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Reply to Singh

To the Editor—We read the letter from Singh [1] with great interest, because she outlined several important issues that may not be easy to clarify. The recent article by Arthurs et al. [2], which was not available when we wrote our review, suggests that late-onset cytomegalovirus (CMV) disease may not be as mild as has been previously reported by others. In our long-lasting experience with anti-CMV prophylaxis [3], late-onset CMV disease was perceived and evaluated as a relatively mild event, at least in kidney transplant recipients, with few symptoms and a benign course after receipt of ganciclovir or valacyclovir therapy. It should be noticed that the figures reported by Arthurs et al. [2] were unusually high: a 29% incidence of late-onset CMV disease, compared with incidences of 16% in the valacyclovir group in the study by Lowance et al. [3] and 17.2% (in the valganciclovir group) and 18.4% (in the oral ganciclovir group) in the pivotal study by Paya et al. [4]. In our own experience, 17% of kidney transplant recipients develop late-onset CMV disease (data not shown). Although the cause is not clear (because these transplant recipients were at high immunological risk), the relatively high figures reported by Arthurs et al. [2] may have affected the results regarding the impact of late-onset CMV in terms of allograft loss or mortality.

The discussion about the consequences of late-onset CMV disease is more than an academic debate. Indeed, it is aimed at answering relevant questions regarding the best means to prevent post-transplantation CMV disease. Data from a recent meta-analysis indicated that both prophylaxis and preemptive treatment reduced the incidence of CMV disease and of acute transplant rejection; however, prophylaxis without preemptive treatment did reduce the incidence of bacterial and fungal infections and death [5]. When prophylaxis and preemptive treatments were compared with one another, there was, indeed, no statistically significant difference with regard to efficacy in the prevention of CMV disease [6, 7]. However, in the study by Reischig et al. [6], there were slight and statistically significant benefits in the prophylaxis group with regard to CMV-DNAemia at 12 months, incidence of biopsy-proven acute rejection, and CMV-associated costs. Moreover, in the recent study by Kliem et al. [7], long-term graft survival at 2, 3, and 4 years was significantly improved in the prophylaxis group. These recent data, together with the simple use of prophylaxis after transplantation, suggest that the prophylactic approach may become a more attractive strategy to prevent CMV disease after organ transplantation.

Finally, as mentioned by Singh [1], the issue of the most appropriate duration of antiviral prophylaxis will be partly solved by the ongoing Improved Protection Against Cytomegalovirus in Transplant (IMPACT) study. If, among high-risk patients undergoing donor-positive/recipient-negative transplantations, the incidence of late-onset CMV disease decreases as the length of anti-CMV prophylaxis increases, this may have a beneficial impact on morbidity and mortality that would be an important new step in defining the optimal CMV disease prevention strategies.

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