Influence of IFNL3/4 Polymorphisms on the Incidence of Cytomegalovirus Infection After Solid-Organ Transplantation

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BACKGROUND
Polymorphisms in IFNL3 and IFNL4, the genes encoding interferon λ3 and interferon λ4, respectively, have been associated with reduced hepatitis C virus clearance. We explored the role of such polymorphisms on the incidence of cytomegalovirus (CMV) infection in solid-organ transplant recipients.

METHODS
White patients participating in the Swiss Transplant Cohort Study in 2008-2011 were included. A novel functional TT/-G polymorphism (rs368234815) in the CpG region upstream of IFNL3 was investigated.

RESULTS
A total of 840 solid-organ transplant recipients at risk for CMV infection were included, among whom 373 (44%) received antiviral prophylaxis. The 12-month cumulative incidence of CMV replication and disease were 0.44 and 0.08 cases, respectively. Patient homozygous for the minor rs368234815 allele (-G/-G) tended to have a higher cumulative incidence of CMV replication (subdistribution hazard ratio [SHR], 1.30 [95% confidence interval {CI}, .97-1.74]; P = .07), compared with other patients (TT/TT or TT/-G). The association was significant among patients followed by a preemptive approach (SHR, 1.46 [95% CI, 1.01-2.12]; P = .047), especially in patients receiving an organ from a seropositive donor (SHR, 1.92 [95% CI, 1.30-2.85]; P = .001), but not among those who received antiviral prophylaxis (SHR, 1.13 [95% CI, .70-1.83]; P = .6). These associations remained significant in multivariate competing risk regression models.

CONCLUSIONS
Polymorphisms in the IFNL3/4 region influence susceptibility to CMV replication in solid-organ transplant recipients, particularly in patients not receiving antiviral prophylaxis.