

[Test Your Knowledge: Lupus Nephritis & Thrombotic Microangiopathy](#)

In the January issue of *AJKD*, [El-Husseini et al](#) describe a case of lupus nephritis-associated thrombotic microangiopathy (TMA) that was successfully treated with eculizumab, a complement inhibitor. The following questions will test your knowledge on lupus nephritis and TMA.

1. Which of the following conditions is associated with TMA?
 - A. Genetically determined factor H excess
 - B. Loss of function mutations of complement factor B
 - C. CD46 abnormalities
 - D. Complement C4 mutations

2. Patients with systemic lupus erythematosus (SLE) and TTP/HUS have:
 - A. More severe kidney injury than patients with SLE without TTP/HUS
 - B. Generally lower serum creatinine than patients with SLE without TTP/HUS
 - C. Better renal pathology chronicity index score than patients with SLE without TTP/HUS
 - D. Lower hemoglobin than patients with SLE without TTP/HUS

3. Lupus nephritis with TMA due to HUS is different from TMA due to TTP because there is:
 - A. Increased kidney dysfunction in HUS
 - B. High ADAMTS-13 activity in HUS
 - C. Low ADAMTS-13 activity in HUS
 - D. Normal ADAMTS-13 activity in HUS

4. Which of the following statements is true regarding eculizumab?
 - A. It is a partially humanized monoclonal antibody that simulates the generation of anti-inflammatory mediator C5a
 - B. In the [TRIUMPH study](#), it reduced nitric oxide consumption, decreased N-terminal pro-brain natriuretic peptide, and increased ferritin
 - C. It forms antibodies against the membrane attack complex
 - D. In patients with paroxysmal nocturnal hemoglobinuria (PNH), eculizumab reduces intravascular hemolysis compared with baseline and placebo, and increases lactate dehydrogenase (LDH) level

5. Which of the following statements is true regarding lupus nephritis with TMA?
 - A. Kidney outcomes are poorer in patients that have a C4d deposition and decreased levels of factor H in the serum
 - B. The proteinuria in patients with lupus nephritis and TMA is less than that in patients with isolated lupus nephritis
 - C. Hypertension is the most common cause of renal TMA in patients with lupus nephritis

D. Renal TMA is not an independent risk factor for kidney outcomes in patients with lupus nephritis

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Solutions to eAJKD's [Test Your Knowledge: Lupus Nephritis & Thrombotic Microangiopathy](#)

1. C. CD46 abnormalities

[Thrombotic microangiopathy \(TMA\) associated with genetic or immune-mediated abnormalities of the complement system include:](#)

- Genetically determined factor H deficiency
- Genetic membrane cofactor protein (CD46) abnormalities
- Complement factor I deficiency
- Gain-of-function mutations of complement factor B
- Complement C3 mutations
- Acquired anti-C3 autoantibodies
- Immune-mediated factor H deficiency

2. A. More severe kidney injury than patients with SLE without TTP/HUS

[The study done](#) by Yu et al to investigate the clinical and pathologic features of TTP-HUS in patients with renal thrombotic microangiopathy (TMA) looked into this specific question. The authors compared 55 patients with lupus nephritis class IV-G to 7 patients with SLE and renal TMA. They found that patients with SLE and renal TMA had more severe kidney injury, worse kidney outcomes, lower serum ADAMTS-13 activity, and higher ADAMTS-13 antibodies. Patients with SLE and renal TMA had worse renal histopathology scores and prognosis compared with patients with lupus nephritis (IV-G) alone. They also suggested that autoantibodies to ADAMTS-13, which are significantly higher in SLE and renal TMA, may hamper the enzymatic activity of ADAMTS-13 leading to increased survival of uncleaved or partially cleaved vWF, resulting in prothrombotic state.

3. D. Normal ADAMTS-13 activity in HUS

It has been reported that deficiency or dysfunction of ADAMTS-13, the vWF-cleaving protease (vWF-cp), may lead to survival of uncleaved or partially cleaved unusually large vWF multimers (UL-vWF) [that induce TTP](#). Hunt et al reported 3 patients presenting with lupus nephritis and TMA. The authors proposed that the TMA was due to HUS as these patients had significant proteinuria, hypertension, and AKI, but normal ADAMTS-13 activity.

4. B. In the TRIUMPH study, it reduced nitric oxide consumption, decreased N-terminal pro-brain natriuretic peptide, and increased ferritin

Eculizumab is fully humanized monoclonal antibody that specifically binds to the complement protein C5 with high affinity, preventing its cleavage into terminal complement components. It inhibits the generation of C5a and C5b, potent inflammatory

mediators, and prevents formation of the terminal complement component C5-9. In the [TRIUMPH](#) (Transfusion Reduction Efficacy and Safety Clinical Investigation, a Randomized, Multicenter, Double-Blinded, Placebo-Controlled, Using Eculizumab in Paroxysmal Nocturnal Haemoglobinuria) study, Eculizumab significantly reduced nitric oxide consumption, levels of N-terminal pro-brain natriuretic peptide, and increased ferritin levels. Eculizumab reduced intravascular hemolysis compared with baseline and placebo, as determined by significantly decreased lactate dehydrogenase (LDH) levels. Significant reductions in LDH levels were achieved within the first week of treatment, with near normal levels achieved at week 2 and maintained throughout longer term treatment, including periods of up to 36 months. Eculizumab achieved rapid and sustained efficacy, regardless of baseline LDH levels or platelet counts. Half of the patients in the eculizumab group became transfusion independent compared with no patients in the placebo group.

5. A. Kidney outcomes are poorer in patients that have a C4d deposition and decreased levels of factor H in the serum

A large study by [Song et al](#) looked at lupus nephritis with TMA. In the 148 patients with lupus nephritis, 36 patients were diagnosed with co-existing renal TMA based on histology. Compared with the non-renal TMA group, patients with renal TMA had significantly higher urine protein and serum creatinine, and more chronic glomerular and tubular interstitial changes on kidney biopsy. Patients with renal TMA had poorer kidney outcome compared with the non-TMA group. Renal TMA was an independent risk factor for kidney outcomes in patients with lupus nephritis. HTN-related TMA was a minority of the 36 cases, with the majority caused by direct SLE-related renal TMA. The kidney outcomes were poorer for those with both C4d deposition and decreased serum complement factor H in the TMA group.