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► To cite this version:

Wolfgang G. Philipp-Dormston, Maxime Battistella, Lise Boussemart, Alessandro Di Stefani, Paolo Broganelli, et al.. Patient-centered management of actinic keratosis. Results of a multi-center clinical consensus analyzing non-melanoma skin cancer patient profiles and field-treatment strategies. Journal of Dermatological Treatment, 2020, 31 (6), pp.576-582. 10.1080/09546634.2019.1679335 . hal-02355726

HAL Id: hal-02355726

<https://univ-rennes.hal.science/hal-02355726>

Submitted on 3 Feb 2020

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Patient-centered management of actinic keratosis. Results of a multi-center clinical consensus analyzing non-melanoma skin cancer patient profiles and field-treatment strategies

Short title: Patient-centered management of actinic keratosis

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Patient-centered management of actinic keratosis. Results of a multi-center clinical consensus analyzing non-melanoma skin cancer patient profiles and field-treatment strategies

Abstract

Introduction: Actinic keratosis (AK) is a chronic skin condition that can be a precursor to cutaneous squamous cell carcinoma. AK can recur and patients are likely to undergo multiple treatments. It is important that AK lesions are managed appropriately, and that patients are involved in treatment decisions.

Materials and methods: The Supporting Professional Expertise in AK (SPEAK) program aims to facilitate this patient-centered care by identifying patient needs and aiding healthcare practitioners (HCPs) in selecting optimal treatment and communication strategies for different types of patients. Twenty-two dermatono oncologists with established expertise in the treatment of AK collaborated to describe commonly encountered psychosocial patient profiles, and to develop respective communication and treatment strategies.

Results and conclusion: Six patient profiles were defined based on different psychosocial characteristics and were used to develop appropriate management approaches. We provide a systematic way of identifying these patient profiles in clinical practice and we outline communication strategies tailored to the primary needs of each type of patient. In addition, we provide recommendations for potential field-treatments that may be best suited for each profile. The recommendations provided here may help improve the communication and relationship between patients and HCPs, resulting in higher treatment adherence and improved patient outcomes.

Keywords: actinic keratosis, cutaneous squamous cell carcinoma, management

Introduction

Actinic keratosis (AK), a chronic skin condition caused predominately by prolonged exposure to ultraviolet (UV) radiation, is a precursor to cutaneous squamous cell carcinoma (SCC). Estimates range from 0.1–10% of AK progressing to SCC [1,2]; in addition, approximately 97% of cutaneous SCCs are contiguous to an AK [3], which may represent carcinoma *in situ* [4].

Whilst many AK lesions resolve spontaneously, some can be potentially invasive, regardless of their intra-epidermal thickness [2,5], and it is not possible to draw conclusions about the histology of AK lesions from their clinical appearance [6]. For this reason, coupled with a lack of supporting long-term prognostic studies, it is important that AK lesions are managed appropriately[2]. Appropriate management of AK can be in the form of lesion-specific or field-directed therapy. Visible AK lesions can arise from subclinical changes that affect a wider area of skin, a process known as cancerization,[3,7] in these instances a field-directed therapy may be advantageous allowing effective treatment of sub-clinical AK lesions that may be missed with lesion-specific therapy. Moreover, current studies have highlighted, that the potential to develop squamous cell carcinomas is associated with subclinical basal proliferating AKs as well as clinical hyperkeratotic AKs, indicating a need for standardized, and approved field therapy^[8,9]. When deciding on a management strategy it is important to consider a multitude of factors, including treatment duration, compliance, cost and risk factors for recurrence and the age of the patient.[2]

In addition, patients increasingly expect to be involved in decision-making about treatments, especially as AK can recur and people with AK are likely to need multiple treatment courses throughout their lifetime. [10] Therefore, a practical tool that takes into

account patient-related factors may be particularly useful for assisting doctors in optimizing the efficiency of their consultations.

Indeed, patient-centric care is now a widely accepted part of high-quality healthcare in general, and seems to improve outcomes, quality of life, satisfaction and treatment adherence. Patient-centric care may also aid the adoption of patient-defined treatment goals and outcomes, [11] and in turn, help manage expectations.

Based on this, the Supporting Professional Expertise in AK (SPEAK) program aims to facilitate patient-centric care in AK management, focusing on ways to appropriately identify the needs of different patients, and aid the physicians in selecting the best field-directed therapy for each patient in an effective and efficient way. The patient profiles and communication strategies developed in the program are outlined in this article and treatment recommendations for different patient profiles are discussed.

Materials and methods

In total, 22 dermatologists with expertise in the management of AK participated in a two-stage process, across four meetings, to develop these clinical profiles and recommendations.

Prerequisite conditions for expert involvement in the multi-center consensus analysis were specialization in dermato-oncology; consistent, long-term clinical treatment experience with non-melanoma skin cancer (NMSC) patients; and sole therapeutic responsibility within a certified skin cancer center. All participating experts met the conditions for inclusion.

In the first stage, consensus meetings were held in Frankfurt, Germany; Paris, France; and Rome, Italy. Discussions were facilitated in the local language, and patient profiles were

developed based on typical patient types commonly encountered by the participating experts in their clinical practice.

During the second stage, six practicing experts represented the national consensus meetings by attending a final meeting in London, United Kingdom, to consolidate the patient profiles developed at a national level. Based on these profiles, the experts developed recommendations for the clinical management and optimal communication approach for each patient type in two smaller groups. Recommendations were discussed within the six-member group and agreed by consensus, after which the experts discussed each of the patient profiles individually and adjusted the recommendations until a unanimous agreement was met.

Therefore, the recommendations in this document represent the expert consensus opinion regarding strategies and techniques that can guide the individualization of AK management. Nevertheless, the experts recognize that each healthcare practitioner (HCP) needs to precisely tailor treatment and communication to each individual patient.

Results

Recommendations

This section includes the characteristics of each patient profile (as defined by clinical experts); questions that can be used to identify each patient profile in clinical practice; and management priorities as well as treatment recommendations for each patient profile.

We summarized the main attributes of six patient profiles (Table 1). An individual patient may not fit exactly into any one particular profile and some people with AK may have characteristics custom of more than one profile: e.g. an academic biologist, geologist or archaeologist working in the field may develop occupational AK. Nevertheless, the profiles

offer a heuristic method to identify an appropriate management approach and consultation style that can guide discussions about AK and facilitate the optimal approach to treatment. For instance, a patient who is anxious about the diagnosis or treatment may benefit from reassurance about the likelihood of malignant transformation, or the systemic effects and safety of treatment, respectively.

AK is typically diagnosed on clinical grounds, [10] so taking a detailed patient history is mandatory prior to identifying the profile category a patient best identifies with; determined using answers to a questionnaire (Table 2). For instance, the concerns and needs of the patients identified can be linked to the appropriate anxious or concerned profile groups, whereas their knowledge and level of engagement can also provide useful insight to categorizing them into the right profile.

It should be noted that immunocompromised patients, who may be at risk of diffuse AK and may be receiving immunosuppressive therapies, can display any of the proposed profiles. When evaluating the communication and treatment strategy for these patients, it is important to consider both the type of profile describing each patient and also the fact that they present with immunosuppression. Therefore, these patients may also need to be treated at multiple areas simultaneously and may require additional therapies for the management of severe local skin reactions.

[INSERT TABLE 1 HERE]

[INSERT TABLE 2 HERE]

Toward patient-centered AK management

This section details how the identified patient profiles can be used to deliver patient-centric management of AK, where the relationship between patient and HCP is built on effective communication, empathy and a feeling of partnership. [12]

Against this background, we outline recommended management priorities and potential treatments to consider for each of the patient profiles (Table 3). For example, in the panel's experience, people who developed AK following occupational exposure need a fast, effective regimen with a short duration of treatment, especially as their potentially low engagement with the disease could translate into poor adherence.

The panel recommends adapting HCP communication style to meet the primary needs of each patient profile (Table 4). For example, HCPs may need to reassure people who are concerned about the cosmetic outcomes that short-term skin reactions, which are common with topical treatments, do not influence long-term aesthetic outcomes and are a result of the treatment being effective, rather than simply being a side effect accompanying the treatment.

Using appropriate terminology when speaking to patients

To deliver education within a patient-centric framework, we recommend HCPs ensure that discussions about AK build on each patient's existing knowledge and reflect their expectations and concerns. This means using appropriate terminology and establishing the introductory terminology, such as explaining the chronic nature of AK. Moreover, the terminology used during a discussion of the same topic could differ markedly for people who develop AK following occupational exposure, and for those patients who are more knowledgeable, reflecting their different levels of health literacy.

An important communication goal is to ensure patients understand the normal role of local skin reactions in AK treatment, and that they appreciate them as a positive indication of

the treatment's function. We advise that HCPs aim to help patients become familiar with any management approaches that might reduce the severity of local reactions and educate patients on when to seek further assistance. Prescribing treatments such as photodynamic therapy (PDT) or ingenol mebutate that have well-characterized and predictable reactions may simplify these discussions.

[INSERT TABLE 3 HERE]

[INSERT TABLE 4 HERE]

[INSERT TABLE 5 HERE]

General treatment recommendations

The panel identified which treatments may be recommended for different patients based on their individual profile and characteristics (Table 5). For instance, these recommendations take into account which therapies may be associated with unpredictable local skin reactions or variable outcomes compared with good aesthetic long-term outcomes, and how aspects of each therapy might be perceived by patients of different profiles.

Practical recommendations for application of topical treatments

HCPs should communicate clearly to patients the exact area over which they, or a carer (e.g. for inaccessible parts of the body), should apply a topical treatment.

Alternatively, HCPs could provide patients who have smartphones with digital cameras, a photographic reference for the area being treated. A photographic reference can be particularly helpful for formulations with long treatment durations or if the HCP and patient agree to postpone the start of treatment.

Educational brochures that provide skin maps; illustrations of the appearance of skin and lesions before, during and after treatment; as well as those showing local skin reactions, are available. Experts stress the importance of such detailed, up-to-date leaflets to provide patients with information about treatment options and facilitate their discussions with HCPs.

Discussion

The panel intends to raise awareness of the optimal management of AK, providing it as an educational resource, as well as helping HCPs implement local and national treatment guidelines in their daily clinical practice. The patient profiles and related recommendations in this document are intended as a pragmatic and heuristic guide to support patient management based on their main characteristics.

In order to support the individualization of treatment for patients with AK, the present recommendations go beyond the treatment-focused, disease-driven framework typically used, [4,13] and take into account patient-related factors that are often neglected by guidelines and recommendations. [14] In particular, the educational messages about AK can be tailored according to each patient's profile by using appropriate terminology that is adjusted to each patient's educational background. This 'consumerist' model of interaction between patient and HCP is generally increasingly common in medicine. [15] Similarly, the suggested guide provides a patient-centric framework with recommendations to support optimal management and physician-patient communication in order to cultivate empathy and a feeling of partnership. [12,16]

For many cases of AK, several treatment approaches are potentially suitable based on existing guidelines. This document therefore further complements existing guidelines and previous consensus papers by providing recommendations about selecting the appropriate

treatment based on the psychosocial needs of different patient profiles and counselling patients about appropriate use.

Ingenol mebutate was one of the treatment options proposed for many of the profiles and this was driven by its association with good cosmetic outcomes [17,18]; the predictable nature of the treatment and related short-term local skin reactions [19–22]; and the fact that the administration regimen of ingenol mebutate allows for flexible use, as patients are able to decide how and when it is used according to their needs and individual condition. In a randomized, evaluator-blinded trial of ingenol mebutate 0.015% gel and diclofenac sodium 3% gel, patients experienced a shorter duration of skin reactions, with a peak after one week, with ingenol mebutate compared with diclofenac sodium, who experienced reactions throughout the 90-day treatment. [3] These attributes support ingenol mebutate, in the panel's opinion, as a viable option for many of the patient profiles; assuming its use is complemented by treatment-focused education delivered at treatment initiation. [23] Despite the presence of local skin reactions, a study of 274 patients using ingenol mebutate reported that 98.2% of patients were adherent to the 3-day administration regimen. [24] Collectively, this evidence supports the panel's recommendation that ingenol mebutate therapy in patients that are well-educated by their dermatologist can lead to consistent, standardized and effective outcomes, with predictable, short-term local skin reactions.

In addition to ingenol mebutate, conventional photodynamic therapy (PDT) was also identified as a viable option for a number of patient profiles, particularly for patients that may be concerned with cosmetic outcomes during or after treatment. The quality of the cosmetic outcomes associated with PDT [24–26] were identified as key drivers for choosing this therapy, as they might reassure and better satisfy patients who are particularly concerned about this. Indeed, PDT was also associated with the highest quality of life ratings, alongside ingenol

mebutate, [14] Similarly, daylight PDT was also recommended, as it has comparable efficacy to conventional PDT for the resolution of AK in the face or scalp, and has been shown to effectively treat AK lesions in a home-based setting. [27] Patients have also reported reduced pain and higher satisfaction with its convenience and outcomes compared with conventional PDT, [28–30] as well as compared with imiquimod. [31] Finally, although imiquimod may not be the treatment of choice for everyone due to the unpredictable onset of local skin reactions and the potential of systemic adverse events, it should be highlighted that imiquimod has high efficacy in reducing AK lesions [32–34] regardless of disease severity, [35] and has been associated with good long-term, post-treatment cosmetic outcomes. [31] Therefore, it could also be considered as a viable option for appropriate patients.

Although commonly used, the panel does not recommend cryotherapy, as a lesion-directed treatment for the patient profiles discussed (Table 5), due to the potential for missing sub-clinical lesions, scarring, highly variable short and long term outcomes based on experience, and the requirement for multiple rounds of treatment.

In conclusion, there is a need for further research and comparative studies to facilitate the development of evidence-based guidelines that use objective criteria to stratify AK patients.

In the meantime, the authors hope that a mutualistic, patient-centric relationship, [15] aided by the guide developed here will improve patient and HCP satisfaction with diagnosis and treatment outcomes. Such a relationship could potentially improve adherence and persistence with topical therapy for AK; avoid patients misinterpreting an unpleasant skin reaction during treatment; optimize the use of time during consultations and follow-up; and ultimately result in improved outcomes, safety and satisfaction.

Acknowledgements

The authors thank Real Science for writing and editorial support, which was funded by LEO Pharma A/S.

Declaration of interest

MB has received honoraria from Leo Pharma A/S, Bristol-Myers-Squibb, Innate Pharma and Takeda. WPD has received honoraria from Allergan, Almirall, Biofrontera, Galderma and Leo Pharma A/S. PB has received honoraria from LEO Pharma A/S, Almirall and Galderma. LB has received research funding from Leo Pharma A/S. LB is a consultant for Pierre Fabre and Novartis. KMT has received honoraria from Leo Pharma A/S, Galderma, Bristol-Myers Squibb, MSD, Roche, Novartis Oncology and Pierre Fabre Oncology. ADS has received honoraria from Almirall, Leo Pharma A/S and Pierre Fabre Oncology.

Author contributions

All authors made contributions to the development and consolidation of the patient profiles detailed in this paper. Based on these profiles, each of the experts developed recommendations for the clinical management and optimal communication approach for each patient type, which were then adjusted until there was unanimous agreement. All authors have contributed equally to the paper and have given it their final approval.

References

1. Salasche SJ. Epidemiology of actinic keratoses and squamous cell carcinoma. *J Am Acad Dermatol* [Internet]. 2000;42(1):S4–7. Available from: <http://linkinghub.elsevier.com/retrieve/pii/S0190962200492285>
2. Feldman SR, Jr ABF. Progression of Actinic Keratosis to Squamous Cell Carcinoma Revisited. 2011;87(April):201–7.
3. Stockfleth E. The importance of treating the field in actinic keratosis. *J Eur Acad Dermatology Venereol*. 2017;31:8–11.
4. Dréno B, Amici JM, Basset-Seguin N, Cribier B, Claudel JP, Richard MA. Management of actinic keratosis: A practical report and treatment algorithm from AKTeam™ expert clinicians. *J Eur Acad Dermatology Venereol*. 2014;28(9):1141–9.
5. Fernández-Figueras MT, Carrato C, Sáenz X, Puig L, Musulen E, Ferrández C, et al. Actinic keratosis with atypical basal cells (AK I) is the most common lesion associated with invasive squamous cell carcinoma of the skin. *J Eur Acad Dermatology Venereol* [Internet]. 2014 Nov 26;29(5):991–7. Available from: <https://doi.org/10.1111/jdv.12848>
6. Schmitz L, Kahl P, Majores M, Bierhoff E, Stockfleth E, Dirschka T. Actinic keratosis: correlation between clinical and histological classification systems. *J Eur Acad Dermatology Venereol* [Internet]. 2016 Mar 8;30(8):1303–7. Available from: <https://doi.org/10.1111/jdv.13626>
7. Philipp-Dormston WG. Field Cancerization: From Molecular Basis to Selective Field-Directed Management of Actinic Keratosis. In: *Current Problems in Dermatology* [Internet]. 2015. p. 115–21. Available from: <https://www.karger.com/DOI/10.1159/000366547>
8. Schmitz L, Gambichler T, Kost C, Gupta G, Stückler M, Stockfleth E, et al. Cutaneous

- squamous cell carcinomas are associated with basal proliferating actinic keratoses. *Br J Dermatol* [Internet]. 2019;180(4):916–21. Available from: <https://doi.org/10.1111/bjd.16536>
9. Schmitz L, Grinblat B, Novak B, Hoeh A-K, Händschke K, von Dobbeler C, et al. Somatic mutations in kinetochore gene KNSTRN are associated with basal proliferating actinic keratoses and cutaneous squamous cell carcinoma. *J Eur Acad Dermatology Venereol* [Internet]. 0(0). Available from: <https://doi.org/10.1111/jdv.15615>
10. de Berker D, McGregor JM, Mohd Mustapa MF, Exton LS, Hughes BR. British Association of Dermatologists' guidelines for the care of patients with actinic keratosis 2017. *Br J Dermatol*. 2017;176(1):20–43.
11. Corriere MA, Avise JA, Peterson LA, Stafford JM, Easterling D, Boone DS, et al. Exploring patient involvement in decision making for vascular procedures Presented at the Thirty-ninth Annual Meeting of the Southern Association for Vascular Surgery, Scottsdale, Ariz, January 14-17, 2015. *J Vasc Surg* [Internet]. 2015;62(4):1032–1039e2. Available from: <http://dx.doi.org/10.1016/j.jvs.2015.04.443>
12. Cerio R. The importance of patient-centred care to overcome barriers in the management of actinic keratosis. *J Eur Acad Dermatology Venereol*. 2017;31:17–20.
13. Peris K, Calzavara-Pinton PG, Neri L, Girolomoni G, Malara G, Parodi A, et al. Italian expert consensus for the management of actinic keratosis in immunocompetent patients. *J Eur Acad Dermatology Venereol*. 2016;30(7):1077–84.
14. Khanna R, Bakshi A, Amir Y, Goldenberg G. Patient satisfaction and reported outcomes on the management of actinic keratosis. *Clin Cosmet Investig Dermatol*. 2017;10:179–84.
15. Russell. Summary of the consultation. In p. 82.

16. Boussemaert L, Bouzillé G, Boyer A, Arnheiter H, Dupuy A. Do personality profiles among physicians correlate with their career choices? MedEdPublish [Internet]. 2016;5(2):1–22. Available from: [http://www.memedpublish.org/manuscripts/461/v1](http://www.mededpublish.org/manuscripts/461/v1)
17. Handler MZ, Bloom BS, Goldberg DJ. Clinical and Histologic Evaluation of Ingenol Mebutate 0.015% Gel for the Cosmetic Improvement of Photoaged Skin. 2017;1–7.
18. Wu DC, Guiha I, Goldman MP. A prospective clinical trial to evaluate the efficacy and safety of topical therapy with ingenol mebutate gel 0.015% for actinic keratosis on an expanded area of the chest. J Clin Aesthetic Dermatology. 2017;10:31–6.
19. Stockfleth E, Bastian M. Pharmacokinetic and pharmacodynamic evaluation of ingenol mebutate for the treatment of actinic keratosis. Expert Opin Drug Metab Toxicol [Internet]. 2018 Sep 2;14(9):911–8. Available from: <https://doi.org/10.1080/17425255.2018.1508449>
20. Neri L, Peris K, Longo K, Calvieri S, Franscione P, Parodi A, et al. Physician-Patient Communication and Patient-Reported Outcomes in the Actinic Keratosis TRTreatment-Adherence INitiative (AK-TRAIN): A Multicenter, Prospective, Real- Life study of Treatment Satisfaction, Quality of Life and Adherence to topical field-direct. J Eur Acad Dermatology Venereol [Internet]. 2018; Available from: <https://doi.org/10.1111/jdv.15142>
21. Carbotti M, Coppola R, Zanframundo S, Devirgiliis V, Panasiti V. Clinical Study Efficacy of Ingenol Mebutate in the Treatment of Actinic Keratoses: A Pre-and Posttreatment Dermoscopic Comparative Analysis. 2018;2018. Available from: <https://doi.org/10.1155/2018/4381019>
22. Longo C, Neri L, Argenziano G, Calvieri S, Calzavara-Pinton PG, Cantisani C, et al. Management of local skin reactions after the application of ingenol mebutate gel for the treatment of actinic keratosis: four illustrative cases. J Eur Acad Dermatology

Venereol [Internet]. 2014 Sep 3;30(2):320–1. Available from:

<https://doi.org/10.1111/jdv.12714>

23. Braun S, Gerber P. Cosmetic effects of ingenol mebutate gel in the treatment of field-cancerized photodamaged skin. *Dermatology Surg.* 2015;1–2.
24. Lebwohl M, Swanson N, Anderson LL, Melgaard A, Xu Z, Berman B. Ingenol Mebutate Gel for Actinic Keratosis. *N Engl J Med* [Internet]. 2012;366(11):1010–9.
Available from: <http://www.nejm.org/doi/abs/10.1056/NEJMoa1111170>
25. Augustin M, Tu JH, Knudsen KM, Erntoft S, Larsson T, Hanke CW. Ingenol mebutate gel for actinic keratosis: The link between quality of life, treatment satisfaction, and clinical outcomes. *J Am Acad Dermatol* [Internet]. 2015 May 1;72(5):816–21.
Available from: <https://doi.org/10.1016/j.jaad.2015.01.036>
26. Lebwohl M, Shumack S, Gold L, Melgaard A, Larsson T, SK T. Long-term follow-up study of ingenol mebutate gel for the treatment of actinic keratoses. *JAMA Dermatology* [Internet]. 2013 Jun 1;149(6):666–70. Available from:
<http://dx.doi.org/10.1001/jamadermatol.2013.2766>
27. Wiegell SR, Wulf HC, Szeimies RM, Basset-Seguin N, Bissonnette R, Gerritsen MJP, et al. Daylight photodynamic therapy for actinic keratosis: An international consensus: International Society for Photodynamic Therapy in Dermatology. *J Eur Acad Dermatology Venereol.* 2012;26(6):673–9.
28. Sotiriou E, Evangelou G, Papadavid E, Apalla Z, Vrani F, Vakirlis E, et al. Conventional vs. daylight photodynamic therapy for patients with actinic keratosis on face and scalp: 12-month follow-up results of a randomized, intra-individual comparative analysis. *J Eur Acad Dermatology Venereol.* 2018;32(4):595–600.
29. Rubel DM, Spelman L, Murrell DF, See JA, Hewitt D, Foley P, et al. Daylight photodynamic therapy with methyl aminolevulinate cream as a convenient, similarly

- effective, nearly painless alternative to conventional photodynamic therapy in actinic keratosis treatment: A randomized controlled trial. *Br J Dermatol.* 2014;171(5):1164–71.
30. Morton CA, Wulf HC, Szeimies RM, Gilaberte Y, Basset-Seguin N, Sotiriou E, et al. Practical approach to the use of daylight photodynamic therapy with topical methyl aminolevulinate for actinic keratosis: A European consensus. *J Eur Acad Dermatology Venereol.* 2015;29(9):1718–23.
31. Sotiriou E, Apalla Z, Maliamani F, Zaparas N, Panagiotidou D, Ioannides D. Intraindividual, right–left comparison of topical 5-aminolevulinic acid photodynamic therapy vs. 5% imiquimod cream for actinic keratoses on the upper extremities. *J Eur Acad Dermatology Venereol* [Internet]. 2009 Jul 29;23(9):1061–5. Available from: <https://doi.org/10.1111/j.1468-3083.2009.03259.x>
32. Swanson N, Abramovits W, Berman B, Kulp J, Rigel DS, Levy S. Imiquimod 2.5% and 3.75% for the treatment of actinic keratoses; Results of two placebo-controlled studies of daily application to the face and balding scalp for two 2-week cycles. *J Am Acad Dermatol* [Internet]. 2010;62(4):582–90. Available from: <http://dx.doi.org/10.1016/j.jaad.2009.07.004>
33. Serra-Guillén C, Nagore E, Hueso L, Traves V, Messeguer F, Sanmartín O, et al. A randomized pilot comparative study of topical methyl aminolevulinate photodynamic therapy versus imiquimod 5% versus sequential application of both therapies in immunocompetent patients with actinic keratosis: Clinical and histologic outcomes. *J Am Acad Dermatol.* 2012;66(4):131–7.
34. Hanke CW, Beer KR, Stockfleth E, Wu J, Rosen T, Levy S. Imiquimod 2.5% and 3.75% for the treatment of actinic keratoses: Results of two placebo-controlled studies of daily application to the face and balding scalp for two 3-week cycles. *J Am Acad*

Dermatol [Internet]. 2010 Apr 1;62(4):573–81. Available from:

<https://doi.org/10.1016/j.jaad.2009.06.020>

35. Peris K, Stockfleth E, Gupta G, Aractingi S, Dakovic R, Dirschka T, et al. Efficacy of imiquimod 3.75% from Lmax according to the number of actinic keratosis lesions. *J Eur Acad Dermatology Venereol.* 2015;29(12):2470–3.

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Table 1: Common AK patient profiles encountered in clinical practice

Profile	1. Unengaged (low medical engagement)	2. Cosmetic concerned during treatment	3. Cosmetic concerned post-treatment	4. Knowledgeable (high medical engagement)	5. Diagnosis-anxious	6. Safety-anxious
Description	Often occupational UV exposure	Concerned with local skin reactions during treatment	Concerned with permanent cosmetic outcomes post-treatment	Well-informed patient	Anxious about malignant diagnosis	Anxious about general and long-term adverse effects of treatment
Clinical characteristic	Severe photodamage Field cancerization present Scalp involvement Trunk and dorsum of the hands involvement Male > female Older age	Moderate, diffuse photodamage Facial involvement Female > male Female > male Younger	Mild to moderate, diffuse photodamage, sun exposure mainly in the past Facial involvement Facial involvement Younger	Moderate photodamage Facial involvement	Mild/early stage disease Facial involvement	Moderate photodamage Facial involvement
Psychosocial characteristics	Employment possibly involves working outdoors Lower level of formal education Unconcerned about disease	Employment involves interaction with others High occupational status and responsibility without allowance for work interruption due	Employment involves interaction with others Exposed occupational position in face-to-face relationships (particularly in the field of customer relationships) Willingness for downtime but not	Highly educated Internet and research literate Well-informed about AK treatments	Worried/hyper-concerned Tendency to be cancer-phobic Regular engagement with healthcare High treatment motivation	High level of social interaction Well-informed – able to use the internet

		<p>to long downtime</p> <p>Well-educated and informed</p> <p>No other health conditions</p>	<p>for poor cosmetic long-term outcomes</p> <p>Well-educated and informed</p> <p>Knowledge regarding UV and skin aging; already cautious with sun exposure</p> <p>No other health conditions</p>			
Other observations	<p>May live far from hospital/practice</p> <p>In some localities, occupational nature of condition may be relevant for reimbursement</p>	<p>Sun exposure</p> <p>may be associated with holidays or outdoor sports</p>	<p>Potentially concerned with appearance and awareness of healthy skin conditions</p>	<p>May be employed in academic or healthcare field</p> <p>May use the term 'actinic keratosis' unprompted</p>	<p>May have low concern with cosmetic outcome, focused on effectiveness</p> <p>Already likely to be using sun protection</p> <p>May present with printed information</p>	<p>May need reassurance regarding absence of systemic effects of treatment and safety of products</p>

Table 2: Questions to support identification of patient profile

Question	Potential profile identification
What is your main concern about your skin?	Focus in response on cosmetic appearance during or after treatment may suggest cosmetic concerned profile Focus in response on skin cancer may suggest safety-anxious profile
What's your occupation? Do you/did you work outdoors?	Outdoor work may suggest profile with low medical engagement Occupations involving high levels of personal interaction (service industry, sales, etc.) may suggest cosmetic concern or safety-anxious profiles
Does your appearance matter in your job or daily life?	Positive response may suggest cosmetic concerned or safety-anxious profile
What do you expect from treatment?	A focus on cosmetic outcomes may suggest cosmetic concerned profile A high level of detail in response may suggest knowledgeable or safety-anxious profile A focus on the potential for pain or discomfort may suggest a safety-anxious profile
Would you accept downtime during treatment?	Using a term common in cosmetic treatment may help identify patients who match the cosmetic concerned profile
Would you be bothered by short-term local skin reactions? Do you care about scarring or	These questions may help distinguish between cosmetic concerned during and post-treatment profiles

hyperpigmentation?	
What do you already know about AK and the treatments?	A focus in response on the visual appearance of local skin reactions and treatment outcomes may suggest cosmetic concerned profile A high level of knowledge may suggest knowledgeable or diagnosis-anxious profile A focus in response on the transformation of AK into SCC may suggest diagnosis-anxious profile
Do you have any preferences for your treatment?	A positive response may indicate knowledgeable profile

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Table 3: Suggested management priorities for commonly encountered AK patient profiles

Profile	Unengaged (low medical engagement)	Cosmetic concerned during treatment	Cosmetic concerned post-treatment	Knowledgeable (high medical engagement)	Diagnosis-anxious	Safety-anxious
Primary need	Rapid treatment	Reassurance about limited nature of local skin reactions	Reassurance about safety of outcomes	Information	Reassurance of treatment efficacy	Reassurance of treatment safety
Focus of treatment	Fast, effective treatment with short duration	Limited cosmetic impact during treatment; predictable downtime	Limited cosmetic impact after treatment; predictable long-term outcome	Evidence-based approach	Fast, effective treatment with rapid signs of efficacy	Treatment decision driven by safety
Additional management suggestions	Early follow-up Need for guidance and motivation from physician	Use pictures to educate about course of treatment and local skin reactions Consider early follow-up for reassurance on normal treatment	Provide additional information about selected treatment safety and outcomes Emphasize photoprotection	Provide supplementary information about treatment efficacy and safety to support treatment choices	Close follow-up Provide additional education on the realistic risk of AK evolution	Early follow-up consultation

		reactions and outcomes				
Notes	Low engagement with disease anticipated to lead to low treatment adherence and preventative measures	Consider prescribing moisturizing and healing creams for cosmetic management of local skin reactions	Consider prescribing moisturizing and healing creams for improvement of long-term cosmetic outcome, including early proper photoprotection to prevent hyperpigmentation (not only for preventative but also for cosmetic reasons)		May be unconcerned about local skin reactions, 'no pain, no gain'	This patient may particularly benefit from easy, direct access to a nurse or dermatologist through a telephone hotline

Table 4: Communication strategies for commonly encountered AK patient profiles^{*}

Profile	Unengaged (low medical engagement)	Cosmetic concerned during treatment	Cosmetic concerned post-treatment	Knowledgeable (high medical engagement)	Diagnosis-anxious	Safety-anxious
Suggested communication style	Simple and direct communication – avoid complex terminology or explanations	Provide reassurance on predictability of local skin reactions and their resolution	Provide reassurance about outcomes of treatment	Medical and scientific style	Simple and direct communication; reassuring	Reassuring; provide confidence in the safety of therapy
Communication strategy	Focus on motivating the patient on the need for treatment now vs potential for surgery later	Focus on dermatologist experience with treatments	Reassure that intense local skin reactions do not negatively influence long-term outcomes	Provide patients with data, including key statistics to support an evidence-based approach	Provide objective evaluation on the risk of AK evolution	Acknowledge anxiety and explore – ‘What are you most concerned about?’

	Consider role of partner/family in communication	Emphasize predictability of local skin reaction time course, if applicable for chosen treatment Explain importance of local skin reaction in response to treatment	Potentially discuss data suggesting improvement in skin quality following treatment, if applicable for chosen treatment	Important to explain all treatment options, with an evaluation of pros and cons	Avoid over-complex terminology which can heighten anxiety Stress efficacy of treatment Discuss management of a chronic condition	Discuss long-term benefits of treatment Reassure on lack of systemic effects, if applicable for chosen therapy Explain importance of local skin reactions in response to treatment
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*All communications should depend on and be tailored according to the chosen treatment

Table 5: Considerations for field-directed therapy* in commonly encountered AK patient profiles

Profile type	Description	Recommended treatments (in alphabetical order)	Rationale	Treatments not recommended	Rationale
Cosmetic concerned during treatment	Concerned with cosmetic effects during treatment	Conventional/daylight PDT Ingenol mebutate	Outcomes with noticeable but short, predictable duration of local skin reactions	Imiquimod	Unpredictable onset of local skin reactions
Cosmetic concerned post-treatment	Concerned with cosmetic outcomes of treatment	Alternative: Diclofenac	Not recommended due to unpredictable outcomes, but an option for patients who would potentially prefer milder but longer lasting local reactions	5-fluorouracil	Use with caution, overuse can lead to severe blistering resulting in scarring

				Diclofenac may not be appropriate as monotherapy in some cases, due to its limited efficacy compared with other options	
Diagnosis-anxious	Anxious about diagnosis	Conventional/daylight PDT Ingenol mebutate Imiquimod	Efficacy-driven treatment decision	Conventional PDT	Potential for pain
	Alternative where lesion-directed treatment is appropriate: Excision/shave		Provides material for histopathology (for patient reassurance)		

Safety-anxious	Anxious about long-term adverse effects of treatment	Daylight PDT Ingenol mebutate	Tolerability-driven treatment decision	Imiquimod	Systemic absorption with immunomodulation
		Alternative: Diclofenac	Good tolerability, but reduced efficacy	Diclofenac	Adherence issues anticipated due to lack of selectivity
Unengaged	Occupational exposure	Conventional PDT	Physician-directed treatment, potentially office-based	Imiquimod	Adherence issues anticipated due to lack of selectivity
		Ingenol mebutate	Short duration of treatment, licensed and approved for multiple locations (face and body)		
Knowledgeable	Well-informed	Conventional/daylight PDT	Support patient decision making with assessment of		

	patient	Ingenol mebutate Imiquimod	efficacy and safety of each treatment		
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*The panel does not recommend cryotherapy for these patient profiles as a lesion-directed treatment due to the potential for missing sub-clinical lesions, scarring, highly variable short and long term outcomes based on experience, and the requirement for multiple rounds of treatment.

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