Breast Cancer Resistance Protein (ABCG2) in Clinical Pharmacokinetics and Drug Interactions: Practical Recommendations for Clinical Victim and Perpetrator Drug-Drug Interaction Study Design

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Supplemental Table 1. Clinically usable compounds and in vitro to in vivo translation inhibition calculations (I_1/IC_{50} and I_2/IC_{50})

Precipitant	I_1 (µM, C_{max})	Plasma Binding (%)	Dose	Ki (µM)	IC_{50} (µM)	$[I_1]/IC_{50}$	$[I_u]/IC_{50}$	I_2 (µM)	$[I_2]/IC_{50}$
afatinib	0.078 [1]	57.2-88.4 [1]	40 mg QD (SS) [1]	-	0.75 [1]	0.10	0.012	330	440
aripiprazole	0.54 [25]	>99 [25]	15 mg QD x 14D [25]	-	3.5 [2]	0.15	0.002	130	38
axitinib	0.16 [26]	99 [27]	5 mg BID x 15D [26]	-	4.4 [3]	0.04	3.6E-04	52	12
curcumin	0.006 [28]	-	2 g SD [28]	0.7 [4]	1.6 [4]	0.004	-	22000	14000
erlotinib	6.06 [29]	90 [29]	150 mg QD x 21D [29]	0.15 [6]	0.13 [6]	47	4.7	1500	12000
elacridar	0.327 [30]	-	400 mg BID x 3D [30]	-	0.31 [7]	1.1	-	2800	9200
fluvastatin	0.461 [31]	99 [31]	20 mg QD (SS) [31]	5.43 [8]	10.86 [a]	0.04	4.2E-04	190	18
gefitinib	0.8 [25]	90 [25]	225 mg QD x 14D [25]	-	1.01 [9]	0.79	0.079	2000	2000
ivermectin	0.022 [25]	93.1 [25]	150 µg/kg SD [25]	1.4 [10]	2.8 [a]	0.01	0.001	24	8.6
lapatinib	2.6 [32,b]	>99 [32]	1250 mg QD (SS) [32]	-	0.025 [11]	104	1.04	5300 [c]	210000 [d]
nilotinib	4 [33]	98 [33]	400 mg BID x 15D [33]	0.69 [12]	1.38 [a]	2.9	0.060	2800	2000
pantoprazole	6 [34]	98 [34]	40 mg SD [34]	-	5.5 [14]	1.1	0.020	370	67
pitavastatin	0.0296 [35]	99.5-99.6 [36]	2 mg SD [35]	2.92 [8]	5.84 [a]	0.0051	2.0E-05	19	3.2
ponatinib	0.161 [15]	99.92 [15]	45 mg QD 2 cycles [15]	-	0.013 [15]	12	0.010	340	26000
quercetin	0.051 [37]	99.1 [38]	500 mg TID x 7D [37]	-	0.6 [16]	0.09	0.001	6600	11000
quizartinib (AC220)	1.8 [39]	99 [40]	200 mg QD x 8D [39]	-	0.5 [17]	3.6	0.04	86	170
rabeprazole	0.9 [41]	96.3 [41]	40 mg AD x 8D [41]	-	8.5 [14]	0.11	0.004	440	52
regorafenib	7.8 [42]	99.5 [42]	160 mg (SS) [42]	-	0.0447 [18]	174	0.87	1300	28000
rilpivirine	0.5 [43]	>99 [43]	25 mg QD x 14D [43]	-	1.5 [19]	0.33	0.003	270	180
sulfasalazine	37.6 [31]	>99.3 [31]	3-4 g SD [31]	-	0.46 [13]	82	0.57	40000	87000
sunitinib	0.17 [44]	95 [44]	50 mg QD x 28D [44]	0.32 [20]	0.64 [a]	0.27	0.013	500	780
tacrolimus	0.038 [31]	75-99 [31]	7 mg SD [31]	-	6 [16]	0.01	6.3E-05	35	5.8
teriflunomide	0.11 [21]	99.5-99.7 [21]	14-70 mg QD x 12D [21]	-	0.146 [21]	0.75	0.002	1000	7100
trametinib	0.032 [22]	96.2-97.4 [22]	2 mg QD x 14D [22]	-	1.1 [22]	0.03	7.6E-04	12	10
trifluoperazine	0.0027 [45]	96.4 [46]	5 mg SD [45]	-	7.56 [23]	3.6E-04	1.3E-05	49	6.5
vismodegib	16.4 [24]	99 [24]	150 mg QD x 7D [24]	-	2.4 [24]	6.8	0.068	1400	590

IC_{50} and K_i values are presented as reported in the respective references.

[a] IC_{50} value was calculated as $2xK_i$, assuming linearity

[b] C_{max} for proposed 250 mg dose = 0.54 µM (Bence et al., 2005)

[c] I_2 value for proposed 250 mg dose = 1000 µM

[d] $[I_2]/IC_{50}$ value for proposed 250 mg dose = 40000

[1] FDA (2013) Drug approval package: GILOTRIF® (afatinib dimaleate) [FDA application no, (NDA) 201292; [2] (Nagasaka et al., 2012); [3] (Reyner et al., 2013); [4] (Kusuhara et al., 2012); [5] (Xia et al., 2007); [6] (Noguchi et al., 2009); [7] (Si et al., 2013); [8] (Hirano et al., 2005); [9] (Yanase et al., 2004); [10] (Jani et al., 2011); [11] (Polli et al., 2008); [12] (Tiwari et al., 2009); [13] (Elsby et al., 2011); [14] (Suzuki et al., 2009); [15] FDA (2012) Drug approval package: ICLUSIG® (ponatinib hydrochloride) [FDA application no, (NDA) 203469]; [16] (Saito et al., 2006); [17] (Bhullar et al., 2013); [18] FDA (2012) Drug approval package: STIVARGA® (regorafenib) [FDA application no, (NDA) 203085]; [19] (Weiss and Haefeli, 2013); [20] (Kawahara et al., 2010); [21] FDA (2012) Drug approval package: AUBAGIO® (teriflunomide) [FDA application no, (NDA) 202992]; [22] FDA (2013) Drug approval package: MEKINIST® (trametinib dimethyl sulfoxide) [FDA application no, (NDA) 204114]; [23] (Pan et al., 2013); [24] FDA (2012) Drug approval package: ERIVEDGE® (vismodegib) [FDA application no, (NDA) 203388]; [25] (Goodman et al., 2005); [26] (Rugo et al., 2005); [27] FDA (2012) Drug approval package: INLYTA® (axitinib) [FDA application no, (NDA) 202324]; [28] (Shoba et al., 1998); [29] (Yamamoto et al., 2008); [30] (Planting et al., 2005); [31] (Goodman et al., 2001); [32] TYKERB® product label (10/18/2013, http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/022059s016s017lbl.pdf); [33] FDA (2012) Drug approval package: TASIGNA® (nilotinib hydrochloride monohydrate) [FDA application no, (NDA) 022068]; [34] PROTONIX® product label (12/10/2013, http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/020987s048,022020s010lbl.pdf); [35] (Mukhtar et al., 2005); [36] FDA (2009) Drug approval package: LIVALO® (pitavastatin calcium) [FDA application no, (NDA) 022363]; [37] (Moon et al., 2008); [38] (Boulton et al., 1998); [39] (Cortes et al., 2013); [40] (Kampa-Schittenhelm et al., 2013); [41] ACIPHEX® product label (04/19/2013, http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/020973s032lbl.pdf); [42] STIVARGA® product label (05/29/2013, http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/203085s001lbl.pdf); [43] FDA (2009) Drug approval package: EDURANT® (rilpivirine hydrochloride) [FDA application no, (NDA) 202022]; [44] SUTENT® product label (08/30/2013, http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/021938s024s025lbl.pdf); [45] (Midha et al., 1988); [46] (Freedberg et al., 1979)

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