The Progression of Dyspigmentation in Patients with Skin of Color Treated with Combination Therapy of Imiquimod, 5-Fluorouracil, and Tretinoin for Keratinocyte Carcinomas

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INTRODUCTION

- Topical triple combination therapy of imiquimod 5% cream, 5-fluorouracil 2% solution, and tretinoin 0.1% cream (IMI/5-FU/TRET) has been shown to be a highly effective and cost-efficient treatment for KCs in patients with Fitzpatrick skin types (FST) I and II.
- Although effective, topical triple cream therapy is not commonly employed in patients with skin of color (FST II-VI) with KCs due to concern for potential post-inflammatory dyspigmentation. Nonetheless, a topical treatment modality may be more desirable than mainstay KC treatment with Mohs surgery or surgical excision in patients who are financially burdened or express a preference for surgical avoidance.
- Although post-inflammatory hyper and hypo-pigmentation is known to be more common and severe in darker-skinned individuals, the cosmetic outcomes of triple combination therapy have yet to be well characterized.

PURPOSE

- To report the dyspigmentation outcomes in a series of three patients with skin of color (and different ethnic origins) who had treatment of their KCs with IMI/5-FU/TRET.
- To evaluate the specific progressions of dyspigmentation with regard to central or surrounding post-inflammatory hyperpigmentation (PIH), hypopigmentation, or erythema over the course of 3-5 years.

METHODS

- Patients underwent a 6-week course of IMI/5-FU/TRET, applying the topical triple combination therapy 5 days on, 2 days off each week for a total of 30 applications.
- Images taken pre and post treatment. Evolution of lesions also monitored throughout clinical follow up, ranging between 3-5 years.
- Patients were able to upload images of their treatment progress and receive clinical feedback via a store-and-forward application (1).

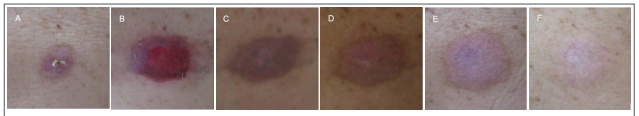

Figure 1. (A) BCC on right lower back. (B) After 30/30 applications (C) 2M, 7D post-treatment (D) 4M, 23D post-treatment (E) 2Y, 2M, 27D post-treatment (F) 5Y, 2M, 22D, normal pigmentation returned

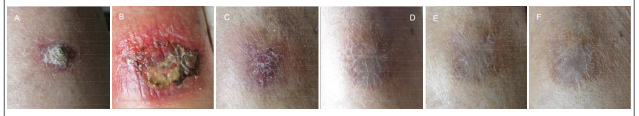

Figure 2. (A) SCC on right lower extremity. (B) After 30/30 applications. (C) 1M, 25D after treatment. (D) 11M, 2D, homogenous PIH. (E) 1Y, 3M, 1D, hypopigmentation centrally with persistent PIH at periphery. (F) 2Y, 2M, 14D, mild hypopigmentation with pronounced hyperpigmentation at periphery. Similar appearance at 3Y, 3M, 15D.

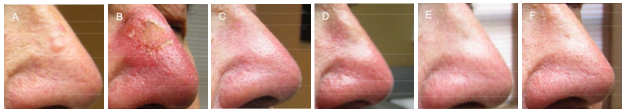

Figure 3. (A) BCC on right nasal sidewall. (B) After 30/30 applications. (C) 2M, 2D after treatment, central area of hypopigmentation. (D) 1Y, 2M, 8D after. (E) 1Y, 11M, 2D after–similar appearance. (F) 3Y, 6D–similar appearance.

RESULTS

- Patient 1's (FST IV) BCC on right lower area of the back developed prominent post-inflammatory hyperpigmentation (PIH) 2M, 7D after and post-inflammatory erythema with annular rim of PIH, which lasted up to 2Y, 2M, 27D. Persistent hypopigmentation developed after, and normal pigmentation returned after 5Y, 2M, 23D.
- Patient 2's (FST IV) SCC on right lower extremity developed intense erythema with moderate PIH after 1M, 25D, homogenous PIH after 11M, 2D, mild hypopigmentation centrally with persistent PIH at the periphery after 1Y, 3M, 1D, and finally more pronounced hyperpigmentation at the periphery which remained from 2Y, 2M, 14D until 3Y, 3M, 15D.
- Patient 3 (FST IV) developed hypopigmentation on the right nasal sidewall, which persisted for 3 years after treatment.
- Areas on the extremity and back progress initially started with PIH, then central hypopigmentation, and finally post-inflammatory erythema. Prolonged PIH was found on extremities, while the nasal area saw persistent hypopigmentation develop.

CONCLUSION

- Preliminary study demonstrates that post-inflammatory dyspigmentation may persist for greater than >3 years. Dyspigmentation outcomes due to triple cream therapy cannot reliably be predicted based on FST alone.
- A larger cohort is needed to truly evaluate the course of dyspigmentation with IMI/5-FU/TRET treatment.
- Although IMI/5-FU/TRET is a highly effective treatment for KCs, patients with skin of color (FST III-VI) must be cautioned regarding long-lasting dyspigmentation following IMI/5-FU/TRET treatment.
- Further study is warranted to characterize factors predicting the cosmetic outcome of triple cream therapy than FST alone.

REFERENCES

1. Nahm WJ, Shen J, Zito PM, Gonzalez AM, et al. A Non-Surgical and Cost-Effective Treatment Approach Employing Topical Imiquimod, 5-Fluorouracil, and Tretinoin for Primary Non-Melanoma Skin Cancers. Journal of drugs in dermatology: JDD. 2021 Mar 1;20(3):260-7