Influence of \textit{GSTM1} and \textit{GSTT1} polymorphisms on the survival rate of patients with malignant glioma under perillyl alcohol-based therapy

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\textbf{ABSTRACT.} \textit{GSTM1} (glutathione \textit{S}-transferase mu 1) and \textit{GSTT1} (glutathione \textit{S}-transferase theta 1) are critical enzymes for detoxification of endogenous and environmental carcinogens. Constitutive \textit{GST} gene polymorphisms may be associated with increased risk for cancer development. We made an explorative study of a Brazilian population with malignant glioma to determine whether \textit{GSTM1} and \textit{GSTT1} genetic polymorphisms influence the response to intranasal administration of perillyl alcohol and the survival rate. Patients were stratified into groups according to clinical presentation, tumor classification, and tumor location. Circulating DNA was extracted from blood plasma or serum, and genotypes were detected by multiplex PCR. The cohort included
95 patients with recurrent malignant glioma included in a Phase I/II clinical trial with perillyl alcohol and 100 matched healthy control subjects. *GSTM1* frequency was similar in patients with glioma (44%) and healthy controls (54%), but *GSTT1* deletion was found in 11.5% patients, contrasting with 36% in controls. A longer survival rate was associated with a lack of *GSTM1* deletion (31 weeks) and a deletion for *GSTT1* (28 weeks). A poor survival rate was associated with *GSTM1* deletion (23 weeks) and with a lack of a *GSTT1* deletion (19 weeks).

A significantly lower frequency of *GSTT1* deletion in glioma patients compared to healthy controls indicates that *GSTT1* deletion may exert a protective role against gliomagenesis, influence therapeutic response to intranasal perillyl alcohol treatment, and increase overall survival, especially considering tumor topography.

**Key words:** Glutathione S-transferases; Genetic polymorphism; Glioma; Perillyl alcohol