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Somatic Mutations of PI3K in Early and Advanced Gallbladder Cancer: Additional Options for an Orphan Cancer.

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Abstract

Gallbladder cancer (GBC) is the second-leading cause of death from malignant tumors in Chilean women. The phosphatidylinositol 3-kinase (PI3K) pathway is involved in proliferation, cell survival, and growth. We investigated mutations in exons 9 and 20 of the PI3K gene in GBC. Mutations in exons 9 (E542K, E545G, E545K) and 20 (H1047L and H1047R) of PI3K were determined by direct sequencing in 130 cases of GBC. The patient group consisted of 110 women and 20 men, and mutations were found in 22 cases (16.9%). Of these, 14 cases had mutations in exon 9 (63.6%) (E542K, 64%; E545K, 29%; and E545G, 7%) and 8 in exon 20 (37.4%; H1047L, 50%; H1047R, 50%). No differences were noted in the frequency and type of mutations analyzed by sex, age, or histologic features. We observed mutations in 22% of the early-stage GBC and 14.6% of the advanced cases. In this series of GBC, 17% of cases were noted as having mutations in either exons 9 or 20 of PI3K. These results suggest that therapeutic testing of inhibitors of the PI3K/AKT pathway may be of benefit in advanced GBC patients.