Abstract Type : Oral
Abstract Submission No. : 1115

Early Outcomes of Tocilizumab (Anti-IL-6R Monoclonal) Treatment for Chronic Active Antibody-Mediated Rejection in Kidney Transplant Recipients

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Objectives: Chronic active antibody-mediated rejection (cABMR) is a leading cause of kidney allograft failure. Anti-humoral therapies such as plasma exchange, intravenous immunoglobulins (IVIG), and rituximab failed to show effectiveness on cABMR. Tocilizumab (TCZ), a humanized anti-Interleukin-6 (IL-6) receptor monoclonal antibody, may be a potential treatment option for cABMR by regulating inflammation and alloantibody production.

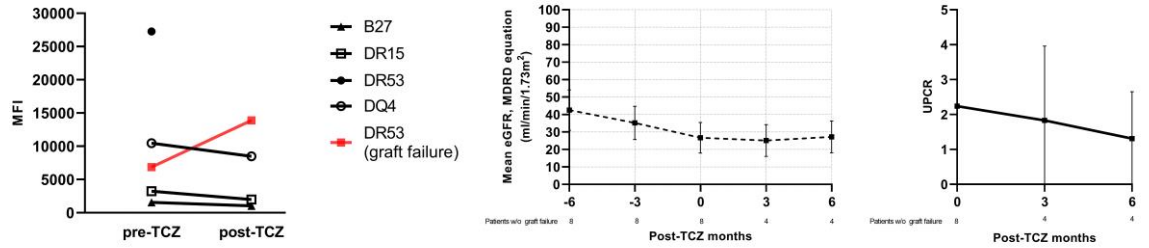
Methods: Thirteen kidney transplant (KT) recipients received TCZ treatment for cABMR in Seoul St. Mary's Hospital between 2019 and 2022. TCZ was administered at a monthly dose of 8mg/kg (maximum 800mg) for up to 6 months. If a patient's Immunoglobulin G level is ≤ 600mg/L, they were given a dose of 0.5mg/kg IVIG before receiving TCZ. Mean follow-up period was 10.0 months.

Results: Five out of thirteen patients had donor specific anti-HLA antibodies (HLA-DSA) at the time of biopsy. The mean fluorescence intensity (MFI) values of HLA-DSA were decreased after TCZ treatment in 3 patients. One patient experienced graft failure after 1 session of TCZ and showed an increase in HLA-DSA MFI. One patient undergoing treatment needs monitoring of HLA-DSA MFI (**Fig. 1A**). Five patients experienced death-censored graft failure. Patients with graft failure more frequently had a history of antibody-mediated rejection, a lower estimated glomerular filtration rate (eGFR), and a higher levels of proteinuria, although this difference was not statistically significant. One patient was diagnosed with pneumonia. No patient deaths were reported. (**Table 1**). In patients without graft failure, eGFR stabilized after starting TCZ with ΔeGFR of 13.0 mL/min/1.73m^2 (6 months pre-treatment) to 0.4 mL/min/1.73m^2 (6 months post-treatment) (**Fig. 1B**) and the amount of proteinuria reduced (**Fig. 1C**).

Conclusions: Even though patients with far advanced cABMR suffered allograft failure during treatment, patients without graft failure showed a decrease in HLA-DSA MFI and stabilization of allograft function. Our study suggests that early application of TCZ can give benefit for cABMR patients.

Figure 1

Fig.1 (A) (B) (C)



(A) MFI values of immunodominant HLA-DSA. (B) Kidney allograft function before and after TCZ treatment. (C) Changes in the amount of proteinuria after TCZ treatment.
Abbreviations: eGFR, estimated glomerular filtration rate; HLA-DSA, donor specific anti-HLA antibody; MDRD, modification of diet in renal disease; MFI, mean fluorescence intensity; TCZ, tocilizumab; UPCR, urine protein creatinine ratio

Table 1

Table 1. Baseline characteristics and clinical outcomes

No	Age	Gender	Previous ABMR Tx	Tx number	Time from KT to treatment (mo)	Time after treatment (mo)	Baseline eGFR (MDRD)	Baseline UPCR	Donor type	HLA-DSA at the time of biopsy	Banff score				Graft failure	Infection
											cg	C4d	ct + ci	g + ptc		
1	47	F	(+)	1	303.0	23.6	12.2	2.4	Live	(+)	1	3	2	5	(+)	(-)
2	52	F	(+)	6	43.1	38.1	33.3	1.9	Live	(-)	2	0	2	4	(+)	(-)
3	57	F	(+)	3	68.7	12.6	11.7	3.5	Live	(-)	1	0	4	4	(+)	(-)
4	62	F	(-)	1	204.5	6.4	13.0	7.6	Live	(-)	3	0	4	6	(+)	(-)
5	66	M	(-)	6	121.9	6.3	25.0	2.0	Live	(+)	3	3	2	6	(+)	(-)
6	71	M	(-)	6	144.8	10.2	31.5	7.1	Live	(-)	1	0	2	5	(-)	(-)
7	52	F	(-)	6	141.2	8.1	30.0	0.3	Live	(-)	2	0	2	4	(-)	(-)
8	37	F	(+)	6	77.8	7.4	13.5	0.4	Live	(-)	1	0	2	5	(-)	(-)
9	58	M	(-)	6	62.8	10.4	32.1	0.7	Live	(+)	2	3	2	5	(-)	(-)
10	65	M	(-)	3	167.0	2.8	28.0	2.7	Live	(+)	1	0	2	5	(-)	(-)
11	58	M	(-)	2	146.6	2.4	42.8	0.3	Live	(-)	2	0	2	4	(-)	(-)
12	61	M	(-)	1	296.0	1.2	25.0	1.0	Live	(+)	3	3	2	5	(-)	(-)
13	58	M	(+)	1	135.6	1.0	26.0	0.3	Live	(-)	2	1	4	6	(-)	(+)

Shaded rows represent patients with graft failure. Abbreviations: ABMR, antibody-mediated rejection; eGFR, estimated glomerular filtration rate; HLA-DSA, donor specific anti-HLA antibody; KT, kidney transplantation; MDRD, modification of diet in renal disease; Tx, treatment; UPCR, urine protein creatinine ratio.