COVID-19 SPECIAL FORUM

European Task Force on Atopic Dermatitis: position on vaccination of adult patients with atopic dermatitis against COVID-19 (SARS-CoV-2) being treated with systemic medication and biologics

Editor,

The coronavirus disease 2019 (COVID-19) pandemic is caused by rapid spread of different strains of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The severity of infection ranges from mild, or even asymptomatic, to very severe. Signs and symptoms include fatigue, fever, exanthemas, upper respiratory illness, loss of smell and taste, pneumonia, severe acute respiratory syndrome and multi-organ failure. Risk factors for a severe or lethal course include age, male gender, obesity, diabetes, cardiovascular disease and immune suppression.[1] At the start of the pandemic, the European Task Force on Atopic Dermatitis (ETFAD) shared their position on continuation of systemic immune-modulating treatments, including immunosuppressive therapy, in atopic dermatitis (AD) patients during the time of the pandemic.[2]

Safe and effective vaccines are urgently needed to control the pandemic and achieve herd immunity. More than 50 COVID-19 vaccine candidates are currently in trials. mRNA vaccines lead to production of antigens by host cells, and two (RNA-1273 and BNT162b2) were recently approved in EU member states to vaccinate adults against COVID-19. A viral vector-based vaccine (AZD1222) has been approved in the United Kingdom, but not yet in the EU.

National strategic guidelines and recommendations are being developed and utilized to vaccinate initially those with increased risk factors for a severe course, as well as those being employed in critical positions. This article provides the position of ETFAD members regarding COVID-19 vaccination of adult patients with AD being treated with systemic immunosuppressive medication and biologics. A separate article discusses how dermatologist may manage allergic issues. Vaccination particularly against pneumococcus and influenza should be performed as recommended in the guidelines.[3]

The ETFAD acknowledges that.

- There is currently no evidence to suggest that AD is an independent risk factor for acquiring SARS-CoV-2, or of having a more severe course of COVID-19, above and beyond other important co-morbid conditions, such as obesity, cardiovascular disease and diabetes.
- Atopic dermatitis is not a contraindication to vaccination. It is unclear whether SARS-CoV-2 vaccination could cause brief AD worsening, but this is not suspected since the vaccination response is mainly T helper cell 1 skewed.[4]
- Systemic immunosuppressants and JAK-inhibitors used to treat AD may attenuate the vaccination response,[5] but no attenuation is expected for dupilumab.[6]

Based on the listed uncertainties and AD disease characteristics,[3,7] the risk–benefit ratio of all currently approved vaccines appears better than the risk of an infection with SARS-CoV-2, also for AD patients. There is no clear evidence to recommend that systemic AD medication is paused before or after COVID-19 vaccination. Temporary 2-week discontinuation of methotrexate slightly improved the immunogenicity of seasonal influenza vaccination in patients with rheumatoid arthritis,[5] but this may not be relevant to mRNA-based vaccines. Clinicians may, therefore, consider pausing immunosuppressant possible during vaccination, typically from the vaccination day until 1 week after for JAK-inhibitors and cyclosporine, or until 2 weeks after for methotrexate and azathioprine, to possibly improve chances or appropriate vaccination response. Alternatively, the lowest dose possible may be used, for example 2.5 mg/kg/day cyclosporine, 1 mg/kg/day azathioprine and 7.5 mg/week methotrexate. The ETFAD recommends to strictly follow guidelines and decisions issued by the local and national health authorities in each country. While patients on immunosuppressive drugs for AD will need a case-by-case approach considering the specific drug and vaccine product, inadequate antibody response in selected individuals is not a major concern, and the risk/benefit of vaccination is considered favourable for the overall AD population. At least 3 weeks are recommended between the two COVID-19 vaccine doses, which increases the risk of AD flares and loss of AD control if the systemic AD medication is paused or reduced in dose for longer periods. Measurement of antibodies against SARS-CoV-2 can be done in cases with particular importance of successful immunization. If a live vaccine against COVID-19 is registered in the future, our recommendations for the use of this vaccine may be different. We encourage registration of COVID-19 AD patients in the ETFAD-supported SECURE-AD register (www.secure-derm.com), which also captures AD patients' experiences of SARS-CoV-2 vaccination.[8]

Acknowledgement

We thank Dr. Karin Loré, Division of Immunology and Allergy, Karolinska Institute, Stockholm, Sweden, for her kind review of this article.

Funding sources

No funding was obtained for this work.

Conflicts of interest

Dr. Thyssen has attended advisory boards for Eli Lilly, Regeneron, Pfizer, LEO Pharma, Abbvie and Sanofi-Genzyme, received speaker honorarium from LEO Pharma, Abbvie, Regeneron and Sanofi-Genzyme, and received research grants from Regeneron and Sanofi-Genzyme. Dr. Vestergaard has been investigator, speaker or consultant for Novartis, Abbvie, Sanofi, Leo Pharma and Eli Lilly. Dr Barbarot has been a principal investigator, advisory board member or consultant for Pierre Fabre Laboratory, Bioderma, Laboratoire La Roche Posay, Sanofi-Genzyme, Abbvie, Novartis, Janssen, Leo Pharma, Pfizer, Amgen, Lilly. Dr. de Bruin-Weller has been a consultant, advisory board member and/or speaker for AbbVie, Almirall, Arena, Eli Lilly, Galderma, Janssen, Leo Pharma, Pfizer, Regeneron and Sanofi-Genzym. Dr. Bieber has been a principal investigator, advisory board member or consultant for Regeneron, Sanofi, GSK, Celgene, Abbvie, AnaptysBio, MedImmune, Chugai, Pierre Fabre, Novartis, Asana Biosciences, LEO, Galapagos/MorphoSys, BioVerSys, Galderma, Kymab, Glenmark, Astellas, Daiichi-Sankyo, Lilly, Pfizer, MenloTx, Dermavant and Allmiral. Dr. T. Bieber was speaker, and/or consultant and/or Investigator for AbbVie, Allmiral, AnaptysBio, Arena, Asana Biosciences, Astellas, BioVerSys, Böhringer-Ingelheim, Celgene, Daichi-Sankyo, Dermavant/Roivant, DermTreat, DS Pharma, RAPT/FLX Bio, Galapagos/MorphoSys, Galderma, Glenmark, GSK, Incyte, Kymab, LEO, Lilly, L´Oréal, MenloTx, Novartis, Pfizer, Pierre Fabre, Sanofi/Regeneron, UCB. T. Bieber is founder of the non-profit biotech company 'Davos Biosciences'. Dr. Gutermuth has been a consultant, advisory board member and/or speaker for AbbVie, Almirall, Eli Lilly, Galderma, Janssen, Leo Pharma, Pfizer, Regeneron and Sanofi-Genzyme. Dr Taïeb has been consultant or investigator for Pierre Fabre, Galderma, Novartis, Johnson and Johnson, Incyte, Abbvie, Modilac, Pfizer, Lilly, Arena, Bioderma and Sanofi. Dr. Seneschal has been investigator, speaker, or consultant for Novartis, Abbvie, Sanofi, Leo Pharma and Eli Lilly. Dr. Weidinger has received institutional research grants from LEO Pharma and L'Oreal, has performed consultancies for Sanofi-Genzyme, Regeneron, LEO Pharma, Incyte, Lilly, Abbvie and Novartis, has lectured at educational events sponsored by Sanofi-Genzyme, Regeneron, LEO Pharma, Abbvie and Galderma, and is involved in performing clinical trials with pharmaceutical industries that manufacture drugs used for the treatment of atopic dermatitis. Dr. Trzeciak has been a speaker, consultant, investigator or advisory board member for LEO Pharma, Pierre Fabre, Pfizer, La Roche Posay, Sanofi-Genzyme, Novartis, Bioderma and Mead Johnson. Dr. Cork is an Investigator and/or consultant Consultant for Regeneron, Sanofi-Genzyme, Pfizer, LEO, Galapagos, Novartis, Boots, L'Oreal, Reckitt Benckiser, Oxagen, Johnson&Johnson, Hyphens, Kymab, Astellas, Galderma, Procter&Gamble, Abbvie, Lilly, Galderma, Menlo and Perrigo. Dr. Paul has received grants and been consultant for Allmiral, Amgen, Abbvie, Boehringer, Celgene, Eli Lilly & Co, Novartis, Janssen, Pfizer, LEO Pharma, Merck, UCB pharma, Pierre Fabre, Regeneron and Sanofi-Genzyme. Dr. Flohr is chief investigator of the UK National Institute for Health Research-funded TREAT (ISRCTN15837754) and SOFTER (Clinicaltrials.gov: NCT03270566) trials as well as the UK-Irish Atopic eczema Systemic Therapy Register (A-STAR; ISRCTN11210918) and a principal investigator in the European Union Horizon 2020-funded BIOMAP Consortium (http://www.biomap-imi.eu/). His department has also received investigator-led funding from Sanofi-Genzyme. Dr. Heratizadeh reports personal fees from Leo Pharma, personal fees from Novartis, personal fees from Pierre Fabre, personal fees from Sanofi-Genzyme, personal fees from Beiersdorf, personal fees from Hans Karrer, personal fees from Nutricia, personal fees from Meda, personal fees from Lilly, grants from Janssen, outside the submitted work. Dr. Darsow gave advice to or received an honorarium for talks or research grant from the following companies: ALK-Abello, Bencard, Meda, Novartis and Sanofi-Regeneron outside the submitted work. Dr. Simon has been an investigator, advisory board member, or consultant for AbbVie, AstraZeneca, Galderma, Lilly, Pfizer, Roche Pharma, and Sanofi-Genzyme. Dr. Torrelo has acted as advisor and/or participant in clinical trials for Sanofi, Lilly, Pfizer, Abbvie and Mylan. Dr. Gelmetti has acted as advisor and/or participant in clinical trials for: Bayer, Sanofi/Regeneron, Galderma and has lectured at educational events sponsored by Pfizer and Leo Pharma. Dr Szalai has performed consultancies for Sanofi-Genzyme, Regeneron, LEO Pharma, Novartis, has lectured at educational events sponsored by Nutricia, is involved in performing clinical trials with pharmaceutical industries that manufacture drugs used for the treatment of psoriasis and atopic dermatitis. Dr. von Kobyletzki has been investigator, speaker, or consultant for Pfizer, Sanofi, Leo Pharma and Eli Lilly. Dr. De Raeve is a consultant, member of scientific advisory boards and/ or received personal fees and non-financial support from LEO Pharma, Pierre Fabre, Sanofi-Genzyme and Bioderma. Dr. Fölster-Holst reports being consultant/Advisor for Beiersdorf AG, Johnson&Johnson, LEO Pharma, Neubourg, Novartis Pharma AG, Nutricia, Pfizer Inc., Regeneron, Sanofi-Aventis as well as speaker for Beiersdorf AG, LEO Pharma, Neubourg, Novartis Pharma AG, Pierre Fabre Laboratories, Pfizer, Procter&Gamble, Regeneron and Sanofi-Aventis. Dr Christen-Zaechs has been an advisor, speaker or investigator for Galderma, L'Oreal, La Roche Posey, Pierre Fabre, Procter and Gamble and Sanofi-Genzyme. Dr. Hijnen has been investigator, speaker, or consultant for Abbvie, Eli Lilly, Incyte, Leo Pharma, MedImmune/Astrazeneca, Pfizer, Sanofi and Thermo Fisher. Dr. Gieler has received institutional research grants from Galderma, has

performed consultancies for Sanofi-Genzyme, Regeneron, LEO Pharma, Lilly, Abbvie and Novartis, has lectured at educational events sponsored by Sanofi-Genzyme, Abbvie, Novartis, Sebamed and Galderma, and is involved in the organization of atopic dermatitis education programmes in Germany for the treatment of atopic dermatitis. Dr. Bangert has been consultant or speaker for Bayer, Mylan, LEO Pharma, Pfizer, Sanofi-Genzyme, Eli Lilly, Novartis, Celgene and AbbVie and principal investigator for Merck, Novartis, Sanofi, Abbvie, Elli Lilly and Galderma. Dr. Spuls has done consultancies in the past for Sanofi 111017 and AbbVie 041217 (unpaid), received departmental independent research grants from pharmaceutical industries different since December 2019 for the TREAT NL registry, is involved in performing clinical trials with many pharmaceutical industries that manufacture drugs used for the treatment of e.g. psoriasis and atopic dermatitis, for which financial compensation is paid to the department/hospital and, is Chief Investigator (CI) of the systemic and phototherapy atopic eczema registry (TREAT NL) for adults and children and one of the main investigator of the SECURE-AD registry. Dr. Ring has been an advisor or speaker for AbbVie, Allergika, Sanofi-Genzyme, Pfizer, Bencard, LEO Pharma and Mylan. Dr. Wollenberg has been a principal investigator, advisory board member, or consultant for AbbVie, Almirall, Galderma, Hans Karrer, LEO Pharma, Lilly, MedImmune, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc. and Sanofi-Genzyme, and received speaker honoraria from Chugai, Galderma, LEO Pharma, Lilly, Loreal, MedImmune, Pfizer, Pierre Fabre, Regeneron Pharmaceuticals, Inc. and Sanofi-Genzyme. Dr. Deleuran has been a principal investigator, speaker, advisory board member, and/or consultant for LEO Pharma, AbbVie, Almirall, Lilly, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Sanofi-Genzyme and Pierre Fabre. This research was performed independently through the authors' academic university and hospital affiliations. Dr. Chernyshov, Dr. Stalder, Dr. Svensson, Dr. Kunz reports no conflict of interest.

J.P. Thyssen,[1,*] C. Vestergaard,[2] S. Barbarot,[3] M.S. de Bruin-Weller,[4] T. Bieber,[5] A. Taieb,[6] J. Seneschal,[6] M.J. Cork,[7] C. Paul,[8] C. Flohr,[9] S. Weidinger,[10] M. Trzeciak,[11] T. Werfel,[12] A. Heratizadeh,[12] U. Darsow,[13] D. Simon,[14] A. Torrelo,[15] P.V. Chernyshov,[16] J.-F. Stalder,[17] C. Gelmetti,[18] Z. Szalai,[19] Å. Svensson,[20] L.B. von Kobyletzki,[21,22] L. De Raeve,[23] R. Fölster-Holst,[24] S. Christen-Zaech,[25] D.J. Hijnen,[26] U. Gieler,[27] J. Gutermuth,[23] C. Bangert,[28] P.I. Spuls,[29] B. Kunz,[30] J. Ring,[31] A. Wollenberg,[32,33] M. Deleuran[2]

[1]Department of Dermatology and Venereology, Bispebjerg Hospital, Copenhagen, Denmark, [2]Department of Dermatology, Aarhus University Hospital, Aarhus, Denmark, [3]Department of Dermatology, Nantes Université, CHU Nantes, UMR 1280 PhAN, INRAE, Nantes, France, [4]National Expertise Center of Atopic Dermatitis, Department of Dermatology and Allergology, University Medical Center Utrecht, Utrecht, The Netherlands, [5]Department of Dermatology and Allergy, University Hospital of Bonn, Bonn, Germany, [6]Department of Adult and Pediatric Dermatology, CHU Bordeaux, University of Bordeaux, Bordeaux, France, [7]Sheffield Dermatology Research. Department of Infection, Immunity and Cardiovascular Disease, The University of Sheffield, Sheffield, UK, [8]Department of Dermatology, Toulouse University, Toulouse, France, [9]St John's Institute of Dermatology, King's College London and Guy's & St Thomas' NHS Foundation Trust, London, UK, [10]Department of Dermatology and Allergy, University Hospital Schleswig-Holstein, Kiel, Germany, [11]Department of Dermatology, Venereology and Allergology, Medical University of Gdansk, Gdansk, Poland, [12]Department of Dermatology and Allergy, Hannover Medical School, Hannover, Germany, [13]Department of Dermatology and Allergy Biederstein, School of Medicine, Technical University of Munich, Munich, Germany, [14]Department of Dermatology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, [15]Department of Dermatology, Hospital Infantil Niño Jesús, Madrid, Spain, [16]Department of Dermatology and Venereology, National Medical University, Kiev, Ukraine, [17]Department of Dermatology, CHU, Nantes, France, [18]Department of Pathophysiology and Transplantation, University of Milan, Head, Unit of Pediatric Dermatology, Milan, Italy, [19]Department of Dermatology of Heim, Pál National Children's Institute Budapest, Budapest, Hungary, [20]Department of Dermatology, Skane University hospital, Malmö, Sweden, [21]University Healthcare Research Center, Faculty of Medicine, Lund University, Lund, Sweden, [22]Department of Occupational and Environmental Dermatology, Lund University, Skåne University Hospital, Malmö, Sweden, [23]Department of Dermatology, Universitair Ziekenhuis Brussel (UZB), Free University of Brussels (VUB), Brussels, Belgium, [24]Department of Dermatology, Venereology and Allergology, University clinics of Schleswig-Holstein, Kiel, Germany, [25]Pediatric Dermatology Unit, Departments of Dermatology and Pediatrics, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland, [26]Department of Dermatology, Erasmus MC University Medical Center, Rotterdam, The Netherlands, [27]Department of Dermatology and Allergology, University of Giessen, Giessen, Germany, [28]Department of Dermatology, Medical University of Vienna, Vienna, Austria, [29]Department of Dermatology. Amsterdam Public Health/Infection and Immunology, Location AMC, Amsterdam, The Netherlands, [30]Dermatologikum Hamburg, Hamburg, Germany, [31]Department of Dermatology and Allergy, Technical University of Munich, Munich, Germany, [32]Department of Dermatology and Allergy, Ludwig-Maximilian University, Munich, Germany, [33]Department of Dermatology I, München Klinik Thalkirchner Strasse, Munich, Germany

*Correspondence: J.P. Thyssen. E-mail: jacob.pontoppidan.thyssen@regionh.dk

References

1 Berlin DA, Gulick RM, Martinez FJ. Severe COVID-19. *N Engl J Med* 2020; **383**: 2451–2460.

2 Wollenberg A, Flohr C, Simon D *et al*. European Task Force on Atopic Dermatitis statement on severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) infection and atopic dermatitis. *J Eur Acad Dermatol Venereol* 2020; **34**: e241–e242.

3 Wollenberg A, Barbarot S, Bieber T *et al*. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I. *J Eur Acad Dermatol Venereol* 2018; **32**: 657–682.

4 Sahin U, Muik A, Derhovanessian E *et al*. COVID-19 vaccine BNT162b1 elicits human antibody and T(H)1 T cell responses. *Nature* 2020; **586**: 594–599.
5 Park JK, Lee YJ, Shin K *et al*. Impact of temporary methotrexate discontinuation for 2 weeks on immunogenicity of seasonal influenza vaccination in patients with rheumatoid arthritis: a randomised clinical trial. *Ann Rheum Dis* 2018; **77**: 898–904.
6 Blauvelt A, Simpson EL, Tyring SK *et al*. Dupilumab does not affect correlates of vaccine-induced immunity: a randomized, placebo-controlled trial in adults with moderate-to-severe atopic dermatitis. *J Am Acad Dermatol* 2019; **80**: 158–167.e1.
7 Wollenberg A, Christen-Zäch S, Taieb A *et al*. ETFAD/EADV Eczema task force 2020 position paper on diagnosis and treatment of atopic dermatitis in adults and children. *J Eur Acad Dermatol Venereol* 2020; **34**: 2717–2744.
8 Mahil SK, Yiu ZZN, Mason KJ *et al*. Global reporting of cases of COVID-19 in psoriasis and atopic dermatitis: an opportunity to inform care during a pandemic. *Br J Dermatol* 2020; **183**: 404–406.

DOI: 10.1111/jdv.17167

COVID-19 and HHV8 first spotted together: an affair under electron microscopy

Dear Editor

Despite the publication of articles about dermatopathology of COVID-related skin lesions,[1] only a few among these investigate patients with SARS-CoV-2 and other viral co-infections showing cutaneous manifestations.

According to the growing attention dedicated by your journal to the topic of novel human coronavirus SARS-Cov-2, we decided to share the rather interesting case of a woman with previous history of Kaposi sarcoma without active skin lesions, who was recently hospitalized for COVID-19 infection. The patient's newly emerging and evident skin manifestation consisted in bluish-red maculopapules (Fig. 1a) that have been biopsied revealed a dermal plaque made of spindle cells arranged in short fascicles lining irregularly shaped vascular slits and vascular structures surrounded by endothelial cells with plum nuclei. The spindle cells displayed mild atypia and rare mitotic figures, and the underlying epidermis was atrophic with a basal hyperpigmentation (Fig. 1b,c). As dermathopatologists, we performed an immunohistochemical analysis to further investigate the histological picture. The analysis results provided that all the spindle cells showed nuclear positivity for HHV8 (Clone 13B1) and cytoplasmatic reactivity for Podoplanin (Clone D2-40) (Fig. 1d, e).

These findings confirm our suspect of Kaposi's sarcoma in plaque phase. Even though we could be satisfied with the diagnosis, we could not ignore the concurrent COVID-19 infection that seemed to correlate with skin rash development, so we decided to perform transmission electron microscope (TEM) analysis and with our surprise we observed not one, but two different viral families:

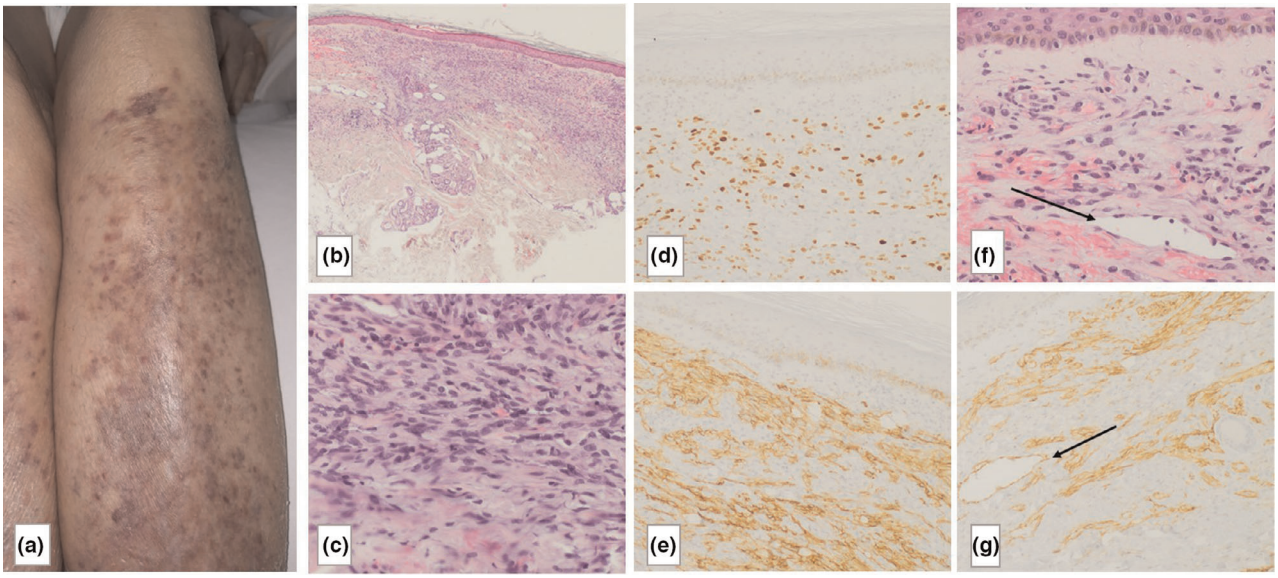

Figure 1 (a) Clinical picture at the admission in the COVID Hub from our patient affected by quiescent Kaposi sarcoma. (b, c) Haematoxilin and eosin staining of a Kaposi sarcoma in plaque stage. Compared with an early patch phase, here the spindle cell proliferation is easy to identify. Immunohistochemical analysis to confirm Kaposi sarcoma: HHV8-specific stain (d) shows nuclear positivity in the spindle cells; the same cellular population is highlighted by Podoplanin (D2–40) showing membrane and citoplasmatic positivity (e). (f, g) Vascular slit-like spaces in haematoxilin and eosin section and with immunohistochemical stain CD31 that allows to highlight vascular structure.

