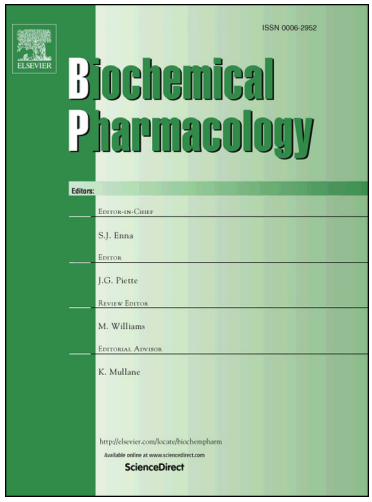
Accepted Manuscript



Ribociclib shows potential for pharmacokinetic drug-drug interactions being a substrate of ABCB1 and potent inhibitor of ABCB1, ABCG2 and CYP450 isoforms *in vitro*

Ales Sorf, Jakub Hofman, Radim Kučera, Frantisek Staud, Martina Ceckova

PII: S0006-2952(18)30156-4
DOI: https://doi.org/10.1016/j.bcp.2018.04.013
Reference: BCP 13122

To appear in: *Biochemical Pharmacology*

Received Date: 9 March 2018
Accepted Date: 13 April 2018

Please cite this article as: A. Sorf, J. Hofman, R. Kučera, F. Staud, M. Ceckova, Ribociclib shows potential for pharmacokinetic drug-drug interactions being a substrate of ABCB1 and potent inhibitor of ABCB1, ABCG2 and CYP450 isoforms *in vitro*, *Biochemical Pharmacology* (2018), doi: https://doi.org/10.1016/j.bcp.2018.04.013

Ribociclib shows potential for pharmacokinetic drug-drug interactions being a substrate of ABCB1 and potent inhibitor of ABCB1, ABCG2 and CYP450 isoforms *in vitro*

Ales Sorf[1], Jakub Hofman[1], Radim Kučera[2], Frantisek Staud[1], Martina Ceckova*[1]

[1]*Department of Pharmacology and Toxicology, Faculty of Pharmacy in Hradec Kralove, Charles University, Czech Republic, CZ*

[2]*Department of Pharmaceutical Chemistry and Drug Control, Faculty of Pharmacy in Hradec Kralove, Charles University, Czech Republic, CZ*

Abbreviations

95%CI, 95% confidential interval; AB, apical-to-basolateral; ABC, ATP-binding cassette; Abcb1, canine P-glycoprotein; ABCB1, human P-glycoprotein; ABCC1, multidrug resistance-associated protein 1; ABCG2, breast cancer resistance protein; BA, basolateral-to-apical; CDK, cyclin-dependent kinase; CDKI, cyclin-dependent kinase inhibitors; CI, combination index; CYP, cytochrome P450; DDI, drug-drug interaction; DMEM, Dulbecco's modified Eagle's medium; DNR, daunorubicin; EMA, European Medicines Agency; ER+, estrogen receptor positive; F_A, fraction of cells affected; FDA, US Food and Drug Administration; HER2-, human epidermal growth factor receptor 2; ITC, International Transporter Consortium; MDCKII, Madin-Darby canine kidney; MIT, mitoxantrone; PMS, phenazine methosulfate; qRT-PCR, quantitative reverse-transcription polymerase chain reaction; TKI, tyrosine kinase inhibitor; XTT, sodium 2,3-bis(2-methoxy-4-nitro-5-sulfophenyl)-5-[(phenylamino)-carbonyl]-2H-tetrazolium inner salt.

***Corresponding author:** Assoc. Prof. Dr. Martina Ceckova Ph.D., Department of Pharmacology and Toxicology, Faculty of Pharmacy in Hradec Kralove, Charles University, Akademika Heyrovskeho 1203, 500 05 Hradec Kralove, Czech Republic. Tel.: +420495067218, Fax: +420495067170, Email: martina.ceckova@faf.cuni.cz