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ORIGINAL ARTICLE

Utility of *CYP2D6* copy number variants as prognostic biomarker in localized anal squamous cell carcinoma

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Abstract

Background: Anal squamous cell carcinoma (ASCC) is an infrequent tumor whose treatment has not changed since the 1970s. The aim of this study is the identification of biomarkers allowing personalized treatments and improvement of therapeutic outcomes.

Methods: Forty-six paraffin tumor samples from ASCC patients were analyzed by whole-exome sequencing. Copy number variants (CNVs) were identified and their relation to disease-free survival (DFS) was studied and validated in an independent retrospective cohort of 101 ASCC patients from the Multidisciplinary Spanish Digestive Cancer Group (GEMCAD). GEMCAD cohort proteomics allowed assessing the biological features of these tumors.

Results: On the discovery cohort, the median age was 61 years old, 50% were males, stages I/II/III: 3 (7%)/16 (35%)/27 (58%), respectively, median DFS was 33 months, and overall survival was 45 months. Twenty-nine genes whose duplication was related to DFS were identified. The most representative was duplications of the CYP2D locus, including *CYP2D6*, *CYP2D7P*, and *CYP2D8P* genes. Patients with *CYP2D6* CNV had worse DFS at 5 years than those with two *CYP2D6* copies