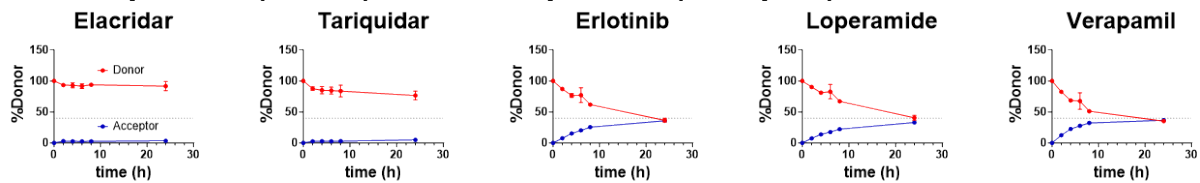


Additional Data file 5:

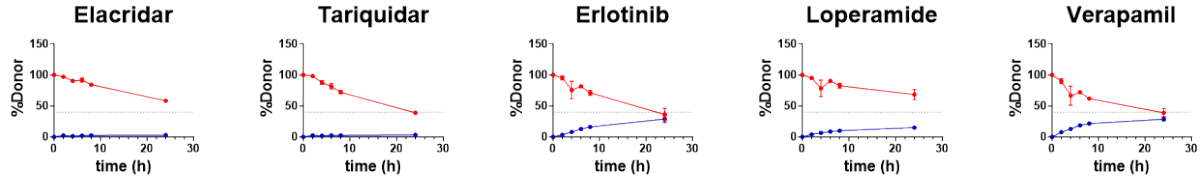
Figure 5 Rapid equilibrium dialyses of the 8 drug mixture plus elacridar and tariquidar.

The drug mixture (100 nM each drug) in human plasma, mouse plasma or complete medium (10% fetal calf serum) was added to the sample chamber (500 μ L; donor compartment) of the RED plate while blank human plasma was added to the buffer compartment (750 μ L; acceptor compartment). Because of the differences in volumes between donor and acceptor compartment, complete equilibrium would be achieved when reaching 40 nM (dashed line). The RED plate was incubated at 37°C and samples were collected at 2, 4, 6, 8 and 24 h from both compartments. Note that both in human and mouse plasma most drugs need at least 24 h to reach equilibrium. Intriguingly, elacridar, tariquidar but also vemurafenib remain mostly in the donor compartment. Elacridar and tariquidar were not stable in mouse plasma. The cause of this instability in mouse plasma is unknown but appeared to be dependent on the batch of mouse plasma used. Equilibrium is more rapidly reached when medium with 10% fetal calf serum is used. Moreover, in this case many drugs are more concentrated in the acceptor compartment which is in line with the presence of more protein. Recovery is not always complete, which may indicate loss due to degradation or adsorption.

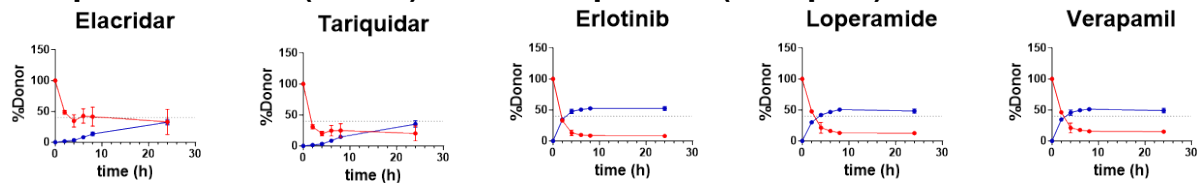
Human plasma (donor) to human plasma (acceptor)



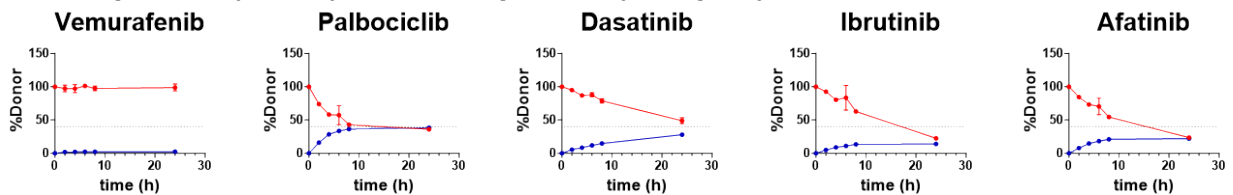
Mouse plasma (donor) to human plasma (acceptor)



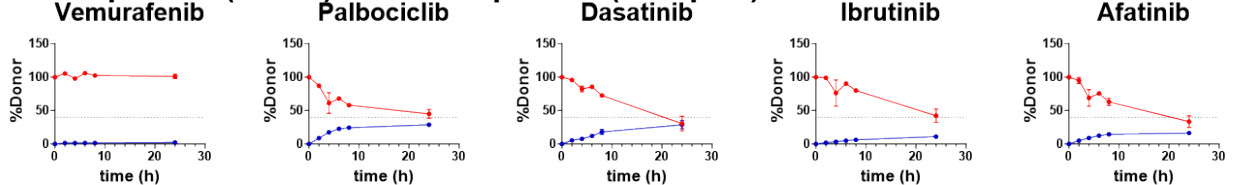
Complete medium (donor) to human plasma (acceptor)



Human plasma (donor) to human plasma (acceptor)



Mouse plasma (donor) to human plasma (acceptor)



Complete medium (donor) to human plasma (acceptor)

