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Molecular Basis of cKit Mutation in Recurrent Gastrointestinal Stromal Tumour (GIST): A Case Report from India

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ABSTRACT The development and progression of gastrointestinal stromal tumours (GISTs) are associated with mutations in the genes KIT and PDGFRA, which predict the response to tyrosine kinase inhibitors (TKI's). The confirmation of diagnosis of GIST is mainly on the basis of findings from the imaging and diagnostic tests of CD34/CD117 expression by immunohistochemistry (IHC). Approximately eighty percent of GIST with advanced disease achieves partial response or stable disease with selective TKI's. The resistance to the drug appears with prolonged usage due to emergence of acquired resistance mutations in the activation loop of cKit gene. Through this case study, the researchers aim to propose that genomic characterisation of GIST must be considered a standard practice to find aberrations that can be better managed with targeted treatment. Here, the researchers discuss a case of a 37-year-old female diagnosed with GIST based on CD34/CD117 positivity by IHC who initially responded to neo adjuvant imatinib therapy but the disease progressed after few months of treatment with each line of TKI. Somatic mutation analysis of 48 tumour-specific actionable genes by Next Generation Sequencing (NGS) was performed to identify the presence of any actionable mutations. The results revealed several primary and secondary (acquired) mutations in the KIT gene indicating resistance to TKI's imatinib, sunitinib and sorafenib but a possible response to regorafenib, a third-line TKI.