Clin Pharmacokinet (2014) 53:203
DOI 10.1007/s40262-013-0118-x

LETTER TO THE EDITOR

Response to "Ethnic-Specific In Vitro–In Vivo Extrapolation and Physiologically Based Pharmacokinetic Approaches to Predict Cytochrome P450-Mediated Pharmacokinetics in Chinese Population: Opportunities and Challenges"

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Published online: 20 November 2013
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We thank Dr Li and his colleagues for their comments, and agree that the development of population physiologically based pharmacokinetic models is always a work in progress pending the availability of additional data. The extra data that Li et al. [1] document relate to liver weight, cardiac output and cytochrome P450 (CYP) phenotype frequencies in Chinese subjects.

The additional data on liver weight for 1,114 subjects obtained at autopsy suggest a 9 % higher mean value than the value from our meta-analysis of data from 342 subjects measured by computed tomography. Nevertheless, both values are lower than the mean value observed from our meta-analysis of Caucasian data.

In contrast to our analysis, which found a lower mean cardiac output in Chinese than in Caucasians, the data of Cao [2] cited by Dr Li and colleagues suggest the reverse. This difference should primarily affect the accuracy of the prediction of systemic clearance after intravenous administration of drugs with relatively high hepatic extraction ratios. Our predictions for plasma concentrations of midazolam, which has a hepatic extraction ratio of about 0.5 after intravenous injection, were similar to the observed data.

With the exception of the frequency of CYP2D6 ultra-rapid metabolisers in Chinese (18 %), the CYP frequencies established from additional data by Li et al. [1] were similar to those that we reported. A review of the study of Guo et al. [3], quoted by Li et al. [1], indicates that their assessment was apparently not based on data for gene duplication but simply on the frequency of *CYP2D6**10 alleles. Thus, the value of 18 % is markedly higher than the figure of 1–2 % documented for Asian populations in general [4, 5] and by our meta-analysis [6].

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