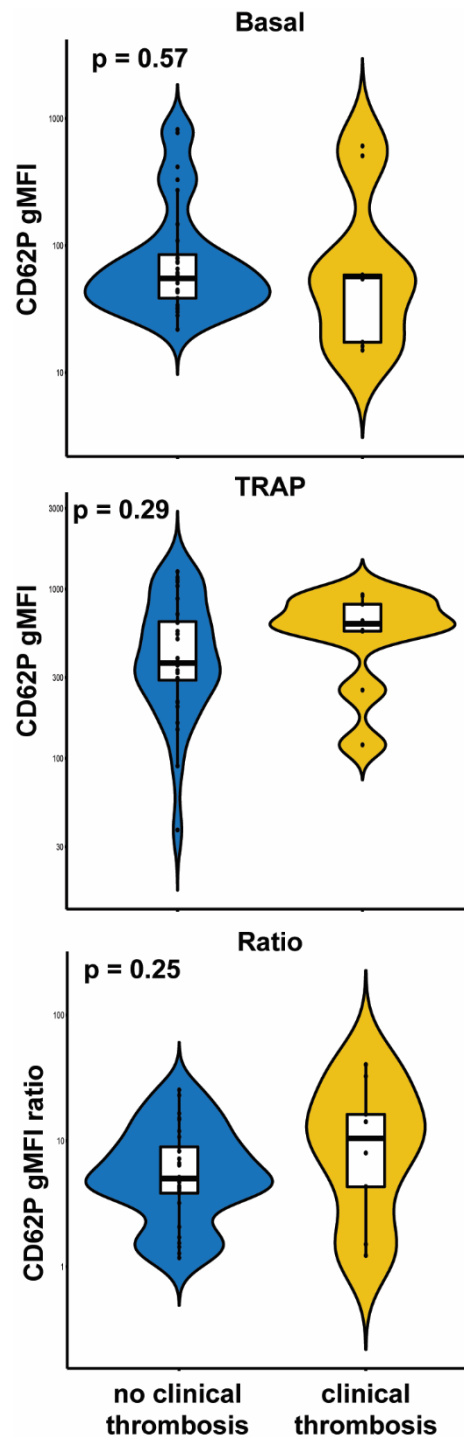


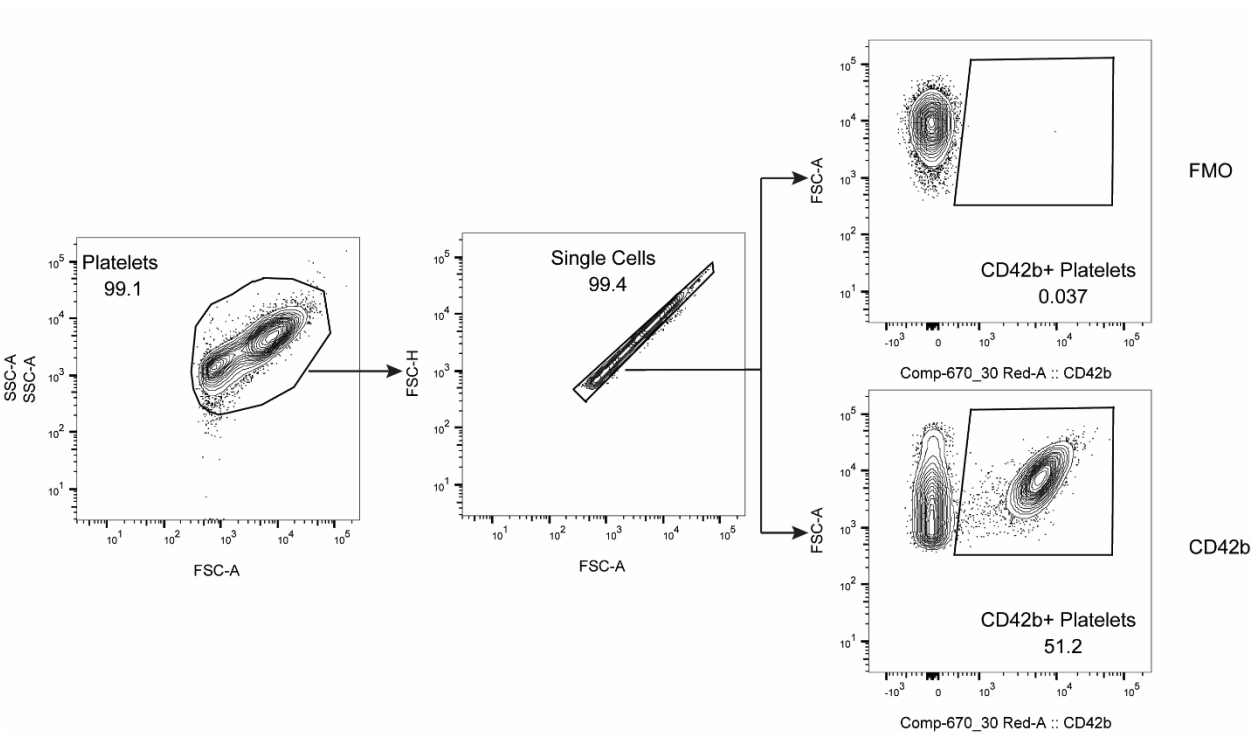
Supplementary materials:

Supplementary Figure 1.



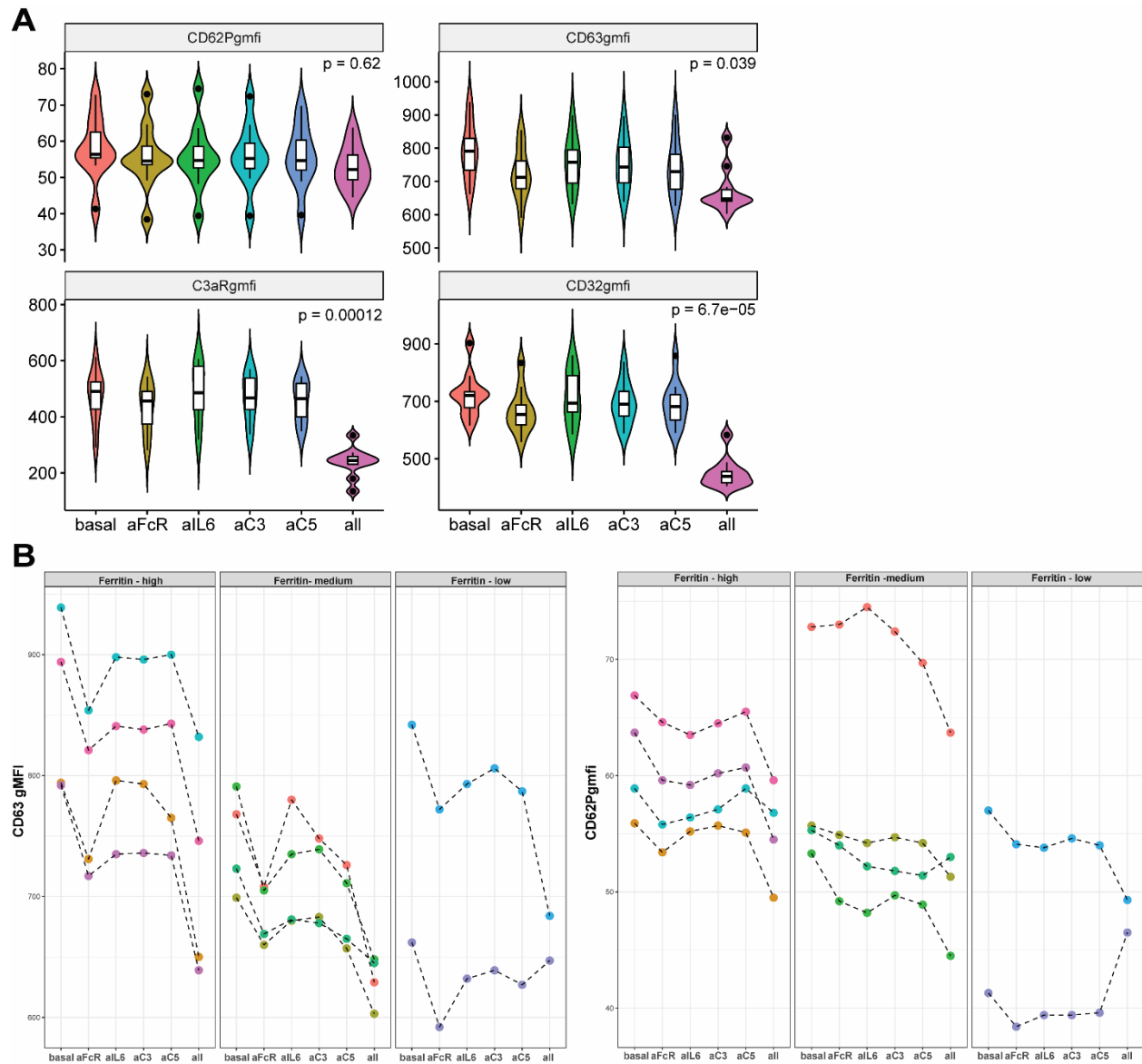
Supplementary Figure 1. Cumulative data for CD62P surface expression of *ex vivo* isolated platelets at baseline (basal), after TRAP activation (TRAP) and their ratio for hospitalized COVID-19 patients that experienced a clinical thrombosis or not. Mann-Whitney non-parametric testing was used and the *p*-values are depicted.

Supplementary Figure 2.



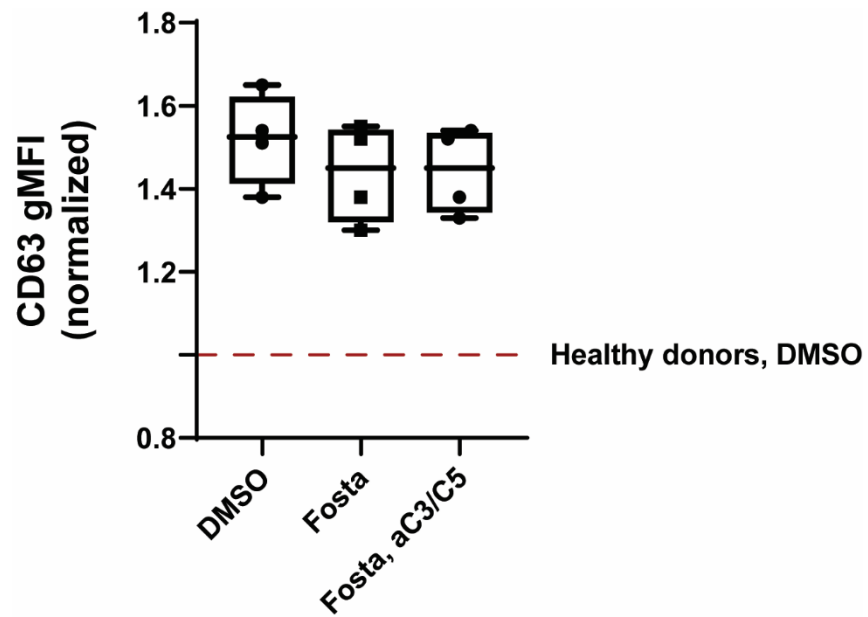
Supplementary Figure 2. Gating strategy for isolated control platelets incubated with COVID-19 plasma.

Supplementary Figure 3.



Supplementary Figure 3. A) Violin plots of gMFI expression of CD62P, CD63, CD32 and C3aR on the surface of control platelets incubated with COVID-19 plasma (n=10 patients) in the presence or absence of neutralizing antibodies to FcγRIIa, IL6, C3a and C5a, as indicated. Kruskal-Wallis non-parametric testing was used to compare the groups and the *p*-values are depicted. **B)** Same samples and conditions depicted in (A) but categorized based on the corresponding patient's ferritin levels. Ferritin – low: <1000ng/mL; Ferritin – medium: 1000-2000ng/mL; Ferritin – high >2000ng/mL

Supplementary Figure 4.



Supplementary Figure 4. Boxplots of gMFI expression of CD63 on the surface of control platelets incubated with COVID-19 plasma (n=4 patients) in the absence or presence of fostamatinib or fostamatinib and neutralizing antibodies to C3a and C5a.

Supplementary Table 1.

	COVID-19 patients with platelets assayed <i>ex vivo</i> (33 unique patients, 38 samples)	COVID-19 patients with plasma assayed <i>in vitro</i> (47 unique patients, 64 samples)
Age (mean, SEM)	60.2 (2.94)	58.7 (2.14)
Gender (male, %)	48%	62%
BMI (mean, SEM)	34 (2.2)	32.7 (1.67)
Platelet count (mean, SEM)	261.9 (17.8)	246 (12.6)
WBC count (mean, SEM)	7.9 (0.6)	9.3 (1.0)
D-dimer (mean, SEM)	4.37 (1.64)	7.04 (2.8)
Ferritin (mean, SEM)	1350.3 (363)	1650.1 (313.8)
LDH (mean, SEM)	347.2 (22.9)	404.5 (33.25)
Hs-CRP (mean, SEM)	91.8 (10.9)	81.53 (12.57)
CVD risk (%)	82%	87%
APACHEIII (mean, SEM)	61.6 (3.9)	63.58 (4.27)
Enrollment NIH Disease Severity Score (mean, SEM)	3.4 (0.18)	3.28 (0.15)
Incident thrombosis (%)	9%	34%
SARS-CoV-2 IgM (ug/mL, mean, SEM)	10.47 (3.73)	10.53 (4.48)
SARS-CoV-2 IgG (ug/mL, mean, SEM)	41.1 (8.76)	47.9 (10.65)

Supplementary Table 1. Clinical information of the COVID-19 patients evaluated.

Supplementary Table 2.

	Condition	Fold-change (mean \pm SEM)	P value vs. No drug
Immediate	---	55.85 \pm 29.63	
	R406	2.61 \pm 0.92	0.0255
	Anti-FcR	0.96 \pm 0.34	0.0245
	Anti-C5a	1.35 \pm 0.50	0.0275
5 mins	---	406.65 \pm 363.08	
	R406	5.613 \pm 2.68	0.0255
	Anti-FcR	3.08 \pm 2.36	0.0245
	Anti-C5a	9.79 \pm 9.14	0.0275
10 mins	---	762.60 \pm 719.81	
	R406	6.68 \pm 3.373	0.0255
	Anti-FcR	4.13 \pm 3.34	0.0245
	Anti-C5a	17.52 \pm 16.98	0.0275
15 mins	---	415.88 \pm 371.80	
	R406	5.86 \pm 2.92	0.0255
	Anti-FcR	3.75 \pm 1.88	0.0245
	Anti-C5a	9.13 \pm 8.54	0.0275

Supplementary Table 2. Inhibition of platelet aggregation in hematoporphyrin-induced photochemical injury model in an endothelial-lined microfluidic channel. Analysis of relative fluorescence intensity of platelet aggregation in the hematoporphyrin-induced photochemical injured endothelial-lined microfluidic channel at different times after infusion of platelets in plasma (n=7) from a severe COVID-19 patient: immediate, 5 min, 10 min and 15 min. Data is expressed as fold increase of platelet accumulation with patient plasma over healthy donor plasma. P values were calculated using Dunnett's multiple comparisons test, n=7.