Letter to the Editor

Response to “Clinical Relevance of CYP3A5 Genotype on Maraviroc Exposures”

We appreciate the comments by Vourvahis et al. (2015). We agree, and we believe that it goes without saying, that there are several variables that affect the pharmacokinetics of any drug, including maraviroc. Yet our study is the only work to date to report investigations of the effect of the cytochrome P450 genotype on maraviroc pharmacokinetics. As such, although the commentary provided by Vourvahis et al. regarding the relationship between ethnicity and maraviroc pharmacokinetics is interesting, the comparison of maraviroc exposure based on ethnicity cannot be used to substitute or surmount analysis of maraviroc exposure based on the CYP3A5 genotype since each of the African American and European American groups contain a mixture of CYP3A5 genotypes (homozygous wild type, heterozygous, and homozygous dysfunctional). For instance, previous studies have noted that 10%–40% of Europeans/European Americans are either homozygous or heterozygous for the CYP3A5*1 allele, resulting in expression of CYP3A5 protein that is readily detectable and comparable in abundance to what has been observed in African Americans with at least one CYP3A5*1 allele (Kuehl et al., 2001; Lamba et al., 2002; Lin et al., 2002). Hence, simple juxtaposition of ethnicity and genotype creates a false parallel that does not actually speak to whether the CYP3A5 genotype contributes to interindividual differences in maraviroc pharmacokinetics, which is a concept that our work was the first to put forth. Thus, we are excited to hear that in light of our findings, other groups are planning to perform analyses of the relationship between the

CYP3A5 genotype and maraviroc pharmacokinetics, and we anxiously await the results of these studies.

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