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Valganciclovir
A Viewpoint by Sharon Walmsley

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In the era of highly active antiretroviral therapy (HAART), the incidence of new cases of cytomegalovirus (CMV) retinitis in HIV-infected patients has decreased dramatically. Nonetheless, patients with advanced HIV infection still present with CMV retinitis as their initial or subsequent AIDS-defining illness (namely those who were previously unaware of their HIV status and those not treated with, or failing, HAART). CMV retinitis can also occur shortly after the initiation of HAART in patients undergoing immune reconstitution.

CMV retinitis can be a frightening and potentially sight-threatening opportunistic infection. The patient is faced with issues related to the infection, the treatment of the infection and their own mortality. Oral valganciclovir takes away one of the 'stresses' of a new diagnosis of CMV retinitis. In the past, patients had many concerns about the need for long term intravenous catheters. These include:

- the potential for infectious and mechanical complications
- confidentiality issues e.g treating oneself in public, or going to the gym or other settings where the chest wall may be exposed
- maintenance of a normal lifestyle.

The fact that treatment can now be given orally allows the patients to better concentrate on optimising their antiretroviral therapy, which can contribute to improved outcomes of CMV retinitis.

Although oral ganciclovir is available, it has its limitations. The requirement for 12 tablets a day to be taken on a three-times daily schedule, in addition to HAART, provides a significant threat to patient compliance. Although comparable outcomes were observed when oral and intravenous formulations of ganciclovir were used as maintenance therapy, the ability of oral ganciclovir to achieve maximal concentrations in the retina is a concern. This is especially so in patients at risk of further loss of sight, such as those with ocular nerve involvement, macular disease and zone 1 disease. The pharmacokinetic and clinical trial data currently available for oral valganciclovir favour its use as maintenance therapy in these high-risk patients. Oral valganciclovir is also suitable for use as induction therapy.

Valganciclovir will therefore become the treatment of choice for the induction and maintenance therapy of HIV-associated CMV retinitis provided there are no contraindications such as anaemia, neutropenia or uncontrolled diarrhoea. It has the ability to combine efficacy and tolerability with convenience. Compared with either the oral or the intravenous formulations of ganciclovir, no additional toxicities are associated with the valine ester of ganciclovir. Whether any changes will emerge in the resistance profile of valganciclovir is uncertain. ▲