

Deletions Affecting Codons 557-558 of the *c-KIT* Gene Indicate a Poor Prognosis in Patients With Completely Resected Gastrointestinal Stromal Tumors: A Study by the Spanish Group for Sarcoma Research (GEIS)

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PURPOSE: To explore the prognostic value of mutations in *c-KIT* and *PDGFR- α* genes with respect to relapse-free survival (RFS) in patients with gastrointestinal stromal tumors (GIST). We have investigated the prognostic relevance of the type and position of the mutations, in addition to other clinicopathologic factors, in a large series of patients with GIST.

METHODS: For this study, 162 patients were selected according to the following criteria: completely resected tumors with negative margins attended between 1994 and 2001; no metastasis at diagnosis; tumor larger than 2 cm, *c-KIT*-positive immunostaining; and no other primary tumors.

RESULTS: The median follow-up was 42 months for patients free of recurrence. Mutations were detected in 96 tumors (60%): 82 cases involving *c-KIT* and 14 cases involving *PDGFR- α* . Univariate analysis demonstrated the following as poor prognostic factors for RFS: tumors larger than 10 cm ($P < .0001$); mitotic count higher than 10 mitoses per 50 high-power fields ($P < .0001$); high risk index ($P < .0001$); intestinal GIST location ($P = .0041$); high cellularity ($P < .0001$); tumor necrosis ($P < .0001$); deletions affecting exon 11 ($P = .0007$); and deletions affecting codons 557 to 558 ($P < .0001$). After the multivariate analysis, only the high risk index (relative risk [RR], 12.36), high cellularity (RR, 3.97), and deletions affecting codons 557 to 558 of *c-KIT* (RR, 2.57) corresponded to independent prognostic factors for RFS in GIST patients.

CONCLUSION: Deletions affecting codons 557 to 558 are relevant for the prognosis of RFS in GIST patients. This critical genetic alteration should be considered to be a new

prognostic stratification variable for randomized trials exploring imatinib mesylate in the adjuvant setting in GIST patients.

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Authors' disclosures of potential conflicts of interest are found at the end of this article.