Preemptive valganciclovir for cytomegalovirus infection in hematological patients


To the Editor

We read with interest the findings by Busca et al. (1) published in the Journal, adding to similar recent findings supporting the efficacy of preemptive valganciclovir in allogeneic hematopoietic stem cell transplant (HSCT) recipients (2, 3).

We add here our single-center preliminary experience in hematological patients. Before November 2005 we usually treated cytomegalovirus (CMV) reactivation (higher than 1500 copies/mL) with intravenous ganciclovir. During a 24-month period starting in November 2005, all our patients undergoing HSCT or aggressive chemotherapy were monitored with weekly real-time quantitative polymerase chain reaction (PCR) assay (Cobas Amplicor CMV Monitor test, Roche Diagnostics, Mannheim, Germany; sensitivity = 600 CMV DNA copies/mL) on peripheral blood during treatment and in the first 3 months after discharge. Thirty-seven patients with CMV viremia higher than 1500 copies/mL (at a median of 45 from end of chemotherapy or HSCT) were identified and treated for 3 weeks with preemptive oral valganciclovir 450 mg b.i.d. (n = 5) or 900 mg b.i.d. (n = 32) according to renal function. No patient had concurrent infections or was receiving steroids at the time of reactivation. No reduction in immunosuppression was performed in allogeneic HSCT recipients at the time of CMV reactivation.

All but 2 patients who reactivated CMV after aggressive chemotherapy (n = 13: 7 myeloablative and 6 nonmyeloablative), or autologous (n = 5: 4 high-dose melphalan and 1 BEAM) or allogeneic (n = 19) HSCT showed weekly drops in CMV levels and finally cleared viremia at the final control on day 21 day since beginning of treatment. Both patients who failed the endpoint were allogeneic HSCT recipients with initial loads lower than 5000 copies/mL who had been treated with valganciclovir 900 mg b.i.d.; they had persistent low-level viremia (4000 copies/mL) for at least 2 months despite salvage treatment with intravenous foscarnet. Only 3 patients, all allogeneic HSCT recipients, developed neutropenia (absolute neutrophil count <500/μL) while on valganciclovir, which could be explained by concurrent immunosuppressive drugs.

The median initial viral load in our cohort was 3900 copies/mL, which is a relatively low level and could have contributed to the high efficacy of valganciclovir. With the use of such a low threshold, we did not observe any case of symptomatic CMV disease.

Recent data support that the efficacy of valganciclovir 450 mg b.i.d. is identical to 900 mg b.i.d. in allogeneic HSCT recipients (90% clearance of antigenemia on day +21) (4), and this is likely true whenever initial CMV load remains quite low, allowing proper treatment of patients with renal failure.

In reduced-intensity conditioning HSCT recipients without gastrointestinal graft-versus-host disease (GvHD), the
British Society of Blood and Marrow Transplantation has just finished a multicentric phase I/II study comparing oral valganciclovir (900 mg twice daily) for 14 days to intravenous ganciclovir (5 mg/kg twice daily) on PCR-based preemptive therapy for active CMV infection; the encouraging results are expected to be published within a few months (personal communication). Concerns remain regarding the availability of oral valganciclovir in patients with gastrointestinal mucositis (which could impair valganciclovir absorption); 2 studies in allogeneic HSCT recipients with stable gastrointestinal GvHD have shown that ganciclovir exposure after 900 mg of valganciclovir was not inferior to that of intravenous ganciclovir (5, 6).

In solid organ transplant recipients, Asberg et al. (7) have recently shown in a multicenter randomized trial that oral valganciclovir is as effective as intravenous ganciclovir for preemptive therapy for CMV reactivation (8), first achieving the A-I level indication of evidence-based medicine for this drug.

References

3. van der Heiden PL, Kalpoe JS, Barge RM, Willemze R, Kroes AS, Schippers EF. Oral valganciclovir as pre-emptive therapy has similar efficacy on cytomegalovirus DNA load reduction as intravenous ganciclovir in allogeneic stem cell transplantation recipients. Bone Marrow Transplant 2006; 37: 693-698.