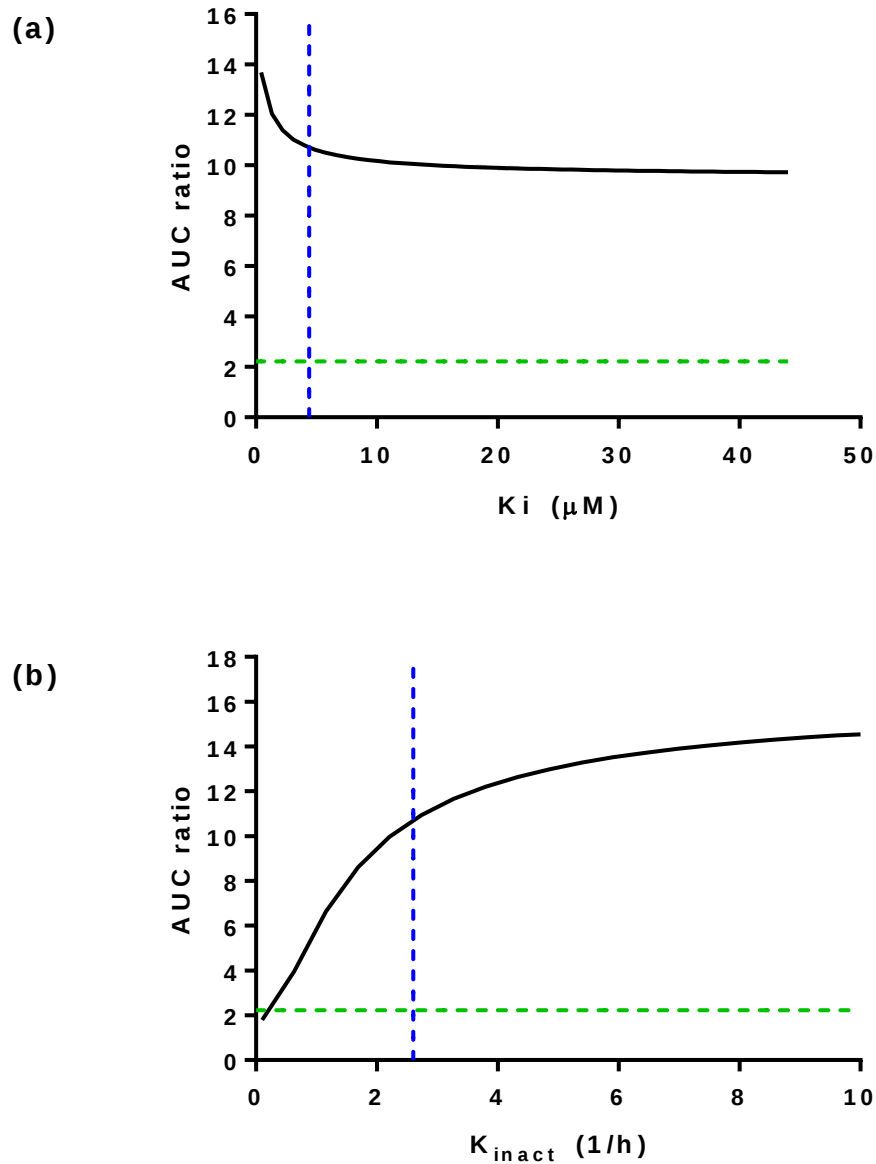


Figure S2. Sensitivity analyses of CYP3A4 (a) competitive inhibition and (b) time-dependent inhibition for midazolam AUC changes after a 2mg single oral dose in the presence of 600 mg ipatasertib QD



Green dashed line- observed midazolam AUC ratio of 2.22; blue dashed line- *in vitro* estimated K_i of 4.4 μM and K_{inact} of 2.6 $1/\text{h}$. Note: Shown here is the sensitivity analysis of the model with K_m of 0.195 μM . Same conclusions are drawn from the other two models with K_m of 1.95 μM and 19.47 μM .