TEXT

MTOR INHIBITORS IN RENAL TRANSPLANTATION: A FIFTEEN YEAR, SINGLE-CENTER EXPERIENCE

Basso E, Messina M, Di Vico MC, Fop F, Bussolino S, Mella A, E. Gallo, Rossetti M.,Segoloni G, Biancone L.

Renal Transplantation Unit "A. Vercellone", Division of Nephrology Dialysis and Transplantation, Department of Medical Sciences, Città della Salute e della Scienza Hospital and University of Turin, Italy

OBJECTIVES

Literature does not provide unequivocal results on safety and efficacy of mTORi, sirolimus (Rapamune® Wyeth) and everolimus (Certican® Novartis) [1,2,3,4,5].
In this study we analyze our fifteen year long experience with these drugs in our Center, providing a comparison with calcineurin inhibitors (CNI) treated patients.

METHODS

Cases: 418 mTORi patients-cases-(May 1997-December 2011, minimum f/up 1 year), in de novo or in conversion protocols. In detail, the group (g1) consists of 75/418 patients (pts) who assumed the drug from the beginnig to the end of follow up.
Control group: 403 pts treated with CNI (tacrolimus or ciclosporine A), matched with g1 for gender, age and transplantation era.

Cases and controls were compared (in a intention to treat analysis) for: organ and pts survival, onset of neoplasia and rate of drop out from the therapy for side effects. Acute rejection rate (AR) and renal function were reported only in g1, since different CNI based treatments could introduce multiple bias in the analysis.

RESULTS

Table 1

sCr mg/dl	Group 1	Controls	p
3 mo	1,98	1,67	0,003
6 mo	1,97	1,65	0,004
1 yrs	1,8	1,59	0,047
Proteinuria g/day	Group 1	Controls	p
3 mo	0,41	0,25	0,003
6 mo	0,34	0,3	0,016
1 yrs	0,41	0,29	0,001
2 yrs	0,35	0,3	0,03
3 yrs	0,43	0,35	0,028

Higher drop-out rate was observed in cases vs controls (18,9% vs 1%, p<0,001). Graft and pts survival: at 5 years respectively 87,7% and 93,8% (cases); 90,6% and 92%(controls),p=NS. In g1, sCr and proteinuria were worse than in controls up to 1 and 3 post transplant year (Table 1); AR rate was not statistically different (13,3% in cases vs 14,6% in controls at the end of the f/up, p=0,72)
In patients switched from CNI to mTORi we defined a sCr value at conversion as predictive of a better outcome. With sCrs< 2,7 mg/dl (area under the ROC curve 0,702), there was a correlation with a lower graft failure rate (16,7 vs 45,2%, OR (CI 95%) 3,3 (1,3-8,2) and better graft survival. As for cancer, in cases vs controls the incidence was 4,8 vs 11,7%(p<0,001); in patients converted to mTORi for cancer, the incidence of a second malignancy was significantly lower vs those continuing on CNI (2,6 vs 12,8%,p=0,02). No difference for cancer relapse and regression, cancer related death and patient survival was noted

CONCLUSIONS

On the basis of our long term analysis,we support the safety and efficacy of mTORi, in the novo and in conversion protocols. Particulary in g1 we did not report different AR rate and graft/patient survival, in spite of sCr and proteinuria slightly higher up to respectively 1-3 post transplant years. Moreover, mTORi resulted protective towards cancer.
Nevertheless, the high mTORi drop out rate suggests caution and request experience in the handling of this drugs and a prompt removal when serious side effects are noted.

References

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DOI: 10.3252/pso.eu.52era.2015