**cKIT - GIST**

**Test Code:** 4199

**Department:** Molecular Oncology

**Test Synonyms:**
- KIT for Gastrointestinal stromal tumor (GIST) (exons 9, 11, 13, 17) reflexed to PDGFRα

**CPT Code(s):**
- 83890
- 83892
- 83898 x 4
- 83903 x 4
- 83907

**Background:**
Approximately 80% of gastrointestinal stromal tumors (GISTs) have an oncogenic mutation in the gene encoding KIT tyrosine kinase. Another 5-7% of GISTs have a mutation in the gene encoding the related kinase PDGFRα (platelet-derived growth factor receptor alpha). KIT and PDGFRα mutations are mutually exclusive in GISTs. In both genes, the observed mutations are invariably in-frame and result in expression of a mutant kinase isoform that has constitutive tyrosine kinase activity. Approximately 10-15% of GISTs have no detectable KIT or PDGFRα gene mutation.

Screening for kinase mutations in suspected GISTs can be helpful for the following reasons.
- The presence of a mutation provides molecular confirmation of the diagnosis.
- Clinical response to treatment with imatinib mesylate (Gleevec™) is predicted by the kinase mutation status, as detailed in the table below.
- The progression-free survival of patients with KIT exon 9-mutant GIST is significantly longer when they are treated with 800mg/d imatinib as opposed to 400mg/d. In contrast, the PFS of patients with KIT exon 11-mutant tumor is not influenced by drug dosage.

<table>
<thead>
<tr>
<th>Mutation Status*</th>
<th>KIT exon 11</th>
<th>KIT exon 9</th>
<th>No mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective response*</td>
<td>65-67%</td>
<td>34-40%</td>
<td>23-40%</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>3%</td>
<td>17%</td>
<td>19%</td>
</tr>
<tr>
<td>Progression-free survival</td>
<td>19-27 mo</td>
<td>9-10 mo</td>
<td>8-15 mo</td>
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</table>

*Defined as complete or partial response by RECIST criteria.

**Methodology:**
The testing protocol involves the following steps.
1. Microscopic examination of the specimen and macrodissection of tumor-rich areas.
2. DNA extraction and purification.
3. PCR amplification of selected KIT exons, serially in this order: exon 11, 9, 13 & 17.
4. Screening for mutations by one of two methods: direct, bidirectional sequencing, or real-time PCR with high resolution melting curve analysis. DNA sequencing is used to confirm any mutations picked up by melting curve analysis.
5. The estimated sensitivity of these methods is 20% mutant allele.

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6. If *KIT* mutations are not detected, the specimen will be reflexed to *PDGFRA* and appropriate testing charges will be incurred. Please see *PDGFRA* Information Sheet for methodology.

**Specimen Requirements:**
- A paraffin block or
- 10 unstained sections of tumor (4-5 microns) (15 sections for small biopsies)

**A REQUISITION FORM MUST ACCOMPANY ALL SAMPLES.** Please include detailed clinical information.

**Test Performed (Days):**
Mon - Fri

**Turn Around Time:**
10 - 14 days

**Shipment Sensitivity Requirements:**
Package and ship specimen to remain cold, but not frozen. Ship via overnight express, using the FedEx priority overnight label provided. Contact Client Services at (855) 535-1522 for shipping kits and instructions.

**References**