5 YEARS COMPARISON OF CYCLOSPORIN VERY LOW EXPOSURE WITH EVEROLIMUS HIGH EXPOSURE VERSUS STANDARD CYCLOSPORIN AND ENTERIC-COATED MYCOPHENOLATE IN RENAL TRANSPLANTATION

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OBJECTIVES

Calcineurin minimization is one of the strategies used to improve long term renal graft outcomes. In this study 58 renal transplanted recipients receiving very low dose of cyclosporine (CsA) and high levels of everolimus (Rad), were compared to 51 recipients receiving standard dose of CsA and enteric-coated mycophenolate sodium (EC-MPS)

METHODS

In this single center retrospective study we compared the outcome of renal transplanted patients who received Rad (C0: 8-12 ng/ml) + CsA (C2: 150-300 ng/mL) + steroids, Vs those who received EC-MPS (1,440 mg/day) + CsA (C2: 500-700 ng/mL) + steroids. Efficacy was evaluated at 5 years. Statistical analysis included T test, χ^2 test and Fisher exact test, Mann Whitney test, Log rank test for the difference of the Kaplan Meier curves, Cox regression for multivariate survival analysis. All the analysis is on an intention to treat basis.

Graphs and tables

|	Gruppo Everolimus. N: 56	Gruppo Micofenolato sodico. N: 50	P value
Donor Age (years)	53 (16-73)	58 (6-77)	0.041
Donor sex M/F	21/19	19/20	0.737
Cold ischemia time (hours)	19 (2-25)	18(1-28)	0.84
Recipient's age at transplantation (years)	46.27 ±11.71	52.46±11.83	0.02
Recipients sex M/F	30/10	30/9	0.842
Number of HLA mismatch	3 (1-6)	3(0-5)	0.39
Graft survival rate	80 %	64%	0.115
Recipient death	4 (7.1%)	6 (12%)	0.497
Therapetic switches	6 (10.7%)	6 (12%)	0.77
Serum creatinine (mg/dl)	1.27 (0.64-3.21)	1.39 (0.77-2.3)	0.426
eGFR (ml/min)	77.34 ± 36.38	60.36 ± 25.34	0.052
Proteinuria (mg/24 ore)	306 (47-2196)	174.5 (12-1012)	0.002
Cyclosporin level C0 (ng/ml)	59 (24-192)	124 (68-201)	<0.001
Cyclosporin level C2 (ng/ml)	317.25 ± 126.36	685.65 ± 161.52	<0.001
Cyclosporin dose (mg/kg)	1.36 ± 0.45	2.13 ± 0.49	<0.001
Everolimus level C0 (ng/ml)	6.1 ± 2.18	-	-
Acute rejection rate	6 (10.7%)	9 (18%)	0.358
Total cholesterol (mg/dl)	217,72 ± 33.63	203.6 ± 35.81	0.132
HDL (mg/dl)	53 (36-118)	49 (24-88)	0.09
LDL (mg/dl)	126 (72-372)	112 (51-164)	0.206
Statin usage	22 (39%)	7 (14%)	0.001
Systolic blood pressure (mm/Hg)	128.91 ± 15.84	128.13 ± 16.07	0.857
Diastolic blood pressure (mm/Hg)	80 (60-100)	80 (60-100)	0.621
Number of anti-hypertensive drugs	2 (0-4)	2 (0-4)	0.86
Erythropoietin usage	4 (7.1%)	1 (2%)	0.358
Haemoglobin (gr/dl)	13.1 ± 1.5	12.78 ± 1.29	0,27
Malignancies	0	1 (2%)	0.494
Cardiovascular events	0	2 (4%)	0.24
Post transplant diabetes	4 (7.1%)	4 (8%)	1.00
Serious infections requiring hospital admission	9 (16%)	9 (18%)	0.95
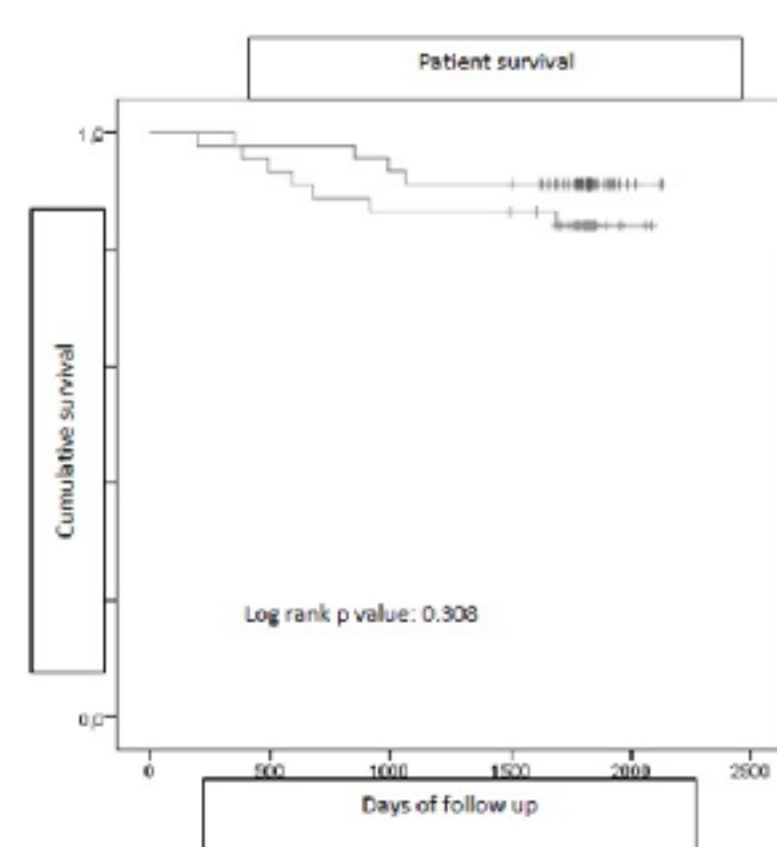
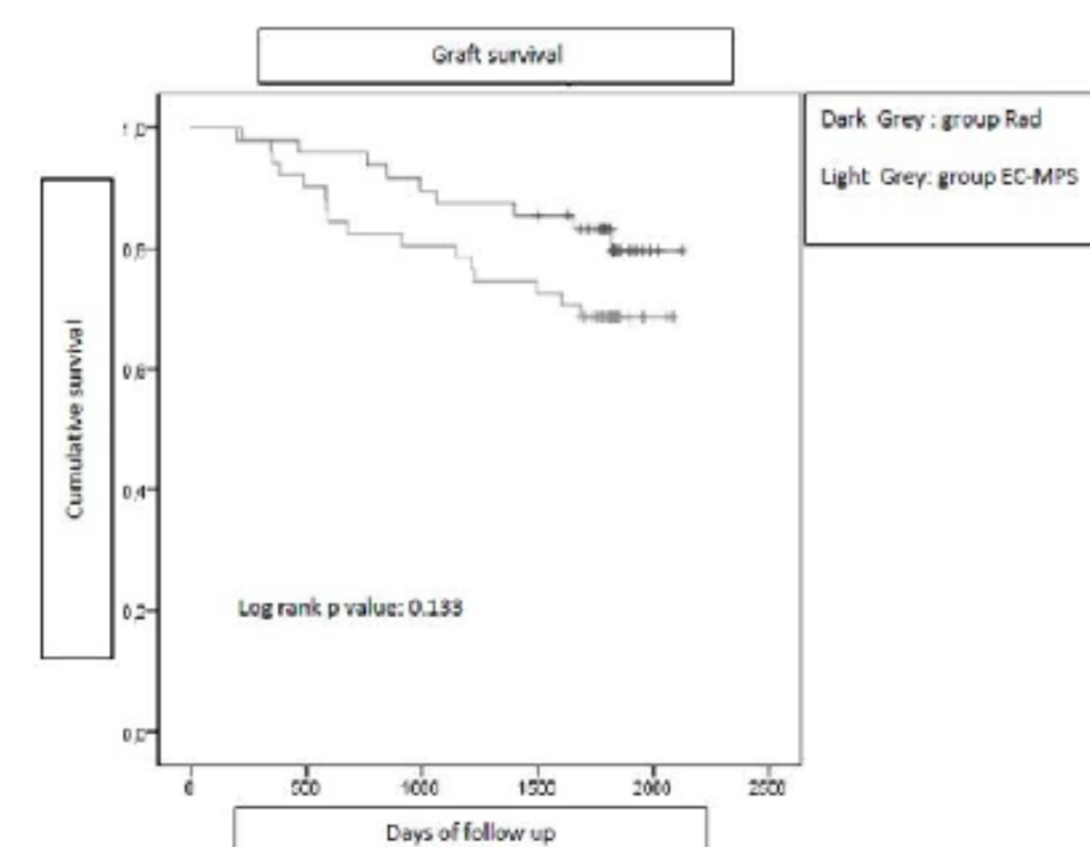Fig 1 Kaplan Meier curves for patients survival. Log rank p value: 0,308

Fig 2.Kaplan Meier curves for death unexpected graft survival.

RESULTS

After 5 years of follow up we evaluated 40 patients in the Rad group and 39 in the EC-MPS group. We found a non-statistical trend towards a better graft survival (81.2 % Vs 68.6 %) and a better graft function (71.82 ± 35.77 Vs 60.0 ± 26.19ml/min, p: 0.114) in favor of the Rad group. The trough and peak levels of cyclosporine were higher in the EC-MPS group, respectively 118.5 (quartile: 98.25-142.25) Vs 59 (41-77) and 670.81 ± 165.80 Vs 321.49 ± 144.32ng/dl (p<0.001).
The Everolimus group had higher level of proteinuria 296 (151-473) Vs. 177 (136-263) mg/24 hours (p: 0.002) and comparable levels of cholesterol but a larger need to use statin. (55% Vs17%, p <0.001) see tab 1.
The Kaplan-Meier curves for patient survival and graft survival are represented in fig 1 and 2.

CONCLUSIONS

In our experience everolimus associated with very low dose of cyclosporine was associated with a non-statistical trend toward a better renal function and graft survival compared to a standard regimen of cyclosporine and EC-MPS. A larger trial might confirm our data with more power from a statistical point of view.

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DOI: 10.3252/pso.eu.50era.2013

Poster presented at:

PosterSessionOnline.com