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Valganciclovir

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Ganciclovir, the standard anti-cytomegalovirus (CMV) drug in transplant recipients, is given either intravenously (for treatment or prevention) or orally (for prevention). Intravenous ganciclovir, although extremely effective, is inconvenient for long term use, as it is associated with the risk of catheter-related sepsis and necessitates frequent homehealth visits. While oral ganciclovir obviated these problems, its poor bioavailability results in low drug exposure, necessitating large oral doses with limited efficacy for established disease. In addition, the CMV disease rate of 15% in the high-risk donor/recipient-negative combination, while lower than that without prophylaxis, is higher than that achieved with intravenous ganciclovir. Oral valganciclovir, which provides drug exposure in transplant recipients comparable with that achieved with intravenous ganciclovir, should represent a significant advance in the prevention and treatment of CMV disease in transplant recipients. It may replace intravenous ganciclovir in most post-transplant situations.

An alternative to primary prevention, preemptive therapy, monitors patients for the presence of CMV antigenaemia or viral DNA. Only patients who demonstrate viral replication are then treated with ganciclovir. The optimal management of such patients when viral replication is detected is not clear. Oral ganciclovir, even at high doses, may not provide adequate drug concentrations to suppress viral replication in many patients. The increased drug exposure obtained with valganciclovir may improve this.

Although oral ganciclovir has been shown to reduce asymptomatic infection in most CMV risk groups, the rate of subclinical infection may remain quite high (up to 60% amongst those at highest risk). This CMV infection rate is associated with chronic rejection of kidney transplants, restenosis of cardiac atherosclerosis and transplant atherosclerosis in heart transplants. Better suppression of subclinical infection associated with the greater ganciclovir exposure provided by valganciclovir may translate into reduced vascular damage or chronic rejection.

The tolerability profile of valganciclovir will ultimately be determined in large efficacy studies that are underway. However, since the ganciclovir exposure from valganciclovir falls between that of oral ganciclovir and intravenous ganciclovir, it is expected that the tolerability profile should reflect this.

A concern with the use of oral ganciclovir is that the low drug exposure may favour the selection of ganciclovir-resistant CMV. The higher ganciclovir levels achievable with valganciclovir may eliminate this problem. Finally, established CMV disease may be treatable with oral administration, obviating the need for long term intravenous access with its associated morbidity. This is particularly relevant to children. Clinical trials with an oral paediatric valganciclovir liquid preparation, designed to determine the optimal dose, are underway in paediatric organ recipients. ▲