

Supplementary Table S4. Influence of nilotinib on the plasma pharmacokinetics of cisplatin in mice.*

Parameter	Wild-type		Oatp1b2(-/-)	
	+ Vehicle	+ Nilotinib	+ Vehicle	+ Nilotinib
Total platinum				
C _{max} (µg/mL)	9.21	10.8	8.49	8.63
AUC (µg·h/mL)	9.98	11.6	10.3	11.8
Unbound platinum				
C _{max} (µg/mL)	6.06	5.51	3.81	4.78
AUC (µg·h/mL)	2.07	2.36	1.62	2.29
AUC _u /AUC _t	0.208	0.203	0.158	0.195
CL (L/h/kg)	7.11	6.26	8.79	6.31
T _{1/2} (h)	0.63	0.59	1.57	1.27

Abbreviations: C_{max}, peak plasma concentration; AUC, area under the plasma concentration-time curve; AUC_u/AUC_t, fraction unbound drug; CL, clearance; T_{1/2}, terminal half-life.

*Parameters are presented were derived from concentrations determined in plasma obtained at various time points after administration of a single dose of cisplatin (15 mg/kg) with or without pretreatment with nilotinib (150 mg/kg; p.o.) in DBA/lacJ (wild-type) mice or age-matched Oatp1b2(-/-) mice. The AUC was calculated using non-compartmental pharmacokinetic analysis extrapolated out to 4 hours. The unbound platinum concentration was determined following ethanolic plasma-protein precipitation, as described (86). Parameters were calculated using the software package PK Solutions 2.0 (Summit Research Services).