Results: At 24M, both EVR groups were comparable to MPA for efficacy, renal function, and overall safety. Incidence of treated BPAR was similar between EVR 3-8 and MPA (19.9% vs. 19.1%) and lower for EVR 6-12ng/mL (15.1%). The pattern of steroid use was similar for all 3 groups. The incidence of CMV infections, CMV events of all categories and BKV infections was lower in both the EVR groups vs. MPA (Table 1). Use of antiviral prophylaxis did not reduce the incidence of CMV infections if the donor and/or recipient were seropositive at baseline.

	EVR 3–8 ng/mL (N=274)	EVR 6–12 ng/mL (N=278)	MPA 1.44 g (N=273)
Infections reported as adverse events (AE) at M24 (%), safety population			
Total AEs	98.9	99.3	98.9
Total infections	67.9	69.8	76.2
– Bacterial	28.5	32.0	28.6
– Fungal	6.2	6.8	6.2
– Viral	10.6	8.3	24.9
thereof BKV infection	0.7	1.4	4.8
thereof CMV infection	1.5	0.4	9.2
CMV events reported in the CMV case report form			
CMV syndrome	1.5	1.8	5.1
CMV lab evidence/antigenemia	1.1	2.2	6.6
CMV disease (organ involvement)	0.7	1.1	2.9

Conclusion: The lower incidence of CMV and BKV infections seen in *de novo* RTxR on EVR therapy may translate into an additional benefit of EVR versus standard therapy.

O-148 EFFECT OF EVEROLIMUS AND DONOR/RECIPIENT SEROLOGY ON CYTOMEGALOVIRUS INFECTION IN HEART TRANSPLANT RECIPIENTS: A SUBANALYSIS OF THE RANOMIZED TRIAL A2310

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Cytomegalovirus (CMV) is the most common infectious agent affecting heart transplant (HT) recipients. Although donor/recipient (D/R) serology is essential in stratifying the risk for CMV, with D+/R– patients at highest risk for clinically relevant infections, immunosuppression additionally affects CMV development. However, the interplay between immunosuppressive regimens and serological risk for CMV is unexplored.

We analyzed 12-month occurrence of CMV infection and syndrome/disease in patients enrolled in A2310 (NCT 00300274). This is a 24-month, multicenter, randomized, open-label study comparing two everolimus arms (target C0 3-8ng/mL or 6-12ng/ml) with reduced cyclosporine to mycophenolate mofetil (MMF) with standard cyclosporine for efficacy, renal function and safety. High everolimus arm was prematurely interrupted because of excess mortality, and is not included in this analysis. CMV prophylaxis was recommended for D+/R- patients.

547 patients comprised the safety population included in this analysis: 279 received everolimus and 268 MMF. Everolimus was associated with lower incidence of CMV infections (8.2% vs. 20.5%, P<0.001), and of CMV syndrome/disease (3.4% vs. 12.5%, P<0.001). As expected, the 108 D+/R– patients were overall more frequently affected by CMV infection and syndrome/disease than the 280 R+ patients (all P<0.05). However, serology impact persisted only in MMF patients, with 22.4% D+/R– vs. 9% R+ with CMV syndrome/disease (P=0.02). Conversely, CMV syndrome/disease occurred in 5.1% of everolimus treated D+/R–, and in 2.7 of R+ (P=0.4; Figure 1).

Everolimus with low-dose cyclosporine reduced about three times the risk for CMV infection and syndrome/disease as compared with standard cyclosporine and MMF. Everolimus remarkably mitigated CMV risk in naïve recipients, who confirmed a high risk for CMV syndrome/disease only in the MMF arm. These data raise the hypothesis that everolimus effect on CMV is independent from recipient's CMV-specific immunity.

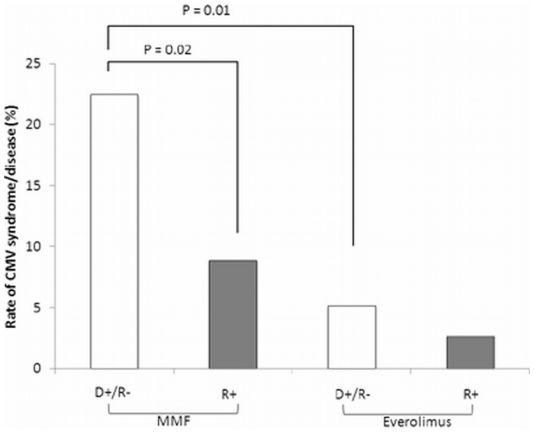

Figure 1

O-149 PRIMARY CMV INFECTIONS AND HHV-6 REACTIVATIONS IN LIVER TRANSPLANT RECIPIENTS RECEIVING VALGANCICLOVIR PROPHYLAXIS

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Background: Cytomegalovirus (CMV) and human herpesvirus-6 (HHV-6) infections are common after liver transplantation. HHV-6 reactivations are usually asymptomatic, but hepatitis or graft dysfunction may occur. Based on *in vitro* studies, the antivirals effective against CMV, have also activity against HHV-6. The efficiency of valganciclovir prophylaxis, given to CMV risk patients (D+/R-), was investigated in preventing primary CMV infections and HHV-6 reactivations.

Methods: Of 196 adult liver transplant patients 32 belonging to CMV high-risk group received antiviral prophylaxis (valganciclovir 900 mg/d and/or i.v. ganciclovir 5mg/kg/d) up to 3 months after transplantation. The patients were monitored for CMV by quantitative PCR and HHV-6 reactivations diagnosed by HHV-6 antigenemia test using monoclonal antibodies against HHV-6B and HHV-6A. Tissue invasive CMV and HHV-6 were demonstrated in biopsies by immunostaining.

Results: During antiviral prophylaxis, no break-through CMV infections were recorded. On the contrary, HHV-6 antigenemia was detected in 12/32 (37%) patients mean 12 days (range 7-22 days) after transplantation. All reactivations were caused by HHV-6B. In three patients HHV-6 antigens were detected in the liver biopsy during graft dysfunction. After cessation of valganciclovir prophylaxis 12/32 (37%) patients developed primary CMV infection mean 181 days (range 95-365 days) post transplantation. Two low level CMV infections were asymptomatic and not treated, 6 infections were successfully treated with valganciclovir, and 4 severe CMV diseases with intravenous ganciclovir. No intragraft CMV infection was found, but one patient developed gastrointestinal CMV. No patient or graft was lost due to CMV or HHV-6.

Conclusions: During valganciclovir prophylaxis, no break-through CMV infections were recorded but HHV-6 reactivations were common, infecting the transplant in three cases. After prophylaxis, primary CMV infections were frequent, but successfully treated with valganciclovir/ganciclovir. Antiviral prophylaxis did not prevent HHV-6 reactivations, but delayed primary CMV infections.

O-150 CMV SPECIFIC IMMUNE RECONSTITUTION IN HTx PATIENTS TREATED WITH PRE-EMPTIVE STRATEGY: LIGHTS AND SHADOWS

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Background: CMV is the most prominent pathogen affecting Heart Transplantation Patients (HTxs). T-cells play a crucial role in controlling Cytomegalovirus (CMV) viremia. The aim of this study is to determine how virus exposure and antiviral pre-emptive treatment affect T-cell recovery after transplantation.

Patients and methods: We recruited 48 CMV R+ patients in a cross-sectional study. We evaluated CMV-DNAemia and CMV specific T-cell response (IFN-gamma ELISPOT test) at the time-points: within 60 days, between 60 and 100 days and after 100 days post-transplant. All HTxs were managed with pre-emptive therapy.

Results: As shown in figure 1, within 60 days after transplant, HTxs not experiencing-post transplant viremia had a median 161 ELISPOT count, while HTxs experiencing moderate viremia (1000-10000) had a median of 91 ELISPOT and patients experiencing overt viremia (>10000) post transplant displayed low (5) median ELISPOT.

From 61-360 days after transplant, HTxs not experiencing viremia continue