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P0485 Clinical validation of a novel ELISpot-based in vitro diagnostic assay to monitor CMV-specific cell-mediated immunity in immunocompromised transplant recipients

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Background: Impaired cytomegalovirus (CMV)-specific cell-mediated immunity (CMV-CMI) is a major cause of uncontrolled CMV reactivation and associated complications in both solid-organ transplantation (SOT) and hematopoietic stem cell transplantation (HSCT). Reliably assessing CMV-CMI is desirable to individually adjust antiviral and immunosuppressive therapy. We demonstrate here the suitability of a novel IFN-γ ELISpot assay (T-Track® CMV), based on the stimulation of peripheral blood mononuclear cells with pp65 and IE-I CMV proteins, to monitor CMV-CMI in immunocompromised SOT and HSCT patients.

Materials/methods: Two independent prospective, longitudinal, observational, multicenter studies were conducted, the first one in 86 intermediate-risk (D-/R+, D+/R+) renal transplant recipients (completed), the second one in 175 intermediate- or high-risk (D+/R+, D+/R-, D-/R+) HSCT recipients (ongoing). In both studies, patients underwent pre-emptive antiviral therapy per institutional guidelines. CMV-CMI, CMV viral load and clinical complications were monitored over approximately six months post-transplantation.

Results: In the kidney transplantation setting, 95% and 88-92% of IFN-γ ELISpot test results were positive pre- and post-transplantation, respectively, demonstrating that the assay can measure CMV-CMI in immunocompromised patients. CMV-specific response was reduced following

immunosuppressive treatment and increased in patients with graft rejection, indicating the ability of the ELISpot assay to monitor the patients' immunosuppressive state. Interestingly, median pp65-specific response was 9-fold higher in patients with self-clearing viral load compared to antivirally-treated patients prior to first detection of viral load ($p<0.001$), suggesting that reactivity to pp65 represents a potential immunocompetence marker. In HSCT patients (ongoing study), interim data analysis indicates that pp65-specific CMI measured after resolution of a primary CMV reactivation (requiring antiviral treatment) is a fair predictor of occurrence of recurrent CMV reactivation within the observational period. Out of 45 patients representative of the total population (D+/R+, D+/R-, D-/R+) and who experienced a (treatment-requiring) primary CMV reactivation, 12 experienced a recurrent CMV reactivation. Interestingly, 30/33 (91%) patients free of recurrent reactivation had a positive pp65-specific test result following primary CMV reactivation.

Conclusions: Altogether, this novel IFN-γ ELISpot assay (T-Track® CMV) is a highly sensitive immune-monitoring tool, suitable for the follow-up of SOT and HSCT recipients, and with a potential use for the risk assessment of CMV-related clinical complications.