Supplementary Table 1. Metabolic pathways of CYP substrate drugs and comparison of predicted and observed drug-drug interaction caused by rifampicin and rifabutin.

Abbreviations

a.m., active moiety; BCRP, breast cancer resistance protein; CR, contribution ratio of cytochrome P450 (see main text); NAT, N-acetyltransferase; OATP, Organic-anion-transporting-polypeptides; PE, prediction error of R_{AUC} (predicted R_{AUC} - observed R_{AUC}); PGP, P-glycoprotein; R_{AUC}, ratio of areas under the concentration-time curve (see main text), R_{AUC} OBS, observed R_{AUC}; R_{AUC} PRED, predicted R_{AUC}; UGT, UDP-glucuronosyltransferase.

CR values awere taken from the DDI-predictor website: www.ddi-predictor.org

Non-CYP pathways were retrieved from drugbank (https://go.drugbank.com) and transformer application databases (https://bioinformatics.charite.de/transformer)

Target interval of predicted R_{AUC} is 0.5 to 2 times the observed RAUC.

Substrate drugs	Estimated contribution of CYP to oral clearance					Non-CYP pathways					DDI with RBT300			DDI with RIF600			Reference
	CR CYP3A4	CR CYP2D6	CR CYP2C9	CR CYP2C19	CR CYP1A2	OATP	NAT	UGT	PGP	BCRP	R_{AUC} OBS	R_{AUC} PRED	PE	R_{AUC} OBS	R_{AUC} PRED	PE	
Alisporivir	0.95	0	0	0	0	X								0.09	0.12	0.33	22
Alprazolam	0.75	0	0	0.1	0									0.12	0.14	0.17	23
Antipyrine	0.3	0	0	0.05	0.3		X				0.77	0.54	-0.30	0.63	0.25	-0.60	12
Antipyrine	0.3	0	0	0.05	0.3		X							0.53	0.25	-0.53	24
Antipyrine	0.3	0	0	0.05	0.3		X							0.53	0.25	-0.53	25
Apremilast	0.3	0	0	0	0				X					0.28	0.3	0.07	26
Aprepitant	0.82	0	0	0	0									0.09	0.14	0.56	27
Atorvastatin	0.68	0	0	0	0			X	X					0.2	0.16	-0.20	28
Axitinib	0.51	0	0	0	0				X					0.21	0.2	-0.05	29
Bedaquiline	0.16	0	0	0	0									0.41	0.45	0.10	30
Brexpiprazole	0.41	0.56	0	0	0									0.27	0.24	-0.11	31
brigatinib	0.53	0	0	0	0									0.2	0.2	0.00	32
Buprenorphine	0.55	0	0	0.25	0			X			0.65	0.31	-0.52	0.3	0.16	-0.47	33
Buspirone	0.99	0	0	0	0				X					0.09	0.12	0.33	34
Cabozantinib	0.35	0	0	0	0									0.23	0.27	0.17	35
Caffeine	0	0	0	0	0.84	X	X				0.98	0.98	0.00	0.61	0.45	0.26	106,23
Carbamazepine	0.25	0	0	0.2	0.38			X	X					0.38	0.23	-0.39	36
Casopitant	0.94	0	0	0	0									0.04	0.12	2.00	37
Celecoxib	0	0	0.97	0	0									0.35	0.46	0.31	38
ceritinib	0.47	0	0	0	0				X					0.3	0.22	-0.27	39
Clarithromycin	0.35	0	0	0	0	X					0.5	0.57	0.14				40
Crizotinib	0.64	0	0	0	0				X					0.18	0.17	-0.06	41
Daclatasvir	0.59	0	0	0	0				X					0.21	0.18	-0.14	42
Dasatinib	0.8	0	0	0	0				X					0.18	0.14	-0.22	43
Diazepam	0.1	0	0	0.64	0		X	X									24

Dienogest	0.6	0	0	0	0									0.17	0.18	0.06	44
Disopyramide	0.22	0	0	0	0									0.33	0.37	0.12	45
doravirine	0.78	0	0	0	0							0.5	0.37	-0.26	0.12	0.14	0.17	46
Erlotinib	0.47	0	0	0	0.35				X						0.25	0.2	-0.20	47
esaxerenone	0.33	0	0	0	0										0.31	0.28	-0.10	48
Estradiol valerate	0.26	0	0	0	0				X						0.56	0.33	-0.41	49
Ethinylestradiol	0.26	0	0	0	0			X				0.65	0.64	-0.02	0.34	0.33	-0.03	44
Etravirine	0.44	0	0	0	0				X			0.63	0.37	-0.41				50
Fesoterodine a.m.	0.53	0.47	0	0	0										0.23	0.2	-0.13	51
Flibanserin	0.82	0	0	0.18	0				X						0.05	0.12	1.40	52
Fluvastatin	0	0	0.8	0	0	X									0.5	0.51	0.02	53
Fostamatinib a.m.	0.44	0	0	0	0										0.25	0.23	-0.08	54
Gefitinib	0.39	0.5	0	0	0						X				0.17	0.25	0.47	55
Gemigliptin	0.56	0	0	0	0										0.2	0.19	-0.05	56
Gliben-Glyburide	0	0	0.63	0	0				X						0.61	0.57	-0.07	57
Glimepiride	0	0	0.99	0	0			X							0.34	0.45	0.32	58
Ibrutinib (fasten)	0.98	0	0	0	0										0.11	0.12	0.09	59
Imatinib	0.35	0	0	0	0	X					X				0.26	0.27	0.04	60
Isavuconazole	0.86	0	0	0	0				X						0.1	0.13	0.30	61
Ivacaftor	0.9	0	0	0	0				X						0.11	0.13	0.18	62
laquinimod	0.66	0	0	0	0										0.2	0.16	-0.20	63
lorlatinib	0.31	0	0	0	0										0.15	0.3	1.00	64
Losartan	0	0	0.4	0	0			X	X						0.69	0.67	-0.03	65
Lurasidone	0.72	0	0	0	0										0.19	0.15	-0.21	66
Mefloquine	0.44	0	0	0	0										0.32	0.23	-0.28	67
Midazolam	0.91	0	0	0	0			X				0.31	0.34	0.10	0.12	0.12	0.00	68,106
Midazolam	0.91	0	0	0	0			X							0.04	0.12	2.00	69
naldemedine	0.62	0	0	0	0										0.17	0.17	0.00	70
Naloxegol	0.95	0	0	0	0										0.11	0.12	0.09	71

Nateglinide	0	0	0.48	0	0								0.76	0.63	-0.17	72
neratinib	0.89	0	0	0	0			X					0.12	0.13	0.08	73
Netupitant	0.51	0	0	0	0			X					0.19	0.2	0.05	74
Nifedipine	0.72	0	0	0	0								0.08	0.15	0.88	75
Nilotinib	0.67	0	0	0	0		X						0.2	0.16	-0.20	76
Olaparib	0.67	0	0	0	0			X					0.13	0.16	0.23	77
Palbociclib	0.49	0	0	0	0			X					0.15	0.21	0.40	78
Palonosetron	0.05	0.2	0	0	0								0.81	0.72	-0.11	74
Phenytoin	0	0	0.72	0.19	0	X	X	X					0.5	0.37	-0.26	79
Pitolisant	0.13	0.52	0	0	0								0.5	0.5	0.00	80
Ponatinib	0.32	0	0	0	0			X					0.37	0.29	-0.22	81
Praziquantel	0.49	0	0	0.18	0								0.15	0.18	0.20	82
Prednisolone	0.18	0	0	0	0			X					0.49	0.42	-0.14	83
Prednisolone	0.18	0	0	0	0			X					0.72	0.42	-0.42	84
Propranolol	0	0.51	0	0.26	0.23		X						0.37	0.41	0.11	85
Ramelteon	0	0	0	0.42	0.58								0.2	0.28	0.40	86
Regorafenib	0.18	0	0	0	0			X					0.5	0.42	-0.16	87
Ribociclib	0.93	0	0	0	0								0.11	0.12	0.09	88
Ruxolitinib	0.35	0	0	0	0								0.3	0.27	-0.10	89
Saquinavir	0.58	0	0	0	0	X	X	X	X	0.53	0.45	-0.15				90
Simvastatin	0.97	0	0	0	0	X		X					0.09	0.12	0.33	68
Simvastatin	0.97	0	0	0	0	X		X					0.14	0.12	-0.14	91
Siponimod	0.12	0	0.77	0	0								0.43	0.35	-0.19	92
Sunitinib	0.42	0	0	0	0								0.25	0.24	-0.04	93
suvorexant	0.75	0	0	0	0			X					0.12	0.15	0.25	94
Tasimelteon	0.15	0	0	0	0.85								0.11	0.3	1.73	95
Telithromycin	0.49	0	0	0	0	X							0.14	0.21	0.50	96
Tizanidine	0	0	0	0	0.97								0.46	0.42	-0.09	97
Tolbutamide	0	0	0.89	0	0		X			0.63	0.63	0	0.36	0.48	-0.33	106,13

Tolvaptan	0.81	0	0	0	0					0.13	0.14	0.08	98
Triazolam	0.93	0	0	0	0					0.05	0.12	1.40	99
Ulipristal	0.86	0	0	0	0					0.1	0.13	0.30	100
Vandetanib	0.09	0	0	0	0	X				0.6	0.59	-0.02	101
Voriconazole	0.31	0	0	0.68	0		0.22	0.22	0				40
Vortioxetine	0.24	0.6	0	0.13	0					0.28	0.29	0.04	102
zanubrutinib	0.8	0	0	0	0					0.07	0.14	1.00	105
Zolpidem	0.4	0	0	0	0.35					0.28	0.22	-0.21	103
Zopiclone	0.44	0	0	0	0					0.18	0.23	0.28	104
Mean PE (SD)									0.11 (0.22)			0.13 (0.50)	
Percentage of R_{AUC} in target interval									0.91			0.94	