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ORIGINAL RESEARCH

Italian Expert Opinion on Chronic Hand Eczema: from Guidelines to Clinical Practice

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ABSTRACT

Introduction: Chronic hand eczema (CHE) is an inflammatory skin condition characterized by different pathomechanisms, clinical presentations, and prognoses. Treatment is often challenging because of limited approved drugs, and severe CHE is associated with reduced quality of life (QoL) and poor overall health measures in terms of psychological, functional, and occupational challenges. This study aims to describe the real-life management practices of Italian dermatologists who frequently treat patients with CHE, compare these practices with existing guidelines, and propose practical clinical recommendations for the management of these patients.

Methods: An 11-question survey was administered to 14 participating dermatologists to gather their insights on the diagnosis, treatment, and management of CHE. Moreover, a

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comprehensive literature search was conducted over the previous 10 years as a starting point for discussion among experts.

***Results*:** CHE was the reason for 6.9% of dermatological consultations by the 14 experts. Median time to CHE diagnosis was 12 (range: 2–24) months. Fissuring and itching (85.7% for both) were the most frequently reported signs and symptoms of CHE. The survey highlighted the need for long-term treatment that is effective and well tolerated, with experts emphasizing the importance of improving disease awareness among physicians and patients. Practical clinical approaches were proposed, emphasizing the significance of a thorough medical history and identification of symptoms in the management of CHE. Experts advocated for specifically developed CHE treatment approaches, concentrating on alleviating symptoms and signs, minimizing adverse events/safety issues, enhancing the QoL of patients, and long-term disease control. Findings from this survey were further discussed and compared to recommendations of the available guidelines for the management of CHE.

***Conclusions*:** Managing CHE requires a comprehensive approach that considers both objective clinical factors and subjective patient expectations. Experts emphasized the need for effective and well-tolerated long-term therapies, improved disease awareness, and communication among physicians and patients.

Keywords: Chronic hand eczema; Contact dermatitis; Quality of life; Expert opinion

Key Summary Points

Chronic hand eczema (CHE) significantly impacts quality of life, with unmet needs in long-term treatment efficacy, patient adherence, and psychological support.

There is a need for expert consensus on CHE management to improve patient outcomes in Italy and address challenges despite existing international guidelines.

This study sought to gather opinions from Italian dermatology experts to identify unmet needs in CHE management and propose targeted strategies to enhance treatment effectiveness and patient quality of life.

This study found that CHE represented 6.9% of dermatological consultations, with fissuring and itching as common symptoms. Experts emphasized the need for long-term treatment, early diagnosis, and improved disease awareness.

These findings highlight the importance of developing targeted therapeutic strategies and patient education to reduce disease burden, potentially guiding future research and treatment advancements for the management of CHE.

INTRODUCTION

Hand eczema (HE) is an inflammatory skin disease affecting the hands and wrists with 1-year prevalence up to 10% [1–3]. Over two-thirds of patients suffering from HE may develop chronic HE (CHE) [4, 5], which lasts for > 3 months or recurs two or more times within a 12-month period [6].

CHE classification is primarily based on the underlying aetiology and clinical subtypes [6, 7]. European Guidelines (EGL) [6] recommend distinguishing between irritant contact dermatitis (ICD), allergic contact dermatitis (ACD), atopic hand eczema (AHE), and protein contact dermatitis/contact urticaria. Diagnosing CHE can be challenging because of its broad clinical

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spectrum, and it requires a comprehensive medical history encompassing signs and symptoms, clinical course, work-related and non-work-related activities, and history of atopic dermatitis (AD) [8]. When contact dermatitis is suspected, patch testing is the first-line approach to recognize contact allergens and irritants, while protein contact dermatitis may require skin prick test and specific IgE measurement [6, 7].

Assessing CHE severity and progression is essential for effective management. Tools like the HE Severity Index (HECSI) and Physician Global Assessment (PGA) provide a systematic approach to evaluate the extent and intensity of signs over time [9–11]. Severe CHE impacts quality of life (QoL), affecting daily activities and work, often resulting in absenteeism or reduced productivity [5, 12, 13]. Visible symptoms can lead to stigmatization, negatively impacting self-image and social interactions [13, 14]. CHE is also linked to higher levels of stress, anxiety, depression, and suicidal thoughts [13, 15–17]. Despite this, health education and counselling still remain insufficiently addressed [14, 18]. Understanding the mental health burden of CHE is a priority for resource allocation and integrating mental and physical health interventions.

Despite the availability of guidelines and advances in treatment, several unmet needs persist in the real-life management of CHE [8]. These include the limited effectiveness and not fully known safety profile of current treatments and the absence of long-term CHE-specific treatment options, resulting in many patients failing to fully control their signs and symptoms [19]. Moreover, difficulty in achieving adherence due to complicated and time-consuming treatment regimens often leads to poor treatment compliance [6, 20].

The EGL serves as a major reference for HE diagnosis, management, and prevention, incorporating recent literature and systematic reviews [6, 20]. Other consensus statements and guidelines have been developed in the UK, Germany, Spain, and Asia [21–24].

This study aimed to develop an expert Italian consensus on the management of CHE to highlight unmet needs in real-life clinical practice, thereby advancing the standard of care in this setting.

METHODS

Study Design

Consensus meetings among expert dermatologists were undertaken with the specific aim of comparing the current status quo on clinical practice with that of specific literature (i.e. guidelines, recommendations, and consensus) on CHE. A total of 14 expert dermatologists from across Italy were invited, and all 14 participated. All dermatologists invited to participate possessed expertise in HE and had experience in treating patients with CHE. Selection criteria included their publication history specifically on HE, active involvement in conferences related to HE, contribution to clinical studies on HE, and previous participation in the development of consensus statements on HE. There were no specific minimum requirements, but expertise and active engagement in the field were prioritized. A preliminary survey was shared with invited dermatologists. The survey was divided into two parts: the first part comprised 6 questions aimed at collecting information on demographics and clinical experience of participating dermatologists; the second part comprised 11 questions specifically aimed at collecting data on the management of patients with CHE. This project was organized into three macro-regional expert meetings (Northern, Central, and Southern Italy), during which the results from the literature search (Supplementary Methods S1), surveys, and EGL [6] were discussed, and the overall output was extracted (Fig. 1), also aided by the use of an Ishikawa fishbone diagram [25] (Fig. 2). This article is based on data derived from a survey conducted among dermatologists and previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Survey

The survey was organized by topic, each addressing specific aspects relevant to the study. Most questions were structured as multiple-choice items or scale-based questions (e.g. Likert scales)

Fig. 1 Flow chart of the different stages of the study. *KOL* key opinion leader

to allow participants to indicate the extent of their agreement or frequency of behaviours. The survey was designed to collect information on demographic and professional experience of dermatologists (region of origin, clinical activity area, percentage of patients with CHE based on the total number of patients, number of patients with CHE treated annually, severity of the disease in patients with CHE, and origin of patients with CHE referred to each dermatologist). In addition, 11 questions were specifically focused on the epidemiological and clinical features of CHE (average time to diagnosis, classification criteria used, most frequent signs and symptoms, comorbidities) and real-world management of CHE (scales used to measure the severity of the disease and the impact on patients' lives, therapeutic objectives attributed by dermatologists and patients, unmet needs, aspects to improve awareness of CHE, initiatives for effective CHE communication).

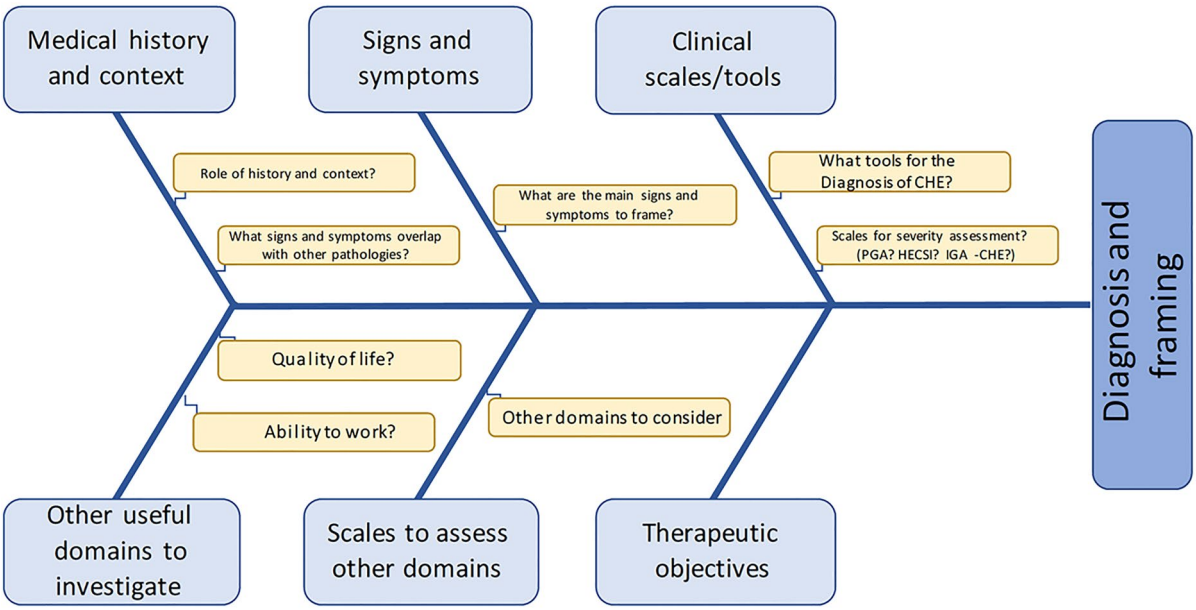

Fig. 2 Ishikawa diagram summarizing the main factors influencing the diagnosis and framing of chronic hand eczema. The problem is placed at the head of the fishbone and the causes or factors branch off from the spine. Categories of causes are light blue colored. The subcategories of causes are listed in yellow. The diagram includes a number of arrows to show the relationship between the different factors. *CHE* chronic hand eczema, *QoL* quality of life

Statistical Analysis

Descriptive data were obtained from questions regarding demographic information and clinical experience of dermatologists and summarized by mean ± SD or number and % and median and range. Questions from the survey on the importance of specific issues in the management of CHE (questions 1–11) were expressed using a 5-point Likert scale (0 for not important to 5 highest level of importance) and expressed as mean score, as previously described elsewhere [26].

RESULTS

Survey Results

Physician Demographics and Clinical Experience

Most participating physicians were dermatologists based in Northern Italy (7 out of 14, 50.0%) (Table 1). Most experts (12 out of 14, 85.7%) worked in university-affiliated clinics, while the remaining two worked in non-university-affiliated hospitals. CHE patients represented 6.9 ± 5.9% of all patients seen and the majority of patients suffered from mild (23.6 ± 21.3%) or moderate (39.1 ± 14.7%) CHE (Table 1). Primary care physicians (11 out of 14, 78.6%) and other dermatologists (9 out of 14, 64.3%) were the most frequent sources of patient referral.

The reported estimated median time to CHE diagnosis was 12 (range, 2 to 24) months. Moat physicians (13 out of 14, 92.9%) reported that they predominantly rely on clinical and anamnestic criteria for diagnosing CHE. This approach includes using clinical judgement and patient history, which are fundamental components of any diagnostic criteria, including those established by the EGL [6]. Only two physicians (14.3%) specifically referenced the EGL for their diagnosis (Table 2).

The survey asked participants to identify the four most frequently observed signs and symptoms of CHE, which were fissuring and itching (12 out of 14, 85.7% for both), dryness (10 out of 14, 71.4%), scaling (9 out of 14, 64.3%), erythema and pain (7 out of 14, 50.0% for both). Blisters were less frequently reported (5 out of 14, 35.7%) (Table 2). The most frequently used methods to assess disease severity were Investigator's Global Assessment (IGA-CHE) [27] and Physician Global Assessment (PGA) [11] (5 out of 14, 35.7% for both), Hand Eczema Severity Index (HECSI) [10] (4 out of 14, 28.6%), and Modified Total Lesion Symptom Score (mTLSS) [11] (2 out of 14, 14.3%) (Table 2). The most commonly used scale for assessing QoL of CHE patients was the Dermatology Life Quality Index (DLQI) [28] (10 out of 14, 71.4%), while for itch and pain the visual analog scale (VAS) (8 out of 14, 57.1%) and numerical rating scale (NRS) [29] (6 out of 14, 42.9%).

The most prevalent comorbidities reported to be associated with CHE were secondary skin infections (9 out of 14, 64.3%) and psychological disorders (7 out of 14, 50.0%). Other comorbidities included mucosal atopic disorders (allergic rhinitis: 5 out of 14, 35.7%; asthma: 2 out of 14, 14.3%) (Table 2).

Therapeutic Goals, Unmet Needs, Disease Awareness, and Communication

A comparison was made between dermatologists' priorities in the management of CHE and their perception of patients' priorities. From this assessment, physicians hypothesized that the most important treatment objectives, aligned with what they believed to be important to their patients, were the improvement of symptoms and QoL, closely followed by an improvement in signs (Fig. 3a, b). Only after achieving these goals do the interviewed dermatologists consider the prevention of flares, repairing the skin barrier, and reducing inflammation (Fig. 3a, b).

The survey revealed that the most commonly reported unmet need in managing patients with CHE was the availability of effective and well-tolerated long-term therapies. (Fig. 3c). Improving disease awareness includes identifying triggers and preventive measures, followed by providing information on the prevalence and impact of CHE on QoL and the publication of articles on the topic aimed at healthcare professionals

Table 1 Demographics and professional experience of participating dermatologists, CHE severity, and referral

Questions and rating	Dermatologists *N* (%)
1. Region of origin?	
North	7 (50.0)
Lombardy	3 (21.4)
Veneto	3 (21.4)
Emilia Romagna	1 (7.1)
Centre	5 (35.7)
Tuscany	1 (7.1)
Umbria	1 (7.1)
Lazio	2 (14.3)
Abruzzo	1 (7.1)
South	2 (14.3)
Campania	1 (7.1)
Sicily	1 (7.1)
2. In what field do you predominantly carry out your clinical activity?	
University clinic	12 (85.7)
Hospital	2 (14.3)
3. How many patients with CHE do you treat annually?	121 ± 115.5
4. What is the percentage of patients affected by CHE out of your total patient population?	6.9 ± 5.9
5. How are your patients with CHE distributed, in percentage, based on the severity of the disease?*	
Mild	23.6 ± 21.3
Moderate	39.1 ± 14.7
Severe	37.3 ± 20.5
6. Who primarily refers patients with CHE for consultation with you?	
Primary care physician	11(78.6)
Dermatologist	9 (64.3)
Allergist	3 (21.4)
The patient autonomously	12 (85.7)
Other	2 (14.3)

Data are presented as number and % or mean and standard deviation

CHE chronic hand eczema

*Disease severity was strictly based on dermatologists' best clinical judgement and recollection of visits with these patients and their overall perception. A measure or scale was not directly used to obtain these estimates

Table 2 Common symptoms, disease severity measures, and comorbidities according to dermatologists' response in patients with chronic hand eczema

Questions and rating	Dermatologists *N* (%)			
1. What is, in your experience, the average time to diagnosis for your patients with CHE? (months)[a]	11.6 (2.0–24.0)			
2. What classification criteria do you usually use for diagnosing CHE?*				
According to EGL	2 (14.3)			
I mainly rely on clinical and anamnestic criteria	13 (92.9)			
3. What are the four signs and symptoms most frequently observed in patients with CHE?				
Itching	12 (85.7)			
Fissuring	12 (85.7)			
Dryness	10 (71.4)			
Scaling	9 (64.3)			
Erythema	7 (50.0)			
Pain	7 (50.0)			
Blisters	5 (35.7)			
4. Rank the 4 main selected signs and symptoms by frequency**				
Ranking	*1st*	*2nd*	*3rd*	*4th*
Itching	6 (42.9)	2 (14.3)	1 (7.1)	2 (14.3)
Fissuring	1 (7.1)	2 (14.3)	6 (42.9)	3 (21.4)
Dryness	3 (21.4)	1 (7.1)	3 (21.4)	2 (14.3)
Scaling	2 (14.3)	2 (14.3)	2 (14.3)	1 (7.1)
Erythema	0 (0.0)	4 (28.6)	0 (0.0)	3 (21.4)
Pain	1 (7.1)	3 (21.4)	1 (7.1)	2 (14.3)
Blisters	1 (7.1)	0 (0.0)	1 (7.1)	1 (7.1)

Table 2 continued

Questions and rating	Dermatologists *N* (%)
5. What are the scales you primarily use to measure the severity of the disease and its impact on the lives of your patients with CHE?	
DLQI	10 (71.4)
VAS (itch and pain)	8 (57.1)
NRS (itch and pain)	6 (42.9)
PGA	5 (35.7)
IGA-CHE	5 (35.7)
HECSI	4 (28.6)
mTLSS	2 (14.3)
6. What are, in your experience, the main comorbidities that your patients with CHE exhibit?	
Secondary skin infections (e.g. bacterial or fungal infections)	9 (64.3)
Psychological disorders (e.g. anxiety, stress, sleep disorders)	7 (50.0)
Allergic rhinitis	5 (35.7)
Autoimmune diseases (e.g. psoriasis, lupus, rheumatoid arthritis)	4 (28.6)
Asthma	2 (14.3)
Other	2 (14.3)
Metabolic disorders (e.g. hyperlipidemia, hypercholesterolemia)	1 (7.1)

CHE chronic hand eczema, *DLQI* Dermatology Life Quality Index, *EGL* European Guidelines, *VAS* visual analog scale, *NRS* numerical rating scale, *PGA* Physician Global Assessment, *IGA* Investigator's Global Assessment, *HECSI* Hand Eczema Severity Index, *mTLSS* Modified Total Lesion Symptom Score

*Dermatologists could provide more than one answer

**The first four most frequent sigs/symptoms are presented, but dermatologists could rank up to seven

[a]Median value is reported (range)

(reviews, clinical studies, epidemiological studies, etc.) (Fig. 4a). According to the experts, improved awareness and events involving experts and patients are important for the effective communication of CHE (Fig. 4b).

Overall Output from the Expert Discussion

Fourteen expert dermatologists convened for three meetings (one dermatologist was unavailable). Discussions were focused on the results from the survey and literature review. Below are the key points that were discussed.

Epidemiology and Classification

Experts supported epidemiological EGL data [6] applicable also to Italy, though it was noted the tobacco-related data seem to be overestimated. They proposed including construction workers as an employment type where CHE can be considered an occupational disease along with homemakers in wet-work occupations.

They agreed with the classification proposed by guidelines [6] but suggested starting with clinical classification and investigating aetiology in a subsequent step, also because several cases of overlap among different aetiological subtypes can coexist, as recently documented in a large Italian study [30]. This approach involved considering the following aspects based on clinical examination: disease presentation, disease onset and duration, recurrence pattern, response to previous therapy, duration of response, symptoms, such as pain and itching, and definition of CHE severity. Only after this stage could the aetiology be investigated.

Medical History and Management of CHE

According to experts, a meticulous medical history is fundamental for achieving an accurate diagnosis, achieving effective treatment, and preventing disease relapse. Key points regarding the investigation of medical history related to CHE patients are summarized in Supplementary Table S1. Expert dermatologists agreed that it is vital to gather comprehensive information on the patient's background. This includes investigating any differential diagnosis, such as psoriasis (both personal and familial), and considering atopy involving the hands, which is one of the four aetiological phenotypes of CHE. Additionally, it involves inquiring about underlying comorbidities and establishing the timeline of the disease, with a focus on chronicity and the occurrence of flares. In addition, understanding the patient's treatment history and any preventive measures they take is essential. Patch testing is essential for diagnosing contact allergy as is prick testing for protein contact dermatitis.

Signs and Symptoms, Scales, and Clinical Tools

Among signs and symptoms, experts agreed that CHE typically manifests with itching, lichenification, scaling, and fissuring (Supplementary Table S2). Investigating the presence of a vesicular exudative component can aid in distinguishing CHE from psoriasis. Pain and bleeding, often associated with fissuring, are important clinical features of CHE. Notably, the involvement of other body parts is important. In a subset of patients, feet may also be affected, indicating involvement in locations beyond the hands (Supplementary Table S2).

Diagnosis should be based on clinical characteristics rather than clinical exclusion. The VAS and NRS are effective for evaluating specific clinical symptoms such as pruritus and pain; it is necessary to supplement these quantitative measures with qualitative methods.

Other diagnostic in vivo procedures (microbiology tests, skin biopsy) in addition to patch tests and skin prick tests should be guided by the clinical presentation and the need for a comprehensive evaluation to accurately diagnose CHE.

Assessment of disease severity must be approached from both a clinician's perspective and using Patient-Reported Outcomes (PROs) measures such as DLQI, VAS, or NRS at least for itch and pain. Clinical evaluation alone is insufficient; it must align with the patient's experience and be used to guide treatment. Among the scales suggested by experts for evaluating QoL, DLQI emerged as the simplest and most

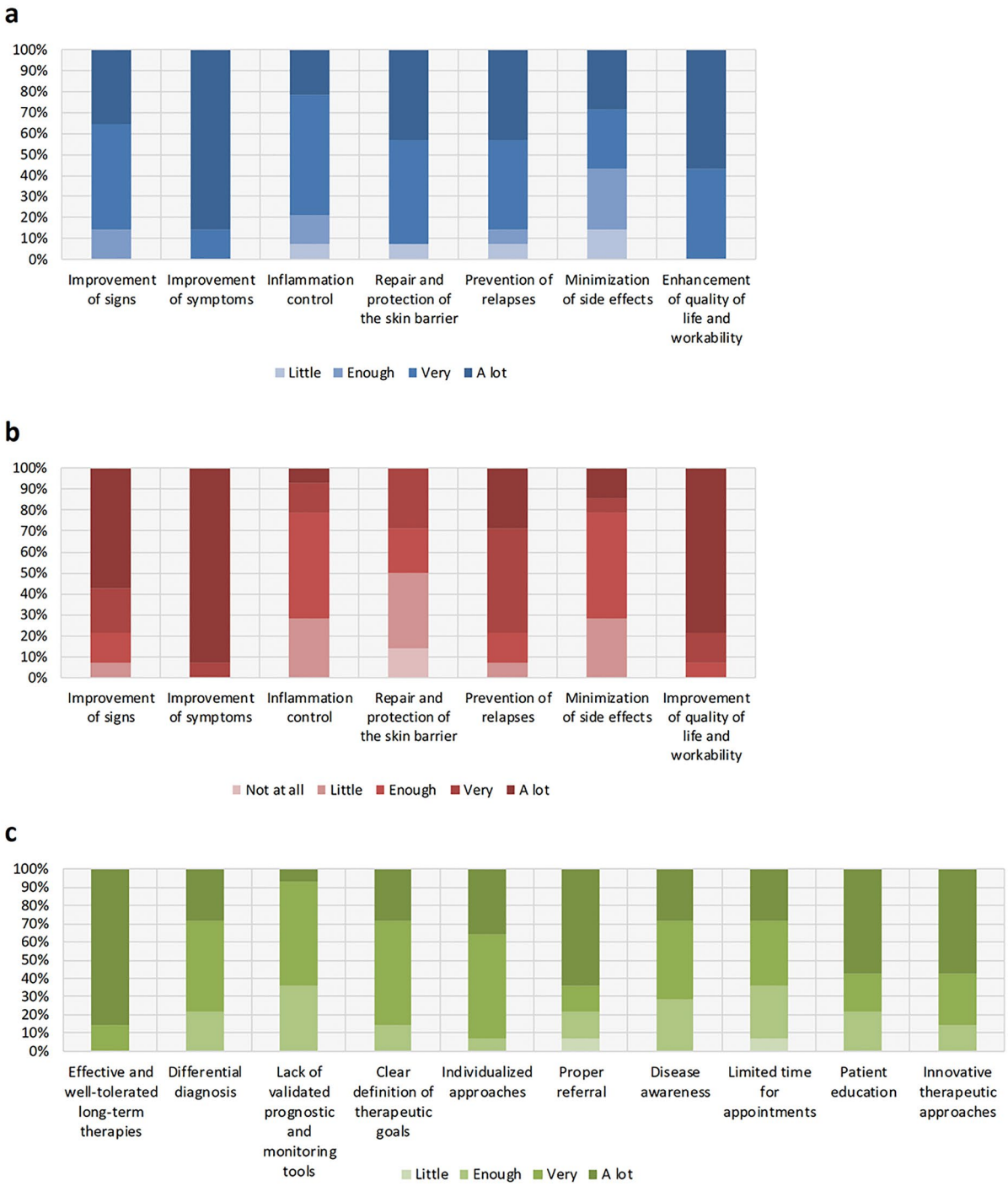

Fig. 3 Results of the survey showing **a** dermatologists' priorities in managing chronic hand eczema (CHE) (survey question 7); **b** dermatologists' perception of patients' priorities (survey question 8); **c** dermatologists' views on unmet needs in CHE management (survey question 9). Question 7: "Please indicate the level of importance you attribute to the following therapeutic objectives in the treatment of patients with CHE". Question 8: "Indicate the level of importance that, in your opinion, the PATIENT affected by CHE attributes to the following therapeutic objectives". Question 9: "Please indicate the level of importance you attribute to the following unmet needs related to the management of patients with chronic hand eczema"

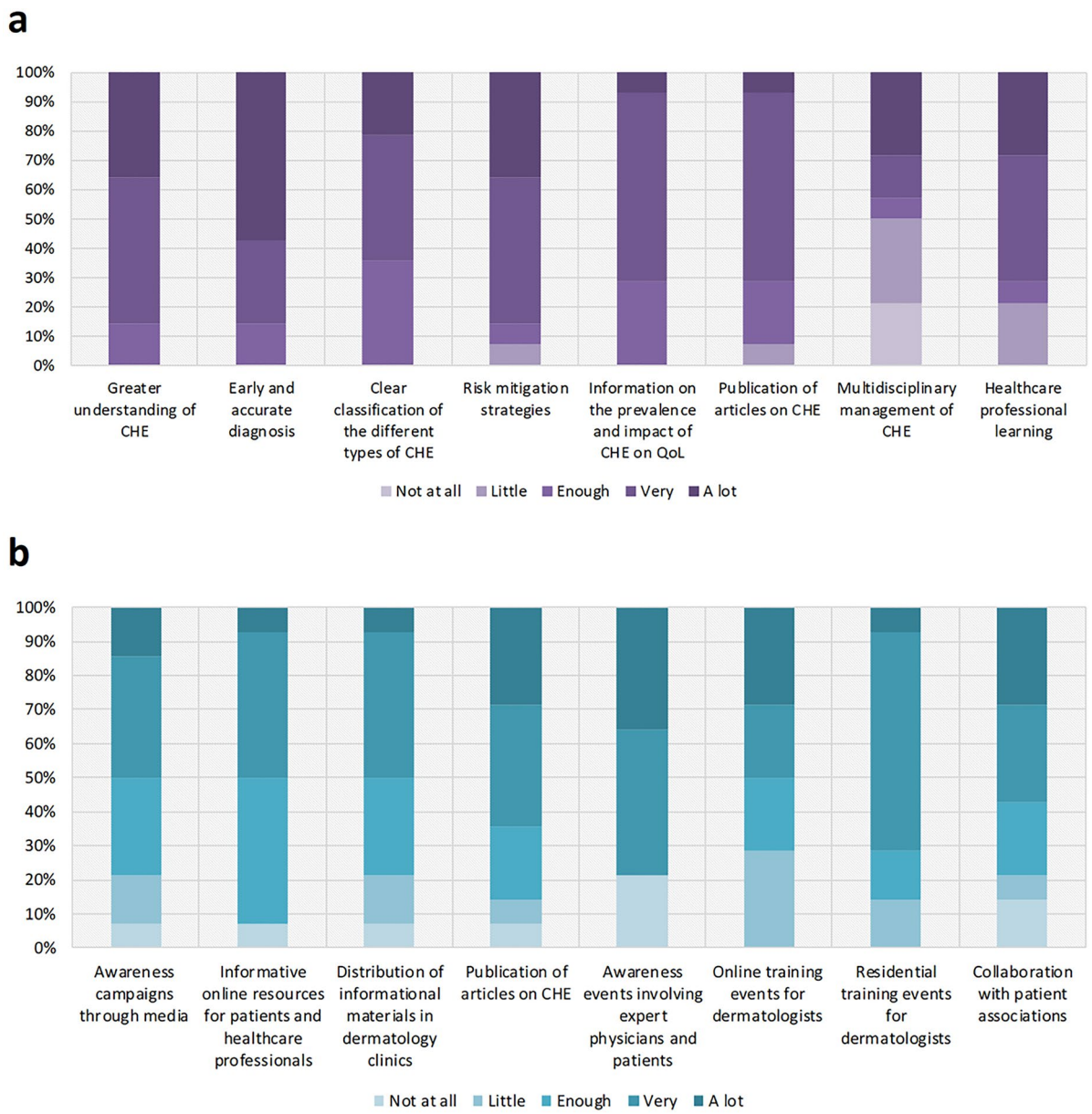

Fig. 4 Results of the survey showing **a** disease awareness improvement (survey question 10) and **b** effective communication strategies (survey question 11). Question 10: "Please indicate the level of importance you attribute to the following aspects for improving disease awareness regarding CHE". Question 11: "Please indicate the level of importance you attribute to the following initiatives for effective communication of CHE"

feasible compared to the others, despite not being specifically tailored for patients with CHE. The Quality of Life in Hand Eczema Questionnaire (QOLHEQ) [31] was also suggested, which is more specifically designed for CHE patients. Furthermore, gathering information from discussions with patients is necessary to assess their ability to work. Understanding a person's capacity to work is imperative, especially when issuing a medical certificate for the patient's illness.

Using the PGA (Physician Global Assessment) is recommended for routine activity as well as HECSI, since it is advocated by Italian Medicines Agency (AIFA) and the European Medicines

Agency (EMA). Additionally, assessing severity and the course of the disease, considering factors like duration, persistence, and frequency of flares, is necessary and emphasizes the importance of evaluating both objective and subjective aspects.

Other Domains and Scales to Investigate

According to the experts, two important domains require investigation for accurately assessing patients with CHE: (1) QoL, fundamental for guiding the most suitable therapy, and (2) the ability to work.

Among the various scales proposed by experts for assessing QoL, the DLQI stood out as the most straightforward and practical, even though it was not specifically developed for patients with CHE. The QOLHEQ [31], which is specifically designed for patients with CHE, was also recommended. Additionally, engaging in patient discussions is essential to evaluate their work capability, which is particularly important when providing medical certificates for their condition.

Engaging in dialogue and open communication with patients helps to understand the comprehensive impact on their quality of life.

Therapeutic Objectives

Considerations and objectives in the treatment and management of CHE patients are presented in Supplemental Table S3. The primary therapeutic goal is to achieve symptom remission, prioritizing QoL and the ability to work closely followed by the achievement of remission of clinical signs. The final therapeutic goal is maintenance of long-term response with minimal adverse events and flare reduction along with preventive measures (Supplemental Table S3).

According to experts, understanding the threshold values of HECSI is considered fundamental in establishing therapeutic goals. By monitoring the HECSI score over time, dermatologists can adjust treatment plans as needed and assess the patient's progress towards achieving their goals. Moreover, by tailoring treatment to the specific severity level indicated by the HECSI score, dermatologists can minimize the risk of unnecessary side effects.

Treatment selection depends on the CHE severity and duration, previous therapies, and patient adherence. Rapid, well-tolerated, effective, manageable treatments aligned with highlighted therapeutic goals from the survey are essential. Formulation, including excipients, plays a vital role in the selection of topical therapies for CHE. The choice of formulation can significantly impact the efficacy, tolerability, and overall patient adherence to the treatment. Therefore, careful consideration of the formulation is essential when selecting the appropriate topical therapy for managing CHE. Identifying eligible patients for each specific therapy is critical to enhance patient compliance and adherence. Recognizing the economic impact on patients, including direct and indirect costs, is also important.

Experts agreed with the treatment pathway proposed by EGL [6]. Topical corticosteroids (TCSs) are useful in managing relapse phases. Experts identified several issues with TCSs: poor adherence and incorrect use, further barrier damage, skin atrophy, reduced long-term efficacy, especially without occlusion, and the need for continuous treatment. Systemic treatments in Italy include systemic corticosteroids, alitretinoin, and cyclosporin, while localized phototherapy is not widely used in Italy because of its adverse events, among them a possible increased risk of cancer [6].

DISCUSSION

This expert opinion provides valuable insight into the current state of CHE management and therapeutic challenges in Italy. Unmet needs highlighted by the Board included effective and safe long-term treatments and the importance of improving disease awareness and communication among healthcare professionals and patients.

Given the comprehensiveness of the EGL [6], the discussion among expert dermatologists was focused on the application of these guidelines in Italy in the management of CHE in real-life

clinical practice, ensuring alignment with current best practices.

Among the different risk factors listed in the EGL [6], experts disagreed that tobacco smoking represents a major risk factor, based on their personal experience and recent evidence [32]. In a recent study conducted in Italy [32] involving 516 housewives (214 affected by CHE and 302 control subjects), no significant difference was observed in the incidence of CHE between smokers and nonsmokers [32]. Moreover, the EGL [6] defined HE as the most common occupational skin disease and included some specific types of employment such as hairdressers, cleaners, healthcare workers, metal workers, and dental technicians as being at greater risk of developing ACD and ICD. The emerging setting of ACD of the hands is represented by contact sensitivity to (meth) acrylates used in nail products by consumers and nail technicians [33, 34]. Hence, experts stated that patients' professional choices, particularly over the long term, are critical for the correct management of the disease.

Regarding the classification, EGL [6] divides CHE into aetiological and clinical subtypes. Results from the survey indicated that experts classified CHE based on both clinical and anamnestic criteria. In the expert discussion, they endorsed the guidelines' classification but recommended a sequential approach, prioritizing clinical classification before exploring aetiology. This approach reflects the diverse nature of CHE, influenced by various internal and external factors acting alone or in combination [35]. However, the clinical relevance of these classifications may be limited because of the lack of a clear relationship found between the type and underlying aetiology of CHE [36]. The UK-based Consensus Statement [21] proposes a classification of HE into seven groups based on demographics, medical history, and lesion morphology. In the guidelines published by the Spanish Academy of Dermatology and Venereology [23], six distinct clinical types of HE were reported based on their morphology. The Asian guidelines [24] classify CHE based on morphology, aetiology, and a combination of both. In general, there is no consensus among dermatologists regarding CHE classification, highlighting the need for global consensus to classify and assess CHE effectively.

Regarding diagnosis, experts, in accordance with the EGL [6] and Korean guidelines [24], emphasized the importance of a thorough medical history and an understanding of the patient's lifestyle to accurately diagnose and treat CHE. EGL [6] reported several differential diagnoses. The UK guidelines [21] recommend that the differential diagnosis should include only psoriasis, microvesicular hand dermatitis (a form of eczema characterized by small vesicles or blisters), and fungal infections. Moreover, experts recommended patch testing CHE patients, considering it to be the gold standard for diagnosing ACD, superimposed ACD on hand AD, and ICD in case of negative patch test result. However, ICD is not the only possible diagnosis when patch tests are negative, as AD can be also included. This is in accordance with EGL [6] and other consensus statements [21, 23, 24], which specify that this in vivo test should be recommended when a patient is nonresponsive to adequate treatment.

Among signs and symptoms, experts agreed with the EGL [6] that chronic forms of CHE typically manifest with itching, lichenification, scaling, and fissuring. They emphasized that pain and bleeding, often associated with fissuring, are important clinical features in CHE, more so than in other conditions.

Regarding clinical scores and clinical tools used in managing CHE patients, the survey and subsequent discussion among experts highlighted the use of VAS or NRS as well as DLQI as the most frequently employed scales for assessing the burden of CHE on patients' quality of life. Based on existing literature [37], these measures are commonly used to evaluate the symptoms and impact of CHE, covering domains related to symptoms and emotions, daily activities, leisure time, work or school, personal relationships, and adverse effects. During discussion, DLQI was indicated by experts as the simplest and most feasible compared to others, despite not being specifically tailored for patients with CHE. Therefore, the experts proposed the QOL-HEQ [31], which is specifically designed to assess the QoL in patients with CHE. Among the scales suggested by experts for evaluating clinical

severity, they identified PGA and HECSI as the most commonly used tools, in alignment with other studies [14, 37–39]. PGA was utilized in alitretinoin clinical studies [11]. HECSI [9] was also recommended by Italian Medicines Agency (AIFA) and the European Medicines Agency (EMA). Experts proposed another important domain requiring investigation in CHE patients: the ability to work. Recently, Ronsh et al. [40] reported a list of candidate outcome domains for HE trials suggested by both patients and physicians. Among those related to QoL as perceived, the ability to work was ranked third, following the perceived negative impact of HE in general and physical hand functioning impairment. Experts agreed that understanding a patient's capacity to work is essential, particularly when issuing a medical certificate for their illness. Among the consensus statements available in the literature, only English et al. [21] reported the indication to investigate the QoL, including the ability to work in CHE patients, indicating the DLQI as the primary tool.

Regarding treatment, the EGL [6] categorizes treatments into topical (including emollients and TCSs) and topical calcineurin inhibitors (TCIs), crisaborole (both off-label, except for atopic HE) and delgocitinib, physical (phototherapy) and systemic therapies (e.g. systemic corticosteroids, alitretinoin, off-label use of cyclosporine and biologics such as dupilumab). Experts agreed that the proposed treatments were traditional and reflective of available CHE therapies, even though they reported limited use of phototherapy in Italy. They suggested distinguishing pharmacological treatments (such as corticosteroids and TCIs) from emollients and skin protection programmes within the group of topical therapies. This recommendation aligns with UK [21] and German [22] consensus statements, where non-pharmacological interventions are reported separately from topical treatments. An important finding emerging from the survey was the urgent need for effective and safe long-term CHE therapies. This critical concern is also acknowledged in the EGL [6] and emphasized in a recent HE Cochrane Review [20].

The prolonged use of TCSs, for instance, can lead to adverse effects such as skin atrophy and disruption of epidermal tight junctions, thus exacerbating epidermal barrier dysfunction [41–43]. While systemic corticosteroids are utilized during flares, their prolonged use is discouraged because of potential adverse effects [6]. Alitretinoin, like other retinoids, is associated with the presence of various adverse effects, including teratogenicity, photosensitivity, skin dryness, and headaches, and requires strict monitoring [44]. Similarly, the long-term use of cyclosporine can be associated with the occurrence of nephrotoxicity and hypertension [45]. The experts during the discussion proposed using the HECSI score to monitor disease progression or regression during treatment by identifying specific thresholds. A recent study [46] demonstrated that HECSI scores effectively reflect changes in disease severity, with an area under the ROC curve of 0.86, indicating high accuracy. This study found that an improvement of 41 points on the HECSI is recommended as the minimally measurable true change, making it a reliable metric for assessing treatment efficacy in clinical practice.

Finally, another important finding that emerged from the survey and discussion was the need to enhance the understanding of the disease from both the patient's perspective and a scientific standpoint, making it useful for dermatologists. Recently, topic-guided interviews were conducted in five European countries (Croatia, Denmark, Germany, the Netherlands, and Spain) involving 60 patients to assess their knowledge on the disease and its progression. Participants expressed a lack of sufficient information about CHE, particularly regarding aetiologies, triggers, and treatment options [40]. Patrizi et al. [47] propose various educational tools for AD management, including traditional materials, support groups, telemedicine, and mobile apps, to improve understanding, adherence to therapy, and the use of distraction techniques for itch. Educational interventions can be delivered through face-to-face sessions, workshops, online materials, and social media and have been shown to enhance therapy adherence [48].

In conclusion, managing CHE requires a comprehensive approach that considers both objective clinical factors and subjective patient experiences. Existing guidelines provide a solid foundation, but there is a need to adapt them to

the specific needs of patients with CHE. Improving disease awareness and communication among healthcare professionals and patients is paramount. Further research is needed to better understand individual triggers and develop effective preventive measures. The search for effective and well-tolerated long-term therapies remains a top priority to improve the QoL for patients with CHE.

The strengths of this expert opinion include the involvement of 14 expert dermatologists with significant expertise in treating patients with CHE. Our approach, combining surveys, literature review, and expert discussions, offers a comprehensive understanding of different issues related to CHE. In addition, this expert opinion aims to provide practical solutions for managing patients with CHE, valuable for healthcare professionals, and emphasizes areas where further research and developments are still necessary.

A limitation of the survey was that data were mainly qualitative, precluding a more rigorous analysis of quantitative data that would have been possible with a higher number of participants. It is important to note that these results reflect the responses given by the dermatologists and may not include all clinically significant signs (for example, lichenification and vesicles) and different clinical phenotypes were not specifically studied. The absence of cost-effectiveness analysis overlooks the relevance of different treatment options for healthcare decision-making.

Diagnostic delay was not specifically quantified as it would have been in a clinical study or trial and reported estimates in the present survey cannot be accurately compared to epidemiological values that were specifically designed to obtain estimates based on large sample size. These estimates reflect personal recall and individual experience treating patients with CHE across Italy and may indeed be subject to a high degree of variability and overestimate the true diagnostic delay.

The survey was developed by experts in CHE but it was not formally validated and as such may affect the reliability of data collected. Indeed, the aim of the survey was not to obtain data typical of the design of an epidemiological study with appropriate sample size. Furthermore, the survey primarily focused on expert opinions, with limited inclusion of patient perspectives, potentially overlooking important insights from those directly affected by CHE. Last, the specific point of view of Italian dermatologists limits the focus to the national level; as such, these results may not be directly applicable to other countries or regions, thereby reducing the generalizability of the study.

CONCLUSIONS

This expert opinion addresses the current challenges in managing patients with CHE, particularly those with moderate to severe disease, which account for approximately 75% of patients with CHE seen by dermatologists. It emphasizes the urgent need for long-term treatments that are both effective and well-tolerated and stresses the importance of enhancing disease awareness and communication among healthcare providers and patients. It highlights national practices and proposes elements that relate to the local adaptation of the EGL. Management strategies need to be targeted, particularly for the management of moderate to severe CHE, and provide both short-term efficacy and long-term disease control. Strategies should also focus on patients' QoL, psychological well-being, daily lives, physical functioning, and their ability to work.

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Declarations

Conflict of Interest. The authors disclose the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Luca Stingeni has acted as Principal Investigator, speaker, and board member for AbbVie, Almirall, Amgen, Bristol Meyer Squibb, Eli Lilly, Janssen, Leo Pharma, Novartis and Sanofi. Maria Concetta Fargnoli has served on advisory boards, received honoraria for lectures and/or research grants from Amgen, Almirall, AbbVie, Boehringer-Ingelheim, BMS, Galderma, Kyowa Kyrin, Incyte, Leo Pharma, Pierre Fabre, UCB, Lilly, Pfizer, Janssen, MSD, Novartis, Sanofi, Regeneron and Sun Pharma. Fabrizio Guarneri has served as advisory board member for Leo Pharma. Anna Balato has served as advisory board member, consultant and/or has received fees, speakers' honoraria or has participated in clinical trials for AbbVie, Almirall, Amgen, Boehringer-Ingelheim, BMS, LeoPharma, Eli Lilly, Incyte, Janssen, Novartis, Sanofi and UCB. Monica Corazza has acted as Principal Investigator, speaker, and board member for AbbVie, Almirall, Amgen, Janssen, Leo Pharma, Novartis and Sanofi. Anna Belloni Fortina has participated in advisory boards, acted as consultant and/or received fees from AbbVie, Amgen, Almirall, Sanofi Genzyme, Leo Pharma, Eli Lilly, Pfizer, Unifarco and Novartis. Piergiacomo Calzavara-Pinton served as advisory board member and consultant and has received fees and speakers' honoraria or has participated in clinical trials for AbbVie, Almirall, Leo Pharma, Cantabria, Galderma, Incyte, Janssen, Novartis, Biogen, Sanofi Genzyme, La Roche Posay, Naos, Boehringer-Ingelheim and Sun Pharma. Antonio Castanzo has served as advisory board member and consultant and has received fees and speakers' honoraria or has participated in clinical trials for AbbVie, Almirall, Amgen Leo Pharma, Lilly, Galderma, Incyte, Janssen, Novartis, Sanofi Genzyme, Boehringer-Ingelheim and UCB. Silvia Mariel Ferrucci has acted as Principal Investigator in clinical trials, Speaker and Member of Advisory board for: AbbVie, Amgen, Almirall, Bayer, Sanofi Genzyme, Leo Pharma, Eli Lilly, Pfizer, Unifarco and Novartis. Luigi Naldi has been consultant and speaker for AbbVie, Almirall, Boheringer Ingelheim, Bristol Myers Squibb, Janssen, Leo Pharma, Novartis and Sanofi. Giovanni Pellacani has served as advisory board member, consultant and investigator for: AbbVie, Allergan, Almirall, Amgen, Beiersdorf, Boheringer, Canfield, Difa-Cooper Ifc, Eli Lilly, Galderma, Janssen-Cilag, Krymi, Kyowa-Kirin, Leo Pharma, L'oreal, Mavig, Menarini, Pfizer, Pierre-Fabre, Sanofi, UCB and Viatris. Ketty Peris received grants from: AbbVie, Almirall, Lilly, Novartis and Sanofi; Advisory Board or consulting fees from: AbbVie, Almirall, Biogen,

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