Evaluation of the Effect of Ritlecitinib on the Pharmacokinetics of Caffeine in Healthy Participants

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October 22, 2022

Abstract

Objective: This clinical study was conducted to evaluate the impact of ritlecitinib on the pharmacokinetics (PK) of caffeine, a cytochrome P450 1A2 (CYP1A2) substrate. Methods: In this single-center, single-arm, open-label, fixed-sequence study, healthy participants received a single 100-mg dose of caffeine on two separate occasions: on Day 1 of Period 1 as monotherapy and on Day 8 of Period 2 after oral administration of ritlecitinib 200 mg once daily (QD) for 8 days. Serial blood samples were collected and analyzed using a validated LC/MS assay. PK parameters were estimated by using a non-compartmental method. Safety was monitored by physical examination, vital signs, electrocardiograms, and laboratory assessments. Results: Twelve participants were enrolled and completed the study. Co-administration of caffeine 100 mg in the presence of steady-state levels of ritlecitinib (200 mg QD) increased caffeine exposure compared with caffeine given alone. Area under the curve (AUCinf) and maximum concentration (Cmax) of caffeine increased by approximately 165% and 10%, respectively, when co-administered with ritlecitinib. The ratios of the adjusted geometric means (90% CI) for caffeine AUCinf and Cmax were 265.14% (234.12%-300.26%) and 109.74% (103.90%-15.91%), respectively, when caffeine was co-administered with steady-state ritlecitinib (test) compared with its administration alone (reference). Multiple doses of ritlecitinib when co-administered with a single dose of caffeine were generally safe and well tolerated in healthy participants. Conclusion: Ritlecitinib is a moderate inhibitor of CYP1A2 and can increase systemic exposures of CYP1A2 substrates.

Effect of Ritlecitinib on PK of Caffeine

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Key words: ritlecitinib, drug interaction, CYP1A2, caffeine, PK

Target journal: *British Journal of Pharmacology*

Character count for title (including spaces): 100/150

Character count for short title (including spaces): 40/40

Word count for article: 2689/4000

Word count for abstract: 233/250

References: 22/no limit

Figures/tables: 6/8

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