

Earliest stage treatment of actinic keratosis/non melanoma skin cancer.

Daisy Kopera*

Professor of Dermatology, Center of Aesthetic Medicine, Medica University Graz Auenbruggerplatz 8, 8036 Graz, Austria

Accepted on November 19, 2020

Introduction

Depending on age, lifestyle, and skin type, squamous cell carcinoma (SCC), a non melanoma skin cancer (NMSC) may develop in sun-exposed skin. Actinic keratosis (AK) represents an early or in situ SCC [1-4]. Pathogenesis of AK can be explained by potentially carcinogenic UV light interacting with keratinocyte DNA where DNA repair mechanisms fail. AK evolve slowly in the basal layer until they become thicker and clinically evident as coarse erythematous patches in early stages which may become hyperkeratotic later on (Figure 1) [1,4-6]. Topical imiquimod has been shown to be useful in clearing AK lesions [7-11]. Imiquimod as a toll-like receptor 7 (TLR-7) agonist induces cytokines, starting an inflammatory skin reaction directed primarily against malignant or virus-infected cells, but has virtually no effect on normal skin.

Imiquimod 5% cream is licensed in the USA (FDA) and Europe (EMA) for the treatment of external genital warts, superficial basal cell carcinoma, and AK, and is being experimentally used in various other dermatological conditions [12-14]. A lesser concentration of imiquimod 3.75% cream is available for the treatment of AK on face and scalp [15].

ABOUT THE STUDY

Two case reports on the treatment of facial uv-exposed skin shall open the discussion if subclinical actinic keratoses can be detected by the use of imiquimod cream in uv-exposed areas even if no lesions can be found clinically.

A 87-year old female showing small scaly AK lesions on her right cheek was treated with imiquimod 3.75% cream. Inflammatory reaction developed from day three onwards and showed field cancerisation, the lesions healed without scarring. A 59-year old female without obvious clinical signs of uv-damage on the face experimentally applied imiquimod 3.75% cream twice daily on the entire face for two weeks. At the end of the treatment phase distinct signs of inflammation appeared, and then taking two weeks for healing without sequelae.

According to the FDA drug safety data report: Imiquimod revealed no evidence of mutagenic or clastogenic potential based on the results of five in vitro genotoxicity tests and three in vivo genotoxicity tests [16,17].

Depending on the country one course of treatment using 28 sachets of imiquimod 3.75% cream will cost approximately US \$ 150. This seems comparatively economical in contrast to the cost of surgical interventions when the disease has come to an advanced stage [18,19] (Figure 1).

Invasive Development of Actinic Keratosis

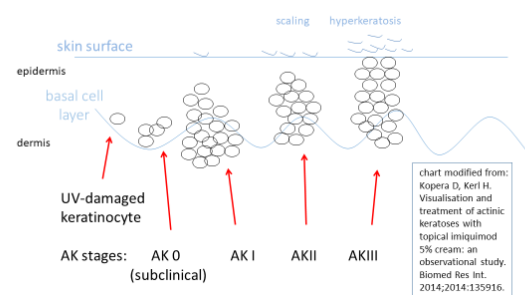


Figure 1. Progression of AK to invasive SCC (NMSC).

CONCLUSION

Taking into account that actinic keratoses as a result of proliferating uv-damaged keratinocytes develop quietly from the dermoepidermal basal cell layer in both directions upwards to the skin surface and invasively into the dermis, earliest stage treatment can prevent non melanoma skin cancer formation.

My personal approach as a clinical dermatologist aims primarily at the „public health factor“. As therapists we are trained to focus on health and happiness of our patients. Successful prevention of diseases categorized as malignant could be named the utmost success in medical treatment. In this case we reach this excellent goal at very low cost and minimal suffering.

These results open the discussion if the use of imiquimod 3.75% cream could be recommended preventively in uv-exposed skin areas to obviate a later development of actinic keratoses AK/squamous cell carcinoma SCC/non melanoma skin cancer NMSC.

References

1. Kopera D, Kerl H. Visualization and treatment of subclinical actinic keratoses with topical imiquimod 5% cream: an observational study. *Biomed Res Int*. 2014.
2. Salasche SJ. Epidemiology of actinic keratoses and squamous cell carcinoma. *J Am Acad Dermatol*. 2000;42:4-7.
3. Ackerman AB, Mones JM. Solar (actinic) keratosis is squamous cell carcinoma. *Br J Dermatol*. 2006;155:9-22.
4. Cockerell CJ. Pathology and pathobiology of the actinic (solar) keratosis. *Br J Dermatol*. 2003;149:34-6.
5. Einspahr JG, Xu MJ, Warneke J, et al. Reproducibility and keratoses. *Cancer Epidemiol Biomarkers Prev* 2006;15:1841-8.

6. Quatresooz P, Pierard-Franchimont C, Paquet P, et al. Crossroads between actinic keratosis and squamous cell carcinoma, and novel pharmacological issues. *Eur J Dermatol.* 2008;18:6-10.
7. Stockfleth E, Meyer T, Benninghoff B, et al. Successful treatment of actinic keratosis with imiquimod cream 5%: a report of six cases. *Br J Dermatol.* 2001;144:1050-3.
8. Hengge UR, Benninghoff B, Ruzicka T, et al. Topical immunomodulators--progress towards treating inflammation, infection, and cancer. *Lancet Infect Dis.* 2001;1:189-98.
9. Hadley G, Derry S, Moore RA. Imiquimod for actinic keratosis: systematic review and meta-analysis. *J Invest Dermatol.* 2006;126:1251-5.
10. Stockfleth E, Sterry W, Carey-Yard M, et al. Multicentre, open-label study using imiquimod 5% cream in one or two 4-week courses of treatment for multiple actinic keratoses on the head. *Br J Dermatol.* 2007;157:41-6.
11. Berman B, Amini S, Valins W, et al. Pharmacotherapy of actinic keratosis. *Expert Opin Pharmacother.* 2009;10:3015-31.
12. Aldara® Cream, 5% (imiquimod). Graceway Pharmaceuticals. U.S. prescribing information. Status October 2010.
13. Aldara® 5% Cream. Summary of product characteristics (UK version). MEDA AB 2010.
14. Schmitt AR, Bordeaux JS. Solar keratoses: Photodynamic therapy, cryotherapy, 5-fluorouracil, imiquimod, diclofenac, or what? Facts and controversies. *Clin Dermatol.* 2013;31:712-7.
15. Del Rosso J, Swanson N, Berman B, et al. Imiquimod 2.5% and 3.75% Cream for the Treatment of Photodamage: A Meta-analysis of Efficacy and Tolerability in 969 Randomized Patients. *J Clin Aesthet Dermatol.* 2018;11:28-31.
16. Kopera D. Earliest Stage Treatment of Actinic Keratosis with Imiquimod 3.75% Cream. *Dermatol Ther.* 2020;33:13517.
17. Clinical pharmacology. Clinical studies. 2004.
18. Gordon LG, Brynes J, Baade PD, et al. Cost-Effectiveness Analysis of a Skin Awareness Intervention for Early Detection of Skin Cancer Targeting Men Older Than 50 Years. *Value Health.* 2017 ;20:593-601.
19. Kopera D, Goswami N, Kerl H. AK progressing to NMSC: at what stage? *J Eur Acad Dermatol Venereol* 2016; 30:172-173.

*Correspondence to

Daisy Kopera

Center of Aesthetic Medicine

Aesthetic Medicine Medica University Graz Auenbruggerplatz
Austria

E-mail: daisy.kopera@medunigraz.at

Tel: +43(316)826606