Activation of MAPK and PI3K in melanoma

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Purpose: Melanoma is a major medical problem because its incidence doubles every ten years in the world. At an early stage, surgery is likely to be curative in many patients. By contrast, the results of non-surgical treatment of melanoma remain extremely disappointing. Indeed, the genetic heterogeneity of melanomas is a major obstacle toward achieving sustainable responses to targeted therapy for melanoma (1).

Experimental Design: In order to better understand how individual cancer patients respond to therapies, we performed a molecular analysis, by real-time PCR, of H1047R Pi3KCA and BRAF V600E mutations involved in the RAS/ RAF/MAP kinase and Pi3K-AKT kinase signaling pathways downstream the tyrosine kinase receptor.

Results: In our series, the prevalence of BRAF and Pi3KCA mutations was 49 and 10%, respectively, representing patients eligible to targeted monotherapy or combination therapy. The coexistence of these two mutations was observed in 2 patients, with a rate of 4%, thus determining the proportion of patients non eligible to targeted monotherapy.

Conclusion: The results obtained in this study have highlighted the fact that the MAPK and the PI3K pathways are frequently deregulated in melanomas. However, the adaptation of treatments to a single therapeutic target is not sufficient. It requires the analysis of all tumor molecular profiles, through the development of numerous biomarkers for targeted therapies and cytotoxic chemotherapy, both in predicting response and toxicity, and predicting combination therapies.