

ALTERNATIVE VIEWPOINTS

Is the Drug Interaction Actual between Posaconazole and Cyclosporine?

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The recent article by Dr. Sansone-Parsons and colleagues, titled "Effect of Oral Posaconazole on the Pharmacokinetics of Cyclosporine and Tacrolimus", suggests that the dose of cyclosporine (CSA) and tacrolimus should be reduced when coadministered with posaconazole (PCZ).¹ After reading the article, we noticed a few important issues that we would like to bring to the attention of the readers of *Pharmacotherapy*.

The correct dosing interval for CSA in adult cardiac transplant patients is twice daily (BID).² However, the abstract stated that CSA was administered three times a day and the method section reported that CSA was given BID. Therefore, we would like to know what dosing frequency was used in this study. Furthermore, although CSA trough (C_0) concentrations are important in dose adjustment, these concentrations were not reported. Thus, it is unclear as to whether a protocol was used in determining CSA dose reductions.

Another point that was not mentioned by the authors was what effect PCZ would have on CSA pharmacokinetics beyond day 10.

Finally, we have difficulty concurring with the results presented in Table 2 titled "Pharmacokinetics of CSA in Four Heart

Transplant Recipients".¹ According to the table, after CSA dose reductions there were no differences in the pharmacokinetic parameters (i.e., C_{max} and AUC_t) of CSA when given alone compared to coadministration of PCZ. However, if CSA dose adjustments were done based on C_0 concentrations to prevent fluctuation of CSA systemic exposure, one would expect to see differences in pharmacokinetic parameters of CSA between the two study phases.

In summary, we believe there is a potential drug-drug interaction between CSA and PCZ. For this reason patients taking both medications will require close monitoring of CSA concentrations. Adjustments of CSA doses might be necessary to prevent acute rejection and drug toxicity.

References

1. Sansone-Parsons A, Krishna G, Martinho M, Kantesaria B, Gelone S, Mant TG. Effect of posaconazole on the pharmacokinetics of cyclosporine and tacrolimus. *Pharmacotherapy* 2007;27(6):825-34.
2. Valantine H. Neoral use in the cardiac transplant recipient. *Transplant Proc* 2000;32(Suppl):27S-44S.

Authors' Reply

The authors declined to reply.

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