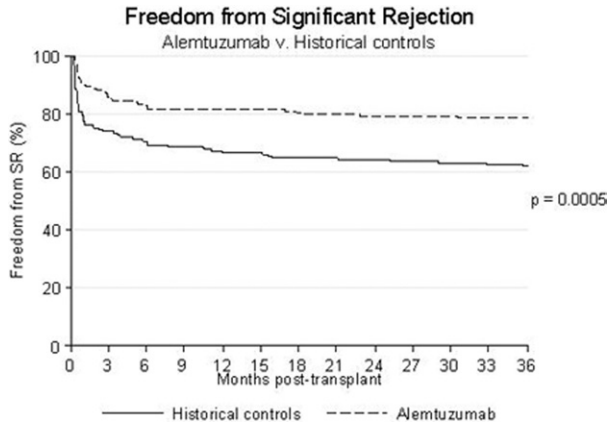
ferent between groups: 99% tacrolimus, 99% mycophenolate. Mean tacrolimus levels (ng/mL) were generally lower for the C-1H v. controls: month 1-6 (8.6 v. 11.4, p<0.00001), month 7-12 (9.9 v.10.9, p=0.0008), month 13-18 (9.8 v. 10.4, p=0.09), month 19-24 (8.8 v. 10.1, p=0.0009) month 25-30 (8.9 v. 10.0, p=0.006), months 31-36 (9.2 v. 9.3, p=0.86). Survival at 3 years was not different between C-1H and controls, 81% v. 77% p=0.35. At 3 years overall freedom from rejection (ISHLT >= 3A/2R) was superior in the C-1H group: 79% v. 62%, p=0.0005.



Conclusions: Routine induction therapy with C-1H after CTX results in similar 3 year survival as controls, but superior freedom from rejection despite lower calcineurin levels and without the use of steroids.

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Everolimus Prevents the Quilty Phenomenon – A Risk Factor for Microvasculopathy in Biopsy (RAD B253 Trial)

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Purpose: Quilty is a risk factor for microvasculopathy (MVP) in biopsy and major cardiac events in heart transplant (HTx) recipients. As yet, no maintenance immunosuppression has been shown to prevent the Quilty phenomenon in biopsy.

Methods and Materials: From the European cohort of the RAD B253 Trial (everolimus [EVE] 3 mg or 1.5 mg daily vs. azathioprine [AZA] in primary HTx pts) we studied 135 pts, mean age 56 yrs (81% men), and 567 biopsies harvested 1 wk (n=125), 4 wks (n=131), 3 months (n=128), 1 yr (n=101) and 2 yrs (n=82) after HTx. Acute cellular rejection (ACR), Quilty (both ISHLT) and MVP (ratio of luminal radius to media thickness <1) were studied in routinely processed right ventricular biopsies (H&E, x200). Immunosuppression was evaluated by IIT analysis (EVE 1.5 mg=43, EVE 3 mg=46, AZA=46).

Results: ACR of any grade was diagnosed in 22%, 37%, 38%, 19%, and 24% of pts at 1 wk, 4 wks, 3 months, 1 yr and 2 yrs post-transplant. Quilty was present in 7%, 7%, 12%, 18% and 19% of pts and MVP in 56%, 71%, 73%, 75% and 71% of pts, respectively. Pts on EVE 1.5 mg vs. EVE 3 mg vs. AZA showed significantly less ACR of any grade during the 2-year follow-up (30% vs. 23% vs. 35%; p=0.032), in 1-year biopsies (31% vs. 23% vs. 36%; p=0.039) and at 4 wks (41% vs. 22% vs. 50%; p=0.023), which was due to a lower rate of mild (30% vs. 18%) and moderate ACR (11% vs. 4%) in pts on 3 mg EVE (p=0.050). Pts on EVE 1.5 mg vs. EVE 3 mg vs. AZA showed the Quilty phenomenon significantly less often during the 2-year follow-up (9% vs. 6% vs. 20%; p<0.001), in 1-year biopsies (9% vs. 6% vs. 18%; p=0.002), at 4 wks (5% vs. 0% vs. 16%; p=0.009) and 2 yrs post-transplant (10% vs. 10% vs. 32%; p=0.043). During the 2-year follow-up (96% vs. 84%; p=0.008) and also in 1-year biopsies (95% vs. 83%; p=0.040) MVP was more frequent in pts with Quilty.

Conclusions: Everolimus suppressed Quilty and mild and moderate ACR more effectively than AZA. It seems that not only its antiproliferative but also its immunosuppressive effects are involved in the prevention of MVP after HTx.

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Improvement of Renal Function after Cyclosporine Reduction Is Influenced by Baseline Proteinuria in Patients Converted to Everolimus: Long Term Follow-Up of the Shirakiss Randomized Study

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Purpose: Cyclosporine (CsA) nephrotoxicity negatively impacts long-term management of heart transplant (HT) recipients. Thus, we designed the SHIRAKISS randomized study to compare two CNI lowering strategies on the progression of renal dysfunction (NCT00420537). Herein we report the 24 months outcome of the patients initially randomized in the study.

Methods and Materials: 34 recipients with 1 to 4 post HT follow-up and 25 to 60 ml/min creatinine clearance (CrCl) were randomized to receive everolimus (EVE) with very low dose of CsA (C0: 50-90 ng/ml; n=17) or mycophenolate (MMF) with low dose CsA (C0: 100-150 ng/ml; n=17) and were initially followed for 12 months. Thirty remained on study treatment for the subsequent 12 months and entered this analysis, which enpoint was CrCl 24 months after randomization.

Results: At 24 months from randomization, CsA levels were lowered by 70% in the EVE arm and by 30% in the MMF arm, and CrCl remained stable in both arms, although non significantly higher in MMF arm (46±12 vs.54±15 mL/min; P=0.13). However, subgroups analysis revealed that baseline proteinuria significantly impacts renal function response to EVE strategy. While in EVE arm patients without proteinuria showed an improvement in CrCl (from 46±8 to 51±8 mL/min;P=0.08), those with baseline proteinuria >150mg/24h showed a decrease in CrCl, which reached significantly lower levels than in patients without (36±11ml/min; P=0.02). On the other hand, baseline proteinuria did not influenced response to CNI lowering in MMF patients.

Conclusions: While confirming that CsA lowering reduces the progression of renal dysfunction after HT both with MMF and EVE, this long-term analysis underscores that CsA lowering with EVE introduction may improve renal function only in patients without baseline proteinuria. Conversely, these data support the notion that detection of even mild proteinuria should represent a potential contra-indication to the use of EVE in kidney sparing strategies.

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Myocardial Recovery after Support with HeartMate I and HeartMate II Left Ventricular Assist *Devices*

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Purpose: Myocardial recovery may occur during LVAD support for non-ischemic dilated cardiomyopathy (DCM). This was originally observed with pulsatile support and it is uncertain whether the type of device influences myocardial recovery.

Methods and Materials: We analysed the outcome of 96 non-ischemic DCM patients who underwent LVAD implantation with Thoratec HeartMate I (HMI) and HeartMate II (HMII) devices between December 1999 and February 2010 in our centre. HMI (pulsatile) device was implanted in 40 patients and HMII (continous flow) device was implanted in 56 patients. Of the HMI group 34 were male, 6 female, age at implant was 40 ± 13 years, duration of support was 289 ± 166 days.