Objective. To develop and validate classification criteria for microscopic polyangiitis (MPA).

Methods. Patients with vasculitis or comparator diseases were recruited into an international cohort. The study proceeded in 5 phases: 1) identification of candidate items using consensus methodology, 2) prospective collection of candidate items present at the time of diagnosis, 3) data-driven reduction of the number of candidate items, 4) expert panel review of cases to define the reference diagnosis, and 5) derivation of a points-based risk score for disease classification in a development set using least absolute shrinkage and selection operator logistic regression, with subsequent validation of performance characteristics in an independent set of cases and comparators.

Results. The development set for MPA consisted of 149 cases of MPA and 408 comparators. The validation set consisted of an additional 142 cases of MPA and 414 comparators. From 91 candidate items, regression analysis identified 10 items for MPA, 6 of which were retained. The final criteria and their weights were as follows: perinuclear antineutrophil cytoplasmic antibody (ANCA) or anti–myeloperoxidase-ANCA positivity (+6), pauci-immune glomerulonephritis (+3), lung fibrosis or interstitial lung disease (+3), sino-nasal symptoms or signs (−C0 3), cytoplasmic ANCA or anti–proteinase 3 ANCA positivity (−1), and eosinophil count ≥1 × 10^9/liter (−C0 4). After excluding mimics of vasculitis, a patient with a diagnosis of small- or medium-vessel vasculitis could be classified as having MPA with a cumulative score of ≥5 points. When these criteria were tested in the validation data set, the sensitivity was 91% (95% confidence interval [95% CI] 85–95%) and the specificity was 94% (95% CI 92–96%).

Conclusion. The 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for MPA are now validated for use in clinical research.
INTRODUCTION

The first description of “periarteritis nodosa” was made by Kussmaul and Maier in 1866 (1). In 1948, Davson et al described 14 cases at autopsy that fitted the clinical description of periarteritis nodosa (2). They divided the cases into 2 groups based on the histologic findings in the kidneys. The clinical presentations of both groups were similar, but their pathologic features differed: 9 patients showed a distinctive pattern of necrotizing glomerulonephritis with no arterial aneurysms, whereas the other 5 patients showed no glomerular lesions in the kidney but had widespread renal arterial aneurysms and renal infarcts. This is the first time that a clear distinction was made between the microscopic form of polyarteritis nodosa (now called microscopic polyangiitis [MPA]) and classic polyarteritis nodosa (PAN). The 1990 American College of Rheumatology (ACR) criteria for the classification of vasculitis did not make this distinction; instead both entities were included under the term “polyarteritis nodosa” (3) or possibly “granulomatosis with polyangiitis” (then called Wegener’s granulomatosis).

The publication that resulted from the 1994 Chapel Hill Consensus Conference (CHCC) aimed to standardize the nomenclature and commented that “different names are being used for the same disease and the same name is being used for different diseases” (4). The distinction between MPA and PAN is recognized in the CHCC definitions. The main discriminating feature between MPA and PAN is the presence in MPA of pauci-immune vasculitis in arterioles, venules, or capillaries. PAN is restricted to a medium-vessel disease, and MPA is a predominantly small-vessel vasculitis that can also involve medium-sized vessels.

The resulting inconsistency between disease definitions and existing classification criteria highlights an important need to update the classification criteria and to include MPA as its own entity. Additionally, over time there have been improvements in our understanding of the different forms of vasculitis, which have been informed in part by routine testing for antineutrophil cytoplasmic antibody (ANCA) in patients with vasculitis and increased utilization of cross-sectional imaging, both of which have occurred since the 1990 ACR criteria were published. Indeed, most investigators regard MPA as part of the group of small-vessel vasculitides related to the presence of ANCA. This article outlines the development and validation of the new ACR/European Alliance of Associations for Rheumatology (EULAR)–endorsed classification criteria for MPA.

METHODS

A detailed and complete description of the methods involved in the development and validation of the classification criteria for MPA is provided in Supplementary Appendix 1, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41983/abstract. Briefly, an international Steering Committee comprising clinician investigators with expertise in vasculitis, statisticians, and data managers was established to oversee the overall Diagnostic and Classification Criteria in Vasculitis (DCVAS) project. The Steering Committee established a 5-stage plan using data-driven and consensus methodology to develop the criteria for each of 6 forms of vasculitis.

Stage 1: generation of candidate classification items for the systemic vasculitides. Candidate classification items were generated by expert opinion and reviewed by a group of vasculitis experts across a range of specialties using a nominal group technique.

Stage 2: DCVAS prospective observational study. A prospective, international multisite observational study was conducted (see Appendix A for study investigators and sites). Ethical approval was obtained from national and local ethics committees. Consecutive patients representing the full spectrum of disease were recruited from academic and community practices. Patients were included if they were 18 years or older and had a diagnosis of vasculitis or a condition that mimics vasculitis. Patients with ANCA-associated vasculitis (AAV) could only be enrolled within 2 years of diagnosis. Only data present at diagnosis were recorded.

Stage 3: refinement of candidate items specifically for AAV. The Steering Committee conducted a data-driven process to reduce the number of candidate items of relevance to cases and comparators for AAV. Items were selected for exclusion if they had a prevalence of <5% within the data set and/or they were not clinically relevant for classification criteria (e.g., related to infection, malignancy, or demographic characteristics). Low-frequency items of clinical importance could be combined, when appropriate.

Stage 4: expert review to derive a gold standard–defined set of cases of AAV. Experts in vasculitis from a wide range of geographic locations and specialties reviewed all submitted cases of vasculitis and a random selection of mimics of
vasculitis. Each reviewer was asked to review ~50 submitted cases to confirm the diagnosis and to specify the certainty of their diagnosis as follows: very certain, moderately certain, uncertain, or very uncertain. Only cases agreed upon with at least moderate certainty were retained for further analysis.

**Stage 5: derivation and validation of the final classification criteria for MPA.** The DCVAS AAV data set was randomly split into development (50%) and validation (50%) sets. Comparisons were performed between cases of MPA and a comparator group randomly selected from the DCVAS cohort in the following proportions: another type of AAV (including granulomatosis with polyangiitis [GPA] and eosinophilic granulomatosis with polyangiitis [EGPA]), 60%; another form of small-vessel vasculitis (e.g., cryoglobulinemic vasculitis) or medium-vessel vasculitis (e.g., PAN), 40%. Least absolute shrinkage and selection operator (lasso) logistic regression was used to identify items from the data set and create a parsimonious model including only the most important items. The final items in the model were formulated into a clinical risk-scoring tool with each factor assigned a weight based on its respective regression coefficient. A threshold that best balanced sensitivity and specificity was identified for classification.

In sensitivity analyses, the final classification criteria were applied to an unselected population of cases and comparators from the DCVAS data set based on the submitting physician diagnosis.

**RESULTS**

**Generation of candidate classification items for the systemic vasculitides.** The Steering Committee identified >1,000 candidate items for the DCVAS case report form (see Supplementary Appendix 2, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41983/abstract).

**DCVAS prospective observational study.** Between January 2011 and December 2017, the DCVAS study recruited 6,991 participants from 136 sites in 32 countries. Information on the DCVAS sites, investigators, and participants is listed in Supplementary Appendices 3, 4, and 5, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41983/abstract.

**Refinement of candidate items specifically for AAV.** Following a data-driven and expert consensus process, 91 items from the DCVAS case report form were retained for regression analysis, including 45 clinical (14 composite), 18 laboratory (2 composite), 12 imaging (all composite), and 16 biopsy (1 composite) items. Some clinical items were removed in favor of similar but more specific pathophysiological descriptors. For example, “Hearing loss or reduction” was removed, and the composite item “Conductive hearing loss/sensorineural hearing loss” was retained. See Supplementary Appendix 6, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41983/abstract, for the final candidate items used in the derivation of the classification criteria for GPA, MPA, and EGPA.

**Expert review to derive a gold standard–defined final set of cases of AAV.** Fifty-five independent experts reviewed vignettes derived from the case report forms for 2,871 cases submitted with a diagnosis of either small-vessel vasculitis (90% of case report forms) or another type of vasculitis or a mimic of vasculitis (10% of case report forms). The characteristics of the expert reviewers are shown in Supplementary Appendix 7, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41983/abstract. A flow chart showing the results of the expert review process is shown in Supplementary Appendix 8, available on the Arthritis & Rheumatology website.

**Table 1.** Demographic and disease features of cases of MPA and comparators*

<table>
<thead>
<tr>
<th></th>
<th>MPA (n = 291)</th>
<th>Comparators (n = 822)†</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD years</td>
<td>65.5 ± 13.2</td>
<td>52.0 ± 16.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex, no. (%) female</td>
<td>164 (56.4)</td>
<td>394 (47.9)</td>
<td>0.016</td>
</tr>
<tr>
<td>Maximum serum creatinine, mean μmoles/liter</td>
<td>126.4</td>
<td>185.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≤1/C6</td>
<td>1.4</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td>cANCA positive, no. (%)</td>
<td>11 (3.8)</td>
<td>257 (31.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>pANCA positive, no. (%)</td>
<td>236 (81.1)</td>
<td>136 (16.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anti–PR3-ANCA positive, no. (%)</td>
<td>6 (2.1)</td>
<td>265 (32.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anti–MPO-ANCA positive, no. (%)</td>
<td>279 (95.9)</td>
<td>142 (17.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximum eosinophil count ≥1 x 10³/liter, no. (%)</td>
<td>15 (5.2)</td>
<td>244 (29.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* cANCA = cytoplasmic antineutrophil cytoplasmic antibody; pANCA = perinuclear ANCA; anti–PR3-ANCA = anti–proteinase 3–ANCA; anti–MPO-ANCA = anti–myeloperoxidase-ANCA.
† Diagnoses of comparators for the classification criteria for microscopic polyangiitis (MPA) included granulomatosis with polyangiitis (n = 300), eosinophilic granulomatosis with polyangiitis (n = 226), polyarteritis nodosa (n = 51), non–ANCA-associated small-vessel vasculitis that could not be subtyped (n = 51), Behçet’s disease (n = 50), IgA vasculitis (n = 50), cryoglobulinemic vasculitis (n = 34), ANCA-associated vasculitis that could not be subtyped (n = 25), primary central nervous system vasculitis (n = 19), and anti-glomerular basement membrane disease (n = 16).
A total of 2,072 cases (72%) passed the process and were designated as cases of vasculitis; these cases were used for the stage 5 analyses.

After expert panel review by 55 investigators, 269 of 404 of the cases retained the submitting physician diagnosis of MPA, and 22 additional cases were reclassified as having MPA by consensus of 2 expert reviewers. Compared to the 291 patients with a reference diagnosis of MPA, the 135 cases that were excluded had lower rates of perinuclear ANCA (pANCA) or anti–myeloperoxidase-ANCA (anti–MPO-ANCA) positivity (76% versus 98%; \( P < 0.01 \)), were less likely to have pauci-immune glomerulonephritis (16% versus 49%; \( P < 0.01 \)), were more likely to have maximum eosinophil counts \( \geq 1 \times 10^9/\text{liter} \) (12% versus 6%; \( P = 0.02 \)), and were more likely to be cytoplasmic ANCA– or proteinase 3–ANCA–positive (20% versus 4%; \( P < 0.01 \)). There were 822 comparators randomly selected for analysis. Table 1 shows the demographic and disease features of the 1,113 cases included in this analysis (291 patients with MPA and 822 comparators), of which 557 (50%; 149 patients with MPA and 408 comparators) were in the development set, and 556 (50%; 142 patients with MPA and 414 comparators) were in the validation set.

Derivation and validation of the final classification criteria for MPA. Lasso regression of the previously selected 91 items yielded 10 independent items for MPA (see Supplementary Appendix 9C, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41983/abstract). Each item was then adjudicated by the DCVAs Steering Committee for inclusion based on clinical relevance and specificity to MPA, resulting in 6 final items. Weighting of an individual criterion was based on logistic regression fitted to the 6 selected items (see Supplementary Appendix 10C, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41983/abstract).

### 2022 AMERICAN COLLEGE OF RHEUMATOLOGY / EUROPEAN ALLIANCE OF ASSOCIATIONS FOR RHEUMATOLOGY

#### CLASSIFICATION CRITERIA FOR MICROSCOPIC POLYANGIITIS

**CONSIDERATIONS WHEN APPLYING THESE CRITERIA**

- These classification criteria should be applied to classify a patient as having microscopic polyangiitis when a diagnosis of small- or medium-vessel vasculitis has been made
- Alternate diagnoses mimicking vasculitis should be excluded prior to applying the criteria

**CLINICAL CRITERIA**

| Nasal involvement: bloody discharge, ulcers, crusting, congestion, blockage or septal defect/perforation | -3 |

**LABORATORY, IMAGING, AND BIOPSY CRITERIA**

| Positive test for perinuclear antineutrophil cytoplasmic antibodies (pANCA) or antmyeloperoxidase (anti–MPO) antibodies ANCA positive | +6 |
| Fibrosis or interstitial lung disease on chest imaging | +3 |
| Pauci-immune glomerulonephritis on biopsy | +3 |
| Positive test for cytoplasmic antineutrophil cytoplasmic antibodies (cANCA) or antiproteinase 3 (anti–PR3) antibodies | -1 |
| Blood eosinophil count \( \geq 1 \times 10^9/\text{liter} \) | -4 |

*Sum the scores for 6 items, if present. A score of \( \geq 5 \) is needed for classification of MICROSCOPIC POLYANGIITIS.*

**Figure 1.** 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for microscopic polyangiitis.
Model performance. Use of a cutoff of ≥5 in total risk score (see Supplementary Appendix 11C, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41983/abstract, for different cut points) yielded a sensitivity of 90.8% (95% confidence interval [95% CI] 84.9–95.0%) and a specificity of 94.2% (95% CI 91.5–96.3%) in the validation set. The area under the curve for the model was 0.98 (95% CI 0.97–0.99) in the development set and 0.97 (95% CI 0.95–0.98) in the validation set for the final MPA classification criteria (Supplementary Appendix 12C, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41983/abstract). The final classification criteria for MPA are shown in Figure 1 (for the slide presentation version, see Supplementary Figure 1, available on the Arthritis & Rheumatology website at http://onlinelibrary.wiley.com/doi/10.1002/art.41983/abstract).

Sensitivity analysis. The classification criteria for MPA were applied to 2,871 patients in the DCVAS database using the original physician-submitted diagnosis (n = 404 cases of MPA and 2,467 randomly selected comparators). Use of the same cut point of ≥5 points for the classification for MPA yielded a similar specificity of 92.5% but a lower sensitivity of 82.4%. This is consistent with the a priori hypothesis that specificity would remain unchanged but sensitivity would be reduced in a population with fewer clearcut diagnoses of MPA (i.e., cases that did not pass expert panel review).

DISCUSSION

Presented here are the 2022 ACR/EULAR MPA classification criteria. These are the first formal criteria for MPA. A 5-stage approach has been used, underpinned by data from the multinational prospective DCVAS study and informed by expert review and consensus at each stage. The comparator group for developing and validating the criteria were predominantly patients with other forms of AAV and other small- and medium-vessel vasculitides, the clinical entities where discrimination from MPA is difficult, but important. The new criteria for MPA have excellent sensitivity and specificity and incorporate ANCA testing and modern imaging techniques. The criteria were designed to have face and content validity for use in clinical trials and other research studies.

These criteria are validated and intended for the purpose of classification of vasculitis and are not appropriate for use in establishing a diagnosis of vasculitis. The aim of the classification criteria is to differentiate cases of MPA from similar types of vasculitis in research settings. Therefore, the criteria should only be applied when a diagnosis of small- or medium-vessel vasculitis has been made and all potential “vasculitis mimics” have been excluded. The exclusion of mimics is a key aspect of many classification criteria, including those for Sjögren’s syndrome (5) and rheumatoid arthritis (6). The 1990 ACR classification criteria for vasculitis perform poorly when used for diagnosis (i.e., when used to differentiate between cases of vasculitis versus mimics without vasculitis) (7), and it is expected that the 2022 criteria would also perform poorly if used inappropriately as diagnostic criteria in people in whom alternative diagnoses, such as infection or other non-vasculitis inflammatory diseases, are still being considered. The relatively low weight assigned to glomerulonephritis in these classification criteria highlights the distinction between classification and diagnostic criteria. While detection of kidney disease is important to diagnose MPA, glomerulonephritis is common among patients with either GPA or MPA and thus does not function as a strong classifier between these conditions.

MPA was not recognized as a separate entity in the 1990 ACR classification criteria for vasculitis, although the disease was recognized as pathologically distinct from PAN over 40 years earlier. This omission of MPA caused difficulties in defining clear homogeneous populations for research; thus, over the last 2 decades, investigators have often relied on the disease definitions of the CHCC nomenclature for eligibility criteria when enrolling patients with MPA into clinical trials (4,8–11). This approach resulted in heterogeneity between patients enrolled in therapeutic trials and epidemiologic studies (12). Due to inconsistent methods employed by researchers when applying the 1990 ACR criteria and the CHCC definitions in parallel, the European Medicines Agency (EMA) convened meetings to develop a consensus on how to utilize the 2 systems, leading to the publication of the EMA algorithm in 2007 (13). The algorithm works by first excluding EGPA and GPA, and then relying on the CHCC histologic descriptions to discriminate between MPA and PAN. The new 2022 ACR/EULAR classification criteria for MPA and other vasculitides provide validated criteria that can replace the EMA interim solution and should harmonize future research studies.

A potential limitation of these new criteria is that, through the expert panel consensus methodology, only the most definite cases were included in the analyses. However, the purpose of these criteria is to enable homogeneous groupings so that individual diseases can be studied. Overall, the use of more definitive cases is consistent with the purpose of classification criteria. Additionally, positive testing for MPO-ANCA is weighted heavily in the criteria, and it is theoretically possible to classify a patient as having MPA on the basis of a positive test for MPO-ANCA only. However, the criteria are intended to only be applied to patients with an established diagnosis of small- or medium-vessel vasculitis; in this setting, the criteria sets should result in a reduction of the score away from a classification of MPA if the patient has features of another form of AAV. When criteria were tested in a much less clearly defined population using the submitting physician diagnosis as the gold standard, the sensitivity of the criteria fell substantially despite 91% of this group being pANCA- or MPO-ANCA positive, which supports the contention that ANCA positivity is not overly dominant for the classification. Nonetheless, ANCA testing is obviously a key discriminator between the different forms of AAV and other small- and medium-vessel vasculitides.
There are some additional study limitations to consider. Although this was the largest international study ever conducted in vasculitis, most patients were recruited from Europe, Asia, and North America. The performance characteristics of the criteria should be further tested in African and South American populations, which may have different clinical presentations of vasculitis. These criteria were developed using data collected from adult patients with vasculitis. Although the clinical characteristics of MPA and the other vasculitides which these criteria were tested against are not known to differ substantially between adults and children, these criteria should be applied to children with some caution. The scope of the criteria is intentionally narrow and applies only to patients who have been diagnosed as having vasculitis. Diagnostic criteria are not specified. The criteria are intended to identify homogeneous populations of disease and, therefore, may not be appropriate for studies focused on the full spectrum of clinical heterogeneity in these conditions. To maximize relevance and face validity of the new criteria, study sites and expert reviewers were recruited from a broad range of countries and different medical specialties. Nonetheless, the majority of patients were recruited from academic rheumatology or nephrology units, which could have introduced referral bias.

The 2022 ACR/EULAR classification criteria for MPA are the product of a rigorous methodologic process that utilized an extensive data set generated by the work of a remarkable international group of collaborators. These are the first classification criteria for this disease. The criteria can now be applied to patients who have been diagnosed as having a small- or medium-vessel vasculitis. These criteria have been endorsed by the ACR and EULAR and are now ready for use to differentiate medium-vessel vasculitis. These criteria have been endorsed by patients who have been diagnosed as having a small- or medium-vessel vasculitis. The criteria can now be applied to adults and children, these criteria should be applied to children with some caution. The scope of the criteria is intentionally narrow and applies only to patients who have been diagnosed as having vasculitis. Diagnostic criteria are not specified. The criteria are intended to identify homogeneous populations of disease and, therefore, may not be appropriate for studies focused on the full spectrum of clinical heterogeneity in these conditions. To maximize relevance and face validity of the new criteria, study sites and expert reviewers were recruited from a broad range of countries and different medical specialties. Nonetheless, the majority of patients were recruited from academic rheumatology or nephrology units, which could have introduced referral bias.

The 2022 ACR/EULAR classification criteria for MPA are the product of a rigorous methodologic process that utilized an extensive data set generated by the work of a remarkable international group of collaborators. These are the first classification criteria for this disease. The criteria can now be applied to patients who have been diagnosed as having a small- or medium-vessel vasculitis. These criteria have been endorsed by the ACR and EULAR and are now ready for use to differentiate one type of vasculitis from another to define populations in research studies.

ACKNOWLEDGMENTS

We acknowledge the patients and clinicians who provided data to the DCVAS project.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Merkel had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Suppiah, Robson, Grayson, Ponte, Craven, Judge, Hutchings, Merkel, Luqmani, Watts.

Acquisition of data. Suppiah, Robson, Grayson, Ponte, Craven, Merkel, Luqmani, Watts.

Analysis and interpretation of data. Suppiah, Robson, Grayson, Ponte, Craven, Khalid, Judge, Hutchings, Merkel, Luqmani, Watts.

REFERENCES


APPENDIX A: THE DCVAS INVESTIGATORS

The DCVAS study investigators are as follows: Paul Gatenby (ANU Medical Centre, Canberra, Australia); Catherine Hill (Central Adelaide Local Health Network: The Queen Elizabeth Hospital, Australia); Dwarkanathan Ranganathan (Royal Brisbane and Women’s Hospital, Australia); Andreas Kronbichler (Medical University Innsbruck, Austria); Daniel Blockmans (University Hospitals Leuven, Belgium); Lilian Barra (Lawson Health Research Institute, London, Ontario, Canada); Simon Carette; Christian Pagnoux (Mount Sinai Hospital, Toronto, Canada); Navjot Dhindra (University of Manitoba, Winnipeg, Canada); Aurore Fil-Mah (University of Calgary, Alberta, Canada); Nader Khalidi (St Joseph’s Healthcare, Hamilton, Ontario, Canada); Patrick Liang (Sherbrooke University Hospital Centre, Canada); Nataliya Milman (University of Ottawa, Canada); Christian
Pineau (McGill University, Canada); Xinping Tian (Peking Union Medical College Hospital, Beijing, China); Guochun Wang (China-Japan Friendship Hospital, Beijing, China); Tian Wang (Anzhen Hospital, Capital Medical University, China); Ming-hui Zhao (Peking University First Hospital, China); Vladimir Tesar (General University Hospital, Prague, Czech Republic); Bo Baslund (University Hospital, Copenhagen [Rigshospitalet], Denmark); Nevin Hammam (Assiut University, Egypt); Amira Shahr (Cairo University, Egypt); Laura Pirla (Turku University Hospital, Finland); Jukka Puttaala (Helsinki University Central Hospital, Finland); Bernhard Hellmich (Kreiskliniken Esslingen, Germany); Jörg Henes (Universitätsklinikum Tübingen, Germany); Peter Lamprecht (Klinikum Bad Bramstedt, Germany); Thomas Neumann (Universitätsklinikum Jena, Germany); Wolfgang Schmidt (Immanuel Krankenhaus Berlin, Germany); Cord Sunderkötter (Universitätsklinikum Münster, Germany); Zoltan Szekanecz (University of Debrecen Medical and Health Science Center, Hungary); Debashish Danda (Christian Medical College & Hospital, Vellore, India); Siddharth Das (Chatrapathi Shahu Maharaj Medical Center, Lucknow, India); Rajiva Gupta (Medanta, Delhi, India); Liza Rajasekhar (NIMS, Hyderabad, India); Aman Sharma (Postgraduate Institute of Medical Education and Research, Chandigarh, India); Shrinkant Wagh (Jharkhand Clinical Development Centre, Pune, India); Michael Clarkson (Cork University Hospital, Ireland); Eamonn Murphy (St. Vincent’s University Hospital, Dublin, Ireland); Carlo Salvarani (Santa Maria Nuova Hospital, Reggio Emilia, Italy); Franco Schievon (La Azienda Ospedaliera di Padua dell’Università Vita-Salute San Raffaele Milano, Italy); Augusto Vaglio (University of Parma, Italy); Koichi Amano (Saitama Medical University, Japan); Yoshihiro Airuma (Kyorin University Hospital, Japan); Hiroaki Dobashi (Kagawa University Hospital, Japan); Shouchi Fujimoto (Miyazaki University Hospital [HUB], Japan); Masayoshi Harigai, Fumio Hirano (Tokyo Medical and Dental University Hospital, Japan); Junichi Hirahashi (University Tokyo Hospital, Japan); Sakae Honma (Tokyo University Hospital, Japan); Tamihiro Kawakami (St. Marianna University Hospital Dermatology, Japan); Shigeto Kobayashi (Juntendo University Koshigaya Hospital, Japan); Hajime Kono (Keio University, Japan); Hirofumi Makino (Okayama University Hospital, Japan); Kazuo Matsui (Kameida Medical Centre, Kamogawa, Japan); Eri Muso (Kitanos Hospital, Japan); Kazuo Suzuki, Kei Ikeda (Chiba University Hospital, Japan); Tsutomu Takeuchi (Keio University Hospital, Japan); Tatsuo Tsuchan (Kyoto University Hospital, Japan); Shunya Uchida (Teikyo University Hospital, Japan); Takashi Wada (Kanazawa University Hospital, Japan); Yehoshua Yamada (St. Marianna University Hospital Interna- medicine, Japan); Kunihito Yamagata (Tsukuba University Hospital, Japan); Wako Yumura (I-U-U Hospital [Chichi Medical University Hospital], Japan); Kan Sow Lai (Penang General Hospital, Malaysia); Luis Felipe Wako Yumura (IUHW Hospital [Jichi Medical University Hospital, Japan]; Hidehiko Yamada (St. Marianna University Hospital Internal Medi- cine, Japan); Kunihito Yamagata (Tsukuba University Hospital, Japan); Wako Yumura (I-U-U Hospital [Chichi Medical University Hospital], Japan); Kan Sow Lai (Penang General Hospital, Malaysia); Luis Felipe Wako Yumura (IUHW Hospital [Jichi Medical University Hospital, Japan]; Hidehiko Yamada (St. Marianna University Hospital Internal Medi- cine, Japan); Kunihito Yamagata (Tsukuba University Hospital, Japan); Wako Yumura (I-U-U Hospital [Chichi Medical University Hospital], Japan); Kan Sow Lai (Penang General Hospital, Malaysia); Luis Felipe Wako Yumura (IUHW Hospital [Jichi Medical University Hospital, Japan]; Hidehiko Yamada (St. Marianna University Hospital Internal Medi- cine, Japan); Kunihito Yamagata (Tsukuba University Hospital, Japan); Wako Yumura (I-U-U Hospital [Chichi Medical University Hospital], Japan); Kan Sow Lai (Penang General Hospital, Malaysia); Luis Felipe Wako Yumura (IUHW Hospital [Jichi Medical University Hospital, Japan]; Hidehiko Yamada (St. Marianna University Hospital Internal Medi- cine, Japan); Kunihito Yamagata (Tsukuba University Hospital, Japan); Wako Yumura (I-U-U Hospital [Chichi Medical University Hospital], Japan); Kan Sow Lai (Penang General Hospital, Malaysia); Luis Felipe Wako Yumura (IUHW Hospital [Jichi Medical University Hospital, Japan]; Hidehiko Yamada (St. Marianna University Hospital Internal Medi-