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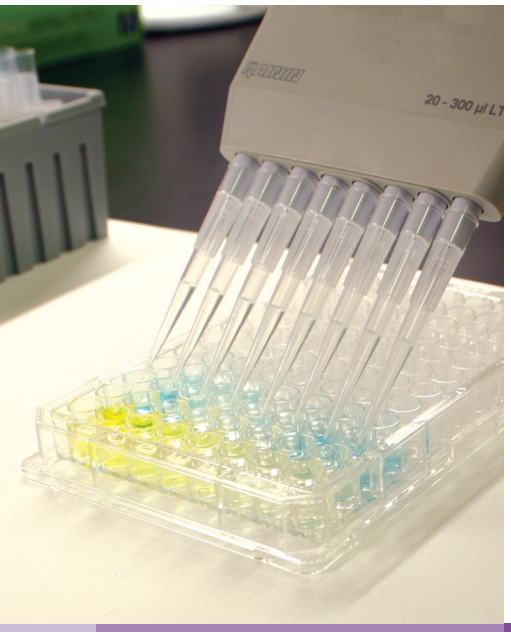


Cincinnati Children's Clinical Laboratories Offer Testing to Monitor Eculizumab Therapy

Eculizumab (Soliris®, Alexion Pharmaceuticals) is FDA approved for treating the complement-mediated hemolysis of paroxysmal nocturnal hemoglobinuria (PNH) and the complement-mediated thrombotic microangiopathy (TMA) of atypical hemolytic uremic syndrome (aHUS). Proper testing can help clinicians ensure that drug dosing is sufficient to keep these diseases at bay.

CONTACT US

For testing information you may contact our clinical lab specialists directly at:

Phone: **513-636-4530**
nephclinicallab@cchmc.org

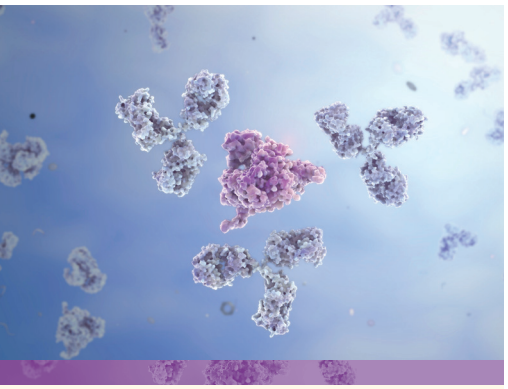
Therapeutic Drug Monitoring for Eculizumab—Overview

- Eculizumab is a humanized IgG4 monoclonal antibody that binds to the complement protein C5 and prevents it from being cleaved into its active fragments.
- Adequate dosage and dosing interval of eculizumab results in a complete blockade of terminal complement pathway activation, thereby halting complement-mediated microvascular injury and cell destruction.
- If a patient is not being sufficiently dosed with eculizumab, breakthrough activation of the complement system and disease reactivation may occur.
- The Nephrology Clinical Laboratory at Cincinnati Children's now offers an assay to monitor serum levels of eculizumab.
- Concomitant CH50 and sC5b-9 testing is also available to determine whether eculizumab is sufficiently present to effectively block the terminal complement pathway.
- These tests, along with clinical judgment and standard laboratory indicators of disease activity such as LDH, platelet count and renal function, can guide eculizumab dosing.

Why Test for Therapeutic Levels?

Eculizumab clearance, and thus serum levels, can be highly variable. In some patients, factors such as heavy proteinuria or severe inflammatory or catabolic states can necessitate significant deviation from the standard dosing regimen in order to ensure sufficient complement pathway blockade.[1,2]

[1]Jodele S et al, BBMT 2015. [2]Jodele S et al, BBMT 2014



Specimen Requirements:

- Testing of CH50 and Eculizumab Level requires 0.5mL each of serum, separated and frozen within 2 hours of collection.
- Testing of sC5b-9 requires 0.5mL of EDTA plasma, separated and frozen within 2 hours of collection.

Specimens should be shipped frozen to:

Cincinnati Children's
Hospital Medical Center
3333 Burnet Avenue NRB 1042
Cincinnati, OH 45229

To download a test requisition and to learn more about our specialized diagnostic testing services please visit: **www.cincinnatichildrens.org/nephrology-labtests**

Testing We Recommend for Patients on Eculizumab

ECULIZUMAB LEVELS[1]

The quantitative measurement of free (unbound to C5) serum eculizumab by enzyme-linked immunosorbent assay (ELISA) may be used to ensure that the drug is present in sufficient concentration to block the terminal complement pathway. This determination may be especially useful when first initiating eculizumab therapy, particularly with persistent clinical or laboratory evidence of disease activity on the current regimen, or if disease reactivation is noted before the next dose.

CH50

CH50 measures the functional activity of both the classical and terminal complement pathways, and is abnormally low if any component of these pathways is defective. This test is beneficial for monitoring patients being treated with eculizumab for aHUS, other forms of thrombotic microangiopathy (TMA), or PNH. Adequate dosage and dosing interval of eculizumab should result in a total blockade of terminal complement pathway activation.

sC5b-9/sMAC

With terminal complement pathway activation, complement proteins C5 through C9 assemble to form the C5b-9 complex, and in the absence of a target membrane, form non-cytolytic complexes in plasma. Quantitative measurement of the resultant soluble membrane attack complex (sMAC or sC5b-9) indicates the degree of terminal complement pathway activation. An elevated plasma level of sC5b-9 indicates activation of the terminal complement pathway, and is suggestive of an insufficient level of eculizumab to block this activation.

Diagnostic Testing Suggesting Adequate Suppression of the Terminal Complement Pathway

These should be interpreted in the context of other clinical and laboratory evidence of disease activity.

- **For aHUS:** eculizumab trough serum concentration >99µg/mL[2]
- **For PNH:** eculizumab trough serum concentration >35µg/mL[3]
- CH50 <10% of the lower limit of normal[4]
- sC5b-9/sMAC normalization, if initially elevated

[1]The eculizumab level and sC5b-9 assays were developed and performance characteristics determined by the Nephrology and CBDI Clinical Laboratories at CCHMC. These tests have not been cleared or approved by the US Food and Drug Administration. The laboratories are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and the College of American Pathologists as qualified to perform high complexity laboratory testing. [2]Legendre CM et al, NEJM 2013. [3]Hillmen P et al, NEJM 2004. [4]Peffault de Latour R et al, Blood 2015; Jodele S et al, BBMT 2014

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