

Comparative population pharmacokinetics of darunavir in SARS-CoV2 patients vs. HIV patients: the role of interleukin-6

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Table S1. Clinical data of the SARS-CoV2 infected patients (n=30)

ID	Age	Gender	Drug	Stage of severity*	Co-morbidities	Co-treatments	ADRs
1	57	M	DRV/COBI	III	None	Hydroxychloroquine, azithromycin, ceftriaxone	Cutaneous rash, thrombocytosis
2	44	M	DRV/COBI	IIa	None	Hydroxychloroquine, ceftriaxone	None
3	64	M	DRV/COBI	III	COPD, acquired hemophilia	Hydroxychloroquine, pantoprazole, prednisone, cyclophosphamide	None
4	33	F	DRV/COBI	IIb	Obesity	Hydroxychloroquine, azithromycin, enoxaparin	None
5	78	M	DRV/COBI	III	Hypertension	Hydroxychloroquine, enoxaparin, amiodarone, ceftobiprole	None
6	68	F	DRV/COBI	IIb	Dyslipidemia, hypertension, hypothyroidism, GERD	Hydroxychloroquine, enoxaparin	None
7	77	M	DRV/COBI	IIa	Parkinson disease, bladder cancer	Hydroxychloroquine, enoxaparin, bisoprolol, furosemide, aldactone, dexamethasone, ceftobiprole, L-dopa, selegiline,	None
8	63	M	DRV/COBI	III	Factor V Leiden thrombophilia	Hydroxychloroquine, azithromycin, enoxaparin, pantoprazole, furosemide, propofol, remifentanyl	None
9	62	F	DRV/COBI	IIa	None	Hydroxychloroquine, azithromycin, ceftriaxone	None
10	82	F	DRV/COBI	IIb	None	Hydroxychloroquine, azithromycin, alprazolam,	None
11	49	M	DRV/COBI	III	HBV-related chronic hepatitis	Hydroxychloroquine, azithromycin, enoxaparin, ceftriaxone, entecavir	None
12	67	M	DRV/COBI	I	Type-II diabetes, atrial fibrillation, obesity	Hydroxychloroquine, azithromycin, metoprolol, metformin, furosemide, allopurinol, liraglutide	Tonic-clonic seizures
13	52	M	DRV/COBI	III	Depression, psychosis	Pantoprazole, remifentanyl, furosemide, levetiracetam, olanzapine, escitalopram, metoclopramide, daptomycin	QT-prolongation
14	60	M	DRV/COBI	III	Hypertension, obesity	Hydroxychloroquine, azithromycin, enoxaparin, pantoprazole, furosemide, propofol, remifentanyl, metoclopramide, cisatracurium	None
15	56	F	DRV/COBI	IIb	Hypothyroidism, autoimmune gastritis	Hydroxychloroquine, enoxaparin, L-thyroxine	None
16	69	F	DRV/COBI	III	Dyslipidemia, hypertension	Hydroxychloroquine, azithromycin, enoxaparin, pantoprazole, furosemide, propofol, remifentanyl, cisatracurium, methylprednisolone	None
17	65	M	DRV/COBI	I	Deep vein thrombosis	Enoxaparin	None
18	55	F	DRV/COBI	IIa	IBD, bronchiectasis	Enoxaparin	None
19	63	F	DRV/COBI	IIa	None	Hydroxychloroquine, enoxaparin	None
20	72	M	DRV/COBI	IIa	Prostatic cancer, hypertension	Hydroxychloroquine, enoxaparin, azithromycin, telmisartan	None
21	75	M	DRV/COBI	III	Type-II diabetes, obesity, epilepsy	Hydroxychloroquine, azithromycin, aspirin, zonisamide	None
22	54	F	DRV/COBI	IIa	Dyslipidemia, hypertension, obesity	Hydroxychloroquine, enoxaparin, paracodine, olmesartan	Diarrhea
23	76	M	DRV/RTV	IIb	Dyslipidemia, hypertension, depression	Hydroxychloroquine, pantoprazole, doxazosin, bisoprolol, sertraline, allopurinol, quetiapine, sertraline	Asthenia
24	55	M	DRV/RTV	IIb	Cerebrovascular disease	Hydroxychloroquine, enoxaparin, aspirin	Diarrhea
25	71	M	DRV/RTV	IIb	hypertension	Hydroxychloroquine	None
26	83	F	DRV/RTV	IIb	Lung cancer	Hydroxychloroquine, zolpidem, pregabalin	None
27	49	F	DRV/RTV	IIb	Hypertension	Hydroxychloroquine, azithromycin, enoxaparin	QT-prolongation
28	57	M	DRV/RTV	I	Gastric cancer, hypertension	Hydroxychloroquine, pantoprazole, caspofungin, tamsulosine, oxycodone/naloxone	Diarrhea
29	63	M	DRV/RTV	IIb	None	Hydroxychloroquine, azithromycin, enoxaparin, pantoprazole, methylprednisolone	None
30	54	F	DRV/RTV	IIa	None	Hydroxychloroquine, pantoprazole, ceftriaxone	None

ADRs, adverse drug reactions; DRV/COBI, Darunavir/cobicistat; DRV/RTV, Darunavir/ritonavir; *classified according to Siddiqi and Merha (4)

Table S2. Clinical data of the HIV infected patients (n=25)

ID	Age	Gender	Drug	Co-morbidities	Co-treatments	ADRs
1	51	M	DRV/COBI/FTC/TAF	GERD	Pantoprazole, colecalciferol	None
2	52	F	DRV/COBI/FTC/TAF	None	None	None
3	47	M	DRV/COBI/FTC/TAF	Depression	Sertraline, alprazolam	None
4	39	M	DRV/COBI/FTC/TAF	None	None	Diarrhea
5	47	M	DRV/COBI/FTC/TAF	Depression, Kaposi sarcoma, hyperuricemia	Aspirin, allopurinol, venlafaxine, quetiapine, delorazepam, atovaquone	None
6	57	M	DRV/COBI/FTC/TAF	None	None	None
7	73	F	DRV/COBI/FTC/TAF	Hypertension, atrial fibrillation, osteoporosis	Betaxolol, flecainide, ramipril, colecalciferol, zolendronic acid	None
8	42	F	DRV/COBI/FTC/TAF	Osteopenia	Colecalciferol	None
9	35	M	DRV/COBI/FTC/TAF	GERD	Lansoprazole, colecalciferol	None
10	32	M	DRV/COBI/FTC/TAF	None	Colecalciferol	None
11	27	M	DRV/COBI/FTC/TAF	None	None	None
12	54	F	DRV/COBI/FTC/TAF	Gastric ulcer, ischemic stroke, hypertension	Pantoprazole, colecalciferol, clopidogrel, olmesartan	None
13	50	M	DRV/COBI/FTC/TAF	Hypertension, diabetes mellitus	Perindopril/indapamine/amlodipine, metformin, atorvastatin, aspirin, insulin lantus, colecalciferol	None
14	51	M	DRV/COBI/FTC/TAF	None	None	None
15	59	M	DRV/COBI/FTC/TAF	Myocardial infarction, osteopenia	Colecalciferol, aspirin, prasugrel, atorvastatin, lansoprazole, bisoprolol	None
16	48	M	DRV/COBI/FTC/TAF	Hypertension, diabetes mellitus, neuropathic pain	Ramipril, lysine acetylsalicylate, atorvastatin, pregabalin, colecalciferol, metformin	None
17	47	F	DRV/COBI/FTC/TAF	Barrett esophagus, psychosis	Risperidone, lorazepam, colecalciferol, pantoprazole	None
18	47	M	DRV/COBI/FTC/TAF	Hypothyroidism, osteopenia	Levothyroxine, colecalciferol	None
19	40	M	DRV/COBI/FTC/TAF	None	Colecalciferol	None
20	33	M	DRV/COBI/FTC/TAF	None	Colecalciferol, trimethoprim-sulfamethoxazole	None
21	49	F	DRV/COBI/FTC/TAF	Psychosis	Olanzapine, delorazepam, colecalciferol	None
22	43	F	DRV/COBI/FTC/TAF	None	Drospirenone-ethynil estradiol	None
23	40	M	DRV/COBI/FTC/TAF	Kaposi sarcoma, depression, PJP	Sertraline, colecalciferol, pantoprazole, atovaquone, valganciclovir	None
24	47	M	DRV/COBI/FTC/TAF	Depression	Sertraline, alprazolam	None
25	31	M	DRV/COBI/FTC/TAF	None	Colecalciferol	None

ADRs, adverse drug reactions; DRV/COBI/FTC/TAF, Darunavir/Cobicistat/Emtricitabine/Tenofovir; PJP *Pneumocystis jirovecii* pneumoniae; GERD, gastroesophageal reflux disease

Supplementary Figure Captions

Fig. S1. Diagnostic plots for the population pharmacokinetic models. Observed versus individual predicted plasma concentrations in SARS-CoV2 patients and in HIV patients are shown. Solid lines refer to linear regression between observed and predicted concentrations. Dashed lines are the identity lines between observed and predicted concentrations.

Fig. S2. Classification and regression tree (CART) analysis of the partition of darunavir oral clearance (CL/F) depending on IL-6 concentrations in SARS-CoV2 patients (n = 30).

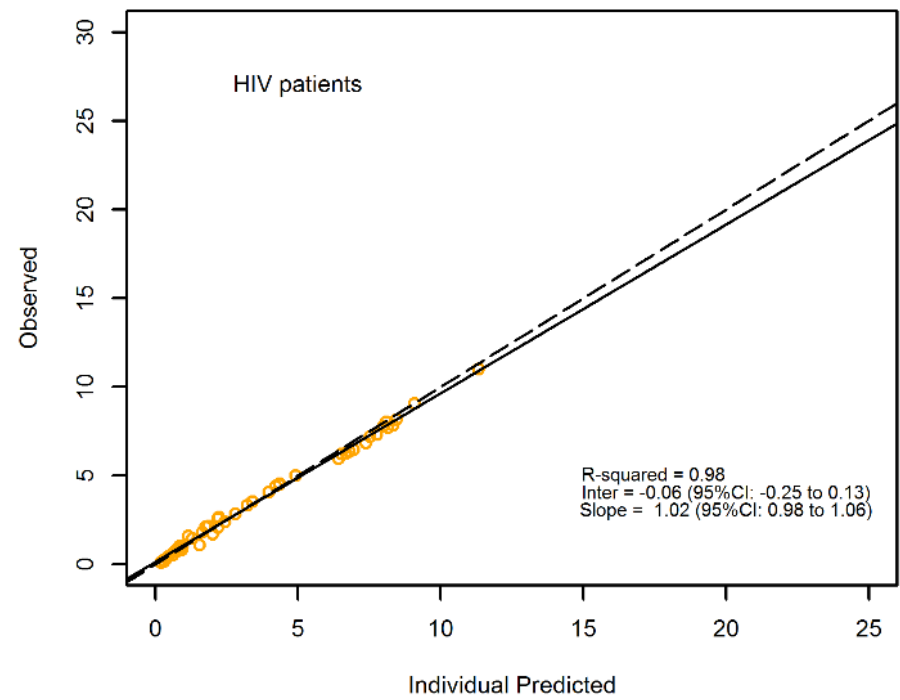
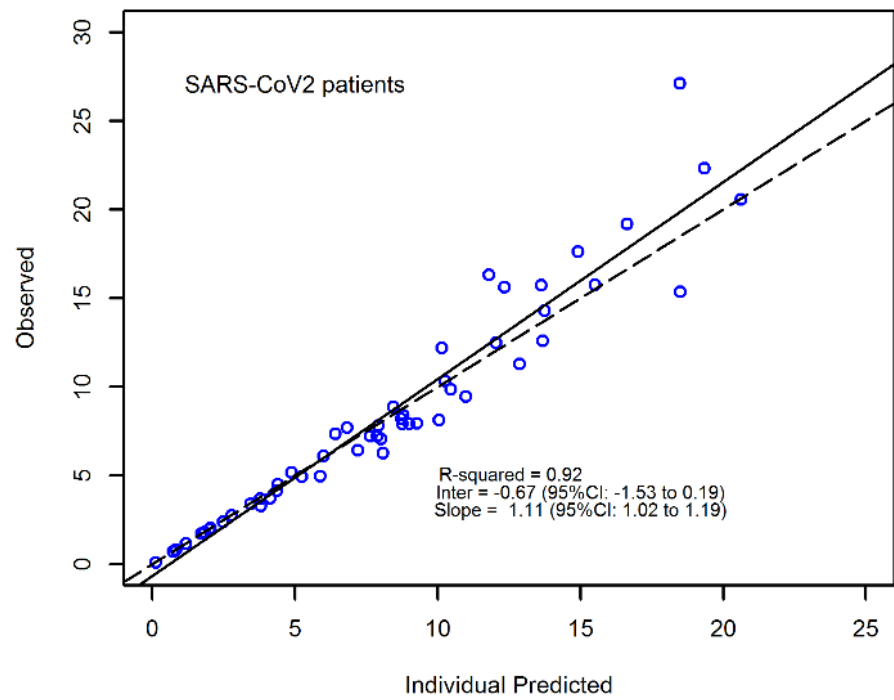


Fig.S1

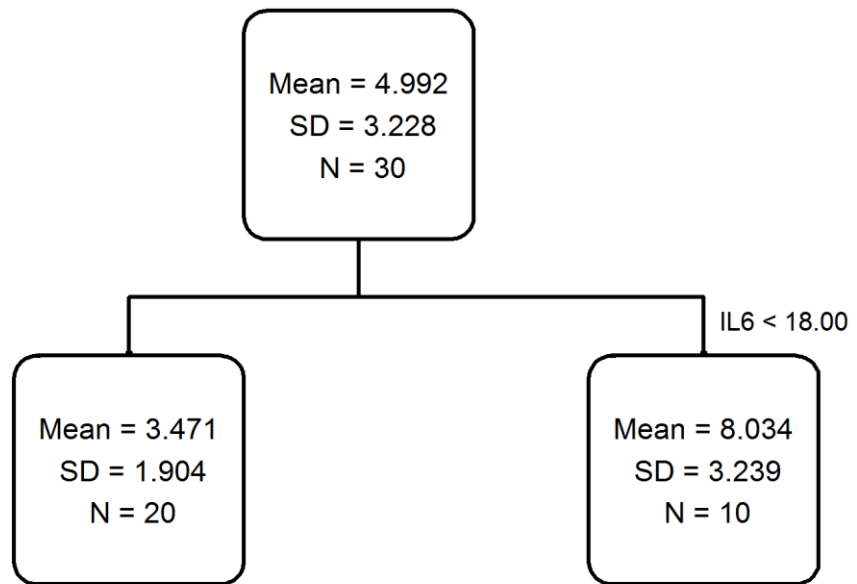


Fig. S2