

Supplementary Table S1. Therapies used by treatment group

	Treatment strategy			
	Glucocorticoids	Glucocorticoids + tocilizumab	p-value*	Total
	N= 597	N= 395		N= 992
Heparin, n(%)				
Prophylaxis	360 (60.3%)	223 (56.5%)		583 (58.8%)
Intermediate	173 (29.0%)	160 (40.5%)	<.001	333 (33.6%)
Full dose	14 (2.3%)	15 (3.8%)	0.184	29 (2.9%)
Remdesivir, n(%)	5 (0.8%)	12 (3.0%)	0.009	17 (1.7%)
Glucocorticoids, n(%)				
Standard dose (Dexamethasone, 6 mg/day)	565 (94.6%)	337 (85.3%)	<.001	902 (90.9%)
High dose (Methylprednisolone 2 mg/kg body weight/day)	32 (5.4%)	58 (14.7%)	<.001	90 (9.1%)
Tocilizumab, n(%)	0 (0.0%)	395 (100.0%)	<.001	395 (39.8%)
Anakinra, n(%)	0 (0.0%)	0 (0.0%)		0 (0.0%)
Delay in starting intervention, days				
Median (IQR)	0 (0.0, 2.0)	2 (1.0, 3.0)		1 (0.0, 3.0)
Started <=2 days after admission, n(%)	161 (27.0%)	210 (53.2%)	<.001	371 (37.4%)

*Chi-square test

Supplementary Table S2. Outcomes by treatment group

Outcomes	Treatment strategy			
	Glucocorticoids	Glucocorticoids + tocilizumab	p-value*	Total
	N= 597	N= 395		N= 992
HFNO, n(%)	69 (11.6%)	202 (51.1%)	<.001	271 (27.3%)
NIV, n(%)	38 (6.4%)	112 (28.4%)	<.001	150 (15.1%)
Invasive mechanical ventilation (IMV), n(%)	34 (5.7%)	52 (13.2%)	<.001	86 (8.7%)
Days between hospital admission and NIV, Median (IQR)	1.0 (0.0, 7.0)	2.0 (1.0, 4.5)	0.187	2.0 (1.0, 5.0)
Days between disease onset and IMV, Median (IQR)	7.0 (4.0, 15.0)	12.0 (8.0, 17.0)	0.028	11.0 (7.0, 16.0)
Days free from HFNO (days), Median (IQR)	24.0 (20.0, 27.0)	24.0 (20.0, 26.0)	0.683	24.0 (20.0, 26.0)
Days free from NIV (days), Median (IQR)	26.0 (23.0, 27.0)	25.0 (23.0, 27.0)	0.459	25.0 (23.0, 27.0)
Days free from IMV (days), Median (IQR)	23.0 (17.5, 25.5)	21.0 (15.0, 24.0)	0.287	21.0 (16.0, 25.0)
Days free from hospital (days), Median (IQR)	20.0 (14.0, 23.0)	14.0 (3.0, 18.0)	<.001	17.0 (10.0, 22.0)
Days free from ICU (days), Median (IQR)	23.0 (21.0, 26.0)	24.0 (20.0, 25.0)	0.551	24.0 (20.0, 26.0)
Death, n(%)	113 (18.9%)	79 (20.0%)	0.676	192 (19.4%)
Death in those requiring HFNO, n(%)	19 (27.5%)	55 (27.2%)	0.960	74 (27.3%)
Death in those requiring NIV, n(%)	13 (34.2%)	38 (33.9%)	0.975	51 (34.0%)
Death in those requiring IMV, n(%)	17 (50.0%)	25 (48.1%)	0.862	42 (48.8%)
Discharged before day 28, n(%)	440 (73.7%)	247 (62.5%)	<.001	687 (69.3%)
<i>Discharged to home, n(%)</i>	320 (72.7%)	190 (76.9%)	0.228	510 (74.2%)
<i>Discharged to RSA, n(%)</i>	120 (27.3%)	57 (23.1%)		177 (25.8%)
Main delays				
Days from symptoms onset to hospitalisation, median(IQR)	6 (3, 9)	6 (3, 8)	0.401	6 (3, 9)
Days from symptoms onset to ICU, median(IQR)	7 (5, 11)	9 (7, 12)	0.028	8 (6, 12)
Days from hospitalisation to ICU, median(IQR)	0 (0, 2)	3 (1, 6)	<.001	1 (0, 4)
Hospitalised in 2021, n(%)	166 (27.8%)	103 (26.1%)	0.549	269 (27.1%)

*Chi-square or Mann-Whitney test

Supplementary Table S3. Unadjusted and adjusted HR of death from fitting Cox regression models - after removing those starting high level glucocorticoids

	Hazard ratios of death (95% CI)	p-value
Unadjusted		
Glucocorticoids	1	
Glucocorticoids + tocilizumab	0.67 (0.46, 0.99)	0.042
Adjusted for time-fixed covariates¹		
Glucocorticoids	1	
Glucocorticoids + tocilizumab	0.56 (0.35, 0.90)	0.016
Adjusted for time-varying covariates²		
Glucocorticoids	1	
Glucocorticoids + tocilizumab	0.66 (0.41, 1.07)	0.090
Weighted³		
Glucocorticoids	1	
Glucocorticoids + tocilizumab	0.59 (0.38, 0.93)	0.022

¹standard Cox model adjusted for age, ethnicity, CCI, baseline CRP and PaO₂-FiO₂ ratio

²standard Cox model adjusted for age, ethnicity, CCI, baseline PaO₂-FiO₂ ratio and CRP and time-varying use of remdesivir, invasive mechanical ventilation, PaO₂-FiO₂ ratio and CRP

³weighted Cox model controlled for age, ethnicity, CCI, baseline PaO₂-FiO₂ ratio and CRP and time-varying use of remdesivir, invasive mechanical ventilation, PaO₂-FiO₂ ratio and CRP using IPW

Supplementary Table S4. Unadjusted and adjusted HR of death from fitting Cox regression models - after removing those aged 75+ or with solid cancer

	Hazard ratios of death (95% CI)	p-value
Unadjusted		
Glucocorticoids	1	
Glucocorticoids + tocilizumab	0.74 (0.48, 1.14)	0.169
Adjusted for time-fixed covariates¹		
Glucocorticoids	1	
Glucocorticoids + tocilizumab	0.60 (0.35, 1.01)	0.057
Adjusted for time-varying covariates²		
Glucocorticoids	1	
Glucocorticoids + tocilizumab	0.77 (0.45, 1.32)	0.341
Weighted³		
Glucocorticoids	1	
Glucocorticoids + tocilizumab	0.64 (0.38, 1.07)	0.087

¹standard Cox model adjusted for age, ethnicity, CCI, baseline CRP and PaO₂-FiO₂ ratio

²standard Cox model adjusted for age, ethnicity, CCI, baseline PaO₂-FiO₂ ratio and CRP and time-varying use of remdesivir, invasive mechanical ventilation, PaO₂-FiO₂ ratio and CRP

³weighted Cox model controlled for age, ethnicity, CCI, baseline PaO₂-FiO₂ ratio and CRP and time-varying use of remdesivir, invasive mechanical ventilation, PaO₂-FiO₂ ratio and CRP using IPW

Supplementary Table S5. Results from fitting the Cox regression model after restricting to participants who had not received a full vaccination cycle prior to hospital admission.

	Hazard ratios of death (95% CI)	p-value
Unadjusted		
Glucocorticoids	1	
Glucocorticoids + tocilizumab	0.84 (0.59, 1.22)	0.362
Adjusted for time-fixed covariates¹		
Glucocorticoids	1	
Glucocorticoids + tocilizumab	0.59 (0.37, 0.93)	0.024
Adjusted for time-varying covariates²		
Glucocorticoids	1	
Glucocorticoids + tocilizumab	0.61 (0.37, 0.98)	0.042
Weighted³		
Glucocorticoids	1	
Glucocorticoids + tocilizumab	0.64 (0.42, 0.98)	0.038

¹standard Cox model adjusted for age, ethnicity, CCI, baseline PaO₂-FiO₂ ratio and CRP

²standard Cox model adjusted for age, ethnicity, CCI, baseline PaO₂-FiO₂ ratio and CRP and time-varying use of remdesivir, invasive mechanical ventilation, PaO₂-FiO₂ ratio and CRP

³weighted Cox model controlled for age, ethnicity, CCI, baseline PaO₂-FiO₂ ratio and CRP and time-varying use of remdesivir, invasive mechanical ventilation, PaO₂-FiO₂ ratio and CRP using IPW

Supplementary Table S6. Causes of deaths by treatment strategy

Causes of death, n(%)	Treatment strategy		
	Glucocorticoids	Glucocorticoids + tocilizumab	p-value*
<i>MI or other cardiovascular</i>	8 (7.1%)	7 (8.9%)	
<i>Cardiac decompensation</i>	16 (14.2%)	14 (17.7%)	
<i>Infection</i>	33 (29.2%)	23 (29.1%)	
<i>Respiratory insufficiency</i>	25 (22.1%)	30 (38.0%)	
<i>Other concomitant morbidity</i>	29 (25.7%)	5 (6.3%)	
<i>Unknown</i>	2 (1.8%)	0 (0.0%)	
<i>Total</i>	79 (100.0%)	113 (100.0%)	

*Chi-square

Supplementary Table S7. Incidence of adverse events by treatment group

Adverse event	Glucocorticoids	Glucocorticoids + tocilizumab	p-value	Total
Pulmonary Embolism	22/589 (3.7%)	24/391 (6.1%)	0.08 ^{&}	46/980 (4.7%)
Sepsis	47/554 (8.5%)	34/81 (8.8%)	0.87 ^{&}	81/941 (8.7%)
Neutropenia	10/432 (2.3%)	17/295 (5.8%)	0.02 ^{&}	27/727 (3.7%)
Severe liver disease	44/429 (10.3%)	53/295 (18.0%)	0.003 ^{&}	97/724 (13.4%)
Thrombosis	2/589 (0.3%)	5/391 (1.3%)	0.12 [*]	7/980 (0.7%)

[&]Chi-square test

^{*}Fisher exact test