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Short communication

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Pharmacokinetic Interaction Study of Combining Crizotinib with Erlotinib in Rats by UPLC-MS/MS

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***SUMMARY*. This study examined whether oral administration of erlotinib 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), erlotinib group (erlotinib 25 mg/kg, n = 8) and co-administration group (erlotinib 25 mg/kg and crizotinib 25 mg/kg, n = 8). The concentration of crizotinib and erlotinib in rat plasma was determined by a sensitive and simple UPLC-MS/MS method. There was no statistical pharmacokinetics difference for crizotinib in the crizotinib group and co-administration group. There was statistical pharmacokinetics difference for erlotinib in the erlotinib group and co-administration group, when co-oral administration erlotinib with crizotinib, C_{max} decreased from 5582.7 to 3466.6 ng/mL ($p < 0.05$), $AUC_{(0-t)}$ decreased from 76252.7 to 54215.2 h.ng/mL ($p < 0.05$). These data indicate erlotinib could not influence the pharmacokinetic profile of crizotinib in rats, and crizotinib could influence the pharmacokinetic profile of erlotinib in rats, which might cause drug-drug interactions when using crizotinib with erlotinib.**

RESUMEN. Este estudio examinó si la administración oral de erlotinib con crizotinib a ratas condujo a alguna interacción farmacocinética. Veinticuatro ratas se dividieron aleatoriamente en 3 grupos: grupo crizotinib (crizotinib 25 mg/kg, n = 8), grupo erlotinib (erlotinib 25 mg/kg, n = 8) y grupo co-administración (erlotinib 25 mg / kg y crizotinib 25 mg/kg, n = 8). La concentración de crizotinib y erlotinib en plasma de rata se determinó por un método UPLC-MS/MS sensible y simple. No hubo diferencia estadística para la farmacocinética de crizotinib en el grupo de grupo crizotinib y co-administración. Tampoco hubo diferencia estadística farmacocinética de erlotinib en los grupos de erlotinib y co-administración, pero cuando se co-administró por vía oral erlotinib con crizotinib, C_{max} disminuyó de 5582,7 a 3.466,6 ng/mL ($p < 0,05$) y $AUC_{(0-t)}$ disminuyó de 76.252,7 a 54.215,2 h.ng/mL ($p < 0,05$). Estos datos indican que erlotinib no influiría en el perfil farmacocinético de crizotinib en ratas, pero crizotinib podría influir en el perfil farmacocinético de erlotinib en ratas, lo que podría causar interacciones farmacológicas cuando se utiliza crizotinib con erlotinib.

KEY WORDS: crizotinib, erlotinib, interaction, pharmacokinetic, rat.

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