A single-center, open-label, parallel control study comparing the pharmacokinetics and safety of a single oral dose of roflumilast and its active metabolite roflumilast N-oxide in healthy Chinese and Caucasian volunteers

Mai Han[1], Xiao-yan Lin[2], Gang Cui[1], Shuai Chen[2], Wei Wu[1], Na Mi[1], Jing Wang[1], Chun-yan Xiao[1], Xin Zhang[1], Xing Lu[1], and Jintong Li[1]

[1]China-Japan Friendship Hospital
[2]Affiliation not available

June 17, 2022

Abstract

Roflumilast is a phosphodiesterase 4 inhibitor developed for COPD treatment. Roflumilast N-oxide is the major metabolite with similar mechanism of action. The exposure difference between different races have been observed, but the need for dose adjustment have been controversial. The present study compared the pharmacokinetics of a single dose of the original oral roflumilast tablets (Daliresp®) 0.5 mg in healthy Chinese and Caucasian subjects under uniform conditions. The Chinese subjects were found to have longer t1/2, higher AUC0-t, AUCinf and Cmax than the Caucasian subjects. Compared to Caucasian subjects, the point estimate on geometric mean of AUC0-t and AUCinf in Chinese subjects was respectively 22% and 25% higher for roflumilast, and 46% and 48% higher for roflumilast N-oxide. The point estimate on geometric mean of Cmax 9% higher for roflumilast, and 24% higher for its N-oxide. After body weight normalization, the difference of pharmacokinetics (PK) exposure reduced but did not eliminate. Compared to the Caucasians, tPDE4i in Chinese subjects was 44% higher. After body- weight normalization, the difference reduced to 27%. Safety analysis showed signs indicating Chinese were less tolerant to roflumilast than Caucasians, or have different pharmacodynamic response. Our study suggests a dose of roflumilast lower than 0.5 mg daily for Chinese patients or future clinical trials. More dose exploration studies are needed to determine the optimal doses of roflumilast for Chinese COPD patients.

Hosted file

`roflumilast racial difference1.docx` available at https://authorea.com/users/489944/articles/573436-a-single-center-open-label-parallel-control-study-comparing-the-pharmacokinetics-and-safety-of-a-single-oral-dose-of-roflumilast-and-its-active-metabolite-roflumilast-n-oxide-in-healthy-chinese-and-caucasian-volunteers

Hosted file

`figure.docx` available at https://authorea.com/users/489944/articles/573436-a-single-center-open-label-parallel-control-study-comparing-the-pharmacokinetics-and-safety-of-a-single-oral-dose-of-roflumilast-and-its-active-metabolite-roflumilast-n-oxide-in-healthy-chinese-and-caucasian-volunteers

Hosted file

`tables.docx` available at https://authorea.com/users/489944/articles/573436-a-single-center-

open-label-parallel-control-study-comparing-the-pharmacokinetics-and-safety-of-a-single-oral-dose-of-roflumilast-and-its-active-metabolite-roflumilast-n-oxide-in-healthy-chinese-and-caucasian-volunteers