



Pharmacokinetic Interaction Study of Combining Crizotinib with Dasatinib in Rats

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SUMMARY. This study examined whether oral administration of dasatinib to the rats with crizotinib led to any pharmacokinetic interactions. Twenty-four rats were divided randomly into 3 groups, crizotinib group (crizotinib 25 mg/kg, n = 8), dasatinib group (dasatinib 15 mg/kg, n = 8) and co-administration group (dasatinib 15 mg/kg and crizotinib 25 mg/kg, n = 8). The concentration of crizotinib and dasatinib in rat plasma was determined by a sensitive and simple UPLC-MS/MS method. There was statistical pharmacokinetics difference for crizotinib in the crizotinib group and co-administration group, when co-oral administration crizotinib with dasatinib, MRT_(0-t) and C_{max} decreased (p < 0.05). There was statistical pharmacokinetics difference for dasatinib in the dasatinib group and co-administration group, when co-oral administration dasatinib with crizotinib, CL and V decreased (p < 0.05), AUC_(0-t) and C_{max} increased (p < 0.01). These data indicate dasatinib could slightly influence the pharmacokinetic profile of crizotinib in rats, and vice versa, which might cause drug-drug interactions when using crizotinib with dasatinib.

RESUMEN. Este estudio examinó si la administración oral a ratas de dasatinib con crizotinib produce alguna interacción farmacocinética. Veinticuatro ratas se dividieron aleatoriamente en 3 grupos, el grupo crizotinib (crizotinib 25 mg/kg, n = 8), el grupo dasatinib (dasatinib 15 mg/kg, n = 8) y el grupo co-administración (dasatinib 15 mg/kg y crizotinib 25 mg/kg, n = 8). La concentración de crizotinib y dasatinib en plasma de rata se determinó por un método UPLC-MS/MS sensible y simple. Hubo diferencia estadística farmacocinética para crizotinib en el grupo de crizotinib y el grupo de co-administración; cuando se co-administró oralmente crizotinib con dasatinib, MRT_(0-t) y C_{max} disminuyeron (p < 0,05). Hubo diferencia estadística farmacocinética para dasatinib en el grupo de dasatinib y en el de co-administración; cuando se co-administró oralmente dasatinib con crizotinib, CL y V disminuyeron (p < 0,05), en tanto que AUC_(0-t) y C_{max} aumentaron (p < 0,01). Estos datos indican que dasatinib podría influir ligeramente el perfil farmacocinético de crizotinib en ratas y viceversa, lo que podría causar interacciones fármaco-fármaco cuando se utiliza crizotinib conjuntamente con dasatinib.

KEY WORDS: Crizotinib, Dasatinib, Interaction, Pharmacokinetic, Rat.

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