aGVHD Pre-Symptomatic Algorithm
Test Code: 403571P

New Assay

Tests in this Panel >> ST2 >> Reg3 alpha (REG3α) >> aGVHD Algorithm

The algorithm value is only available as part of this test and cannot be ordered individually.

Clinical and Procedure

Clinical Utility
The aGVHD Pre-Symptomatic Algorithm is used to aid in the evaluation of patients for acute graft versus host disease (aGVHD) following hematopoietic cell transplant (HCT) using the biomarkers ST2 and regenerating islet-derived 3 alpha (REG3α).

About aGVHD Pre-Symptomatic Algorithm

The diagnosis of aGVHD in allogeneic HCT patients has largely relied on clinical assessment, often in combination with biopsy. However, this approach is problematic since damage is often severe by the onset of clinical signs and biopsies are invasive, expensive and carry the risk of severe complications. Non-invasive approaches, such as the use of biomarkers to test for aGVHD have been the subject of clinical research for a number of years, but suffer from a lack of clinical validation, established algorithmic value cutoffs and standardization between laboratories. However, recent research by Drs. James Ferrara and John Levine, working with an international consortium through the Icahn School of Medicine at Mount Sinai has led to the development and clinical validation of an algorithm (based on ST2 and REG3α levels) that provides prediction of risk for severe aGVHD and non-relapse mortality (NRM) in allo-HCT patients at critical times post-transplant. Use of the results from the aGVHD Algorithm tests may aid in treatment decisions and modifications prior to or early in the disease process, and thus improve outcomes for patients.

To evaluate the risk of severe aGVHD and NRM post-transplant:

- The aGVHD Pre-Symptomatic Algorithm for use post-transplant and before the patient shows onset of aGVHD symptoms.
- The aGVHD Symptomatic Onset Algorithm for use post-transplant, and after the patient displays symptoms of aGVHD.
- The aGVHD Post-Treatment Algorithm for use after systemic treatment for aGVHD has been initiated.

The aGVHD predictive algorithm tests utilize serum levels of ST2 and REG3α, and have been clinically validated to help health care professionals better predict the risk of NRM prior to the onset of aGVHD. While there are multiple clinical factors that increase the risk of NRM post-transplant include HLA mismatch, non-family donors, recipient age and GVHD prophylactic therapy, use of the predictive algorithm has been demonstrated to be more accurate despite variations in these clinical factors. The two biomarkers used in the algorithm are both important to the pathobiology of aGVHD. ST2 is member of the Toll-interleukin 1 receptor family, and functions as a down-regulator of the pro-inflammatory cytokines IL-1, IL-6 and TNF-α. ST2 has been shown to be elevated in inflammatory conditions. REG3α, an anti-inflammatory/anti-bacterial protein expressed in Paneth cells within the epithelium of the small intestine, has been shown to be elevated in medical conditions where immune dysregulation causes damage to the mucosal epithelial barrier.

About Graft versus Host Disease (GVHD)

GVHD is one of the major causes of morbidity and mortality associated with allogeneic bone marrow, stem cell, or other kinds of hematopoietic cell transplants. GVHD occurs in 30 – 50% of HLA-matched sibling transplants and 60 – 90% of matched unrelated donors. GVHD often manifests in the skin, liver and/or gastrointestinal (GI) tract, and is caused by immune dysregulation that is initiated when allogeneic donor T cells recognize host tissues as foreign. GVHD may be either acute or chronic. Acute GVHD (aGVHD), which typically occurs in the first 3 months post-transplant, has an incidence of 19 – 66% and carries a poor prognosis if the disease is severe. The mean onset of aGVHD is around 1 month after the transplant occurs. Diagnosis of aGVHD has traditionally been based on the clinical presentation and ruling out other etiologies through differential diagnosis. In many cases biopsies of the
liver, skin or GI tract are performed. Chronic GVHD (cGVHD) occurs 3 months to >1 year post-transplant and has a pathophysiology that is distinct from aGVHD, although poorly understood. The overall incidence of cGVHD is 40 – 50%.

Pre-transplant conditioning regimens may damage host tissue, which in turn leads to inflammatory cytokine release (TNF-α, INF-γ, IL-1 and IL-6) directly from damaged tissues. The inflammatory cytokines stimulate antigen presenting cells which present host antigens to donor lymphocytes. In response, donor T cells proliferate, differentiate and undergo activation. Once donor T cells are activated, pro-inflammatory cytokines are produced in large quantities resulting in additional inflammation, recruitment of neutrophils to the site, and ultimately severe tissue damage. Administration of immunosuppressive agents are commonly used to treat cases of GVHD.

In skin, aGVHD frequently manifests as a maculopapular skin rash due to cellular/tissue damage. In the GI tract, aGVHD which frequently manifests as nausea, vomiting, anorexia, secretory diarrhea and in severe cases abdominal pain and at times hemorrhage, is caused by cellular damage to the mucosal epithelial barrier of the small intestines. The occurrence of aGVHD in the liver results in elevated bilirubin levels, indicative of liver damage.

Procedure
The assays for quantification of REG3α and ST2 are sandwich ELISAs performed in a microtiter plate format. Conversion of a chromogenic substrate produces a color, the intensity of which is proportional to the concentration of REG3α or ST2 in the sample material. The results from ST2 and REG3α are then used to calculate the algorithm result. This test has not been cleared or approved for diagnostic use by the U.S. Food and Drug Administration.

Turnaround Time
Same day (within 24 hours from receipt of specimen), Monday through Friday.

Specimen Information

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<th>Specimen Type</th>
<th>Order Code</th>
<th>CPT Code</th>
<th>NY Approved</th>
<th>Volume</th>
<th>Assay Range</th>
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<td>Serum</td>
<td>403571P</td>
<td>83006, 83520</td>
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<td>0.5 mL (min. 100 uL)</td>
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Special Instructions
- Whole blood should be collected in serum tube
- Allow to clot for 30 to 60 minutes and centrifuged to isolate the serum
- 0.5 mL of serum sample should be removed to a sterile tube and frozen immediately

Shipping
Ship Monday through Friday. Friday shipments must be labeled for Saturday delivery. All specimens must be labeled with patient's name and collection date. A Viracor Eurofins test requisition form must accompany each specimen. Multiple tests can be run on one specimen. Ship specimens FedEx Priority Overnight® to: Viracor Eurofins, 1001 NW Technology Dr, Lee's Summit, MO 64086.

Causes for Rejection
Invalid specimen type, inadequate volume, gross hemolysis or gross lipemia, sample not frozen upon receipt.

Disclaimer
Specimens are approved for testing in New York only when indicated in the Specimen Information field above.

The CPT codes provided are based on Viracor Eurofins’ interpretation of the American Medical Association's Current Procedural Terminology (CPT) codes and are provided for general informational purposes only. CPT coding is the sole responsibility of the billing party. Questions regarding coding should be addressed to your local Medicare carrier. Viracor Eurofins assumes no responsibility for billing errors due to reliance on the CPT codes illustrated in this material.
References


