Eculizumab in Posttransplant TMA: Unproven Benefit
A Response to Maritati et al.: "Eculizumab First" in the Management of Posttransplant Thrombotic Microangiopathy

To the Editor: In their retrospective study, Maritati *et al.*[1] advocate "eculizumab first" in patients with posttransplant thrombotic microangiopathy (PT-TMA). A critical analysis indicates that the data do not provide evidence to suggest that the use of eculizumab was instrumental in the improvement of graft function. First, the study was uncontrolled. Second, the graft failure rate of 27% is within the range reported in eculizumab-naïve PT-TMA cohorts (7%–38%).[2–5] Most authors attribute graft recovery to calcineurin inhibitor dose reduction and treatment of underlying rejections, a policy also applied by Maritati *et al.*[1]

Moreover, the characteristics of the study cohort are notable. Donor quality was poor (69% extended criteria donors). Remarkably, in this study, all patients developed PT-TMA almost immediately after transplantation (3 days, interquartile range: 2–4). This underlines the association between early PT-TMA and older donor age and donor arteriolosclerosis. Tokarski *et al.*[S1] reported 77 patients with PT-TMA; however, in only 24 patients, onset was within 2 weeks after transplantation. In this early group, graft survival was 100% and not driven by complement inhibitory therapy. We must emphasize that calcineurin inhibitor toxicity is enhanced in extended criteria donors.[S2] Importantly, in the latter study by Le Meur *et al.*,[S2] patients with early delayed graft function were switched from calcineurin inhibitor to belatacept, which resulted in an increase in estimated glomerular filtration rate from 18 to 35 ml/min per 1.73 m^2 (comparable to the reported 6-month estimated glomerular filtration rate of 27 ml/min per 1.73 m^2 in Maritati *et al.*[1] study).

Therefore, for now, eculizumab should not be considered the primary option in PT-TMA treatment. Controlled prospective studies, including cost-effectiveness evaluation, are needed.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary References.

1. Maritati F, Corradetti V, Bini C, et al. "Eculizumab First" in the management of posttransplant thrombotic microangiopathy. *Kidney Int Rep*. 2024;9:982–993. https://doi.org/10.1016/j.ekir.2024.01.013
2. Schwimmer J, Nadasdy TA, Spitalnik PF, Kaplan KL, Zand MS. De novo thrombotic microangiopathy in renal transplant recipients: a comparison of hemolytic uremic syndrome with localized renal thrombotic microangiopathy. *Am J Kidney Dis*. 2003;41:471–479. https://doi.org/10.1053/ajkd.2003.50058
3. Bren A, Pajek J, Grego K, et al. Follow-up of kidney graft recipients with cyclosporine-associated hemolytic-uremic syndrome and thrombotic microangiopathy. *Transplant Proc*. 2005;37:1889–1891. https://doi.org/10.1016/j.transproceed.2005.02.112
4. Le Quintrec M, Lionet A, Kamar N, et al. Complement mutation-associated de novo thrombotic microangiopathy following kidney transplantation. *Am J Transplant*. 2008;8:1694–1701. https://doi.org/10.1111/j.1600-6143.2008.02297.x
5. Avila A, Gavela E, Sancho A. Trombotic microangiopathy after kidney transplantation: an underdiagnosed and potentially reversible entity. *Front Med*. 2021;8:642864. https://doi.org/10.3389/fmed.2021.642864

Romy N. Bouwmeester[1], Jack F.M. Wetzels[2] and Nicole C.A.J. van de Kar[1]

[1]Radboud University Medical Center, Amalia Children's Hospital, Radboud Institute for Molecular Life Sciences, Department of Pediatric Nephrology, Nijmegen, The Netherlands; and [2]Radboud University Medical Center, Radboud Institute for Health Sciences, Department of Nephrology, Nijmegen, The Netherlands

Correspondence: Romy N. Bouwmeester, Radboud University Medical Center, Amalia Children's Hospital, Department of Pediatric Nephrology, P.O. Box 9101, 6500 HB, Nijmegen, The Netherlands. E-mail: Romy.Bouwmeester@radboudumc.nl

Received 22 February 2024; accepted 26 February 2024; published online 8 April 2024

Kidney Int Rep (2024) **9,** 1929; https://doi.org/10.1016/j.ekir.2024.02.1442

© 2024 International Society of Nephrology. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).