Molecular profiling, including *TERT* promoter mutations, of acral lentiginous melanomas

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BACKGROUND: Acral lentiginous melanoma (ALM) has singular clinical and molecular characterization. *TERT* (human telomerase reverse transcriptase) promoter mutations have being described as recurrent in melanomas and infrequent in ALM, but their real incidence and clinical relevance is unclear.

HYPOTHESIS: *TERT* mutation status was associate with clinical/molecular features and survival of acral lentiginous melanomas.

METHODS: Sixty-one samples from 48 patients with ALM were analyzed. After DNA isolation, the mutation profiles of the hotspot region of BRAF, NRAS, KIT, PDGFRA, and TERT genes were determined by PCR amplification followed by direct Sanger sequencing. KIT, PDGFRA, and VEGFR2 gene amplification was performed by quantitative PCR. Clinical information such as survival, clinical stage, and Breslow tumor classification were obtained from medical records.

RESULTS: *TERT* promoter mutations were found in 9.3% of the cases, *BRAF* in 10.3%, *NRAS* in 7.5%, *KIT* in 20.7%, and *PDGFRA* in 14.8% of ALM. None of the cases showed *KIT*, *PDGFRA*, or *VEGFR2* gene amplification. We found an association between *KIT* mutations and advanced Clark level (IV and V, p=0.043) and *TERT* promoter mutations with low mitotic index (p=0.015). No relevant associations were found between *TERT* mutation status and clinical/molecular features nor survival. Mutations of *KIT* and *PDGFRA* are the most common genetic alterations, and they can be therapeutic targets for these patients.