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REVIEW

Risk Assessment in Atopic Dermatitis: Guidance from a Multidisciplinary Expert Panel

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ABSTRACT

Guidelines recommend that patients with severe atopic dematitis (AD) be treated with Janus kinase inhibitors (JAKi). Recently, the safety of JAKi as a class was reviewed by the European Medicines Agency, leading to a modification of the Summaries of Product Characteristics. For upadacitinib, changes involve reduced posology and restriction of its use to patients with no other alternative amongst the elderly and those at an increased risk of major adverse cardiovascular events (MACE), cancer and venous thromboembolism (VTE). Risk assessment may be daunting and clarity regarding definitions and data is needed. An interdisciplinary workshop, termed the Multiple In-treatment Risk Assessment & Management, was conceived to provide dermatologists with a platform for multidisciplinary exchange on risk assessment in patients with MACE, cancer and

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VTE to correctly recognise patients with increased risk. In this review, we characterised common and less common patient profiles in order to assess the risk. With the cooperation of a cardiologist, oncologist, respiratory medicine specialist and haematologists, we identified the risk factors for MACE, cancer and VTE. The results show that taking a careful medical history is the basis of risk assessment and that a careful medical history should be performed regardless of the intended therapy in AD. We propose that risk levels be used in the general population as a benchmark to evaluate risk levels in patients with AD, and provide a checklist to support such risk assessments in routine clinical practice. Our work provides a clear framework for risk assessment to the community of dermatologists and, therefore, contributes to improving the standard of care in AD.

Keywords: Atopic dermatitis; JAKi; Risk assessment; MACE; Cancer; VTE

Key Summary Points

Why carry out this study?

In the wake of article 20 of Regulation (EC) No 726/2004 of the European Parliament and of the Council proceedings, we provide guidance concerning the assessment of risk for developing adverse events in patients with atopic dermatitis considered for treatment with upadacitinib based on discussions between dermatologists and other specialists (a cardiologist, an oncologist, a respiratory medicine specialist and a haematologist).

Such a correct risk assessment is a dermatologist's unmet need.

What was learned from this study?

An appropriate history taking and the knowledge of specific risk factors are the key to correctly assessing risks for non-cutaneous comorbidities and complications.

Increasing the confidence of dermatologists and enhancing the ease of risk assessment will result in an improvement of standard of care.

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INTRODUCTION

Atopic dermatitis (AD) is the most common chronic inflammatory skin disorder, and mainly affects children and adults in developed countries [1]. AD is phenotypically heterogeneous and can present as a mild, moderate or severe disease. Several scoring systems exist to assess and classify the severity of signs and symptoms of this disease, including the Eczema Area and Severity Index (EASI), modified EASI (mEASI), Scoring Atopic Dermatitis (SCORAD) or the objective component of SCORAD (oSCORAD), Atopic Dermatitis Severity Index (ADSI) and body surface area (BSA) [2]. Treating a disease as complex as AD is not an easy task although much progress has been made over the years due to ever increasing knowledge of its basic biology [3]. Disease severity is the basis for the choice of treatment. Moderate-to-severe AD may require systemic treatment. The latest European and American guidelines strongly recommend treating severe AD, amongst others, with Janus kinase inhibitors (JAKi), such as abrocitinib, baricitinib and upadacitinib [4, 5].

Both efficacy and long-term safety are of extreme importance when treating any disease. Based on pharmacovigilance data and to ensure patient safety, in February 2022, the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) initiated a reassessment (EMA/PRAC/68283/2022) under Article 20 of Regulation (EC) No 726/2004 of the European Parliament and of the Council of the benefit–risk ratio of the entire class of oral JAKi. The EMA announced its final decision in March 2023, thereby confirming measures to

minimise the risk of major adverse cardiovascular events (MACE), cancer and venous thromboembolism (VTE) as serious adverse events [6]. For upadacitinib, the measures include reduced posology (Sect. 4.2. of the Summary of Product Characteristics [7]) and their use only if no other alternative exists in the elderly and in patients at an increased risk of MACE, cancer and VTE (Sect. 4.4) [7].

The assessment of risk concerning these three categories of serious adverse events may require some input from several medical specialities. Therefore, an interdisciplinary workshop, referred to as the Multiple In-treatment Risk Assessment & Management (M.I.R.A.), was conceived to provide dermatologists with a platform for discussing risk assessment for the adverse events in question with colleagues of different medical specialities.

The aim of this article is to present a practical approach to risk assessment prior to prescribing upadacitinib, as elaborated by the M.I.R.A. expert panel, and to present the profiles of selected patients for whom care may need to be taken. A checklist arose during the multidisciplinary discussion (Fig. 1), and we propose this checklist as a base to perform risk assessment in routine clinical practice.

METHODS

The Workshop

The M.I.R.A. workshop was conducted to identify the best methods for routine risk assessment in patients with AD considered for treatment with upadacitinib (for details see the Electronic Supplementary Material (ESM)). The project started in July 2023 and ended in December 2023.

Working Method

The dermatologists participating in the M.I.R.A. workshop were first asked to describe the most common profile of a patient who seeks help in their clinics and then to describe a second, less common profile of a patient whose risk assessment for MACE, cancer or VTE constituted a challenge. The profiles were identified using the Patient Profile Form (ESM Fig. 1). Next, patient profiles were analysed to identify in each person the risk factors for conditions proposed in the EMA's recommendations. Dermatologists voiced their needs regarding both the interpretation of the recommendations and the practicalities of risk assessment. The needs expressed by the dermatologists together with the answers from other participating specialists are shown in Table 1.

Ethical Approval

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

HOW TO DETERMINE INCREASED RISK OF MACE?

A MACE is a common composite safety endpoint in clinical trials. There are three definitions of MACE. Since 2012, the EMA uses the classical three-item definition for this endpoint that includes myocardial infarction, stroke and cardiovascular death. In a second definition, used in some studies, a fourth item, namely hospitalisation for unstable angina pectoris or revascularisation procedures, is added, while other studies used another definition in which a fifth item, namely heart failure, is added [8]. The most important risk factors for MACE include type 2 diabetes, smoking, dyslipidaemia, hypertension and obesity [9].

A number of studies have reported an increased prevalence of cardiovascular disease in AD. However, a recent systematic review stated that available evidence on the relationship between these two conditions, as well as between AD and risk factors for cardiovascular disease, is inconclusive. This uncertainty is due to the diversity of study designs and definitions adopted [10]. AD is also unlikely to be an

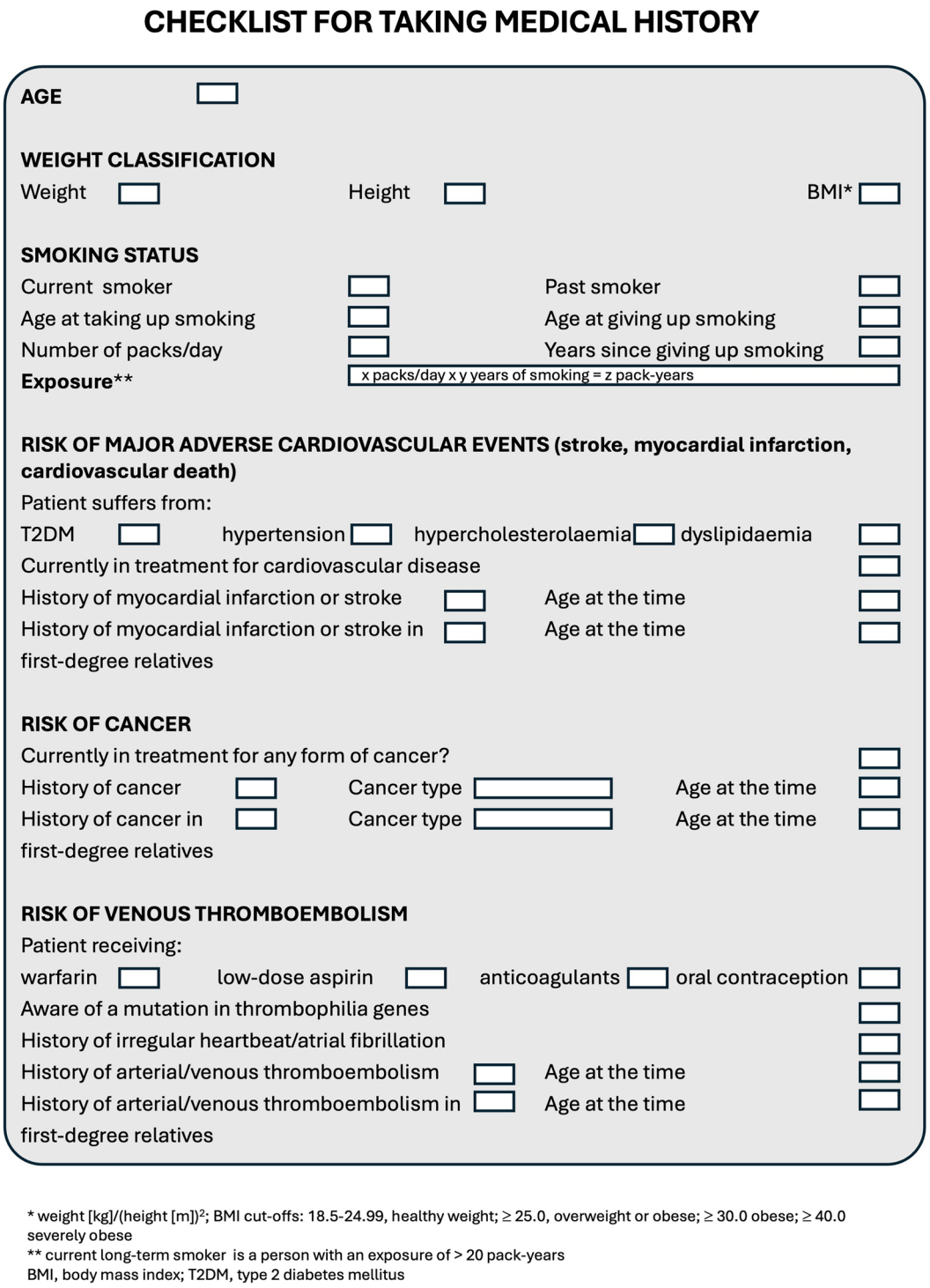

Fig. 1 Checklist for taking medical history for risk assessment

Table 1 Need for interpretation of the European Medicines Agency's recommendations as asked by dermatologists or specific medical specialists

Serious adverse event	EMA measures[a] to minimise the risk of that serious adverse event as stated in the SPCh	Dermatologists' need for an interpretation	Specialists' answer
Major adverse cardiovascular events	p.7 Upadacitinib should only be used if no suitable treatment alternatives are available in patients with **history of atherosclerotic cardiovascular disease** or **other cardiovascular risk factors** (...) p.4 A dose of 15 mg is recommended for patients at higher risk of (...) major adverse cardiovascular events (MACE) (...)	How to identify patients with increased cardiovascular risk?	Patients with increased cardiovascular risk can be identified by taking detailed medical history and confirming the presence of hypercholesterolaemia, dyslipidaemia, hypertension, obesity, type 2 diabetes mellitus or smoking
		How to calculate cardiovascular risk?	Cardiovascular risk can be calculated using the available cardiovascular risk cards or ad hoc applications, e.g. ESC CVD Risk Calculation App Patients with type 2 diabetes mellitus and those with past history of cardiovascular disease may need to be managed in collaboration with a cardiologist
Malignancy excluding non-melanoma skin cancer	p.7 Upadacitinib should only be used if no suitable treatment alternatives are available in patients with **malignancy risk factors** (e.g. **current malignancy or history of malignancy**) p.9 In patients 65 years of age and older, patients who are **current or past long-time smokers**, or with other malignancy risk factors (e.g. current malignancy or history of malignancy) upadacitinib should only be used if no suitable treatment alternatives are available p.4 A dose of 15 mg is recommended for patients at higher risk of (...) malignancy	How to determine increased risk for malignancy?	Patients with increased risk for malignancy can be identified by taking detailed medical history and confirming the presence of first- and second-degree relatives of both sexes with malignancies
		How to quantify the risk in patients with current malignancy or history of malignancy?	The risk in patients with current malignancy or history of malignancy can be assessed by enquiring about the type of cancer, time from diagnosis, treatment outcomes. The risk/benefit ratio of upadacitinib can be evaluated with attending oncologist
		How to determine increased risk for malignancy in a young patient?	Young patients have no particular risk factors except for familial history that should be acquired with the medical history
		What is the definition of a "current long-time smoker"?	A person who smokes currently and has a cumulative exposure of 20 pack-years[b], relevant for patients > 50 years of age
		What is the definition of a "past long-time smoker"?	A person who had smoked for a cumulative exposure of > 20 pack-years, relevant for patients > 50 years of age

Table 1 continued

Serious adverse event	EMA measures[a] to minimise the risk of that serious adverse event as stated in the SPCh	Dermatologists' need for an interpretation	Specialists' answer
Venous thromboembolism	p.4 A dose of 15 mg is recommended for patients at higher risk of **venous thromboembolism** (VTE) (…)	What should be asked when taking medical history to determine increased risk of VTE?	Dermatologists should ask about history of thrombosis at a young age (< 50 years), in particular, following weak provoking factors (minor surgery, tooth extraction, combination oral anticoagulants, or immobility) or unprovoked VTE, and about family history of VTE (first-degree relatives affected at a young age)
		Should a dermatologist perform full thrombophilia testing?	Patients should be referred to a specialist for thrombophilia testing if risk factors for VTE found in medical history Testing should not be done routinely

CVD Cardiovascular disease, *EMA* European Medicines Agency, *ESC* European Society of Cardiology, *SPCh* Summary of Product Characteristics

[a]Article 20 of Regulation (EC) No 726/2004 of the European Parliament and of the Council: Sections 4.2 Posology and method of administration and Section 4.4 Special warnings and precautions for use of the SPCh

[b]Pack-years value is determined by multiplying the number of years of smoking by the average number of packs per day

independent risk factor for cardiovascular disease [11].

The authors of an analysis of long-term safety data amounting to 7000 patient-years of exposure and including 5 years of follow-up in patients with moderate-to-severe AD treated with upadacitinib confirmed that the risk of developing MACE was low (0.1 and<0.1 events/100 patient-years for those patients receiving a dose of 15 and 30 mg, respectively, at 1 year) and stable (0.2 and<0.1 events/100 patient-years for those patients receiving a dose of 15 mg and 30 mg, respectively, at year 5) [12].

Dermatologists should take a careful medical history to specifically determine if any of the above-mentioned risk factors are present in their patients. Patients without such risk factors are highly unlikely to develop MACE. There are tools for calculating the risk of cardiovascular disease, such as SCORE2 for individuals aged 40–69 years and SCORE2-OP for those individuals aged > 70 years, which are available as risk cards or applications [9, 13]. Elderly individuals with hypertension and/or hypercholesterolaemia have a high risk for cardiovascular disease regardless of AD or of the treatments offered to them. Multidisciplinary care may be needed in patients at high risk of cardiovascular disease [14]. Risk factors must be regularly reassessed as they may change over time.

Patient Profiles

The most frequent patient profile identified by the participating dermatologists in their clinical practice was that of a young man with no cardiovascular risk factors. Conversely, the less common and more challenging profile from the point of view of cardiovascular risk assessment was identified as a middle-aged female with a medical history of arrhythmia and familial history of cardiovascular disease on her mother's side (Table 2).

Risk Factor Analysis

There were no risk factors identified in the first patient profile, whereas the presence of hypertension, arrhythmia and familial history of cardiovascular disease were identified as potential risk factors for MACE in the second patient profile. Both profiles were deemed low risk by the cardiologist given that the first patient was free of risk factors and the second

Table 2 Patient profiles with low and high risk of major adverse cardiovascular events

Cardiology-dermatology team	Patient profile	
	Common profile (first patient profile)	**Equally common profile but "difficult" in terms of risk assessment (second patient profile)**
Demographic data	Male Age: 35 years	Female Age: 45 years
Diagnosis	Moderate-to-severe AD with exacerbation in the past 10 years	Moderate-to-severe AD
Medical history	Familial tendency towards allergies Past treatment with corticosteroids and cyclosporin	Hypertension since the age of 35 years, episodes of arrythmia Past treatment with beta-blockers
Familial history	Not known	Heart failure and atrial fibrillation in the mother
Risk category following analysis	*Low risk*	*Low risk*

AD Atopic dermatitis, *MACE* Major adverse cardiovascular events

had controlled hypertension and arrhythmia, neither of which is a risk factor for MACE.

Management

Both patients require periodical reassessment of their cardiovascular risk. For the first patient, reassessment is needed for an early detection of newly presented risk factors, as in the general population. For the second patient, it is necessary to understand the nature of arrythmia and to exclude atrial fibrillation; cardiological consultation may be useful for a better assessment of the cardiovascular health of the woman and to follow up the cardiovascular condition.

HOW TO DETERMINE INCREASED RISK OF MALIGNANCY?

Available data show that AD is associated with increased risk of non-melanoma skin cancer (NMSC) and a slightly decreased risk of several solid malignancies [15, 16]. However, there may be a bias regarding the prevalence of NMSC as patients with AD cared for by dermatologists are more likely to receive an early diagnosis of a skin malignancy than individuals who are not seen by dermatologists. Also, the use of phototherapy in AD may be another potential risk factor [17]. There are also data implying that patients with AD have an increased risk of developing lymphomas, especially T-cell lymphomas [15, 18–20].

An integrated analysis of long-term safety data on upadacitinib in moderate-to-severe AD confirmed that the risk of developing NMSC was low (0.3 and 0.4 events/100 patient-years, for the dose of 15 mg and 30 mg, respectively, at 1 year) and stable (0.4 and 0.3 events/100 patient-years, for the dose of 15 mg and 30 mg, respectively, at 5 years) [12]. It was also low and stable for malignancies excluding NMSC: 0.1 and 0.5 events/100 patient-years at 1 year and 0.3 and 0.4 events/100 patient-years at 5 years, for the dose of 15 mg and 30 mg, respectively [12].

Currently, there is no reliable tool to determine the overall risk of developing cancer during the lifetime of an individual, apart from hereditary syndromes (e.g., breast-ovarian cancer syndromes, hereditary gastrointestinal tumours), or specific risk-factor driven malignancies (e.g., human papilloma virus and cervical cancer). Familial anamnesis is crucial to highlight recurrent malignancies in a given family that may suggest that hereditary cancer syndromes are present [21–23].

Dermatologists should take careful medical and familial histories, asking the patient to specify the degree of kinship, type of tumour and age of presentation. Breast, ovarian and colon cancer are the cancer types that most frequently run in families, and presentation of tumours at a young age that otherwise are common in the elderly may be a sign of a hereditary cancer [22, 23].

To assess the risk of recurrence in a cancer survivor, dermatologists should ask again about the type of tumour, its staging, the current stage of the follow-up and if the follow-up ended, how much time has elapsed since it has ended. Also, it is useful to know if the patient is still under oncological care. The risk of recurrence as a function of time since cure varies for various types of tumours and even for different histologies of the same cancer [24–28].

Although smoking is also a risk factor for cardiovascular disease and VTE, during the M.I.R.A. workshop only the oncological risk of smoking was considered to explain the language used by EMA and help identify patients at increased risk of cancer due to tobacco smoking. The EMA used the language "current or past long-term smoker", which may require an explanation. A person with an exposure of > 20 pack-years (calculated as the average number of packs/day multiplied by the number of years of smoking) who continues to smoke can be defined as "current long-term smoker". To be considered a "past smoker" a period of 10–15 years must elapse since the last use of a cigarette to cancel out the risk related to smoking [29–31].

Patient Profiles

For the analysis of increased risk of cancer, the dermatologists identified three patient profiles, none of which were very frequent, but they were

Table 3 Patient profiles with intermediate and high risk of developing cancer

Oncology-dermatology team	Patient profile		
	Uncommon and "difficult" profile in terms of risk assessment (second patient profile)	**Uncommon and "difficult" profile in terms of risk assessment (first patient profile)**	**Common patient (third patient profile)**
Demographic data	Male Age: 64 years	Female Age: 49 years old Healthy weight	Female Age: 19 years old BMI: 24
Diagnosis	Moderate-to-severe AD treated with 15 mg upadacitinib	Moderate-to-severe AD	Moderate-to-severe AD
Medical history	Dyslipidaemia	Allergic rhinitis	Autoimmune thyroiditis, on contraceptive pill
Family history	Father died of lung cancer Mother died from natural causes at 90 years of age	Breast cancer in the mother and/or in the grandmother	No relevant family history
Tobacco smoking	Ex-smoker, 22.5 pack-years between 20 and 50 years of age	Never smoked	Current smoker since the age of 14, vaper in the past year
Risk category following analysis	**Intermediate risk**	**High risk**	**Low risk**

AD Atopic dermatitis, *BMI* body mass index

those which the dermatologists considered useful for a discussion with the oncologist (Table 3). The first patient profile was that of a middle-aged woman with a family history of breast cancer in the mother and/or the grandmother. The second patient profile was that of a 64-year-old male, past smoker with a cumulative exposure of 22.5 pack-years (10–15 cigarettes/day for 30 years) and a family history of the father dying of lung cancer. The third patient profile was that of a 19-year-old woman, a smoker since the age of 14 years and a vaper during the previous year.

Risk Factor Analysis

The risk factors or potential risk factors identified in patient profiles included the existence of cases with breast cancer in the family of the first patient, age, past smoker status and familial history of lung cancer in the second patient and current smoker status in the third patient. The oncologist deemed the first patient to be at high risk for the development of breast cancer because of two index cases in the family and the second patient to be at intermediate risk of developing lung cancer. The family history of lung cancer was considered irrelevant as other factors (e.g. smoking, occupational exposure, air pollution or poor diet) are often involved in the pathogenesis of this malignancy [32]. In the case of the third patient, the cumulative exposure to tobacco smoking is too short to consider the patient at increased risk of cancer. In fact, the overall exposure to tobacco smoking should be considered and measured in pack/years.

Management

In the case of the woman with two index cases of breast cancer in her profile, population or personalised screening for breast cancer should be recommended [33, 34]. Consistently, a patient with features similar to those in the second profile may be eligible for a low-dose computed tomographic screening for lung cancer, similar to the general population [31]. The third patient should be advised about the dangers of smoking and encouraged to give it up. In current or past long-time smokers, the presence of additional (other than smoking) risk factors should be determined.

HOW TO DETERMINE INCREASED RISK FOR VTE?

Venous thromboembolism consists of two interrelated conditions: deep-vein thrombosis and pulmonary embolism [35]. VTE can be classified as unprovoked or provoked. Unprovoked VTE occurs in the absence of any known provoking risk factors, whereas in a provoked VTE episode a known acquired risk factor, transient (bed rest > 3 days, immobility of a limb after an injury, trauma or surgery, oestrogen therapy or pregnancy or foreign object or device) or persistent (active cancer, congestive heart disease, obesity or varicose veins) can be found [36–38]. High body mass index and recent hospitalisation are also risk factors for VTE [39]. Oral contraceptives or hormone replacement therapy that contain exogenous oestrogens increase the risk of VTE threefold compared to non-users, especially during the first year of their use, decreasing with time [40, 41]. Rare genetic thrombophilia defects further increase the risk of VTE [41, 42].

In the general population, the incidence of VTE is approximately 1 in 1000 general population and increases with age [43, 44]. No association has been found between AD and risk of VTE [45]. Available literature shows that patients with AD have a lower risk of VTE than patients with other immune-mediated inflammatory diseases, such as rheumatoid arthritis (RA), and that AD is not an independent risk factor for VTE [46, 47]. Moreover, patients with AD treated with upadacitinib are not at an increased risk of developing VTE. In fact, in one study, in patients with moderate-to-severe AD treated with upadacitinib, the risk of developing VTE was low (< 0.1 and < 0.1 events/100 patient-years for dose 15 mg and 30 mg, respectively, at 1 year) and stable (0.1 and 0.1 events/100 patient-years for the dose of 15 mg and 30 mg, respectively, at year 5) [12]. Therefore, the haematology-dermatology team in the workshop focused their attention on risks related to oral contraception and thrombophilia syndromes, which are known risk factors [41, 42].

For a correct risk assessment, similar to those for MACE and cancer, dermatologists should take the familial history of thrombophilia, including degree of kinship, age at VTE episode and determination of whether the even is unprovoked or provoked. Relatives of patients with primary VTE are at a higher risk of VTE than relatives of those with secondary VTE. In patients with AD and increased risk of VTE, full thrombophilia testing could be requested [39, 41]. Such tests are not to be done in all patients, and clotting specialists should be consulted.

Patient Profiles

The dermatologists pointed out a 30-year-old woman with severe AD on oral contraceptive pill as the frequent patient profile in their everyday care and a 25-year-old woman with a history of deep vein thrombosis (DVT) as that in whom a discussion with a haematologist would be interesting with the aim to ensure that the risk of VTE was assessed correctly (Table 4).

Risk Factor Analysis

The risk factors for VTE identified during the analysis included contraceptive pill in the first patient, and DVT in the second. The haematologist deemed the first profile at low risk and the second at high risk for the development of VTE independently of AD and any AD treatment.

Table 4 Patient profiles with low and high risk of venous thromboembolism

Haematology-dermatology team	Patient profile	
	Common patient type (first patient profile)	**Uncommon and "difficult" profile in terms of risk assessment (second patient profile)**
Demographic data	Female Age: 30 years BMI = 24	Female Age: 25 years Healthy weight
Diagnosis	Severe AD	Severe AD
Medical history	Alopecia areata, asthma Past treatment with cyclosporin, omalizumab, corticosteroids, dupilumab, on contraceptive pill	Childhood asthma, inhalant allergies
Familial history	Hypertension and dyslipidaemia Younger sister with similar clinical picture	Not known
History of VTE	No history of VTE	Past episode of DVT
Risk category following analysis	**Low risk**	**High risk**

AD Atopic dermatitis, *BMI* body mass index, *DVT* deep vein thrombosis, *VTE* venous thromboembolism

Management

For the first female patient, no specific assessment is needed as she was assessed by the physician who prescribed the contraceptive pill. However, a complete medical history can be acquired as specified above. In the second patient, the medical history should be taken to exclude a current high risk of VTE. All episodes of unprovoked or provoked VTE, diseases linked to a possible risk of VTE, family history of VTE and past spontaneous miscarriages should be evaluated. While the first patient can be managed by a dermatologist alone, the second would benefit from a specialist visit with a haematologist.

DISCUSSION

Atopic dermatitis is a complex chronic disease that requires intervention and management of multiple dimensions,; however, to date, the condition is still not adequately controlled in many patients [48]. Upadacitinib has been shown to be a highly effective therapy for AD with a well-characterised safety profile in several indications and patient profiles [49]. The EMA Article 20 procedure limited the use of oral JAKi in certain patient populations, including those with AD. Hence, the M.I.R.A. multidisciplinary expert panel worked on how to best perform and standardise risk assessment and evaluate patient risk profile in clinical practice, for timely identification of patients at a potentially increased risk of MACE, malignancy and VTE, ultimately informing and supporting therapeutic decision-making.

Although for dupilumab there are substantial data on safety in patients with AD with comorbidities, the same is not true for patients treated with JAKi [50, 51]. ORAL Surveillance (ClinicalTrials.gov number: NCT02092467) was a phase 3b/4 randomised, open-label, noninferiority trial with safety endpoints that failed to establish the noninferiority of tofacitinib, a JAKi, compared to tumour necrosis factor (TNF) inhibitors in patients with at least one cardiovascular risk factor for the outcomes of adjudicated MACE and malignancies [52]. The results of this study prompted EMA's Article 20 referral procedure.

Compared to patients with RA, in patients with AD the risk–benefit ratio for oral JAKi is favourable for patients aged < 65 years without cardiovascular or malignancy risk factors [53]. This may be due to AD not being a high-risk disease, whereas RA has a higher risk disease [53]. On the other hand, the results of an integrated safety analysis restricted to upadacitinib in six trials in RA, two trials in psoriatic arthritis, one trial in ankylosing spondylitis and three trials in AD suggest that upadacitinib has a similar safety profile across all four diseases, with some variations in adverse event rates due to differences in patient population and disease-associated comorbidities [49]. Safety data on upadacitinib in the AD population did not confirm increased risk for any of the serious adverse events identified by EMA compared to other therapies used in AD or the general population; however, risk assessment in the AD population maybe useful regardless of the treatment [12].

A very recent cross-sectional study on data from the Danish national registers and Danish Skin Cohort analysed the prevalence of risk factors that potentially impact the choice of treatment with JAKi in > 20,000 patients with AD. This study showed that 64.4% of younger patients with AD had no risk factors, whereas 60.3% of the oldest patients (≥ 65 years of age) had ≥ 3 risk factors. The non-modifiable risk factors identified were cancer (5.6%), MACE (2.6%), VTE (2.0%), history of smoking (15.6%) and elderly age (≥ 65 years; 12.4%) [54]. It should be noted here that some risk factors, such as increased body weight, high blood glucose level, hypertension, unhealthy diet and high alcohol consumption, physical inactivity and smoking, are common to cardiovascular disease and cancer. A careful assessment of risk factors in patients with AD considered for JAKi treatment can be done as proposed here.

Upadacitinib is a highly effective therapy for AD [55]. Patient safety must most certainly be ensured and, equally, all patients must be offered therapies that can effectively improve AD and health-related quality of life [56]. Uncontrolled AD has been linked to a number of adverse outcomes, such as poor sleep quality [57]. Sleep health is important for cardiovascular health, which highlights the importance of disease control [58].

Our work may be helpful for the dermatology community and be used as a starting point for risk assessment. The limitations of this study comprise lack of a systematic literature review as a basis for the answers provided by the specialists. In addition, a limited number of dermatologists and other specialists were involved. Lastly, we are well aware of the oversimplification of addressing one risk at the time given their coexistence and intricate relationship; this was done to obtain help from individual specialists, but each patient must be assessed holistically.

CONCLUSIONS

In conclusion, we present a practical approach to risk assessment prior to prescribing upadacitinib. All specialists confirmed that taking a careful medical history is the basis of risk assessment. Clearly, a risk–benefit ratio assessment should be done prior to any treatment in AD. We propose that risk levels in the general population be used as a benchmark to evaluate risk levels in patients with AD and the use of a checklist to support the decision-making process in routine clinical practice.

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Declarations

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