O212
Oral Session
Advances in CMV infection in transplant recipients

RECONSTITUTION OF CMV-SPECIFIC IMMUNITY POST HEART TRANSPLANTATION MAY GUIDE CUSTOMIZATION OF IMMUNOSUPPRESSIVE AND ANTIVIRAL STRATEGIES: A PROSPECTIVE RANDOMIZED STUDY.

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Objectives: Reconstitution of cytomegalovirus (CMV) specific immunity post transplantation is associated to a lower risk of subsequent viral reactivation, in CMV seropositive recipients. In this prospective randomized study, we analyzed the interplay of immunosuppressive, anti-CMV strategies, and CMV immunity at risk for CMV infection during the first year after transplant.

Methods: by a factorial 2x2 randomization process, we allocated consecutive CMV seropositive heart transplant (HT) recipients to receive either three months of valganciclovir prophylaxis or a pre-emptive based approach, and to receive either mycophenolate (MMF) or everolimus (EVE) on top of a cyclosporine-based immunosuppressive therapy. During the 12 month follow-up period, all patients were monitored for CMV infection and CMV-immunity reconstitution was assessed by IFN-g ELISPOT assay (ELITecGroup S.p.A., R&D Torino, Italy).

Results: 22 patients were randomized to pre-emptive approach vs. 21 to prophylaxis, and 23 EVE vs. 20 MMF. Six patients (26%) discontinued EVE within 2 months from randomization for adverse events. CMV DNA was detected in 25 patients (58%) and in 12 (48%) of them viral load peaked over 10,000 copies/ml. Patients randomized to prophylaxis and those who were not discontinued from EVE showed less CMV viremia ($p<0.04$), while only EVE was associated with a lower rate of high grade CMV (6 vs. 42%; $p<0.01$). Immunity recovery at month one was associated with 60% risk reduction of any viremia and 75% risk reduction of high grade CMV. In patients without early immunity (n=22), prophylaxis and EVE reduced the risk of viremia by 80 and 75% respectively ($p<0.03$). This protective effect was not observed in patients who recovered early CMV immunity. In addition, the degree of CMV immunity at prophylaxis discontinuation (month 3) predicted late-onset CMV infection (0 vs. 53%; $p=0.01$).

Conclusion: lack of CMV-specific immune reconstitution after HT is associated with increased risk of CMV infection and identifies patients likely to benefit of specific anti-CMV approaches, such as prolonged valganciclovir prophylaxis or EVE-based immunosuppression.