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LETTER TO THE EDITORS

Valganciclovir for Cytomegalovirus Prophylaxis in Liver Transplant Recipients

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TO THE EDITORS:

We thank Jain et al. for their interest and correspondence regarding our recently published study.[1] The authors note that the incidence of cytomegalovirus (CMV) disease in our retrospective study was much lower than that reported by others. As acknowledged in our article, we did not use routine surveillance to detect CMV viremia and the true rate of CMV infection could have been higher than what we reported. However, it is unlikely that we did not account for most or all cases of clinically significant or symptomatic CMV infection due to the frequent follow-up schedule in our liver transplant program.

The overall incidence of CMV disease in our high to moderate risk liver transplant recipients at 12 months posttransplantation of 3% and 4% with valganciclovir and ganciclovir, respectively, is similar to that previously reported by Gane et al.[2] (4.8% with ganciclovir at 6 months). In addition, the incidence of CMV disease in our high risk group of 7% and 22% with valganciclovir and ganciclovir, respectively, was similar to that reported by others using ganciclovir (9.3-21.4%).[2-4] Finally, the valganciclovir pivotal study reported a 12% incidence of CMV disease at 6 months in their high-risk control group using the same dosing regimen of ganciclovir as ours.[5] Therefore, we feel the overall low rate of CMV disease in our study was similar to that reported in other large studies which used prospective surveillance methods.[2-6]

In a previously published study by Jain et al.,[7] the incidence of CMV infection was high, at 17% overall and 25.9% in high risk patients using a valganciclovir regimen of 900 mg/day or 450 mg every other day depending on renal function for 3 to 6 months posttransplantation. The authors concluded that valganciclovir prophylaxis was ineffective in liver transplant recipients. However, their study did not include a contemporary or historical control group. In addition, the clinical characteristics of patients assigned to the different dosing regimens and how the medication was dosed in patients with renal insufficiency were not provided. It is possible that some of their patients received an inadequate dose of valganciclovir on the 450 mg every other day regimen if the dose was not adjusted for improved renal function and this could, in part, explain the high incidence of CMV disease seen in their cohort. In addition, the more prolonged follow-up in their study of 19 ± 6 months may have contributed to the higher cumulative incidence of CMV disease compared to our study and others, although the number of patients who developed CMV disease after 1 yr was not reported.

Jain et al. raise the interesting possibility that liver transplant recipients may have lower ganciclovir exposure with oral valganciclovir due to ineffective or deficient esterase activity early posttransplantation or via drug interactions with mycophenolate mofetil. However, this hypothesis is not supported by a recent pharmacokinetic study in which the area under the concentration-time curve of ganciclovir after valganciclovir intake at 1 to 3 months posttransplantation was similar across organ types (liver, 46.0 ± 16.1 μg · hour/mL; heart, 40.2 ± 11.8 μg · hour/mL; kidney, 48.2 ± 14.6 μg · hour/mL).[8] Nonetheless, we agree that adequate exposure to therapeutic levels of ganciclovir in the blood are important to minimize the risk of CMV viremia as recently shown by Wiltshire et al.[9] In addition, surveillance for CMV infection after cessation of antiviral prophylaxis is particularly important during the first year posttransplantation, when patients are receiving high levels of immunosuppression.

Our study was not designed to determine if valganciclovir provides adequate prophylaxis against CMV in liver transplant recipients but rather to review outcomes with low-dose valganciclovir compared to a historical control that received oral ganciclovir. We agree that in order to better define the optimal dose, frequency, and duration of valganciclovir prophylaxis to use in liver transplant recipients additional prospective, multicenter trials are needed.

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Abbreviations: CMV, cytomegalovirus.

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