Welcome to the EULAR 2017 Report

The Annual European Congress of Rheumatology 2017, hosted by the European League Against Rheumatism (EULAR), once again showed its recognition and appreciation as the prime platform for rheumatology information exchange and professional education in Europe and for the world. More than 14,000 attendees from 130 countries came to this year’s EULAR Congress in Madrid to hear the best in rheumatology research and clinical advances. The scientific programme also included presentations carefully selected from more than 4,850 abstracts submitted.

The EULAR 2017 Report brings you highlights of some of the best presentations, focusing on the clinical and therapeutic findings that are able to change the way rheumatologists and other health professionals are practising medicine. We hope that you will enjoy these accounts and statements of the latest in rheumatology clinical and translational research.

A number of the research reports that you will find in the EULAR 2017 Report also include access to video interviews with the presenters as well as other rheumatologists.

For details about the EULAR Congress, please visit www.congress.eular.org.

Best wishes and see you again 13-16 June in Amsterdam for EULAR 2018!

Prof. Johannes W.J. Bijlsma
President of EULAR
Professor of Rheumatology
Utrecht University, Netherlands
KEVZARA in combination with methotrexate (MTX) is indicated for the treatment of moderately to severely active rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying antirheumatic drugs (DMARDs). KEVZARA can be given as monotherapy in case of intolerance to MTX or when treatment with MTX is inappropriate.

**KEVZARA® (sarilumab) - Abbreviated Prescribing Information**

**NAME AND PRESENTATION:** KEVZARA 150 mg solution for injection in pre-filled syringe, KEVZARA 200 mg solution for injection in pre-filled pen. KEVZARA 200 mg solution for injection in pre-filled syringe, KEVZARA 200 mg solution for injection in pre-filled pen. 100 mg solution for injection; each single-dose pre-filled syringe contains 100 mg sarilumab in 1.14 ml solution (131.6 mg/ml). 200 mg solution for injection; each single-dose pre-filled syringe contains 200 mg sarilumab in 1.14 ml solution (175 mg/ml). 200 mg solution for injection; each single-dose pre-filled pen contains 200 mg sarilumab in 1.14 ml solution (175 mg/ml). Sarilumab is a human monoclonal antibody selective for the interleukin-6 (IL-6) receptor, produced in Chinese Hamster Ovary cells by recombinant DNA technology.

**THERAPEUTIC INDICATIONS:** KEVZARA is an interleukin-6 (IL-6) receptor antagonist. KEVZARA in combination with methotrexate (MTX) is indicated for the treatment of moderately to severely active rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying antirheumatic drugs (DMARDs). KEVZARA can be given as monotherapy in case of intolerance to MTX or when treatment with MTX is inappropriate.

**POSSIBILITY AND METHOD OF ADMINISTRATION:** Treatment should be initiated and supervised by healthcare professionals experienced in the diagnosis and treatment of rheumatoid arthritis. Patients treated with KEVZARA should be given the patient alert card. Posology: the recommended dose of KEVZARA is 200 mg once every 2 weeks administered as a subcutaneous injection. Reduction of dose from 200 mg once every 2 weeks to 150 mg once every 2 weeks is recommended for management of neutropenia, thrombocytopenia, and liver enzyme elevations. For important information on dose modification, please refer to the full SmPC. Special populaations: The safety and efficacy of KEVZARA have not been studied in patients with hepatic impairment, including patients with positive hepatitis B virus (HBV) or hepatitis C virus (HCV) serology. The safety and efficacy of KEVZARA in children up to 18 years of age have not been established. No data are available. No dose adjustment is needed for elderly patients or patients with mild or moderate renal impairment. Method of administration: Subcutaneous use. Injection sites (abdomen, thigh and upper arm) should be rotated with each injection. KEVZARA should not be injected into skin that is tender, damaged, or has bruises or scars. A patient may self-inject KEVZARA or the patient’s caregiver may administer KEVZARA if their healthcare professional determines that it is appropriate. Proper training should be provided to patients and/or caregivers on the preparation and administration of KEVZARA prior to use.

**CONTRAINDICATIONS:** Hypersensitivity to the active substance or to any of the excipients listed in the full SmPC. Active, severe infections. SPECIAL WARNINGS AND PRECAUTIONS FOR USE: Patients should be closely monitored for the development of signs and symptoms of infection during treatment with KEVZARA. Treatment with KEVZARA should be withheld if a patient develops a serious infection or an opportunistic infection. A patient with a history of a serious opportunistic infection during treatment with KEVZARA should also undergo prompt and complete diagnostic testing appropriate for an immunocompromised patient; appropriate antimicrobial therapy should be initiated, and the patient should be closely monitored. Serious and sometimes fatal infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens have been reported in patients receiving immunosuppressive agents including KEVZARA for RA. Treatment with KEVZARA was associated with a higher incidence of decrease in ANC, a reduction in platelet counts, a higher incidence of transaminase elevations, increases in lipid parameters. Use KEVZARA with caution in patients with known HIV infection. Patients presenting with new-onset abdominal symptoms such as persistent pain with fever should be evaluated promptly. If anaphylaxis or other hypersensitivity reaction occurs, administration of KEVZARA should be stopped immediately. KEVZARA should not be administered to patients with known hypersensitivity to sarilumab. Avoid concurrent use of live vaccines as well as live attenuated vaccines during treatment with KEVZARA as clinical safety has not been established. RA patients have an increased risk for cardiovascular disorders and risk factors (e.g. hypertension, hyperlipidaemia) should be managed as per usual standard of care. For further details on special warnings and precautions for use see full SmPC. DRUG INTERACTIONS: Upon initiation or discontinuation of KEVZARA in patients being treated with CYP substrate medicinal products, therapeutic monitoring of effect (e.g., warfarin) or drug concentration (e.g., theophylline) should be performed and the individual dose of the medicinal product should be adjusted as needed. Caution should be exercised in patients who start KEVZARA treatment while on therapy with CYP3A4 substrates (e.g., oral contraceptives or statins), as KEVZARA may reverse the inhibitory effect of IL-6 and restore CYP3A4 activity, leading to decreased exposure and activity of CYP3A4 substrates. For further details see full SmPC. PREGNANCY AND LACTATION: Women of childbearing potential should use effective contraception during and up to 3 months after treatment.KEVZARA should not be used during pregnancy unless the clinical condition of the woman requires treatment with sarilumab. Because IgG1 are excreted in human milk, a decision should be made whether to discontinue breast-feeding or to discontinue sarilumab therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. EFFECTS ON ABILITY TO DRIVE: KEVZARA has no or negligible influence on the ability to drive or operate machinery. UNDESIRABLE EFFECTS: Very common: neutropenia. Common: upper respiratory tract infection, urinary tract infection, nasopharyngitis, oral herpes, thrombocytopenia, hypercholesterolemia, hypertriglyceridemia, transaminases increased. Injection site erythema, injection site pruritus. The most common serious adverse reactions were infections. For further details on adverse events see full SmPC. OVERDOSE: There is no specific treatment for KEVZARA overdose. In the event of an overdose, the patient should be closely monitored, treated symptomatically, and supportive measures instituted as required. SPECIAL PRECAUTIONS FOR STORAGE: Store in a refrigerator (2°C to 8°C). Do not freeze. Once removed from the refrigerator, KEVZARA should be administered within 14 days and should not be stored above 25°C. Store pre-filled syringe/pre-filled pen in the original carton in order to protect from light. PHARMACOLOGICAL PROPERTIES: Pharmacotherapeutic group: immunosuppressants, interleukin inhibitors. ATC code: L04AC14. MARKETING AUTHORISATION HOLDER: sanofi-aventis group, 54, rue La Boëtie, 75008 Paris, France.

**LEGAL CATEGORY:** Medicinal product subject to medical prescription. DATE LAST REVISED: June 2017

Abbreviated Prescribing Information based on the EU SmPC as of June 2017. Before prescribing always refer to your full local prescribing information as this information may vary from country to country.

© 2017 Sanofi and Regeneron Pharmaceuticals, Inc. All Rights Reserved. 08/2017 SAGLB.SARI.17.07.0918
Panel revises spondyloarthritis treat-to-target recommendations

By Mitchel L. Zoler

The newly revised recommendations from an unaffiliated, international expert panel on a treat-to-target approach for axial spondyloarthritis and psoriatic arthritis has one conspicuous feature that the prior recommendations lacked: evidence.

The first treat-to-target recommendations for spondyloarthritis (SpA) and psoriatic arthritis (PsA) from 2013 were based entirely on expert opinion (Ann Rheum Dis. 2014 Jan;73[1]:6-16), but in the new update 4 of the 11 recommendations now have an evidence base as well as a fifth recommendation for the part that pertains to PsA, Prof. Désirée van der Heijde said at the congress.

In 2013, “we had no evidence,” but enough new findings accumulated during 2011-2016 to now back up almost half of the recommendations, said Prof. van der Heijde, professor of rheumatology at Leiden (the Netherlands) University Medical Center and spokesperson for the revision task force. The new recommendations were published shortly after the congress (Ann Rheum Dis. 2017 Jul 6. doi: 10.1136/annrheumdis-2017-211734).

Among the evidence-based recommendations, the most striking was a new formulation for how to measure disease activity. The new recommendations call the ASDAS (Ankylosing Spondylitis Disease Activity Score) the “preferred” disease activity measure for patients with axial SpA and cite both the DAPSA (Disease Activity Index for Psoriatic Arthritis) as well as minimal disease activity as “considered to define the target” when treating PsA.

“This recommendation just made it,” squeaking onto the list with a 52% vote of approval from the task force members, said Prof. van der Heijde. “It had the longest discussion,” with a significant minority of panelists taking a different view.

ASDAS shook out as the preferred measure for axial SpA because of evidence linking a patient’s ASDAS with syndesmophyte formation. “The idea is that by targeting ASDAS you should have better outcomes,” she explained.

If ASDAS is to become the go-to assessment for managing axial SpA, then many more physicians will need to use it. Just before Prof. van der Heijde unveiled the revised recommendations, Prof. Maxime Dougados spoke about challenges in applying the treat-to-target strategy to axial SpA. One challenge is getting physicians to make the necessary assessments in routine practice. He cited data collected from 32 rheumatology practices in the Paris area showing that fewer than 1% of patients had undergone ASDAS assessment (Clin Exp Rheumatol. 2015 Nov/Dec;33[6]:851-7).

“Applying a treat-to-target approach in axial SpA is feasible but requires systematic collection of outcome parameters in daily practice.”

Prof. van der Heijde unveiled the revised recommendations, Prof. Maxime Dougados spoke about challenges in applying the treat-to-target strategy to axial SpA. One challenge is getting physicians to make the necessary assessments in routine practice. He cited data collected from 32 rheumatology practices in the Paris area showing that fewer than 1% of patients had undergone ASDAS assessment (Clin Exp Rheumatol. 2015 Nov/Dec;33[6]:851-7).

“Applying a treat-to-target approach in axial SpA is feasible but requires systematic collection of outcome parameters in daily practice,” such as ASDAS, said Prof.
commentary

ASDAS makes sense but evidence needed

The evidence we now have is the difference between the new recommendations and the prior version. We have evidence from trials in patients with psoriatic arthritis using minimal disease activity as a target. And we have indirect evidence from observational studies in patients with SpA that suggest the higher the ASDAS, the more progression occurs. In addition, results reported at the EULAR 2017 Congress showed that reductions in the ASDAS appeared to correlate with the effect of a tumour necrosis factor inhibitor on reduced radiographic progression in patients with ankylosing spondylitis. But this is just an association; data from a randomised, prospective trial should be available next year.

Although the data today are incomplete, I agree that the ASDAS is the best measure we have for disease activity in patients with axial SpA. Based on data reported at EULAR, it seems that an ASDAS of less than 1.3 is the right target for many axial SpA patients, although every patient has a different target that must be individualised. Every patient has a different risk-and-benefit agenda; the target must be very patient centred.

The recommendations say to manage patients with axial SpA or psoriatic arthritis by treating them to a target. To do that a clinician needs a standardised assessment of a patient’s disease and to perform follow-up measurements to see if the target is met. The data Prof. Dougados cited from Paris document that assessments such as an ASDAS are rarely made. Getting an ASDAS means knowing either a patient’s C-reactive protein level or erythrocyte sedimentation rate. That requires blood work before a clinic visit, something patients often don’t want.

Will these recommendations change practice and make the ASDAS more widely used? That depends to some extent on whether any benefits or penalties linked to ASDAS use go into place.

Next year, we expect to see results from trials that are testing whether the treat-to-target approach produces better outcomes. Evidence like that will be important to further spur adoption.

Dr. Lianne S. Gensler is director of the ankylosing spondylitis clinic at the University of California, San Francisco (USA). She has been a consultant to Novartis and Janssen and has received research support from AbbVie and UCB. Dr. Gensler was a member of the task force that issued the revised recommendations. She made these comments in an interview.
EULAR launches its School of Rheumatology

By Gregory Twachtman

EULAR has launched a new way for rheumatologists all around the world to remain up-to-date on their profession with the organisation’s new School of Rheumatology.

EULAR President Johannes W.J. Bijlsma, a professor of rheumatology at the University Medical Centre Utrecht (Netherlands), provided congress attendees with an overview of the new school.

Noting that EULAR has more than a decade of educational material, including online courses, books, live courses, and other educational material, Prof. Bijlsma said a decision was made “to put that all under the same ‘roof’ – the roof of the School of Rheumatology.”

Much like a physical school, this virtual campus will offer different learning opportunities for a wide range of visitors.

“What we are thinking about is developing what we call the ‘school yard,’ and the school yard can be accessed by anyone,” Prof. Bijlsma said. This free portion will provide information for three types of visitors: medical students, patients, and health professionals.

For medical students, “we aim to have information on rheumatic diseases available for all medical students all over the world, but it will be based on the curriculum of European medical schools,” he said.

The area focused on patients will include information on medical treatments, such as updates on biosimilars, as well as discussions about rheumatic and musculoskeletal diseases and information that will be useful to those who are fighting these diseases.

Similarly, practitioners will be able to access an element of free information to help them in the delivery of care.

But the deeper information will be available for those who choose to pay for membership to the new school.

“We will have separate classes for all the members,” Prof. Bijlsma said, including classes, information for those who are unable to attend the EULAR Congress (including recorded sessions), a subscription to the EULAR Journal The Annals of the Rheumatic Diseases, and other items that are still being developed. People who attended the EULAR Congress in Madrid received a free membership to the school for the first year; future costs have not yet been determined.

Beyond the school yard of free information, there are seven “classrooms” currently under development that are part of the pay area for each of the following types of visitors:

• Medical students, which will have a standard curriculum for musculoskeletal diseases and provide videos to help support teachers and students.
• Trainees in rheumatology, which will provide information for those looking to become a rheumatologist in Europe.
• Teachers, which will be a resource to those who are educating current and future rheumatologists.
• Rheumatologists, which will offer a pocket primer on rheumatic diseases as an app.
• Scientists, which will have online course offerings on epidemiology and clinical trial research and will offer webinars on basic science methodology.
• Health professionals, which includes preparing an accreditation system and expanding online courses.

“What we are thinking about is developing what we call the ‘school yard,’ and the school yard can be accessed by anyone.”

Prof. Bijlsma

• Patients, which includes lay versions of EULAR Recommendations, information on developing patient partner programmes in research, and webinars on specific topics such as biosimilars.

Online courses available through the school will be updated annually. “We have different groups of people who meet twice or three times a year deciding what is available for each target group, what information they want to give that target group and how best to deliver it,” he said of the process to build the school’s curriculum.

“Then we make a list of priorities, look at the budget, and decide what steps we need to take.”

Prof. Bijlsma stressed that this information, both free and premium, is not just for patients, health professionals, and rheumatologists in Europe, but the site and its information “will be available to anyone, regardless of location.”
EULAR kicks off its ‘Don’t Delay, Connect Today’ early intervention campaign

By Leslie J. Yerman

Attendees at EULAR 2017 learned about the importance of its “Don’t Delay, Connect Today” early intervention campaign at a joint session for clinicians, health professionals, and patients that featured presentations on how all three groups can contribute to the early diagnosis and treatment of rheumatic diseases, particularly the role of organisations and public engagement.

The purpose of the “Don’t Delay, Connect Today” campaign is to promote early intervention by encouraging those with typical symptoms to take action and consult their doctors as soon as possible. All PARE members are adopting the campaign and putting its message into effect in an attempt to dispel arthritis myths and educate the public about the seriousness of the disease.

John Church, CEO of Arthritis Ireland, discussed the EULAR Campaign and how organisations can become involved. “This campaign is especially important as it targets not only patients, but also health professionals in the hopes of encouraging those with typical RMD [rheumatic and musculoskeletal disease] symptoms to take action and, hopefully, prevent long-term irreversible damage,” Mr. Church said. “Campaign materials have been developed for both PARE patient organisation and EULAR Health Professional members. It is a well-coordinated effort to promote early intervention, which is so vital with RMDs.”

“Arthritis is a chronic disease with multiple comorbidities,” he explained. “With the development of powerful biologic drugs, improvements in care pathways for patients, and very effective self-management options, early diagnosis and intervention can lead to significant improvements in lifestyle, physical movements, increased well-being, and work force participation.”

Despite the significant impact of arthritis on people and its economic costs, it continues to be under-funded within health systems. “It is a subspecialty that is shrouded in public myth,” Mr. Church said.

The campaign “is a pan-European effort aimed at creating a big impact. It will demonstrate strength in numbers if we all act together.”

Another talk during the session described Rheumatosphere, a programme in Glasgow, United Kingdom, that focuses on raising awareness about arthritis and arthritis research. The programme aims to inspire the next generation of scientists and clinicians, raise public awareness of arthritis and immunology, as well as empower patients and their caregivers through dissemination of information that is both enjoyable and understandable to the lay public.

Louise Bennett of the University of Glasgow (United Kingdom) asked attendees to “engage with the public, which is an essential part of scientific life, particularly because the majority of research is publicly funded.” She also stressed “the importance of targeting diverse groups, such as patients, children, and adults, in outreach activities.”

Neither Mr. Church nor Ms. Bennett have any disclosures of interest.
In the final audience Q&A session, the panellists agreed that we are entering a new era in GCA, with the Chair stating that, "We are truly on the cusp of new therapies becoming available for our patients."

**Key symposium highlights:**

**GCA is an area of high unmet medical need**
- If left untreated, GCA can lead to blindness, aortic aneurysm or stroke
- Current treatment involves glucocorticoids (GCs), which have limited efficacy and may result in side effects
- There are a lack of robust studies to identify reliable and efficacious therapy
- Tocilizumab has been investigated in GiACTA, the largest Phase III clinical trial to date in GCA

**Histopathology adds value but multi-disciplinary collaboration is key**
- GCA is often difficult to diagnose due to variable presentation
- Temporal artery biopsy is the gold standard for GCA diagnosis
- Histopathology can be difficult to interpret conclusively
- Pattern recognition in tissue sample is essential

**Use of imaging will improve GCA diagnosis**
- Imaging offers the speed and accuracy essential for diagnosis
- Guidelines and medical societies recognise a role for imaging
- Integrated imaging with a fast-track diagnostic approach reduces the risk of sight loss

**A brighter horizon for GCA**
- New therapeutic options offer GC-sparing approaches
- Advances in our understanding of disease mechanisms, recognition, diagnosis and disease management will improve the outlook for patients with GCA

"The long-sought future goal will be sustained remission without chronic GC use”

Prof John H. Stone
Boston, MA, USA

"Information from several different perspectives is needed to make an affirmative diagnosis”

Dr Yara Banz
Bern, Switzerland

"Training programmes are key to driving successful use of imaging in the future”

Dr Andreas Diamantopoulos
Oslo, Norway

"The potential harmful effects of GCs can sometimes be overlooked”

Prof Georg Schett
Erlangen, Germany

Visit [www.rocherheumatology.com](http://www.rocherheumatology.com) for more EULAR content
From Evolution to Revolution in Treatment of RA Patients
held on Friday 16 June 2017

Current therapeutic strategies are still suboptimal or not well tolerated in a significant proportion of patients with rheumatoid arthritis (RA). This symposium explored the challenges that persist despite the large number of treatment options available, and what can be done to further improve patient outcomes.

Key symposium highlights:

**Real-world evidence (RWE) is increasingly important to clinicians, regulators and payers**
- Regional and local registries are a valuable source of RWE
- The large CORRONA RA US registry has revealed information relevant to clinical practice (e.g. non-adherence, effectiveness and safety of biologics, orals and DMARDs, quality of life)
- RWE complements data from clinical trials

**Several challenges remain in the treatment of RA**
In an interactive debate-style discussion, Prof Choy and Prof Rubbert-Roth focussed on topics selected by the audience:
- Many patients do not take MTX as prescribed due to side effects or inadequate response
- Reimbursement barriers in some countries may reduce patients’ chances of achieving clinical remission
- Reliable biomarkers are needed to identify patients who would benefit from earlier biologic treatment

**New approaches to treating RA are being developed**
- Considerable unmet medical need remains in DMARD-IR and TNF-IR RA patients
- Breakthroughs in immunology are demystifying the heterogeneity of RA
- Advances in protein engineering and precision combination treatment approaches to restore immune homeostasis may help achieve improved remission rates and safety
- Roche is continuing its longstanding commitment to address unmet needs in rheumatic diseases

In the final audience Q&A session, the panellists commented that there is a revolution taking place in the approach to treating RA, with the Chair stating, “This is set to enhance outcomes in the near future.”

Visit [www.rocherheumatology.com](http://www.rocherheumatology.com) for more EULAR content
Blueprint for RMD research offers hope for funding where it’s needed

By Nicola Garrett

A blueprint that sets out a clear research agenda to address areas of unmet need across the spectrum of rheumatic and musculoskeletal diseases (RMDs) aims to provide a persuasive argument for attracting more research funding and innovation in the areas where it is most needed.

Created by a group of international experts under the leadership of EULAR Treasurer Prof. Iain McInnes, the blueprint, known as RheumaMap, will set out the research priorities for the next decade and beyond.

At the congress, Prof. McInnes took delegates through the views expressed by different voices involved in the creation of the blueprint – health professionals, patients, and the medical and scientific community.

A great deal of progress has been made in the last two decades in delivering new treatments for some RMDs. However, this progress has been primarily focused around rheumatoid arthritis, psoriatic arthritis, and axial spondyloarthritis. Much of this progress arose because research had allowed us to understand the underlying biological mechanisms behind those diseases and the best strategies to apply to their treatment, said Prof. McInnes, director of the Institute of Infection, Immunity, and Inflammation at the University of Glasgow (United Kingdom).

Progress on research into other RMDs had been a little slower in some measure because the research focus was not sufficiently well defined for policy makers and potential funders to furnish necessary support.

“The proof that high-quality research can deliver therapeutics is already there. ... The idea of RheumaMap was to sit down and ask experts in each of the different RMDs working across disciplines within rheumatology to set out the research priorities that will allow us to address the current unmet needs in RMDs,” Prof. McInnes said in an interview.

In his talk, Prof. McInnes addressed the critical issues surrounding the areas of unmet research needs and summarised the key recommendations from the RheumaMap task force.

In order to reflect an ever-changing research landscape, RheumaMap is a “living document” that will be updated in real time. The task force intends to review the document each year, but, if a big breakthrough happens in the meantime, it will be included in the research agenda.

As stakeholders and policies evolve, the task force will also need to revisit RheumaMap to make sure it is still fit for its purpose and that it is still speaking to the right people, Prof. McInnes said.

“Research is a journey of discovery that is always only really fully relevant at that given moment in time. We’re never quite sure where that journey is going to take us.”

Prof. Iain McInnes

“Research is a journey of discovery that is always only really fully relevant at that given moment in time. We’re never quite sure where that journey is going to take us.”
New classification system for systemic lupus erythematosus moves forward

By Michele G. Sullivan

A proposed classification scheme for systemic lupus erythematosus (SLE) relies on a combination of antinuclear antibody titer and the weighted scoring of signs and symptoms in seven clinical and three immunologic domains.

Anyone with an ANA titer of at least 1:80 on immunofluorescence and 84 points accumulated from the domains can be classified as having the disease, according to the proposed system. An international collaboration between the American College of Rheumatology and the European League Against Rheumatism, the system is the first classification scheme update since 2012, said Dr. Sindhu Johnson, who discussed it during the congress.

“This is a work in progress at this point, not the final system,” said Dr. Johnson of the University of Toronto, cochair of the project's steering committee. “While the prior iterations of lupus classification criteria have served us well, both groups felt it was time for an update that would reflect our current thinking on the disease.”

The proposed system is not intended to be a diagnostic tool, Dr. Johnson said in an interview. Rather, it’s meant to better stratify patients into research studies. “The prior criteria were missing patients. And, since classification criteria are used to decide whether patients can get into a clinical trial, we all felt that we were doing patients an injustice if the criteria were excluding some and denying them an opportunity to receive a novel therapy.”

There are currently two classification criteria in use: the 1982 American College of Rheumatology criteria and the Systemic Lupus International Collaborating Clinics Criteria (SLICC 2012). New understandings of SLE pathogenesis have rendered the 1982 ACR criteria outdated, according to a recently published paper (Arthritis Care Res. 2017 July 10. doi: 10.1002/acr.23317). While the SLICC 2012 criteria incorporated some of the new concepts and have increased sensitivity, compared with the 1982 ACR criteria, their specificity actually declined, partially because the document assigned equal weight to each of the clinical and immunologic criteria. The ACR/EULAR project takes a different tack. Criteria are weighted to reflect the clinical impact of different signs and symptoms, Dr. Johnson said.

“In clinical practice, if someone has class III/IV lupus nephritis, that’s a very different patient than someone who has leukopenia. As clinicians, we weight things differently, and so do these criteria, putting more weight on serious or internal organ manifestations of SLE.”

The ACR/EULAR criteria begin with a confirmed ANA titer of at least 1:80. “This has never been a requirement before, but the consensus now is that you need to have a positive ANA to be classified.”

Once that baseline is established, patients can be assessed in seven clinical domains and three immunologic domains. Each contains a subgroup of weighted signs and symptoms. These are ordered from those with least impact to those with most impact. Within each domain, only the highest-scoring criterion is counted toward the total score. When assessing, clinicians should not score any symptom if a cause other than SLE is more likely. The symptoms are not time-bound either, Dr. Johnson said. A symptom may have occurred only one time in the past, and that’s sufficient to earn a score. At least one clinical criterion must be present to be classified as SLE-positive.

The clinical domains

Constitutional: Fever (13 points). The only symptom in this domain, it’s never before been assessed in SLE criteria, Dr. Johnson said. “Our inclusion of fever is new, but our work in phase 1 of this project found that fever is a feature that can distinguish early lupus from mimickers. We want to identify patients as early in the disease course as possible so we can intervene, and fever appears to improve the ability to detect those patients.”

Cutaneous: Nonscarring alopecia (13), oral ulcers (14), subacute cutaneous or discoid lupus (29), and acute cutaneous lupus (38).

“Skin has long been recognised as an important part of lupus, but it got a lot of weight that some people felt was inappropriate. These criteria still include skin, but a patient can’t be classified on skin findings alone. There is concern that skin findings by themselves may not be lupus but something else, and some people even consider that cutaneous and systemic lupus are two different things.”

continued on following page
**Arthritis:** Synovitis in at least two joints (34).
**Neurologic:** Delirium (12), psychosis (20), and seizure (34).
**Serositis:** Pleural or pericardial effusion (34) and acute pericarditis (38).
**Hematologic:** Leukopenia (12), thrombocytopenia (26), and autoimmune hemolysis (28).
**Renal:** Proteinuria more than 0.5 g/24 hours (27), renal biopsy with class II or V lupus nephritis (55), and renal biopsy with class III or IV lupus nephritis (74).

The immunologic domains

**Antiphospholipid antibodies:** Anticardiolipin immunoglobulin G more than 40 GPL units, anti-beta2GP1 IgG more than 40 units, or lupus anticoagulant positive (13).
**Complement proteins:** Low C3 or low C4 (19) and low C3 and low C4 (27).

**Highly specific antibodies:** Anti-dsDNA antibody (38) and anti-Smith antibody (40).

**Moving forward**

Screening 10 domains with their attendant components may seem a bit clunky now, Dr. Johnson noted, but the final iteration should be more streamlined. Plus, she said, the system will be presented on a computer application that makes calculation much easier. “We’re aiming for feasibility and simplicity, but, at the same time, when you have a complex disease, you don’t want oversimplification. You may lose sensitivity and specificity.”

After further streamlining, Dr. Johnson said, the next step will be validating in a large retrospective patient cohort. “Right now, we are still collecting data for the validation cohort, which will be drawn from 36 centres. We’ll analyse sensitivity and specificity, comparing this system with the other two. We hope to present all these data at the ACR meeting in the fall.”

While research classification is the system’s raison d’être, it will undoubtedly influence diagnosis and clinical assessment as well, Dr. Johnson said. “ACR and EULAR are very clear that they only support the validation of classification criteria. The diagnosis of SLE is still within the hands of the physician. But, we know that classification criteria do inform our concept of the disease, so it’s likely these will shift the way we think about diagnosing lupus as well. We do hope to identify patients with earlier disease, so they have the opportunity to be involved in research” that may modify their disease course and, ultimately, prevent permanent damage and improve quality of life.

Dr. Johnson had no disclosures related to the development of the classification criteria.

**commentary**

The aim is to get patients into trials at earlier stages

This joint ACR/EULAR effort is very large, involving over 40 international SLE experts and centres, including many Systemic Lupus International Collaborating Clinics Criteria members. The goals are to develop new criteria that will be both sensitive and specific for SLE, which is a very heterogeneous and often elusive disease, using newer rigorous expert opinion-based and data-driven methodologies (as has been accomplished recently for rheumatoid arthritis, scleroderma, and gout).

The new criteria will include a point system on a continuous scale with a cutoff for “definite SLE” decided upon by SLE expert consensus and many cases used for validation. There is a particular interest in trying to include SLE patients at earlier stages of disease, as there is impetus in SLE clinical trials and studies to test strategies and medications capable of preventing the longer-term sequelae and complications of the disease.

This is a tall order! While genetic and cytokine-based biomarkers are being developed for the identification of SLE, unfortunately, we were not able to incorporate them as they are not available for routine use at this time. The SLE classification criteria are used worldwide for inclusion in clinical trials and studies.

The work has been preceding in phases: phase 1, item generation; phase 2, item reduction and definition of criteria; phase 3, multicriteria decision analysis and threshold identification; and phase 4, validation. Phases 1-3 involved many iterative, group discussions, data collection and review, and novel “forced choice” methodologies for arriving at group consensus. In phase 4 (validation), the goal is to compare classification using these criteria with the existing ACR and SLICC criteria, as well as SLE expert physician diagnosis. We will see how they do after all this effort!

**Dr. Karen H. Costenbader**

Dr. Costenbader is the lupus programme director at Brigham and Women’s Hospital, Boston, USA. She is a member of the classification criteria steering committee and is the senior author on a paper describing the process to develop the draft classification criteria (Arthritis Care Res. 2017 July 10. doi: 10.1002/acr.23317).
Pain is common in patients with psoriatic arthritis (PsA) and can be disruptive to their lives and jobs, even among those whose inflammatory symptoms have been treated with biologic drugs for 3 months or longer, according to findings from a multinational survey.

At the congress, Prof. Philip G. Conaghan of the University of Leeds (United Kingdom) presented findings from the survey of 782 consecutive PsA patients from 13 countries in Europe, the Middle East, Asia, and the Americas, as well as Australia. All patients included in the analysis were on biologic agents – mainly tumour necrosis factor inhibitors – for at least 90 days.

About one-third of the cohort reported little pain or mild pain, 30% reported moderate pain, and the rest – 37% of the cohort – reported severe pain despite treatment with biologic agents.

In an interview, Prof. Conaghan said that it’s important for clinicians not to assume that pain in a PsA patient on a biologic means that the drug is not working.

“The main limitation of our study is that we haven’t worked out how well-controlled patients’ psoriatic arthritis is, so, although we know they’re on a biologic for more than 3 months, we don’t know if they were responding well to it.” But, even in the absence of systemic inflammation, he said, there are other potential causes for pain that should not be over­looked.

“There’s no reason why PsA patients wouldn’t have pain due to tendinitis, enthesitis, and osteoarthritis – the same mechanical-type joint pain that we see in the whole community of people over 40,” Prof. Conaghan said. “I am concerned that, once we give someone a label of inflammatory arthritis, we stop looking at all the other things that can happen to their musculoskeletal system.”

Moreover, he said, “people who’ve had arthritis severe enough to need a biologic treatment will have muscle deconditioning and weakness. It’s very common that PsA patients have trouble opening jars and getting out of chairs.”

Such weakness “can lead to mechanical joint pain, which fortunately can be improved – along with the pain – through muscle strengthening and rehabilitation.”

For their study, Prof. Conaghan and his colleagues collected information from clinicians on treatment and from patients. The questionnaires incorporated several measures of disability, pain, functional impairment, and health-related quality of life that have been validated for use in PsA patients.

Severe pain was significantly associated with increased use of prescription nonsteroidal anti-inflammatory drugs and opioids, as well as nonprescription pain medication. Patients 65 years and older had a significantly greater likelihood of being unemployed or retired because of PsA if they reported severe pain, compared with those reporting mild or moderate pain.

A number of quality of life and work-related measures were also associated with pain severity. Prof. Conaghan and his colleagues found that the risk of disability increased with bodily pain, and more severe pain was associated with greater activity impairment, worse social functioning, more work impairment, and work time missed, among other measures (P less than .0001 for all).

“What we saw is that, the more pain you have, the more your world shrinks in,” Prof. Conaghan said.

Dr. Conaghan reported financial relationships with AbbVie, Eli Lilly, Novartis, Pfizer, Bristol-Myers Squibb, and Roche. Some of his study coauthors have similar disclosures. Four coauthors are employees of Novartis.
Unresolved fatigue lingers for most PsA patients

By Mitchel L. Zoler

Fatigue is an important symptom in patients with psoriatic arthritis but often goes unaddressed when treatment only involves disease-modifying drugs.

A survey of more than 1,000 patients with psoriatic arthritis (PsA) in Denmark found that more than half had moderate or severe levels of fatigue, and a principal component analysis of the sources of fatigue found three factors responsible for the majority of reported patient fatigue: chronic inflammation, chronic pain, and chronification of the PsA, Tanja S. Jørgensen, PhD, said at the congress.

“These findings are highly suggestive that central sensitisation is an important, extra-articular manifestation of psoriatic arthritis and should be a focus of patient management,” said Dr. Jørgensen, a clinical epidemiologist at the Parker Institute in Copenhagen.

“Pain is the most important symptom in patients with psoriatic arthritis, but fatigue is second-most important. It has a huge impact on patient quality of life,” she said.

“Just treating inflammation doesn’t do it all. We need to do more, think differently, think outside the box” of relying primarily on disease-modifying antirheumatic drugs, especially biological drugs, to resolve symptoms in PsA patients. “We should not think that biologicals do it all.”

The upshot is that PsA patients may have their inflammatory markers under control with treatment but still report that they don’t feel well, have pain, are tired, and have no energy.

But Dr. Jørgensen admitted that she couldn’t say with any certainty what additional interventions might help resolve pain and fatigue in PsA patients.

“I tell them to walk and be active; I think that may help. But we don’t really know what to do,” she said in an interview.

Her study included 1,062 PsA patients enrolled during December 2013-December 2014 in the Danish DANBIO registry of patients with inflammatory arthritides who received treatment with a biological drug. These participants also agreed to both complete a pain DETECT Questionnaire and to rate their fatigue on a visual analogue scale.

Dr. Jørgensen and her associates designated a visual analogue scale score of at least 57 out of 100 as representing moderate or severe fatigue and found that 542 (51%) of the patients had fatigue self-ratings that fell in this range. Patients with this higher fatigue level also had significantly worse PsA with significantly higher numbers of swollen and tender joints, higher pain DETECT scores, and higher scores on their Health Assessment Questionnaire and their 28-joint Disease Activity Score using C-reactive protein.

When the researchers ran a principal component analysis on these data, they identified three primary factors contributing to fatigue. Chronic inflammation contributed 31% of the fatigue effect, chronification contributed 17%, and chronic pain contributed 15%, Dr. Jørgensen reported.

Dr. Jørgensen has received research support from AbbVie, Biogen, Novartis, Pfizer, Roche, and UCB.
Comorbidities in psoriatic arthritis flag worse prognosis

By Mitchel L. Zoler

Comorbidities are relatively common in psoriatic arthritis patients, and they are more prevalent in patients with a worse disease course while on initial treatment with a tumour necrosis factor inhibitor, based on data from more than 1,700 Danish patients.

The presence of comorbidities in psoriatic arthritis (PsA) patients on initial tumour necrosis factor inhibitor (TNFi) treatment “was associated with higher disease activity, shorter adherence to the first TNFi, and reduced clinical response,” Dr. Lars Erik Kristensen said at the congress.

“We need to put more focus on comorbidities” in PsA patients, Dr. Kristensen added during a press conference. PsA has traditionally been considered similar to rheumatoid arthritis, but the comorbidity profile of many PsA patients sets the two rheumatic disorders apart. “Comorbidities play a more central role in PsA than they do in rheumatoid arthritis,” said Dr. Kristensen, a rheumatologist and chief scientific officer of the Parker Institute in Copenhagen. “PsA is not like rheumatoid arthritis.”

To better understand the possible impact of comorbidities on PsA, he and his associates reviewed 1,750 Danish patients with PsA enrolled in a national registry at the time they began treatment with a TNFi. At the time they started treatment, 1,066 (61%) had no comorbidities, 493 (28%) had one comorbidity, and 191 (11%) had two or more comorbidities.

A comparison of the subgroups with no comorbidities and those with two or more showed several important and statistically significant differences in their baseline characteristics. Patients with at least two comorbidities had longer disease duration, and they had more active disease as measured by parameters including the 28-joint Disease Activity Score and the Health Assessment Questionnaire. Patients with two or more comorbidities also were older and had a higher average body mass index.

Further analyses showed that patients with two or more comorbidities were 72% more likely to discontinue their TNFi treatment, compared with patients with no comorbidities – a statistically significant difference, Dr. Kristensen reported.

After 6 months of TNFi treatment, patients with two or more comorbidities had lower rates of achieving the American College of Rheumatology 20%, 50%, or 70% improvement criteria, compared with patients with no comorbidities. For example, an ACR20 response occurred in 40% of patients with no comorbidities and in 31% of patients with two or more comorbidities after 6 months in an adjusted analysis.

Dr. Kristensen has been a consultant to or a speaker for several drug companies.
Ustekinumab trumps TNF-blockade for enthesitis in patients with PsA

By Michele G. Sullivan and Brian Hoyle

The anti-IL-23 antibody ustekinumab cleared enthesitis significantly better than did TNF-blockade in a small, open-label trial of patients with psoriatic arthritis.

After 6 months on the drug, 71% of those taking the antibody achieved a score of 0 on the Spondyloarthritis Research Consortium of Canada (SPARC) scale, representing a complete absence of enthesitis, Dr. Elizabeth Araujo said at the congress. Just 38% of those on TNF-inhibitors achieved that score.

“These data support the concept that enthesitis-driven PsA patients may respond slightly differently to the traditional arthritis-driven PsA study population with superior outcomes of IL-23 than TNF targeting,” Dr. Araujo said in an interview before the meeting. “They also point to the pivotal pathophysiological role of the IL-23/IL-27 pathway in enthesitis.”

Enthesitis is often more bothersome to arthritis patients than their primary disease, said Dr. Araujo of the Centre of Internal Medicine, Universitätsklinikum Erlangen, Germany.

“Despite being a hallmark of PsA patients, enthesitis still receives rather peripheral attention as an outcome, especially when compared with ‘classical’ arthritis. Nonetheless, in clinical practice, enthesitis is an important factor for PsA-associated pain in many patients,” explained Dr. Araujo.

Yet it’s frequently ignored or under-treated. When it is addressed, enthesitis is often treated using TNF-inhibitors. But recent increases in the treatment options for PsA patients got Dr. Araujo thinking that PsA patients with enthesitis might respond better to a different therapy.

She investigated this with the open-label ECLIPSA trial, which randomised 51 PsA patients (47 with active enthesitis) to a 6-month treatment regimen of ustekinumab or a TNF-inhibitor. The primary endpoint of the observational study was a SPARC score of 0.

Patients were a mean of 61 years, with a mean disease duration of 2.5 years. The mean baseline SPARC score was 4. The mean Psoriatic Area and Severity Score (PASI) was 3.

Patients’ arthritis symptoms responded equally well to both drugs, with similar marked decreases in tender and swollen joint counts. But there was a clear, significant between-group separation on the SPARC score, with 71% of the ustekinumab group reaching a 0, compared with 38% of the TNF-inhibition group.

Ustekinumab also effected better skin clearance than TNF-inhibition, she said. Among the TNF-inhibition group, about 20% achieved a PASI 90 and 20%, a PASI 100. Among those taking ustekinumab, about 80% achieved a PASI 90 and 55%, a PASI 100.

The data point the way to more stratified treatment approaches for PsA patients, where PsA that predominantly involves enthesitis is treated by drugs like ustekinumab, Dr. Araujo said. Since both TNF-inhibitors and ustekinumab are approved for treatment of PsA, treatment could be tailored.

“Stratification of PsA patients according to clinical features (enthesitis driven vs. arthritis driven) appears within reach and will allow a more selective use of cytokine-blocking agents in PsA in the future,” said Dr. Araujo.

“More attention on enthesal-driven PsA patients is needed in the future as this patient group is well known to clinicians working in the PsA field but is massively underrepresented in clinical studies. Comparative studies of biological [disease-modifying antirheumatic drugs] in PsA need to take into account the differences in the clinical profile of PsA patients and should not be confined to the traditional polyarticular arthritis–driven disease population,” she added.

Dr. Araujo had no financial disclosures.
Study validates EULAR definition of arthralgia suspicious for progression to RA

By Brian Hoyle

Results of a longitudinal study have confirmed that the recently established EULAR definition of arthralgia suspicious for progression to rheumatoid arthritis can help to distinguish patients who are at highest risk for progression from those who do not progress to RA.

Patients clinically suspected of arthralgia who met the definition for arthralgia suspicious for progression to RA displayed an increased risk for arthritis development, compared with patients who did not meet the EULAR definition (hazard ratio, 2.1; 95% confidence interval, 0.9-4.7). The approach had a sensitivity of 83% and positive predictive value of 30%, study head Prof. Annette van der Helm–van Mil reported at the congress.

Use of these criteria had a similar outcome in terms of arthritis development within 2 years in another group of arthritis patients who also met the 2010 criteria for RA or who began receiving disease-modifying antirheumatic drugs within 2 years of diagnosis.

The findings should help investigators looking at early arthritis progression to design better clinical trials by enabling more homogeneous populations of patients to be included, said Prof. van der Helm–van Mil, professor of rheumatology at Leiden University Medical Centre and at Erasmus Medical Centre in Rotterdam, both in the Netherlands.

“Previous data have shown that rheumatologists do recognise patients at risk for RA based on their clinical expertise and pattern recognition. So, they do recognise patients who have a combination of clinical characteristics that characterise the symptomatic prearthritic stage of RA. (This pattern is also called clinically suspect arthralgia,” Prof. van der Helm–van Mil said in an interview.

However, the disadvantage of rheumatologists’ use of pattern recognition to identify patients at risk for RA is that it can be subjective, she said.

Several proof-of-concept trials are testing the hypothesis that the disease is more susceptible to disease-modifying treatment in the symptomatic prearthritis phase and that such early treatment might even prevent progression to chronic RA. But, selecting the “correct symptomatic patient” for early treatment with disease-modifying antirheumatic drugs is important, she said. Such a patient does not have clinical arthritis but is truly at risk for RA. Not all arthralgia patients are similar, and the type of arthralgia that is the hallmark for a heightened risk of progression to RA had not been defined formally prior to the EULAR definition.

A EULAR task force sought to provide some objective clarity by defining arthralgia at risk for RA (Ann Rheum Dis. 2017;76:491-6). The process relied on clinical expertise at all stages. However, until now, the definition had not been validated longitudinally. The current study used progression from arthralgia to clinical arthritis or RA as the outcome.

The definition of arthralgia at risk for RA hinges on seven parameters: symptom duration less than 1 year, symptoms in metacarpophalangeal joints, morning stiffness lasting an hour or more, symptoms that are worst in the morning, family history of RA, difficulty forming a fist, and positive squeeze test of metacarpophalangeal joints.

The researchers used those seven parameters to follow 241 Dutch patients considered likely to develop RA and 113 patients with recent-onset arthralgia in small joints who had not been evaluated by rheumatologists and who were referred to secondary care.

“The EULAR definition was developed for use in scientific studies and this definition is immediately applicable for this purpose,” Prof. van der Helm–van Mil said.

“With regards to application in daily practice, the clinical definition should be combined with results of additional investigations to accurately identify imminent RA in the phase of arthralgia. Which combination of markers yields the best accuracy is a subject for further studies,” Prof. van der Helm–van Mil said.

An important aspect of the task force’s definition is that rheumatologists should use it in patients in whom they consider imminent RA more likely than other diagnoses. The definition was not discriminative for RA when the investigators of the current study ignored this entry criterion, leading to a sensitivity of just 10% and positive predictive value of 3%.

“This suggests that the definition should be used in secondary care but may not be useful in primary care. However, more research is needed here,” Prof. van der Helm–van Mil said.

The authors reported no disclosures of interest.
Adding ultrasound to treat to target doesn’t improve RA remission outcomes

By Jennie Smith and Michele G. Sullivan

Adding ultrasound exams to a treat-to-target (T2T) protocol did not improve remission outcomes in patients with rheumatoid arthritis. In fact, seven-joint ultrasound actually reduced the chance that patients would achieve clinical remission in several remission assessment tools, Dr. Alexandre Sepriano said at the congress.

“We saw no advantage in using ultrasound of seven joints in addition to clinical examination, compared to clinical examination alone,” said Dr. Sepriano of Leiden (Netherlands) University Medical Centre. “We can speculate on the reasons why, but, in truth, this is the same message we have now seen in two other studies.”

Subclinical, ultrasound-detected synovitis has been shown to be predictive of disease flare in people with rheumatoid arthritis (RA), suggesting that ultrasound may have a role in defining treatment strategies, but recent trials integrating musculoskeletal ultrasound assessments into a T2T protocol have not shown better outcomes than when standard clinical definitions of remission are used.

Dr. Sepriano presented findings from BIODAM, a 2-year observational cohort of RA patients across 10 countries who are managed under a T2T protocol.

Several studies, including BIODAM, have helped to establish T2T – which intensifies treatment if patients are not in remission and eases treatment intensity when patients are in remission – as an optimal management strategy in RA. Dr. Sepriano and his colleagues set out to learn whether using ultrasound data in T2T would result in better outcomes than does use of the established T2T strategy that uses only clinical data by creating a combined new strategy using both ultrasound and clinical measures.

To do this, they looked at a subgroup of 130 patients from six countries who were treated at the BIODAM centres that had expertise in ultrasound. Patients’ clinical and ultrasound data were collected every 3 months through 2 years (for 1,037 visits in total) and were managed by rheumatologists under established T2T protocols. These patients were a mean of 55 years old, with a mean disease duration of 6 years.

As in the broader BIODAM study, the researchers used multiple clinical definitions of remission, including 28-joint and 44-joint Disease Activity Scores and the European League against Rheumatism/Amer-
ican College of Rheumatology–Boolean criteria. For the ultrasound measure, they used the previously validated US-7, which looks at seven joints for signs of synovitis.

In general, the proportion of patients in clinical remission rose over the study period, no matter what assessment tool was used. However, Dr. Sepriano and his colleagues found that the combined clinical and ultrasound benchmark for T2T decreased the likelihood of DAS-44 clinical remission after 3 months by 41% when compared with the conventional strategy. The story was similar for other assessments: The reduction was 49% on the DAS-28, 55% on Boolean remission, and 66% on Simple Disease Activity Index remission.

The reasons for this finding are difficult to discern, Dr. Sepriano said, and are complicated by the fact that this study was not a randomised, controlled trial but a longitudinal cohort in real-world practice settings.

Given the many variables involved, Dr. Sepriano said, “it may be not entirely linear to have an explanation as to why, when we used ultrasound, we actually got worse results.”

But, he noted, results from two randomised trials in more restricted populations of RA patients have also shown no benefit from adding ultrasound.

“What the data are telling us is that the clinician should be encouraged to use clinical data in his or her decisions – so we stress the importance of following a T2T strategy according to clinical data,” Dr. Sepriano said. “Adding ultrasound may not be an advantage in this scenario.”

Dr. Sepriano and his associates had no conflicts of interest to declare.

“We saw no advantage in using ultrasound of seven joints in addition to clinical examination, compared to clinical examination alone. We can speculate on the reasons why, but, in truth, this is the same message we have now seen in two other studies.”
Add-on tofacitinib as good as adalimumab for active RA

By Sara Freeman

When it comes to patients with rheumatoid arthritis who are responding inadequately to methotrexate therapy, results of the Oral Rheumatoid Arthritis trial (ORAL) Strategy study suggest that adding the Janus kinase inhibitor tofacitinib is just as effective as adding the tumour necrosis factor inhibitor adalimumab.

At 6 months’ follow-up, 46% of patients randomised to tofacitinib plus methotrexate met the trial’s primary endpoint of an American College of Rheumatology response of at least 50% (ACR50), compared with 44% of those who were given adalimumab plus methotrexate. This result met the trial’s prespecified criteria for noninferiority. An ACR50 response means that there was at least 50% improvement in tender or swollen joint counts as well as a 50% improvement in at least three of the other five criteria (acute phase reactant, such as erythrocyte sedimentation rate; patient assessment; physician assessment; pain scale; and disability/functioning questionnaire).

The study also assessed the use of tofacitinib as monotherapy vs. the two combination treatments, but noninferiority was not shown despite monotherapy helping 38% of patients to achieve the primary endpoint.

Nevertheless, “in circumstances where methotrexate is precluded, tofacitinib monotherapy is a clinically viable option,” lead study author Dr. Roy Fleischmann said at the congress.

“This actually substantiates what I’ve done in clinical practice since [tocafitinib] was approved,” said Dr. Fleischmann, a rheumatologist in group practice in Dallas, USA. “If I have patients on methotrexate and they show an incomplete response, I add tofacitinib; I don’t switch, I add. Then if the patient has a good response – a really good response – then I discontinue [methotrexate].”

Dr. Fleischmann said he does the same when adding a tumour necrosis factor inhibitor to methotrexate and that there are some patients who just do better with combination treatment.

ORAL Strategy was a phase IIIB/IV study that randomised 1,152 adults with active RA, despite treatment for more than 4 months with 15-25 mg/kg of methotrexate per week. Patients had to have four or more painful or tender joints and four or more swollen joints at baseline, and a high-sensitivity C-reactive protein level of 3 mg/L or more.

Patients were randomised to one of the study’s three treatment arms: tofacitinib 5 mg twice daily as monotherapy (n = 384), the same regimen of tofacitinib added to methotrexate (n = 376), or adalimumab 40 mg every 2 weeks added to methotrexate (n = 386). (Two patients in each group did not receive their assigned treatment.) Treatment was for 1 year, and concomitant treatment with nonsteroidal anti-inflammatory drugs, oral glucocorticoids, or both was allowed so long as their doses remained stable and no dose adjustments were necessary.

ACR20 responses were also recorded and were achieved by 65% with tofacitinib monotherapy, 73% with tofacitinib plus methotrexate, and 71% with adalimumab plus methotrexate, and ACR70 responses were 18%, 25%, and 21%, respectively. Comparable improvements from baseline to the end of the study were also seen for Simple Disease Activity Index, Clinical Disease Activity Index, Disease Activity Score in 28 joints using erythrocyte sedimentation rate, and Health Assessment Questionnaire scores in patients given the combination treatments.

The study’s findings were published online (Lancet. 2017 Jun 16. doi: 10.1016/S0140-6736[17]31659-8) to coincide with their presentation in a late-breaking abstract at the congress.


“First, this combination’s efficacy and toxicity are similar to injectable biologics such as adalimumab,” said Dr. Scott of King’s College London and Dr. Stevenson of the University of Sheffield (England). Indeed, no new side effects were seen, and side effects were consistent with those seen in previous studies.

“Second,” they wrote, “the onset of action of these drugs seems equally rapid. Third, most patients are able to remain on tofacitinib therapy for 12 months.”

Dr. Scott and Dr. Stevenson suggested these findings are “extremely encouraging” as “they show the ongoing benefits of innovation in drug treatment.”

The findings support the previous RA-BEAM trial (N Engl J Med. 2017;376:652-62) with another Janus kinase inhibitor, baricitinib, Dr. Fleischmann said during his presentation, which had also shown combination therapy with methotrexate was perhaps more beneficial than adding adalimumab.
In the Lancet editorial, Dr. Scott and Dr. Stevenson wrote: “Although a combination of [Janus kinase] inhibitors with methotrexate is likely to be the way they are used in clinical practice, monotherapy results in clinical and functional responses, as shown in the ORAL Strategy trial, and thus might be appropriate in some patients.”

The study was funded by Pfizer. Dr. Fleischmann has received research grants, research support, and consultancy fees from Pfizer and from AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, GlaxoSmithKline, Janssen, Novartis, Sanofi-Genzyme, and UCB. Dr. Scott has advised Eli Lilly, Roche Products, Napp Pharmaceuticals, Baxalta, and Novartis. Dr. Stevenson did not have any industry disclosures.
Cardiovascular events in rheumatoid arthritis have decreased over decades

By Sara Freeman

Recent improvements in the management of rheumatoid arthritis may have had a positive impact on common cardiovascular comorbidities, according to the results of a systematic review and meta-analysis.

Risk ratios (RRs) for several CV events in rheumatoid arthritis (RA) patients were found to be lower for data published after 2000 and up to March 2016 when compared with data published up until 2000. Indeed, comparing these two time periods, French researchers found that the RRs for myocardial infarction (MI) were a respective 1.32 and 1.18, for heart failure a respective 1.25 and 1.17, and for CV mortality a respective 1.21 and 1.07.

“Systemic inflammation is the cornerstone of both rheumatoid arthritis and atherosclerosis,” Prof. Cécile Gaujoux-Viala, professor of rheumatology at Montpellier University, Nîmes, France, and chief of the rheumatology service at Nîmes University Hospital, said during a press briefing at the congress. “Over the past 15 years, new treatment strategies such as ‘tight control,’ ‘treat-to-target,’ methotrexate optimisation, and use of biologic DMARDs [disease-modifying antirheumatic drugs] have led to better control of this inflammation,” Prof. Gaujoux-Viala added.

The aim of the meta-analysis was to look at the overall risk for CV events in RA patients versus the general population, she said, as well as to see if there had been any temporal shift by analysing data obtained within two time periods – before 2000 and after 2000.

A systematic literature review was performed using the PubMed and Cochrane Library databases to search for observational studies that provided data about the occurrence of CV events in RA patients and controls. Of 5,714 papers that included reports of stroke, MI, heart failure, or CV death, 28 had the necessary data for the meta-analysis. Overall, the 28 studies included 2,278,711 RA patients, with a mean age of 55 years.

Results showed that RA patients had a 17% increased risk for stroke versus controls overall ($P = .002$), with a RR of 1.17. The RRs were 1.12 before 2000 and 1.23 after 2000, making stroke the only CV event that did not appear to show a downward trend.

Compared with the general population, RA patients had a 24% excess risk of MI, a 22% excess risk of heart failure, and a 18% excess risk of dying from a CV event (all $P$ less than .00001).

These data provide “confirmation of an increased CV risk in RA patients compared to the general population,” Prof. Gaujoux-Viala said.

She had no relevant conflicts of interest to disclose.
Hip, knee replacements fall in Danish RA patients

By Mitchel L. Zoler

The rates of both total hip and total knee replacement surgeries dropped among Danish patients with rheumatoid arthritis (RA) since the mid-1990s, reductions that were coincident with more widespread use of biologic drugs as well as with other improvements in care, according to analyses of Danish national health records.

“The introduction of guidelines [on biologic drug use] in 2002 and increasing use of biologic drugs [as a result] may have contributed to this positive development,” Lene Dreyer, PhD, said at the congress. Other factors that may have also contributed include widespread use of conventional disease-modifying antirheumatic drugs (DMARDs) and adoption of a treat-to-target strategy by many clinicians.

In 1996, the first year studied and before any biologic DMARDs were routinely used for RA, the rate of total knee replacement was nearly 6/1,000 person-years among RA patients, compared with a 0.42/1,000 person-years rate in the general adult Danish population, a roughly 14-fold excess among the RA patients, Dr. Dreyer reported. But by 2016, “this gap had almost disappeared,” she said. “It seems like rheumatologists in Denmark are doing a good job” treating RA patients.

That may have been especially true subsequent to 2002, when the Danish Institute for Rational Pharmacotherapy issued recommendations that opened the door to wider use of biologic DMARDs, such as tumour necrosis factor inhibitors, to treat RA patients, noted Dr. Dreyer of Gentofte University Hospital, Copenhagen. During 2003-2011, use of total knee replacement surgery in RA patients fell by an average annualised rate of 0.2 surgeries/1,000 person-years. But among the general Danish population the average annualised rate of knee surgeries rose by 0.08/1,000 person-years.

“This is a very important finding,” commented Prof. Robert Landewé, professor of rheumatology at the Academic Medical Center in Amsterdam. “It is extremely difficult to test the effect of the introduction of the [biologic DMARD] guidelines,” he cautioned. But he highlighted the positive finding that the excess of hip and knee replacement surgeries in patients with RA, compared with the general population, had recently narrowed.

Dr. Dreyer and her associates used records from the Danish National Patient Register to compare 29,427 patients with incident RA during 1996-2011 with more than 290,000 matched control individuals. All people studied had not un-

continued on following page
The researchers used an “interrupted time series analysis” to examine the possible impact of the introduction of widespread access to biologic DMARDs starting in 2003.

The analysis showed that the rate of total hip replacements in 1996 was nearly 9 surgeries/1,000 person-years among RA patients and nearly 3/1,000 person-years in the general population, a threefold excess for RA patients. This rate fell by an average annual rate of 0.38/1,000 person-years among RA patients both before and after 2002, so that by 2011 the rate was roughly half the 1996 rate, about 4.5/1,000 patient-years. The rate in the general population rose during 1996-2011, and by 2011 was nearly 4/1,000 person-years and so nearly the same as RA patients. Wider availability of biologic DMARDs for RA patients starting in 2003 did not have an apparent impact on the rate of total hip replacement.

In contrast, wider use of biologic DMARDs appeared to have an effect on the rate of total knee surgeries among RA patients. During 1996-2001, the rate rose by an annual average of 0.19/1,000 person-years, very similar to the 0.21/1,000 person-years annual rise in the general Danish population. However, during 2003-2011, the average annual rate of total knee surgery fell by 0.20/1,000 person-years in the RA patients but continued to rise at an annual average rate of 0.08/1,000 person-years in the general population, Dr. Dreyer reported.

Additional Danish registry data exist for patients who received biologic DMARDs, and Dr. Dreyer said that she and her associates hope to use this to further examine the impact of these drugs on patient outcomes.

Dr. Dreyer has received lecture fees from Merck Sharp & Dohme and UCB. Prof. Landewé has received consulting fees from several drug companies.

“This is a very important finding. It is extremely difficult to test the effect of the introduction of the [biologic DMARD] guidelines.”

EULAR School of Rheumatology

- Become a member and be kept up-to-date on further developments
- One year free membership for all congress attendees
- Free access to the EULAR App – a new tool for rheumatology

From June 2017 all EULAR education offers under a new roof.
Visit the EULAR booth for more information.

Follow @eular_org on [Twitter] and [Facebook]
Selection of strategy for high-risk early RA remission induction hinges on safety

By Sara Freeman

Two-year results from the Care in early RA (CareRA) trial demonstrated the sustained effectiveness of a treat-to-target approach in patients with early rheumatoid arthritis at high risk for progression.

The percentage of patients who achieved clinical remission with one of three disease-modifying antirheumatic drug (DMARD) and glucocorticoid-containing regimens ranged from 60% to 65% at 1 year, and the percentage of those patients who were able to maintain their remission at all time points in year 2 ranged from 55% to 70%, none of which were significantly different from each other.

“The overall aim of treating rheumatoid arthritis is to achieve remission, a state of absence of disease activity, which should lead to symptom relief, better functioning, and preventing joint damage,” Veerle Stouten, a PhD student at the University of Leuven (Belgium), said at the congress, where she won a clinical abstract award for the research.

Ms. Stouten added that, according to international guidelines, achieving clinical remission means treating patients early, as soon as possible after the diagnosis of rheumatoid arthritis is made; intensively, with a DMARD, preferably methotrexate if not contraindicated, combined with short-term glucocorticoids; and to target, meaning treatment should be targeted at achieving remission or at least low disease activity in every patient.

The CareRA trial was a prospective, randomised, multicenter trial set up to see which of three methotrexate-based, steroid-containing intensive regimens would be best for inducing remission in patients with high-risk RA. The pragmatic trial was conducted in 13 Belgian rheumatology practices recruiting 400 patients, 300 of whom were designated as high risk for progression based on factors such as their antibody status and presence of joint erosions. CareRA trial investigators defined clinical remission as less than 2.6 on the 28-joint Disease Activity Score using C-reactive protein (DAS28-CRP).

The three regimens all contained a weekly 15-mg dose of methotrexate and prednisone 30 mg or 60 mg that was then tapered weekly after the first 6-7 weeks.

In the COBRA Classic regimen, methotrexate was partnered with sulphasalazine, given as a 2-g daily dose. Prednisone was initially given at a dose of 60 mg and then tapered to 5.7 mg starting at week 7.

For the COBRA Slim regimen, just methotrexate and prednisone were used, with the latter started at a dose of 30 mg and then tapered to 5 mg starting at week 6.

Lastly, the COBRA Avant-Garde regimen saw methotrexate combined with leflunomide, 10 mg daily, and the same step-down prednisone regimen as COBRA Slim.

In the first year, treatment in each group was adjusted to achieve a target of low disease activity (DAS28-CRP of 3.2 or lower), with measurements taken every 3 months. The steroid component was stepped down further after 28 weeks and stopped altogether by 34 weeks. The aim was also to reduce the number of DMARDs used, such that everyone was on DMARD monotherapy if possible. In the second year, rheumatologists could treat patients at their own discretion, with adjustments to treatment made according to DAS28-CRP at
Ms. Stouten reported that all three of the intensive induction regimens “were very effective in our high-risk population and that they showed persistently high remission rates at year 2.”

The percentage of patients with a DAS28-CRP of less than 2.6 at 2 years was 65.3% for the COBRA Classic regimen, 73.5% for COBRA Slim, and 73.1% for COBRA Avant-Garde.

For inducing remission, however, she suggested that the COBRA Slim regimen might have the edge from a benefit-to-risk perspective. A total of 60.2% of COBRA Slim patients were in remission at year 1, and 67.8% of them remained in remission throughout year 2. Also, fewer COBRA Slim patients needed biologic therapy, both overall (n = 11) and in the first year (n = 2), when compared with the other two regimens. In the COBRA Classic arm, 65.3% were in remission at year 1, and 54.7% of those patients maintained it throughout year 2, whereas in the COBRA Avant-Garde arm the rates were 61.3% at year 1, with 70.2% of those maintaining remission throughout year 2. A total of 18 patients in the COBRA Classic group started biologics, including 10 in the first year, compared with 15 in the COBRA Avant-Garde group, 7 of those in the first year.

“For maintaining remission, there were no statistically significant differences observed in remission rates at year 2 between treatment groups,” Ms. Stouten observed. “However, COBRA Avant-Garde had numerically better CDAI [clinical disease activity index] remission rates at year 2 [48.2% vs. 33.7% for COBRA Slim and 34.7% for COBRA Classic; P = .068].”

The total numbers of patients reporting adverse events related to treatment were lower with the COBRA Slim regimen (n = 164) than with COBRA Classic (n = 209) and COBRA Avant-Garde (n = 208). Fewer COBRA Slim patients also had to stop treatment (5 vs. 9 with COBRA Classic and 12 with COBRA Avant-Garde) or have interrupted treatment (12 vs. 17 and 19, respectively) because of adverse events.

Ms. Stouten had no personal disclosures. The study was supported by a Flemish governmental grant provided by IWT (Innovatie door Wetenschap en Technologie).

---

EULAR Online Courses 2017

- Courses start in September 2017
  - 12th EULAR Online Course on Rheumatic Diseases
  - 4th EULAR Online Course in Paediatric Rheumatology
  - 3rd EULAR Online Course for Health Professionals
  - 7th EULAR Online Course on Systemic Sclerosis
  - 9th EULAR Online Course on Connective Tissue Diseases
  - 6th EULAR Online Introductory Ultrasound Course
- Individual course cost: EUR 115

NEW: Discounted price for low and middle income countries with GDP below USD 10'000 (EUR 86).
Sign up for online courses at eular.org

Follow @eular_org on Twitter and Facebook

EULAR

Fighting rheumatic & musculoskeletal diseases together
Childhood second-hand smoke boosts RA incidence

By Mitchel L. Zoler

Second-hand smoke exposure to children was about as potent a trigger for future rheumatoid arthritis (RA) as active smoking by an adult, based on an analysis of data collected from more than 70,000 French women followed for an average of more than 20 years.

“This is the first demonstration of a rheumatoid arthritis risk associated with passive smoking,” Dr. Raphaèle Seror said at the congress. “This is an important finding because we can avoid passive smoke exposure,” Dr. Seror said. The imperative to eliminate second-hand smoke exposure to children is particularly acute for those with a genetic risk for developing RA, specifically children with a parent diagnosed with RA, suggested Dr. Seror, a professor of rheumatology at the University of Paris–South.

She and her associates used data collected in the E3N, a longitudinal French epidemiological study that enrolled nearly 100,000 women in 1990 when they were 40-65 years old and collected health data by questionnaire every 2-3 years for an average of 21 years. They identified from this cohort women with “confirmed” RA based on a self report of having incident RA during follow-up plus a coincident record of reimbursement for a prescription for an RA-specific treatment, such as methotrexate or a biological disease-modifying drug.

This identified 389 women with confirmed incident RA, including 350 with a complete smoking history that made the current analysis possible. The study also included 70,248 women who did not develop RA and who had provided a complete smoking history.

The analysis showed that women who reported a history of second-hand smoke exposure estimated at more than an hour daily as children but without a history of active smoking had a 43% higher rate of incident RA, compared with never-smoker women without a history of passive smoke exposure, Dr. Seror reported. This association just missed reaching statistical significance, a limitation that Dr. Seror attributed to a power issue as the analysis included only 30 women who had incident RA and a history of second-hand smoke exposure without adult smoke exposure. By comparison, women in the study with a history of active smoking without childhood exposure linked had a 37% increased incidence of RA, a finding that confirmed the well-known link between smoking and RA incidence.

The study also found that women with both second-hand smoke exposure as children and adult smoking linked with a 73% higher RA incidence, an indication that the contributions from second-hand smoke in children and active smoking by adults were not only similar in magnitude but also worked additively to promote RA development.

Dr. Seror had no relevant disclosures.
Studies examine methotrexate starting dose for RA in monotherapy and combinations

By Sara Freeman

A low versus high starting dose of methotrexate given as monotherapy or in combination with glucocorticoids or conventional synthetic disease-modifying antirheumatic drugs to newly diagnosed rheumatoid arthritis patients doesn’t seem to make a difference in short-term disease activity and physical functioning responses, but a higher starting dose of at least 15 mg/week may provide a better chance at achieving a good response at 6 months, according to two separate observational studies presented at the congress.

One of the studies looked at 3- to 6-month disease activity and physical functioning responses to methotrexate used as mono- or combination therapy, and the other assessed EULAR clinical responses at 6 months in mostly monotherapy-treated patients.

Low vs. high dose in combination treatments

“Methotrexate is the anchor drug in the treatment of rheumatoid arthritis patients. Current guidelines for methotrexate monotherapy recommend initiating 15 mg/week orally then escalating to 25-30 mg/week or the highest tolerable dose, but no recommendations exist for the drug’s use in combination therapy,” said Sytske Anne Bergstra, first author of a study using the international, observational METEOR database, a cohort with real-world clinical data.

“Our study questioned whether a higher initial methotrexate dose in combination with other effective medication would be more effective than a lower initial dose in the short term,” said Ms. Bergstra, a PhD student at Leiden (the Netherlands) University Medical Centre. The investigators selected 1,404 RA patients from the METEOR database who had a symptom duration of less than 5 years, had less than 2 months between diagnosis and first visit, and did not change medications (only dose adjustments were allowed). They were divided into three groups: methotrexate monotherapy, methotrexate plus conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), and methotrexate plus glucocorticoids (and possibly csDMARDs). The investigators defined initial starting doses of methotrexate as low (10 mg/week or less) or high (15 mg/week or more) based on the last reported dose of methotrexate at no later than 8 weeks of follow-up.

In each group, females constituted about 80% of patients, and the mean age was 45-48 years. The group that received methotrexate plus csDMARDs had a median symptom duration nearly twice that of the other groups (730 days vs. 365 for monotherapy and 458 for methotrexate plus glucocorticoids). Rheumatoid factor positivity ranged from 77% to 84% and anticitrullinated peptide autoantibody positivity from 72% to 85%.

The use of a high methotrexate starting dose generally trended upward in patients enrolled in the database through 2015, whereas the high point for use of a low dose was 2010 and declined thereafter. Overall, a high starting dose was used in 28% of monotherapy patients, 14% with methotrexate plus csDMARDs, and 46% with methotrexate plus glucocorticoids.

In propensity score–adjusted analyses that helped to control for confounding by indication, there were no differences in the effectiveness of low or high methotrexate starting doses for all three groups after follow-up between 3 and 6 months on Disease Activity Score (DAS), 28-joint DAS, or the Health Assessment Questionnaire (HAQ).

“Our findings seem to contradict the general trend of starting with high methotrexate doses. They indicate that higher doses did not provide better short-term clinical outcome in either monotherapy or combination therapy,” Ms. Bergstra observed.

She continued: “For the moment, we suggest that rheumatologists consider starting with a lower initial methotrexate dose, especially when prescribing in combination with other synthetic DMARDS or glucocorticoids.”

Effect of initial dose on EULAR response

Rebecca Davies of the Centre for Musculoskeletal Research at the University of Manchester (United Kingdom) presented data from a separate study that examined the effect of giving a low versus a high dose of methotrexate on patients’ rate of response to EULAR criteria at 6 months.

“Methotrexate is the recommended first line treatment for rheumatoid arthritis; however, we have not yet established [a] clear
optimal strategy for the starting dose of this therapy,” Ms. Davies said.

International, evidence-based recommendations advise starting oral methotrexate at 10-15 mg/week with escalation of 5 mg every 2-4 weeks up to 20-30 mg/week, she explained, but practice varies regarding the starting dose of methotrexate in the United Kingdom. This is most likely a result of the lack of published evidence on the importance of the initial methotrexate dose on its efficacy and safety, she suggested.

The aim of the study was therefore to assess the two most commonly used methotrexate starting doses used in the United Kingdom (7.5 mg/week or less vs. 15 mg/week or more) and how they affected the DAS28 of patients.

“Methotrexate is the recommended first line treatment for rheumatoid arthritis; however, we have not yet established [a] clear optimal strategy for the starting dose of this therapy.”

A total of 810 patients with rheumatoid arthritis who were starting methotrexate were recruited from the U.K. national, multicentre, longitudinal, observational Rheumatoid Arthritis Medication Study. For inclusion in the study, patients had to have complete DAS28 data at baseline and at 6 months.

The median age of patients was similar among the low- and high-dose groups, at 58 and 61 years, respectively. Most of the participants were female (70% vs. 60%), with a median disease duration of 6 years. Median baseline DAS28 scores were 4.2 in low- and 4.1 in high-dose groups, and baseline HAQ scores were 1.3 and 0.9, respectively.

Ms. Davies noted that 627 (77%) of the patients newly initiated on methotrexate received 15 mg/week, 10 received 20 mg, and 2 received 25 mg. The low dose of 7.5 mg/week was started by 165 patients (20%), 4 started on 5 mg, and 2 started on 2.5 mg. In more than 90% of patients, methotrexate was given orally in both the low- and high-dose groups.

Patients who were initiated on the lower methotrexate dose were more often prescribed concomitant nonbiologic DMARDs (17% vs. 10% of those in the high-dose group). Half of patients in both high- and low-dose groups used oral steroids, and a quarter used intramuscular steroids.

According to the EULAR response criteria, a good response is seen if the final DAS28 drops to 3.2 or below and there is also an improvement of 1.2 or more from baseline values. This was achieved in 23% of patients in the low-dose group and in 33% of patients in the high-dose group. Moderate EULAR clinical responses were seen in 32% and 25%, and nonresponses seen in a respective 45% and 42%.

However, findings on a multinomial logistic regression model “showed that RA patients starting methotrexate on a higher dose have a higher probability of having a good EULAR clinical response, as opposed to nonresponse, at 6 months,” Ms. Davies said.

The unadjusted relative risk ratio in patients starting a high versus low dose was 0.8 for a moderate EULAR response and 1.5 for a good EULAR response. The respective adjusted RRR was 1.0 and 2.7, suggesting that there is no difference between the doses in achieving a moderate response, but the higher dose has the edge at helping patients achieve a good EULAR response by 6 months.

During the discussion following Ms. Davies’ presentation, Dr. Roy Fleischmann of the department of internal medicine at the University of Texas Southwestern Medical Center, Dallas, USA, asked whether a high dose had actually been used at all in the study. Dr. Fleischmann observed that both 7.5 mg/week and 15 mg/week could be considered low doses.

However, one of the chairs of the session, Peter Taylor, PhD, of the University of Oxford (United Kingdom) noted that the bioavailability of methotrexate does not change much when the dose is above 15 mg via the oral route.

Prof. Kimme Hyrich of the University of Manchester (United Kingdom), senior author on the study, pointed out that the point of the analysis was to compare the starting doses of methotrexate among patients, and there might have been patients who received higher doses (25 mg or more) during the 6-month follow-up period. It is expected that future work will look at the change in the dose response over the 6-month time period, she said.

Ms. Bergstra and Ms. Davies reported that they had no relevant financial disclosures. Several co-authors for the METEOR database study disclosed financial relationships with numerous companies that market drugs for RA.
Attitudes and beliefs affecting methotrexate adherence identified

By Sara Freeman

Negative beliefs and uncertainty regarding treatment with methotrexate, as well as dislike for the drug, contribute the most to rheumatoid arthritis patients’ nonadherence to the therapy, with one study finding that about one-third were nonadherent at the time they were eligible to start biologic therapy.

The French cross-sectional survey of 244 patients who were not responding to methotrexate found that 34% actually had poor adherence, including 54% who skipped doses and 38% who temporarily stopped treatment without their doctors’ recommendation. In comparison, patients who were deemed adherent had a lower rate of skipping doses (15%) or temporarily stopped treatment without their doctors’ recommendation (4%), both of which were statistically significant differences, Dr. Catherine Beauvais reported at the congress. Nonadherence was defined as taking less than 80% of doses, according to the CQR19 (Compliance Questionnaire for Rheumatology).

“We have identified profiles of adherence,” Dr. Beauvais of Saint-Antoine Hospital in Paris commented in an interview.

“Among nonadherent patients, there are two profiles,” she added. “We have patients who are not responding to methotrexate, but they also have negative beliefs, low levels of support, and they have professional impairment. [Then,] there are patients who do not like their treatment [although it is being well tolerated].”

The other profiles identified were of patients with good adherence to methotrexate with a higher or lower impact on patient outcomes.

In a poster presentation, Dr. Beauvais and her coauthors suggested that the “detection of patients’ profiles may allow targeted strategies to improve or maintain adherence.”

The FORGET survey was conducted over a 3-month period starting in July 2016. A total of 78 rheumatologists recruited patients who were inadequately responding to methotrexate and, thus, eligible to start biologic treatment for rheumatoid arthritis. Both the rheumatologists and the patients completed questionnaires, with 200 questionnaires being completed by patients and their rheumatologist.

As might be suspected for an RA population, 72% of respondents were women, with a mean age of 54 years. Over half (58%) had at least one comorbidity, and the mean disease activity score in 28 joints at the time of the survey was 4.07.

Significant factors for nonadherence were feeling constrained about taking treatment, cited by 29% of respondents; feeling “less good” with a change in dosage (31%); and feeling that treatment was “doing me more harm than good” (19% of respondents).

Surprisingly, most rheumatologists seemed to be unaware of their patients’ lack of adherence to their medication, despite saying that they asked about adherence in more than 80% of their patients.

Rheumatologists proposed the addition of a biologic to methotrexate more often if patients were nonadherent than if patients showed good compliance (91% vs. 68%; P less than .01).

Effect of patient attitudes on compliance

A team of U.K. researchers evaluated how attitudes toward treatment with methotrexate affected patients’ compliance in a separate poster presentation at the congress.

PhD student Holly Hope and her associates at the University of Manchester (United Kingdom) reported data from the Rheumatoid Arthritis Medications Study (RAMS), in which a random sample of 50 patient diaries were examined to construct a framework, which was then used to evaluate 200 patient diaries for beliefs surrounding methotrexate treatment.

RAMS is a 1-year observational study of patients with RA who are starting treatment with methotrexate. Patients recruited into the study completed weekly diaries, noting whether they took methotrexate (adherence) and, if not, their reasons for not doing so. Patients were deemed nonadherent if they did not take methotrexate correctly for 90% of the time over a period of 6 months.

Lower adherence was significantly associated with negative or uncertain views about treatment, with an odds ratio of 2.7. Conversely, being positive or certain about treatment lowered patients’ odds of being nonadherent (OR, 0.32).

“Encouraging patients to actively monitor their progress with therapy and providing them with support to understand likely effects of methotrexate may help optimise disease-modifying antirheumatic drug use,” they concluded.

Ms. Hope and Dr. Beauvais had no conflicts of interest to disclose. The FORGET survey was funded by Chugai Pharma France.
No cancer risk found from biological DMARDs

By Mitchel L. Zoler

Additional real-world evidence confirmed that biological disease-modifying drugs used to treat rheumatoid arthritis (RA) produced no spikes in new cancers or in cancer recurrences in registry data from tens of thousands of Swedish patients.

Among RA patients with a history of cancer, patients treated with a tumour necrosis factor inhibitor (TNFi) were not at an increased risk for cancer recurrence, Prof. Johan Askling said at the congress. In a second study, patients with RA treated with a non-TNFi, biological, disease-modifying drug, specifically abatacept, rituximab, or tocilizumab, had no significantly different rate of new cancer onset when compared with RA patients who never received a biological disease-modifying drug nor when compared with the general Swedish adult population, said Prof. Askling, a professor of clinical epidemiology at the Karolinska Institute in Stockholm.

He qualified the findings on cancer recurrence as limited to patients with a history of relatively common cancers – colorectal, lung, breast, or prostate – as well as to patients who were several years removed from their initial cancer diagnoses, and the average duration on TNFi treatment was nearly 5 years.

The adjusted hazard ratio for cancer recurrence among the TNFi recipients was reduced by a nominal 30%, compared with that of the controls, a difference that was not statistically significant, Prof. Askling reported.

The second study used data from similar sources for patients treated during 2006-2014 and included nearly 100,000 Swedes from the general population, more than 42,000 RA patients who did not receive a biological drug, more than 14,000 treated with either a first or second TNFi drug, and 1,693 patients treated with tocilizumab, 1,894 on abatacept, and 3,119 on rituximab.

The rates of new onset cancer in any of these treatment groups, including the patients on tocilizumab, abatacept, or rituximab, was not significantly different from the rate among RA patients who never received a biological drug, nor from the general Swedish population rate, Prof. Askling said.

This is “one of the first large-scale assessments” of the cancer risk posed by non-TNFi biological drugs, aside from what was reported from the pivotal trials for these drugs, Prof. Askling said.

Prof. Askling has received research support from AbbVie, Lilly, MSD, Pfizer, Roche, and UCB.

continued on following page
Commentary

Results further confirm low cancer risks

Rheumatologists began having concerns about the possible impact of biological drugs on cancer when these types of drugs first became available 20 or more years ago. Registries have allowed us to follow these patients, and, so far, we have consistently seen that the risk for cancer is very low. The major adverse effect from treatment with biological drugs is infection.

The most confirmed finding has been that biological drugs do not cause new cancers. We have known less about the risk patients with a history of cancer face for recurrence by taking a biological drug. The data on this have so far been scarce. Most guidelines advise that, when patients have had cancer, the possible use of a biological drug should be the subject of a shared-decision discussion with the patient. The new data reported by Prof. Askling add to the risk information we have available to discuss with patients.

The risk that biological drugs pose for infections is more complex. The infection risk also depends on a patient’s use of glucocorticoids, their age, and their comorbidities. The infection risk faced by a patient from treatment with a biological drug requires an individualised discussion that takes into account the severity of all the relevant risk factors.

Prof. João E. Fonseca is a professor of rheumatology at the University of Lisbon. He has been a speaker for or has received research funding from Abbvie, MSD, Pfizer, Roche, and UCB.
Troponin acts as atherosclerotic biomarker in patients with lupus

By Sara Freeman

Measuring levels of troponin, a well-known cardiac biomarker, could help identify patients with systemic lupus erythematosus (SLE) at particularly high risk for cardiovascular (CV) events, according to the results of a cross-sectional study presented at the congress.

Prof. Karim Sacré presented the findings of the study that looked for possible biomarkers of atherosclerosis in patients with SLE and provided preliminary evidence that high-sensitivity troponin T (HS-cTnT) was predictive regardless of whether or not patients already had visible atherosclerotic plaques on vascular ultrasound.

“Patients with SLE have been known to be at risk for cardiovascular disease for at least a decade,” Prof. Sacré of Bichat Hospital, University of Paris-Diderot, France, said in an interview at the meeting. Today, SLE is considered an independent risk factor for CV events, much like diabetes, he added.

However, determining which patients with lupus will and which will not develop cardiac problems is still tricky in routine practice. This is because the traditional ways of assessing CV events do not fully account for the increased risk seen in lupus patients. Indeed, the Framingham risk score, which is based on several risk factors, such as tobacco use, hypertension, and dyslipidaemia, has been shown to underestimate the cardiovascular risk of lupus patients, he observed.

“So, we need something that will help clinicians to better define the real risk of cardiovascular disease in such populations,” he said at an earlier press conference.

Thus, the objective of the study he presented was to try to find a biomarker in the blood that might aid clinicians in identifying which patients who had SLE and no obvious cardiac symptoms might be at risk for future CV events.

The study involved 63 patients with SLE who were consecutively recruited and 18 individuals without SLE who were used as controls. None had any symptoms of cardiovascular disease at recruitment, and all were assessed prospectively by vascular ultrasound for the presence of atherosclerotic plaques in the carotid artery.

The concentration of HS-cTnT was measured in the serum by using an electrochemiluminescence method, which could detect a concentration level greater than 3 ng/L.

At recruitment, the Framingham risk score was low (2.1) in both
patients and controls, none of whom showed any signs of already having cardiovascular disease. The results of the carotid ultrasound, however, showed a different story for the SLE patients, with 23 (36.5%) identified as having carotid plaques, compared with just 2 (11.1%) of the control group.

Serum HS-cTNT could be detected in more SLE patients than controls (58.7% vs. 33.3%; \( P = .057 \)), and the SLE patients who had detectable levels were nine times more likely than controls to have a carotid plaque, Prof. Sacré reported, although the 95% confidence interval was wide (1.55 to 90.07; \( P = .033 \)).

Interestingly, a higher percentage of SLE patients with carotid plaques than those without had detectable HS-cTNT (87% vs. 42.5%; \( P \) less than .001). Conversely, more patients with detectable HS-cTnT than without had a carotid plaque (54.5% vs. 11.5%; \( P \) less than .001).

In multivariate analyses, only SLE status and age were significantly associated with having carotid plaques, and body mass index and HS-cTnT (\( P = .033 \)) were statistically associated with the presence of carotid plaques in SLE patients.

The research is, of course, preliminary, Prof. Sacré emphasised, and further investigation is needed. The study looked at subclinical disease rather than actual CV events, and that is something to look at next in a larger cohort of patients with a longer follow-up period, he said.

Prof. Sacré disclosed that he had received support for travel to the EULAR Congress from Roche Diagnostics France.

“Patients with SLE have been known to be at risk for cardiovascular disease for at least a decade.”

---

The EULAR App

- The EULAR App provides information and guidelines on rheumatic and musculoskeletal diseases for use by rheumatologists, medical doctors and health professionals in rheumatology for their everyday work.
- **EULAR App features include:**
  - Recommendations
  - Outcome measures library with calculators
  - Imaging library
  - Classification material for RMDs
  - EULAR pocket primer on rheumatic diseases
    - all accessible from any location (online and offline)
- Created as part of the EULAR School of Rheumatology.
- [www.eular.org](http://www.eular.org)
Catastrophic antiphospholipid syndrome (CAPS) is associated with a high mortality rate, but new research presented at the congress shows that patient survival can be significantly improved by a triple-therapy treatment approach. Researchers at the congress also presented clinical practice guidelines for the diagnosis and management of the rare disease, which accounts for just 1% of patients with antiphospholipid syndrome (APS).

CAPS is characterised by a fast onset of widespread thrombosis, mainly in the small vessels, and, often, microangiopathic hemolytic anaemia is seen in the laboratory. If undiagnosed or left untreated, patients may present with multiorgan failure needing intensive care treatment, which can be fatal in up to 50% of cases.

At the congress, Dr. Ignasi Rodriguez-Pintó presented new data from the CAPS Registry that looks at the combined effect of anticoagulation, corticosteroids, and plasma exchange or intravenous immunoglobulins on the survival of patients with CAPS, as well as the new clinical practice guidelines.

**CAPS Registry study**

The aim of the study Dr. Rodriguez-Pintó presented on behalf of the CAPS Registry Project Group was to determine what, if any, survival benefit would be incurred from a triple-therapy approach when compared with other different combinations of anticoagulation, corticosteroids, and plasma exchange or intravenous immunoglobulins, or none of these treatments.

Although the triple-therapy treatment approach is already being used in practice, its use is largely empirical, Dr. Rodríguez-Pintó of the department of autoimmune disease at the Hospital Clinic, Barcelona, explained.

The investigators derived their data from episodes of CAPS occurring in patients in the CAPS Registry from the European Forum on Antiphospholipid Antibodies. This international registry was set up in 2000 and has been assembling the clinical, laboratory, and therapeutic findings of patients with CAPS for almost 20 years.

“We observed 525 episodes of CAPS in 502 patients. That means that some patients had two to three episodes of CAPS,” Dr. Rodriguez-Pintó said. Data on 38 episodes of CAPS had to be excluded from the analysis because of missing information.

continued on following page
mation, which left 487 episodes occurring in 471 patients.

The mean age of the 471 patients included in the analysis was 38 years. The majority (67.9%) were female and had primary (68.8%) APS. Triple therapy was given to about 40% of patients who experienced CAPS, with about 57% receiving other combinations of drugs, and 2.5% receiving no treatment for CAPS.

Overall, 177 of the 487 (36.3%) episodes of CAPS were fatal.

‘‘Triple therapy was associated with a higher chance of survival when compared to other combinations or to none of these treatments,’’ Dr. Rodríguez-Pintó said.

While 28% of patients with CAPS died in the triple therapy group, mortality was 41% with other combinations of treatments and 75% with none of these treatments.

All-cause mortality was reduced by 47% with triple therapy, compared with none of these treatments. The adjusted odds ratio (aOR) when comparing survival between triple therapy and no treatment was 7.7, with a 95% confidence interval of 2.0 to 29.7. The aOR comparing other drug combinations versus none of these treatments was 6.8 (95% CI, 1.7-29.6).

‘‘For a long time, we have been saying that triple therapy would probably be the best approach, but we had no firm evidence,’’ Dr. Rodríguez-Pintó said.

‘‘So, this is the first time that we have clear clinical evidence of the benefit of these approaches, and I think that these results are important because they will give us more confidence in how we treat patients and help develop guidance on [the treatment’s] use in the future.”

Guidelines

A steering committee composed of representatives from the European Commission–funded RARE-Bestn Practices project and McMaster University in Hamilton, Canada, used GRADE methodology to develop the guidelines for CAPS diagnosis and management. The committee answered three diagnostic and seven treatment questions that originated from a panel of 19 international stakeholders, including Dr. Rodríguez-Pintó, through systematic reviews of the literature that used Cochrane criteria.

Although the review of studies did not include the study of CAPS Registry data that Dr. Rodríguez-Pintó and his colleagues conducted, he said that the recommendations still confirm the value of using a triple therapy approach to treatment.

The panel created three diagnostic recommendations for patients suspected of having CAPS, all of which were conditional and based on very low certainty of evidence: use preliminary CAPS classification criteria to diagnose CAPS; use or nonuse of biopsy, depending on the circumstances, because of its high specificity but possibly low sensitivity for thrombotic microangiopathy; and test for antiphospholipid antibodies, which should not delay initiation of treatment.

All seven first-line treatment recommendations that the panel developed relied on a very low certainty of evidence, and most were conditional:

• Triple-therapy combination treatment with corticosteroids, heparin, and plasma exchange or intravenous immunoglobulins instead of a single agent or other combination treatments.
• Therapeutic dose anticoagulation was one of only two treatment recommendations to be considered ‘‘strong,’’ but use of direct oral anticoagulants is not advised.
• Therapeutic plasma exchange is recommended for use with other therapies and should be strongly considered for patients with microangiopathic hemolytic anaemia.
• Intravenous immunoglobulin is advised for use in conjunction with other therapies and should be given special consideration for patients with immune thrombocytopenia or renal insufficiency.
• Antiplatelet agents are conditionally recommended as an add-on therapy, but their potential mortality benefit is tempered by increased risk of bleeding when used with anticoagulants. Strong consideration should be given to their use as an alternative therapy to anticoagulation when anticoagulation is contraindicated for a reason other than bleeding.
• Rituximab should not be used because of little available data on its use, uncertainty regarding long-term consequences, and its expense – except for refractory cases where other therapies have been insufficient.
• Corticosteroids should not be used because of their lack of efficacy in CAPS when used alone and potential for adverse effects, except for certain circumstances where they may be indicated.

The authors of the guidelines emphasised that these recommendations are not meant to apply to every CAPS patient. They also noted that the available evidence did not allow for temporal analysis of treatments and that conclusions could not be drawn regarding ‘‘first-line’’ versus ‘‘second-line’’ therapies.

None of the authors of the registry study or the guidelines had relevant conflicts of interest to declare.
Biomarkers discriminate lung inflammation and fibrosis in SSc-related interstitial lung disease

By Brian Hoyle

The management of systemic sclerosis (SSc)-related interstitial lung disease (ILD) could potentially benefit from the development of two specific nuclear imaging biomarkers.

“Our data show that stage-dependent visualisation of ILD with radiotracers that specifically target key markers of lung inflammation and/or fibrosis is possible. Using specific imaging biomarkers might allow individualised patient management and thus, could potentially be the first step towards precision medicine in SSc-ILD,” said Janine Schniering, who presented the results of the study.

Ms. Schniering is a PhD student in the Department of Rheumatology at University Hospital Zurich, a designated EULAR Center of Excellence.

SSc is an autoimmune disease of the connective tissue. When the lungs are involved, the result is often death. Distinct genomic and molecular subtypes of ILD have been identified. These advancements have brought targeted therapies within reach.

Ideally, diagnosis of SSc-ILD should be early in the course of the disease when SSc-ILD can be more effectively treated, and the damage that has occurred so far can perhaps be reversed. But, roadblocks to personalised care remain.

“Clinical tools for individualised patient stratification are still missing. This unmet need leaves patient management mostly at a trial and error-stage, which is in sharp contrast to the developing concept of precision medicine,” Ms. Schniering explained.

At last year’s EULAR Congress, Ms. Schniering and her colleagues reported the success of a radiotracer that specifically targets integrin alpha_v beta_3. SPECT (single photon emission computed tomography) was used to detect the radiotracer molecule in lung tissue of an established murine model of bleomycin-induced lung fibrosis and in tissue samples from ILD patients.

In the current study, the researchers assessed the applicability of nuclear imaging (PET/CT and SPECT/CT) of key molecules of ILD as potential biomarkers for the stage-dependent assessment of ILD in the murine preclinical model. 177Lu-(RGDK)-ligand was used as SPECT tracer to target integrin alpha_v beta_3 with 18F-Azafol used as PET tracer to target folate receptor beta (FR-beta).

“We found that expression of folate receptor beta, a marker exclusively expressed on activated macrophages, and integrin alpha_v beta_3, a marker expressed on a variety of immune cells and (myo-) fibroblasts, were significantly upregulated at the protein and/or mRNA level of lungs from patients with SSc-ILD. Most notably, similar increases in the expression levels of FR-beta and integrin alpha_v beta_3 were detected in the murine model of bleomycin-induced lung fibrosis,” she said.

In mice, FR-beta expression was upregulated at the inflammatory stages, with higher integrin alpha_v beta_3 expression evident in both the inflammatory and fibrotic stages of lung disease. The molecular targeted imaging discriminated between lung inflammation and/or fibrosis with time. The findings corresponded with changes in expression of FR-beta and integrin alpha_v beta_3 at the tissue level.

In contrast, the clinically routinely employed, but unspecific, imaging techniques of 18F-fluorodeoxyglucose-PET and high-resolution CT did not discriminate lung inflammation and fibrosis.

The findings demonstrate that the stage-dependent assessment of ILD is possible with molecular-targeted imaging.

Ms. Schniering reported receiving grant/research support from the Swiss National Science Foundation, and many of her coauthors reported relationships with pharmaceutical companies and/or holding the patent license for mir-29 for the treatment of systemic sclerosis.
Studies provide insight into link between cancer immunotherapy and autoimmune disease

By Jennie Smith and Mitchel L. Zoler

Rheumatologists all over the world are beginning to find that the new class of anticancer immune checkpoint inhibitor therapies have the potential to elicit symptoms of rheumatoid arthritis (RA) and other rheumatic diseases in patients with no previous history of them, according to two reports from the congress.

These immune checkpoint inhibitor (ICI) agents, which include ipilimumab, nivolumab, and pembrolizumab, target regulatory pathways in T cells to boost antitumour immune responses, leading to improved survival for many cancer patients, but the induction of rheumatic disease can sometimes lead to the suspension of the agents, according to investigators.

Dr. Cassandra Calabrese, an osteopathic physician at the Cleveland Clinic, Cleveland, USA, presented results from a retrospective chart review of 19 patients referred with symptoms of autoimmune disease after treatment with this class of drugs. Three patients had a preexisting autoimmune disease and were referred preemptively prior to starting immunotherapy. The remaining 16 patients had no history of autoimmune disease and developed symptoms a median of 16 weeks after starting treatment.

“This phenomenon was unknown to me and my group before [February 2016], when we started noting referrals of patients from oncology,” Dr. Calabrese said. “We were seeing symptoms of everything from Sjögren’s syndrome to inflammatory arthritis and myositis in patients being treated with these drugs for their cancer.” The same year, Dr. Calabrese and her team began coordinating an ongoing study to assess these patients.

Dr. Calabrese said that the cohort has shown so far that patients who develop autoimmune disease after immune checkpoint inhibitors “require much higher doses – of steroids in particular – to treat their symptoms,” and this can all too often result in being taken out of a clinical trial or having to stop cancer treatment.

Most of the patients in the cohort were treated with steroids only, while three patients received biologic agents, and four received methotrexate or antimalarials.

Dr. Calabrese said that the serology results were available for all the patients in the cohort and
"This phenomenon was unknown to me and my group before [February 2016], when we started noting referrals of patients from oncology. We were seeing symptoms of everything from Sjögren’s syndrome to inflammatory arthritis and myositis in patients being treated with these drugs for their cancer."

"were largely unremarkable."

She noted that the rheumatic symptoms did not always resolve after pausing or stopping the cancer treatment. "We have some patients that have been off their checkpoint inhibitors for over a year and still have symptoms, so it's looking like it might be a more long-term effect," she said.

Rheumatologist Rakiba Belkhir of Hôpitaux Universitaires Paris-Sud in Paris encountered the phenomenon of checkpoint inhibitor–induced autoimmune disease much the same way Dr. Calabrese did: through referrals from a cancer center.

"In my unit, we also manage patients with myeloma, and I developed a weekly consultation with a cancer center," Dr. Belkhir said. In 2015, she saw her first patient with RA and no previous history who had been treated with checkpoint inhibitors. That patient's symptoms resolved after treatment with non-steroidal anti-inflammatory drugs alone.

Dr. Belkhir shared results from this and five other patients presenting with symptoms of RA after their cancer treatment with immune checkpoint inhibitors, taken from a larger cohort of patients (n = 13) with a spectrum of rheumatic disease–like adverse effects. None of the six patients in this study had a previous clinical history of RA. They manifested their RA symptoms after a median of 1 month on cancer immunotherapy.

Some were able to continue their checkpoint inhibitors and be treated simultaneously for RA with steroids, antimalarials, methotrexate, and NSAIDs, Dr. Belkhir said. None received biologic agents, and each medication strategy, she said, was arrived at in consultation with the treating oncologist.

Dr. Belkhir’s team also looked closely at serology and found all six patients to be at least weakly, and mostly strongly, seropositive for RA. Three patients underwent testing for anticyclic citrullinated protein antibodies prior to starting cancer immunotherapy and two of these three were anti-CCP positive. Now, she said, the oncologists she’s working with are testing for anticyclic citrullinated peptides and rheumatoid factor prior to initiating cancer immunotherapy, so that this relationship is better understood.

"It is possible that antibodies were already present and that the anti-PD1 immunotherapy, "one type of immune checkpoint inhibitor, "acted as a trigger for the disease." Animal studies have suggested a role for PD1 in the development of autoimmune disease, "but it's not well investigated," Dr. Belkhir said.

Dr. Belkhir and Dr. Calabrese both acknowledged that the understanding of checkpoint inhibitor–induced autoimmune disease is in its infancy. Clinical trials largely missed the phenomenon, the researchers said, because the trials were not designed to capture musculoskeletal adverse effects with the same granularity as other serious adverse events.

"This will be a long discussion in the months and the years ahead with oncologists."
Prior mycobacterial infection linked to Sjögren’s syndrome

By Sara Freeman

Previous infection with nontuberculous mycobacteria was associated with an 11 times increased risk of later developing Sjögren’s syndrome in a large population-based study reported at the congress.

Study investigator Dr. Hsin-Hua Chen and his colleagues at the Taichung (Taiwan) Veterans Hospital found that the adjusted odds ratio for having Sjögren’s syndrome after nontuberculous mycobacteria infection (NTM) was 11.24, with a 95% confidence interval of 2.37-53.24.

The risk for having Sjögren’s syndrome was found to be highest in those aged 40-65 years versus those older than 65 (aOR, 39.24; \( P = .09 \)) and in those with no prior history of bronchiectasis (aOR, 37.98; \( P = .09 \)). Although, in both analyses, the 95% CIs were very wide (3.97-387.75 and 3.83-376.92, respectively), and the \( P \) values were not significant.

“These data might support the need for screening for Sjögren’s syndrome in patients with NTM infection, particularly among those aged 40-65 years and those without a history of bronchiectasis,” Dr. Chen observed.

Dr. Chen and his colleagues decided to look at the association between tuberculous or nontuberculous mycobacteria with Sjögren’s syndrome for several reasons. First, mycobacterial infections have been linked to the development of autoimmunity. Second, there has been an increased incidence of tuberculosis reported in patients with Sjögren’s syndrome. Third, both Sjögren’s and infection with NTM occurred predominantly in middle-aged women, suggesting a shared potential mechanism.

To investigate a possible association, a matched case-control study was conducted with data obtained from the Taiwan National Health Insurance Database. There were 5,751 new cases of Sjögren’s syndrome that were identified and validated by at least two qualified rheumatologists and matched to 86,265 controls from the general population according to age, gender, and year of diagnosis. Patients with rheumatoid arthritis and systemic lupus erythematosus were excluded. International Classification of Disease codes were used to identify individuals who had prior TB or NTM infections.

The mean age of patients in both groups was 55 years, and approximately 87% of participants in both groups were female. There was a significant difference in baseline Charlson Comorbidity Index scores between cases and controls (0.5 vs. 0.4; \( P \) less than .001), and more cases than controls had bronchiectasis (4.1% vs. 1.3%; \( P \) less than .001). Results were adjusted accordingly.

While there was an association between NTM infection and Sjögren’s syndrome, there was no association with tuberculous mycobacteria infection.

Of course, it is not clear if infection with NTM actually causes the condition, and reverse causality cannot be ruled out, Dr. Chen said, so further mechanistic studies would be needed to investigate NTM’s possible role in the development of Sjögren’s syndrome.

Dr. Chen and coauthors had nothing to disclose.
Obesity blunts TNFi response in axial spondyloarthritis

By Mitchel L. Zoler

Obese patients with axial spondyloarthritis were substantially less responsive to treatment with a tumour necrosis factor inhibitor than were healthy-weight patients in a multicentre Swiss study with 531 patients.

In a multivariate analysis that controlled for several demographic and clinical factors, including baseline disease severity, obese patients with axial spondyloarthritis (SpA) were 70% less likely to achieve a 40% or better improvement in their Assessment in SpondyloArthritis International Society improvement criteria (ASAS 40) when compared with patients with a healthy body mass index (BMI), Dr. Raphael Micheroli reported in a poster at the congress.

This is the first report to document an adverse effect from obesity on responsiveness to treatment with a tumour necrosis factor inhibitor (TNFi) in patients with axial SpA, said Dr. Micheroli, a rheumatologist at the University Hospital in Zürich.

The finding supplies a third reason why patients with newly diagnosed axial SpA should try to lose weight if they are obese (or overweight) – to potentially improve their responsiveness to a TNFi. The other two reasons are to reduce cardiovascular disease risk in patients who are already at risk for these complications because of their disease and to also help improve their ability to perform physical activities, he explained in an interview.

Dr. Micheroli proposed three possible reasons why obese patients with axial SpA might be less responsive to a TNFi than healthy-weight patients: They receive an inadequate TNFi dosage, their increased adipose tissue produces excess proinflammatory cytokines that exacerbate their axial SpA, or it is possible that obese patients are more likely to be misdiagnosed with axial SpA and because they don’t really have this disease their symptoms cannot improve with TNFi treatment. They may instead have, for example, degenerative back pain, a condition that can be challenging to distinguish from axial SpA, he said.

A role for obesity in blunting the beneficial effects of TNFi treatment has been well described for psoriatic arthritis, for example, in an Italian study with 138 patients (Ann Rheum Dis. 2014 June;73[6]:1157-62), and in a Danish study with more than 1,200 patients (Rheumatology [Oxford]. 2016 Dec;55[12]:2191-9).

Dr. Micheroli’s study included 624 patients with axial SpA enrolled in the Swiss Clinical Quality Management in Rheumatic Diseases axial spondyloarthritis cohort who met the ASAS classicfication criteria for axial SpA and started treatment with their first TNFi after they entered the cohort. Follow-up data after 1 year on treatment were available for 531 of these patients. The entry group included 332 patients (53%) with a healthy BMI, 204 (33%) with an overweight BMI (25-30 kg/m²), and 88 (14%) obese patients (BMI more than 30 kg/m²). The patients averaged about 40 years old and had been symptomatic for an average of about 13 years. About one-third of patients started on adalimumab treatment, about one-quarter started etanercept, more than one-fifth began infliximab, and some patients started treatment with either golimumab or certolizumab pegol.

After 1 year on TNFi treatment, ASAS 40 improvement occurred in 44% of 282 healthy-BMI patients, 34% of 178 overweight patients, and in 29% of 71 obese patients, Dr. Micheroli reported. In a baseline-adjusted multivariate model, this difference translated into an odds ratio of 0.30 for obese patients achieving an ASAS 40 response, compared with the healthy-BMI patients after 1 year, a statistically significant difference. Further analysis showed no statistically significant differences in TNFi discontinuation rates among the three BMI subgroups.

Dr. Micheroli had no disclosures.
TNFi treatment halves ankylosing spondylitis progression

By Mitchel L. Zoler

At least 2 years of tumour necrosis factor–inhibitor treatment of patients with ankylosing spondylitis nearly halved the rate of spinal radiographic progression in a study involving 432 Swiss patients.

In addition, patients on a tumour necrosis factor inhibitor (TNFi) who achieved low disease activity, reflected in an Ankylosing Spondylitis (AS) Disease Activity Score of 1.3 or less, showed virtually no spinal radiographic progression during a 2-year follow-up, Dr. Adrian Ciurea reported at the congress.

He cautioned, however, that the evidence only shows correlation and can’t prove a causal relationship between TNFi treatment and slowed spinal radiographic progression because of potential residual confounding.

Dr. Ciurea and his associates analysed records for AS patients enrolled in the Swiss Clinical Quality Management in Rheumatic Diseases cohort who underwent at least two spinal radiographs separated by a 2-year gap. They assessed the radiographs using the modified Stoke AS Spinal Score (mSASSS), and they defined progression as a gain of at least two units on the mSASSS during a 2-year period between radiographs.

The 432 AS patients in the study averaged 40 years old, two-thirds were men, and they had AS symptoms for an average of nearly 14 years. Their average AS Disease Activity Score (ASDAS) at entry was 2.8.

A multivariate analysis that controlled for several variables, including sex, smoking history, baseline mSASSS, and exercise, identified three parameters that had significant correlations with radiographic progression: Men had more than double the rate of progression, compared with women; higher baseline mSASSS was linked with a higher rate of progression; and a greater-than-2-year history of treatment with a TNFi was linked with a 48% reduced rate of progression, reported Dr. Ciurea, a rheumatologist at the Zürich University Hospital.

The duration of treatment also mattered. Patients who received at least 4 years of TNFi treatment had a statistically significant 68% reduced rate of radiographic spinal progression. In contrast, patients who received a TNFi for fewer than 4 years but more than 2 years had a 42% lower rate of progression that was of borderline statistical significance. TNFi treatment that started during the 2 years immediately preceding the radiograph failed to show a significant link with reduced progression.

Further analysis also showed a tight correlation between patients’ disease activity while on TNFi treatment and radiographic progression. Patients who maintained an average ASDAS of 2.1 or less during the 2 years prior to radiographic assessment showed an average mSASSS gain of 0.31 units over that 2-year period, compared with an average 1.45-unit mSASSS gain among patients whose average ASDAS remained above 2.1, a statistically significant difference between these two groups. Patients with even more inactive disease on TNFi treatment – those who maintained an average ASDAS of 1.3 or less – had an average 0.01-unit rise in their mSASSS after 2 years of treatment, compared with an average 0.52-unit mSASSS rise after 2 years in patients with an ASDAS of more than 1.3 but less than 2.1, he said.

The cohort study received partial support from Merck Sharpe & Dohme. Dr. Ciurea has been a consultant to or speaker for AbbVie, Celgene, Eli Lilly, Janssen-Cilag, Merck Sharp & Dohme, Novartis, Pfizer, and UCB.
Comorbidities emerge in adulthood for many patients with JIA

By Michele G. Sullivan

More than half of young adults with juvenile idiopathic arthritis have comorbid conditions that impact their daily quality of life. The issues range from directly disease-related – like uveitis – to more tangentially associated problems, like depression, Dr. Kirsten Minden said at the congress.

“These comorbidities significantly impact the lives of young patients with JIA but are under-recognised and under-reported by adult rheumatologists. Guidance on risk assessment in adults with JIA is needed,” said Dr. Minden of the German Rheumatism Research Centre, Berlin.

She discussed the findings of two large German registries, Biologika in der Kinder-Rheumatologie (BiKeR) and Juvenile Arthritis-Methotrexate/Biologics Long-Term Observation (JUMBO).

Children enter BiKeR as soon as they receive a JIA diagnosis; they transfer to JuMBO when they turn 18 years old. Since 2001, 1,022 children have transitioned from the paediatric to young adult databases. These patients are largely female (68%), with a mean age of 23 years and a mean disease duration of 13 years. Most (77%) had received at least one biologic disease-modifying antirheumatic drug; the mean number of those drugs received was three. They were diagnosed with a wide variety of JIA subtypes: polyarthritis RF-negative (27%); enthesitis-related (20%); extended oligoarthritis (17%); polyarthritis RF-positive (9%); psoriatic arthritis (9%); persistent oligoarthritis (9%); and systemic arthritis (5%). The remainder had other subtypes.

More than half of the patients had at least one comorbidity; the mean number of issues per patient was two. Eye disorders were most common (17%), with uveitis making up 16% of that. Immune disorders were also common (12%). Psychiatric disorders occurred in 10%, with most of that (9%) being depression. Another 9% had skin or subcutaneous tissue disorders, including psoriasis (3%).

Autoimmune thyroiditis occurred in 2.5%, as did inflammatory bowel disease. General gastrointestinal disorders were present in 5%.

Men and women experienced different comorbidity clusters. Depression was more common among women (12% vs. 3%), as were pain disorders (6% vs. 2%) and autoimmune disorders (3% vs. 1%). Men, however, experienced more inflammatory bowel disease than women (4% vs. 2%).

Comorbidities were also expressed differently among the different JIA subtypes. Those with systemic disease were more likely to have hypertension (21%), osteoporosis (10%), and amyloidosis (4%). Uveitis was most common among those with extended oligoarthritis (35%). Psoriasis was most common among those with psoriatic arthritis (20%).

A progressive enrollment assessment showed some encouraging trends, however. The patients who enrolled in the earliest epoch (2001-2005) were also oldest at initial assessment (26). The majority of those (71%) had at least one comorbidity. But from 2006-2009, patients were younger when assessed, and fewer had comorbidities (55%). In the last epoch of 2010-2016, patients were a mean of 20 when assessed, and about 45% endorsed at least one comorbidity.

Hypertension, uveitis, and depression have all decreased since a rate of 21% in 2001-2005 to 13% most recently. Depression declined from 11.5% to 6%, and uveitis, from 17% to 2%.

This improvement, she said, may reflect newer trends in earlier diagnosis, earlier treatment, and more effective disease-modifying drugs.

“Age and disease duration do play a role in the presence of comorbidities, but whether the lower rates are due to younger age now is question-
Session highlights concerns about the paediatric to adult rheumatology transition

By Leslie J. Yerman

Care services for the transition of young patients with rheumatic and musculoskeletal diseases (RMDs) from paediatric to adult care ought to take the unique needs of individual patients into account. Yet, evaluations that seek to identify the best aspects of transition programmes need to be more rigorous in order to improve their effectiveness, speakers said at a joint health professionals, PARE, and paediatric rheumatology session.

Wendy Olsder, the chair of Youth-R-Well.com – an organisation for young people with RMDs in the Netherlands – spoke about her own personal experience as a young adult with arthritis. “I was diagnosed with juvenile arthritis when I was 14 years old and transitioned from paediatric to adult care a couple of years ago,” she said. “Many young people feel nervous about this change. Health professionals have the power to ensure a smooth transition. Preparing patients is key to success.”

Both patients and health professionals have perceptions about the transition from paediatric to adult treatment. If these issues are not addressed, it can have a negative impact on the care and well-being of patients, Ms. Olsder said in an interview.

While addressing some of the main issues in the transition process using her own personal story, she discussed input she has received from other young patients through her involvement in Youth-R-Well.com, as well as some best practices for achieving a successful transition.

“I believe that being aware of patients’ perceptions and worries helps to increase the knowledge of healthcare professionals,” Ms. Olsder continued. “It is important to understand patient feelings and provide the support that could solve transition issues.”

“Every young adult is different and experiences the transition differently. It is essential that health professionals understand each patient’s individual needs and offer an effective transition,” she continued.

However, the involvement of health professionals is not the only key, she said. “Parents and patient organisations play an important role. In addition, information guides could help with the process.”

Dr. Kirsten Minden of the German Rheumatism Research Centre in Berlin talked about the evaluation of diverse transition interventions for patients with childhood-onset RMDs that persist into adulthood. “Transition care services are complex interventions, which include several interacting components, have variable outcomes, and present problems for evaluators,” Dr. Minden said in an interview. “There are also practical and methodological difficulties.

“A key question in evaluating complex interventions is whether they are effective in everyday practice,” she continued. “Therefore, it is important to understand how transitional care services work, what their active ingredients are, and how they exert their effects. Well-designed studies are needed to build an adequate body of evidence.”

Dr. Minden covered issues regarding questions asked in transition research. “More rigorous study design, dedicated funding, and inclusion of paediatric and adult researchers are needed to demonstrate the impact of transitional care,” she explained. “In addition, the effectiveness of transition programmes and their elements has to be demonstrated. There are a variety of challenges.

“Another major barrier is the lack of a common and validated definition of transition success. Currently, there is no well-validated tool that measures transition readiness for transfer to adult care,” she added. “Research needs are wide ranging and include both substantive and methodological concerns.”

“Despite widespread agreement on the importance of transition and need for adequate transition programmes, rigorous research is still limited,” Dr. Minden stated. “Given the lack of reliable methodology in transition research, a joint initiative will be essential, ideally by EULAR and PReS, to agree to facilitate a standardised measurement approach, foster future research initiatives, and enable comparative assessment across Europe.”

Neither Ms. Olsder nor Dr. Minden had disclosures of interest.
Employment support for young RMD patients too often neglected or underused

By Eli Zimmerman

College graduates and young working professionals with rheumatic and musculoskeletal diseases (RMDs) are ready to work. They just need some help, according to speakers at a PARE session.

The session featured speakers deeply involved in creating programmes to help young people with RMDs navigate through the complex nature of being in the workforce with an RMD.

Lembe Kullamaa, a patient advocate, discussed a workshop meeting on the topic that she recently helped to organise.

“The workshop came together as a common idea of the European Patients’ Forum Youth Group and European Multiple Sclerosis Platform Youth Group,” Ms. Kullamaa said in an interview. “We felt that the topic of young people with chronic conditions in the labour market is not often addressed.”

Ms. Kullamaa also touched on some of the challenges facing young people with RMDs while trying to secure a job.

Jeanette Andersen, a youth leader and advocate, delved into the stigmas faced by young professionals with RMDs and the hurdles these patients must overcome.

“It is often a problem for young people with RMDs that they have to take off time from work for doctor appointments, blood tests, or disease activity, which makes them ‘bad’ or ‘unstable’ workers in the eyes of their coworkers and employer,” Ms. Andersen said in an interview.

She explored the strengths and shortcomings of some of the current legislation that has been enacted to curb discrimination against those with an RMD.

Maureen McAllister, manager of the Joint Working Service at Arthritis Care Scotland, spoke about some of the support systems in place in Scotland that are already helping young RMD patients and the importance of both medical and nonmedical therapy.

“The Joint Working Service offers employability guidance, support, information, and signposting and is funded within Arthritis Care,” Ms. McAllister said in an interview.

“Complementing medical treatments with access to condition-specific services, which have a good understanding of the impact of the condition, can help people with arthritis to increase their capacity, confidence, and resilience in managing everyday life and work issues.”

None of the speakers had conflicts of interest to declare.
Researchers aim to help working patients with rheumatic diseases

By Jennie Smith

Biologic medications, multiprofessional interventions, and early, aggressive treatment of rheumatic diseases have allowed more people with rheumatoid arthritis and other rheumatic diseases to maintain their careers and continue with their daily valued activities.

But that does not mean working patients don’t continue to experience pain, lost work days, and disability, even if they are in clinical remission. Indeed, according to two researchers now focusing on work- and rehabilitation-related issues among people with rheumatic disease, the working environment presents a series of unique concerns for patients – many of which require a closer look.

Mathilda Björk, PhD, an occupational therapist at Linköping (Sweden) University, discussed the complexities of the concept of remission and making decisions about rehabilitation in a population that may have few clinical indicators of an active disease but continues to struggle at work and finding an activity balance in life.

“When rheumatologists discuss remission, generally it’s according to disease activity measured by the DAS28, for example, which measures disease activity and inflammation. But we know that inflammation and disability are not highly correlated,” Dr. Björk said in an interview. That means that patients may have a low disease activity but still experience disability.

Dr. Björk’s recent studies derive from two Swedish cohorts of people with early rheumatoid arthritis (RA) in the TIRA-project (Swedish acronym for Early Intervention in Rheumatoid Arthritis) – with one group treated before the advent of biologic medications and the other treated after 2006 when these became widely available. In the latter cohort, more than three-quarters of patients were working. “It is a high-functioning group,” she said. “But they reported a lot of limitations and problems at work.”

Disability can arise “from stress, or tiredness, or pain,” all of which can be exacerbated by the demands of managing a work environment in combination with active leisure time and a lot of social roles, Dr. Björk said.

Dr. Björk’s talk highlighted “the need for clinicians to arm the patient with self-management strategies and to carefully assess what the patient wants to do,” at work and at home when considering indications for rehabilitation. “Today’s patients are demanding in a good way and want to stay active and participate in valued activities,” Dr. Björk said. “But this also causes needs for activity balancing, self-management, and energy conservation as a part of the rehabilitation, which is in line with today’s guidelines and recommendations.”

At the same session, Yeliz Prior, PhD, of the University of Salford (United Kingdom), presented on the lack of communication between RA patients and clinicians related to work-specific concerns and ways to intervene.

In an interview, Dr. Prior said that clinicians need to ask their employed RA patients more pointed questions to determine the presence of work instability, a common precursor of disability and a key intervention point in preventing disability. Work instability occurs when people must change their duties or position because of an inability to meet normal job demands or must miss days of work.

“People with RA often don’t
People with RA often don’t know their rights at work and particularly struggle to decide whether they should disclose their condition. “We’ve made the tool and the user manual freely available online at the Salford University’s research repository for therapists to download and use in clinical practice. Its use is becoming more common amongst occupational therapists working in rheumatology in the U.K., but there is a need for wider uptake to standardise work rehabilitation provision across the U.K.,” she said.

Yet in many clinics the conversations about work still aren’t taking place. Some of the problem lies with patients’ awareness, Dr. Prior said, who “don’t necessarily think it’s the clinicians’ responsibility to address their difficulties at work, so they don’t tend to disclose work problems to their GP, rheumatologist, or even the therapists, who are most likely to be of help, unless they have been specifically asked about how they are coping at work or have been in long-term sickness leave. We know that once people with RA are on long-term sick leave, they are unlikely to return to work. Therefore, job retention work rehabilitation is more effective but requires an early identification of problems at work.”

More clinicians should be asking about patient’s work status, she said. “Work is an important aspect of life – just like we ask patients about their daily lives, we should be asking how they are getting along at work.” Currently, Dr. Prior is involved in evaluating a pilot programme to implement Health and Work Champions in the NHS, funded by the College of Occupational Therapists and the Public Health England. This campaign is aimed at raising the awareness about the importance of asking the “work” question amongst the NHS staff to encourage the early identification of work instability in people consulting to the NHS in the U.K.

Neither Dr. Björk nor Dr. Prior reported having any relevant conflicts of interest.
Methods for improving care, outreach to ethnic groups and immigrants outlined

By Brian Hoyle

The challenges of treating rheumatic and musculoskeletal diseases (RMDs) in patients from different ethnic backgrounds, including those who have recently immigrated, were a central topic of a PARE Session on “Difficult to reach patient groups.”

A combination of poor awareness of RMDs and their causes, dissatisfaction with communication about the nature of a disease and its treatment, and differing beliefs about medicinal use can lead to nonadherence to treatment regimens prescribed by clinicians. These problems play a big part in racial and ethnic disparities that remain in many countries despite the availability of effective treatments for many RMDs. Two of the presentations at the session highlighted efforts to boost the awareness of treatment and importance of seeking treatment.

Treatment success is grounded in patient buy-in concerning adherence to the medication regimen for a disease such as rheumatoid arthritis (RA). Speaker Kanta Kumar, PhD, in her presentation on “The challenges and solutions for engaging patients from ethnic backgrounds in rheumatology care,” described how she and her colleagues at the University of Manchester (United Kingdom) have reported the differing perceptions of medicinal use between individuals from different ethnic groups. These views can potentially impact medication adherence and patients’ satisfaction with information they receive in clinic,” said Dr. Kumar, a lecturer at the university.

“In the UK, we have recently shown that patients from different ethnic backgrounds with RA were dissatisfied with the information they receive about medicines. Patients’ beliefs about medicines and illness perceptions were found to be associated with satisfaction with information received by clinicians,” Dr. Kumar explained in an interview. A national audit by the British Society for Rheumatology also revealed a greater physical and mental impact of RA on patients from different ethnic backgrounds.

“This can impact ... the way patients perceive their disease activity and information received on treatments. If we understand the needs of patients from ethnic backgrounds, we can help improve the health outcomes,” Dr. Kumar said.

Treatment of RMDs in Sweden has also been challenged by increased immigration. Those fleeing repression and war elsewhere can find a safe haven in countries including Sweden. But, their freedom does not include freedom from existing medical conditions. One approach is to contact immigrants during their integration into Swedish society to provide information on available medical services and treatments, according to Tidiane Diao, an International Liaison Officer at the Swedish Rheumatism Association (SRA), a nonprofit organisation headquartered in Stockholm.

“The iconoclastic experience enriched the SRA and gave it a great knowledge of how to reach out to minority groups, giving them the tools to live their lives to the fullest in Sweden, the SRA participated indirectly to reduce the burden on the welfare system and also increased the number of our members and embraced the diversity in the organisation,” Mr. Diao said.

SRA did not take on these challenges alone. With state funding from a programme tailored for nonprofits, SRA established a network of stakeholders, including health providers, employment offices, high schools, and an adult education association.

“The iconoclastic experience enriched the SRA and gave it a great knowledge of how to reach out to minority groups, giving them the tools to be fully part of society despite the burden of the RMDs,” Mr. Diao said. “Today, the SRA is cited as a reference in Sweden when it comes to reaching out to different minorities suffering from RMDs. Many organisations are now lining up to work with the SRA in these matters.”

Neither Dr. Kumar nor Mr. Diao had any conflicts of interest to report.
Greater patient engagement in research challenges researchers to expand their role

By Heidi Splete

Collaborative research between patients and investigators in rheumatology is evolving to more clearly define the role of patients and integrate their perspectives in planning and protocols, according to Dr. Maarten de Wit of VU University Medical Centre, Amsterdam, the Netherlands.

“There is a growing appreciation of the patients’ lived experiences of an illness for conducting high-quality health research,” Dr. de Wit said in an interview. “Whether it is for designing a clinical trial or for developing a new patient-reported outcome questionnaire, it is important to understand patients’ needs and preferences.” Especially with long-term conditions such as rheumatologic and musculoskeletal diseases, “researchers should make an effort to incorporate patients’ perspectives using more than one method,” Dr. de Wit observed. “It will ensure more relevant research topics (research addressing unmet needs of patients), better fit between research findings and clinical practice, and, finally, a smaller gap between the world of researchers and that of patients (better mutual understanding),” he emphasised.

In his presentation at the congress, Dr. de Wit addressed aspects of patient partnerships, including defining the role of patients as partners, training researchers in collaborative work, preserving the patients’ voices, and demonstrating the impact of collaborative research to funders and the public.

Patients want their voices to be heard when it comes to research, Dr. de Wit said. “In clinical practice, health professionals tend to underestimate the number of patients that want to have a greater say in the management of their own disease. The same is true for clinical research. Patients and their organisations want more influence on the health research agenda and on the conduct of studies. They don’t want any longer to only write a letter of endorsement or to be approached at the end of the study to help disseminate research findings,” he explained. In addition, “patients can tell researchers what is important for them to measure in a study or what instrument reflects their opinions best. Patients can also advise on less burdensome logistics, informed consent forms, or more successful recruitment strategies.”

Dr. de Wit offered some details for how researchers might collaborate with patients and capture their perspectives. “One way is to consult individual patients through qualitative studies such as individual interviews, focus group meetings, or surveys. Patients provide valuable data, although the communication goes mainly into one direction and without offering patients any influence on the conduct of the study,” he said. “Another way is to collaborate with patient experts – volunteers with [an] affinity to research and [who are] competent to work on an equal footing with researchers right from the start and till the end of the research project. The take-home message for researchers and health professionals is that they should combine multiple methods of patient participation to obtain representativeness of the patients’ perspectives in their studies,” he added.

Although there is no current consensus or methodology to assess the outcomes of patient participation in research, some structures are in progress, Dr. de Wit said. “We already see that more researchers engage patients automatically, not only on the level of consultation but by starting meaningful and often intense partnerships,” he noted. “Compared to many other disease areas, we have the advantage that initiatives from EULAR and OMERACT [Outcomes Measurement in Rheumatology] have resulted in practical recommendations that guide researchers and patients to start working together. These recommendations are more and more implemented, not only on national but also on international level.”

Dr. de Wit had no financial conflicts to disclose.