Treatment of early accelerated AMR with eculizumab in antibody incompatible renal transplantation

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Introduction

Early accelerated antibody-mediated rejection (AMR) within 2 weeks after antibody-incompatible renal transplantation can be defined as sudden deterioration in graft function with oligoanuria that requires re-commencing on dialysis, does not improve with pheresis and often results in graft loss. The most common mechanism of AMR is binding of antibodies to antigens on endothelial cells in the kidney followed by complement activation. Eculizumab is a monoclonal antibody that specifically targets and blocks action of complement. It can be used as a salvage therapy in AMR refractory to standard treatment.

Methods

Over a period of 6 years 10 patients who underwent antibody incompatible living donor renal transplantation were treated with eculizumab. 4 of them were blood group (ABOi) and 6 were HLA-antibody incompatible (HLAi). The initial protocol was 5 doses on weekly bases. One of the patients had a 9 weeks course and one a 4 weekly course. All patient were receiving standard AMR treatment including antibody removal with no improvement in renal function.

Results

Mean age of patients treated was 43±17 years (ranged 18 – 66) and 9 of 10 were female. Mean baseline donor specific antibody (DSA) level for HLAi patients was 49280± 21230 MFI (ranged 26526 – 84022). 2 patients lost their grafts and underwent nephrectomy (both ABOi) and 2 patients died with no evidence of graft recovery (both HLAi) before finishing a scheduled treatment with eculizumab. Follow-up of patients ranged between 2 months and 2 years. Mean creatinine on the last visit was 133±53umol/L.

References

[Difference in outcomes after antibody-mediated rejection between abo-incompatible and positive cross-match transplantations.](#) Couzi L, Manook M, Perera R, Shaw O, Ahmed Z, Kessaris N, Dorling A, Mamode N. Transpl Int. 2015 Oct;28(10):1205-15.

[The use of eculizumab in renal transplantation.](#) Barnett AN, Asgari E, Chowdhury P, Sacks SH, Dorling A, Mamode N. Clin Transplant. 2013 May-Jun;27(3):E216-29.

Results cont.

Efficacy of eculizumab in our cohort was 60%. Relative risk of treatment failure with standard AMR treatment versus salvage therapy with eulizumab was 2.5 (95%CI 1.17 – 5.34) p=0.02; number needed to harm = 1. 67 (3.37 – 1.11). There was no statistically significant difference in either baseline DSA pre transplant or highest level of DSA post transplant between patients whose graft function did and did not recover. Mean DSA value on the last follow up was 14710±11342 MFI (ranged 3251 – 26218).

Figure 1. Comparison of DSA levels between patients whose graft recovered (blue) and patients whose graft did not recover (orange). The latter died during the eculizumab rescue therapy. DSA value given in Mean Fluorescence Intensity (MFI).

Discussion

Eculizumab can be successful in treatment of accelerated antibody mediated rejection. Multicentre analysis of treatment outcomes may allow better identification of patients who would likely benefit from short course of eculizumab as a salvage therapy.