Supplementary Tables to:

Cellular uptake of imatinib into leukemic cells is independent of human organic cation transporter 1 (OCT1)

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Supplementary Table S1. Overview of conflicting reports regarding the importance of OCT1 genetics, OCT1 expression, or cellular imatinib uptake for imatinib pharmacokinetics and response

OCT1 genetics	Reference	OCT1 variant	Number of patients	Effects on imatinib response	Effects on imatinib pharmacokinetics	Significant association
	Zach et al. (1)	rs12208357 (c.181C>T, p.R61C)	32	No effect on MMR	No effect on steady state imatinib plasma level	No
	Kim et al. (2)	rs683369 (c.480G>C, p.L160F)	229	Higher rate of loss of response		Yes
	Gromicho et al. (3)	rs683369 (c.480G>C, p.L160F)	33	No correlation with treatment response		No
	Bazeos et el. (4)	rs3413049 (c.1201G>A, p.G401S)	60	Higher rate of MMR		Yes
	Takahashi et al. (5)	rs628031 (c.1222A>G, p.M408V)	62	Higher rate of MMR		Yes
		rs628031 (c.1222A>G, p.M408V)	62		No effect on $C_{minutes}$	No
	White et al. (6)	rs12208357 (c.181C>T, p.R61C) rs72552763 (c.1260_1262delGAT, p.M420del) and others	136	No effect on MMR		No
	Maffioli et al. (7)	rs12208357 (c.181C>T, p.R61C) rs72552763 (c.1260_1262delGAT, p.M420del) rs628031 (c.1222A>G, p.M408V)	65	No correlation with overall inadequate response		No
		rs6935207 (c.-105-1690G>A)	65	Correlation with overall inadequate response		Yes
	Giannoudis et al. (8)	rs35191146 (c.1260_1262delGAT, p.M420del)	177	Higher risk of treatment failure		Yes
	Angelini et al. (9)	combination of several alleles	189	Higher rate of MMR		Yes
	Seong et al. (10)	rs2282143 (c.1022C>T, p.P341L)	82	No effect on CCR or MMR	No effect on imatinib trough concentration	No
	Nambu et al. (11)	rs2282143 (c.1022C>T, p.P341L)	15		No effect on steady state imatinib plasma level	No
	Yamakawa et al.	rs2282143	34		No effect on imatinib	No

	(12)	(c.1022C>T, p.P341L)			clearance	
	Singh et al. (13)	Haplotype of rs3798168, rs628031 (c.1222A>G, p.M408V), rs80301372 (IVS7+850C>T)	38		Significant association with imatinib clearance	Yes
***OCT1/SLC22A1* mRNA level**	**Reference**	**Cell type**	**Number of patients**	**Effects on imatinib response**		**Significant association**
	Crossman et al. (14)	BM MNC	15	8-fold higher pre-treatment OCT1 mRNA levels in patients who achieved CCR by 12 months of imatinib treatment than non-responders		Yes
	Wang et al. (15)	PBC	70	High pre-treatment OCT1 mRNA levels associated with significantly better overall and progression-free survival rates than low OCT1 levels Note: this association is lost when primers are used that do not cover OCT1 variant rs35191146(8)		(Yes)/No
	Zhang et al. (16)	PBC	68	No difference in OCT1 mRNA levels at time of diagnosis between patients achieving CCR by 12 months of imatinib therapy or not achieving CCR		No
	Marin et al. (17)	PBC	60	High OCT1 mRNA at time of diagnosis in patients with CP-CML associated with better rates of MMR and CMR by 6 years of imatinib treatment		Yes
	White et al. (18)	PB MNC	56	No difference in achieving MMR between patients with high or low OCT1 mRNA levels at time of diagnosis		No
	White et al. (19)	PB MNC	46	No difference in achieving MMR or CMR between patients with high or low OCT1 mRNA levels at time of diagnosis		No
	Zhong et al. (20)	BM MNC	84	Higher OCT1 mRNA levels in patients achieving CCR than in non-responders		Yes
	Nardinelli et al. (21)	PBC	88	High OCT1 mRNA at time of diagnosis in patients with CP-CML associated with higher rates of MMR by 12 and 18 months of imatinib treatment		Yes
	Gromicho et al. (3)	PB MNC, BM MNC	33	Higher OCT1 mRNA levels in patients sensitive to imatinib treatment		Yes
Cellular imatinib uptake	**Reference**	**Cell type**	**Number of patients**	**Effects on imatinib response**		**Significant association**
	White et al. (18)	PB MNC	56	Higher cellular imatinib uptake associated with higher rates of achieving MMR and CMR by 2 years of imatinib treatment		Yes
	White et al. (19)	PB MNC	56	Higher cellular imatinib uptake associated with higher rates of achieving MMR and CMR by 5 years of imatinib treatment		Yes

	Engler et al. (22)	PB MNC	34	Higher cellular imatinib uptake associated with higher rates of achieving MMR by 12 months of imatinib treatment	Yes
	Engler et al. (22)	$CD34^+$	34	Cellular imatinib uptake not associated with MMR by 12 months of imatinib treatment	No
	White et al. (23)	PB MNC	100	Higher cellular imatinib uptake associated with higher rates of achieving MMR by 2 years of imatinib treatment	Yes

BM MNC, bone marrow mononuclear cells

CCR, complete cytogenetic response

CMR, complete molecular response

CP, chronic phase

MMR, major molecular response

PBC, peripheral blood cells

PB MNC, peripheral blood mononuclear cells

Supplementary Table S2

Multiple reaction monitoring (MRM) transitions and MS parameters for determination of imatinib, *N*-desmethyl imatinib and their internal standards with LC-MS-MS

Analyte	MRM transition (*m/z*)	Dwell time (ms)	Fragmentor (V)	Collision energy (V)
Imatinib	494.3 > 394.1	50	162	22
Imatinib-d_8	502.3 > 394.1	50	162	22
N-Desmethyl imatinib	480.3 > 394.1	50	165	22
N-Desmethyl imatinib-d_8	488.3 > 394.1	50	165	22

Supplementary Table S3

Characteristics of SLC family members whose mRNA expression has been quantified by real-time PCR in the present study. SLC transporters (24) were selected based on the core and extended list of the PharmaADME Consortium (http://www.pharmaadme.org) and are considered as important for drug uptake

SLC family	Family name	Investigated family members	Selected drug substrates
SLC2	Facilitative GLUT transporter	SLC2A4, SLC2A5	
SLC5	Sodium glucose transporter	SLC5A8, SLC5A12	Nicotinate
SLC6	Sodium- and chloride-dependent neurotransmitter transporter	SLC6A6	Paroxetine, fluoxetine
SLC7	Cationic aminuteso acid transporter/ glycoprotein-associated	SLC7A5	Gabapentin
SLC10	Sodium bile salt cotransport	SLC10A1, SLC10A2	Bile acid-coupled cytostatic drugs, statins
SLC15	Proton oligopeptide cotransporter	SLC15A1, SLC15A2, SLC15A3, SLC15A4	β-lactam antibiotics
SLC16	Monocarboxylate transporter	SLC16A1, SLC16A3, SLC16A7	Salicylate, statins
SLC19	Folate/thiaminutese transporter	SLC19A1	Methotrexate
SLCO	Organic anion transporter	SLCO1A2, SLCO1B1, SLCO1B3, SLCO1C1, SLCO2A1, SLCO2B1, SLCO3A1, SLCO4A1, SLCO4C1, SLCO5A1, SLCO6A1	Benzylpenicillin, methotrexate, paclitaxel, rifampicin, statins, troglitazone, valsartan
SLC22	Organic cation/anion/zwitterion transporter	SLC22A1, SLC22A2, SLC22A3, SLC22A4, SLC22A5, SLC22A6, SLC22A7, SLC22A8, SLC22A9, SLC22A11, SLC22A12, SLC22A13, SLC22A14, SLC22A15, SLC22A16, SLC22A17, SLC22A18, SLC22A18AS	Antiviral drugs, metformin, methotrexate, platinum compounds
SLC27	Fatty acid transporter	SLC27A1	

SLC28	Na+-coupled nucleoside transporter	SLC28A1, SLC28A2, SLC28A3	Antiviral drugs, gemcitabine
SLC29	Facilitative nucleoside transporter	SLC29A1, SLC29A2, SLC29A3, SLC29A4	Antiviral drugs, gemcitabine
SLC47	Multidrug and Toxin Extrusion (MATE)	SLC47A1, SLC47A2	Antiviral drugs, metformin, platinum compounds

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