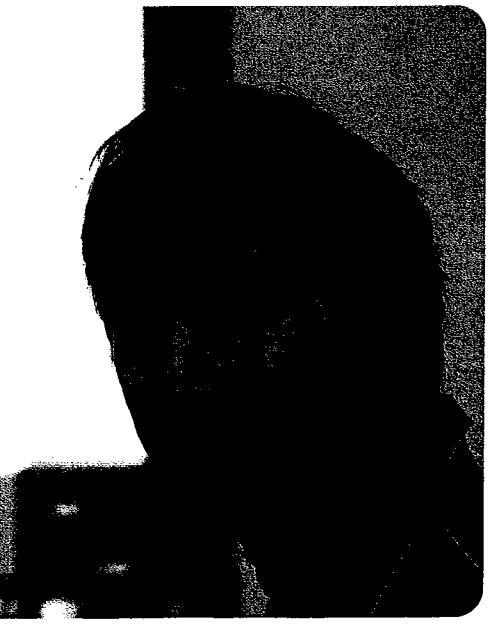

Oral valganciclovir for CMV retinitis

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[illegible]	**Case Report** Woman, 27 years, originating from Burundi. Fever and cervical adenopathy during a visit in Belgium. Diagnosis of HIV infection, with CD4+ = 36/mm³. Hospitalisation for adenopathy biopsy, which revealed granulomas suggestive for tuberculosis (TB). Anti-TB treatment started. Adenopathy disappeared, no fever, felt better and went back to Burundi, with cotrimoxazol prophylaxis.
[illegible]	Arrived in Belgium with fever, dyspnea, dysphagia, and deterioration of general condition. Hospitalisation: CD4+ = 9/mm³ and HIV RNA >750 000 copies/mL. Chest X-Ray: interstitial syndrome. Empiric treatment for *Pneumocystis carinii pneumonia*, but BAL remained negative, and no clinical improvement. Gastroscopy: severe CMV esophagitis. Fundoscopy: CMV retinitis (cfr photo initial visit). Conclusion: systemic CMV disease, including CMV pneumonia. Treatment: iv ganciclovir 250 mg twice daily (5 mg/kg) infused over 4 h for 3 weeks. Rapid improvement of general condition.
[illegible]	Antiretroviral therapy started (lamivudine, stavudine, efavirenz).
[illegible]	Maintenance therapy with 900 mg oral valganciclovir daily.
[illegible]	CD4+ = 203/mm³ and undetectable viral load (<50 copies/ml); therapy unchanged.

CMV in AIDS Patients

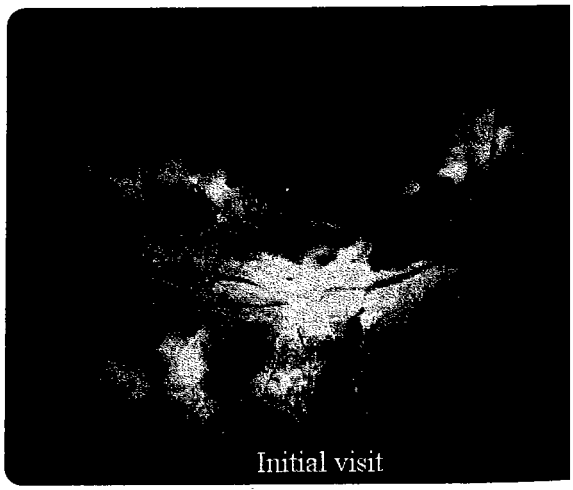
Despite very effective and well tolerated antiretroviral therapy, we still see AIDS patients with complications due to progressive immunodeficiency, including *Pneumocystis carinii pneumonia* and *Mycobacterium avium complex* (MAC) or *Cytomegalovirus* (CMV) infection. The cumulative incidence of CMV retinitis at 27 months for patients with CD4+ lymphocyte counts of 100/mm³ or 50/mm³ is respectively 26.3% and 41.9%[1]. In one series, the cross-sectional prevalence of CMV-retinitis in patients with CD4+ <50/mm³ was reported to be 30%[2].

CMV retinitis and CMV systemic disease are the most frequent complications in extremely advanced AIDS patients (CD4+ <10/mm³), although not in Africans. In the case we report, the first complication was extrapulmonary tuberculosis, which was detected quickly and treated efficiently. Had the patient remained in Belgium, antiretroviral therapy initiation would not have been postponed, and would probably have avoided the CMV infection.

CMV affects the eye in about 30% of cases. It usually affects one eye at first, but then progresses to the contralateral eye. The symptoms, including floaters (spots, bugs, spider webs), light flashes, blind spots, blurred vision, obstructed areas of vision, sudden decrease of vision, are due to inflammation and detachment of the retina. The risk of total retinal detachment, leading to permanent vision loss and even blindness, is elevated and occurs quickly.

CMV retinitis is the most frequent and first expression of CMV disease, but colitis, esophagitis, pneumonia and encephalitis are also possible.

Before the availability of valganciclovir, the treatment of CMV retinitis and CMV systemic disease consisted of intravenous ganciclovir and was a heavy burden for the patient. For induction thera-



Initial visit

py, the dose is 5 mg/kg twice daily via intravenous infusion, lasting several hours, for 3 weeks. Maintenance therapy is at the same dose once daily iv, 7 days a week (or 6 mg/kg once daily 5 days a week). IV administration requires a port-a-cath implant for daily injections under meticulous hygienic measures. Even then, the infectious risk remains high. Some ophthalmologists inject gangiclovir directly into the eye, or administer an intraoccular ganciclovir sustained-release eye implant.

New oral drugs

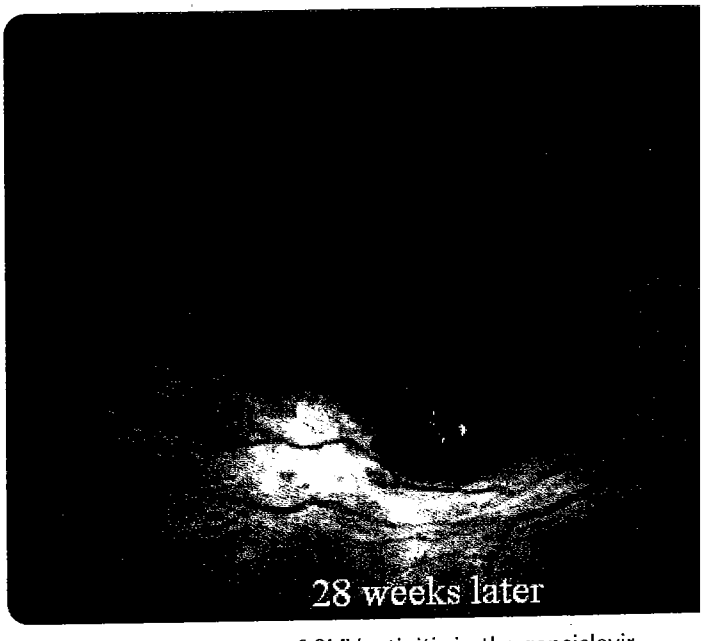
Due to low bioavailability, oral ganciclovir (Cymevene®) is suitable only as maintenance therapy. Pill burden is high (3000 mg or 2x500 mg capsules 3 times daily).

In contrast, valganciclovir (Valcyte®), the new oral prodrug of ganciclovir, has high bioavailability allowing its use for induction therapy, with a dramatic decrease in pill count. The dose of valganciclovir for induction therapy is 900 mg (2 tablets) twice daily for 3 weeks, followed by maintenance therapy of 900 mg once daily. Data suggest maintenance therapy can be discontinued when antiretroviral therapy has restored immunity: CD4+ >100/mm³, undetectable HIV viral load and negative CMV PCR[3].

Oral valganciclovir enables a much shorter hospitalisation period and reduces the risk of catheter-induced infections and mechanical complications[4]. Only when the patient is unconscious or has dysphagia due to esophagitis (as described in this patient), is intravenous therapy preferred.

Efficacy of valganciclovir

In a controlled study oral valganciclovir was compared to intravenous ganciclovir as induction therapy for newly diagnosed CMV retinitis in patients with AIDS[5]. After 4 weeks, all patients received valganciclovir as maintenance therapy. During the first 4 weeks, 10% had progression of CMV retinitis in the ganciclovir group and 9.9% in the valganciclovir group. A satisfactory response was obtained in 77% and 71.9% of the patients respectively, and median time to progression of retinitis was 125 and 160 days. The mean values for the area under the curve for the ganciclovir dosage interval were similar at both induction and maintenance doses. The frequency and severity of adverse events were similar. Conclusion: Oral valganciclovir is as effective and as well tolerated as intravenous ganciclovir, but more convenient and patient-friendly in these very ill and multimedicated patients.



Ocular clinical history

- **First visit: 26.6.2002**
  - CMV retinitis in vascular distribution characterised by fluffy-white retinal infiltration and large areas of intraretinal hemorrhages
  - Visual acuity: 0.4
  - Other eye: normal
- **After starting valganciclovir**
  - Development of inactive chorioretinal scar (complete healing noted on 19.9.2002).
  - Neither progression nor relapse of CMV retinitis was observed during the entire treatment period (28 weeks)
  - Visual acuity improved to 0.9
  - Other eye remained normal
- **Last visit: 13.1.2003**
  - Chorioretinal scar tissue with stable visual acuity
  - Other eye: normal

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