

Definition, aims, and implementation of GA²LEN/HAEi Angioedema Centers of Reference and Excellence

To the Editor,

GA²LEN, the Global Allergy and Asthma European Network, and HAE international (HAEi), the global umbrella organization for the world's hereditary angioedema (HAE) patient groups, have launched their joint ACARE (Angioedema Center of Reference and Excellence) program, within GA²LEN's center of reference and excellence (CORE) initiative. Angioedema is a common, heterogeneous, often debilitating and chronic condition and is frequently a challenge for physicians and affected patients, especially patients suffering from recurrent attacks. Additionally, it can be a challenge for some patients to understand the underlying etiology of their angioedema (Table 1). GA²LEN's CORE networks, such as UCARE for urticaria and ADCARE for atopic dermatitis, help to improve the management of difficult-to-treat conditions. Here, we describe the aims, requirements, provisions, application process, audit, and accreditation protocol for GA²LEN/HAEi ACAREs. ACAREs aim to provide excellence in angioedema management, increase the knowledge of angioedema through research and education, and promote advocacy activities that raise angioedema awareness. To become a certified ACARE, angioedema centers must fulfill 32 requirements, defined by specific provisions that will be assessed during an audit visit. The ACARE program will result in a strong network of angioedema specialists, promote angioedema research and awareness, and harmonize and improve angioedema management globally. ACAREs will

expand access to modern angioedema medicines in countries where they are available and help to bring them to countries where they are not.¹

This document summarizes the aims of GA²LEN/HAEi Angioedema Centers of Reference and Excellence (ACAREs) and elaborates the requirements that ACAREs must fulfill to become certified. It also provides (see Appendix S1) background information on GA²LEN and HAEi, including HAEi member organizations and regional patient advocates, on why we need an Angioedema Center of Reference and Excellence (ACARE) program and network, and on the accreditation and certification process, governance and funding, and on the interaction with other GA²LEN networks of centers of reference and excellence. The protocols, aims, requirements, and provisions related to becoming a certified ACARE are based on (a) the experience of the GA²LEN UCARE network and (b) input from angioedema patients, general practitioners, and angioedema specialists.

What are the aims of GA²LEN/HAEi ACAREs? The aims of ACAREs are to set the global standard for excellence in comprehensive angioedema care through research, education, advocacy, and interaction among ACAREs. By serving as referral centers for the diagnosis and management of patients with angioedema, ACAREs will complement the local healthcare system. ACAREs aim to increase knowledge and awareness of angioedema.

TABLE 1 Classification of angioedema

Bradykinin-mediated angioedema				Mast cell mediator-mediated angioedema		Unknown mediator
C1-INH deficiency/defect		C1-INH normal		IgE mediated	Non-IgE mediated	
Inherited	Acquired	Inherited	Acquired			
HAE-1	AAE-C1-INH	HAE nC1-INH (HAE-FXII, HAE-ANGPT1, HAE-PLG, HAE-KNG1, HAE-UNK)	AE due to medication that interferes with BK degradation, eg ACEi	Angioedema with or without wheals in patients with urticaria	Angioedema with or without wheals in patients with urticaria	Idiopathic AE
HAE-2				Anaphylaxis		

Abbreviations: AAE-C1-INH, acquired angioedema due to C1-inhibitor deficiency; ACEi-AE, angiotensin-converting enzyme inhibitor-induced angioedema; BK, bradykinin; HAE nC1-INH, hereditary angioedema with normal C1-inhibitor levels, either due to a mutation in factor XII (F12), angiotensin-converting enzyme 1 (ANGPT1), plasminogen (PLG), kininogen-1 (KNG1), or unknown (UNK) (HAE-FXII, HAE-ANGPT1, HAE-PLG, HAE-KNG1, HAE-UNK); HAE-1, hereditary angioedema due to C1-inhibitor deficiency; HAE-2, hereditary angioedema due to C1-inhibitor dysfunction.

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Audit results: ☐ All requirements fulfilled, no areas with a need for further improvement, center should be certified
☐ All requirements fulfilled, some areas require further improvement, center should be certified
☐ Areas with a need for further improvement:

☐ Most requirements fulfilled, center should be certified after
☐ providing documentation that the following requirements are fulfilled

☐ re-audit in _____ months

Comments: _____

These guidelines and consensus documents include, for example, the international WAO/EAACI guideline for HAE, the EAACI/GA²LEN/EDF/WAO guideline for urticaria, the International/Canadian hereditary angioedema guideline,²⁻⁵ the international consensus on the diagnosis and management of pediatric patients with hereditary angioedema with C1 inhibitor deficiency, the international consensus on the use of genetics in the management of HAE,⁶ and the international consensus and practical guidelines on the gynecologic and obstetric management of female patients with hereditary angioedema caused by C1 inhibitor deficiency.⁷ The deliverables for this requirement are that (a) current guideline and consensus document versions are present (paper or electronic version) at the center, (b) ACARE staff can answer questions on the recommendations these documents provide, and (c) ACARE physicians can show, upon request, by use of a patient file, that patient management decisions are based on guideline recommendations (Figure 1B).

ACKNOWLEDGMENTS

The GA²LEN/HAEi ACARE is supported by its twin network, the GA²LEN UCARE network (www.ga2len-ucare.com). We thank Beate

Schinzel for expert help with formatting and revising the manuscript as well as its submission.

CONFLICT OF INTEREST













Dr Maurer reports grants and personal fees from Allakos, personal fees from Aralaz, grants and personal fees from AstraZeneca, grants and personal fees from BioCryst, grants from Blueprint, grants and personal fees from CSL Behring, grants and personal fees from FAES, grants and personal fees from Genentech, grants from Kalvista, grants from Lilly, grants from Menarini, grants and personal fees from Novartis, grants from Leo Pharma, grants from Moxie, grants from Pharming, personal fees from Pharvaris, grants and personal fees from Roche, from Sanofi, grants and personal fees from Shire/Takeda, grants and personal fees from UCB, grants and personal fees from Uriach, outside the submitted work. Dr Aberer reports other from Takeda, other from CSL Behring, outside the submitted work. Dr Ansotegui reports personal fees from Mundipharma, personal fees from Roxall, personal fees from Sanofi, personal fees from MSD, personal fees from Faes Farma, personal fees from Hikma, personal fees from Astra Zeneca, personal fees from Stallergens, outside the submitted work. Dr Aygören-Pürsün reports personal fees from Adverum, grants and personal fees from BioCryst, grants and personal fees from CSL Behring, grants and personal fees from Kalvista, personal fees from Pharming, grants and personal fees from Shire/Takeda, during the conduct of the study. Dr Banerji reports grants from Takeda, BioCryst, personal fees from Takeda, BioCryst, CSL, Pharming, Pharvaris, Kalvista, outside the submitted work. Dr Aberer reports other from Takeda, other from CSL Behring, outside the submitted work. Dr Bernstein reports grants and personal fees from Shire/Takeda, grants and personal fees from CSL Behring, grants and personal fees from BioCryst, grants and personal fees from Kalvista, grants from IONIS, grants and personal fees from Novartis/Genentech, grants and personal fees from Astra Zeneca, grants and personal fees from Sanofi Regeneron, from HAEA MAB, during the conduct of the study. Dr Betschel reports personal fees from CSL Behring, personal fees from Takeda/Shire, during the conduct of the study; personal fees from Octapharma, grants from Green Cross, personal fees from Novartis, personal fees from CADTH, outside the submitted work; and Chair of the Canadian Hereditary Angioedema Network. Dr Bork reports personal fees from CSL, personal fees from Shire, outside the submitted work. Dr Busse reports personal fees from CSL Behring, grants and personal fees from Shire, personal fees from Pharming, personal fees from Pearl Therapeutics, personal fees from BioCryst, personal fees from CVS Health, personal fees from Novartis, personal fees from Law offices of Levin, Riback, Adelman and Flangel, outside the submitted work. Dr Bygum reports grants and other from CSL Behring, grants and other from Shire/TAKEDA, other from ViroPharma, from HAE Scandinavia, outside the submitted work. Dr Caballero reports personal fees and other from BioCryst, personal fees, non-financial support and other from CSL-Behring, personal fees from Merck, personal fees and other from Novartis, personal fees from Octapharma, personal fees, non-financial support and

other from Shire HGT, personal fees and other from Pharming NV, outside the submitted work. Dr Campos reports and Personal fees for consulting and lectures from Takeda. Dr Cancian served for Scientific Advisory Boards, and received travel grants, for/from CSL Behring and Shire-Takeda. His Institution (Department of Medicine, University of Padua, Italy) received grants from CSL Behring and Shire-Takeda. Dr Cohn reports personal fees from Takeda, personal fees from Pharming, personal fees from CSL, personal fees from BioCryst, outside the submitted work. Dr Craig reports grants, personal fees and other from CSL Behring, grants and personal fees from Dyax, grants, personal fees and other from Takeda, grants and personal fees from BioCryst, grants and personal fees from Pharming, personal fees from Grifols, grants and non-financial support from GSK, grants and non-financial support from Regeneron, grants and non-financial support from Novartis/Genentech, outside the submitted work; and On the Medical Advisory Board for HAE-A of America, AAAAI Board, ALA Mid Atlantic Board. Dr Dissemond reports grants and personal fees from Novartis, outside the submitted work. Dr Du-Thanh reports personal fees from SHIRE/T. Dr Ensina reports personal fees from NOVARTIS, personal fees and non-financial support from TAKEDA, personal fees from SANOFI, outside the submitted work. Dr Farkas reports grants and personal fees from CSL Behring, grants and personal fees from Shire/Takeda, grants and personal fees from Pharming, personal fees from BioCryst, personal fees from Kalvista, outside the submitted work. Dr Gimenez-Arnau reports grants and personal fees from URIACH, grants and personal fees from NOVARTIS, personal fees from DSANOFI, grants from CARLOS III FEDER, personal fees from FAES, personal fees from GSK, personal fees from ALMIRALL, personal fees from ASTRA ZENECA, outside the submitted work. Dr Fukunaga reports personal fees from A Takeda company (Shire), personal fees from CSL Behring, outside the submitted work. Dr Gompels reports other from Speaker at Novartis Urticaria conference 2019, outside the submitted work; and A member of the Immunology Clinical reference group. Dr Gower reports grants, personal fees, research grants and other from Takeda/Shire/Dyax, research grants and other from BioCryst Pharmaceuticals, other from CSL Behring, other from Pharming, other from Fresenius kabi, outside the submitted work. Dr Grumach reports grants, personal fees and other from Shire/Takeda, personal fees and other from CSL Behring, outside the submitted work. Dr Hide reports grants and personal fees from Shire/Takeda, Mitsubishi-Tanabe, Taiho-yakuhin, personal fees from CSL-Behring, BioCryst, Novartis, Teikoku-Seiyaku, Eizai, Kaken, Kyowahakkou-Kirin, grants from Glaxo-Smith-Klein, outside the submitted work. Dr Jakob reports grants, personal fees and non-financial support from Novartis, personal fees and non-financial support from Thermo Fisher Scientific, grants and personal fees from ALK-Abello, personal fees from Celgene, personal fees and non-financial support from Bencard/Allergy Therapeutics, personal fees from Allergopharma, outside the submitted work. Dr Kaplan reports other from Genentech, other from Novartis, other from Sanofi Aventis, other from BioCryst, outside the submitted work. Dr Katelaris reports grants and personal fees from CSL Behring, grants and personal fees

from Takeda, grants from BioCryst, during the conduct of the study. Dr Kleinheinz reports personal fees from Novartis, during the conduct of the study; personal fees from Abbvie, personal fees from Leo GmbH, personal fees from Janssen, personal fees from Medac, personal fees from Galderma, personal fees from Celgene, personal fees from Bencard, outside the submitted work. Dr Kocatürk reports personal fees from Novartis, personal fees from Sanofi, outside the submitted work. Dr Longhurst reports grants and personal fees from BioCryst, grants, personal fees and non-financial support from CSL Behring, grants from Ionis, grants from Kalvista, personal fees from Pharming, grants, personal fees and non-financial support from Takeda, personal fees from GSK, personal fees from Octapharma, outside the submitted work. Dr MacGinnitie reports personal fees from BioCryst, personal fees from Shire, outside the submitted work. Dr Magerl reports personal fees from CSL Behring, personal fees from Shire/part of Takeda, personal fees from Novartis, personal fees from BioCryst, personal fees from KalVista, personal fees from Pharming, outside the submitted work. Dr Makris reports personal fees from Novartis, outside the submitted work. Dr Marsland reports grants and personal fees from Novartis, personal fees and non-financial support from Sanofi, personal fees from Galderma, personal fees from Roche, non-financial support from Almirall, outside the submitted work. I. Martinez Saguer has received honoraria, research funding, and travel grants from BioCryst, CSL Behring, Pharming, and Takeda/Shire, KalVista and/or served as a consultant and/or participated in advisory boards for these companies. Dr Metz reports personal fees from Moxie, personal fees from Novartis, personal fees from Roche, personal fees from Sanofi, personal fees from Shire, outside the submitted work. Dr Papadopoulos reports personal fees from Novartis, personal fees from Nutricia, personal fees from HAL, personal fees from MENARINI/FAES FARMA, personal fees from SANOFI, personal fees from MYLAN/MEDA, personal fees from BIOMAY, personal fees from AstraZeneca, personal fees from GSK, personal fees from MSD, personal fees from ASIT BIOTECH, personal fees from Boehringer Ingelheim, grants from Gerolymatos International SA, grants from Capricare, outside the submitted work. Dr Reich reports personal fees from Abbvie, personal fees from Bioderma, personal fees from Chema Elektromet, personal fees from Galderma, personal fees from Bausch Health, personal fees from Janssen, personal fees from Leo Pharma, personal fees from Medac, grants and personal fees from Menlo Therapeutics, personal fees from Novartis, personal fees from Pierre-Fabre, personal fees from Trevi, personal fees from Kymab Limited, personal fees from MSD, personal fees from Metriopharm, personal fees from Drug Delivery Solutions, personal fees from Eli Lilly, outside the submitted work. Dr Riedl reports grants and personal fees from CSL Behring, grants and personal fees from Shire/Takeda, grants and personal fees from BioCryst, grants and personal fees from Pharming, personal fees from Pharvaris, personal fees from Adverum, personal fees from KalVista, personal fees from Attune, grants from Ionis, outside the submitted work; and US HAEA Medical Advisory Board Member - uncompensated. Dr Röckmann-Helmbach reports other from Pharming, during the conduct of the

study. Dr Schmid-Grendelmeier reports personal fees from Takeda, during the conduct of the study. Dr Serpa reports speaker fees from Shire/Takeda, Novartis and Sanofi. Dr Sheikh reports other from Takeda, from CSL, outside the submitted work. Dr Smith reports personal fees from Takeda/Shire, personal fees from CSL/Behring, grants from Takeda/Shire, grants from BioCryst, outside the submitted work. Dr Soria reports personal fees from Novartis, personal fees from Sanofi Genzyme, personal fees from Abbvie, outside the submitted work. Dr Staubach reports personal fees and non-financial support from Takeda, personal fees and non-financial support from Shire, personal fees and non-financial support from Pharming, personal fees and non-financial support from CSL Behring, personal fees and non-financial support from Novartis, outside the submitted work. Dr Stobiecki reports personal fees from lectures given for CSL Behring, Takeda (Shire), personal fees from conducting clinical trials as a principal investigator for BioCryst, personal fees from consultant work for: BioCryst, CSL Behring, Takeda (Shire), Pharming, outside the submitted work. Dr Sussman reports grants and personal fees from Research grants from pharmaceutical companies. Novartis, Genentech, Amgen, Sanofi, CSL behring, Leo, Kedrion, Green Cross, DBV, Aimune. D'dConsulting and honararia from Novartis, Novo, CSL Behring, Amgen., during the conduct of the study; grants from Novartis Pharmaceutical, grants from Genentech, grants from CSL behring, grants from Amgen, grants from Leo, grants from DBV, grants from Aimune, grants from Sanofi, non-financial support from Novartis, non-financial support from Novo, non-financial support from PEDIAPHARM, non-financial support from Sanofi, grants from Kedrion, outside the submitted work. Dr Thomsen reports grants and personal fees from Novartis, grants and personal fees from Sanofi, grants and personal fees from UCB, grants and personal fees from Janssen, grants and personal fees from Abbvie, outside the submitted work. Dr Treudler reports personal fees from Shire-Takeda, personal fees from ALK-Abello, personal fees from Novartis, grants and personal fees from Sanofi-Genzyme, grants from Hautnetz Leipzig e.V., other from Fraunhofer Institut, outside the submitted work. Dr van Doorn reports personal fees from Leopharma, grants and personal fees from Novartis, personal fees from Abbvie, personal fees from BMS, personal fees from Celgene, personal fees from Lilly, personal fees from MSD, personal fees from Pfizer, personal fees from Sanofi-Genzyme, personal fees from Janssen Cilag, outside the submitted work. Dr Weber-Chrysochoou reports personal fees from Takeda and CSL Behring, outside the submitted work. Dr Zuberbier reports personal fees from AstraZeneca, personal fees from AbbVie, personal fees from ALK, personal fees from Almirall, personal fees from Astellas, personal fees from Bayer Health Care, personal fees from Bencard, personal fees from Berlin Chemie, personal fees from FAES, personal fees from HAL, personal fees from Leti, personal fees from Meda, personal fees from Menarini, personal fees from Merck, personal fees from MSD, grants and personal fees from Novartis, personal fees from Pfizer, personal fees from Sanofi, personal fees from Stallergenes, personal fees from Takeda, personal fees from Teva, personal fees from UCB, grants from Henkel, personal fees from

Kryolan, personal fees from L'Oréal, outside the submitted work; and Organizational affiliations: Üommitee member: WHO-Initiative "Allergic Rhinitis and Its Impact on Asthma" (ARIA) Member of the Board: German Society for Allergy and Clinical Immunology (DGAKI) Dead: European Centre for Allergy Research Foundation (ECARF) Decretary General: Global Allergy and Asthma European Network (GA2LEN) Member: Committee on Allergy Diagnosis and Molecular Allergology, World Allergy Organization (WAO). Other authors declare that they have no conflicts of interest.

Marcus Maurer¹ 
 Werner Aberer²
 Rosana Agondi³
 Mona Al-Ahmad⁴ 
 Maryam Ali Al-Nesf⁵ 
 Ignacio Ansotegui⁶
 Rand Arnaout⁷
 Luisa Karla Arruda⁸ 
 Riccardo Asero⁹ 
 Emel Aygören-Pürsü¹⁰
 Aleena Banerji¹¹
 Andrea Bauer¹²
 Moshe Ben-Shoshan¹³
 Alejandro Berardi¹⁴
 Jonathan A. Bernstein¹⁵ 
 Stephen Betschel¹⁶
 Carsten Bindslev-Jensen¹⁷
 Mojca Bizjak¹⁸ 
 Isabelle Boccon-Gibod¹⁹
 Konrad Bork²⁰ 
 Laurence Bouillet¹⁹ 
 Henrik Balle Boysen²¹
 Nicholas Brodzski²²
 Sigurd Broesby-Olsen¹⁷ 
 Paula Busse²³
 Thomas Buttgerit¹
 Anette Bygum²⁴ 
 Teresa Caballero²⁵
 Régis A. Campos^{26,27}
 Mauro Cancian²⁸
 Ivan Cherrez-Ojeda^{29,30} 
 Danny M. Cohn³¹
 Célia Costa³²
 Timothy Craig³³
 Paulo Ricardo Criado^{34,35,36}
 Roberta F. Criado³⁷
 Dorottya Csuka³⁸
 Joachim Dissemond³⁹
 Aurélie Du-Thanh⁴⁰
 Luis Felipe Ensina⁴¹
 Ragıp Ertaş⁴²
 José E. Fabiani⁴³
 Claudio Fantini⁴⁴

Henriette Farkas³⁸ 
 Silvia Mariel Ferrucci⁴⁵
 Ignasi Figueras-Nart⁴⁶
 Natalia L. Fili⁴⁷ 
 Daria Fomina^{48,49}
 Atsushi Fukunaga⁵⁰ 
 Asli Gelincik⁵¹ 
 Ana Giménez-Arnau⁵² 
 Kiran Godse⁵³
 Mark Gompels⁵⁴
 Margarida Gonçalves⁵⁵
 Maia Gotua⁵⁶ 
 Richard Gower⁵⁷
 Anete S. Grumach⁵⁸
 Guillermo Guidos-Fogelbach⁵⁹
 Michihiro Hide⁶⁰
 Natalia Ilina⁶¹
 Naoko Inomata⁶²
 Thilo Jakob⁶³
 Dario O. Josviack⁶⁴
 Hye-Ryun Kang⁶⁵ 
 Allen Kaplan⁶⁶ 
 Alicja Kasperska-Zajac⁶⁷ 
 Constance Katelaris⁶⁸
 Aharon Kessel⁶⁹
 Andreas Kleinheinz⁷⁰
 Emek Kocatürk⁷¹
 Mitja Košnik¹⁸ 
 Dorota Krasowska⁷²
 Kanokvalai Kulthanan⁷³
 M. Sendhil Kumaran⁷⁴
 José Ignacio Larco Sousa⁷⁵
 Hilary J. Longhurst^{76,77,78}
 William Lumry⁷⁹
 Andrew MacGinnitie⁸⁰ 
 Markus Magerl¹
 Michael P. Makris⁸¹
 Alejandro Malbrán⁸²
 Alexander Marsland⁸³
 Inmaculada Martinez-Saguer⁸⁴
 Iris V. Medina⁸⁵
 Raisa Meshkova⁸⁶
 Martin Metz¹ 
 Iman Nasr⁸⁷ 
 Jan Nicolay⁸⁸
 Chikako Nishigori⁸⁹
 Isao Ohsawa⁹⁰
 Kemal Özyurt⁹¹
 Nikolaos G. Papadopoulos⁹² 
 Claudio A. S. Parisi⁹³
 Jonathan Grant Peter⁹⁴
 Wolfgang Pfützner⁹⁵ 
 Todor Popov⁹⁶

- Nieves Prior⁹⁷
German D. Ramon⁹⁸
Adam Reich⁹⁹
Avner Reshef¹⁰⁰ 
Marc A. Riedl¹⁰¹ 
Bruce Ritchie¹⁰²
Heike Röckmann-Helmbach¹⁰³
Michael Rudenko¹⁰⁴
Andaç Salman¹⁰⁵ 
Mario Sanchez-Borges¹⁰⁶ 
Peter Schmid-Grendelmeier¹⁰⁷ 
Faradiba S. Serpa¹⁰⁸
Esther Serra-Baldrich¹⁰⁹
Farrukh R. Sheikh¹¹⁰
William Smith¹¹¹
Angèle Soria¹¹² 
Petra Staubach¹¹³
Urs C. Steiner¹¹⁴
Marcin Stobiecki¹¹⁵
Gordon Sussman¹¹⁶ 
Anna Tagka¹¹⁷ 
Simon Francis Thomsen¹¹⁸ 
Regina Treudler¹¹⁹
Solange Valle¹²⁰
Martijn van Doorn¹²¹
Lilian Varga³⁸ 
Daniel O. Vázquez¹²² 
Nicola Wagner¹²³
Liangchun Wang¹²⁴ 
Christina Weber-Chrysochoou¹⁰⁷
Young-Min Ye¹²⁵ 
Anna Zalewska-Janowska¹²⁶
Andrea Zanichelli¹²⁷
Zuotao Zhao^{128,129} 
Yuxiang Zhi¹³⁰ 
Torsten Zuberbier¹³¹ 
Ricardo D. Zwiener¹³²
Anthony Castaldo¹³³
- ¹Department of Dermatology and Allergy, Dermatological Allergology, Allergie-Centrum-Charité, Charité—Universitätsmedizin Berlin, Berlin, Germany
²Department of Dermatology, Medical University of Graz, Graz, Austria
³University of São Paulo, São Paulo, Brazil
⁴Microbiology Department, Faculty of Medicine, Kuwait University, Safat, Kuwait
⁵Allergy and Immunology Section, Department of Medicine, Hamad General Hospital, Doha, Qatar
⁶Department of Allergy and Immunology, Hospital Quiron Bizkaia, Bizkaia, Spain
⁷King Faisal Specialist Hospital & Research Center, Al Faisal University, Riyadh, Saudi Arabia
⁸Ribeirão Preto Medical School, University of São Paulo, São Paulo, Brazil
⁹Ambulatorio di Allergologia, Clinica San Carlo, Paderno Dugnano (MI), Italy
¹⁰Center for Children and Adolescents, University Hospital Frankfurt, Frankfurt, Germany
¹¹Division of Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Boston, MA, USA
¹²Department of Dermatology, University Allergy Center, University Hospital Carl Gustav Carus, Technical University, Dresden, Germany
¹³Division of Allergy, Immunology and Dermatology, Department of Pediatrics, McGill University Health Center, Montreal, QC, Canada
¹⁴Instituto de Asma, Alergia y Enfermedades Respiratorias, Corrientes, Argentina
¹⁵Allergy Section, Division of Immunology, Department of Internal Medicine, Partner Bernstein Allergy Group, Partner Bernstein Clinical Research Center, University of Cincinnati, Cincinnati, OH, USA
¹⁶Division of Clinical Immunology and Allergy, St. Michael's Hospital, University of Toronto, Toronto, ON, Canada
¹⁷Department of Dermatology and Allergy Center, Odense University Hospital, Odense, Denmark
¹⁸Division of Allergy, University Clinic of Respiratory and Allergic Diseases Golnik, Golnik, Slovenia
¹⁹Clinical Immunology/Internal Medicine Department, National Reference Center for Angioedema, Grenoble University Hospital, Grenoble, France
²⁰Department of Dermatology, Johannes Gutenberg University Mainz, Mainz, Germany
²¹HAE International (HAEi), Horsens, Denmark
²²Skåne University Hospital, Lund University, Lund, Sweden
²³Division of Clinical Immunology, Icahn School at Mount Sinai, New York, NY, USA
²⁴HAE Centre, Odense University Hospital, Odense, Denmark
²⁵Allergy Department, Hospital Universitario La Paz, IdiPaz, CIBERER U754, Madrid, Spain
²⁶Universidade Federal da Bahia, Salvador, Brazil
²⁷Serviço de Imunologia, Hospital das Clínicas Professor Edgard Santos, Salvador, Brazil
²⁸Department of Systems Medicine, University Hospital of Padua, Padua, Italy
²⁹School of Medicine, Universidad de Especialidades Espíritu Santo, Samborombón, Ecuador
³⁰RespiraLab, Research, Guayaquil, Ecuador
³¹Department of Vascular Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands
³²Immunoallergy Department, Hospital de Santa Maria, Centro Hospitalar Universitário de Lisboa Norte (CHLN), EPE, Lisbon, Portugal
³³Department of Medicine and Pediatrics, Penn State University, Hershey, PA, USA

- ³⁴Faculdade de Medicina do ABC, Santo André, Brazil
- ³⁵Alergoskin Alergia e Dermatologia SS Ltda, Santo André, Brazil
- ³⁶UCARE Center, São Paulo, Brazil
- ³⁷Faculdade de Medicina do ABC (FMABC), Santo André, Brazil
- ³⁸3rd Department of Internal Medicine, Hungarian Angioedema Reference Center, Semmelweis University, Budapest, Hungary
- ³⁹Department of Dermatology, Venereology and Allergology, University of Essen, Essen, Germany
- ⁴⁰Service de Dermatologie-allergologie, CHU Montpellier, Montpellier Cedex 5, France
- ⁴¹Division of Allergy, Clinical Immunology and Rheumatology, Department of Pediatrics, Federal University of São Paulo, São Paulo, Brazil
- ⁴²Department of Dermatology, Kayseri City Education and Research Hospital, Kayseri, Turkey
- ⁴³Private Practice, Lomas de Zamora, Argentina
- ⁴⁴Servicio de Alergia e Inmunología—Hospital Alende y Clínica Colón, Mar del Plata, Argentina
- ⁴⁵Ambulatorio di Dermatologia Allergologica e Professionale, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano (MI), Italy
- ⁴⁶The Dermatology Department of the Hospital de Bellvitge, Universitat de Barcelona, Barcelona, Spain
- ⁴⁷Unidad Alergia e Inmunología Clínica, Hospital Público Materno Infantil, Salta, Argentina
- ⁴⁸Center of Allergy and Immunology, City Clinical Hospital No. 52, Moscow Ministry of Healthcare, Moscow, Russian Federation
- ⁴⁹Department of Allergology and Clinical Immunology, I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation
- ⁵⁰Division of Dermatology, Graduate School of Medicine, Kobe University, Kobe, Japan
- ⁵¹Division of Immunology and Allergic Diseases, Department of Internal Medicine, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey
- ⁵²Department of Dermatology, Hospital del Mar, IMIM, Universitat Autònoma, Barcelona, Spain
- ⁵³Department of Dermatology, D Y. Patil University School of Medicine, Mumbai, India
- ⁵⁴Department of Immunology, North Bristol NHS Trust, Southmead Hospital, Bristol, UK
- ⁵⁵Clinica de Dermatologia, Centro Hospitalar Universitário Coimbra, Coimbra, Portugal
- ⁵⁶Center of Allergy and Immunology, Tbilisi, Georgia
- ⁵⁷Marycliff Clinical Research, Spokane, WA, USA
- ⁵⁸Clinical Immunology, Medical School, University Center Health ABC, Santo Andre, Brazil
- ⁵⁹National School of Medicine, Instituto Politécnico Nacional, Mexico City, Mexico
- ⁶⁰Department of Dermatology, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan
- ⁶¹NRC Institute of Immunology FMBA, Moscow, Russia
- ⁶²Department of Environmental Immuno-Dermatology, Yokohama City University Graduate School of Medicine, Yokohama, Japan
- ⁶³Department of Dermatology and Allergy, University Medical Center Giessen (UKGM), Justus-Liebig-University Giessen, Giessen, Germany
- ⁶⁴Instituto de Medicina Respiratoria—Rafaela, Santa Fe, Argentina
- ⁶⁵Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, Seoul, Korea
- ⁶⁶Medical University of South Carolina, Charleston, SC, USA
- ⁶⁷European Center for Diagnosis and Treatment of Urticaria, Zabrze, Poland
- ⁶⁸Immunology & Allergy Unit, Department of Medicine, Campbelltown Hospital, Campbelltown, NSW, Australia
- ⁶⁹Division of Allergy & Clinical Immunology, Rappaport Faculty of Medicine, Bnai Zion Medical Center, Technion, Haifa, Israel
- ⁷⁰Clinic for Dermatology, Elbe Kliniken Buxtehude, Buxtehude, Germany
- ⁷¹Department of Dermatology, School of Medicine, Koç University, Koc, Turkey
- ⁷²Department of Dermatology, Venerology and Pediatric Dermatology, Medical University of Lublin, Lublin, Poland
- ⁷³Department of Dermatology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand
- ⁷⁴Department of Dermatology, Postgraduate Institute of Medical Education and Research, Chandigarh, India
- ⁷⁵Clinica San Felipe, Lima, Peru
- ⁷⁶Department of Immunology, Addenbrookes Hospital Cambridge University NHS Foundation Trust, Cambridge, UK
- ⁷⁷UCLH, London, UK
- ⁷⁸Addenbrooke's Hospital Cambridge and University College Hospital, London, UK
- ⁷⁹Allergy/Immunology Division, Department of Internal Medicine, University of Texas Southwestern Medical School, Dallas, TX, USA
- ⁸⁰Division of Immunology, Department of Pediatrics, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA
- ⁸¹Allergy Unit "D. Kalogeromitros", 2nd Department of Dermatology and Venereology, University Hospital "Attikon", National and Kapodistrian University of Athens, Athens, Greece
- ⁸²Unidad de Alergia, Asma e Inmunología Clínica, Buenos Aires, Argentina
- ⁸³Department of Dermatology, The Urticaria Clinic, Salford Royal Foundation Trust, University of Manchester, Manchester, UK
- ⁸⁴Hemophilia Centre Rhine Main (HZRM), Moerfelden-Walldorf, Germany
- ⁸⁵Allergy and Clinical Immunology Department, Centro Médico Vitae, de Julio, Argentina
- ⁸⁶Department of Clinical Immunology and Allergology, Smolensk State Medical University, Smolensk, Russian Federation
- ⁸⁷Adult Immunology and Allergy Unit, Department of Medicine, Royal Hospital, Muscat, Oman

- ⁸⁸Klinik für Dermatologie, Universitätsklinikum Mannheim, Mannheim, Germany
- ⁸⁹Division of Dermatology, Kobe University Graduate School of Medicine, Kobe, Japan
- ⁹⁰Department of Internal Medicine, Saiyu Soka Hospital, Soka, Japan
- ⁹¹Department of Dermatology, Faculty of Medicine, Kırşehir Ahi Evran University, Kırşehir, Turkey
- ⁹²Allergy Unit, 2nd Pediatric Clinic, National and Kapodistrian University of Athens, Athens, Greece
- ⁹³Adults and Pediatrics Allergy Unit, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina
- ⁹⁴Department of Medicine, University of Cape Town, Cape Town, South Africa
- ⁹⁵Department of Dermatology and Allergology, Allergy Center Hessen, University Clinic Marburg, Marburg, Germany
- ⁹⁶University Hospital Sv. Ivan Rilski, Sofia, Bulgaria
- ⁹⁷Allergy Department, Hospital Universitario Severo Ochoa, Madrid, Spain
- ⁹⁸Instituto de Alergia e Inmunología del Sur, Buenos Aires, Argentina
- ⁹⁹Department of Dermatology, University of Rzeszow, Rzeszów, Poland
- ¹⁰⁰Angioedema Center, Barzilai Medical Center, Ashkelon, Israel
- ¹⁰¹Department of Medicine, University of California—San Diego, La Jolla, CA, USA
- ¹⁰²Departments of Medicine and Medical Oncology, University of Alberta, Edmonton, AB, Canada
- ¹⁰³Department of Dermatology and Allergology, University Medical Center Utrecht, Utrecht, The Netherlands
- ¹⁰⁴London Allergy and Immunology Centre, London, UK
- ¹⁰⁵Dermatology Department, Marmara University School of Medicine, Pendik Research and Training Hospital, Istanbul, Turkey
- ¹⁰⁶Allergy and Clinical Immunology Department, Centro Medico Docente La Trinidad, Caracas, Venezuela
- ¹⁰⁷Allergy Unit, Department of Dermatology, University Hospital of Zürich, Zürich, Switzerland
- ¹⁰⁸Hospital Santa Casa de Misericórdia de Vitória, Espírito Santo, Brazil
- ¹⁰⁹Dermatology Department, Hospital Sant Pau, Barcelona, Spain
- ¹¹⁰Department of Medicine, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia
- ¹¹¹Clinical Immunology and Allergy, Royal Adelaide Hospital, Adelaide, SA, Australia
- ¹¹²Service de Dermatologie et Allergologie, Hôpital Tenon, APHP, Sorbonne Université, Paris, France
- ¹¹³Department of Dermatology, University Medical Center, Mainz, Germany
- ¹¹⁴Department of Clinical Immunology, University Hospital Zurich, Zurich, Switzerland
- ¹¹⁵Department of Environmental Allergology, Jagiellonian University Medical College Kraków, HAE Center, University Hospital, Kraków, Poland
- ¹¹⁶Division of Allergy and Immunology, University of Toronto, Toronto, ON, Canada
- ¹¹⁷First Department of Dermatology and Venereology, National and Kapodistrian University of Athens, "A. Syggros" Hospital, Referral Center of Occupational Dermatological Diseases, Athens, Greece
- ¹¹⁸Department of Dermatology, Bispebjerg Hospital, Copenhagen, Denmark
- ¹¹⁹Department of Dermatology, Venerology and Allergology and Leipzig Interdisciplinary Center of Allergology—Comprehensive Allergy Center, UMC Leipzig, Leipzig, Germany
- ¹²⁰Federal University of Rio de Janeiro, Rio de Janeiro, Brazil
- ¹²¹Department of Dermatology, Erasmus MC, Rotterdam, The Netherlands
- ¹²²Clínica Privada Monte Grande, Buenos Aires, Argentina
- ¹²³Department of Dermatology, University of Erlangen, Erlangen, Germany
- ¹²⁴Dermatology Department of Sun Yat-sen Memorial Hospital, Guangzhou, China
- ¹²⁵Department of Allergy and Clinical Immunology, Ajou University School of Medicine, Suwon, Korea
- ¹²⁶Chair of Clinical Immunology and Rheumatology, Department of Psychodermatology, Medical University of Lodz, Lodz, Poland
- ¹²⁷Department of Biomedical and Clinical Sciences, Luigi Sacco Hospital, University of Milan, Milan, Italy
- ¹²⁸Department of Dermatology and Venereology, First Hospital, Peking University, Beijing, China
- ¹²⁹Beijing Key Laboratory of Molecular Diagnosis on Dermatoses, Beijing, China
- ¹³⁰Department of Allergy, Peking Union Medical College Hospital & Chinese Academy of Medical Sciences, Beijing, China
- ¹³¹Department of Dermatology and Allergy, Allergie-Centrum-Charité, Charité—Universitätsmedizin Berlin, Berlin, Germany
- ¹³²Servicio de Alergia e Inmunología, Hospital Universitario Austral, Buenos Aires, Argentina
- ¹³³HAE International (HAEi), Fairfax City, VA, USA

Correspondence

Marcus Maurer, Department of Dermatology and Allergy, Allergie-Centrum-Charité, Dermatological Allergology, Charité—Universitätsmedizin Berlin, Charitéplatz 1, D-10117 Berlin, Germany.
Email: marcus.maurer@charite.de

ORCID

Marcus Maurer  <https://orcid.org/0000-0002-4121-481X>
Mona Al-Ahmad  <https://orcid.org/0000-0003-3720-7032>
Maryam Ali Al-Nesf  <https://orcid.org/0000-0001-9354-0214>
Luisa Karla Arruda  <https://orcid.org/0000-0002-7505-210X>
Riccardo Asero  <https://orcid.org/0000-0002-8277-1700>
Jonathan A. Bernstein  <https://orcid.org/0000-0002-3476-1196>

Mojca Bizjak  <https://orcid.org/0000-0003-2595-468X>
 Konrad Bork  <https://orcid.org/0000-0002-6084-4577>
 Laurence Bouillet  <https://orcid.org/0000-0001-8245-4767>
 Sigurd Broesby-Olsen  <https://orcid.org/0000-0002-1558-8471>
 Anette Bygum  <https://orcid.org/0000-0002-3004-0180>
 Ivan Cherrez-Ojeda  <https://orcid.org/0000-0002-1610-239X>
 Henriette Farkas  <https://orcid.org/0000-0003-2929-1721>
 Natalia L. Fili  <https://orcid.org/0000-0003-0327-3963>
 Atsushi Fukunaga  <https://orcid.org/0000-0003-2026-8154>
 Asli Gelincik  <https://orcid.org/0000-0002-3524-9952>
 Ana Giménez-Arnan  <https://orcid.org/0000-0001-9548-5423>
 Maia Gotua  <https://orcid.org/0000-0003-2497-4128>
 Hye-Ryun Kang  <https://orcid.org/0000-0002-2317-4201>
 Allen Kaplan  <https://orcid.org/0000-0002-6566-4743>
 Alicja Kasperska-Zajac  <https://orcid.org/0000-0002-2000-0070>
 Mitja Košnik  <https://orcid.org/0000-0002-4701-7374>
 Andrew MacGinnitie  <https://orcid.org/0000-0002-9451-3733>
 Martin Metz  <https://orcid.org/0000-0002-4070-9976>
 Iman Nasr  <https://orcid.org/0000-0003-0346-9675>
 Nikolaos G. Papadopoulos  <https://orcid.org/0000-0002-4448-3468>
 Wolfgang Pfützner  <https://orcid.org/0000-0002-8721-724X>
 Avner Reshef  <https://orcid.org/0000-0002-3324-7072>
 Marc A. Riedl  <https://orcid.org/0000-0003-3460-1544>
 Andaç Salman  <https://orcid.org/0000-0002-6407-926X>
 Mario Sanchez-Borges  <https://orcid.org/0000-0002-9308-6418>
 Peter Schmid-Grendelmeier  <https://orcid.org/0000-0003-3215-3370>
 Angèle Soria  <https://orcid.org/0000-0002-8726-6658>
 Gordon Sussman  <https://orcid.org/0000-0002-2202-2513>
 Anna Tagka  <https://orcid.org/0000-0003-3307-6522>
 Simon Francis Thomsen  <https://orcid.org/0000-0002-4838-300X>
 Lilian Varga  <https://orcid.org/0000-0002-5484-364X>

Daniel O. Vázquez  <https://orcid.org/0000-0001-9864-0783>
 Liangchun Wang  <https://orcid.org/0000-0002-5169-2751>
 Young-Min Ye  <https://orcid.org/0000-0002-7517-1715>
 Zuotao Zhao  <https://orcid.org/0000-0002-9595-6050>
 Yuxiang Zhi  <https://orcid.org/0000-0001-7539-6650>
 Torsten Zuberbier  <https://orcid.org/0000-0002-1466-8875>

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.