

Prophylactic eculizumab treatment significantly improves renal allograft survival in patients with atypical haemolytic uremic syndrome compared with historic controls

Dr Emily K Glover^{1,2}, Dr Kate Smith-Jackson^{1,2}, Dr Edwin Wong^{1,2}, Dr Sally Johnson^{1,2}, Dr Michal Malina^{1,2}, Prof David Kavanagh^{1,2}, Prof Neil S. Sheerin^{1,2}

¹National Renal Complement Therapeutics Centre, Newcastle University, Newcastle Upon Tyne , UK, ²Newcastle Hospitals NHS Foundation Trust, Newcastle Upon Tyne, UK

Atypical haemolytic uraemic syndrome (aHUS) is a rare cause of end stage renal failure and has been recognised to have poor outcomes in renal transplantation due to early disease recurrence. Eculizumab treatment has transformed management of the condition in particular, allowing patients with aHUS to undergo transplantation. We report the largest case series of prophylactic eculizumab use in renal transplantation for aHUS.

We conducted a retrospective case series review of renal allografts for patients with confirmed aHUS and prospectively followed up those treated with eculizumab. 37 received prophylactic eculizumab treatment from the time of transplantation, 14 received eculizumab treatment with curative intent from the time of disease recurrence and 49 historic cases did not receive eculizumab. Both living and deceased donor renal allografts were included. The minimum follow up period was 1 year. Graft survival and reason for failure were collected by review of clinical records and results were censored for patient death with a functioning graft and for functioning graft at the end of the study period. Results were further analysed to compare those with only pathological mutations in complement pathway genes for CFH, CFB, CFI or C3.

At the end of the study period (1st August 2018), 4 grafts that had received prophylactic eculizumab had failed, as had 3 that received curative eculizumab and 38 of those historic controls that had not received eculizumab. Kaplan-Meier survival analysis showed that eculizumab treatment significantly improved renal allograft survival in patients with aHUS when administered prophylactically ($p<0.001$) or curatively ($p=0.03$). 5-year survival was 88% with prophylactic eculizumab, 78% with curative eculizumab and 36% without eculizumab treatment. In historic cases who did not receive eculizumab treatment graft survival was significantly ($p=0.007$) worse for those with pathological mutations compared to those who had mutations of uncertain significance. The improvement in 5 year graft survival with prophylactic eculizumab compared to no eculizumab was of greater significance when comparing only those cases with pathological mutations.

Prophylactic eculizumab treatment from time of renal transplantation dramatically improves graft survival at 5 years to begin to approach the UK average for all causes of renal failure. With prophylactic eculizumab treatment, renal transplantation has become a viable therapeutic option for those with end stage renal failure caused by aHUS.