University of Ljubljana | Faculty of Medicine
INSTITUTE OF MICROBIOLOGY AND IMMUNOLOGY

univerzitetni klinični center ljubljana
University Medical Centre Ljubljana

COMPLEMENT C5 INHIBITION WITH ECULIZUMAB/RAVULIZUMAB IN KIDNEY TRANSPLANT PATIENTS – A SINGLE CENTER EXPERIENCE

Špela Borštnar[1,2], Željka Večerić Haler[1,2], Gregor Mlinšek[1,2], Miha Arnol[1,2], Katarina Kouter[3], Saša Simčič[3] and Andreja Aleš Rigler [1,2]

[1]Department of Nephrology, University Medical Centre Ljubljana, Slovenia

[2]Faculty of Medicine, University of Ljubljana, Slovenia

[3]Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Slovenia

TTS 2024 In Person + Live Streaming ISTANBUL TURKEY September 22-25 + Virtual October 21-23

P.305

INTRODUCTION

- C5 inhibition with eculizumab/ravulizumab is recently well-established treatment for thrombotic microangiopathy (TMA) in atypical hemolytic uremic syndrome (aHUS) and for C3 nephropathy
- Its use in kidney transplant patients has still not been widely reported
- The aim of our retrospective study was to investigate the use of eculizumab and ravulizumab in Slovenian kidney transplant patients

- *We have no financial conflicts of interest related to this study, or any relationships with commercial entities that could influence the research outcomes*

METHODS

- We retrospectively analysed the records of kidney transplant patients from the Centre for kidney transplantation of University Medical Centre Ljubljana, where all Slovenian kidney transplant patients are managed
- We included patients treated with anti complement C5 therapy any time after kidney transplantation (Tx)
- Their clinical, laboratory, and histological characteristics and outcomes were analysed

RESULTS

- From 2018 to the end of July of 2024, we treated 13 patients after kidney transplantation with eculizumab and/or ravulizumab
- 7 men, 6 women, average age 44 years at treatment start

indicatons/diagnosis	number of patients	male	female	average age (years)
primary aHUS	1 (8%)	0	1	22
secondary aHUS	8 (61%)	5	3	52 (40-61)
C3 glomerulopathy	3 (23%)	2	1	34 (21-54)
chronic antibody-mediated rejection (AMR)	1 (8%)	0	1	50

RESULTS – PRIMARY AHUS

- 1 female patient born in 1991, ESRD l.2012, positive genetics (homozygous deletion of CFHR1 in CFHR3 genes), positive anti factor H antibody
- Tx from deceased donor in May 2021
- Before Tx: rituximab, eculizumab few hours before transplantation and then once a week four weeks, then maintenance dose every two weeks
- She has hypertensive crisis immediately after transplantation
- From October 2021 on ravulizumab treatment; tacrolimus, mycophenolate mofetil
- Surveillance kidney biopsy one year after TX: no signs of TMA
- Now: without any laboratory sign of TMA, s-creatinine 110 µmol/l, anti factor H antibody negative
- She will be on life (kidney) time treatment

RESULTS – SECONDARY AHUS

- Eight patients were diagnosed with secondary aHUS in the early post-transplant period (till one month after Tx). 4 of them due to *de novo* TMA in association with ischemia-reperfusion injury and/or calcineurin inhibitor toxicity, other 4 had elements of antibody-mediated rejection (AMR) with atypical presentation

	lab. signs TMA	**acute kidney injury**	**arterial hyper-tension**	**elevated plasma c5b9**	**low APA**	**positive anti factor H antibody**	**positive DSA**	**positive genetics**
number of patients	5/8 (63%)	8/8 (100%) 6/8 (75%)-on hemodialysis	0/8 (0%)	4/8 (50%)	1/8 (13%)	1/6 (17%) (for 2 not available)	2/8 (25%)	2/5 (40%) (for 3 not available)

	other immuno-suppression	**plasma-pheresis**	**anti C5 therapy**	**„hematologic response“**	**„renal response“**	**treatment duration**
number of patients	6/8 (75%) 3/8 (38%)-switch to belatacept	2/8 (25%)	6/8(75%)-eculizumab 1/8 (13%) -both 1/8 (13%)- ravulizumab	5/5 (100%)	6/8 (75%) 2/6 (33%) - no more hemodialysis	3/8 (38%) - average 2 months 2/8 (25%)- still

RESULTS – C3 GLOMERULOPATHY

	lab. signs TMA	acute kidney injury	rise in proteinuria	arterial hypertension	elevated plasma c5b9	low APA	positive genetics for C3 risk
number of patients	0/3 (0%)	1/3 (33%)	2/3 (67%)	0/3 (0%)	2/3 (67%)	1/3 (33%)	2/3 (67%)

	added other immunosuppression	anti C5 therapy	„renal response“	treatment duration
number of patients	3/3 (100%)	3/3 (100%) - ravulizumab	2/3 (67%)	2/3 (67%) - still one stopped due to mycoplasma infection

- In one patient C3 recurrence was found on surveillance kidney biopsy one year after transplantation with no rise in serum creatinine and proteinuria, his laboratory results are stable, we are waiting for results of second kidney biopsy one year after treatment initiation

RESULTS – CHRONIC ANTIBODY-MEDIATED REJECTION

- 50 years old woman was 8 years after second Tx diagnosed with chronic active antibody-mediated rejection with positive donor specific antibodies (DSA)
- Her serum creatinine concentration rose from 90 to 150 µmol/L, no laboratory TMA signs
- She was treated with 5 pulses of methylprednisolone, intravenous immunoglobulins, 7 membranous plasmapheresis; cyclosporin was switched to tacrolimus
- She also received induction therapy with eculizumab (4 doses one week apart)
- Serum creatinine dropped to 115 µmol/L
- Genetic results are not available

- 5 years after treatment her serum creatinine, proteinuria, DSA are slightly increasing, cell-free DNA is 2% (elevated), rebiopsy showed still chronic antibody-mediated rejection
- These days we started treatment with daratumumab (anti CD28 antibody)

RESULTS – INFECTIONS

- 6 from 13 patients (46%) had no infection during/after therapy with eculizumab or ravulizumab
- In 7 (54%) patients infections were successfully treated:
- 2 patients had cytomegalovirus (CMV) infection,
- 2 urosepsis,
- 1 sepsis of unknown origin,
- 1 clostridium difficile diarrhoea and CMV infection,
- 1 patient soft tissue infection with Mycoplasma arginine;
- It should be considered that all patients received also other immunosuppressive therapy in addition to C5 inhibitor
- **No infections with encapsulated organisms occurred during the follow up**

CONCLUSIONS

- C5 inhibition with eculizumab and ravulizumab is effective and safe in kidney transplant patients with primary aHUS, *de novo* TMA (with or without AMR) and C3 nephropathy.

LITERATURE

- González CC, et al. Efficacy and safety of eculizumab in kidney transplant patients with primary atypical hemolytic-uremic syndrome. Transplant Proc. 2022;54(1):25-26
- Tan EK, at al. Use od eculizumab for active antibody-mediated rejection that occurs early post-kidney transplantation: A Consecutive series of 15 cases. Transplantation. 2019;103(11):2397-2404
- Gonzalez Suarez ML, et al. Outcomes of kidney transplant patients with atypical hemolytic Uremic Syndrome Treated with Eculizumab: A Systematic Review and Meta-Analysis. J Clin Med. 2019;8(7):919.
- Tank ZC, et al. New findings in preventing recurrence and improving renal function in AHUS patients after renal transplantation treated with eculizumab: a systemic review and meta- analyses. Ren Fail. 2023;45(1):2231264
- Kanbay M, et al. The role of anticomplement therapy in the management of the kidney allograft. Clin Transplant. 2024;38(3):e15277
- Jehn U, et al. First report on successful conversion of long-term treatment of recurrent atypical hemolytic uremic syndrome with eculizumab to ravulizumab in a renal transplant patient. Transpl Int. 2022;35:10846