Supplement S4: Supplementary table: Trial Primary and Secondary Endpoints – Per Protocol Set (PPS)

Per Protocol Set					
Primary and secondary endpoints	**Statistic**	**Estimate (95% Confidence Interval)**		**Treatment Effect**	**Estimate (95% CI)**
		Plasma	**SOC**		
Alive and free of MV at 15 Days	%	85.0 (80.5; 88.7)	84.5 (78.0; 89.3)		1.05 (0.59; 1.86)
Alive and free of MV at 30 Days	KM [%]	83.7 (79.2; 87.6)	82.6 (76.4; 88.0)		0.900 (0.56; 1.44)
Sustained Improvement or Discharge within 30 Days	CIF [%]	83.0 (78.2; 86.9)	85.7 (79.2; 90.3)		0.970 (0.796; 1.182)
Hospital Discharge (30 Days)	CIF [%]	81.2 (76.3; 85.2)	80.8 (73.8; 86.1)		1.050 (0.855; 1.291)
All-Cause Mortality					
Day 15	KM [%]	3.4 (1.9; 6.2)	5.0 (2.5; 9.7)		0.638 (0.251; 1.620)
Day 30	KM [%]	9.1 (6.3; 13.1)	8.2 (4.8; 13.7)		1.070 (0.545; 2.102)
Supplemental Oxygen (30 Days)					
Incidence	CIF [%]	89.6 (85.4; 92.6)	88.8 (82.8; 92.8)		1.011 (0.935; 1.094)
Life-Weaning from SO_2	CIF [%]	82.0 (76.7; 86.1)	82.7 (75.3; 88.1)		1.068 (0.867; 1.316)
Mechanical Ventilation (30 Days)					
Incidence	CIF [%]	13.6 (10.0; 17.8)	13.0 (8.4; 18.8)		1.030 (0.600; 1.766)
Life-Weaning from MV	CIF [%]	54.9 (37.5; 69.3)	71.4 (45.8; 86.5)		0.363 (0.149; 0.885)
ICU (30 Days)					
Admission	CIF [%]	34.7 (29.3; 40.1)	33.6 (26.4; 40.9)		0.992 (0.728; 1.353)
Life Discharge	CIF [%]	77.5 (68.0; 84.4)	83.3 (70.0; 91.1)		0.937 (0.649; 1.354)
Clinical Status					
Day 0	Med. (IQR)	5 (5; 5)	5 (5; 5)		
Day 15	Med. (IQR)	2 (0; 5)	2 (0; 5)		1.12 (0.80; 1.58)
Day 30	Med. (IQR)	2 (0; 2)	2 (0; 3)		0.97 (0.68; 1.38)
NT50 Values					
Day 0 - Log_2-transformed	Med. (IQR)	3 (1; 5)	3 (1; 5)		
Day 6 - Log_2-transformed	Med. (IQR)	6 (5; 6)	6 (5; 6)		-0.14 (-0.65; 0.37)
Ratio (D6/D0) - Log_2-transf'd	Med. (IQR)	2 (1; 3)	2 (0; 4)		-0.20 (-0.86; 0.45)

KM = incidence estimated using Kaplan-Meier methodology; 95% confidence interval calculated using log(-log)-transformation. CIF = incidence estimated using Cumulative Incidence Function accounting for competing risk; SD = standard deviation; Med. = Median; IQR = Interquartile range; HR = hazard ratio; OR = odds ratio.

All estimates of treatment effects were adjusted for study site and period.

Hazard ratios were obtained using a Cox regression including factors for randomised treatment, study period and site. Subdistribution hazard ratios were obtained using a Fine&Grey regression model (accounting for competing risk) including factors for randomised treatment, study period and site. Mean differences between treatments were obtained using a general linear model including the baseline value as a covariate and factors for randomised treatment, study period and site. Common odds ratios were obtained using a proportional odds logistic regression analysis including baseline clinical status as covariate and factors for randomised treatment, study period and site.