Eculizumab Improves Survival When Stem Cell Transplant Patients Develop High-Risk TA-TMA

Transplant-associated thrombotic microangiopathy (TA-TMA) is one of the most dangerous complications that can occur in patients receiving hematopoietic stem cell transplant (HSCT). It occurs in about 30% of patients and, when untreated, can have a mortality rate exceeding 80%.

A closer study of TA-TMA in recent years has revealed that an over-activated complement system drives severe organ damage, especially in the kidney. This information prompted a multidisciplinary team of experts at Cincinnati Children's to explore whether the complement-blocking drug eculizumab could help.

The research was led by first author Sonata Jodele, MD, and senior author Stella Davies, MBBS, PhD, MRCP, and included 12 co-authors from several divisions at Cincinnati Children's.

The team reported encouraging results from using the drug to treat 64 HSCT recipients with high-risk TA-TMA. At one-year post-transplant, the survival rate for treated patients improved to 66%, up from 16% in a previously reported untreated cohort.

Patients who responded to treatment received a median of 11 doses of eculizumab, and their TA-TMA resolved within a median of 66 days. Those who did not respond tended to have more severe complement activation, and some had intestinal bleeding that limited the drug's effectiveness.

The team noted that treatment with eculizumab started only after multi-organ damage had occurred, suggesting that earlier detection of high-risk TA-TMA could further improve survival rates.

"We were quite excited to see a strong response to this treatment, but the outcomes are not yet ideal," Jodele says. "Now, we hope to determine whether a combination of using complement blockers and targeting other endothelial injury pathways may assist those who do not respond to eculizumab alone."

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"Complement blockade for TA-TMA: Lessons Learned from a Large Pediatric Cohort Treated With Eculizumab" was published in the March 26, 2020, issue of *Blood*.