Commentary on the “Evidence- and Consensus-Based (S3) Guidelines for the Treatment of Actinic Keratosis” Published by the International League of Dermatological Societies in Cooperation with the European Dermatology Forum

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Keywords

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Abstract

In 2015, the International League of Dermatological Societies and the European Dermatology Forum published a guideline for the treatment of actinic keratosis, which is classified as an evidence- and consensus-based S3 guideline. From the point of view of the GD Task Force “Licht.Hautkrebs.Prävention,” an interdisciplinary expert panel of the Society for Dermopharmacy for the prevention and treatment of skin cancer, this guideline reveals strengths and weaknesses but, in summary, does not meet the claim for an evidence- and consensus-based S3 guideline.

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Introduction

Medical guidelines play an increasingly important role in the treatment of patients. In Germany, they have gained considerably in importance through the law to improve patients' rights (“Patientenrechte-Gesetz”) of February 26, 2013, in which guidelines are referred to, in addition to numerous other regulations (duty of information, duty of explanation etc.): “As a rule, physicians should apply the current state of scientific knowledge and medical experience that is required to achieve the treatment goal, and which has been proven in trials. For this, guidelines which have been prescribed by scientific societies are definitive.”

In addition, medical guidelines are also becoming increasingly important as guidance with regard to medical care for funding agencies and political decision-making committees. In Germany, medical guidelines are created by scientific societies which are organized in the Associa-

S3	Evidence- and consensus-based guidelines	Representative body for systematic research, selection, literature review, structured consensus building
S2e	Evidence-based guidelines	Systematic research, selection, literature review
S2k	Consensus-based guidelines	Representative committee, structured consensus building
S1	Recommendations for action by expert groups	Consensus building in an informal process

Fig. 1. Hierarchy of medical guidelines based on the Association of Scientific Medical Societies in Germany.

tion of Scientific Medical Societies (AWMF) according to the vote of the Advisory Council on the Assessment of Developments in the Health Care System. These are based on actual scientific data and procedures which have been proven in practice and provide more security in medicine, but should also take economic aspects into consideration. The AWMF defines a hierarchy for medical guidelines (Fig. 1).

The work group responsible for establishing a set of guidelines needs to have a balanced composition in order to comprehensively identify problems in practical medical care and to avoid potential biases. This balance is usually achieved by the inclusion of various medical societies (interdisciplinary approach) and patient representatives or self-help groups. Dependencies and conflicts of interest, possibly due to cooperation with industrial companies in the context of studies and consultancy activities, as well as financing by a health care or insurance company must be disclosed.

The Strengths and Weaknesses of the ILDS/EDF Guideline

In 2015, the International League of Dermatological Societies (ILDS) and the European Dermatology Forum (EDF) published a guideline for the treatment of actinic keratosis (AK) [1], which is classified as an evidence- and consensus-based S3 guideline. The primary objective is stated as the provision of recommendations for the treatment for various subgroups of patients with AK. The target groups of the guidelines are physicians who are involved in the diagnosis and treatment of AK patients – primarily dermatologists and histopathologists – and

general practitioners. The secondary objective is stated as “implementation of knowledge relating to the clinical background of AK, including recommendations for the histopathological definition, diagnosis and the assessment of patients presenting with AK.” These are very worthy objectives; however, on closer examination questions arise as to whether this guideline meets the claim for an evidence- and consensus-based S3 guideline, how this should be properly interpreted, and whether a German guideline is needed.

The basis of evidence of the ILDS/EDF guideline is a systematic review, which is based on a systematic Cochrane review carried out in 2012 and “updated” by systematic literature research up to January 25, 2013. Because of this, studies which were carried out after January 2013 are not taken into account. This considerably limits the “evidence base” so that an update of the literature is urgently required. In addition, many of the studies which are cited have considerable methodological deficits (see the “risk of bias” illustration in the publication) and therefore must be interpreted with caution.

Regardless of this, many relevant questions cannot be answered by assessment of the evidence from the extended systematic review and therefore recommendations must be published on the basis of expert opinion. These are referred to as “consensus-based recommendations” and are discussed, rated, and subjected to a formal consensus process similar to that for evidence-based recommendations, in order to reduce bias. This depends on a representative committee of experts, as well as an objective consensus process. Here, the question arises with regard to the criteria according to which the “expert group” was comprised, and whether this representatively reflects the appropriate medical societies. Normally the expert

Table 1. Strengths and weaknesses of the ILDS/EDF guideline for the treatment of actinic keratosis

Strengths

Based on systematic literature research
Good compilation of randomized controlled trials
International consensus on the necessity for treatment
Useful histological classification of the various treatment groups
Good basis for national guidelines

Weaknesses

Outdated literature research
No representative composition of the group of experts
Influenced by economic interests
No moderator who is independent from the group of authors
Often no strong consensus
No mention of “off-label use” and no consideration of special features of national approvals

societies concerned are contacted and asked to send a delegate as part of a formal process. However, here this was obviously not the case. In addition, no patients’ representation was involved, and moderation was performed by a member of the team of authors.

With consensus-based recommendations, it is important to assess the strength of the consensus. All recommendations should be discussed in a formal consensus process involving an independent external moderator and should then be subjected to consensus in a voting process (nominal group technique). In this process, divergent opinions can be expressed and minority votes are possible. In other guidelines, the strength of consensus is evaluated as follows: 75–95% agreement is deemed to be consensus; >95% strong consensus. However, in the present guideline, agreements of ≥ 50 , ≥ 75 , and $\geq 90\%$ were stated. It is noticeable that some consensus-based recommendations in this guideline are based on a consensus of $\geq 50\%$ and many others on a consensus of $\geq 75\%$. This shows how heterogeneous the expert opinion is in several cases, and that the basis for an evidence-based recommendation is often lacking.

One positive aspect which must be emphasized is the proposed classification of 4 different patient groups for treatment. This consensus is based on an agreement which is $\geq 90\%$. A differentiation is made between the following groups of patients:

- Patients with individual AK lesions
- Patients with multiple AK lesions (multiple is defined as at least 6 differentiable AK lesions in a region of the body or field)
- Patients with field carcinogenesis
- Patients with concomitant immunosuppression

It is certainly also problematic if an international guideline attempts to generalize the special national features for the approval of medications and the remuneration of medical services. Even within Europe, there are considerable differences in the approval status of individual preparations for the treatment of AK, and in the USA procedural treatment (primarily cryosurgery) of patients with AK is predominant due to the remuneration situation. Therefore, it should be standard practice in the recommendation of guidelines to clearly indicate whether a recommendation for treatment is a so-called off-label use. Unfortunately, this is not stated for any of the recommended treatments in the present guideline, although this is important information for both physicians and patients.

The group of authors of this guideline recommends that it is implemented in the form of corresponding national guidelines, in order to take specific national features better into account. This guideline is certainly a very helpful basis for this. It is encouraging that in Germany a group of experts has been constituted in a representative process via the relevant expert societies for the production of an “S3 Guideline for Actinic Keratosis and Squamous Cell Carcinoma” and has already started its work.

The strengths and weaknesses of the ILDS/EDF guideline from the point of view of the authors of this commentary are summarized in Table 1.

Disclosure Statement

The authors of this commentary state no conflict of interest.

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