**PDGFRA - GIST**

**Test Code:** 5250  
**Department:** Molecular Oncology

**Test Synonyms:**  
*PDGFRA* mutation screening for  
gastrointestinal stromal tumor (GIST)  
(exons 12, 14, 18)

**CPT Code(s):**  
83890  
83892  
83898 x 3  
83903 x 3  
83907

**Background:**  
Approximately 80% of gastrointestinal stromal tumors (GISTs) have an oncogenic mutation in the gene encoding *KIT* tyrosine kinase.\(^1\) Another 5-7% of GISTs have a mutation in the gene encoding the related kinase *PDGFRA* (platelet-derived growth factor receptor alpha).\(^2\) *KIT* and *PDGFRA* 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.

The most common mutation in *PDGFRA* is D842V, which generates a mutant form of the kinase that is fully resistant to imatinib in vitro.\(^1\) Tumors with this mutation are generally slow to recur or progress. There are only limited data on patients whose GIST harbored this mutation and were treated with imatinib. Combining data from the B2222 phase II trial, the SWOG 0033 phase III trial and the EORTC phase III trial of imatinib for advanced GIST, there were no objective responses among 10 patients with this mutation.\(^2,4\) One patient had stable disease. In another recent report of 19 patients with D842V-mutant GIST, 26% had stable disease and 74% had progressive disease as their best response to imatinib.\(^6\)

Other *PDGFRA* mutations occurring in exons 12, 14 and 18 are nearly all predicted to be sensitive to inhibition by imatinib based on pre-clinical data.\(^4\) This is supported by the limited clinical trial data that are available.\(^3,5\)

**Methodology:**  
This test is performed as a reflex for GISTs that are negative for a *cKIT* mutation. 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 *PDGFRA* exons 12, 14 & 18.  
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.

**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:

References