



## Conference 2008 Poster Abstracts

### **Pharmacogenetic profiling of GISTs in clinical service: aiding diagnosis and predicting imatinib response**

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#### Background:

Most gastrointestinal stromal tumours (GISTs) express receptor tyrosine kinase KIT oncoprotein and are diagnosed by positive immunostaining for CD117, sometimes immunostaining can be equivocal; in these cases molecular testing can provide confirmation of the tumour pathology.

The majority of GISTs have activating somatic mutations in one of two tyrosine kinase genes, c-KIT and platelet derived growth factor receptor-alpha (PDGFRA). The majority, 80-85%, have acquired activating mutations in c-KIT, whereas 5-10% have acquired activating mutations in PDGFRA. The presence and location of c-KIT/PDGFRA mutations correlates with tumour location and differences in tumour behaviour, as well as clinical response to imatinib. Activating mutations in exon 11 of c-KIT correlate with increased imatinib response and progression-free survival, whereas exon 9 mutations predict worse imatinib response.

#### Aims:

We aimed to establish a clinical service for the molecular characterization of GISTs

#### Methods

Here we describe the optimisation and development of a routine diagnostic test in an accredited laboratory to screen exons 9, 11, 13 and 17 of c-KIT and exons 12, 14 and 17 18 of PDGFRA for activating somatic mutations from paraffin embedded tissue.

#### Results:

We have currently issued 11 reports describing 5 exon 11 (c-KIT) activating mutations, 2 exon 18 (PDGFRA) activating mutations, 1 exon 14 (PDGFRA) activating mutation and 3 negative screens.

#### Conclusions:

The identification of an activating mutation not only confirms a diagnosis of GIST but also predicts the clinical outcome and malignant profile of GISTs, which aids the clinical management of the patient.