Developments and challenges in dermatology: an update from the Interactive Derma Academy (IDeA) 2019

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Abstract The 2019 Interactive Derma Academy (IDeA) meeting was held in Lisbon, Portugal, 10–12 May, bringing together leading dermatology experts from across Europe, the Middle East and Asia. Over three days, the latest developments and challenges in relation to the pathophysiology, diagnosis, evaluation and management of dermatological conditions were presented, with a particular focus on acne, atopic dermatitis (AD) and actinic keratosis (AK). Interesting clinical case studies relating to these key topics were discussed with attendees to establish current evidence-based best practices. Presentations reviewed current treatments, potential therapeutic approaches and key considerations in the management of acne, AK and AD, and discussed the importance of the microbiome in these conditions, as well as the provision of patient education/support. It was highlighted that active treatment is not always required for AK, depending on patient preferences and clinical circumstances. In addition to presentations, two interactive workshops on the diagnosis and treatment of sexually transmitted infections/diseases (STIs/STDs) presenting to the dermatology clinic, and current and future dermocosmetics were conducted. The potential for misdiagnosis of STIs/STDs was discussed, with dermoscopy and/or reflectance confocal microscopy suggested as useful diagnostic techniques. In addition, botulinum toxin was introduced as a potential dermocosmetic, and the possibility of microbiome alteration in the treatment of dermatological conditions emphasized. Furthermore, several challenges in dermatology, including the use of lasers, the complexity of atopic dermatitis, wound care, use of biosimilars and application of non-invasive techniques in skin cancer diagnosis were reviewed. In this supplement, we provide an overview of the presentations and discussions from the fourth successful IDeA meeting, summarizing the key insights shared by dermatologists from across the globe.
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Introduction

The fourth Interactive Derma Academy (IDeA) meeting was held in Lisbon, Portugal, 10–12 May 2019, with dermatologists from Europe, the Middle East and Asia in attendance. Over three days, presentations on important issues relating to the diagnosis and treatment of acne, atopic dermatitis (AD) and actinic keratosis (AK), and additional presentations summarizing current challenges in dermatology, were delivered. Interesting clinical cases relating to these topics were also discussed to demonstrate current evidence-based best practices and treatment options. In addition, two interactive workshops were conducted on the diagnosis of sexually transmitted infections/diseases (STIs/STDs) presenting to the dermatology clinic, and the possibilities of current and future dermocosmetics. Here, we provide an overview of the presentations and discussions from the successful IDeA 2019 meeting.

Acne

Low adherence to treatment regimens: Falk Ochsendorf

Low adherence to acne treatments is associated with poor outcomes.[1] Adherence is determined by: quality of physician-patient relationship, patient understanding of treatment and pathology, and ease of treatment.[2-6] Evidence suggests that interventions focusing only on single aspects of disease management, such as information sharing with the patient, motivation of the patient or provision of extra patient support, are not associated with large improvements in adherence.[7]

Physicians should be aware of non-adherence and how this can be improved and/or prevented, including selecting effective, tolerable compounds as part of a simple treatment regimen,[8] selecting the patient's preferred topical vehicle and developing good physician–patient relationships with scheduled return visits. For example, improved treatment adherence was observed with once-daily combined clindamycin phosphate 1.2%-tretinoin 0.025% gel compared with separate daily applications of clindamycin phosphate gel 1% and tretinoin cream 0.025% (88% vs. 61%).[8] Further, patient adherence can be improved by asking three questions at first contact: 'How should therapy be applied?', 'How often should therapy be applied?' and 'What should be done in case of problems?'.[9,10]

Antibiotic resistance: Julien Lambert

Antibiotics (ABs) targeting *Cutibacterium acnes (C. acnes;* formerly *Propionibacterium acnes)* are impacted by microbial resistance, necessitating a change in attitude towards their use in acne.[11,12] Physicians should balance the needs of individual patients with public health concerns as the consequences of AB resistance extend beyond acne treatment, impacting other skin bacteria and the entire human microbiota.[12,13] AB resistance also affects clinical response in acne, leading to a reduction in and/or absence of response, and/or relapse,[12,13] as observed in the decreased efficacy of topical erythromycin over time.[14] Limiting the use of ABs in acne therapy has therefore been suggested,[12,15] particularly as *C. acnes* is only one of four pathogenic factors (excess sebum production, abnormal desquamation, *C. acnes* colonization and inflammation)[15,16]; thus, its elimination does not cure the condition. With this in mind, guidelines have provided recommendations for the use of ABs in acne management.[17-19]

Guidelines recommend that topical ABs are not used as monotherapy, with combination treatment (topical retinoids and antimicrobials) endorsed to address three of the four major pathogenic factors in acne.[18-21] Retinoids normalize desquamation and facilitate entry of the AB into the pilosebaceous duct, while antimicrobials target *C. acnes* and reduce inflammation.[20-22] The combination of clindamycin/tretinoin significantly reduced the presence of *C. acnes* after 6 weeks of treatment compared with clindamycin alone, including in patients with highly resistant *C. acnes*.[20] Furthermore, unlike clindamycin monotherapy,[23] clindamycin/tretinoin treatment has not been associated with an increase in clindamycin-resistant *C. acnes*.[24]

Other recommendations include avoiding using topical ABs as maintenance therapy,[19] and restricting use of oral ABs in acne.[12]

While useful in the treatment of severe acne, oral ABs are not recommended as monotherapy,[19] or for concurrent treatment with topical ABs.[12] Rather, oral ABs should be combined with topical retinoids and/or benzoyl peroxide (BPO) for involved areas.[12] Additionally, use of oral ABs should be limited to 3–4 months due to the risk of antimicrobial resistance at other body sites.[12]

Evaluation of treatment efficacy: Giuseppe Micali

At present, there is a lack of standardized methods for evaluating treatment efficacy in acne, with at least 25 grading systems developed to date.[25-28] Current clinical evaluations include lesion counts,[29] global severity grading and comprehensive acne severity system (CASS) assessment,[30] which have limitations. For example, lesion counts are restricted by subjective evaluation,[31] and global severity grading cannot estimate the effect of treatment on individual lesions.[32] Further, global severity grading is influenced by the presence of a single lesion of the highest grade.[33] In addition, CASS assessment is thought to be imprecise and requires investigator global assessment training to improve reliability. In contrast, use of digital systems in instrumental evaluations may allow more objective evaluation of acne lesions, and movement towards standardized therapeutic monitoring. Instrumental evaluations may include advanced digital photography and, to a limited extent, dermatoscopy and reflectance confocal microscopy.[25,34,35]

The role of the microbiome in acne: Harald Gollnick

Commensal microbiota inside the body and on the surface of the skin are typically balanced and in a healthy state;[36] however, cutaneous dysbiosis can induce immune activation, leading to inflammation.[37,38] It can also allow non-commensal bacteria to colonize the skin and cause infection.[39]

C. acnes is considered the ‘gatekeeper’ of the facial microbiome, colonizing the lower part of the follicular canal and interfollicular epidermis.[40-42] *C. acnes* strains comprise up to 90% of the facial microbiota;[43] however, certain strains or excessive numbers are associated with acne.[44,45]

Modulation of the microbiome therefore represents a novel treatment strategy for acne.[46,47] In particular, altering the composition of *C. acnes* strains on the skin, through topical application of strains that are capable of inhibiting pathogenic strains, could reduce inflammation. This is supported by a pilot study in which topical application of selected *C. acnes* strains over 5 weeks reduced non-inflamed lesions and improved comedone counts without causing irritation, flare-up or deterioration in inflammatory lesions.[47] Microbiome modulation also significantly reduced non-inflamed lesion counts in patients with acne after 42 days, despite a relative increase in *C. acnes* bacteria.[47] This confirms that downregulation of pathogenic *C. acnes* strains is possible through increasing the number of beneficial strains of *C. acnes*; however, it is not clear if continuous or intermittent treatment is necessary.

Figure 1 Clinical presentation of mild-to-moderate papulopustular acne in a 19-year-old patient.

Clinical cases

Harald Gollnick discussed several cases, covering aspects of diagnosis, treatment, psychological impact and therapeutic challenges associated with acne and acne-mimicking conditions. Furthermore, differential diagnoses were presented, such as syringomas, eruptive vellus hair cysts, facial sebocystomatosis and rosacea (including demodicosis and trombidiosis).

Falk Ochsendorf contributed a clinical case on the diagnosis and treatment of a 19-year-old female presenting with acne. This patient had suffered from acne since age 12, receiving no previous treatment aside from cosmeceuticals. The patient was diagnosed with mild-to-moderate papulopustular acne (with approximately 10–20 inflammatory lesions on the cheek; Fig. 1) and prescribed topical treatment. Treatment with a fixed-dose combination of topical BPO/retinoid (e.g. BPO/adapalene), BPO/clindamycin or retinoid/clindamycin (e.g. tretinoin/clindamycin) could be administered in-line with the latest guidance for the treatment of mild-to-moderate papulopustular acne.[19]

Giuseppe Micali discussed the diagnosis and treatment of a 16-year-old male presenting with an abrupt onset of intense itchy erythema of facial skin (Fig. 2a). This patient had a medical history of mild comedonal acne (previous 1 year) treated

Figure 2 Clinical presentation of acne and AD flare on the face (a) and body (b) of a 16-year-old patient.

with topical retinoids. In addition to an erythematous rash, comedones and papules were present on his face, as well as large eczematous lesions with oozing and crusting on his chest, upper back and shoulders (Fig. 2b). While side-effects from topical retinoid treatment were considered, diagnosis was established as acne and AD flare. AD and acne can coexist and flares of AD may occur in patients with acne.[48] The AD flare was treated with systemic antibiotics and a topical calcineurin inhibitor (TCI). Once improvement was achieved, topical combination therapy was initiated to treat acne.[19]

Atopic dermatitis

Is AD a single disease? Kilian Eyerich

Diagnosis of AD remains based on subjective criteria, including those proposed by Hanifin and Rajka (1980), the UK Working Party (1994) and the American Academy of Dermatology (2014).[49-54] Eczema and dermatitis are further classified into sub-categories/variants, such as nummular eczema, dyshidrotic eczema and chronic contact dermatitis. Recently, there has been movement towards 'endstream oriented therapy', in which eczema is classified as a type 2 immune driven disease.[55]

T-helper type 2 (Th2) immunity is stimulated by specific antigens. Parasites, environmental antigens and humoral immunity can trigger the Th2-mediated pro-inflammatory response, initiating release of serum cytokines (interleukin [IL]-4, IL-5 and IL-13).[56-58] Approaches to stratifying AD use serum cytokine levels,[59] genetic markers,[60] microbiome analyses[61] and patient ethnicity.[62,63] Although AD is highly heterogeneous (Fig. 3)[64], four main endotypes exist: genetic immunology type, non-genetic immunology type, genetic barrier type and non-genetic barrier type, which all result in exaggerated Th2 immunity.[65]

Skin microbiome in health and disease: Claudia Traidl-Hoffmann

There is increasing awareness of a role of the microbiome in skin diseases.[66,67] The interplay between chemical, physical and immunological factors and microbial barrier function is

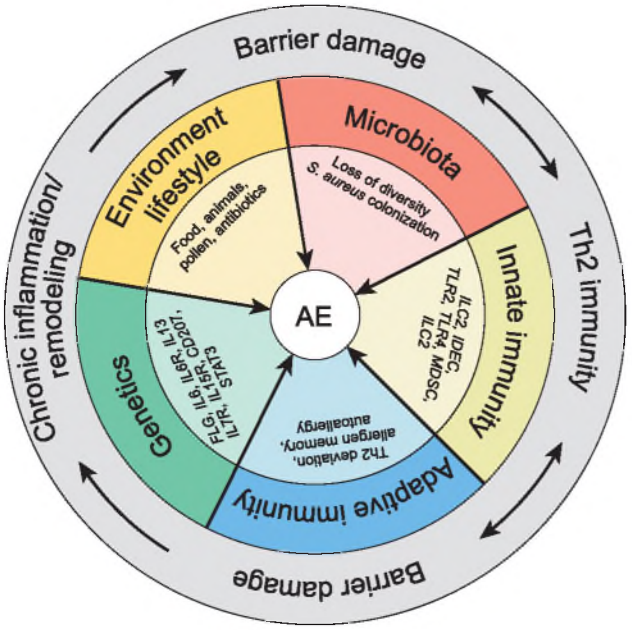

Figure 3 The complex pathophysiology of AD, involving genetic traits, environmental influences and changes in immunity that result in epidermal barrier damage and Th2-driven immune response.[64] Reprinted from Trends in Immunology, 36(12), Eyerich K, Eyerich S, Biedermann T, The multi-modal immune pathogenesis of atopic eczema, pp 788-801. Copyright 2015 with permission from Elsevier.

complex,[68] but can potentially be explained by the biodiversity hypothesis. This hypothesis proposes that contact with natural and traditional environments enriches the human microbiome,[69] whereas urbanization and global warming,[69] contact with household animals[70] and consumption of fast food[71] reduce biodiversity. A diverse diet and breastfeeding during infancy may also increase microbiome diversity.[72,73] However, research is needed to establish the direction of causal relationships between the microbiome and skin disease, i.e. is the microbiome affected by skin disease, or does the microbiome affect skin disease?[74,75]

In AD, the expression of genes involved in skin barrier function (claudin [CLDN]1, CLDN4, filaggrin [FLG] and tight junction protein [TJP]1) is reduced, with a negative correlation between *Staphylococcus aureus (S. aureus)* frequency and expression of CLDN4/5 and TJP1/2.[76] Additionally, skin pH is higher in patients with AD compared with healthy individuals, which favours growth of *S. aureus* and may impact microbiome diversity.[77,78] In addition, skin pH-dependent *S. aureus* abundance can serve as a predictor for increasing AD severity. Thus, the microbiome can also serve as a diagnostic and predictive tool.[74,79] Novel therapies promoting microbiome diversity are in development, including dual spleen tyrosine kinase (Syk)/Janus kinase (Jak) inhibitor ASN002, which reduces *S. aureus* frequency and Eczema Area and Severity Index (EASI) score.[80,81]

Itch: pathophysiology and treatment: Sonja Ständer

Pruritus (itch) is a hallmark of AD that severely impacts quality of life;[82] it is usually associated with flare-ups,[83] but may remain after relief from eczema. Pruritus is mediated by multiple cutaneous C Fibre classes, which may be histamine-sensitive or non-histaminergic.[84]

Long-standing pruritus can lead to cutaneous structural and functional neuroanatomical changes.[85,86] This was recently shown using a model of selective non-histaminergic C Fibre activation, in which neuronal sensitization and more intense pruritus were experienced by patients with AD versus healthy controls.[87] Patients with AD are also hypersensitive to mechanical stimuli, clinically known as alloknesis or worsening of itch by scratching.[88] Interestingly, most patients with AD show regular response to pain stimuli.[87]

A recent paper summarized therapeutic recommendations of 14 AD guidelines from Europe, North America, the Asia-Pacific region, and Africa.[89] While most guidelines recommend first-generation (sedating) antihistamines as anti-pruritic therapies for sleep disturbances (exceptions: German, European and Japanese guidelines), there is limited evidence that second-generation (non-sedating) antihistamines improve pruritus in AD. A recent Cochrane systematic review of 25 studies (representing 3285 patients) found no evidence that H1 antihistamines were more effective than placebo as an 'add-on' therapy for eczema, with the exception of fexofenadine, which appeared to lead to a small improvement in patient-assessed pruritus.[90] European AD guidelines discuss, but do not recommend routine treatment of itch with opioid receptor antagonists (naltrexone or nalmefene), or a selective serotonin receptor inhibitor (paroxetine).[89,91]

Based on expert opinion, therapies such as aprepitant, naltrexone (oral), naloxone (i.v.), selective serotonin reuptake inhibitors (e.g. paroxetine, fluvoxamine), gabapentin, pregabalin, cyclosporine and methotrexate, are effective in relieving pruritus associated with AD, and some are recommended in treatment guidelines.[92,93] In addition, topical transient receptor potential cation channel subfamily M member 8 (TRPM8) agonists have been considered for the treatment of pruritic skin. In a randomized, double-blind, pilot study, a cooling compound containing two TRPM8 agonists ameliorated severe pruritus and improved quality of life in patients with dry, pruritic skin compared with vehicle.[94]

Importantly, treatment for pruritus should be started early, as prevention of neuroanatomical changes and neuronal sensitization is essential. It is also necessary to treat pruritus for a sufficient duration (several weeks) to impact the central nervous system.

Sensitive skin – pathomechanism and management: Thomas Luger

Sensitive skin is a disturbing skin condition occurring primarily on the face. Current treatments ameliorate dysfunction of epidermal barriers (e.g. driven by microbial or physical factors, innate immunity, adaptive immunity and cutaneous nerves). These treatments include emollients (the mainstay treatment) and topical anti-inflammatory therapies, such as TCI and topical corticosteroids (TCS).[91] However, TCS are not recommended for the treatment of sensitive skin areas or long-term management,[91] and their use is associated with limitations, including skin barrier impairment, skin atrophy, increased risk of skin infections, tachyphylaxis and corticophobia.[95-98] Furthermore, use of TCS on sensitive skin areas is a concern among patients.[99] European AD guidelines therefore recommend TCI, particularly pimecrolimus, for the treatment of sensitive skin areas, such as the eyelid, perioral skin and genital area.[91]

TCI are fast and effective anti-pruritic agents, as demonstrated in adults and children.[93] Tacrolimus and pimecrolimus have dual mechanisms of action, targeting both nuclear factor of activated T cells[100,101] and the transient receptor potential cation channel subfamily V member 1,[102] to reduce inflammation and relieve itch.[91] Importantly, there is no evidence of impairment of epidermal barrier function or skin atrophy with TCI, nor a causal link between TCI and lymphomas/skin tumour occurrence.[98,103-106] The absence of skin atrophy with TCI favours their use over TCS for topical long-term management of AD.[91]

Long-term treatment with pimecrolimus was considered both effective and safe in a trial involving 2418 infants with mild-to-moderate AD, with >85% of patients cleared/almost cleared of AD overall and >95% of patients cleared/almost cleared of facial AD after 5 years of treatment.[103] Furthermore, pimecrolimus had a substantial steroid-sparing effect, with no evidence of impairing the developing immune system.[103] It is therefore recommended in children and for the treatment of facial lesions.[91] Pimecrolimus has demonstrated benefits over both TCS and tacrolimus. Firstly, pimecrolimus is an alternative to TCS for the treatment of sensitive skin areas,[107] and has been shown to reduce TCS-induced skin atrophy compared with vehicle after six weeks in a double-blind study.[108] In children, compared with tacrolimus 0.03% ointment, pimecrolimus 1% cream led to a greater reduction from baseline in body surface area affected by AD in the head/neck region after 43 days of treatment (pimecrolimus: 53.7%; tacrolimus: 34.9%).[109] Pimecrolimus 1% cream was reported to cause fewer application-site reactions than tacrolimus 0.03% ointment after 4 days, including itching and erythema/irritation, although the incidence of warmth, stinging and burning sensation was similar in both groups.[109] Additionally, pimecrolimus has the potential to increase adherence to treatment as it is non-greasy, thus preferred over tacrolimus.[109]

Hot topic: Education of patients with AD and parents – an updated review of successful programmes: Matthias Augustin

Holistic programmes that aim to maintain the skin barrier and a high level of treatment compliance in AD are needed. The World Health Organization advocates patient-centred care, with joint decision-making between physicians and patients.[110] The rationale for educational interventions for AD encompasses the complexity of AD treatment,[111] high volume of information for patients[112] and association between low adherence and poor outcomes.[113,114] The main elements that should be covered by educational programmes were highlighted, including medical, nutritional and psychological issues,[115] as well as the importance of patient motivation.[116]

In a systematic review, it was unclear whether educational interventions improve health-related quality of life in people with chronic inflammatory skin conditions.[117] However, tentative conclusions suggested face-to-face group sessions and text messages may be effective, and that delivery of educational programmes by a multidisciplinary team over six weeks to three months may be associated with positive outcomes.[117] Although guidelines, expert consensus papers and patient groups propose standardized interventions for patients with chronic AD, in most countries, few patients receive a structured educational programme due to a lack of financial support/resources.

It was agreed that patients should be well informed about their disease and treatment, and most attendees thought that there was an excellent level of evidence to support the benefits of educational programmes in AD. An interactive survey showed that attendees had a range of experience with educational programmes in AD (Fig. 4a). In this survey, 94% of responses indicated that education was provided for at least some of their patients with AD, with 34% stating that education is provided on a regular basis for all patients (Fig. 4b). Most attendees (68% of responses) stated that a high proportion (>50%) of their patients with AD received therapeutic education, with 42% indicating that >80% of patients received this education (Fig. 4c). Attendees suggested that, if it was offered free of charge, there would be moderate uptake by their patients of an evidence-based educational AD programme (Fig. 4d). Most attendees (75% of responses) indicated they had not used digital technology for educating patients with AD (Fig. 4e), with 19% stating use with some patients and only 5% stating use with all patients.

Hot topic: Education of patients with AD and parents – update on new AD treatments: Thomas Luger

Atopic dermatitis treatments may target phenotypes or genotypes of AD and a personalized approach is required. An overview of treatment milestones was provided (Fig. 5), with key clinical data on novel therapies presented.

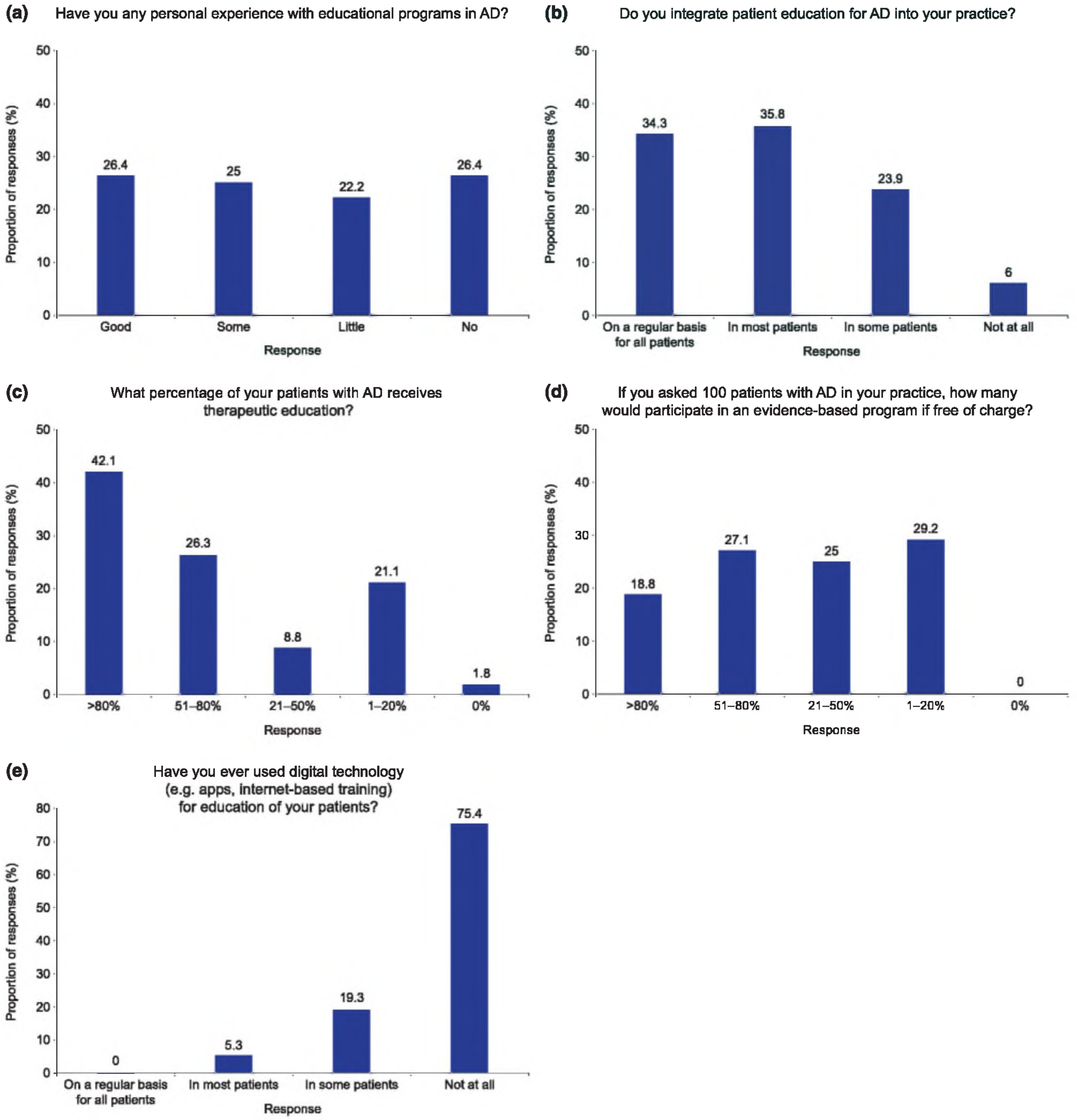

Figure 4 Assessment of experience with educational programmes in AD via interactive survey (a–e) of attendees.

In CHRONOS (a phase 3 study in adults), the monoclonal antibody (mAb) dupilumab, which targets IL-4 and IL-13, was reported to be effective in moderate-to-severe AD, with significantly more patients who received dupilumab plus TCS achieving the co-primary endpoints (Investigator's Global Assessment [IGA] score of 0/1 and EASI 75% improvement [EASI-75] from baseline) after 16 weeks than patients who received placebo plus TCS.[118] In a phase 2 dose-finding study of tralokinumab, another mAb, higher doses (150 and 300 mg) demonstrated meaningful improvements compared with placebo across clinical and patient-reported outcomes for eczema and pruritus.[119] Similarly, the first-in-class anti-IL-17C mAb MOR106 demonstrated

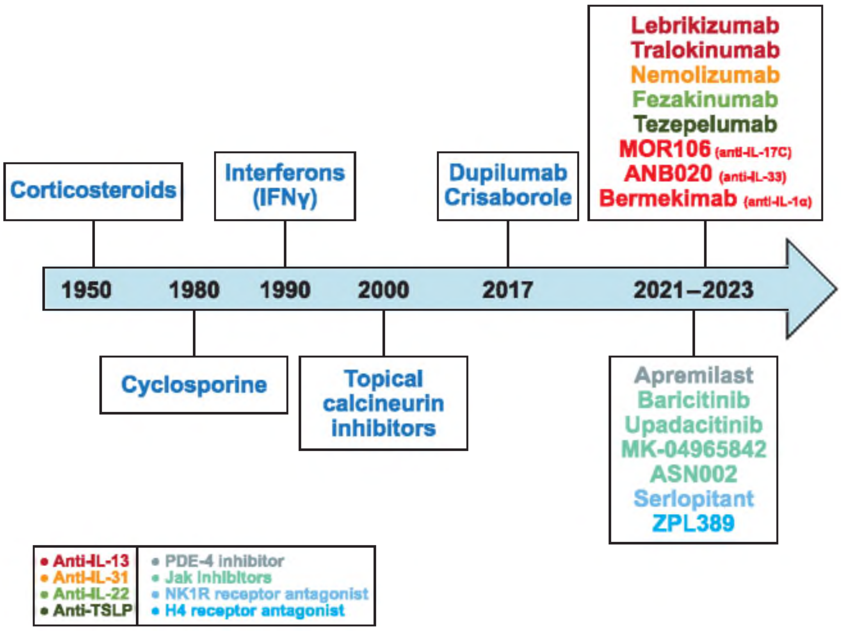

Figure 5 Overview of AD treatment milestones to date. H4, histamine H4; IFNy, interferon-gamma; IL, interleukin; Jak, Janus kinase; PDE-4, phosphodiesterase-4; NK1R, neurokinin 1 receptor; TSPL, Thymic stromal lymphopoietin.

promising improvements in AD skin efficacy parameters (EASI-50 and Scoring Atopic Dermatitis) vs. placebo in a phase 1 dose-finding study.[120] Further, in a phase 1 safety and tolerability study of bermekimab (anti-IL-1a mAb) in moderate-to-severe AD, reductions in itch and pain were reported with higher doses of bermekimab (400 mg vs. 200 mg).[121]

In addition to mAbs, Jak inhibitors, neuropeptides, phosphodiesterase-4 inhibitors (PDE-4i) and aryl hydrocarbon receptor (AhR) agonists are in development for use in AD. Jak inhibitors block multiple AD pathways, but baricitinib has been associated with numerous side-effects, such as headache, increased blood creatinine and creatine phosphokinase levels, and nasopharyngitis.[122] A randomized, double-blind phase 2 trial of baricitinib (a Jak-1 and Jak-2 inhibitor) reported improvements in eczema and itch vs. placebo in moderate-to-severe AD.[122] Additionally, in a dose-finding study, twice-daily application of a topical Jak inhibitor, ruxolitinib 1.5% cream, was shown to be well tolerated and to provide greater relief from itch compared with vehicle within 36 hours of initiation of treatment.[123] Neurokinin 1 receptor agonists are currently undergoing clinical investigation, with a phase 2 trial in chronic pruritus reporting serlopitant to be significantly more efficacious than placebo in reducing pruritus when administered at 1 mg and 5 mg once-daily.[124] Crisaborole, the first commercially available PDE-4i,[125] has been reported to be effective in mild-to-moderate AD, significantly and rapidly improving eczema and pruritus compared with vehicle in two double-blind phase 3 studies involving more than 1500 patients aged ≥ 2 years.[126] In a phase 2 dose-finding study, Tapinarof 1% cream (AhR modulating agent) demonstrated efficacy in AD, in terms of patients achieving EASI-75, compared with vehicle.[127] Transplantation of the topical microbiome; for example, of antimicrobial coagulase-negative staphylococci reduced *S. aureus*, is also a potential novel therapeutic strategy for AD.[128]

Actinic keratosis

Review of recent publications on AK – discussion of clinical importance: Thomas Dirschka

A new scoring system, the actinic keratosis area and severity index (AKASI), has been proposed for assessing the severity of AK on the head.[129] AKASI is an objective measure for AK severity and the risk of squamous cell carcinoma (SCC).[130] AK lesions show varying patterns in basal growth, including crowding, budding and papillary sprouting of cells in the basement of the epidermis.[131] Basal proliferation in AK is linked to SCC.[132]

Field-directed treatments are essential for AK and should be applied not only to visible lesions, but also the surrounding sun-exposed area.[133,134] At present, therapy-resistant AK lesions remain enigmatic and require further research. Efforts must be taken to investigate the epidermal/dermal/inflammatory cross talk, and discussions regarding the benefits of sunscreen will continue.

Hard to treat AK – discussion of location and lesion characteristics: Girish Gupta

In some cases, active treatment of AK is not required; instead, primary care monitoring of sun-exposed areas, coupled with prevention and self-care advice may be all that is needed. Ultimately, the most appropriate management strategy should be determined by patient preferences and clinical circumstances.[135] Where treatment is indicated, there should be an induction phase followed by a maintenance phase. For lesions on the scalp/face and limbs/trunk, recommended induction therapies include 5% 5-fluorouracil cream, 3.75% imiquimod cream, photodynamic therapy (PDT) and 3% diclofenac in 2.5% hyaluron gel.[136] Maintenance treatments for lesions on the scalp/face include 5% 5-fluorouracil cream and PDT, with the addition of 0.5% 5-fluorouracil cream combined with 10% salicylic acid for lesions on the limbs/trunk.[136] When used as maintenance treatment, 5% 5-fluorouracil cream can be used three times weekly over a longer period of time (3–6 months). Although there is no evidence that 5% 5-fluorouracil cream extends time to first keratinocyte carcinoma, it has been shown to decrease the risk of SCC by 75% vs. placebo.[137] Further evidence is required to optimize AK treatment strategies, particularly in organ transplant recipients, who are considered very high risk patients. Oral retinoids have a poor evidence base, comprising mainly of case series with no clear endpoints and short-term follow-up. Additionally, combination therapy with oral retinoid and oral nicotinamide requires further investigation.

AK lesions of particular risk – discussion on detection of 'risky' AK: Giuseppe Micali

AK may develop into non-melanoma skin cancer and is considered a precursor to SCC. Evidence suggests that, in addition to the classical stepwise progression from AK I to AK II and AK III, invasive SCC (iSCC) may arise from direct invasion of proliferating atypical basaloid keratinocytes that are limited mostly to the epidermal basal layer (AK I).[138] The depth of follicular extension of atypical keratinocytes in AK correlates with the depth of invasion of associated SCC,[139] and there is a predictive relationship between the number of AKs and the risk of SCC.[140]

Two AK clinical cases were presented. The first concerned the diagnosis and treatment of a 68-year-old male with three AK lesions >1 cm^2 ('AK patch') (Fig. 6a). This patient's medical history included renal transplantation and AK previously treated with cryotherapy and curettage. The chosen treatment was two two-week cycles of imiquimod 3.75% cream, with clearance of lesions observed 15 days after the end of treatment (Fig. 6b). While the majority of patients with AK are treated with PDT, this case highlights that other treatments may be effective in transplant patients. It was noted that in renal transplant patients, presence of a defined skin site with an AK patch >1 cm^2 results in an approximate 20-fold increased risk of development of SCC compared with skin sites without this feature.[141] Furthermore, patients with ≥3 AK patches are six times more likely to develop SCC within an 18-month period than those with <3 AK patches.[141]

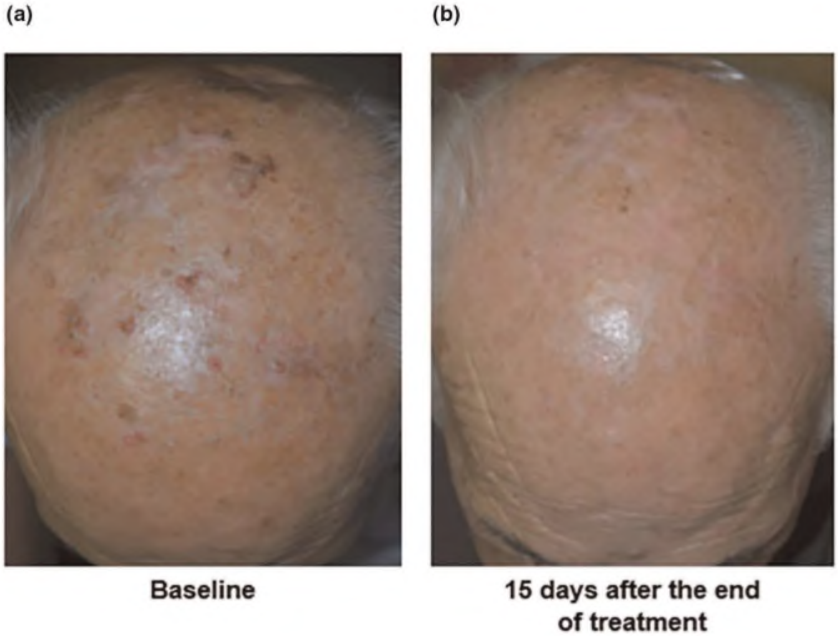

Figure 6 Presentation of AK patches in a 68-year-old patient (a) and following treatment with imiquimod 3.75% cream (b).

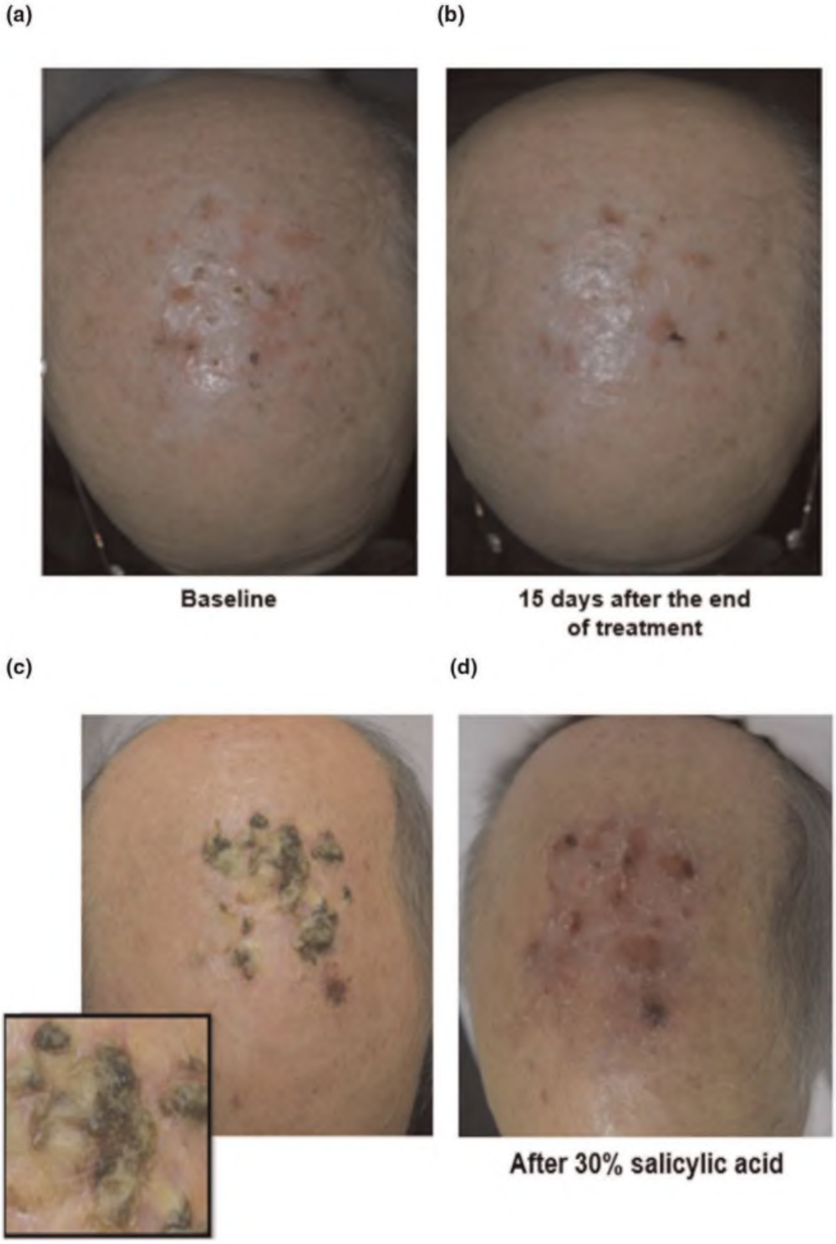

Figure 7 Initial presentation of AK lesions in a 76-year-old patient (a) and following treatment with imiquimod 3.75% cream (b). One year later, hyperkeratotic lesions presented (c) and were treated with 30% salicylic acid ointment (d).

The second clinical case referred to the diagnosis and treatment of a 76-year-old male presenting with AK lesions (Fig. 7a). His medical history revealed AK lesions that had returned following PDT one year prior, and was otherwise unremarkable. Following initial treatment with two two-week cycles of imiquimod 3.75% cream, some lesions remained, as observed 15 days after the end of treatment (Fig. 7b). One year later, the patient presented with hyperkeratotic lesions (Fig. 7c), which were treated with 30% salicylic acid ointment. After one week (Fig. 7d), two biopsies ruled out AK and iSCC, and allowed diagnosis of erosive pustular dermatitis of the scalp. This skin disorder is rare and occurs mainly in elderly people with sun damaged skin; it is characterized by pustular and crusted lesions. Several factors that trigger this disorder have been reported, including use of topical medications (fluorouracil, imiquimod, ingenol mebutate and tretinoin), surgery, cryotherapy, radiotherapy, and PDT.[142-147]

Overview of workshops

Sexually transmitted diseases

Colm O'Mahony shared his experiences of daily practice in a UK STI/STD clinic, covering the diagnosis and treatment of STIs/STDs. The importance of physician-patient communication and managing clinical mistakes (e.g. misdiagnosis or misinterpretation of laboratory results) was highlighted.

Giuseppe Micali discussed current diagnostic techniques for common STIs/STDs, including anogenital warts, molluscum contagiosum, herpes simplex, phthiriasis and scabies. The use of dermoscopy and/or reflectance confocal microscopy in the diagnosis of these diseases, and some STIs/STDs with doubtful clinical presentation, was discussed.

Mihael Skerlev discussed the diagnosis and treatment of external genital warts. Guidelines recommend the following patient-applied therapies: imiquimod 3.75% or 5% cream, podofilox 0.5% solution or gel, or sinecatechins 15% ointment.[148] Imiquimod 5% cream in combination with ablation methods (sequential therapy) has been shown to reduce the recurrence of successfully treated anogenital warts[149] and may represent a practical treatment approach. Although treatment options are available for external genital warts, management is difficult and sometimes frustrating; therefore, updated treatment algorithms may be helpful. Preventable measures (human papillomavirus vaccination)[150,151] also exist and should be promoted.

The future of dermocosmetics

Elena Araviiskaia discussed the uses and applications of modern dermocosmetics, considered an important part of dermatological patient management. This included details on a novel face compact cream containing salix alba and decanediol, which provides effective coverage of acne, and is non-comedogenic, well perceived and well tolerated by patients.[152] Additionally, new areas of research in this field were outlined, including modulation of the skin microbiome,[153,154] prevention (e.g. of the development of AD[155] or relapse of acne[156]), protection from the external environment,[157,158] nanotechnologies (e.g. for acne treatment)[159,160] and new vehicles (e.g. lasers) for drug delivery.[161,162]

Daniela Pinto presented evidence in support of interventions that alter the human microbiome, representing novel diagnostic and therapeutic approaches for the treatment of skin and scalp conditions, as the microbiome is involved in scalp diseases (e.g. hair growth disorders).[163-165]

Firas Al-Niaimi discussed the use of botulinum toxin (BTX) in non-cosmetic dermatology. Use of neurotoxins in medicine is increasing. As such, dermatologists should expect an increasing number of enquiries from patients regarding BTX. BTX has multiple non-cosmetic uses, including prevention of hypertrophic scars, amelioration of flushing in rosacea, improvement of localized pruritic dermatoses, and treatment of dermatoses aggravated by sweating.[166,167]

Challenges in dermatology

Laser in dermatology: Firas Al-Niaimi

The use of laser has enormously contributed to dermatology, with different types of lasers providing a range of clinical benefits. Vascular lasers target haemoglobin in capillary malformations, venous malformations, hemangiomas, spider angioma and angiokeratomas.[168] They may also be used to treat non-primary vascular conditions, such as inflammatory acne[169] and inflammatory rosacea.[170] Pigment-specific lasers also have a number of uses, including the treatment of Naevus of Ota. Similarly, ablative lasers, which target water, can treat a number of dermatological conditions, such as sarcoidosis and angiofibromas.[171,172] Furthermore, use of laser-assisted drug delivery,[173] and of fractional lasers to treat scarring, is becoming more prominent in dermatology.

Atopic eczema – new hope for a complex disease: Johannes Ring

In addition to topical dermatotherapy (skin care with emollients), topical anti-inflammatory agents are the cornerstone of proactive, long-term treatment of atopic eczema.[91,93] Ultraviolet (UV) therapy also has anti-inflammatory and anti-pruritic effects.[174,175] Despite the availability of these options, the appearance of targeted biologics against mediators of the Th2 inflammatory response (e.g. IL-4, IL-13) offer new hope for the treatment of atopic eczema.[118,119,176]

Antiseptics and biofilms in wound care: Stan Monstrey

The physiological and pathophysiological principles behind wound healing, and relevant clinical procedures to facilitate the wound healing process, were described. This included details on enzymatic debridement, restoration of moisture balance and infection prevention (through use of antimicrobials, antiseptics and protease inhibitors).

Povidone-iodine (PVP-I), a topical antimicrobial, has a broad spectrum of activity, providing protection from bacteria, viruses, fungi, spores, protozoa, and amoebic cysts.[177] Furthermore, unlike other antiseptics, no acquired resistance or cross-resistance to PVP-I has been reported.[178] PVP-I dressings have been shown to be more effective than silver dressings in the disruption of chronic wound biofilms,[179] which develop as a consequence of the bacterial life cycle (during the multicellular life phase, bacterial cells are sessile and exist as a biofilm).[180]

Biologics vs. biosimilars in the treatment of psoriasis: Matthias Augustin

Biosimilars registered by authorities (e.g. the European Medicines Agency[181] and US Food and Drug Administration[182]) for psoriasis are well-controlled and show substantial similarity to biologics.[183,184] There is currently no evidence to contraindicate the use of biosimilars in psoriasis.[185] Despite this, potential safety issues associated with biosimilars should be considered in real-world care and post-marketing surveillance undertaken,[186] with potential negative expectations of the patient (nocebo effect)[187] managed. Negative expectations can be avoided by providing sufficient patient information[188] and avoiding uncontrolled switches.

Novel non-invasive techniques in the diagnosis of skin cancers: Caterina Longo

Real-world cases were used to demonstrate current imaging and screening techniques for diagnosing skin cancers, including digital dermatoscopy and confocal microscopy. Digital dermatoscopy is widely used, and can efficiently compare images to detect changes over time in an individual.[189] Confocal microscopy is useful for diagnosing melanoma and basal cell carcinoma.[190,191] It may also be used to make accurate skin cancer diagnoses in difficult cases.[192]

Conclusions

During the IDeA 2019 meeting, the latest developments and challenges relating to the pathophysiology, diagnosis, evaluation and management of dermatological conditions (including acne, AD and AK) were presented and discussed, and clinical implications noted. Presentations reviewed current treatments, potential therapeutic approaches and key considerations (e.g. antibiotic resistance, selection of appropriate maintenance therapy, recognition of hard to treat lesions) in the management of each condition, as well as discussing the importance of the microbiome in dermatological conditions and of patient education/support. In the management of AK, it was highlighted that active treatment is not always required, depending on patient preferences and clinical circumstances. In addition to the presentations on acne, AD and AK, the diagnosis and treatment of STIs/STDs and the future of dermocosmetics were discussed. Several challenges in dermatology were also reviewed.

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