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ORIGINAL RESEARCH

Management of Patients Affected by Moderate-to-Severe Atopic Dermatitis with JAK Inhibitors in Real-World Clinical Practice: An Italian Delphi Consensus

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ABSTRACT

Introduction: Several systemic therapies have been approved for the treatment of severe AD. In particular, Janus kinase inhibitors (JAKi), including abrocitinib, baricitinib, and upadacitinib, recently received approval for the treatment of patients with severe AD after being evaluated in several clinical trials. However, a few concerns have been raised regarding their long-term safety and the management of these drugs in real-world clinical practice. In this article we described the results of a Delphi consensus aimed at describing the knowledge

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on JAKi and focusing, in particular, on providing clinical recommendations for dermatologists in daily practice regarding the use of these drugs.

Methods: Twelve Italian dermatologists reviewed the most recent literature regarding the efficacy and safety profiles of JAKi and proposed 24 statements.

Results: Agreement was reached for statements focusing on three main topics: (1) place in therapy of JAKi in patients with moderate-to-severe AD; (2) effectiveness and safety of JAK inhibitors in different phenotypes; (3) different approaches to the management of patients treated with JAKi in clinical practice. The panel proposed several recommendations regarding all the statements.

Conclusion: Given the wide use of JAKi in clinical practice, it is crucial to establish a specific follow-up for each patient's phenotype in order to achieve the best possible clinical outcome and minimize potential adverse events.

Keywords: Abrocitinib; Baricitinib; Consensus; Delphi; JAK inhibitors; Real life; Upadacitinib

Key Summary Points
JAK inhibitors are very effective drugs approved for the treatment of severe atopic dermatitis.
Given recent concerns emerging on the safety profile of JAK inhibitors, we carried out a Delphi consensus on the management of patients treated with these drugs in clinical practice.
A detailed medical history should be obtained from each patient before starting the JAK inhibitor.
JAK inhibitors could be prescribed to patients aged 65 years old or older in the absence of medical history or significant risk factors for cardiovascular disease and/or malignancies.

INTRODUCTION

Atopic dermatitis (AD) is one of the most common inflammatory skin diseases worldwide [1]. AD usually presents with eczematous patches and intense itch that can significantly impair patients' quality of life and productivity [1]. For decades, the management of AD has relied on topical emollients and corticosteroids for mild-to-moderate disease, while the systemic treatments approved in Europe were cyclosporine, methotrexate, azathioprine, and short courses of oral corticosteroids [2]. However, these treatments are unfeasible for the long-term management of this disease. During the last 5 years, several new drugs have been approved for severe AD. In particular, according to European guidelines, patients with severe AD should be treated with biological drugs (such as dupilumab and tralokinumab) or Janus kinase (JAK) inhibitors, such as abrocitinib, baricitinib, and upadacitinib [3]. JAK inhibitors have shown efficacy and safety in multiple phase III clinical trials and in a few initial real-world experiences [4–9]. However, a few concerns have been raised regarding their long-term safety and the management of these drugs in real-world clinical practice [7, 10]. Upadacitinib and abrocitinib are selective inhibitors of JAK-1, and they are each currently approved at two different dosages (30 mg and 15 mg for upadacitinib and 200 mg and 100 mg for abrocitinib). Baricitinib is an inhibitor of both JAK-1 and JAK-2, and it is approved for both AD and alopecia areata across two different dosages, 4 mg and 2 mg daily [11–13].

In this article, we describe the results of a Delphi consensus aimed at describing the knowledge on JAK inhibitors and focusing, in particular, on providing clinical recommendations for dermatologists in daily practice regarding the use of these drugs.

METHODS

The use of JAK inhibitors for the treatment of severe AD is increasing constantly. However, current guidelines do not often give specific

advice for the management of these patients, in particular regarding the place in therapy of JAK inhibitors and their role in difficult-to-treat subpopulations with multiple comorbidities and concomitant medications. We aimed to discuss current evidence on real-world data on JAK inhibitors, along with the clinical experience of a cohort of Italian dermatologists specialized in AD with at least 1 year of experience with JAK inhibitors. We performed a Delphi consensus on 24 statements in order to provide clinical guidance for dermatologists in routine practice. Delphi consensus represents a widely used method in medicine to generate consensus among experts when clinical guidelines are incomplete or lack enough clinical evidence.

A scientific committee of 12 Italian dermatologists reviewed the most recent literature on the efficacy and safety profiles of JAK inhibitors and generated 24 statements focusing on three main topics: (1) place in therapy of JAK inhibitors in patients with moderate-to-severe AD; (2) effectiveness and safety of JAK inhibitors in different patient subgroups; (3) different approaches to the management of patients treated with JAK inhibitors in a real-world clinical setting (Table 1).

During the first meeting in July 2023, all the panel members produced their opinions on the three identified topics. Then, all the opinions were rewritten into statements and shared with all the members. Each panelist was asked to evaluate the statement using a Likert scale (1–5; 1 = total disagreement; 5 = total agreement). In accordance with the recommendations of the Italian Ministry of Health, the consensus on the agreement was reached when $\geq$ 75% of voters expressed a vote equal to 4 or 5 [14]. After the first round, a second round of voting was performed after reviewing the statements that did not reach agreement. After the second round, the list of approved statements was completed.

Data were analyzed using descriptive statistics.

Institutional review board approval was exempted for this study as its procedures did not include human subjects and did not deviate from good clinical practice. All the involved dermatologists gave their approval for the study to be published. All the dermatologists who were part of the consensus were involved in the writing and/or revision of the manuscript. All the dermatologists who participated in the consensus were aware of the objective of the study, and they all knew that the manuscript will be published. The participants gave written informed consent.

RESULTS

Consensus on the agreement was obtained for 21 out of 24 statements during the first online meeting of the Delphi (Table 1). A consensus was not reached for three statements, two regarding the place in therapy of JAK inhibitors in some patient groups and one on the management of the treatment during concomitant infections. These three statements were modified according to the suggestions of the committee members and were re-presented during the second Delphi round. This time, consensus was obtained. Statements for each topic are discussed in the following sections.

Place in Therapy of JAK Inhibitors

European guidelines for the management of AD do not indicate which drug to prefer for different patient phenotypes (classic AD, predominant involvement of head and neck, hands AD, prurigo nodularis-like, generalized lichenoid, generalized inflammatory, erythroderma, and nummular eczema-like) as cyclosporine, interleukin (IL)-4/13 inhibitors, IL-13 inhibitors, and JAK inhibitors are equally recommended for the treatment of severe AD. During the last couple of years, several reports have evaluated the effectiveness of each treatment for different clinical phenotypes of AD [15–18]. In particular, Vittrup et al. [15] analyzed 347 adult patients treated with dupilumab, showing a lower effectiveness in those with predominant involvement of head/neck areas. Moreover, dupilumab showed lower effectiveness in patients with significant head, neck, and hand involvement, as recently described by Chiricozzi et al. [16]. On the other hand, baricitinib appears to be more effective in these areas, as described by Thyssen et al. [17]

Table 1 Summary of the Delphi consensus process for statements regarding the use of JAK inhibitors in clinical practice

Statement	Expert agreement first round (%)	Second round reformulation	Expert agreement second round (%)	Included in final recommendations
1 First-line JAK inhibitor may be preferred over biologic (anti-IL-4/13 or anti-IL-13) in the patient with moderate-severe atopic dermatitis with prevalent involvement of sensitive areas (e.g., face/neck, hands, genitalia)	100.00			Yes
2 First-line JAK inhibitor may be preferred over biologic (anti-IL-4/13 or anti-IL-13) in the patient with itch-NRS $\geq$ 7	58.34	JAK inhibitors may be preferred over biologics, even in the first-line setting, in the "itch-dominant" phenotype characterized by itch-NRS $\geq$ 7 and BSA between 10 % and 40%	100.00	Yes
3 JAK inhibitor may be a viable alternative, even in the first line, in patients with different clinical phenotypes of AD (nummular-like atopic dermatitis, prurigo nodularis-like, generalized inflammatory, psoriasiform)	83.33			Yes
4 JAK inhibitor may be preferred first-line over biologic (anti-IL-4/13 or anti-IL-13) in patients with concomitant psoriasis or an AD–psoriasis overlap pattern	83.33			Yes
5 JAK inhibitor may be a viable alternative, even first-line, in patients who also have atopic comorbidities (conjunctivitis, asthma, rhinitis)	41.66	JAK inhibitors may be a viable alternative in patients who also have atopic comorbidities (conjunctivitis, asthma, rhinitis)	83.33	Yes
6 In patients who have a history of recurrent conjunctivitis at baseline, JAK inhibitors may be preferred over dupilumab	100.00			Yes

Table 1 continued

Statement	Expert agreement first round (%)	Second round reformulation	Expert agreement second round (%)	Included in final recommendations
7 JAK inhibitors show faster action than biologics (anti-IL-4/13 or anti-IL-13) in all clinical subtypes of AD: improvement of at least 3 points on the NRS-pruritus scale compared with baseline (approx. 1 week versus 3–4 weeks)	100.00			Yes
8 JAK inhibitors show higher efficacy (compared with currently available biologics) in both the short and long term in clinical and real-world studies	75.00			Yes
9 Upadacitinib and abrocitinib achieve EASI 90 in a significantly higher proportion of patients as early as 16 weeks of treatment	91.67			Yes
10 JAK inhibitors have shown equal efficacy and rapidity both in first-line and after failure of biological drugs	91.67			Yes
11 Data from the first real-world experience showed no new safety signals regarding JAK inhibitors, and the rate of adverse events was comparable to that from the registrational clinical trials	100.00			Yes
12 Most adverse events associated with JAK inhibitors, both in clinical trials and in real-world in AD, have been mild to moderate and have not led to discontinuation of the drug	83.33			Yes
13 There are no contraindications to first-line prescription of JAK inhibitors to women of childbearing age	91.67			Yes

Table 1 continued

Statement	Expert agreement first round (%)	Second round reformulation	Expert agreement second round (%)	Included in final recommendations
14 There is no evidence of increased thrombotic risk in patients in treatment with JAK inhibitor and estroprogestin pill simultaneously in clinical trials	75.00			Yes
15 No significant increase in thrombotic risk was found in patients with AD who were treated with JAK inhibitor, compared with the general population	91.67			Yes
16 In clinical trials, JAK inhibitors show high levels of long-term clinical response maintenance, both in terms of EASI 75/90 and PROs	100.00			Yes
17 It is not mandatory to prescribe contraceptive therapy to a woman of childbearing age who begins therapy with a JAK inhibitor, although it is necessary to inform the patient about the potential teratogenic effect of the drug	100.00			Yes
18 In patients who smoke less than 5 cigarettes per day, in the absence of other risk factors, a JAK inhibitor may be prescribed for the treatment of atopic dermatitis	91.67			Yes
19 With regard to EMA recommendations, a patient at increased risk for cancer should be considered a patient who has already had cancer	100.00			Yes

Table 1 continued

Statement	Expert agreement first round (%)	Second round reformulation	Expert agreement second round (%)	Included in final recommendations
20 With regard to EMA recommendations, a patient at increased cardiovascular risk should be considered to be at risk of major CV events (heart attack, stroke)	75.00			Yes
21 In the patient who is to start JAK inhibitor, prior administration of herpes zoster vaccination is not mandatory	75.00			Yes
22 It is recommended to suspend the JAK inhibitor until the resolution of symptoms in case of infections requiring systemic antibiotic therapy	66.67	In case of concomitant infections, which do not require hospitalization, with fever and related symptoms (e.g., cough, dyspnea), it is advisable to suspend the JAK inhibitor until complete clinical resolution and, where applicable, until laboratory tests normalize	100.00	Yes
23 In case of major surgery, it is advisable to discontinue the JAK inhibitor 1 week before surgery and resume it 1 week later if there are no complications	75.00			Yes
24. When administering vaccines (excluding live attenuated virus vaccines), it is advisable to discontinue the JAK inhibitor 1 week before administration and resume it 1 week after	91.67			Yes

AD atopic dermatitis, *BSA* body surface area, *CV* cardiovascular, *EASI* Eczema Area and Severity Index, *EMA* European Medicines Agency, *IL* interleukin, *JAK* Janus kinase, *NRS* numerical rating scale, *PRO* patient-reported outcome

During the first Delphi round, agreement was reached for the statement 1 regarding the use of JAK inhibitors as first-line treatments in patients with severe involvement of difficult-to-treat areas (face/neck, hands, genitalia). No agreement was obtained in the first round for statement 2, which concerned the preferable use of JAK inhibitors over biologics in patients with severe itch. This statement was rewritten according to the members' suggestions, shifting the focus to the "itch-dominant" phenotype (patients with itch-NRS $\geq$ 7 and BSA up to 40%) [17], obtaining the agreement during the second Delphi round.

Consensus was also reached for statements 3 and 4 regarding the viable use of JAK inhibitors in patients with several AD phenotypes (including prurigo-like and nummular eczema-like AD) and those with concomitant AD and plaque psoriasis.

There was no agreement in the first round on statement 5, which suggested the possible use of JAK inhibitors as a first-line treatment in patients with atopic comorbidities (including asthma and allergic rhinitis). The statement was reconsidered after removing the words "first-line," and it was approved during the second round.

Statement 6, regarding the preferable use of JAK inhibitors compared with dupilumab in patients with a medical history of conjunctivitis, was approved on the basis of the available literature on the different safety profiles of these drugs.

Real-World Effectiveness and Safety of JAK Inhibitors

Ten statements were generated on this topic, and they all reached agreement during the first Delphi round. In particular, statements 7–10 - highlighted the high effectiveness profiles of all the approved JAK inhibitors, according to data from both clinical trials and real-world experience in terms of both clinical improvement and patient-reported outcomes (PROs) [4–9]. In particular, upadacitinib and abrocitinib have demonstrated high rates of EASI 75 and EASI 90 (reduction of at least 75% and 90% of the Eczema Area and Severity Index compared to baseline), along with rapid decrease of the itch and improvement in the quality of life, across all patient groups (biological-naive versus biological-experienced, different phenotypes) [4, 19]. Also, baricitinib has shown significant results in terms of EASI 75 and reductions of itch, particularly in the post hoc analysis of BREEZE-AD7 on the itch-dominant profile, showing the importance of a personalized approach in AD therapies [17,20]

Regarding safety, agreement was reached in statements 11–15 concerning the low rates of treatment-emergent severe adverse events (AEs) and AEs leading to discontinuation in clinical trials and real-world studies. There was also agreement on the absence of absolute contraindication to the prescription of JAK inhibitors in women of childbearing potential. The panel also agreed that, according to existing literature, no increase in the thrombotic risk has been demonstrated during treatment with JAK inhibitors in patients with AD, including women who were taking oral contraceptives [21].

Management of Patients Treated with JAK Inhibitors in Real-World Clinical Practice

Eight statements were proposed to the panel concerning the management of patients in real-life clinical settings, and seven of the statements reached agreement after the first Delphi round. In particular, the panel agreed that it is not mandatory to prescribe contraceptives to women of childbearing potential before starting the treatment after appropriate counseling.

Also, there was agreement regarding the definition of patients with a higher risk of cancer (including those with a medical history and/or a family history of neoplasm diagnosis at young age in two first-degree family members) and higher cardiovascular risk for major adverse cardiovascular events (MACEs; including those with diabetes, smokers, dyslipidemia, hypertension, obesity). In those cases, the anamnesis is fundamental. If the patient presents an increased risk for thrombosis, MACEs, or neoplasm, multidisciplinary management is very

important for modifying the variable risk factors inducing a risk reduction linked to the patient's comorbidities and/or predisposition [22].

The members agreed that anti-herpes zoster vaccination should not be mandatory before starting the treatment. Concerning concomitant vaccinations (excluding live vaccines) and major surgeries occurring during the treatment, the panelists agreed that it is appropriate to interrupt the JAK inhibitor 1 week before and restart 1 week after the procedure (statements 21 and 23). Finally, after the first Delphi round, no agreement was reached on statement 22 suggesting that in the case of concurrent infections requiring systemic antibiotic therapy, suspending the JAK inhibitor until the resolution of the symptoms was recommended. The statement was modified as follows: "In case of concomitant infections, which do not require hospitalization, with fever and related symptoms (e.g., cough, dyspnea), it is advisable to suspend the JAK inhibitor until complete clinical resolution and, where applicable, until laboratory tests normalize." In this form, this statement reached agreement during the second Delphi round.

DISCUSSION

Abrocitinib, baricitinib, and upadacitinib currently represent three of the six recommended systemic treatments for adult patients with severe AD, according to European guidelines [3]. No specific recommendation is given regarding which treatment to prefer for different patient phenotypes. According to our group, JAK inhibitors could be preferred in those with a high itch-NRS and with significant involvement of sensitive areas (head, hands, genitalia). This is consistent with data from scientific literature since upadacitinib and abrocitinib have both shown more effectiveness and rapidity in treating both AD and subjective symptoms, compared with dupilumab in both head-to-head clinical trials and real-world experience [4–6, 19, 23]. Network meta-analyses, despite their limitations, have also shown better outcomes for abrocitinib and upadacitinib compared with anti-IL-13 monoclonal antibodies [24, 25]. Moreover, a recent post hoc analysis of the BREEZE-AD7 clinical trial, a phase III study that compared the efficacy of baricitinib 4 mg plus topical corticosteroids (TCS), with baricitinib 2 mg plus TCS and placebo plus TCS, has shown best results on signs (EASI 75) and symptoms (variations of itch-NRS of at least 4 points) in a clinical AD phenotype characterized by mild-to-moderate lesions (BSA up to 40%) and severe itch (itch-NRS > 7) [17,20]. As already mentioned, this phenotype is known as "itch-dominant" [26] and appears to respond better to baricitinib compared with all the intention-to-treat population of the clinical trials.

Regarding different clinical phenotypes, recent real-world case series have shown the effectiveness of JAK inhibitors, and upadacitinib in patients with overlapping psoriasis and AD features [27]. This could probably be explained by a broader spectrum of actions of JAK inhibitors, given the role of JAK-1 and JAK-2 in the signaling of different cytokines involved in AD and psoriasis pathogenesis. Regarding atopic comorbidities, limited data are available on the possible role of JAK inhibitors in patients with concomitant asthma or allergic rhinitis [28]. Few trials are ongoing with topical JAK-1 inhibitors in patients affected by asthma. As a matter of fact, JAK-1-selective inhibitors that could be used via dry powder inhalation in patients with asthma are currently under evaluation [28]. In this setting of Th2-mediated asthma, JAK-1 inhibition seems to be more efficacious than JAK-3 inhibition [28]. Thus, according to our panel, dupilumab should be preferred. Still, JAK inhibitors could also represent a possible option, especially in patients with mild-to-moderate asthma or rhinitis, as underlined in recent real-world experience [29].

Concerning the real-world effectiveness and safety of JAK inhibitors, data from scientific literature have confirmed data from clinical trials from all three drugs [5–7, 9]. In particular, abrocitinib and upadacitinib have shown very high rates of EASI 90 and EASI 100, comparable or superior to phase III clinical trials [4, 17]. Regarding the safety profile of these three drugs, no significant safety findings have emerged

from real-life clinical practice compared with clinical trials [30]. To date, safety data for JAK inhibitors in patients with AD are available from clinical trials with a 3-year follow-up, while only limited long-term real-world experiences have been published. In particular, three studies have reached a 52-week observation period [7, 31, 32]. According to those studies, the vast majority of treatment-emergent AEs have been mild or moderate, and only a limited percentage of them have led to discontinuation [21, 33]. Also, currently, there is a consensus on the absence of absolute contraindication to the prescription of JAK inhibitors in women of childbearing potential after appropriate counseling on the importance of abstinence or the use of contraception [34].

Regarding oral contraceptives, it is worth mentioning that most of the women included in phase III clinical trials were taking them concomitantly as a result of the inclusion and exclusion criteria of these studies [4, 19]. According to a study on 22 healthy female subjects, upadacitinib showed no effects on the pharmacokinetics of levonorgestrel and ethinylestradiol [35]. No significant increase in thromboembolism has been reported to date. Moreover, a recent multicenter French real-world study on more than 200 patients confirmed the positive benefit–risk profile of JAK inhibitors, even in a population with cardiovascular comorbidities and multiple risk factors [30].

Regarding the recommendation for the use of JAK inhibitors in patients with AD, in 2022, under the Article 20 of Regulation (EC) No. 726/2004, the Pharmacovigilance Risk Assessment Committee (PRAC) of EMA developed a reassessment (EMA/PRAC/68283/2022) of the benefit–risk balance of oral JAK inhibitors [30, 36]. The final recommendations of the PRAC were released at the end of 2022, and the European Commission's final decision was issued in March 2023. A recent report from Wollenberg et al. analyzed the PRAC recommendation, underlining that the JAK inhibitors maintain a favorable benefit–risk profile as a first-line therapy in patients under 65 years of age without cardiovascular or malignancy risk factors [36]. They assessed that the benefit–risk profiles of available treatments should be compared for patients with risk factors. Regarding this recommendation, our group reached a consensus on which category of patients should be defined as high risk, including those with recent cardiovascular events and concomitant malignancy. It should also be taken into account that the incidence rates of MACEs, thromboembolism, and malignancies in patients with AD not treated with JAKi and in those treated with JAK inhibitors are comparable in terms of events per 1000 patients-years, according to current literature [21, 30, 36, 37].

The aim of our group was also to give practical recommendations for the management of patients receiving JAK inhibitors. On this topic, guidelines lack consistent evidence to date. In accordance with the summary of product characteristics of the three drugs, the panel agreed that the herpes zoster vaccination may be performed before starting the treatment. Still, it should not be mandatory, in agreement with local immunization guidelines [3, 36]. Similarly, according to the drugs' SPC, we reached agreement regarding contraception, as women of reproductive potential should, of course, be advised to use effective contraception during treatment and for 1 month following the final dose of JAK inhibitor [11–13]. However, the oral contraception should not be mandatory. We also tried to advise patients undergoing medical procedures, including vaccines or surgeries. For both situations, we recommended withdrawing the drug 1 week before and 1 week after the procedure, based on the short half-lives of the three JAK inhibitors [38, 39].

Our study has a few limitations because of the limited number of clinicians included and because of the very limited real-world experience currently available, especially on abrocitinib and baricitinib. Moreover, a selection bias should be mentioned, as most of the panel's dermatologists specialized in treating AD and were already familiar with JAK inhibitors. Another limitation is due to the intrinsic nature of a Delphi consensus, which is based on both clinical evidence and experts' opinions.

CONCLUSION

This Delphi consensus produced 24 statements regarding the management of patients receiving JAK inhibitors in real-world clinical practice. Our suggestions aimed to fill a void in current guidelines in order to give clinicians some advice in this setting. It is crucial to critically update and revise current treatment guidelines in light of the most recent real-world data on new treatment options.

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Data Availability. Additional data supporting the findings of this manuscript are available to the corresponding author upon reasonable request.

Declarations

Conflict of Interest. Luigi Gargiulo has been a consultant for Almirall. Luciano Ibba has been a consultant for Almirall. Piergiorgio Malagoli has been a speaker for AbbVie, Lilly, Novartis, Janssen-Cilag, Celgene, Leopharma, and Almirall. Andrea Chiricozzi has served as advisory board member and consultant and has received fees and speaker's honoraria or has participated in clinical trials for AbbVie, Almirall, Bristol Myers Squibb, Leo Pharma, Lilly, Janssen, Novartis, Pfzer and Sanof Genzyme. Paolo Dapavo has been a speaker for Novartis, Abbvie, Sanofi, UCB, Janssen, Lilly, and LeoPharma. Silvia M. Ferrucci has been principal investigator in clinical trials for ABBVIE, Almirall, Galderma, Leo Pharma, Sanofi, Amgen, Novartis, Bayer and received honoraria for lectures for Novartis and Menarini. Maddalena Napolitano acted as speaker, consultant and/or advisory board member for Abbvie, Eli Lilly, Leo Pharma, Novartis, and Sanofi. Michela Ortoncelli has served as a consultant and/or speaker for AbbVie, LEO Pharma, Novartis and Sanofi. Maria T. Rossi has received personal fee for advisory board meeting from Sanofi, Abbvie, Novartis, and Cantabria. Antonio Costanzo has served as an advisory board member, consultant and has received fees and speaker's honoraria or has participated in clinical trials for Abbvie, Almirall, Biogen, LEO Pharma, Lilly, Janssen, Novartis, Pfizer, Sanofi Genzyme, and UCB-Pharma. Alessandra Narcisi has served on advisory boards, received honoraria for lectures and research grants from Almirall, Abbvie, Leo Pharma, Celgene, Eli Lilly, Janssen, Novartis, Sanofi-Genzyme, Amgen and Boehringer Ingelheim. Anna G. Burroni, Massimo Gola and Claudio Sciarrone have nothing to declare.

Ethical Approval. Institutional review board approval was exempted for this study as its procedures did not include human subjects and did not deviate from good clinical practice. All the involved dermatologists gave their approval for the study to be published. All the

dermatologists who were part of the consensus were involved in the writing and/or revision of the manuscript. All the dermatologists who participated in the consensus were aware of the objective of the study, and they all knew that the manuscript will be published. The participants gave written informed consent.

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