mean (IQR/SD; range) anti-SARS-CoV2 anti-S RBD total Ig concentration (U/ml)													
Day													
0													
28													
56													
112													
180													
Anti-SARS-CoV2 anti-S RBD interpretation													
Day 0													
Positive													
Negative													
Insufficient													
Not tested													

Short title:	ISAP / SAP Template

	All cohorts	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
		1A	1B	Overall	2A	2B	Overall	3A	3B	Overall	4A	4B	Overall
Day 28													
Positive													
Negative													
Insufficient													
Not tested													
Day 56													
Positive													
Negative													
Insufficient													
Not tested													
Day 112													
Positive													
Negative													
Insufficient													
Not tested													
Day 180													
Positive													
Negative													
Insufficient													
Not tested													

Short title:	ISAP / SAP Template

	All cohorts	Cohort 1			Cohort 2			Cohort 3			Cohort 4		
		1A	1B	Overall	2A	2B	Overall	3A	3B	Overall	4A	4B	Overall

Haematological malignancies sub-cohort
1A=Active therapy with immuno-suppressive or modulating agents
1B=Aggressive therapy expected to cause temporary ablation of immune function
Solid tumour sub-cohort
2A=Early cancer on systemic treatment
2B=Advanced cancer on systemic treatment
Renal and hepatic disorders
3A=Renal disorders (currently receiving immunosuppression; dialysis; transplant recipient receiving immunosuppression)
3B=Hepatic disorders (autoimmune liver disease and liver transplantation on immune suppressive therapy)
Inflammatory disorders
4A=Receiving rituximab
4B=Receiving non-rituximab immunosuppressants

Short title:	ISAP / SAP Template

Table 13: IgG responses against multiple COVID-19 antigens (all cohorts, Oxford patients only)

	All cohorts (Oxford patients only)									
	SARS-CoV-2 N	SARS-CoV-2 Spike	SARS-CoV-2 Spike (B.1.1.529; BA.1),	SARS-CoV-2 Spike (BA.5)	SARS-CoV-2 Spike (BQ.1.1)	SARS-CoV-2 Spike (XBB.1)	SARS-CoV-2 Spike (XBB.1.5)	SARS-CoV-2 Spike (XBB.1.16)	SARS-CoV-2 Spike (XBB.1.16.1)	SARS-CoV-2 Spike (XBB.2.3))
Median/mean (IQR/SD; range; n) log-transformed IgG concentration (AU/ml)										
Day 0										
All cohorts										
Cohort 1										
Cohort 2										
Cohort 3										
Cohort 4										
Day 28										
All cohorts										
Cohort 1										
Cohort 2										
Cohort 3										

Short title:	ISAP / SAP Template

	All cohorts (Oxford patients only)									
	SARS-CoV-2 N	SARS-CoV-2 Spike	SARS-CoV-2 Spike (B.1.1.529; BA.1),	SARS-CoV-2 Spike (BA.5)	SARS-CoV-2 Spike (BQ.1.1)	SARS-CoV-2 Spike (XBB.1)	SARS-CoV-2 Spike (XBB.1.5)	SARS-CoV-2 Spike (XBB.1.16)	SARS-CoV-2 Spike (XBB.1.16.1)	SARS-CoV-2 Spike (XBB.2.3))
Cohort 4										
Day 56										
All cohorts										
Cohort 1										
Cohort 2										
Cohort 3										
Cohort 4										
Day 112										
All cohorts										
Cohort 1										
Cohort 2										
Cohort 3										
Cohort 4										
Day 180										
All cohorts										
Cohort 1										
Cohort 2										

Short title:	ISAP / SAP Template

	All cohorts (Oxford patients only)									
	SARS-CoV-2 N	SARS-CoV-2 Spike	SARS-CoV-2 Spike (B.1.1.529; BA.1),	SARS-CoV-2 Spike (BA.5)	SARS-CoV-2 Spike (BQ.1.1)	SARS-CoV-2 Spike (XBB.1)	SARS-CoV-2 Spike (XBB.1.5)	SARS-CoV-2 Spike (XBB.1.16)	SARS-CoV-2 Spike (XBB.1.16.1)	SARS-CoV-2 Spike (XBB.2.3))
Cohort 3										
Cohort 4										

Short title:	ISAP / SAP Template

Table 14: IgG responses against multiple COVID-19 antigens (all cohorts, all patients)

	All cohorts (all patients)				
	SARS-CoV-2 Spike	SARS-CoV-2 S1 RBD	SARS-CoV-2 S1 NTD	SARS-CoV-2 S1 N	SARS-CoV-1 Spike
Median/mean (IQR/SD; range; n) log-transformed IgG concentration (AU/ml)					
Day 0					
All cohorts					
Cohort 1					
Cohort 2					
Cohort 3					
Cohort 4					
Day 28					
All cohorts					
Cohort 1					
Cohort 2					
Cohort 3					
Cohort 4					
Day 56					
All cohorts					
Cohort 1					

Cohort 2					
Cohort 3					
Cohort 4					

Cohort 1 Haematological malignancies
Cohort 2 Solid tumours
Cohort 3 Renal and hepatic disorders
Cohort 4 Inflammatory disorders

Table 15: T cell responses by cohort and sub-cohort at each timepoint

	Haematological malignancies cohort			Solid tumours cohort			Renal and hepatic disorders cohort			Inflammatory disorders cohort			All cohorts
	1A	1B	Overall	1A	1B	Overall	1A	1B	Overall	1A	1B	Overall	
Spot-forming cells per million PBMC* (mean/median (SD/IQR;range;n)													
Day													
28													
56													
112													
180													

* PBMC=Peripheral blood mononuclear cells

Short title:	ISAP / SAP Template

Table 16: Neutralising antibody levels by cohort and sub-cohort at each timepoint

	Haematological malignancies cohort			Solid tumours cohort			Renal and hepatic disorders cohort			Inflammatory disorders cohort			All cohorts
	1A	1B	Overall	1A	1B	Overall	1A	1B	Overall	1A	1B	Overall	
COVID-19 variant 1 log-transformed IC50 (mean/median (SD/IQR; range; n)													
Day													
Baseline													
28													
56													
112													
180													
COVID-19 variant 2 log-transformed IC50 (mean/median (SD/IQR; range; n)													
Day													
Baseline													
28													
56													
112													

180													
COVID-19 variant 3 log-transformed IC50 (mean/median (SD/IQR; range; n)													
Day													
Baseline													
28													
56													
112													
180													

Table 17: Comparison of anti-SARS-CoV-2 anti-S-RBD Ig concentrations between the two vaccines at each timepoint

	Vaccine		Difference in means (95% CI)	p-value
	Comirnaty	Spikevax		
Median/mean (IQR/SD; range; n) anti-SARS-CoV2 anti-S RBD total Ig concentration (U/ml)				
Day				
0				
28				
56				
112				
180				

Short title:	ISAP / SAP Template

Table 18: Baseline adverse events (haematological malignancies cohort)

Baseline adverse event	Haematological malignancies cohort						
	Grade (n (%))		Grade (n (%))		Grade (n (%))		Total CRFs
	1-2	3+	1-2	3+	1-2	3+	
Total toxicities							
Total subjects							
Blood and lymphatic system disorders							
Thrombocytopenia							
Cardiac disorders							
Arrhythmia							
Chest pain							
Myocarditis							
Palpitations							
Pericarditis							
Eye disorders							
Blurred vision							
Gastrointestinal disorders							
Abdominal pain							
Diarrhoea							
Nausea							
Vomiting							

Short title:	ISAP / SAP Template

Baseline adverse event	Haematological malignancies cohort						
	Grade (n (%))		Grade (n (%))		Grade (n (%))		Total CRFs
	1-2	3+	1-2	3+	1-2	3+	
General disorders and administration site conditions							
Chills							
Fatigue							
Fever/pyrexia							
Leg swelling							
Lymphadenopathy							
Immune system disorders							
Anaphylaxis							
Hypersensitivity							
Injury, poisoning and procedural complications							
Injection site pain							
Swelling							
Skin bruising							
Musculoskeletal and connective tissue disorders							
Arthralgia							
Leg pain							
Myalgia							
Nervous system disorders							

Short title:	ISAP / SAP Template

Baseline adverse event	Haematological malignancies cohort						
	Grade (n (%))		Grade (n (%))		Grade (n (%))		Total CRFs
	1-2	3+	1-2	3+	1-2	3+	
Facial paralysis							
Headache							
Seizures							
Psychiatric disorders							
Anxiety							
Confusion							
Respiratory, thoracic and mediastinal disorders							
Dyspnea							
Skin and sub-cutaneous tissue disorders							
Petechiae							
Rash							
Spontaneous bleeding							
Vascular disorders							
Hypertension							
Hypotension							
Other toxicities (specify)							

Short title:	ISAP / SAP Template

Table 19: Baseline adverse events (solid tumours cohort)

Baseline adverse event	Solid tumours cohort						
	Grade (n (%))		Grade (n (%))		Grade (n (%))		Total CRFs
	1-2	3+	1-2	3+	1-2	3+	
Total toxicities							
Total subjects							
Blood and lymphatic system disorders							
Thrombocytopenia							
Cardiac disorders							
Arrhythmia							
Chest pain							
Myocarditis							
Palpitations							
Pericarditis							
Eye disorders							
Blurred vision							
Gastrointestinal disorders							
Abdominal pain							
Diarrhoea							
Nausea							
Vomiting							

Short title:	ISAP / SAP Template

Baseline adverse event	Solid tumours cohort						
	Grade (n (%))		Grade (n (%))		Grade (n (%))		Total CRFs
	1-2	3+	1-2	3+	1-2	3+	
General disorders and administration site conditions							
Chills							
Fatigue							
Fever/pyrexia							
Leg swelling							
Lymphadenopathy							
Immune system disorders							
Anaphylaxis							
Hypersensitivity							
Injury, poisoning and procedural complications							
Injection site pain							
Swelling							
Skin bruising							
Musculoskeletal and connective tissue disorders							
Arthralgia							
Leg pain							
Myalgia							
Nervous system disorders							

Short title:	ISAP / SAP Template

Baseline adverse event	Solid tumours cohort						
	Grade (n (%))		Grade (n (%))		Grade (n (%))		Total CRFs
	1-2	3+	1-2	3+	1-2	3+	
Facial paralysis							
Headache							
Seizures							
Psychiatric disorders							
Anxiety							
Confusion							
Respiratory, thoracic and mediastinal disorders							
Dyspnea							
Skin and sub-cutaneous tissue disorders							
Petechiae							
Rash							
Spontaneous bleeding							
Vascular disorders							
Hypertension							
Hypotension							
Other toxicities (specify)							

Short title:	ISAP / SAP Template

Table 20: Baseline adverse events (renal and hepatic disorders cohort)

Baseline adverse event	Renal and hepatic disorders cohort						
	Grade (n (%))		Grade (n (%))		Grade (n (%))		Total CRFs
	1-2	3+	1-2	3+	1-2	3+	
Total toxicities							
Total subjects							
Blood and lymphatic system disorders							
Thrombocytopenia							
Cardiac disorders							
Arrhythmia							
Chest pain							
Myocarditis							
Palpitations							
Pericarditis							
Eye disorders							
Blurred vision							
Gastrointestinal disorders							
Abdominal pain							
Diarrhoea							
Nausea							
Vomiting							

Short title:	ISAP / SAP Template

Baseline adverse event	Renal and hepatic disorders cohort						
	Grade (n (%))		Grade (n (%))		Grade (n (%))		Total CRFs
	1-2	3+	1-2	3+	1-2	3+	
General disorders and administration site conditions							
Chills							
Fatigue							
Fever/pyrexia							
Leg swelling							
Lymphadenopathy							
Immune system disorders							
Anaphylaxis							
Hypersensitivity							
Injury, poisoning and procedural complications							
Injection site pain							
Swelling							
Skin bruising							
Musculoskeletal and connective tissue disorders							
Arthralgia							
Leg pain							
Myalgia							
Nervous system disorders							

Short title:	ISAP / SAP Template

Baseline adverse event	Renal and hepatic disorders cohort						
	Grade (n (%))		Grade (n (%))		Grade (n (%))		Total CRFs
	1-2	3+	1-2	3+	1-2	3+	
Facial paralysis							
Headache							
Seizures							
Psychiatric disorders							
Anxiety							
Confusion							
Respiratory, thoracic and mediastinal disorders							
Dyspnea							
Skin and sub-cutaneous tissue disorders							
Petechiae							
Rash							
Spontaneous bleeding							
Vascular disorders							
Hypertension							
Hypotension							
Other toxicities (specify)							

Short title:	ISAP / SAP Template

Table 21: Baseline adverse events (inflammatory disorders cohort)

Baseline adverse event	Inflammatory disorders cohort						
	Grade (n (%))		Grade (n (%))		Grade (n (%))		Total CRFs
	1-2	3+	1-2	3+	1-2	3+	
Total toxicities							
Total subjects							
Blood and lymphatic system disorders							
Thrombocytopenia							
Cardiac disorders							
Arrhythmia							
Chest pain							
Myocarditis							
Palpitations							
Pericarditis							
Eye disorders							
Blurred vision							
Gastrointestinal disorders							
Abdominal pain							
Diarrhoea							
Nausea							
Vomitting							

Short title:	ISAP / SAP Template

Baseline adverse event	Inflammatory disorders cohort						
	Grade (n (%))		Grade (n (%))		Grade (n (%))		Total CRFs
	1-2	3+	1-2	3+	1-2	3+	
General disorders and administration site conditions							
Chills							
Fatigue							
Fever/pyrexia							
Leg swelling							
Lymphadenopathy							
Immune system disorders							
Anaphylaxis							
Hypersensitivity							
Injury, poisoning and procedural complications							
Injection site pain							
Swelling							
Skin bruising							
Musculoskeletal and connective tissue disorders							
Arthralgia							
Leg pain							
Myalgia							
Nervous system disorders							

Short title:	ISAP / SAP Template

Baseline adverse event	Inflammatory disorders cohort						
	Grade (n (%))		Grade (n (%))		Grade (n (%))		Total CRFs
	1-2	3+	1-2	3+	1-2	3+	
Facial paralysis							
Headache							
Seizures							
Psychiatric disorders							
Anxiety							
Confusion							
Respiratory, thoracic and mediastinal disorders							
Dyspnea							
Skin and sub-cutaneous tissue disorders							
Petechiae							
Rash							
Spontaneous bleeding							
Vascular disorders							
Hypertension							
Hypotension							
Other toxicities (specify)							

Short title:	ISAP / SAP Template

Table 22: Baseline adverse events (all cohorts)

Adverse event	All cohorts		
	Grade (n (%))		Total CRFs
	1-2	3+	
Total toxicities			
Total subjects			
Blood and lymphatic system disorders			
Thrombocytopenia			
Cardiac disorders			
Arrhythmia			
Chest pain			
Myocarditis			
Palpitations			
Pericarditis			
Eye disorders			
Blurred vision			
Gastrointestinal disorders			
Abdominal pain			
Diarrhoea			
Nausea			
Vomiting			

Short title:	ISAP / SAP Template

Adverse event	All cohorts		
	Grade (n (%))		Total CRFs
	1-2	3+	
General disorders and administration site conditions			
Chills			
Fatigue			
Fever/pyrexia			
Leg swelling			
Lymphadenopathy			
Immune system disorders			
Anaphylaxis			
Hypersensitivity			
Injury, poisoning and procedural complications			
Injection site pain			
Swelling			
Skin bruising			
Musculoskeletal and connective tissue disorders			
Arthralgia			
Leg pain			
Myalgia			

Short title:	ISAP / SAP Template

Adverse event	All cohorts		
	Grade (n (%))		Total CRFs
	1-2	3+	
Nervous system disorders			
Facial paralysis			
Headache			
Seizures			
Psychiatric disorders			
Anxiety			
Confusion			
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
Skin and sub-cutaneous tissue disorders			
Petechiae			
Rash			
Spontaneous bleeding			
Vascular disorders			
Hypertension			
Hypotension			
Other toxicities (specify)			

Short title:	ISAP / SAP Template

Table 23: Worst reported adverse events excluding baseline up to day 28 (haematological malignancies cohort)

Worst reported adverse event	Haematological malignancies cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Total toxicities								
Total subjects								
Blood and lymphatic system disorders								
Thrombocytopenia								
Cardiac disorders								
Arrhythmia								
Chest pain								
Myocarditis								
Palpitations								
Pericarditis								
Eye disorders								
Blurred vision								
Gastrointestinal disorders								
Abdominal pain								
Diarrhoea								
Nausea								

Short title:	ISAP / SAP Template

Worst reported adverse event	Haematological malignancies cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Vomiting								
General disorders and administration site conditions								
Chills								
Fatigue								
Fever/pyrexia								
Leg swelling								
Lymphadenopathy								
Immune system disorders								
Anaphylaxis								
Hypersensitivity								
Injury, poisoning and procedural complications								
Injection site pain								
Swelling								
Skin bruising								
Musculoskeletal and connective tissue disorders								
Arthralgia								

Short title:	ISAP / SAP Template

Worst reported adverse event	Haematological malignancies cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Leg pain								
Myalgia								
Nervous system disorders								
Facial paralysis								
Headache								
Seizures								
Psychiatric disorders								
Anxiety								
Confusion								
Respiratory, thoracic and mediastinal disorders								
Dyspnea								
Skin and sub-cutaneous tissue disorders								
Petechiae								
Rash								
Spontaneous bleeding								
Vascular disorders								
Hypertension								

Short title:	ISAP / SAP Template

Worst reported adverse event	Haematological malignancies cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Hypotension								
Other toxicities (specify)								

Table 24: Worst reported adverse events excluding baseline up to day 28 (solid tumours cohort)

Worst reported adverse event	Solid tumours cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Total toxicities								
Total subjects								
Blood and lymphatic system disorders								
Thrombocytopenia								
Cardiac disorders								
Arrhythmia								
Chest pain								
Myocarditis								

Short title:	ISAP / SAP Template

Worst reported adverse event	Solid tumours cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
Palpitations								
Pericarditis								
Eye disorders								
Blurred vision								
Gastrointestinal disorders								
Abdominal pain								
Diarrhoea								
Nausea								
Vomiting								
General disorders and administration site conditions								
Chills								
Fatigue								
Fever/pyrexia								
Leg swelling								
Lymphadenopathy								
Immune system disorders								
Anaphylaxis								
Hypersensitivity								

Short title:	ISAP / SAP Template

Worst reported adverse event	Solid tumours cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
Injury, poisoning and procedural complications								
Injection site pain								
Swelling								
Skin bruising								
Musculoskeletal and connective tissue disorders								
Arthralgia								
Leg pain								
Myalgia								
Nervous system disorders								
Facial paralysis								
Headache								
Seizures								
Psychiatric disorders								
Anxiety								
Confusion								
Respiratory, thoracic and mediastinal disorders								
Dyspnea								

Worst reported adverse event	Solid tumours cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
Skin and sub-cutaneous tissue disorders								
Petechiae								
Rash								
Spontaneous bleeding								
Vascular disorders								
Hypertension								
Hypotension								
Other toxicities (specify)								

Table 25: Worst reported adverse events excluding baseline up to day 28 (renal and hepatic disorders cohort)

Worst reported adverse event	Renal and hepatic disorders cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Total toxicities								
Total subjects								

Short title:	ISAP / SAP Template

Worst reported adverse event	Renal and hepatic disorders cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Blood and lymphatic system disorders								
Thrombocytopenia								
Cardiac disorders								
Arrhythmia								
Chest pain								
Myocarditis								
Palpitations								
Pericarditis								
Eye disorders								
Blurred vision								
Gastrointestinal disorders								
Abdominal pain								
Diarrhoea								
Nausea								
Vomiting								
General disorders and administration site conditions								
Chills								

Short title:	ISAP / SAP Template

Worst reported adverse event	Renal and hepatic disorders cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Fatigue								
Fever/pyrexia								
Leg swelling								
Lymphadenopathy								
Immune system disorders								
Anaphylaxis								
Hypersensitivity								
Injury, poisoning and procedural complications								
Injection site pain								
Swelling								
Skin bruising								
Musculoskeletal and connective tissue disorders								
Arthralgia								
Leg pain								
Myalgia								
Nervous system disorders								
Facial paralysis								

Short title:	ISAP / SAP Template

Worst reported adverse event	Renal and hepatic disorders cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Headache								
Seizures								
Psychiatric disorders								
Anxiety								
Confusion								
Respiratory, thoracic and mediastinal disorders								
Dyspnea								
Skin and sub-cutaneous tissue disorders								
Petechiae								
Rash								
Spontaneous bleeding								
Vascular disorders								
Hypertension								
Hypotension								
Other toxicities (specify)								

Short title:	ISAP / SAP Template

Table 26: Worst reported adverse events excluding baseline up to day 28 (inflammatory disorders cohort)

Worst reported adverse event	Inflammatory disorders cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Total toxicities								
Total subjects								
Blood and lymphatic system disorders								
Thrombocytopenia								
Cardiac disorders								
Arrhythmia								
Chest pain								
Myocarditis								
Palpitations								
Pericarditis								
Eye disorders								
Blurred vision								
Gastrointestinal disorders								
Abdominal pain								
Diarrhoea								
Nausea								

Short title:	ISAP / SAP Template

Worst reported adverse event	Inflammatory disorders cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Vomiting								
General disorders and administration site conditions								
Chills								
Fatigue								
Fever/pyrexia								
Leg swelling								
Lymphadenopathy								
Immune system disorders								
Anaphylaxis								
Hypersensitivity								
Injury, poisoning and procedural complications								
Injection site pain								
Swelling								
Skin bruising								
Musculoskeletal and connective tissue disorders								
Arthralgia								

Short title:	ISAP / SAP Template

Worst reported adverse event	Inflammatory disorders cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Leg pain								
Myalgia								
Nervous system disorders								
Facial paralysis								
Headache								
Seizures								
Psychiatric disorders								
Anxiety								
Confusion								
Respiratory, thoracic and mediastinal disorders								
Dyspnea								
Skin and sub-cutaneous tissue disorders								
Petechiae								
Rash								
Spontaneous bleeding								
Vascular disorders								
Hypertension								

Short title:	ISAP / SAP Template

Worst reported adverse event	Inflammatory disorders cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Hypotension								
Other toxicities (specify)								

Table 27: Worst reported adverse events excluding baseline up to day 28 (all cohorts)

Worst reported adverse event	All cohorts			
	Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+		
Total toxicities				
Total subjects				
Blood and lymphatic system disorders				
Thrombocytopenia				
Cardiac disorders				
Arrhythmia				
Chest pain				
Myocarditis				

Short title:	ISAP / SAP Template

Worst reported adverse event	All cohorts			
	Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+		
Palpitations				
Pericarditis				
Eye disorders				
Blurred vision				
Gastrointestinal disorders				
Abdominal pain				
Diarrhoea				
Nausea				
Vomitting				
General disorders and administration site conditions				
Chills				
Fatigue				
Fever/pyrexia				
Leg swelling				
Lymphadenopathy				
Immune system disorders				
Anaphylaxis				
Hypersensitivity				

Short title:	ISAP / SAP Template

Worst reported adverse event	All cohorts			
	Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+		
Injury, poisoning and procedural complications				
Injection site pain				
Swelling				
Skin bruising				
Musculoskeletal and connective tissue disorders				
Arthralgia				
Leg pain				
Myalgia				
Nervous system disorders				
Facial paralysis				
Headache				
Seizures				
Psychiatric disorders				
Anxiety				
Confusion				
Respiratory, thoracic and mediastinal disorders				

Short title:	ISAP / SAP Template

Worst reported adverse event	All cohorts			
	Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+		
Dyspnea				
Skin and sub-cutaneous tissue disorders				
Petechiae				
Rash				
Spontaneous bleeding				
Vascular disorders				
Hypertension				
Hypotension				
Other toxicities (specify)				

Table 28: Worst reported adverse events excluding baseline up to day 56 (haematological malignancies cohort)

Worst reported adverse event	Haematological malignancies cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Total toxicities								
Total subjects								

Worst reported adverse event	Haematological malignancies cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Blood and lymphatic system disorders								
Thrombocytopenia								
Cardiac disorders								
Arrhythmia								
Chest pain								
Myocarditis								
Palpitations								
Pericarditis								
Eye disorders								
Blurred vision								
Gastrointestinal disorders								
Abdominal pain								
Diarrhoea								
Nausea								
Vomiting								
General disorders and administration site conditions								
Chills								
Fatigue								

Worst reported adverse event	Haematological malignancies cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Fever/pyrexia								
Leg swelling								
Lymphadenopathy								
Immune system disorders								
Anaphylaxis								
Hypersensitivity								
Injury, poisoning and procedural complications								
Injection site pain								
Swelling								
Skin bruising								
Musculoskeletal and connective tissue disorders								
Arthralgia								
Leg pain								
Myalgia								
Nervous system disorders								
Facial paralysis								
Headache								
Seizures								

Short title:	ISAP / SAP Template

Worst reported adverse event	Haematological malignancies cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Psychiatric disorders								
Anxiety								
Confusion								
Respiratory, thoracic and mediastinal disorders								
Dyspnea								
Skin and sub-cutaneous tissue disorders								
Petechiae								
Rash								
Spontaneous bleeding								
Vascular disorders								
Hypertension								
Hypotension								
Other toxicities (specify)								

Short title:	ISAP / SAP Template

Table 29: Worst reported adverse events excluding baseline up to day 56 (solid tumours cohort)

Worst reported adverse event	Solid tumours cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Total toxicities								
Total subjects								
Blood and lymphatic system disorders								
Thrombocytopenia								
Cardiac disorders								
Arrhythmia								
Chest pain								
Myocarditis								
Palpitations								
Pericarditis								
Eye disorders								
Blurred vision								
Gastrointestinal disorders								
Abdominal pain								
Diarrhoea								
Nausea								
Vomiting								

Short title:	ISAP / SAP Template

Worst reported adverse event	Solid tumours cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
General disorders and administration site conditions								
Chills								
Fatigue								
Fever/pyrexia								
Leg swelling								
Lymphadenopathy								
Immune system disorders								
Anaphylaxis								
Hypersensitivity								
Injury, poisoning and procedural complications								
Injection site pain								
Swelling								
Skin bruising								
Musculoskeletal and connective tissue disorders								
Arthralgia								
Leg pain								
Myalgia								

Worst reported adverse event	Solid tumours cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Nervous system disorders								
Facial paralysis								
Headache								
Seizures								
Psychiatric disorders								
Anxiety								
Confusion								
Respiratory, thoracic and mediastinal disorders								
Dyspnea								
Skin and sub-cutaneous tissue disorders								
Petechiae								
Rash								
Spontaneous bleeding								
Vascular disorders								
Hypertension								
Hypotension								
Other toxicities (specify)								

Short title:	ISAP / SAP Template

Table 30: Worst reported adverse events excluding baseline up to day 56 (renal and hepatic disorders cohort)

Worst reported adverse event	Renal and hepatic disorders cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Total toxicities								
Total subjects								
Blood and lymphatic system disorders								
Thrombocytopenia								
Cardiac disorders								
Arrhythmia								
Chest pain								
Myocarditis								
Palpitations								
Pericarditis								
Eye disorders								
Blurred vision								
Gastrointestinal disorders								
Abdominal pain								
Diarrhoea								
Nausea								
Vomiting								

Worst reported adverse event	Renal and hepatic disorders cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
General disorders and administration site conditions								
Chills								
Fatigue								
Fever/pyrexia								
Leg swelling								
Lymphadenopathy								
Immune system disorders								
Anaphylaxis								
Hypersensitivity								
Injury, poisoning and procedural complications								
Injection site pain								
Swelling								
Skin bruising								
Musculoskeletal and connective tissue disorders								
Arthralgia								
Leg pain								
Myalgia								

Short title:	ISAP / SAP Template

Worst reported adverse event	Renal and hepatic disorders cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Nervous system disorders								
Facial paralysis								
Headache								
Seizures								
Psychiatric disorders								
Anxiety								
Confusion								
Respiratory, thoracic and mediastinal disorders								
Dyspnea								
Skin and sub-cutaneous tissue disorders								
Petechiae								
Rash								
Spontaneous bleeding								
Vascular disorders								
Hypertension								
Hypotension								
Other toxicities (specify)								

Short title:	ISAP / SAP Template

Table 31: Worst reported adverse events excluding baseline up to day 56 (inflammatory disorders cohort)

Worst reported adverse event	Inflammatory disorders cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Total toxicities								
Total subjects								
Blood and lymphatic system disorders								
Thrombocytopenia								
Cardiac disorders								
Arrhythmia								
Chest pain								
Myocarditis								
Palpitations								
Pericarditis								
Eye disorders								
Blurred vision								
Gastrointestinal disorders								
Abdominal pain								
Diarrhoea								
Nausea								
Vomiting								

Short title:	ISAP / SAP Template

Worst reported adverse event	Inflammatory disorders cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
General disorders and administration site conditions								
Chills								
Fatigue								
Fever/pyrexia								
Leg swelling								
Lymphadenopathy								
Immune system disorders								
Anaphylaxis								
Hypersensitivity								
Injury, poisoning and procedural complications								
Injection site pain								
Swelling								
Skin bruising								
Musculoskeletal and connective tissue disorders								
Arthralgia								
Leg pain								
Myalgia								

Short title:	ISAP / SAP Template

Worst reported adverse event	Inflammatory disorders cohort							
	Grade (n (%))		Grade (n (%))		Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+	1-2	3+	1-2	3+		
Nervous system disorders								
Facial paralysis								
Headache								
Seizures								
Psychiatric disorders								
Anxiety								
Confusion								
Respiratory, thoracic and mediastinal disorders								
Dyspnea								
Skin and sub-cutaneous tissue disorders								
Petechiae								
Rash								
Spontaneous bleeding								
Vascular disorders								
Hypertension								
Hypotension								
Other toxicities (specify)								

Short title:	ISAP / SAP Template

Table 32: Worst reported adverse events excluding baseline up to day 56 (all cohorts)

Worst reported adverse event	All cohorts			
	Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+		
Total toxicities				
Total subjects				
Blood and lymphatic system disorders				
Thrombocytopenia				
Cardiac disorders				
Arrhythmia				
Chest pain				
Myocarditis				
Palpitations				
Pericarditis				
Eye disorders				
Blurred vision				
Gastrointestinal disorders				
Abdominal pain				
Diarrhoea				
Nausea				
Vomitting				

Short title:	ISAP / SAP Template

Worst reported adverse event	All cohorts			
	Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+		
General disorders and administration site conditions				
Chills				
Fatigue				
Fever/pyrexia				
Leg swelling				
Lymphadenopathy				
Immune system disorders				
Anaphylaxis				
Hypersensitivity				
Injury, poisoning and procedural complications				
Injection site pain				
Swelling				
Skin bruising				
Musculoskeletal and connective tissue disorders				
Arthralgia				
Leg pain				
Myalgia				

Short title:	ISAP / SAP Template

Worst reported adverse event	All cohorts			
	Grade (n (%))		95% CI (any grade)	Total CRFs
	1-2	3+		
Nervous system disorders				
Facial paralysis				
Headache				
Seizures				
Psychiatric disorders				
Anxiety				
Confusion				
Respiratory, thoracic and mediastinal disorders				
Dyspnea				
Skin and sub-cutaneous tissue disorders				
Petechiae				
Rash				
Spontaneous bleeding				
Vascular disorders				
Hypertension				
Hypotension				
Other toxicities (specify)				

Short title:	ISAP / SAP Template

Table 33: SAE line listing

Event Number	Cohort	Event Name	Grade	Seriousness	Event onset date	Event resolved date	IMP	Last admin date	Reviewer category	Overall Category	Comments

Short title:	ISAP / SAP Template

Table 34: SAEs, SARs and SUSARs by cohort and overall

	Haematological malignancies		Solid tumours		Renal and hepatic disorders		Inflammatory disorders		All cohorts
	1A	1B	2A	2B	3A	3B	4A	4B	
SAEs (n (%))									
SARs (n (%))									
SUSARs (n (%))									

Short title:	ISAP / SAP Template

Table 35: Post-treatment SARS-CoV-2 nucleocapsid antibodies (anti-SARS-CoV-2 N protein total IgG) dynamics

	Haematological malignancies		Solid tumours		Renal and hepatic disorders		Inflammatory disorders		Overall
	1A	1B	2A	2B	3A	3B	4A	4B	
SARS-CoV-2 nucleocapsid antibodies									
Negative/low at baseline (n (%))									
Post treatment increase to high (n (%))									
Day									
28									
56									
112									
180									
Negative at baseline to									
Low (n (%))									
High (n (%))									
Low at baseline to high (n (%))									
Cut-off index (median (IQR; range))									
Day									
28									
56									
112									

Short title:	ISAP / SAP Template

	Haematological malignancies		Solid tumours		Renal and hepatic disorders		Inflammatory disorders		Overall
	1A	1B	2A	2B	3A	3B	4A	4B	
180									

Short title:	ISAP / SAP Template

Table 36: SARS-CoV-2 infection variants, incidence rates, risk difference, symptoms and severity

	Cohort												
	Haematological malignancies (n=)			Solid tumours (n=)			Renal and hepatic disorders (n=)			Inflammatory disorders (n=)			All cohorts
	1A	1B	Overall	2A	2B	Overall	3A	3B	Overall	4A	4B	Overall	
SARS-CoV-2 infection (n (%); 95% CI)													
Variant													
Victoria													
Delta													
Omicron													
Other (specify)													
Incidence rate ratios (95%CI; p-value)													
Cohort 1 vs cohort 2													
Cohort 1 vs cohort 3													
Cohort 1 vs cohort 4													
Cohort 2 vs cohort 3													
Cohort 2 vs cohort 4													
Cohort 3 vs cohort 4													
Risk difference (95%CI; p-value)													
Cohort 1 vs cohort 2													

Short title:	ISAP / SAP Template

	Cohort												
	Haematological malignancies (n=)			Solid tumours (n=)			Renal and hepatic disorders (n=)			Inflammatory disorders (n=)			All cohorts
	1A	1B	Overall	2A	2B	Overall	3A	3B	Overall	4A	4B	Overall	
Cohort 1 vs cohort 3													
Cohort 1 vs cohort 4													
Cohort 2 vs cohort 3													
Cohort 2 vs cohort 4													
Cohort 3 vs cohort 4													
Test used for confirmation													
PCR test (or other validated molecular assay)													
Lateral flow test													
Symptoms (n (%))													
High temperature or shivering													
New continuous cough													
Loss or change to sense of smell or taste													
Shortness of breath													
Feeling tired or exhausted													
Aching body													
Sore throat													
Blocked or runny nose													

Short title:	ISAP / SAP Template

	Cohort												
	Haematological malignancies (n=)			Solid tumours (n=)			Renal and hepatic disorders (n=)			Inflammatory disorders (n=)			All cohorts
	1A	1B	Overall	2A	2B	Overall	3A	3B	Overall	4A	4B	Overall	
Loss of appetite													
Diarrhoea													
Feeling sick or being sick													
Other (specify)													
Symptoms associated with an SAE													
Severity (n (%))													
Uninfected; no viral RNA detected													
Ambulatory mild disease													
Asymptomatic; viral RNA detected													
Symptomatic; independent													
Symptomatic; assistance needed													
Hospitalised moderate disease													
Hospitalised; no oxygen therapy													

Short title:	ISAP / SAP Template

	Cohort												
	Haematological malignancies (n=)			Solid tumours (n=)			Renal and hepatic disorders (n=)			Inflammatory disorders (n=)			All cohorts
	1A	1B	Overall	2A	2B	Overall	3A	3B	Overall	4A	4B	Overall	
Hospitalised; oxygen by mask or nasal prongs													
Hospitalised severe disease													
Hospitalised; oxygen by NIV or high flow													
Intubation and mechanical ventilation, pO_2/FiO_2 150 or SpO_2/FiO_2 200													
Mechanical ventilation pO2/FiO2 < 150 (SpO2/FiO2 < 200) or vasopressors													
Mechanical ventilation pO_2/FiO_2 150 and vasopressors, dialysis, or ECMO.													
Dead													

Short title:	ISAP / SAP Template

Table 37: COVID-19 Risk behaviour changes over time, by cohort and overall

	Baseline (n (%))					Day 112 (n (%))					Day 180 (n (%))									
	Cohort					Cohort					Cohort									
How often did you visit friends or relatives outside of your household?	1	2	3	4	All	1	2	3	4	All	1	2	3	4	All					
In the past 12 months																				
Every day																				
A few times a week																				
A few times a month																				
Once a month																				
Not at all																				
In the past month																				
Every day																				
A few times a week																				
A few times a month																				
Once a month																				
Not at all																				
How often did you have visitors (friends, family, caregivers, housekeepers or others) in your home?																				
In the past 12 months																				

Short title:	ISAP / SAP Template

	Baseline (n (%))					Day 112 (n (%))					Day 180 (n (%))									
	Cohort					Cohort					Cohort									
Every day																				
A few times a week																				
A few times a month																				
Once a month																				
Not at all																				
In the past month																				
Every day																				
A few times a week																				
A few times a month																				
Once a month																				
Not at all																				
How often did you use public transportation (bus, taxi, train)?																				
In the past 12 months																				
Every day																				
A few times a week																				
A few times a month																				
Once a month																				
Not at all																				
In the past month																				
Every day																				

Short title:	ISAP / SAP Template

	Baseline (n (%))					Day 112 (n (%))					Day 180 (n (%))									
	Cohort					Cohort					Cohort									
A few times a week																				
A few times a month																				
Once a month																				
Not at all																				
How often did you go out for shopping (e.g. grocery shopping or any other shopping?																				
In the past 12 months																				
Every day																				
A few times a week																				
A few times a month																				
Once a month																				
Not at all																				
In the past month																				
Every day																				
A few times a week																				
A few times a month																				
Once a month																				
Not at all																				

Short title:	ISAP / SAP Template

	Baseline (n (%))					Day 112 (n (%))					Day 180 (n (%))									
	Cohort					Cohort					Cohort									
How often did you physically attend work/school/ college/university classes?																				
In the past 12 months																				
Every day																				
A few times a week																				
A few times a month																				
Once a month																				
Not at all																				
In the past month																				
Every day																				
A few times a week																				
A few times a month																				
Once a month																				
Not at all																				
Have you ever isolated from household members?																				
In the past 12 months																				
Every day																				
A few times a week																				
A few times a month																				
Once a month																				

Short title:	ISAP / SAP Template

	Baseline (n (%))					Day 112 (n (%))					Day 180 (n (%))									
	Cohort					Cohort					Cohort									
Not at all																				
In the past month																				
Every day																				
A few times a week																				
A few times a month																				
Once a month																				
Not at all																				

Table 38: Average (mean/median;SD/IQR) COVID risk behaviour scores over time and by cohort

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Question	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
How often did you visit friends or relatives outside of your household?								
In the past 12 months								
Baseline								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Question	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Day 112								
Day 180								
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
In the past month								
Baseline								
Day 112								
Day 180								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Question	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
How often did you have visitors (friends, family, caregivers, housekeepers or others) in your home?								
In the past 12 months								
Baseline								
Day 112								
Day 180								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Question	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
In the past month								
Baseline								
Day 112								
Day 180								
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Question	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
How often did you use public transportation (bus, taxi, train)?								
In the past 12 months								
Baseline								
Day 112								
Day 180								
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Question	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
In the past month								
Baseline								
Day 112								
Day 180								
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Question	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
How often did you go out for shopping (e.g. grocery shopping or any other shopping?								
In the past 12 months								
Baseline								
Day 112								
Day 180								
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
In the past month								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Question	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Baseline								
Day 112								
Day 180								
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
How often did you physically attend work/school/ college/university classes?								
In the past 12 months								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Question	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Baseline								
Day 112								
Day 180								
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
In the past month								
Baseline								
Day 112								
Day 180								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Question	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
Have you ever isolated from household members?								
In the past 12 months								
Baseline								
Day 112								
Day 180								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Question	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
In the past month								
Baseline								
Day 112								
Day 180								
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Question	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								

Scoring system	
Every day	5
A few times a week	4
A few times a month	3
Once a month	2
Not at all	1

Short title:	ISAP / SAP Template

Table 39: Responses to EQ5D-5L questionnaires by visit and cohort

Dimension	Baseline (n (%))					Day 112 (n (%))					Day 180 (n (%))									
	Cohort					Cohort					Cohort									
	1	2	3	4	All	1	2	3	4	All	1	2	3	4	All					
Mobility (walking about)																				
No problems																				
Slight problems																				
Moderate problems																				
Severe problems																				
Unable to walk about																				
Self-care (washing or dressing)																				
No problems																				
Slight problems																				
Moderate problems																				
Severe problems																				
Unable to wash or dress myself																				
Usual Activities (e.g work, study, housework, family or leisure activities)																				
No problems																				
Slight problems																				

Short title:	ISAP / SAP Template

Dimension	Baseline (n (%))					Day 112 (n (%))					Day 180 (n (%))									
	Cohort					Cohort					Cohort									
Moderate problems																				
Severe problems																				
Unable to do usual activities																				
Pain/discomfort																				
No pain or discomfort																				
Slight pain or discomfort																				
Moderate pain or discomfort																				
Severe pain or discomfort																				
Extreme pain or discomfort																				
Anxiety/depression																				
Not anxious/depressed																				
Slightly anxious/depressed																				
Moderately anxious/depressed																				
Severely anxious/depressed																				
Extremely anxious/depressed																				

Table 40: Median EQ5D-5L scores by visit and cohort; comparisons between cohorts and time vs cohort effects

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Dimension	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Mobility score (median (IQR;n)								
Baseline								
Day 112								
Day 180								
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
Self-care score (median (IQR;n)								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Dimension	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Baseline								
Day 112								
Day 180								
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
Usual activities score (median (IQR;n)								
Baseline								
Day 112								
Day 180								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Dimension	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
Pain/discomfort score (median (IQR;n)								
Baseline								
Day 112								
Day 180								
Mann-Whitney test p-value								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Dimension	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
Anxiety/depression score (median (IQR;n)								
Baseline								
Day 112								
Day 180								
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Dimension	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
Visual analogue scale score (median (IQR;n))								
Baseline								
Day 112								
Day 180								
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								

Short title:	ISAP / SAP Template

Scoring system

Mobility	
No problems	1
Slight problems	2
Moderate problems	3
Severe problems	4
Unable to walk about	5
Self-care (washing or dressing)	
No problems	1
Slight problems	2
Moderate problems	3
Severe problems	4
Unable to wash or dress myself	5
Usual Activities (e.g work, study, housework, family or leisure activities)	
No problems	1
Slight problems	2
Moderate problems	3
Severe problems	4
Unable to do usual activities	5
Pain/discomfort	
No pain or discomfort	1

Short title:	ISAP / SAP Template

Slight pain or discomfort	2
Moderate pain or discomfort	3
Severe pain or discomfort	4
Extreme pain or discomfort	5
Anxiety/depression	
Not anxious/depressed	1
Slightly anxious/depressed	2
Moderately anxious/depressed	3
Severely anxious/depressed	4
Extremely anxious/depressed	5

Short title:	ISAP / SAP Template

Table 41: Median PROMIS Global Health v1.2 scores by visit and cohort; comparisons between cohorts and time vs treatment effects

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Dimension	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Global Mental Health score (median (IQR;n))[1]								
Baseline								
Day 112								
Day 180								
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
Global Physical Health score (median (IQR;n))[2]								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Dimension	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Baseline								
Day 112								
Day 180								
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
Global01 score (median (IQR;n))[3]								
Baseline								
Day 112								
Day 180								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Dimension	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Mann-Whitney test p-value								
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								
Global09 score (median (IQR;n))[4]								
Baseline								
Day 112								
Day 180								
Mann-Whitney test p-value								

Short title:	ISAP / SAP Template

	Cohort					Effect (adjusted mean difference (95% CI; p-value)) (all cohorts)		Interaction
Dimension	1	2	3	4	All	Time	Cohort	Cohort x time effect p-value
Cohort 1 vs Cohort 2								
Cohort 1 vs Cohort 3								
Cohort 1 vs Cohort 4								
Cohort 2 vs Cohort 3								
Cohort 2 vs Cohort 4								
Cohort 3 vs Cohort 4								

Items from PROMIS Global Health v1.2 questionnaire:
1=Combined score from Global Mental Health Items 02, 04, 05 and 10
2=Combined score from Global Physical Health Items 03, 06, 07 and 08 from PROMIS v1.2 questionnaire
3= Individual score from Global Health Item 01 (In general, would you say your health is:)
4=Individual score from Global Health item 09 (To what extent are you able to carry out your everyday physical activities such as walking, climbing stairs, carrying groceries, or moving a chair

Short title:	ISAP / SAP Template

Table 42: Exploratory analysis of anti SARS-CoV-2 anti S-RBD Ig levels between vaccine types and cohorts at each timepoint

	Vaccine		Adjusted GMR (95% CI)*	p-value**
	Comirnaty	Spikevax		
Mean anti-SARS-CoV2 anti-S RBD total Ig concentration (U/ml) (log transformed)-Day 0				
All cohorts***				
Haematological malignancies cohort				
Solid tumours cohort				
Renal and hepatic disorders cohort				
Inflammatory disorders cohort				
Mean anti-SARS-CoV2 anti-S RBD total Ig concentration (U/ml) (log transformed)-Day 28				
All cohorts***				
Haematological malignancies cohort				
Solid tumours cohort				
Renal and hepatic disorders cohort				
Inflammatory disorders cohort				

	Vaccine		Adjusted GMR (95% CI)*	p-value**
	Comirnaty	Spikevax		
Mean anti-SARS-CoV2 anti-S RBD total Ig concentration (U/ml) (log transformed)-Day 56				
All cohorts***				
Haematological malignancies cohort				
Solid tumours cohort				
Renal and hepatic disorders cohort				
Inflammatory disorders cohort				
Mean anti-SARS-CoV2 anti-S RBD total Ig concentration (U/ml) (log transformed)-Day 112				
All cohorts***				
Haematological malignancies cohort				
Solid tumours cohort				
Renal and hepatic disorders cohort				
Inflammatory disorders cohort				
Mean anti-SARS-CoV2 anti-S RBD total Ig concentration (U/ml) (log transformed)-Day 180				
All cohorts***				
Haematological malignancies cohort				
Solid tumours cohort				
Renal and hepatic disorders cohort				
Inflammatory disorders cohort				

* GMR=Geometric mean ratio
** p-value from likelihood ratio test to evaluate cohort and vaccine type interaction term
*** ANCOVA model covariates will be baseline value and cohort

Short title:	ISAP / SAP Template

Table 43: Protocol deviations likely to impact data integrity

Non-compliance number	Date identified	Identified by..	Protocol Version	Section of Protocol relevant to event	Site Name	Participant ID	Categorisation	Description Free Text	Impact on data integrity	Classification	Follow-up Required	Date Follow-up completed