SKIN CANCER (OTHER THAN MELANOMA)

INGENOL MEBUTATE DECREASES P53-POSITIVE KERATINOCYTES IN SKIN CANCERIZATION FIELD SHOWING A DIRECT CORRELATION WITH CLINICAL RESPONSE IN PATIENTS WITH MULTIPLE ACTINIC KERATOSES

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Introduction: UV radiation is considered the main risk factor for Non Melanoma Skin Cancers (NMSC). Chronic UV exposure induces an histologically detectable accumulation of “p53 patches“, defined as clonal outgrowths of keratinocytes with elevated nuclear expression of mutated p53, able to progress to actinic keratosis (AK) and ultimately squamous cell carcinomas (SCC).

Objective: Assessment of Ingenol mebutate gel (150 and 500 mcg/g) effects in the decrease of “p53 patches” within the skin cancerization field (CF) in patients with multiple AKs of face/scalp or trunk/extremities, to explore if the supposed p53+ keratinocytes reduction might contribute to achieve a durable AK decrease in treated areas.

Materials and Methods: For the study, we enrolled n=10 patients, treated with Ingenol mebutate at the above concentrations, and evaluated at 2 and 6 months after treatment.

Results: Clinical responses were observed in the majority of patients (n=7), with AK reduction or complete clearance (n=6 and n=1, respectively). Remarkably, two patients did not react to the treatment and in one patient, after an initial partial response, new lesion were detected. In untreated skin CF samples (n=3), numerous p53+ keratinocytes were observed, similar to those found in invasive SCC samples (53.56±8.79 and 74.34±22.05, respectively; p=0.2). After treatment, a different p53+ keratinocytes decrease in CF samples at 2 months was observed (24.67±31.19; p=0.19). Significantly, the amount of p53+ keratinocytes strongly and directly correlated with the clinical response in terms of AK reduction both at 2 and 6 months follow up (R2 =0.81).

Conclusion: Untreated skin CF is characterized by a remarkable presence of p53+

keratinocytes as detected in invasive SCC, confirming that in non-pathologic sun-exposed skin numerous cells undergo the first step mutation involved in NMSC oncogenesis. Ingenol mebutate is able to decrease p53+ keratinocytes with variable efficacy, and the degree of reduction directly correlates with the clinical efficacy.