For patients with atypical hemolytic-uremic syndrome, treatment with the terminal complement inhibitor eculizumab can improve renal function, even allowing some patients to discontinue dialysis, reports a study in the *New England Journal of Medicine*.

The report describes two prospective phase 2 trials of eculizumab in patients with atypical hemolytic-uremic syndrome, aged 12 years or older. Trial 1 included 17 patients with low platelet counts and kidney damage. Trial 2 included 20 patients with kidney damage but no more than a 25 percent reduction in platelet count during at least 8 weeks of plasma exchange or infusion. Both trials included 26 weeks of eculizumab; with long-term extension phases, treatment continued for a median of 64 and 62 weeks, respectively.

In trial 1, platelet count increased by a mean of 73 × 10^9 over 26 weeks. In trial 2, 80 percent of patients remained free of thrombotic microangiopathy events—including dialysis initiation—while receiving eculizumab.

Eculizumab was also associated with time-dependent improvement in estimated GFR, particularly in patients receiving earlier treatment. In trial 1, four out of five patients were able to discontinue dialysis. Long-term treatment with eculizumab had no cumulative toxicity or serious infection-related adverse events, including meningococcal infections.

Atypical hemolytic-uremic syndrome—caused by genetic defects in complement system regulation—puts patients at risk of complement-mediated thrombotic microangiopathy affecting the kidneys and other organs. The new trials support previous case reports showing benefits of complement inhibitor therapy with eculizumab.


**Urinalysis Is More Specific for AKI than NGAL**

For early detection of acute kidney injury (AKI), urinalysis is a more specific test than urinary neutrophil gelatinase-associated lipocalin (NGAL), reports a study in *Nephrology Dialysis Transplantation*.

A rapid enzyme-linked immunosorbent assay (ELISA) for urinary NGAL underwent analytic validation by the use of random and 24-hour urine samples from 125 healthy volunteers. The results showed that NGAL levels were stable for up to 7 days, including ambient and frozen samples. The ELISA showed linear performance at concentrations from 0.24 to 10,000 ng/mL, with a quantitation limit of 0.24 ng/mL. Inter- and intra-assay precision were excellent, although the presence of white blood cells was associated with higher NGAL levels. The ninety-fifth percentile reference values were 65.0 ng/mL or less in women and 23.4 ng/mL or less in men.

In a clinical validation study, NGAL measurement and urinalysis were performed on samples from 363 emergency department patients who were admitted to the hospital. Urinary NGAL concentrations increased with AKI stage according to the Acute Kidney Injury Network criteria. However, the ELISA had only fair performance in differentiating absence of AKI versus stage 1, 2, or 3 AKI. Sensitivity and specificity were both 65 percent, with an area under the curve of 0.70. By comparison, urinalysis with microscopy offered excellent specificity of 91 percent but sensitivity of only 22 percent: area under the curve 0.57.

Urinary NGAL is a promising biomarker for earlier detection of AKI. The new ELISA reliably measures NGAL in clinical urine samples, although pyuria is a potential confounder.

Higher urinary NGAL is an indicator of AKI; its diagnostic performance is only fair, but it might be improved by excluding patients with prerenal causes of AKI. Meanwhile, microscopic urinalysis is a readily available and inexpensive test with high specificity for AKI [Schinstock CA, et al. Urinalysis is more specific and urinary neutrophil gelatinase-associated lipocalin is more sensitive for early detection of acute kidney injury. *Nephrol Dial Transplant* 2013; 28:1175–1185].

**Eculizumab for Atypical Hemolytic-Uremic Syndrome**

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