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LETTER TO THE EDITORS

Question of Using Valganciclovir for Cytomegalovirus (CMV) Infection Prophylaxis in Post–Liver Transplant Recipients

TO THE EDITORS:

We read the article by Park et al. with great interest.[1]

The authors retrospectively studied the efficacy of low-dose oral valganciclovir (n = 49) compared with the standard dose of ganciclovir (n = 60) for the prevention of cytomegalovirus (CMV) disease in adult liver transplant recipients. The authors found 2 patients in each group with CMV disease within 1 year of follow-up. Both patients in the ganciclovir group were high risk for CMV (donor positive, recipient negative), while in valganciclovir group, 1 patient was high-risk and 1 was low risk.[1]

Absorption of valganciclovir has been found to be 10 times higher than oral ganciclovir, with bioavailability of nearly 60% in healthy volunteers and in patients who are human immunodeficiency virus positive with CMV. Based on these findings, we agree that the greater absorption and antiviral activity of valganciclovir offers an attractive option for prophylaxis against CMV after solid-organ transplantation.[2-4]

However, when we analyzed 203 consecutive post–liver transplant recipients treated with prophylactic valganciclovir between July 2001 and May 2003, we found an overall rate of 17% symptomatic CMV, when either the donor or the recipient was exposed to CMV. It was 25.9% in the high-risk group, (donor positive, recipient negative, based on CMV serology). Some of the patients developed CMV even while on valganciclovir prophylaxis.[5,6] Since our publication, we have screened more high-risk recipients for CMV during and after valganciclovir prophylaxis and have found a higher rate than the rate published earlier.

In concurrence with our findings, a double-blind, prospective trial was conducted by Roche laboratories (manufacturers of valganciclovir and ganciclovir) in 372 posttransplantation patients with high risk for CMV disease (heart, n = 56; liver, n = 177; kidney, n = 120; and kidney/pancreas, n = 11) comparing valganciclovir and ganciclovir prophylaxis. The overall results at 6 months suggested that the rate of CMV disease (including invasive CMV) was 12.1% with valganciclovir prophylaxis compared to 15.2% with ganciclovir. However, in liver transplant recipients, the rate of invasive CMV disease was 12% in the valganciclovir group compared to 3% in oral ganciclovir group. Based on these findings, valganciclovir was not recommended for CMV prophylaxis in high-risk liver transplant recipients.[7]

One fails to understand why liver transplant recipients had higher rates of CMV compared to kidney or heart transplant recipients under valganciclovir prophylaxis. Both mycophenolate mofetil and valganciclovir require esterase to convert them into active forms (mycophenolic acid and ganciclovir, respectively). Post–liver transplant recipients often have initial hepatic and/or bowel dysfunction, and therefore the enzyme may be quantitatively deficient or qualitatively ineffective. Improved absorption of valganciclovir over time has been reported in liver transplant recipients. Also, valganciclovir could be competing with mycophenolate mofetil for esterase to be converted to active ganciclovir. Previous pharmacokinetic studies on valganciclovir were performed 21 to 180 days after liver transplant.[2-4] There is a lack of pharmacokinetic data in the early post–transplant period.

In the present report, it is possible that the authors might have found a lower rate of CMV because not all patients were screened for CMV disease after discontinuation of prophylaxis. In addition, because of the retrospective nature of the study, some patients might have been missed, as some patients might not have presented to their clinic or might not have been documented adequately.

It is particularly important to note that the overall rate of CMV disease was only 4% in the entire group,[1] much lower than that observed by others.

We feel that the findings of this retrospective study, which indicates that valganciclovir provides adequate prophylaxis for liver transplant recipients, should be treated with caution in clinical practice until more prospective clinical trials are conducted. It is important to have a high degree of suspicion for CMV infection during and, particularly, after discontinuation of valganciclovir prophylaxis.

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