



Drug-resistant cytomegalovirus in transplant recipients: a French cohort study

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OBJECTIVES: Cytomegalovirus (CMV) drug resistance is a therapeutic challenge in the transplant setting. No longitudinal cohort studies of CMV resistance in a real-life setting have been published in the valganciclovir era. We report findings for a French multicentre prospective cohort of 346 patients enrolled at initial diagnosis of CMV infection (clinical trial registered at clinicaltrials.gov: NCT01008540).

PATIENTS AND METHODS: Patients were monitored for detection of CMV infection for ≥ 2 years. Real-time detection of resistance by UL97 and UL54 gene sequencing and antiviral phenotyping was performed if viral replication persisted for >21 days of appropriate antiviral treatment. Plasma ganciclovir assays were performed when resistance was suspected.

RESULTS: Resistance was suspected in 37 (10.7%) patients; 18/37 (5.2% of the cohort) had virological resistance, associated with poorer outcome. Most cases involved single UL97 mutations, but four cases of multidrug resistance were due to UL54 mutations. In solid organ transplant recipients, resistance occurred mainly during primary CMV infection (odds ratio 8.78), but also in two CMV-seropositive kidney recipients. Neither CMV prophylaxis nor antilymphocyte antibody administration was associated with virological resistance.

CONCLUSIONS: These data show the feasibility of surveying resistance. Virological resistance was frequent in patients failing antiviral therapy. More than 1/5 resistant isolates harboured UL54 mutations alone or combined with UL97 mutations, which conferred a high level of resistance and sometimes were responsible for cross-resistance, leading to therapeutic failure.

Résumé en
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