Supplementary Materials

Supplementary Methods.

Analysis of imatinib and CGP74588. Imatinib and its pharmacological active metabolite CGP74588 were simultaneously quantitated in plasma samples by a validated assay based on liquid chromatography with tandem triple quadrupole mass spectrometry. The analytes of interested were extracted from the plasma matrix by liquid-liquid extraction from 25-μL aliquots of plasma with stable-labeled imatinib-d8 used as the internal standard. The multiple reaction monitoring settings (m/s) for the quantitation of imatinib, CGP74588 and imatinib-d8 were 494>394 (m/z), 480>394 (m/z) and 502>394 (m/z), respectively. Using calibration curves ranging from 20.0 to 5,000 ng/mL for both imatinib and CGP74588, peak area ratios were plotted as a function of the nominal concentration. For imatinib, a linear function was applied to the plot, while for CGP74588, a non-linear quadratic regression model was used. For imatinib, the within and between-run precisions at five tested concentrations, including the lower limit of quantitation (20.0 ng/mL), were ≤10.8 and ≤2.7%, respectively, while the average accuracy ranged from 97.5 to 107.5%. For CGP74588, the within and between-run precisions were ≤12.6 and ≤3.7%, respectively, with the accuracy ranging from 93.1 to 104.0.

Supplementary Figure 1

Possible transporter interactions between imatinib and rosuvastatin. Transporters involved in imatinib (red arrows) and rosuvastatin (blue arrows) pharmacokinetics are depicted, showing that imatinib and rosuvastatin share OATP1A2, ABCB1 and ABCG2 as a transporter at the intestinal level and OATP1B3, ABCB1 and ABCG2 at the hepatic basolateral and biliary membrane, respectively. Due to their involvement in the absorption, metabolism and excretion of both drugs, these transporters may affect imatinib and/or rosuvastatin pharmacokinetics during concomitant use.