Four-drug immunosuppressive treatment as rescue therapy in kidney transplant recipients with repeated episodes of acute rejection or chronic active allograft rejection

Rojas W, Soler Pujol G, Diaz C, Sleiman J, Cano Giraldo G, Laham G. Nephrology section, Internal Medicine Department, CEMIC, Buenos Aires, Argentina.

Introduction

CEMIC

Repeated or persistent acute rejection episodes (AR) can lead to chronic rejection (CR), challenging the management of immunosuppressive therapy (IT).

Reinforcing IT with a four-drug (4D) regimen that includes m-TOR inhibitors (m-TORi), calcineurin inhibitors (CNI), mycophenolate (MF) and steroids could be a good strategy in this scenario. However, there is no consensus on this matter.

We present our experience with 4D in kidney transplant recipients (KT) who presented biopsy proven chronic active rejection (CAR) or recurrent episodes of AR.

Our aim was to evaluate kidney graft function (KF) at 3, 6 and 12 months , histological features and safety of a 4D IT.

Methods

Retrospective, observational study, included 19 kidney transplant (KT) patients treated with 4D from 2008 to 2022.

Variable	N= 19
Recipient age in years	47.6 ± 12.8
Female recipients %	42.1
Time from transplant to 4D (months)	44.4
Follow-up after 4D	1 year
Deceased donors %	52.6
Use of induction %	100

1.Overall population characteristics

Reasons for conversion to a 4D regimen were:

- Biopsy proven CAR or
- Recurrent episodes of AR.

Recipient KF was measured with:

- Estimation of glomerular filtration rate by the CKD-EPI formula (eGFR) and/or
- Proteinuria-creatininuria ratio (PCR) at 3, 6 and 12 months.

Safety outcomes included:

- Infectious events (IE) including BK after the start of 4D
- Neoplastic events (NE) after the start of 4D.

Results

Variable	Pre 4D	3rd month	6th month	12th month	*p*
Creatinine mg/dl	1.8(1.4-2.2)	1.6(1.5-2.4)	1.5(1.4-2.0)	1.5(1.4-2.1)	0.693
PCR mg/g	138(100-336)	132(0-197)	115(0-159)	157(45-495)	0.103
eGFR ml/min	40(27-63)	44(30-60)	51(31-59)	48(31-64)	0.662

Variable	%	*p*
Presence of DSA pre 4D	42.1	0.522
Presence DSA post 4D	53.3	
Average cPRA I% pre 4D	15.8	0.886
Average cPRA I% post 4D	17.6	
Average cPRA II % pre 4D	57.9	0.766
Average cPRA II % post 4D	52.9	

As this was a small cohort, pathology findings were described in each particular case and did not let us draw a conclusion.

- Incidence of BK viremia post 4D was not significant p=0.556.
- There was no evidence of higher incidence of infectious events.
- No neoplastic events were recorded after the start of 4D.
- There were 2 graft losses and only one patient discontinued the 4D regimen due to intolerance.
- There were 3 deaths with a functioning graft (15.8%), all due to infectious causes.

CEMIC

Conclusion

In our experience, KT recipients who presented CAR or repeated episodes of AR then switched to an IT with 4D stabilized their eGFR and PCR, no new DSA were found and there was no evidence of a higher incidence of BK viremia or neoplastic events.