SUPPLEMENTARY APPENDIX

Overview of lung transplant management

Post-transplantation immunosuppression and induction therapy followed standard protocols at each of the nine participating centres. All patients received life-long *Pneumocystis jirovecii* pneumonia prophylaxis with cotrimoxazole. Valganciclovir for cytomegalovirus prophylaxis was given according to local guidelines. Monitoring transbronchial biopsies were obtained routinely or as clinically indicated depending on the standard protocol at each centre.

Patients with allograft dysfunction were investigated for acute cellular rejection, lymphocytic bronchiolitis/neutrophilic reversible allograft dysfunction, and airway injury caused by infection/colonisation. Chronic lung allograft dysfunction was diagnosed based on international criteria when the forced expiratory volume in the first second and/or the forced vital capacity declined to 80% or less of the best postoperative value during routine outpatient assessments at least three months after transplantation.[1] Comprehensive lung function testing including spirometry and lung volume measurements, high-resolution computed tomography of the chest, and bronchoscopy with bronchoalveolar lavage and transbronchial biopsy were performed to look for causes of lung allograft dysfunction, including persistent acute rejection, azithromycin-responsive allograft dysfunction, infection, anastomotic stricture, and recurrent sarcoidosis.

COVID-19 screening and management

COVID-19 infection was documented by positive real-time polymerase-chain-reaction testing of nasopharyngeal swabs obtained to evaluate symptoms consistent with COVID-19 or after contact with a patient known to have COVID-19. All patients with mild-to-moderate

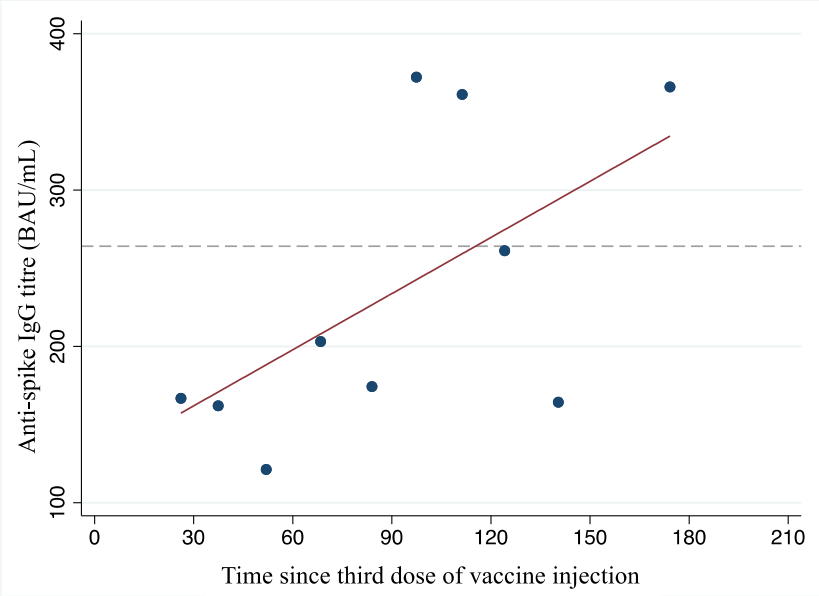
COVID-19 infection were treated within 5 days of symptom onset with casirivimab-imdevimab monoclonal antibodies, starting in June 2021. Patients with severe COVID-19 also received dexamethasone, antibiotics, oxygen as needed, and supportive care. Tocilizumab and remdesivir were given if deemed appropriate by the physician in charge.

Table S1: Main features of the screened patients and of the included and excluded patients

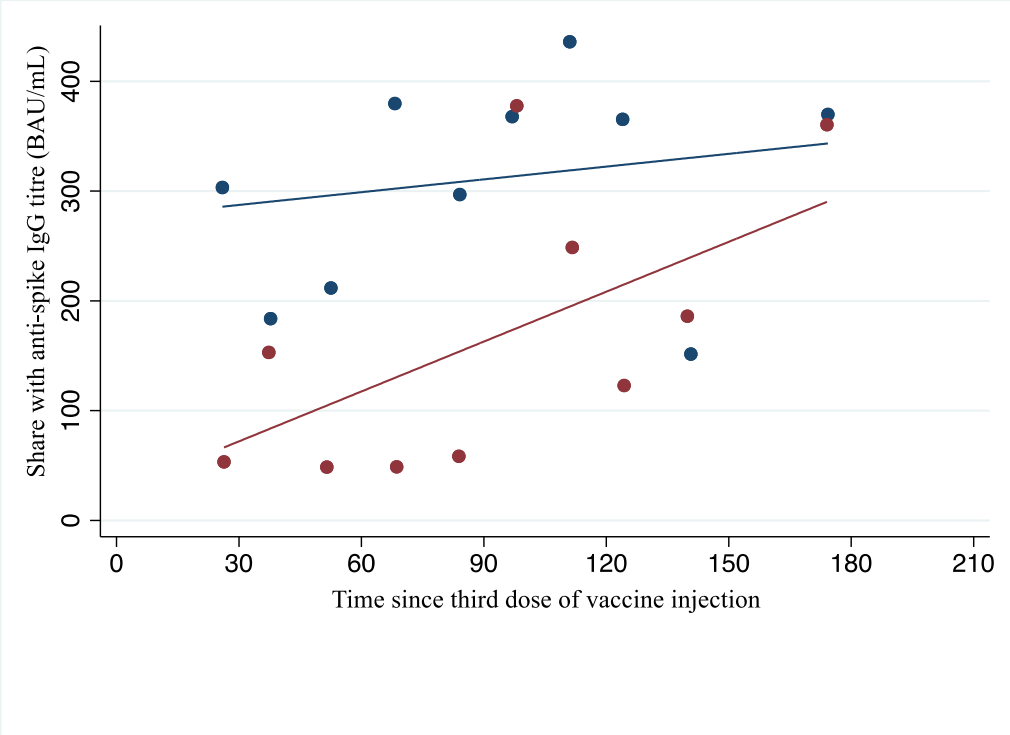
	Overall n = 2420	Included n = 1071	Excluded n = 1349	*p* value
Male, n (%)	1139 (48)	551 (51)	702 (53)	0.46
Age at lung transplantation (y), med [IQR]	47 [30 - 57]	47 [31 - 58]	46 [30 - 57]	0.04
Age at vaccination (y), med [IQR]	54 [40 - 63]	54 [40 - 63]	54 [39 - 62]	0.29
Transplantation indications, n (%),				0.09
Cystic fibrosis	769 (32)	327 (31)	442 (33)	
Chronic obstructive pulmonary disease	696 (29)	323 (30)	373 (28)	
Fibrosis	405 (17)	160 (15)	245 (18)	
Pulmonary arterial hypertension	257 (10)	121 (11)	136 (10)	
Other	293 (12)	140 (13)	153 (11)	
Transplantation procedure, n(%)				0.02
Double-lung	2074 (86)	918 (86)	1156 (86)	
Single-lung	196 (8)	75 (7)	121 (9)	
Heart-lung	115 (5)	62 (6)	53 (4)	
Multiorgan	35 (1)	16 (1)	19 (1)	
Maintenance immunosuppression at the time of vaccination, n (%)				
Cyclosporine	435 (18)	197 (20)	239 (18)	0,16
Tacrolimus	1946 (80)	786 (79)	1160 (86)	0.07
Corticosteroids	2057 (85)	903 (85)	1154 (86)	0,64
Mycophenolate	1562 (64)	675 (63)	887 (66)	0.53
Azathioprine	321 (13)	157 (15)	164 (12)	0.13
Everolimus	453 (18)	195 (18)	258 (19)	0,59
Sirolimus	21 (1)	11 (1)	10 (1)	0.19
Intensified immunosuppression within 6 months before vaccination, n (%), n = 2262	267 (12)	90 (8)	177 (15)	0,01
Methylprednisolone, n(%)	135 (6)	52 (5)	83(7)	0.05
Rituximab, n(%)	61 (3)	12 (1)	49 (4)	<0.01
Anti-thymocyte globulins, n(%)	21 (1)	2 (0)	19(2)	<0.01
Intravenous immunoglobulins, n(%)	77 (3)	25 (2)	52 (4)	0.01
Plasmapheresis, n(%)	16 (1)	1 (0)	15 (1)	<0.01

Figure S1: Times of anti-spike IgG assays

Panel A



Panel B



Each panel shows a binscatter plot with 10 bins of equal size (104 or 105 observations per bin). Panel A shows the relationship between anti-spike IgG titres and time from the third vaccine dose to the anti-spike IgG assay in the overall population. The solid line represents the best linear fit (beta=1.196, *p*=0.03) and the dashed line the 264 BAU/mL threshold used to categorise patients as responders. Panel B shows the same relationship in the two subgroups defined by time from lung transplantation to the first vaccine dose longer than the median of 5.3 years (blue dots, 50/% of the sample; beta=0.388, *p*=0.659) vs. shorter than 5.3 years (red dots, 50% of the sample; beta=1.514, *p*=0.025).