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Clinical Trial of Allogeneic Mesenchymal Stem Cell Therapy for Chronic Active Antibody-Mediated Rejection in Kidney Transplant Recipients

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Objectives: The aim of this study is to investigate the therapeutic effect of allogenic mesenchymal stem cell therapy (MSC) in kidney transplant recipients (KTR) diagnosed with chronic active antibody-mediated rejection (CAMR).

Methods: A total of 5 patients diagnosed with CAMR by allograft biopsy were enrolled. Each patient received MSC for 4 cycles (1×10^6 cells/kg every other week) via peripheral vein. Human bone marrow-derived MSC (Catholic MASTER Cells) were obtained from the Catholic Institute of Cell Therapy (CIC, Seoul, Korea). The Catholic MASTER Cells were certified by the KFDA. Blood samples were collected at baseline and before 2nd and 4th MSC doses, and 1, 3, and 6 months after the end of treatment. Routine blood chemistry tests including serum creatinine, third party donor-specific Elispot and lymphocyte subsets analysis were performed using blood samples.

Results: Of the total of 5 patients, 2 patients maintained their allograft function well during the follow-up period. Two of the three patients who experienced graft loss started hemodialysis. The other patient developed Pneumocystis jirovecii pneumonia (PJP) 5 weeks after treatment, and expired on Week 6. There were no infectious complications other than PJP, and there were no serious adverse events related to MSC administration.

In the flow cytometry results, CD8+CCR7+ T cells, CD3Vδ2 T cells and Vδ2+γδ T cells decreased after MSC administration, and CD8+CCR7- T cells, CD3Vδ1 T cells and Vδ1+γδ T cells showed a conversely increasing trend.The two patients who maintained allograft function showed lower baseline serum creatinine levels compared to the other patients. In addition, these patients had an average baseline Elispot of less than 10 spots/$2.5\text{x}10^5$ cells, which was lower than that of patients with graft loss.

Conclusions: MSC showed the therapeutic effect on CAMR in some patients through changes in immune cells. And further studies are required on the MSC.

Table1&2. Baseline characteristics and Clinical outcomes

Table1. Baseline characteristics

No	KT date	Donor type	HLA relation	ABO compatibility	Crossmatch	DSA	Bx date	Prior Treatment
1	1994.07	LD	Haplo-identical	Compatible	Negative	DR7 1469 DR53 30776	2020.01	RTX/IVIg
2	2019.03	DD	Non-identical	Compatible	Negative	Negative	2020.04	None
3	2015.07	LD	Haplo-identical	Compatible	Negative	B75 13020	2020.05	RTX/IVIg
4	2016.07	DD	Non-identical	Compatible	Negative	Negative	2019.11	RTX/IVIg
5	2016.04	LD	Non-identical	Incompatible	T-FCXM 3.26 B-FCXM 4.17	Negative	2019.10	RTX/IVIg, Tocilizumab

Abbreviations: KT, kidney transplantation; HLA, human leukocyte antigen; DSA, donor-specific antibody; Bx, biopsy; LD, living donor; DD, deceased donor; RTX, rituximab; IVIg, intravenous immunoglobulin therapy

Table2. Clinical outcomes

No	Serum Creatinine				Graft survival	Infection	MSC SAE	Patient survival
	Baseline	1 month	3 months	6 months				
1	2.46	3.15	4.22	4.4	HD at Week 52	X	X	O
2	4.15	5.18	ND	ND	CRRT at Week 5	PJP	X	Expired at Week 6
3	2.3	2.12	1.86	2.02	O	X	X	O
4	5.04	6.73	ND	ND	HD at Week 13	X	X	O
5	1.63	1.80	1.75	2.10	O	X	X	O

Abbreviations: MSC, mesenchymal stem cell; SAE, serious adverse event; HD, hemodialysis; ND, not done; CRRT, continuous renal replacement therapy; PJP, Pneumocystis jirovecii pneumonia