



CONFERENCE 2007

ABSTRACTS

POSTER

Somatic Mutation Testing of gists in clinical service:

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Aims: Gastrointestinal stromal tumors (GISTs) are soft tissue sarcomas of mesenchymal origin and comprise about 0.1-3% of all gastrointestinal (GI) cancers (700 patients/year in the UK). Most GISTs are routinely diagnosed by positive immunostaining for CD117. The majority of GISTs have activating somatic mutations in the c-KIT gene; the remainder have activating mutations in platelet derived growth factor receptor-alpha (PDGFRA). The type of c-KIT/PDGFRA mutation correlates with differences in survival, as well as clinical response to imatinib. Mutations in c-KIT exon 11 correlate with better imatinib response and progression-free survival, compared to exon 9 mutations. We aimed to evaluate the feasibility of offering genetic tests for GISTs through a clinically accredited diagnostic laboratory.

Methods: Positive controls with known mutations were screened by bi-directional sequencing to optimise the screening protocol. DNA was extracted from formalin fixed paraffin embedded tumour sections. A mutation screening strategy was devised to identify c-KIT mutations in exons 11 and 9 by bi-directional DNA sequencing. Samples in which mutations were not detected were analysed for c-KIT mutations in exons 13 and 17 and PDGFRA mutations in exons 12 and 18.

Results: Consistent with previous studies most somatic mutations (>45%) associated with GISTs occur in exon 11 of c-KIT. However, no specific mutation hotspot was identified, indicating that the whole exon requires examination.

Conclusions: Mutation screening for c-KIT mutations can be performed robustly by DNA sequencing in a clinical laboratory and may be useful to clarify cases of GISTs with indeterminate CD117 staining.