Table S1: Additional authors from the OCTAVE-DUO trial consortium

Affiliation	Name
Patient and Public Representatives on the Trial Management Group with no affiliation	Richard Beesley
	Vicky Churchill
	Elspeth Insch
	Holly Loughton
	Eilean MacDonald
Cancer Research UK Clinical Trials Unit (CRCTU), University of Birmingham, Edgbaston, Birmingham. B15 2TT, UK.	Siân Lax
	Faye Lowe
	Sophia Magwaro
Centre for Cancer Immunology, University of Southampton, Southampton, SO16 6YD, UK	Mark Gradwell
Centre for Clinical Haematology, University Hospitals Birmingham NHS Foundation Trust, Birmingham B15 2SY, UK	Francesca Kinsella
	Hayley Rolfe
Centre for Inflammatory Disease, Department of Immunology and Inflammation, Imperial College London, Hammersmith Campus, Du Cane Road, London W12 0NN UK	Stacey McIntyre
	Paige Mortimer
Clinical Immunology Service, University of Birmingham, Edgbaston, Birmingham. B15 2TT, UK.	Saly Al-Taei
Clinical Immunology, Royal Free Hospital, Hampstead, London. NW3 2QG, UK	Susan Tadros
	Sarita Workman
Clinical Immunology, Royal Free Hospital, Hampstead, London. NW3 2QG, UK and Institute of Immunity and Transplantation, University College London, Hampstead, London NW3 2PF.	Siobhan O Burns
College of Medical, Veterinary & Life Sciences; University of Glasgow, Glasgow; G12 8QQ, UK.	Maxine Arnott
	James Brock
	Andrew Melville
	Aurelie Najm
	Matthew Rutherford
	Flavia Sunzini
COVID Surveillance Unit, Francis Crick Institute, London. NW1 1AT, UK	Lou S Herman
	Agnieszka Hobbs
	Martina Ragno
	Mary Y Wu
Department of Haematology, Sheffield Teaching Hospitals NHS Foundation Trust, Royal Hallamshire Hospital, Sheffield. S10 2JF, UK.	Rachael Selby
Department of Haematology, St James's University Hospital, Leeds. LS9 7TF, UK	Jennifer Clay
Department of Haematology, University Hospital Southampton NHS Foundation Trust, Southampton, SO16 6YD, UK	Clare Hutchison
	Robert Lown
	May N Lwin
Department of Infection, Immunity and Cardiovascular Disease, The Medical School, The University of Sheffield, Sheffield. S10 2RX, UK.	Naomi Meardon
Department of Infectious Diseases, Imperial College London, School of Medicine Chelsea and Westminster Hospital SW10 9NH UK	Peter Kelleher
Dept of Immunology and Inflammation, Imperial College London, UK	Liz Lightstone
Hammersmith Hospital, Du Cane Road, London. W12 0HS, UK	Thomas Walters
Hope Clinical Trial Facility, Leicester Royal Infirmary, Leicester. LE1 5WW, UK	Jayne Denyer
	Rahima Ibrahim
Imperial College Healthcare NHS Trust, Hammersmith Hospital, London W12 OHS	Sarah Gleeson
	Paul Martin
	Stephen McAdoo
Leeds Teaching Hospitals NHS Trust, Leeds General Infirmary, St George Street. LS1 3EX, UK	Helena Baker
National Institute of Health Research, Southampton Clinical Research Facility, University Hospital Southampton NHS Foundation Trust, Southampton, SO16 6YD, UK	Sarah Horswill
	Nina Parungao
	Stephen Saich

NIHR Southampton Clinical Research Facility, University Hospital Southampton NHS Foundation Trust, Southampton, SO16 6YD, UK	James Cullinane
Nuffield Department of Medicine, University of Oxford, Oxford, OX1 2JD, UK.	Sophie Irwin
	Paul Klenerman
	Thomas Marjot
Radcliffe Department of Medicine, University of Oxford, Oxford. OX3 9DU, UK	Ronjon Chakraverty
Rheumatology, University Hospital Southampton NHS Foundation Trust, Southampton, SO16 6YD, UK	Christopher Holroyd
Royal Free Hospital, Hampstead, London. NW3 2QG, UK	Janki Kavi
Sheffield Teaching Hospitals NHS Foundation Trust, Royal Hallamshire Hospital, Sheffield S10 2JF UK	Doreen Trown
Southampton General Hospital, Tremona Road, Southampton. SO16 6YD, UK	Gavin Babbage
St George's Hospital, Cranmer Terrace, Tooting. SW17 0RE, UK	Julia Chackathayil
	Patricia Faria
St James's University Hospital, Beckett St, Harehills, Leeds. LS9 7TF, UK	Karen Ingham
The Francis Crick Institute, London. NW1 1AT, UK	Murad Miah
	Mauro Miranda
	Nicola O'Reilly
	Callie Smith
UCL Cancer Institute, University College London Hospital, London. WC1E 6DD, UK	Kimberley Driver
	Kaylee Gauntlett
University of Glasgow, Glasgow. G12 8QQ, UK	Andrew Farthing
	Suzann Rundell
	Emily Smith
	Andrew Tong
	Kieran Woolcock
University of Oxford, Oxford, OX1 2JD, UK	Daniel Hanke
	Stephen Laidlaw
	Zainab Malik
	Dung Nguyen
	Nicholas Provine
	Tom Tipton
	Victoria Walker

Table S2: Participating sites and recruitment

Name of Site	Principal Investigator	Disease Cohorts Recruited	Total participants recruited
Glasgow Royal Infirmary	Professor Stefan Siebert	Immune-mediated rheumatic diseases	179
John Radcliffe Hospital, Oxford	Professor Eleanor Barnes	Lymphoid malignancy Immune-mediated rheumatic diseases Chronic liver disease Gastrointestinal disease on immune suppressive therapy Haemopoietic stem cell transplant Primary immunodeficiency	218
Hammersmith Hospital, London	Dr Michelle Willicombe	Chronic renal disease	164
Southampton General Hospital	Professor Sean Lim	Lymphoid malignancy Immune-mediated rheumatic diseases Haemopoietic stem cell transplant	63
Royal Hallamshire Hospital, Sheffield	Professor John Snowden	Haemopoietic stem cell transplant	8
University College Hospital, London	Dr Kwee Yong	Lymphoid malignancy Haemopoietic stem cell transplant CAR T-cell therapy	29
St James's Hospital, London	Professor Gordon Cook	Haemopoietic stem cell transplant	5
Leicester Royal Infirmary	Dr Matthew A'Hearne	Lymphoid malignancy	23
St Georges Hospital, London	Dr Mickey Koh	Solid cancer Haemopoietic stem cell transplant	6
Royal Free Hospital, London	Professor Siobhan Burns	Primary immunodeficiency	5
The Queen Elizabeth Hospital, Birmingham	Dr Helen Parry	Solid cancer Lymphoid malignancy Chronic liver disease Haemopoietic stem cell transplant Primary immunodeficiency	104

Table S3: Eligible patient cohorts within OCTAVE-DUO

Solid Cancer Cohort (SC)

Diagnosis of:

- Breast cancer
- Lung cancer

Lymphoid Malignancy Cohort (LM)

Diagnosis of:

- Aggressive B-cell non-Hodgkin's lymphoma (B-NHL)
- Chronic lymphocytic leukaemia (CLL)
- Hodgkin's Lymphoma
- Indolent B-NHL (except CLL and small lymphocytic lymphoma)
- Myeloma

Immune-mediated rheumatic diseases Cohort (IR)

Diagnosis of:

- Rheumatoid arthritis
- Psoriatic arthritis
- Seronegative arthritis
- Spondyloarthritis
- Anti-neutrophil cytoplasm antibodies (ANCA)-associated vasculitis
- Systemic lupus erythematosus (SLE)
- Psoriasis
- Crohn's disease / ulcerative colitis
- Autoimmune hepatitis

Chronic Renal Disease Cohort (CRD)

Diagnosis of:

- End stage kidney disease secondary to any cause
- Renal transplant following end stage kidney disease

Chronic Liver Disease Cohort (CL)

Diagnosis of:

- Liver cirrhosis
- Liver transplantation
- Chronic liver disease (of any stage) on immune suppressive therapy

Gastrointestinal Disease Cohort (GIS)

Diagnosis of:

- Gastrointestinal disease on immune suppressive therapy

Primary immunodeficiency Cohort (PID)

Defined as

- any patient who is on immunoglobulin replacement therapy or any patient with an IgG <4g/l and on prophylactic antibiotics

Haematopoietic Stem Cell Transplant Cohort (HSCT)

Patients previously treated with:

- Autologous or allogenic haematopoietic stem cell transplant for any indication and with any conditioning regimens and intensities, who have not relapsed post-transplant
- CAR T-cell therapies

Chimeric-Antigen Receptor (CAR) T-Cell therapies Cohort

Patients previously treated with:

- CAR T-cell therapies

Table S4: SARS-CoV-2 spike antibody assays – definition of inadequate response

Assay	Antibody non responder (AU/ml)	Antibody low responder (AU/ml)
Abbott	<50	≥50 but <700
Diasorin	Either <33·8 AU/ml for Trimeric S or 15 AU/ml for S1/S2.	For Trimeric S: equal to or >33·8 AU/ml and <400 or For SI/S2: >15 AU/ml and <400 Please Note: if results are available by both methods, both need to be <400
Roche	<0·8	≥0·8 and <400
SIEMENS*	0.0	N/A

* The SIEMENS assay has a binary response (negative or positive). All patients are randomised as non-responders.

AU, arbitrary units.

Note: Other assays with a relative relevant mark of conformity (e.g., UKCA, CE or CE UKNI) could be added following discussion with, and approval by, the Trial Management Group.

Table S5: Classification of disease-directed therapies and the disease cohorts where they were listed

Drug Class	Specific Drugs	IR	GIS	LM & HSCT	SC	CRD	CL
Corticosteroids	Beclomethasone Betamethasone Cortisone Dexamethasone Hydrocortisone Methylprednisolone Prednisolone Triamcinolone	Y (N=33)	Y (N=5)	Y (N =22)	Y (N=0)	Y (N=52)	Y (N =33)
B-cell targeted therapy	Rituximab (Anti-CD20) Daratumumab (Other) Elotuzumab (Other) Isatuximab (Other) Venetoclax (BTK Inhibitor) Ibrutinib (BTK Inhibitor) Acalabrutinib (BTK Inhibitor) Obinutuzumab (Anti-CD20)	Y (N=32)	Y (N=0)	Y (N=99)	-	Y (N=1)	Y (N=3)
Anti-metabolites	Azathioprine Mycophenolate mofetil 6-Mercaptopurine	Y (N=3)	Y (N=18)	-	-	Y (N=85)	Y (N=34)
DMARDs	Methotrexate Leflunomide (Other) Sulphasalazine (Other)	Y (N=96)	Y (N=4)	Y (N=0)	Y (N=0)	Y (N=0)	Y (N=0)
Cytotoxic chemotherapy	Cyclophosphamide Capecitabine Carboplatin Cisplatin Cytarabine Daunorubicin Docetaxel Doxorubicin Epirubicin Etoposide Fludarabine Fluorouracil Gemcitabine Idarubicin Melphalan Mitoxantrone Nab-paclitaxel	-	-	Y (N=6)	Y (N=0)-	Y (N=0)	-

Drug Class	Specific Drugs	IR	GIS	LM & HSCT	SC	CRD	CL
	Paclitaxel						
	Vincristine						
	Vinorelbine						
	Lenalidomide						
	Olaparib						
	Vemurafenib						
	Azacitidine						
	Decitabine						
Hormonal therapies	Aromatase Inhibitor Fulvestrant Tamoxifen Toremifene	-	-	-	Y (N=5)	-	-
Calcineurin inhibitors	Cyclosporine Tacrolimus	Y (N=0)	Y (N=4)	-	-	Y (N=134)	Y (N=32)
Biologic therapies	Sirolimus (Other) Atezolizumab (Other) Durvalumab (Other) Pembrolizumab (Other) Abemaciclib (Other) Afatinib (Other) Bortezomib (Other) Everolimus (Other) Gefitinib (Other) Gemtuzumab ozogamicin (Other) Neratinib (Other) Palbociclib (Other) Pertuzumab (Other) Pomalidomide (Other) Ribociclib (Other) Thalidomide (Other) Trastuzumab (Other) Abatacept (Other) Adalimumab (Anti-TNF) Apremilast (Other) Certolizumab (Anti-TNF) Etanercept (Anti-TNF) Golimumab (Anti-TNF) Guselkumab (Anti-IL23) Infliximab (Anti-TNF) Ixekizumab (Anti-IL17) Sarilumab (Anti-IL6)	Y (N=121)	Y (N=80)	Y (N=5)	Y (N=4)	Y (N=84)	Y (N=2)

Drug Class	Specific Drugs	IR	GIS	LM & HSCT	SC	CRD	CL
	Secukinumab (Anti-IL17)						
	Tocilizumab (Anti-IL6)						
	Ustekinumab (Anti-IL23)						
	Vedolizumab						
	Bosutinib (Other)						
	Brentuximab (Other)						
	Crenolanib (Other)						
	Dasatinib (Other)						
	Gilteritinib (Other)						
	Imatinib (Other)						
	Lestaurtinib (Other)						
	Midostaurin (Other)						
	Nilotinib (Other)						
	Ponatinib (Other)						
	Quizartinib (Other)						
	Sorafinib (Other)						
	Alemtuzumab (Anti-CD52)						
	Anti-thymocyte globulin (ATG) (Other)						
Jak inhibitors	Baricitinib Tofacitinib Upadacitinib Ruxolitinib	Y (N=3)	Y (N=0)	Y (N=2)	-	-	-

BTK: Bruton tyrosine kinase, CR: chronic renal disease, CL: chronic liver disease, DMARDs: Disease-modifying antirheumatic drugs, GI: Gastrointestinal disease on immune suppressive therapy, HSCT: haemopoietic stem cell transplant, IR: Immune-mediated rheumatic diseases, LM; lymphoid malignancies, SC: Solid cancer, IL: Interleukin, TNF: Tumour necrosis factor.

NB. Y indicates whether each patient cohort were likely to be treated with each concomitant drug classification. N indicates the number of patients within each cohort.

Table S6: Patient comorbidities split by treatment arm

Characteristic	BNT162b2 (Arm 1) N = 377	mRNA-1273 (Arm 2) N = 374	NVX-CoV2373 (Arm 3) N = 53	Overall N = 804
Cardiovascular Disease	**61 (16·58%)**	**56 (15·39%)**	**8 (16·00%)**	**125 (15·98%)**
Unknown	9	10	3	22
History of stroke	**17 (4·60%)**	**14 (3·83%)**	**3 (6·00%)**	**34 (4·33%)**
Unknown	7	8	3	18
Diabetes	**63 (16·98%)**	**70 (19·07%)**	**6 (12·00%)**	**139 (17·64%)**
Unknown	6	7	3	16
Asthma	**35 (9·43%)**	**32 (8·72%)**	**3 (6·00%)**	**70 (8·88%)**
Unknown	6	7	3	16
Chronic obstructive pulmonary disease (COPD)	**6 (1·62%)**	**8 (2·19%)**	**0 (0%)**	**14 (1·78%)**
Unknown	6	8	3	17
Other chronic lung disease	**17 (4·71%)**	**17 (4·82%)**	**1 (2·00%)**	**35 (4·58%)**
Unknown	16	21	3	40
Hypertension	**125 (33·69%)**	**137 (37·33%)**	**18 (36.00%)**	**280 (35.53%)**
Unknown	6	7	3	16
Cancer (in the last 5 years)	**73 (19·41%)**	**69 (18·80%)**	**32 (62·75%)**	**174 (22·05%)**
Unknown	6	7	2	15
Chronic renal disease	**93 (25·98%)**	**90 (25·57%)**	**1 (2·00%)**	**184 (24·21%)**
Unknown	19	22	3	44
Liver disease	**34 (9·16%)**	**23 (6·28%)**	**1 (2·00%)**	**58 (7·37%)**
Unknown	6	8	3	17
Inflammatory bowel disease	**33 (8·90%)**	**32 (8·72%)**	**1 (2·00%)**	**66 (8·38%)**
Unknown	6	7	3	16
Rheumatologic disease	**106 (28·50%)**	**97 (26·43%)**	**4 (8·00%)**	**207 (26·24%)**
Unknown	5	7	3	15
Human immunodeficiency virus (HIV)	**2 (0·54%)**	**1 (0·27%)**	**0 (0%)**	**3 (0·38%)**
Unknown	7	7	3	17

Table S7: Patient vaccine timing and COVID-19 history split by treatment arm

Characteristic	BNT162b2 (Arm 1) N = 377	mRNA-1273 (Arm 2) N = 374	NVX-CoV2373 (Arm 3) N = 53	Overall N = 804
Time between 1st and 2nd vaccine (weeks)	**11·00 (9·00, 11·00)**	**11·00 (9·00, 11·00)**	**11·00 (10·00, 11·00)**	**11·00 (9·00, 11·00)**
Time between 2nd and 3rd vaccine (weeks)	**20·00 (17·00, 23·00)**	**20·00 (17·00, 23·00)**	**18·00 (16·50, 23·50)**	**20·00 (17·00, 23·00)**
Previous COVID-19	**16 (4·24%)**	**19 (5·08%)**	**1 (1·89%)**	**36 (4·48%)**
Severity of Previous COVID-19				
Asymptomatic	4 (25·00%)	1 (5·26%)	0 (0%)	5 (13·89%)
Hospitalized for COVID-19 with no Oxygen	1 (6·25%)	1 (5·26%)	0 (0%)	2 (5·56%)
Hospitalized for COVID-19 with Oxygen	2 (12·25%)	3 (15·79%)	0 (0%)	5 (13·89%)
Not Known	0 (0%)	1 (5·26%)	0 (0%)	1 (2·78%)
Symptomatic - Not hospitalized for COVID-19	9 (56·25%)	13 (68·42%)	1 (100·00%)	23 (63·89%)

Table S8: Baseline characteristics split by disease cohort

Characteristic	IR	LM	CRD	GIS	CL	PID	HSCT	SC	CT
	N = 189	N = 178	N = 164	N = 95	N = 82	N = 40	N = 44	N = 10	N = 2
Age (years)									
15-44	35 (18·52%)	11 (6·18%)	30 (18·29%)	56 (58·95%)	9 (10·98%)	10 (25·00%)	8 (18·18%)	2 (20·00%)	1 (50·00%)
45-64	103 (54·50%)	54 (30·34%)	68 (41·46%)	36 (37·90%)	43 (52·44%)	17 (42·50%)	19 (43·18%)	5 (50·00%)	0 (0%)
65-74	36 (19·05%)	62 (34·83%)	47 (28·66%)	3 (3·16%)	26 (31·71%)	9 (22·50%)	17 (38·64%)	3 (30·00%)	1 (50·00%)
75+	15 (7·94%)	51 (28·65%)	19 (11·59%)	0 (0%)	4 (4·88%)	4 (10·00%)	0 (0%)	0 (0%)	0 (0%)
BMI									
Underweight (<18·5)	1 (0·53%)	3 (1·76%)	4 (3·48%)	3 (3·19%)	1 (1·23%)	0 (0%)	0 (0%)	0 (0%)	0 (NA%)
Normal weight (18·5-24·9)	49 (26·20%)	52 (30·59%)	24 (20·87%)	50 (53·19%)	21 (25·93%)	16 (53·33%)	14 (40·00%)	2 (40·00%)	0 (NA%)
Overweight (25-29·9)	67 (35·83%)	82 (48·24%)	46 (40·00%)	28 (29·79%)	32 (49·51%)	10 (33·33%)	15 (42·86%)	0 (0%)	0 (NA%)
Obese (30-39·9)	55 (29·42%)	30 (17·65%)	38 (33·04%)	12 (12·77%)	25 (30·86%)	4 (13·33%)	5 (14·29%)	1 (20·00%)	0 (NA%)
Very obese	15 (8·02%)	3 (1·77%)	3 (2·61%)	1 (1·06%)	2 (2·47%)	0 (0%)	1 (2·86%)	2 (40·00%)	0 (NA%)
Missing	2	8	49	1	1	10	9	5	2
Ethnicity									
Black	0 (0%)	2 (1·15%)	16 (9·76%)	0 (0%)	1 (1·23%)	0 (0%)	0 (0%)	0 (0%)	0 (NA%)
East Asian	0 (0%)	1 (0·58%)	5 (3·05%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (NA%)
Mixed Race	1 (0·56%)	2 (1·15%)	1 (0·61%)	2 (2·15%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (NA%)
Other	8 (4·50%)	8 (4·60%)	10 (6·10%)	0 (0%)	0 (0%)	3 (7·89%)	3 (7·90%)	1 (11·11%)	0 (NA%)
South Asian	0 (0%)	4 (2·30%)	42 (25·61%)	2 (2·15%)	3 (3·70%)	0 (0%)	1 (2·63%)	0 (0%)	0 (NA%)
White	169 (94·94%)	157 (90·23%)	90 (54·88%)	89 (95·70%)	77 (95·06%)	35 (92·11%)	34 (89·47%)	8 (88·89%)	0 (NA%)
Missing	11	4	0	2	1	2	6	1	2
Sex									
Female	129 (68·25%)	54 (30·86%)	55 (33·54%)	38 (40·43%)	34 (41·98%)	23 (60·53%)	15 (39·47%)	8 (80·00%)	0 (NA%)
Male	60 (31·75%)	121 (69·14%)	109 (66·46%)	56 (659·57%)	47 (58·02%)	15 (39·47%)	23 (60·53%)	2 (20·00%)	0 (NA%)
Missing	0	3	0	1	1	2	6	0	2
Smoking status									
Current smoker	18 (9·68%)	14 (8·86%)	2 (6·90%)	9 (9·78%)	11 (13·75%)	0 (0%)	1 (3·70%)	0 (0%)	0 (NA%)
Never smoked	106 (56·99%)	76 (48·10%)	21 (72·41%)	53 (57·61%)	40 (50·00%)	27 (71·05%)	17 (62·96%)	4 (50·00%)	0 (NA%)
Not known	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (3·70%)	3 (37·5%)	0 (NA%)

Characteristic	IR	LM	CRD	GIS	CL	PID	HSCT	SC	CT
	N = 189	N = 178	N = 164	N = 95	N = 82	N = 40	N = 44	N = 10	N = 2
Previous smoker	62 (33·87%)	68 (43·04%)	6 (20·69%)	30 (32·61%)	29 (36·25%)	11 (28·95%)	8 (39·63%)	1 (12·5%)	0 (NA%)
Missing	3	20	135	3	2	2	17	2	2
WHO performance status									
0	63 (33·33%)	115 (66·47%)	113 (72·90%)	80 (86·02%)	52 (65·82%)	31 (83·78%)	25 (71·43%)	4 (50·00%)	0 (NA%)
1	78 (41·27%)	48 (27·75%)	35 (22·58%)	11 (11·83%)	17 (21·52%)	3 (8·11%)	8 (22·86%)	4 (50·00%)	0 (NA%)
2	35 (18·52%)	9 (5·20%)	7 (4·52%)	2 (2·15%)	7 (8·86%)	3 (8·11%)	2 (5·71%)	0 (0%)	0 (NA%)
3	13 (6·88%)	1 (0·58%)	0 (0%)	0 (0%)	2 (2·53%)	0 (0%)	0 (0%)	0 (0%)	0 (NA%)
4	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1·27%)	0 (0%)	0 (0%)	0 (0%)	0 (NA%)
Missing	0	5	9	2	3	3	9	2	2

IR: inflammatory/rheumatoid diseases, LM: lymphoid malignancies· CRD: chronic renal disease, GIS: gastrointestinal disease on immune suppressive therapy, CL: chronic liver disease, PID: primary immunodeficiency, HSCT: haemopoietic stem cell transplant, SC: solid cancer, CT: chimeric-antigen receptor T-cell therapies

Table S9: Patient comorbidities split by disease cohort

Characteristic	IR	LM	CRD	GIS	CL	PID	HSCT	SC	CT
	N = 189	N = 178	N = 164	N = 95	N = 82	N = 40	N = 44	N = 10	N = 2
Cardiovascular Disease	**18 (9·58%)**	**36 (20·70%)**	**56 (34·15%)**	**3 (3·37%)**	**5 (6·23%)**	**4 (11·11%)**	**3 (7·50%)**	**0 (0%)**	**0 (0%)**
Unknown	1	4	0	6	2	4	4	1	0
History of stroke	**7 (3·74%)**	**14 (8·05%)**	**11 (6·71%)**	**0 (0%)**	**2 (2·47%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**
Unknown	2	4	0	1	1	5	4	1	0
Diabetes	**20 (10·64%)**	**19 (10·92%)**	**60 (36·59%)**	**5 (5·32%)**	**25 (30·86%)**	**6 (16·67%)**	**4 (10·00%)**	**0 (0%)**	**0 (0%)**
Unknown	1	4	0	1	1	4	4	1	0
Asthma	**24 (12·77%)**	**13 (7·47%)**	**4 (2·44%)**	**9 (9·58%)**	**6 (7·41%)**	**9 (25·00%)**	**5 (12·50%)**	**0 (0%)**	**0 (0%)**
Unknown	1	4	0	1	1	4	4	1	0
Chronic obstructive pulmonary disease (COPD)	**4 (2·13%)**	**5 (2·88%)**	**2 (1·22%)**	**2 (2·13%)**	**1 (1·23%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**
Unknown	1	4	0	1	1	5	4	1	0
Other chronic lung disease	**4 (2·44%)**	**4 (2·30%)**	**12 (7·32%)**	**0 (0%)**	**4 (4·94%)**	**8 (22·22%)**	**2 (5·00%)**	**0 (0%)**	**1 (50·00%)**
Unknown	25	4	0	1	1	4	4	1	0
Hypertension	**50 (26·60%)**	**50 (28·74%)**	**136 (82·93%)**	**7 (7·45%)**	**26 (32·10%)**	**6 (16·67%)**	**5 (12·50%)**	**0 (0%)**	**0 (0%)**
Unknown	1	4	0	1	1	4	4	1	0
Cancer (in the last 5 years)	**5 (2·66%)**	**100 (57·14%)**	**14 (8·54%)**	**2 (2·13%)**	**7 (8·64%)**	**9 (25·00%)**	**27 (67·50%)**	**9 (100·00%)**	**1 (50·00%)**
Unknown	1	3	0	1	1	4	4	1	0
Chronic renal disease	**2 (1·24%)**	**7 (4·05%)**	**161 (98·17%)**	**1 (1·11%)**	**6 (7·41%)**	**2 (5·56%)**	**5 (12·50%)**	**0 (0%)**	**0 (0%)**
Unknown	28	5	0	1	1	4	4	1	0
Liver disease	**5 (2·67%)**	**4 (2·30%)**	**7 (4·27%)**	**6 (6·38%)**	**32 (36·51%)**	**1 (2·78%)**	**3 (7·50%)**	**0 (0%)**	**0 (0%)**
Unknown	2	4	0	1	1	4	4	1	0
Inflammatory bowel disease	**11 (5·85%)**	**3 (1·72%)**	**2 (1·22%)**	**41 (43·62%)**	**3 (3·70%)**	**3 (8·33%)**	**3 (7·50%)**	**0 (0%)**	**0 (0%)**
Unknown	1	4	0	1	1	4	4	1	0
Rheumatologic disease	**178 (94·18%)**	**6 (3·45%)**	**7 (4·27%)**	**5 (5·32%)**	**7 (8·64%)**	**3 (8·33%)**	**0 (0%)**	**1 (11·11%)**	**0 (0%)**
Unknown	0	4	0	1	1	4	4	1	0
HIV	**1 (0·54%)**	**1 (0·58%)**	**1 (0·61%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**
Unknown	2	4	0	1	1	4	4	1	0

IR: inflammatory/rheumatoid diseases, LM: lymphoid malignancies· CRD: chronic renal disease, GIS: gastrointestinal disease on immune suppressive therapy, CL: chronic liver disease, PID: primary immunodeficiency, HSCT: haemopoietic stem cell transplant, SC: solid cancer, CT: chimeric-antigen receptor T-cell therapies

Table S10: Anti-spike Ig response category at trial entry and measured baseline anti-spike Ig levels response

Prior anti-spike Ig response category at trial entry	Response category based on baseline anti-spike Ig levels Pre-3rd vaccine dose		
	Non-responder	Low-responder	Responder
Non-responder	238 (77·78%)	65 (21·24%)	3 (0·98%)
Low-responder	14 (3·31%)	358 (84·63%)	51 (12·06%)

Table S11: Number of responders for each treatment arm split by sex

	BNT162b2 (Arm 1) N =345		mRNA-1273 (Arm 2) N = 335		NVX-CoV2373 (Arm 3) N = 48	
	Female N = 161	Male N = 184	Female N = 160	Male N = 175	Female N = 12	Male N = 36
Non-responder	26 (16·15%)	47 (25·54%)	27 (16·88%)	40 (22·86%)	5 (41·67%)	22 (61·11%)
Low-responder	29 (18·01%)	36 (19·57%)	22 (13·75%)	27 (15·43%)	3 (25·00%)	8 (22·22%)
Responder	106 (65·84%)	101 (54·89%)	111 (69·38%)	108 (61·71%)	4 (33·33%)	6 (16·67%)

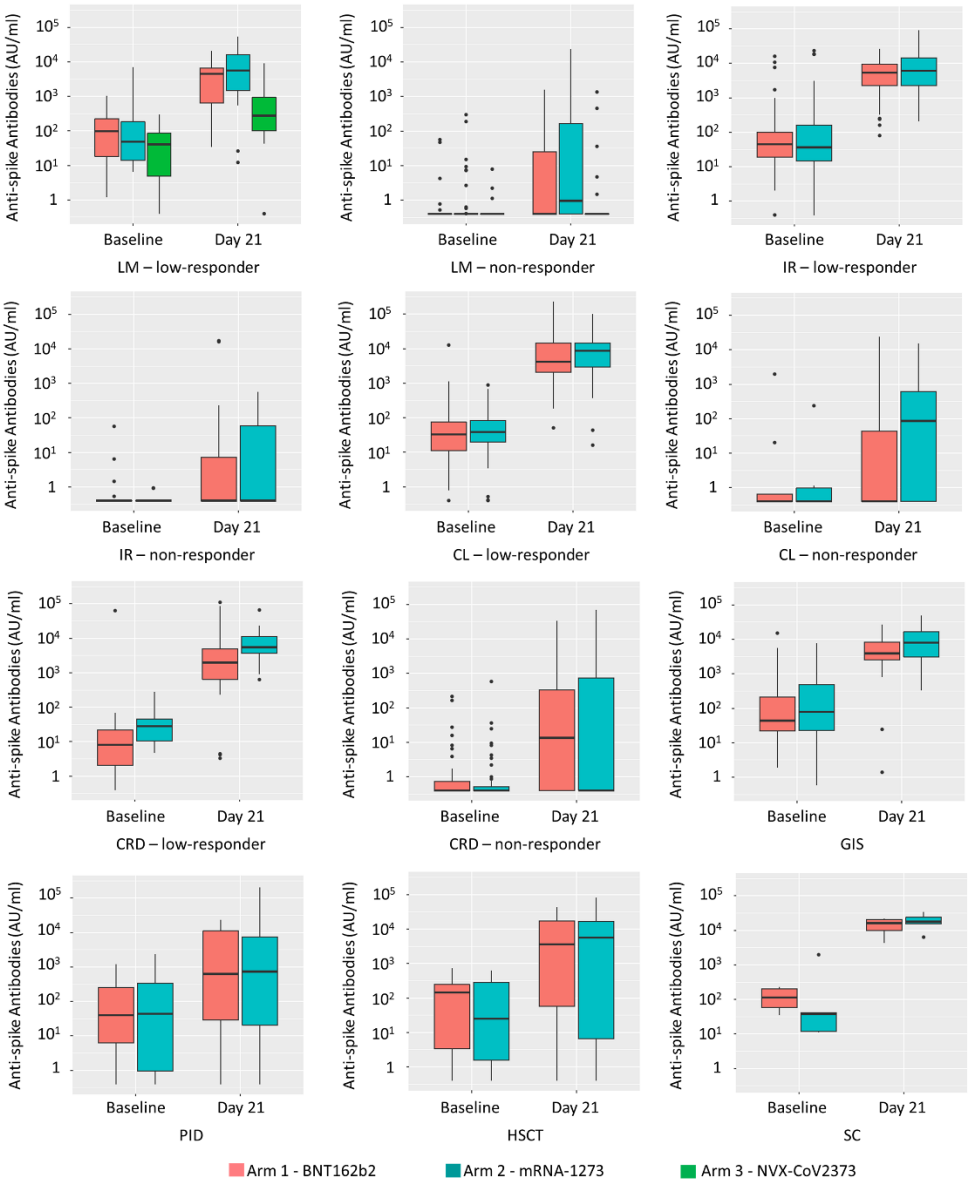

Figure S1. Anti-spike antibody response by disease cohort, responder category at randomisation and vaccine type

Boxplots of pairwise comparisons of anti-spike antibody response between the treatment arms for the different disease groups and level of response at randomisation. Lymphoid malignancy (LM) low responder (LR) mRNA-1273 vs BNT162b2 p=0·92, NVX-CoV2373 vs BNT162b2 p=0·09, NVX-CoV2373 vs mRNA-1273 p=0·01*, non-responder (NR) = mRNA-1273 vs BNT162b2 p=0·14 , NVX-CoV2373 vs BNT162b2 p=0·44, NVX-CoV2373 vs mRNA-1273 p=0·20, Inflammatory rheumatic disease (IR) LR p=0·61, NR p=0·95, chronic liver disease (CL) LR p=0·80 NR p=0·69, chronic renal disease (CRD) LR p=0·017* NR p=0.57, Gastrointestinal disease (GIS) all p=0·11 primary immunodeficiency (PID) all p=0·91, haemopoietic stem cell transplant (HSCT) all p=0·81, solid cancer (SC) all p=0·77.

Statistically significant differences* were only seen between the BNT162b2 and mRNA-1273 arm for low-responders at randomisation in the chronic renal disease cohort and in the lymphoid malignancy cohort of low-responders between NVXCoV2373 and mRNA-1273.

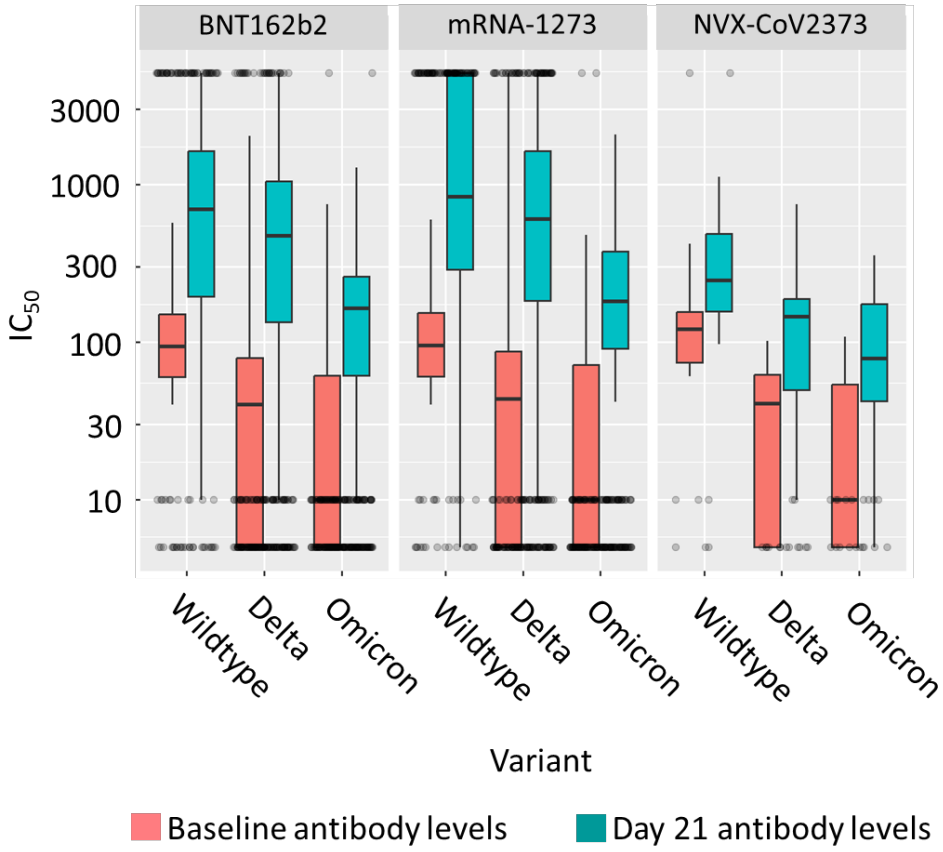

Figure S2. Neutralising antibody titres in participants seropositive post third vaccine by SARS-CoV-2 variant and vaccine type

Assessment of quantifiable neutralising antibody titres (median 50% inhibitory concentration [IC_{50}]) pre-third dose and at day 21 against Ancestral (wildtype), delta (B.1.617.2), and omicron (B.1.1.529, BA.1) variants are shown for each vaccine type, to BNT162b2, mRNA-1273 and NVX-CoV2373.

.

Table S12: Comparison of T-cell response at baseline and post third vaccine dose by disease group

Baseline T-cell Response		Post-vaccine T-cell Response, n (%)	
		Negative	Positive
Chronic liver disease			
	Negative	11 (52·38)	10 (47·62)
	Positive	2 (5·41)	35 (94·59)
	Total	13 (22·41)	45 (77·59)
Chronic renal disease			
	Negative	42 (54·55)	35 (45·45)
	Positive	19 (34·55)	36 (65·45)
	Total	61 (46·21)	71 (53·79)
Gastrointestinal disease on immune suppressive therapy			
	Negative	1 (10·00)	9 (90·00)
	Positive	2 (4·17)	46 (95·83)
	Total	3 (5·17)	55 (94·83)
Haemopoietic stem cell transplant			
	Negative	5 (55·56)	4 (44·44)
	Positive	0 (0·00)	16 (100·00)
	Total	5 (20·00)	20 (80·00)
Inflammatory/rheumatoid diseases			
	Negative	2 (15·38)	11 (84·62)
	Positive	9 (5·42)	157 (94·58)
	Total	11 (6·15)	168 (93·85)
Lymphoid malignancies			
	Negative	23 (41·07)	33 (58·93)
	Positive	5 (7·46)	62 (92·54)
	Total	28 (22·76)	95 (77·24)
Primary immunodeficiency			
	Negative	1 (20·00)	4 (80·00)
	Positive	0 (0·00)	29 (100·00)
	Total	1 (2·94)	33 (97·06)
Solid cancer			
	Negative	0 (-)	0 (-)
	Positive	0 (0·00)	7 (100·00)
	Total	0 (0·00)	7 (100·00)

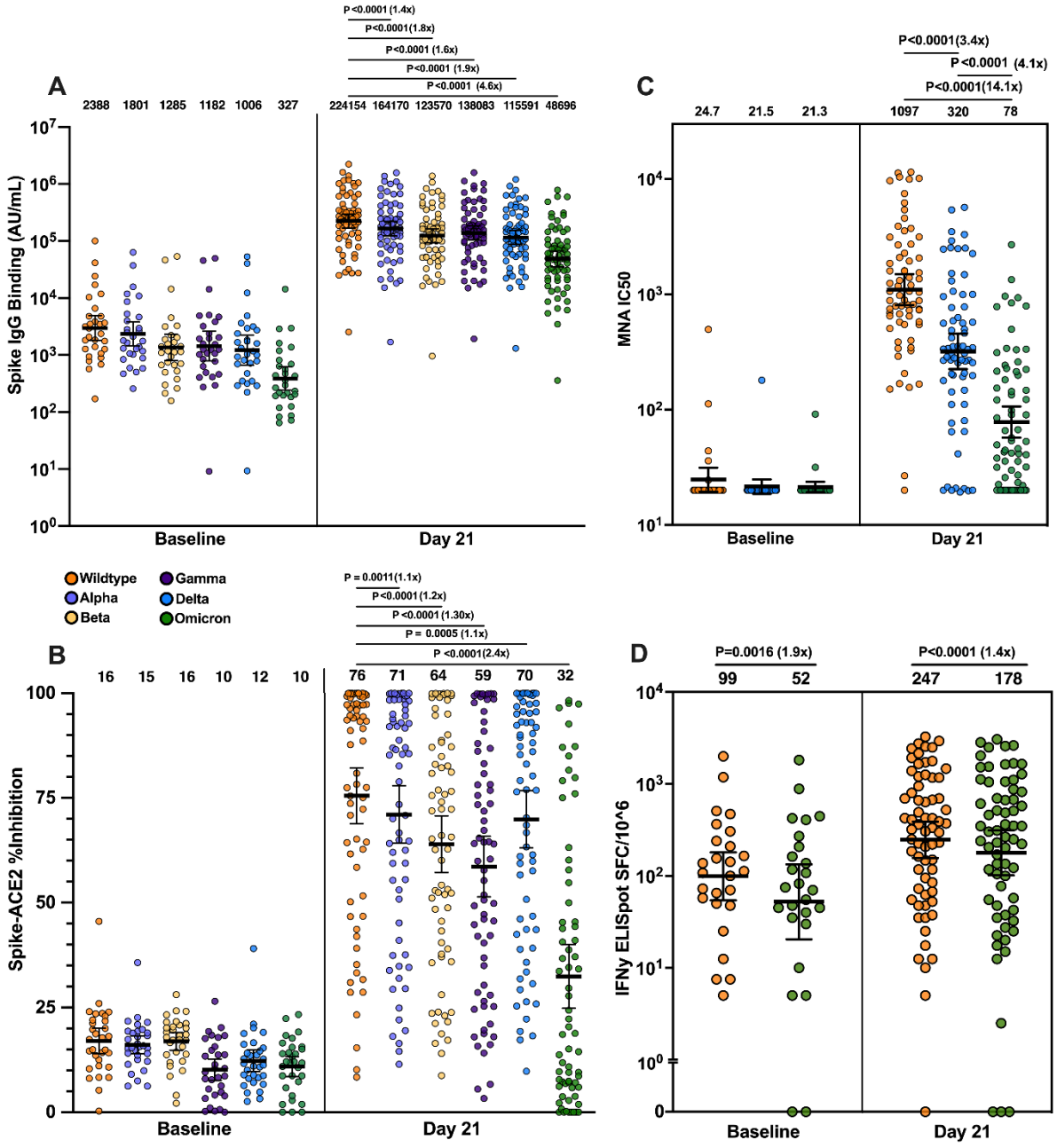

Figure S3. Assessment of response to SARS-CoV-2 variants

Assessment of response to SARS-CoV-2 variants in 72 participants at pre-third dose and 21 days post third dose COVID-19 vaccine timepoints. (A) IgG binding to variant spike measured by MSD assay, (B) percentage (%) inhibition of ACE2 binding to variant spike by participant sera, (C) microneutralisation (MNA) IC_{50} of aSARS-CoV-2 wildtype, Delta variant (B.1.617.2) and Omicron (B.1.1.529, BA.1) and (D) IFNγ ELISpot assay to measure T-cell responses to overlapping peptide pools covering SARS-CoV-2 wildtype and Omicron spike proteins. Lines are geometric mean titre (GMT) with 95% confidence intervals (CI) for A, C & D; mean with 95% CI for B. Fold decrease of GMT is in brackets. Test is Friedman test with corrected Dunn's multiple comparisons test or Wilcoxon test.

Logistic regression modelling

The logistic regression models evaluated the combination of baseline variables that are significantly associated with the odds of response following a third vaccine. The model building process was conducted using a backward stepwise selection approach. The variables considered for use in the model were Vaccine Arm (BNT162b2, mRNA-1273, NVX-CoV2373), anti-spike antibody Response at randomisation (non-responder, low-responder), Prior vaccine received (AstraZeneca, BNT162b2), Disease cohort, Ethnicity, BMI, Age, Sex, Time interval from second vaccine dose, Prior COVID-19 infection, Treatment drugs category.

A dataset was established using the population for analysis which includes all eligible patients who have both baseline and post third vaccination results available. The dataset was then expanded to include all the other variables which were to be included in the model. Participants with any unknown data were removed from the model such that only complete cases were used. For the anti-spike antibody, response was considered as a binary variable; no or yes, where yes includes low-responders and responders. Where values of the anti-spike antibody assay < 0·8 AU/ml is no response and ≥ 0·8 AU/ml is a response.

Table A. Two arm model logistic regression analysis of the anti-spike antibody response to the third vaccine dose with BNT162b2 or mRNA-1273, N=158. Due to a lack of numbers and issues with co-linearity, patients in the solid cancer cohort (n = 4) were excluded from the dataset. additionally, participants from the GIS cohort (n = 82) were removed due to co-linearity issues. These co-linearity issues occur as all the participants in these specific groups become responders post-vaccination. The following treatment variables were removed from the modelling process due to small numbers: jak inhibitors (n=4), cytotoxic chemotherapy (n=5) and hormonal therapies (n=3).

Characteristic	OR	95% CI	p-Value
Prior vaccine			
AstraZeneca			
BNT162b2	1·96	1·08, 3·64	0·029
Disease group			
IR			
LM	0·44	0·18, 1·04	0·065
CRD	1·67	0·38, 7·92	0·50
CL	7·06	1·80, 31·30	0·007
PID	1·11	0·28, 5·26	0·90
HSCT	1·11	0·27, 5·44	0·90
B-cell targeted therapy			
No			
Yes	0·10	0·05, 0·18	<0·001
Corticosteroids			
No			
Yes	0·56	0·31, 1·00	0·051
Anti-metabolites			
No			
Yes	0·14	0·06, 0·31	<0·001
Calcineurin inhibitors			
No			
Yes	0·26	0·07, 0·82	0·026
DMARDs			
No			
Yes	2·54	0·81, 9·10	0·12
Age			
15-44			
45-64	0·74	0·34, 1·57	0·40
65-74	0·55	0·23, 1·26	0·20
75+	0·24	0·09, 0·57	0·002
Prior COVID-19			
No			
Yes	4·70	0·90, 42·3	0·10

CI: Confidence interval, OR: Odds ratio· IR: inflammatory/rheumatoid diseases, LM: lymphoid malignancies· CRD: chronic renal disease, GIS: gastrointestinal disease on immune suppressive therapy, CL: chronic liver disease, PID: primary immunodeficiency, HSCT: haemopoietic stem cell transplant, SC: solid cancer, DMARDs: Disease-modifying antirheumatic drugs.

Table B. Three arm model logistic regression analysis of the anti-spike antibody response to the third vaccine dose with BNT162b2, mRNA-1273 and NVX-CoV2373, N=163, including only the lymphoid malignancies cohort. The following treatment variables were excluded from the modelling as no patients received them: anti- metabolites, jak inhibitors, hormonal therapies, calcineurin inhibitors and DMARDs.

Characteristic	OR	95% CI	p-value
Treatment arm			
BNT162b2 (Arm 1)			
mRNA-1273 (Arm 2)	1·99	0·79, 5·13	0·15
NVX-CoV2373 (Arm 3)	0·38	0·11, 1·16	0·10
Response at randomisation			
Non-responder			
Low-responder	155	27·00, 3411·00	<0·001
Biological therapies			
No			
Yes	0·08	0·00, 1·25	0·12

CI: Confidence interval, OR: Odds ratio·

Table C. Two arm model logistic regression analysis of the T-cell response to the third vaccine dose with BNT162b2 and mRNA-1273, N= 500. Due to a lack of numbers and issues with co-linearity, the solid cancer cohort (n = 4) and mixed-race ethnicity (n = 4) were excluded. These co-linearity issues occur as all the patients in these specific groups become responders post-vaccination. The following treatment variables were removed from the modelling process due to small numbers: Cytotoxic Chemotherapy (n=1) and Hormonal Therapies (n=3).

Characteristic	OR	95% CI	p-Value
Response at randomisation			
Non-responder			
Low-responder	2·04	1·03, 4·11	0·043
Age (years)			
15-44			
45-64	0·59	0·22, 1·47	0·30
65-74	0·35	0·12, 0·96	0·046
75+	0·25	0·07, 0·81	0·024
Prior vaccine			
AstraZeneca			
BNT162b2	0·47	0·24, 0·94	0·032
BMI			
Normal weight (18·5-24·9)			
Underweight (<18·5)	0·87	0·15, 7.20	0·90
Overweight (25-29·9)	2·51	1·20, 5·35	0·015
Obese (30-39·9)	0·76	0·35, 1·60	0·50
Very obese (40+)	0·77	0·18, 4·06	0·70
B-cell targeted therapy			
No			
Yes	8·99	3·17, 30·50	<0·001
Anti-metabolites			
No			
Yes	2·92	1·26, 7·07	0·014
Calcineurin inhibitors			
No			
Yes	0·16	0·04, 0·52	0·004
Time interval from second vaccine	**1·06**	**0·99, 1·13**	**0·10**
Disease group			
IR			
LM	0·19	0·06, 0·58	0·004
CRD	0·51	0·11, 2·49	0·40
GIS	1·16	0·26, 8·28	0·90
CL	0·87	0·25, 6·45	0·80
PID	2·87	0·46, 56·40	0·30
HSCT	0·69	0·16, 3·56	0·60
Corticosteroids			
No			
Yes	0·31	0·16, 0·61	<0·001

CI: Confidence interval, OR: Odds ratio, BMI: Body mass index, IR: inflammatory/rheumatoid diseases, LM: lymphoid malignancies, CRD: chronic renal disease, GIS: gastrointestinal disease on immune suppressive

therapy, CL: chronic liver disease, PID: primary immunodeficiency, HSCT: haemopoietic stem cell transplant, SC: solid cancer.

Table D. Three arm model logistic regression analysis of the T-cell response to the third vaccine dose with BNT162b2, mRNA-1273, and NVX-CoV2373, N= 104, including only the lymphoid malignancies cohort. Due to a lack of numbers and issues with co-linearity, patients of certain ethnicities were excluded from the dataset. Specifically, south Asian (n= 1), black (n = 1), east Asian (n= 1), mixed race (n = 1). Similarly, patients with a BMI categorised as underweight (n = 3) were removed for the same issues. The following treatment variables were excluded from the modelling as no patients or few patients received them: anti-metabolites, jak inhibitors, hormonal therapies, cytotoxic chemotherapies (n=2), calcineurin inhibitors and DMARDs.

Characteristic	OR	95% CI	p-Value
Response at randomisation			
Non-responder			
Low-responder	0·17	0·03, 0·71	0·021
Age (years)			
45-64			
65-74	0·05	0·00, 0·31	0·004
75+	0·27	0·04, 1·62	0·20
Prior vaccine			
AstraZeneca			
BNT162b2	0·13	0·03, 0·51	0·010
Sex			
Female			
Male	0.10	0.01, 0.50	0.01
BMI			
Normal weight (18·5-24·9)			
Overweight (25-29·9)	2·81	0·62, 14·00	0·20
Obese (30-39·9)	78·80	5·33, 2721·00	0·006
Very obese (40+)	0·12	0·00, 28·40	0·50
B-cell targeted therapy			
No			
Yes	9·97	2·55, 49·90	0·002
Time interval from second vaccine	**1·15**	**1·00, 1·37**	**0·065**
Biological therapies			
No			
Yes	0·06	0·00, 1·38	0·079

CI: Confidence interval, OR: Odds ratio, BMI: Body mass index.

Table S13: Baseline characteristics of participants with no serology or T-cell response post third vaccine

Characteristic, n (%)	N = 44
Treatment arm	
BNT162b2 (Arm 1)	15 (34·09)
mRNA-1273 (Arm 2)	24 (54·55)
NVX-CoV2373 (Arm 3)	5 (11·36)
Disease Group	
IR	1 (2·27)
LM	12 (27·27)
CRD	28 (63·63)
GIS	0 (0)
CL	2 (4·55)
PID	0 (0)
HSCT	1 (2·27)
SC	0 (0)
CT	0 (0)
Age (years)	
15-44	7 (15·91)
45-64	13 (29·55)
65-74	17 (38.64)
75+	7 (15·91)
BMI	
Underweight (<18·5)	0 (0)
Normal weight (18·5-24·9)	12 (34·29)
Overweight (25-29·9)	10 (28·57)
Obese (30-39·9)	13 (37·14)
Very obese (40 +)	0 (0)
Unknown	9
Ethnicity	
Black 4 (9·1%)	4 (9·09)
East Asian	1 (2·27)
Other	4 (9·09)
South Asian	9 (20·46)
White	26 (59·09)
Smoking status	
Current smoker	2 (7·69)
Never smoked	11 (42·31)
Previous smoker	13 (50·00)
Unknown	18
WHO performance status	
0	26 (63·41)
1	15 (36·59)
Unknown	3

IR: inflammatory/rheumatoid diseases, LM: lymphoid malignancies· CRD: chronic renal disease, GIS: gastrointestinal disease on immune suppressive therapy, CL: chronic liver disease, PID: primary immunodeficiency, HSCT: haemopoietic stem cell transplant, SC: solid cancer, CT: chimeric-antigen receptor T-cell therapies

Table S14: Comorbidities of participants with no serology or T-cell response post third vaccine

Characteristic, n (%)	N = 44
Cardiovascular Disease	15 (34·09)
History of stroke	5 (11·36)
Diabetes	13 (29·55)
Asthma	5 (11·36)
Chronic obstructive pulmonary disease (COPD)	1 (2·27)
Other chronic lung disease	3 (6·82)
Hypertension	27 (61·36)
Cancer (in the last 5 years)	6 (13·64)
Chronic renal disease	29 (65·91)
Liver disease	1 (2·27)
Inflammatory bowel disease	0 (0)
Rheumatologic disease	3 (6·82)
Human immunodeficiency virus (HIV)	1 (2·27)

Table S15: Treatment details of participants with no serology or T-cell response post third vaccine

Characteristic, n (%)	N = 44
B-cell targeted therapy	6 (13·64)
Corticosteroids	22 (50·00)
Biological therapies	17 (38·64)
Anti-metabolites	25 (56·82)
Jak inhibitors	1 (2·27)
Cytotoxic chemotherapy	1 (2·27)
Hormonal therapies	0 (0)
Calcineurin inhibitors	29 (65·91)
DMARDs	0 (0)

DMARDs: Disease-modifying antirheumatic drugs.

Table S16: Adverse events for each treatment arm split by sex

	BNT162b2 (Arm 1) N = 370		mRNA-1273 (Arm 2) N = 368		NVX-CoV2373 (Arm 3) N = 51	
Adverse Event	**Female N = 170**	**Male N = 200**	**Female N = 173**	**Male N = 195**	**Female N = 13**	**Male N = 38**
Arrhythmia						
No	160 (94·12%)	189 (94·50%)	160 (92·49%)	176 (90.26%)	13 (100.00%)	36 (94.74%)
Yes	4 (2·35%)	1 (0·50%)	6 (3·47%)	4 (2.05%)	0 (0.00%)	1 (2.63%)
Missing	6 (3·53%)	10 (5·00%)	7 (4·05%)	15 (7.69%)	0 (0.00%)	1 (2.63%)
Arthralgia						
No	128 (75·29%)	163 (81·50%)	125 (72·25%)	151 (77.44%)	10 (76.92%)	35 (92.11%)
Yes	36 (21·18%)	27 (13·50%)	41 (23·70%)	29 (14.87%)	3 (23.08%)	2 (5.26%)
Missing	6 (3·53%)	10 (5·00%)	7 (4·05%)	15 (7.69%)	0 (0.00%)	1 (2.63%)
Chest pain						
No	160 (94·12%)	186 (93·00%)	161 (93·06%)	173 (88.72%)	13 (100.00%)	37 (97.37%)
Yes	4 (2·35%)	4 (2·00%)	5 (2·89%)	7 (3.59%)	0 (0.00%)	0 (0.00%)
Missing	6 (3·53%)	10 (5·00%)	7 (4·05%)	15 (7.69%)	0 (0.00%)	1 (2.63%)
Chills						
No	139 (81·76%)	169 (84·50%)	126 (72·83%)	152 (77.95%)	11 (84.62%)	35 (92.11%)
Yes	25 (14·71%)	21 (10·50%)	40 (23·12%)	28 (14.36%)	2 (15.38%)	2 (5.26%)
Missing	6 (3·53%)	10 (5·00%)	7 (4·05%)	15 (7.69%)	0 (0.00%)	1 (2.63%)
Dyspnoea						
No	156 (91·76%)	182 (91·00%)	158 (91·33%)	168 (86.15%)	11 (84.62%)	36 (94.74%)
Yes	8 (4·71%)	8 (4·00%)	8 (4·62%)	12 (6.15%)	2 (15.38%)	1 (2.63%)
Missing	6 (3·53%)	10 (5·00%)	7 (4·05%)	15 (7.69%)	0 (0.00%)	1 (2.63%)
Fever/pyrexia						
No	147 (86·47%)	177 (88·50%)	133 (76·88%)	160 (82.05%)	13 (100.00%)	34 (89.47%)
Yes	17 (10·00%)	13 (6·50%)	33 (19·08%)	20 (10.26%)	0 (0.00%)	3 (7.89%)
Missing	6 (3·53%)	10 (5·00%)	7 (4·05%)	15 (7.69%)	0 (0.00%)	1 (2.63%)
Headache						
No	90 (52·94%)	140 (70·00%)	85 (49·13%)	119 (61.03%)	10 (76.92%)	29 (76.32%)
Yes	74 (43·53%)	50 (25·00%)	81 (46·82%)	61 (31.28%)	3 (23.08%)	8 (21.05%)
Missing	6 (3·53%)	10 (5·00%)	7 (4·05%)	15 (7.69%)	0 (0.00%)	1 (2.63%)
Myalgia						
No	99 (58·24%)	139 (69·50%)	98 (56·65%)	118 (60.51%)	10 (76.92%)	30 (78.95%)
Yes	65 (38·24%)	51 (25·50%)	68 (39·31%)	62 (31.79%)	3 (23.08%)	6 (15.79%)
Missing	6 (3·53%)	10 (5·00%)	7 (4·05%)	15 (7.69%)	0 (0.00%)	2 (5.26%)
Myocarditis						
No	164 (96·47%)	190 (95·00%)	165 (95·38%)	180 (92.31%)	13 (100.00%)	37 (97.37%)
Yes	0 (0·00%)	0 (0·00%)	1 (0·58%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Missing	6 (3·53%)	10 (5·00%)	7 (4·05%)	15 (7.69%)	0 (0.00%)	1 (2.63%)
Nausea						
No	129 (75·88%)	173 (86·50%)	127 (73·41%)	148 (75.90%)	11 (84.62%)	34 (89.47%)
Yes	35 (20·59%)	17 (8·50%)	39 (22·54%)	33 (16.92%)	2 (15.38%)	3 (7.89%)
Missing	6 (3·53%)	10 (5·00%)	7 (4·05%)	14 (7.18%)	0 (0.00%)	1 (2.63%)
Palpitations						
No	162 (95·29%)	189 (94·50%)	163 (94·22%)	177 (90.77%)	13 (100.00%)	36 (94.74%)
Yes	2 (1·18%)	1 (0·50%)	3 (1·73%)	3 (1.54%)	0 (0.00%)	0 (0.00%)
Missing	6 (3·53%)	10 (5·00%)	7 (4·05%)	15 (7.69%)	0 (0.00%)	2 (5.26%)
Vaccination complication						
No	70 (41·18%)	83 (41·50%)	42 (24·28%)	74 (37.95%)	8 (61.54%)	29 (76.32%)
Yes	94 (55·29%)	108 (54·00%)	124 (71·68%)	106 (54.36%)	5 (38.46%)	8 (21.05%)
Missing	6 (3·53%)	9 (4·50%)	7 (4·05%)	15 (7.69%)	0 (0.00%)	1 (2.63%)

Table S17: Number of serious adverse events by category for each treatment arm and disease group

Characteristic, n (%)	Non-fatal/life-threatening SUSAR N = 1	SAR N = 2	Unrelated SAE N = 21	Overall N = 24
Treatment arm				
BNT162b2 (Arm 1)	0 (0)	0 (0)	8 (38·10)	8 (33·33)
mRNA-1273 (Arm 2)	0 (0)	2 (100·00)	10 (47·62)	12 (50·00)
NVX-CoV2373 (Arm 3)	1 (100·00)	0 (0)	3 (14·29)	4 (16·67)
Disease group				
IR	0 (0)	1 (50·00)	4 (19·05)	5 (20·83)
LM	1 (100·00)	0 (0)	8 (38·10)	9 (37·50)
CRD	0 (0)	1 (50·00)	0 (0)	1 (4·17)
GIS	0 (0)	0 (0)	2 (9·52)	2 (8·33)
CL	0 (0)	0 (0)	1 (4·76)	1 (4·17)
PID	0 (0)	0 (0)	1 (4·76)	1 (4·17)
HSCT	0 (0)	0 (0)	4 (19·05)	4 (16·67)
SC	0 (0)	0 (0)	1 (4·76)	1 (4·17)
CT	0 (0)	0 (0)	0 (0)	0 (0)

IR: inflammatory/rheumatoid diseases, LM: lymphoid malignancies· CRD: chronic renal disease, GIS: gastrointestinal disease on immune suppressive therapy, CL: chronic liver disease, PID: primary immunodeficiency, HSCT: haemopoietic stem cell transplant, SC: solid cancer, CT: chimeric-antigen receptor T-cell therapies

Members of the OCTAVE-DUO Trial Steering Committee and independent Data Monitoring Committee

Trial Steering Committee

Prof Andrew Cope (Chair): Professor of Rheumatology and Head of the Centre for Rheumatic Diseases, King's College London

Gill Murphy (PPI representative): Patient & Public Research Panel Member, UCL Blood & Transplant Research Unit

Prof Kevin Dhaliwal: Professor of Molecular Imaging & Healthcare Technology, Centre for Inflammation Research (CIR), University of Edinburgh, Consultant in Respiratory Medicine, Tuberculosis /Infection and Interventional Medicine. Royal Infirmary of Edinburgh, NHS Lothian.

Prof David Adams: Professor of Hepatology, Institute of Immunology and Immunotherapy, University of Birmingham

Tim Waterson (PPI representative): Legal Trustee, Primary Sclerosing Cholangitis (PSC) Support,

Independent Data Monitoring Committee

Professor Christopher Edwards: Consultant Rheumatologist at University Hospital Southampton NHS Foundation Trust, Professor of Clinical Rheumatology at the University of Southampton, Associate Director of Southampton National Institute for Health Research, Director of Southampton Musculoskeletal Research Unit.

Dr Tobias Menne: Consultant Haematologist, Freeman Hospital, Newcastle upon Tyne.

Professor Kerry Hood: Professor of Trials and Director of the Centre for Trials Research, College of Biomedical and Life Sciences, Cardiff University.

Table S18: OCTAVE-DUO Trial Eligibility Criteria

Inclusion Criteria
Aged ≥18 years.
Have an inadequate response to two doses of SARS-CoV-2 vaccine measured at least 14 days after receipt of the second vaccine, defined by SARS-CoV-2 spike antibody response. An inadequate response is defined as: - Antibody non-response: SARS-CoV-2 anti-spike antibodies below the level of detection using the PHE Roche platform [or equivalent assay, see appendix p 5] <0.8 Arbitrary Units (AU)/ml; or - Antibody low-response*: SARS-CoV-2 anti-spike antibodies <0.8 and <400 AU/mL using the Roche platform [or equivalent assay, see appendix p 5]).
Anticipated life expectancy of 6 months or greater.
Fall into one (or more) of the patient cohorts listed in appendix p 4 who will meet disease relevant classification, disease state, and staging according to established international standards.
Participant is willing and able to comply with trial requirements.
For the randomised sub-study only, female participants of childbearing potential* must be willing to ensure that they or their partner use acceptable effective contraceptive methods^ until 3 months after the re-boost immunisation. * Defined as a fertile woman, following menarche and until becoming post-menopausal unless permanently sterile. Permanent sterilisation methods include hysterectomy, bilateral salpingectomy and bilateral oophorectomy. Postmenopausal is defined as no menses for 12 months without an alternative medical cause. ^ Acceptable birth control methods include: - Combined (oestrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation - Progestogen-only hormonal contraception associated with inhibition of ovulation - Intrauterine device (IUD) - Intrauterine hormone-releasing system (IUS) - Bilateral tubal occlusion - Vasectomised partner - Sexual abstinence - Progestogen-only oral hormonal contraception, where inhibition of ovulation is not the primary mode of action - Male or female condom with or without spermicide - Cap, diaphragm or sponge with spermicide Note: Haematopoetic stem cell transfer (HSCT) and chimeric-antigen receptor (CAR)-T cell recipients who have received any SARS-CoV-2 vaccine pre-procedure and are receiving a re-vaccination course post HSCT/CAR-T are eligible for recruitment.
Exclusion Criteria
Receipt of any vaccine within 30 days before trial entry, with the exception of: a SARS-CoV-2 vaccine which is allowed ≥14 days prior; or a flu vaccination which is allowed ≥7 days prior.
For aggressive B-cell non-Hodgkin's lymphoma (B-NHL) or Hodgkin lymphoma only, participants on active systemic treatment or within 4 weeks of completion of systemic treatment.
Any known contraindications as specified in the applicable product information including but not limited to: - Known allergy or hypersensitivity to any of the trial IMPs or any of the trial drug excipients; and - History of anaphylaxis to prior COVID-19 vaccinations, or any component of the vaccine.
In the judgement of the Investigator, the patient is unsuitable to participate in the trial or is unlikely to comply with trial procedures.
For the randomised sub-study only, patients who are pregnant or lactating at trial entry or planning to become pregnant within 3 months after re-vaccination.