THE LANCET

Supplementary appendix

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Contents

Table S1. Clinical characteristics of the main cohort and subgroup of patients who had cellular responses assessed.

Characteristic		Main Cohort N=920 (%)	Subgroup N=106 (%)	p value
Gender	Male Female	604 (65.7) 316 (34.3)	71 (67.0) 35 (33.0)	0.78
Age	Years (Median)	59 (48-67)	53 (42-62)	**<0.0001**
Ethnicity	Caucasian* Black Indoasian Other	404 (43.9) 84 (9.1) 301 (32.7) 131 (14.2)	43 (40.6) 14 (13.2) 31 (29.2) 18 (17.0)	0.51
Cause of ESKD	Polycystic kidney disease Glomerulonephritis* Diabetic nephropathy Urological Unknown Other	107 (11.6) 272 (29.6) 171 (18.6) 72 (7.8) 208 (22.6) 90 (9.8)	8 (7.5) 34 (32.1) 17 (16.0) 8 (7.5) 26 (24.5) 13 (12.3)	0.59
Vaccinated ≤1 year post transplant	Yes No	92 (10.0) 828 (90.0)	45 (42.5) 61 (57.5)	**<0.0001**
Time vaccinated post transplant	Years (Median)	6.6 (6.1-7.3)	2.0 (0.4-7.9)	**<0.0001**
Immunosuppression at diagnosis	CNI monotherapy* CNI/anti-proliferative CNI/steroids CNI/anti-proliferatives/steroids	458 (49.8) 240 (26.1) 56 (6.1) 149 (16.2)	44 (41.5) 30 (28.3) 2 (1.9) 26 (24.5)	0.11

	Anti-proliferatives/steroids Other	4 (0.4) 13 (1.4)	- 4 (3.8)	
Induction immunotherapy	Alemtuzumab* IL2 receptor blocker None/Unknown	636 (69.3) 103 (11.2) 181 (19.7)	64 (60.4) 30 (28.3) 12 (11.3)	0.067
Transplant number	1st ≥2nd	806 (87.6) 114 (12.4)	93 (87.7) 13 (12.3)	0.97
Diabetes	No Yes	592 (64.3) 328 (35.7)	75 (70.8) 31 (29.2)	0.19
Vaccine type	BNT162b2 ChAdOx1	490 (53.3) 430 (46.7)	51 (48.1) 55 (51.9)	0.32
Time between vaccinations	Days (median)	74 (66-77)	63 (63-77)	**<0.0001**
Time of serological test post-boost	Days (median)	31 (27-35)	31 (29-34)	0.38

ESKD – end stage kidney disease, CNI- calcineurin inhibitor *Comparator

Table S2. Demographic characteristics of HCW comparator cohort

Characteristic		HCW (prior infection) n=25 (%)	HCW (infection-naïve) n=40 (%)
Gender	Male Female	11 (44.0) 14 (56.0)	15 (37.5) 25 (62.5)
Age	Years (Median)	32.9 (26.0-47.1)	42.8 (33.4-45.7)
Vaccine type	BNT162b2 ChAdOx1	18 (72.0) 7 (28.0)	32 (80.0) 8 (20.0)
Time between vaccinations	Days (median)	68 (61-75)	66 (61-69)
Time of serological test post-boost	Days (median)	28 (21-29)	24 (21-29)

Table S3. Clinical characteristics associated with seroconversion following SARS-CoV-2 vaccination in 768 infection-naïve kidney transplant recipients

Characteristic		Failure to seroconvert N=343 (%)	Seroconversion N=425 (%)	p value
Gender	Male Female	228 (66.5) 115 (33.5)	280 (65.9) 145 (34.1)	0.86
Age	Years (Median)	60 (49-67)	59 (48-67)	0.30
Ethnicity	Caucasian Black Indoasian Other	164 (47.8) 31 (9.0) 94 (27.4) 54 (15.7)	200 (47.1) 26 (6.1) 143 (33.6) 56 (13.2)	0.14
Cause of ESKD	Polycystic kidney disease Glomerulonephritis Diabetic nephropathy Urological Unknown Other	40 (11.7) 106 (30.9) 69 (20.1) 27 (7.9) 66 (19.2) 35 (10.2)	51 (12.0) 123 (28.9) 75 (17.6) 39 (9.2) 98 (23.1) 39 (9.2)	0.74
Vaccinated ≤1 year post transplant	Yes No	42 (12.2) 301 (87.8)	17 (4.0) 408 (96.0)	**<0.0001**
Time vaccinated post transplant	Years (Median)	6.8 (2.4-13.6)	6.7 (3.2-11.9)	0.78
Immunosuppression at diagnosis	CNI monotherapy* CNI/anti-proliferative CNI/steroids CNI/anti-proliferatives/steroids Anti-proliferatives/steroids Other	97 (28.3) 123 (35.9) 21 (6.1) 95 (27.7) 3 (0.9) 4 (1.2)	284 (66.8) 74 (17.4) 26 (6.1) 36 (8.5) 1 (0.2) 4 (0.9)	**<0.0001**

Induction immunotherapy	Alemtuzumab* IL2 receptor blocker None/Unknown/Other	194 (56.6) 60 (17.5) 89 (25.9)	333 (78.4) 23 (5.4) 69 (16.2)	**<0.0001**
Transplant number	1st ≥2nd	292 (85.1) 51 (14.9)	380 (89.4) 45 (10.6)	0.07
Diabetes	No Yes	210 (61.2) 133 (38.8)	294 (69.2) 131 (30.8)	**0.021**
Vaccine type	BNT162b2 ChAdOx1	141 (41.1) 202 (58.9)	269 (63.3) 156 (36.7)	**<0.0001**
Time between vaccinations	Days (median)	74 (66-78)	75 (68-77)	0.76
Time of serological test post-boost	Days (median)	31 (27-35)	31 (27-35)	0.49

ESKD – end stage kidney disease, CNI-Calcineurin inhibitors, *indicates comparator group

Table S4. Comparison of clinical characteristics of infection-naïve patients receiving ChAdOx1 versus BNT162b2 vaccines

Characteristic		ChAdOx1 N=358 (%)	BNT162b2 N=410 (%)	p value
Gender	Female Male	117 (32.7) 241 (67.3)	143 (34.9) 267 (65.1)	0.52
Age	Years (Median)	59 (49-67)	60 (48-67)	0.45
Ethnicity	Caucasian Black Indoasian Other	175 (48.9) 35 (9.8) 98 (27.4) 50 (14.0)	189 (46.1) 22 (5.4) 139 (33.9) 60 (14.6)	**0.046**
Cause of ESKD	Polycystic kidney disease Glomerulonephritis Diabetic nephropathy Urological Unknown Other	47 (13.1) 113 (31.6) 66 (18.4) 26 (7.3) 74 (20.7) 32 (8.9)	44 (10.7) 116 (28.3) 78 (19.0) 40 (9.8) 90 (22.0) 42 (10.2)	0.62
Vaccinated ≤1 year post transplant	Yes No	39 (10.9) 319 (89.1)	20 (4.9) 390 (95.1)	**0.0025**
Immunosuppression at diagnosis	CNI monotherapy* CNI/anti-proliferative CNI/steroids CNI/anti-proliferatives/steroids Anti-proliferatives/steroids Other	166 (46.4) 94 (26.3) 25 (7.0) 69 (19.3) 2 (0.6) 2 (0.6)	215 (56.4) 103 (25.1) 22 (5.4) 62 (15.1) 2 (0.5) 6 (1.5)	0.33
Induction immunotherapy	Alemtuzumab* IL2 receptor blocker	235(65.6) 48 (13.4)	292 (71.2) 35 (8.5)	0.078

	None/Unknown/Other	75 (20.9)	83 (20.2)	
Transplant number	1st ≥2nd	311 (86.9) 47 (13.1)	361 (88.0) 49 (12.0)	0.62
Diabetes	No Yes	231 (64.5) 127 (35.5)	273 (66.6) 137 (33.4)	0.55
Seroconversion	Yes No	156 (43.6) 202 (56.4)	269 (65.6) 141 (34.4)	**<0.0001**
Time between vaccinations	Days (median)	74 (66-78)	74.5 (68-77)	0.95
Time of serological test post-boost	Days (median)	31 (26-34)	31 (28-35)	0.065

ESKD – end stage kidney disease, CNI=calcineurin inhibitors, *indicates comparator group

Table S5. Clinical characteristics associated with seroconversion in 358 infection-naïve patients receiving ChAdOx1

Variable	Reference Group	Denominator	Response Rate (%)	Univariable		Multivariable	
				OR (95% CI)	p value	OR (95% CI)	p value
Age	≥60	178	69 (38.8)	0.64 (0.44-1.03)	0.068	0.53 (0.33-0.84)	0.008
Gender	Male	241	104 (43.2)	0.95 (0.61-1.48)	0.82		
Ethnicity	Caucasian	175	76 (43.4)	0.99 (0.65-1.50)	0.96		
Cause ESRD	Glomerulonephritis	113	51 (45.1)	1.10 (0.70-1.72)	0.69		
Time of vaccine post-transplant	<1 year	39	7 (17.9)	0.25 (0.11-0.58)	0.0013	0.23 (0.09-0.56)	0.0012
Number of transplants	≥2	47	19 (40.4)	0.86 (0.46-1.61)	0.64		
Transplant induction agent	Alemtuzumab	235	124 (52.8)	3.18 (1.97-5.12)	<0.0001	-	
Maintenance Immunosuppression	CNI monotherapy	166	104 (62.7)	4.52 (2.89-7.06)	<0.0001	4.12 (2.44-6.95)	<0.0001
Diabetes	Yes	127	51 (40.2)	0.8 (0.52-1.25)	0.33		

CNI=calcineurin inhibitors

Table S6. Clinical characteristics associated with seroconversion in 410 infection-naïve patients receiving BNT162b2

Variable	Reference Group	Denominator	Response Rate (%)	Univariable		Multivariable	
				OR (95% CI)	p value	OR (95% CI)	p value
Age	≥60	208	134 (64.4)	0.90 (0.60-1.35)	0.61		
Gender	Male	267	176 (65.9)	1.04 (0.68-1.59)	0.86		
Ethnicity	Caucasian	189	124 (65.6)	0.99 (0.66-1.50)	0.99		
Cause ESRD	Glomerulonephritis	116	72 (62.1)	0.81 (0.52-1.26)	0.34		
Time of vaccine post-transplant	<1 year	20	10 (50.0)	0.51 (0.21-1.25)	0.14	-	
Number of transplants	≥2	49	26 (53.1)	0.55 (0.30-1.0)	0.05	-	
Transplant induction agent	Alemtuzumab	292	209 (71.6)	2.43 (1.57-3.79)	0.0001	-	
Maintenance Immunosuppression	CNI monotherapy	215	180 (83.7)	6.13 (3.87-9.69)	<0.0001	6.34 (3.71-11.06)	<0.0001
Diabetes	Yes	137	80 (58.4)	0.62 (0.41-0.96)	0.03	0.51 (0.32-0.83)	0.006

CNI=calcineurin inhibitors

Table S7. Clinical characteristics associated with seroconversion in 768 infection-naïve patients receiving a SARS-CoV-2 vaccine

Variable	Reference Group	Denominator	Response Rate (%)	Univariable		Multivariable	
				OR (95% CI)	p value	OR (95% CI)	p value
Age	≥60	386	203 (52.6)	1.25 (0.94-1.66)	0.12	0.71 (0.51-0.99)	0.043
Gender	Male	508	280 (55.1)	0.97 (0.72-1.32)	0.97		
Ethnicity	Caucasian	364	200 (54.9)	0.97 (0.73-1.29)	0.84		
Cause ESRD	Glomerulonephritis	229	123 (53.7)	0.91 (0.67-1.24)	0.55		
Time of vaccine post-transplant	<1 year	59	17 (28.8)	0.30 (0.17-0.53)	<0.0001	0.30 (0.16-0.57)	0.0002
Number of transplants	≥2	96	45 (46.9)	0.68 (0.44-1.04)	0.08	-	
Transplant induction agent	Alemtuzumab	527	333 (63.2)	2.78 (2.03-3.82)	<0.0001	1.22 (0.82-1.80)	0.32
Maintenance Immunosuppression	CNI monotherapy	381	284 (74.5)	5.11 (3.75-6.96)	<0.0001	5.20 (3.57-7.57)	<0.0001
Diabetes	Yes	264	131 (49.6)	0.70 (0.52-0.94)	0.02	0.65 (0.46-0.91)	0.014
Vaccine	BNT162b2	410	269 (65.6)	2.47 (1.85-3.31)	<0.0001	2.46 (1.78-3.41)	<0.0001

CNI - calcineurin inhibitors

Table S8. Characteristics of infection-naïve patients undergoing assessment of serological and cellular responses by vaccine type

Characteristic		BNT162b2 N=40 (%)	ChAdOx1 N=39 (%)	p value
Gender	Male Female	30 (75.0) 10 (25.0)	25 (64.1) 14 (35.9)	0.30
Age	Years (Median)	57 (46-64)	50 (39-56)	**0.016**
Ethnicity	Caucasian Black Indoasian Other	18 (45.0) 2 (5.0) 14 (35.0) 6 (15.0)	19 (48.7) 6 (15.4) 8 (20.5) 6 (15.4)	0.30
Cause of ESKD	Glomerulonephritis* Other	10 (25.0) 30 (75.0)	16 (41.0) 23 (59.0)	**0.026**
Vaccinated ≤1 year post transplant	Yes No	3 (7.5) 37 (92.5)	25 (64.1) 14 (35.9)	**<0.0001**
Immunosuppression at diagnosis	CNI monotherapy* Other	21 (52.5) 19 (47.5)	10 (25.6) 29 (74.4)	**0.015**
Induction immunotherapy	Alemtuzumab Other	29 (72.5) 11 (27.5)	16 (41.0) 23 (59.0)	**0.0005**
Transplant number	1^{st} $\geq 2^{nd}$	36 (90.0) 4 (10.0)	33 (84.6) 6 (15.4)	0.47
Diabetes	No Yes	23 (57.5) 17 (42.5)	32 (82.1) 7 (17.9)	**0.018**

ESKD – end stage kidney disease, CNI - calcineurin inhibitors

Table S9. Analysis of clinical characteristics associated with detectable T-cell responses in infection-naïve patients after the first-year post-transplant

Nine of 79 (11.4%) infection-naïve patients had detectable T-cell responses post-vaccination, none of the 28 patients vaccinated within the first-year post-transplant and 9/51 (17.6%) of patients vaccinated after the first post-operative year, p=0.019. Analysis was preformed of independent variables associated with T-cell responses in infection-naïve patients after the first-year post-transplant.

Variable	Reference Group	Univariable	
		OR (95% CI)	p value
Age	≥60 years	0.23 (0.03-1.98)	0.18
Gender	Male	0.50 (0.11-2.19)	0.36
Cause of ESKD	Glomerulonephritis	1.41 (0.30-6.62)	0.66
Number of transplants	≥2	0.93 (0.09-9.03)	0.95
Transplant induction agent	Alemtuzumab	1.75 (0.32-9.55)	0.52
Maintenance Immunosuppression	CNI monotherapy	0.17 (0.19-3.78)	0.17
Vaccine	BNT1262b2	1.40 (0.25-7.72)	0.70
Diabetes	Yes	1.3 (0.30-5.57)	0.72

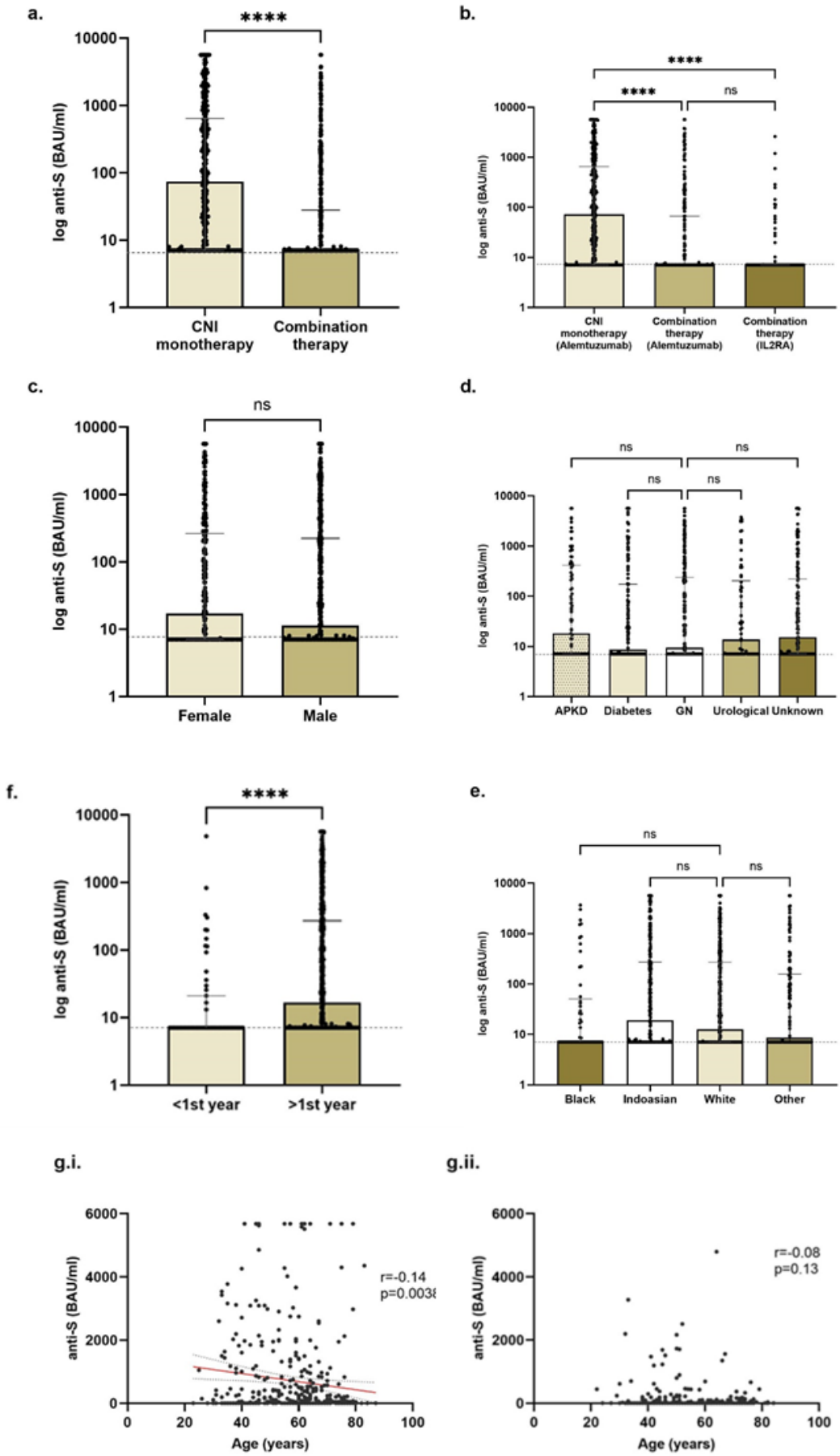
Table S10. Characteristics associated with lack of detectable immunological (serological and T-cell) response in 79 infection-naïve transplant patients

Variable	Reference Group	Denominator	Event rate (%)	Univariable		Multivariable	
				OR (95% CI)	p value	OR (95% CI)	p value
Age	≥60	23	10 (43.5)	0.95 (0.36-2.54)	0.92		
Gender	Male	55	25 (45.5)	1.17 (0.44-3.08)	0.76		
Ethnicity	Caucasian	37	16 (43.2)	0.92 (0.38-2.25)	0.86		
Cause ESKD	Glomerulonephritis	26	8 (30.8)	0.43 (0.16-1.15)	0.09	-	
Time of vaccine post-transplant	<1 year	28	5 (17.9)	0.15 (0.5-0.46)	0.0009	0.19 (0.04-0.96)	0.045
Number of transplants	≥2	10	4 (40.0)	0.82 (0.21-3.16)	0.77		
Transplant induction agent	Alemtuzumab	45	27 (60.0)	4.88 (1.87-13.79)	0.0017	1.89 (0.49-7.35)	0.30
Maintenance Immunosuppression	CNI monotherapy	31	25 (80.6)	15.83 (5.11-49.06)	<0.0001	13.3 (3.68-48.14)	<0.0001
Diabetes	Yes	24	11 (45.8)	1.09 (0.42-2.87)	0.86		
Vaccine	BNT162b2	40	25 (62.5)	4.83 (1.85-12.65)	0.0013	1.63 (0.42-6.55)	0.46

CNI - calcineurin inhibitors

Figure S1. Correlation between anti-S concentrations and clinical characteristics in infection-naïve patients.

a. Kidney transplant patients who were receiving calcineurin inhibitor (CNI) monotherapy had significantly higher anti-S concentrations, 75 (7.1-646) BAU/ml, compared with patients receiving CNI in combination with anti-proliferative agents (mycophenolate mofetil or azathioprine), with or without corticosteroids, 7.1 (7.1-28) BAU/ml, $p<0.0001$
b. Comparing patients receiving combination therapy alone, there was no difference between those who had received Alemtuzumab induction, 7.1 (7.1-67) BAU/ml compared with IL-2 receptor antibodies, 7.1 (7.1-7.12) BAU/ml, $p=0.06$. Comparing patients who received Alemtuzumab as induction alone, those who are maintained on CNI monotherapy, 73 (7.1-656) BAU/ml, had significantly higher anti-S than those on combination therapy, $p<0.0001$.
c. There was no difference in anti-S between females, 17 (7.1-264) BAU/ml compared with males, 11 (7.1-223) BAU/ml, $p=0.76$
d. There was no correlation between cause of end stage kidney disease (ESKD) and anti-S concentrations. Patients with ESKD secondary to diabetes had a median anti-S concentration of 9 (7.1-174) BAU/ml, polycystic kidney disease (APKD), 18 (7.1-415) BAU/ml, Glomerulonephritis (GN), 9 (7.1-238), Urological causes of ESKD, 14 (7.1-205) BAU/ml, and unknown causes of ESKD, 15 (7.1-221) BAU/ml, $p=0.83$
e. There was no correlation between ethnicity and anti-S concentrations. Patients from Indoasian, Black and White backgrounds having a median anti-S concentration of 19 (7.1-272), 7.1 (7.1-51) and 13 (7.1-270) respectively, $p=0.13$.
f. Patients who were within their first-year post-transplant when vaccinated had significantly lower anti-S, 7.1 (7.1-21) BAU/ml compared with those patients who were vaccinated after the 1st year, 17 (7.1-271) BAU/ml, $p<0.0001$.
g. A significant inverse correlation was seen between anti-S response and age in patients who received BNT162b2, $r=-0.14$, $p=0.0038$ (i), but not in patients who received ChAdOx1, $r=-0.08$, $p=0.13$ (ii).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CNI monotherapy
Combination therapy
b.
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ns
log anti-S (BAU/ml)
CNI monotherapy (Alemtuzumab)
Combination therapy (Alemtuzumab)
Combination therapy (IL2RA)
c.
ns
log anti-S (BAU/ml)
Female
Male
d.
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ns
ns
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log anti-S (BAU/ml)
APKD
Diabetes
GN
Urological
Unknown
f.
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log anti-S (BAU/ml)
<1st year
>1st year
e.
ns
ns
ns
log anti-S (BAU/ml)
Black
Indoasian
White
Other
g.i.
anti-S (BAU/ml)
6000
4000
2000
0
r=-0.14
p=0.003
0
20
40
60
80
100
Age (years)
g.ii.
anti-S (BAU/ml)
r=-0.08
p=0.13
Age (years)

Figure S2. Correlation between anti-S concentrations and diagnostic characteristics in patients with prior infection.

a. Anti-S concentrations in patients who were diagnosed by PCR compared with serology were 324 (111-844) and 758 (172-1985) BAU/ml respectively, p=0.59, in patients receiving ChAdOx1; and 1659 (546-3684) and 2752 (641-5680) BAU/ml respectively, p=0.76, in patients receiving BNT162b2.

b. Anti-S concentrations in patients who were anti-NP positive compared with negative at the time of testing, were 503 (37-2094) and 701 (153-1694) BAU/ml respectively, p=0.91, in patients receiving ChAdOx1; and 2512 (499-5680) and 2350 (780-5022) BAU/ml respectively, p=0.99, in patients receiving BNT162b2

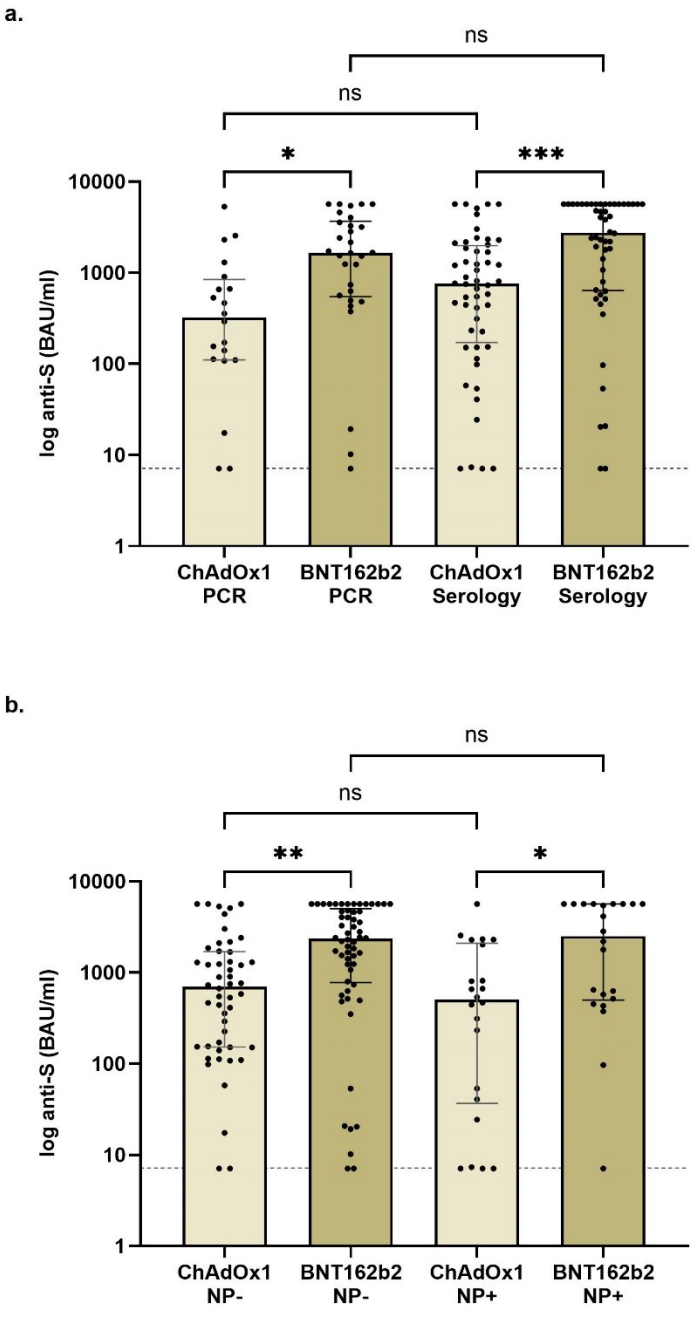

Figure S3. Immunological responses to SARS-CoV-2 vaccination in 106 kidney transplant recipients who underwent paired serological and T cell assessments

a. Anti-S concentrations in infection-naïve patients who received BNT162b2 were higher compared with those patients who had received ChAdOx1, with anti-S concentrations of 34 (7.1-861) BAU/ml and 7.1 (7.1-13) BAU/ml respectively, p=0.0005. These anti-S concentrations in patients were significantly lower than infection naïve HCW who received the corresponding vaccine, with HCW receiving BNT162b2 and ChAdOx1 having a median anti-S of 815 (318-2033), p=0.0003, and 88 (47-395) BAU/ml, p=0.01, respectively. Black dotted line represents 7.1 BAU/ml, the cut off for a positive result.

b. There was no difference in median SFU/10^6 PBMCs in previously exposed patients who received BNT162b2 compared with ChAdOX1, with 160 (20-422) SFU/10^6 PBMCs and 95 (8-144) SFU/10^6 PBMCs respectively, p=0.42. There were no differences between T-cell responses in previously exposed patients and HCW receiving the corresponding vaccine, with HCW receiving BNT162b2 and ChAdOx1 having a median 246 (131-332) SFU/10^6 PBMCs, p=0.63 and 114 (74-216) SFU/10^6 PBMCs, p=0.85 respectively. Data points of 0 SFU/10^6 PBMCs are represented as 0.1 for visualisation on a log scale. Black dotted line indicates threshold for a positive ELISpot, 40 SFU/10^6 PBMCs which was calculated from unvaccinated, infection naïve HCW.

c. There was no difference in anti-S concentrations in patients with prior infection who received BNT162b2, 1238 (497-2829) BAU/ml, compared with ChAdOx1, 366 (119-1273) BAU/ml, p=0.07. There were also no differences between patients and HCW with prior exposure who received BNT162b2, median anti-S 2189 (1236-3303) BAU/ml), p=0.72, or HCW who received ChAdOx1, median anti-S 753 (574-867) BAU/ml, p=0.91. Black dotted line represents 7.1 BAU/ml, the cut off for a positive result.

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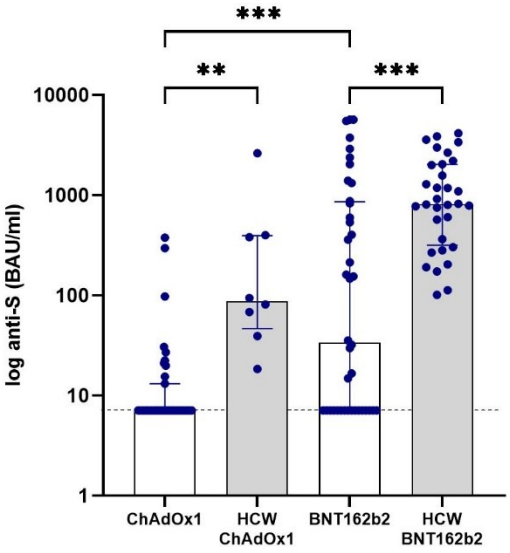
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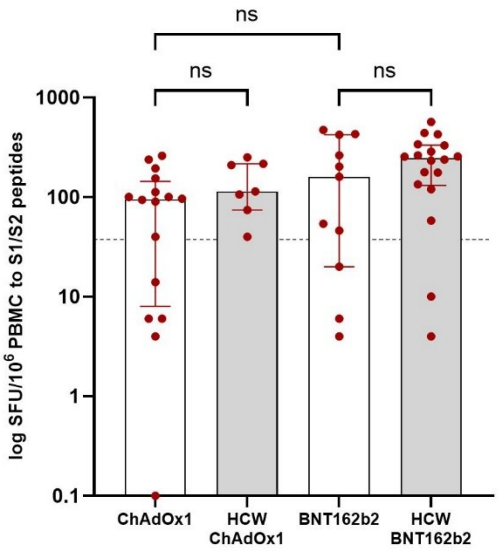
HCW ChAdOx1
BNT162b2
HCW BNT162b2

b.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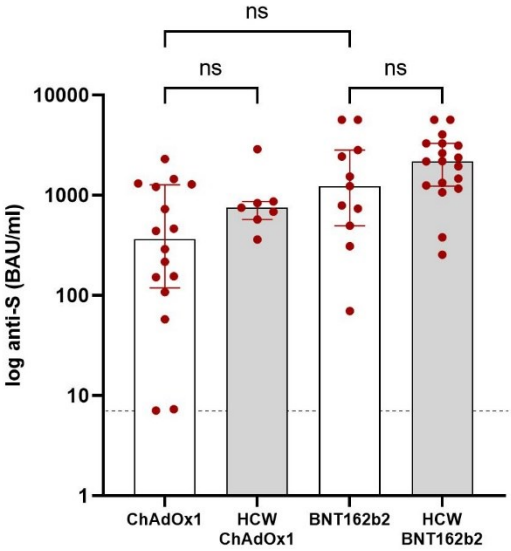
HCW ChAdOx1
BNT162b2
HCW BNT162b2

c.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ns
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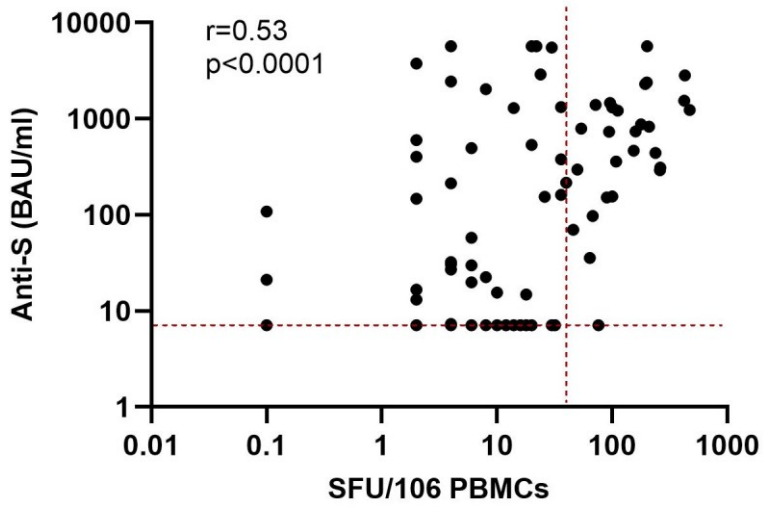
1000
100
10
1
log anti-S (BAU/ml)
ChAdOx1
HCW ChAdOx1
BNT162b2
HCW BNT162b2

Figure S4. Correlation between anti-S (BAU/ml) and T-cell responses (SFU/10^6 PMBCs)



Supplemental Methods

Study population and objectives

We undertook a cohort study of 920 kidney transplant patients who had received 2 doses of either BNT162b2 or ChAdOx1. The aim of the study was to evaluate immune responses to 2 dose vaccination with either BNT162b2 or ChAdOx1. Patients were included if they were able to provide consent for research and were participating in the vaccination programme. Participants were vaccinated as part of their usual care, with two doses of either 0.5mL ChAdOx1-S (Oxford AstraZeneca) or 30ug BNT162b2 (Pfizer-BioNTech) at the specified dosing interval.

All patients were recruited from within Imperial College Renal and Transplant Centre into one of two prospective studies. The first is the OCTAVE study, an Observational Cohort Study of T-cells, Antibodies and Vaccine Efficacy in SARS-CoV-2 in people with chronic diseases and/or secondary immunodeficiency, which is part of the UK COVID-19 Immunity National Core Study Programme. The OCTAVE study was approved by the Health Research Authority, Research Ethics Committee (Reference:21/HRA/0489). The second study is a prospective longitudinal study 'The effect of COVID-19 on Renal and Immunosuppressed patients', sponsored by Imperial College London. This study was approved by the Health Research Authority, Research Ethics Committee (Reference: 20/WA/0123).

A subgroup of the first 106 (11.5%) patients recruited underwent more in-depth immunological analysis of serological and cellular responses to SARS-CoV2 vaccination. A group of 65 healthcare workers (HCW), with a median age of 38 (30-46) years, were used as a comparator. Fifty and 15 HCW received the BNT162b2 and ChAdOx1 vaccines, respectively. The median interval between vaccinations in the HCW was 68 (61-70) days, with a median time to sampling post-vaccination of 28 (21-28) days.

Anonymised data were collected on age, gender, ethnicity, primary renal disease, diabetes, induction and maintenance immunosuppression, date(s) and number of renal transplants. Under the terms of our ethical approval for healthy volunteers data were collected only on age, gender and ethnicity.

Serological testing

Serum was tested for antibodies to both the nucleocapsid protein (anti-NP) and spike protein (anti-S). Anti-NP was tested using the Abbott Architect SARS-CoV-2 IgG 2 step chemiluminescent immunoassay (CMIA) according to manufacturer's instructions. This is a non-quantitative assay and samples were interpreted as positive or negative with a threshold index value of 1.4. The presence of anti-NP was used as a marker of natural infection. For vaccine responses, spike protein antibodies (anti-S IgG) were assessed using the Abbott Architect SARS-CoV-2 IgG Quant II CMIA. Anti-S antibody titres are quantitative with a threshold value of 7.1 BAU/ml for positivity, and an upper level of detection of 5680 BAU/ml.

T cell ELISpot

SARS-CoV-2 specific T-cell responses were detected using the T-SPOT® Discovery SARS-CoV-2 (Oxford Immunotec) according to the manufacturer's instructions. In brief, peripheral blood mononuclear cells (PBMCs) were isolated from whole blood samples with the addition of T-Cell Xtend™ (Oxford Immunotec) if samples were taken more than 12 hours prior to processing. All samples were processed within 24 hours of venepuncture. 250,000 PBMCs were plated into individual wells of a T-SPOT® Discovery SARS-CoV-2 plate. The assay measures immune responses to SARS-CoV-2 spike protein peptide pools (S1 protein and S2 protein), in addition to positive PHA (phytohemagglutinin) and negative controls. Cells were incubated and interferon-γ secreting T cells were detected. Spot forming units (SFU) were detected using an automated plate reader (Autoimmun Diagnostika). Spot count in the negative well was subtracted from spot count for spike protein wells and this was used to calculate spike protein specific responses per 10^6 PBMC. Assays with a negative PHA response were deemed to be failed assays and excluded from analysis (n=1 for HCW and n=2 for transplant recipients). Infection-naïve, unvaccinated participants were used to identify a threshold for a positive response using mean +3 standard deviation SFU/10^6 PBMC, as previously described. This resulted in a cut-off for positivity of 40 SFU/10^6 PBMC (1).

Definition of prior infection

Prior infection was defined serologically or via past PCR positive confirmed infection. The detection of anti-NP on current or historic samples, and the presence of anti-S at baseline (pre-vaccine) or historic samples, was required for the definition of prior infection by serological methods. Serological screening of transplant patients had commenced in our centre in June 2020, and these data were used to aid identification of patients with prior SARS-CoV-2 exposure prior to vaccination. As part of this protocol, patients were initially screened for anti-NP, and those with a subthreshold anti-NP index value (0.25-1.4), underwent confirmatory testing for natural infection by assessing for receptor binding domain (anti-RBD) antibodies. This was performed using an in-house double binding antigen ELISA (Imperial Hybrid DABA; Imperial College London, London, UK), which detects total RBD antibodies (2-4). The HCW had serological analysis at baseline, which was used to define prior infection alone.

Statistical Analysis

Statistical analysis was conducted using Prism 9.0 (GraphPad Software Inc., San Diego, California). Unless otherwise stated, all data are reported as median with interquartile range (IQR). The aim of the study was to investigate the seroconversion rates in transplant patients receiving either BNT162b2 or ChAdOx, and identify clinical variables associated with reduced immunogenicity. In addition, T-cell responses were investigated in a subcohort of patients.

The Chi-squared test was used for proportional assessments; seroconversion and ELISpot positivity in patients receiving BNT162b2 and ChAdOx1 in both infection-naïve and infection-experienced patients.

The Mann-Whitney and Kruskal-Wallis tests were used to assess the difference between 2 or >2 groups, with Dunn's post-hoc test to compare individual groups. A comparison of anti-S concentrations and T-cell responses, in both infection naïve and infection-experienced patients receiving BNT162b2 and ChAdOx1 was undertaken.

To investigate clinical features associated with seroconversion following vaccination, proportional assessments of clinical characteristics in patients seroconverting compared with those failing to seroconvert was performed. A comparative analysis of clinical features associated with seroconversion by vaccine type was undertaken. Multivariable analysis was carried out using multiple logistic regression using variables which had a p value of <0.15 on univariable analysis.

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Data sharing

Individual participant data that underlie the results reported in this article, after de-identification will be shared upon reasonable request to the corresponding author

Contributor statement

MP- Investigation, data curation, data analysis, writing - original draft, review, and editing, conceptualisation, accessed and verified data

TT- Investigation, data curation, writing-review and editing

CC- Investigation, data analysis, writing-review and editing, conceptualisation, accessed and verified data

PMa, SG, RDC, HE, PMo, SMcI, DM, AC, GP- Investigation, writing-review and editing

LL- Writing-review and editing, supervision

DT- Writing-review and editing, supervision

SPM- Writing-review and editing, supervision, conceptualisation

PK- Investigation, writing - original draft, review, and editing, conceptualisation

MW- Investigation, data curation, data analysis, writing - original draft, review, and editing, conceptualisation, accessed and verified data

The corresponding authors had full access to all the data and the final decision to submit for publication.

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