

O214

Oral Session

Advances in CMV infection in transplant recipients

EFFECTIVENESS OF EARLY-ONSET VS. DELAYED-ONSET UNIVERSAL CYTOMEGALOVIRUS (CMV) PROPHYLAXIS IN D+/R- SOLID ORGAN TRANSPLANT (SOT) RECIPIENTS: IMPORTANCE OF CYTOMEGALOVIRUS (CMV)-SPECIFIC T-CELL RESPONSE.

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Objectives: Late CMV disease occurs in at least 20% of D+/R- SOT after ending long term prophylaxis. We hypothesized that a short delay (14 days) in the initiation of the universal prophylaxis against CMV in D+/R- SOT recipients, would allow some degree of CMV exposition generating an increased CMV-specific T-cell mediated immunity (CMI), in comparison with those SOT recipients that receive an early onset (< 3 days) prophylaxis, and that this early acquisition of CMI will protect against late CMV disease.

Methods: A prospective multicenter study was conducted in D+/R- SOT recipients of six tertiary hospitals in Spain, from Sept/09 to Sept/12. Samples of whole blood were prospectively collected at days 30, 90, 120, 200, and 300 for CMI evaluation through measurement of CMV-specific interferon (IFN)g-producing CD8+ and CD4+ T by intracellular cytokine staining. *Early prophylaxis* (EP; first 3 days after Tx) was performed in all participating centers during the first 18 months of the study, and *delayed prophylaxis* (DP: 14 days after Tx) was performed in all participating centers during the following 18 months. We evaluated which were the risk factors for the development of CMV disease - including dynamics of CMI, relationship of CMI with CMV disease, and protective role of DP- through survival analysis and proportional risk Cox regression models.

Results: We included 95 patients (50 with EP and 45 with DP). A total of 305 blood samples were processed for CMI determination (median of 4 samples/patient). Patients were followed-up for a median of 807 days. A total of 26 patients (27.4%) developed CMV disease. DP was not significantly associated with a higher CMI response, nor with a lower rate of global CMV disease, but we observed a trend towards a lower incidence of end-organ CMV disease in patients receiving DP (HR: 0.26; CI: 0.05-1.2; p=0.09). Independent risk factors for CMV disease were the use of anti-lymphocyte antibodies (Hazard ratio [HR]: 3.7; confidence interval 95%[CI]:1.6-8.5; p=0.002), acute rejection (HR: 2.3; CI:0.99-5.3; p=0.05) and donor age (HR: 1.02; CI:0.99-1.04; p=0.06).CMI response was detected only in 18% of patients at day 200 and in 36% at day 365. The percentage of SOT recipients with CMI response at day 365 was higher in liver than in kidney transplant recipients (CMI response 60% vs. 24.6%; p=0.002). Detectable CMI at day 120 was protective against CMV disease (Positive predictive value: 93%).

Conclusions: Delaying the onset of CMV prophylaxis two weeks in D+/R- SOT recipients could have a protective effect against the development of end organ CMV disease. Although long term universal prophylaxis significantly hinders CMI response in D+/R- patients, specially in kidney transplant recipients, those patients achieving an adequate CMI response appears to be protected against the development of CMV disease.