ACR 2025

Insights From The American College of Rheumatology Convergence 2025

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Congress Review

Review of the American College of Rheumatology (ACR) Convergence 2025

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THE AMERICAN College of Rheumatology (ACR) Convergence returned to Chicago, Illinois, USA, this year, and with it brought thousands of rheumatology healthcare professionals together at McCormick Place and online. Over 6 days, attendees engaged with over 3,000 abstracts spanning basic, translational, and clinical research, and a program brimming with plenary sessions, late-breaking data, skills courses, and interactive formats at the annual meeting "where rheumatology meets."

In the Opening Ceremony, ACR President, William Harvey, reflected on a year eclipsed by uncertainty and change, and returned to three mission pillars that shaped both his presidency and this year's meeting: education, research, and community. Education remains the forefront of the ACR's work. The 2025 Convergence built on this foundation with an expanded online program, traditional plenaries, an impressive Poster Hall, Meet the Professor sessions, and the Practice Innovation Summit, designed to give healthcare providers direction and strategies to move forward in the current healthcare landscape.

> **Since its establishment in 1985, the Foundation has invested approximately 243 million USD to support nearly 5,000 awards**

Several themes running through the Opening Ceremony framed the scientific and clinical discussions that shaped the meeting. The rapid expansion of artificial and augmented intelligence in healthcare was highlighted as both an opportunity and a responsibility to bear. This set of tools can accelerate discovery, support new educational models, and streamline practice, but they must be guided to strengthen compassionate, patient-centered care for patients with rheumatic disease. The ACR President also spoke candidly and refreshingly about the spread of medical misinformation, emphasizing the community's commitment to evidence-based practice and the role of clinicians in translating data into trusted information and maintaing transparency with patients and the public.

Research and advocacy were presented as parallel strands of the ACR's mission. Harvey noted mounting pressures on academic

institutions, federal agencies, journals, and funding priorities that risk slowing the pace of discovery and narrowing the scope of discourse. Against this backdrop, the ACR's Washington, D.C. office and its advocacy team have worked to ensure that the voice of rheumatology is heard in policy debates. In 2025 alone, the College issued more than 120 op-eds, letters, comments, and public statements, and during the Advocates for Arthritis event, members, interprofessional colleagues, and patients met with bipartisan lawmakers to champion sustained National Institutes of Health (NIH) funding, protect Medicare and Medicaid access, and press for pharmacy benefit manager reforms to improve affordability and access to rheumatic therapies.

The Rheumatology Research Foundation (RRF), celebrating its 40th anniversary this year, featured prominently in the ceremony. Since its establishment in 1985, the Foundation has invested approximately 243 million USD to support nearly 5,000 awards across training, career development, and project funding. Nearly 1,000 students and residents have attended the ACR Convergence through Foundation scholarships, and the organization continues to prioritize pipeline development, with awards for investigators and implementation research that bring evidence-based care into everyday practice.

Community, workforce, and wellbeing were celebrated in the Opening Ceremony. The Association of Rheumatology Professionals (ARP) marked its 60th anniversary, and celebrated a diverse community of more than 1,600 members representing over 20 disciplines. ARP members lead innovations in telehealth, raise awareness of health disparities, and build inclusive environments

for learners and colleagues at all career stages, underscoring the holistic role of allied health professionals in delivering indispensable care.

As is tradition, the Opening Ceremony honored excellence across the rheumatology community with a series of awards. ARP awards recognized outstanding clinicians, scholars, students, and lifelong contributors, with the ARP Lifetime Achievement Award. The ACR Distinguished Fellow Awards celebrated the next generation of clinical and research leaders, and the ACR Master awards acknowledged senior members whose careers have demonstrated outstanding service to the profession. The ACR Presidential Gold Medal, the College's highest honor, was awarded to Eric L. Matteson, Mayo Clinic, Rochester, Minnesota, USA, who has spent decades of leadership within the ACR and the RRF. His career has combined scholarship, clinical care, and reshaped understanding and management of vasculitis and rheumatoid arthritis.

The invited keynote talk focused on the people who make this possible. Tate Shanafelt, Chief Wellness Officer at Stanford University, California, USA, and a pioneer in the field of clinician wellbeing, used data from large national cohorts to explore occupational distress, burnout, and their impacts on quality of care, turnover, and workforce sustainability. Shanafelt emphasized that personal resilience and meaning in work cannot by themselves offset excessive administrative burden, electronic health record demands, and lack of true time away from clinical duties on a system-level. He recommended to "chart a course" for clinician wellbeing through organizational change, leadership accountability, and support for professional fulfilmen. This is aligned with the ACR's broader commitment to sustain a thriving rheumatology workforce.

As the ACR Convergence 2025 continued to unfold in the theaters of McCormick Place and online, these key themes of education, research, advocacy, community, and wellbeing were staples in conversation and debates. The following congress highlights showcase a selection of key abstracts and important data. These are practice-changing insights that demonstrate how this meeting brings the global rheumatology community together to improve the lives of people with rheumatic and musculoskeletal diseases.

> **Today, ARP members lead innovations in telehealth, raise awareness of health disparities, and build inclusive environments for learners and colleagues at all career stages**

Earlier Kidney Biopsy May Improve Lupus Nephritis Detection

FINDINGS presented at the ACR Convergence 2025 suggest that current guidelines for kidney biopsy in systemic lupus erythematosus (SLE) may miss early, clinically significant cases of lupus nephritis (LN).[1]

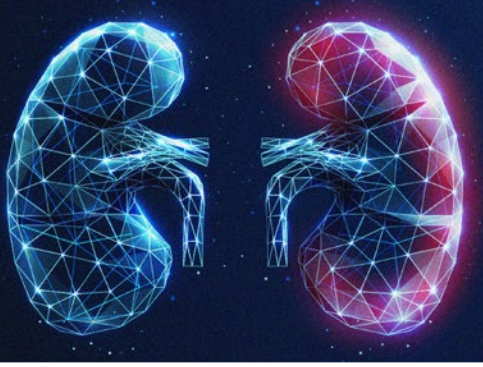
Researchers from the Accelerating Medicines Partnership (AMP), led by Michelle Petri of Johns Hopkins University, Baltimore, Maryland, USA, found that patients with modest elevations in urine protein-to-creatinine ratio (UPCR) but other risk indicators often already have histologic evidence of LN on biopsy.

Guidelines from the ACR, European Alliance of Associations for Rheumatology (EULAR), and Kidney Disease: Improving Global Outcomes (KDIGO) currently recommend kidney biopsy in patients with SLE when UPCR is ≥0.50 g/g. However, emerging data have shown that patients with lower proteinuria may still harbor proliferative or membranous LN, conditions that can lead to irreversible renal damage if not treated early. The AMP study evaluated whether earlier biopsy could identify subclinical disease in patients at risk.

The study enrolled 28 patients with SLE without known LN whose UPCR ranged from 0.250–0.499 g/g and who had at least one additional LN predictor, such as non-White race, low complement (C3 or C4), positive anti-double-stranded DNA antibodies, or active urine sediment. All participants had normal renal function, were on minimal corticosteroids, and had no prior immunosuppressive therapy.

Biopsy results revealed that 20 of 28 participants (69%) already had LN, including proliferative forms: six Class III and seven Class V. Two Class II, two Class III, and three Class V cases later progressed to higher UPCR levels despite treatment, indicating early but active disease at the time of biopsy. Patients with low C3 or C4 before enrolment were significantly more likely to have LN (p=0.0223 and p=0.0296, respectively). No biopsy complications were reported.

These findings challenge the current 0.50 g/g UPCR biopsy threshold, suggesting it may delay diagnosis and treatment of early LN. The AMP team's algorithm (biopsy for UPCR 0.250–0.499 g/g plus another LN predictor) identified a high proportion of patients with meaningful renal pathology, supporting revision of current LN biopsy guidelines to promote earlier detection and intervention.



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Upadacitinib Maintains Long-Term Remission in Giant Cell Arteritis

TWO-YEAR results from the Phase III SELECT-GCA trial, presented at the ACR Convergence 2025, show that continued treatment with upadacitinib 15 mg (UPA15) sustained remission and significantly reduced the risk of disease flare and glucocorticoid exposure in patients with giant cell arteritis (GCA). These data reinforce the long-term efficacy and safety of the JAK inhibitor as a potential treatment option for this chronic inflammatory vasculitis.[2]

Of the 428 patients treated in the first year, 181 entered the extension phase, and 91% completed the full 104 weeks

SELECT-GCA enrolled patients aged ≥50 years (mean age: 71 years) with active GCA, and included a 52-week randomized, placebo-controlled first phase followed by a 52-week blinded extension phase. In the initial phase, participants received UPA15, UPA7.5, or placebo alongside a glucocorticoid taper. Those who achieved at least 24 consecutive weeks of remission entered the extension phase, where participants previously on upadacitinib were re-randomized either to continue their assigned dose or switch to placebo, while the original placebo group continued the same regimen.

Of the 428 patients treated in the first year, 181 entered the extension phase, and 91% completed the full 104 weeks. Among patients originally treated with UPA15, 68.6% who continued the same dose maintained remission through 2 years, compared with only 28.6% who switched to placebo. Continuous UPA15 treatment reduced the risk of disease flare by approximately 90% from Weeks 52–104 compared with discontinuation. Patients remaining on UPA15 also showed greater improvements across secondary endpoints, including glucocorticoid sparing, with a cumulative one-gram reduction in glucocorticoid use during the second year.

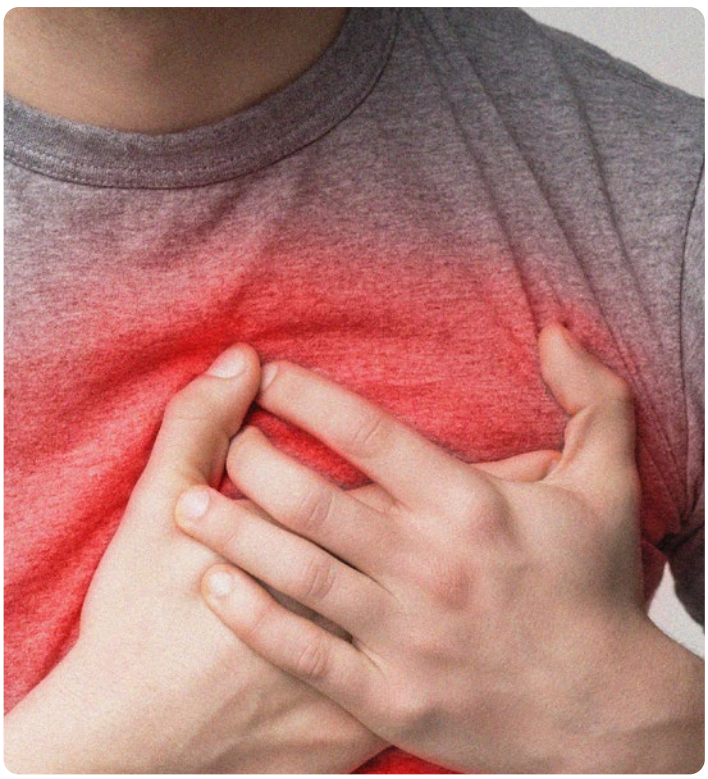
Safety findings were consistent with earlier reports. Serious treatment-emergent adverse events were less frequent in both upadacitinib groups than in the placebo group. Serious infections occurred less often with UPA15, although higher rates of herpes zoster and mild elevations in creatine kinase were observed. One venous thromboembolism occurred in a patient with pre-existing risk factors. No major cardiovascular events or deaths were reported.

In this older patient population, upadacitinib 15 mg maintained durable remission over 2 years without new safety concerns. These results further support its role as a long-term, steroid-sparing therapy for managing GCA.

GLP-1 Receptor Agonists Linked to Lower Cardiovascular Risk and Mortality in Psoriatic Arthritis

A NEW retrospective study, presented at the ACR Convergence 2025, suggests that glucagon-like-peptide-1 receptor agonists (GLP-1 RA), a class of drugs widely used for Type 2 diabetes management, may provide cardiovascular and survival benefits for patients with psoriatic arthritis (PsA). The study analyzed data from 83 large healthcare organizations worldwide, using the TriNetX database (TriNetX, LLC, Cambridge, Massachusetts, USA) to examine patient records from January 2015–December 2024.[3]

Researchers identified 4,104 patients with PsA taking GLP-1 RAs, including semaglutide, liraglutide, exenatide, and lixisenatide, and 86,432 patients with PsA not on these medications. Patients in the GLP-1 RA group were slightly older at diagnosis, with a mean age of 55.4±11.5 years compared to 52.6±15.1 years for the non-GLP-1 RA group. Female patients were more prevalent in the GLP-1 RA group, while males predominated in the non-user group. White patients comprised the majority in both groups, with 80.9% of GLP-1 RA users and 73.5% of non-users.



Using 1:1 propensity score matching to balance demographics, comorbidities, and medication use, the study found that PsA patients on GLP-1 RAs had a significantly lower risk of major adverse cardiovascular events and reduced overall mortality compared with those not taking the drugs. The analysis accounted for pre-existing cardiovascular events to ensure only new events after GLP-1 RA initiation were included.

GLP-1 RAs are known for their cardiovascular, renal, and weight-loss benefits in Type 2 diabetes. Previous research has shown that weight reduction, whether through lifestyle modification or surgery, can improve disease activity in inflammatory conditions such as PsA, rheumatoid arthritis, and psoriasis.

The study suggests that GLP-1 RAs may offer dual benefits for patients with PsA by addressing both metabolic and inflammatory risk factors. The authors note that further research is needed to understand the mechanisms behind these effects and to confirm long-term outcomes. If validated, GLP-1 RAs could become a valuable adjunct therapy for PsA patients, particularly those with obesity, Type 2 diabetes, or heightened cardiovascular risk.

These findings highlight the growing interest in therapies that target both metabolic and inflammatory pathways in chronic autoimmune diseases.

LEVI-04 Reduces Bone Marrow Lesions and Symptoms in Knee Osteoarthritis

A NOVEL therapy for knee osteoarthritis (OA), presented at the ACR Convergence 2025, LEVI-04, has demonstrated significant improvements in both structural and symptomatic measures of the disease in a Phase II clinical trial. Bone marrow lesions (BML), areas of increased bone turnover, oedema, and fibrosis detectable on MRI, are a hallmark of OA and affect approximately 80% of symptomatic patients with knee OA. These lesions are associated with radiographic severity and fluctuating knee pain.[4]

> **LEVI-04 is a first-in-class p75NTR-Fc fusion protein that has previously shown clinically meaningful improvements in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain**

LEVI-04 is a first-in-class p75NTR-Fc fusion protein that has previously shown clinically meaningful improvements in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain, function, stiffness, Patient Global Assessment (PGA), and pain on movement (Staircase-Evoked Pain Procedure [StEPP]), while maintaining a favorable safety profile. The latest analysis focused on LEVI-04's impact on BMLs and the relationship to OA symptoms.

The study enrolled 518 participants with symptomatic knee OA (WOMAC pain ≥4/10, Kellgren-Lawrence [KL] grade ≥2) in a multicenter, randomized, double-blind, placebo-controlled trial. Participants received either placebo or LEVI-04 (0.3, 1, or 2 mg/kg) every 4 weeks through Week 16. BMLs were measured using coronal proton density-weighted fat-suppressed MRI sequences at baseline and Week 20, with the largest lesion area per participant quantified electronically.

At baseline, 74–79% of participants had BMLs across treatment groups. By Week 20, LEVI-04 produced a significant, dose-dependent reduction in both the proportion of participants with BMLs and the mean BML area (0.3 mg/kg, $p<0.01$; 1 mg/kg and 2 mg/kg, $p<0.001$) compared with placebo. Patients with higher baseline KL grades experienced the greatest reductions. Modest but statistically significant positive correlations were observed between changes in BML area and clinical improvements, including WOMAC pain (Rho=0.21), function (Rho=0.22), stiffness (Rho=0.19), PGA (Rho=0.20), and StEPP (Rho=0.25).

These findings indicate that LEVI-04 not only reduces BMLs but also aligns with improvements in patient-reported symptoms, supporting its potential as a therapy that addresses both structural changes and symptomatic relief in knee OA.

By Week 20, LEVI-04 produced a significant, dose-dependent reduction in both the proportion of participants with BMLs and the mean BML area (0.3 mg/kg, $p<0.01$; 1 mg/kg and 2 mg/kg, $p<0.001$) compared with placebo

Revised Criteria Boost Specificity for Axial Spondyloarthritis

RESULTS from the CLASSIC study, presented at the ACR Convergence 2025, have shown a major international effort to refine diagnostic criteria for axial spondyloarthritis (axSpA).[5]

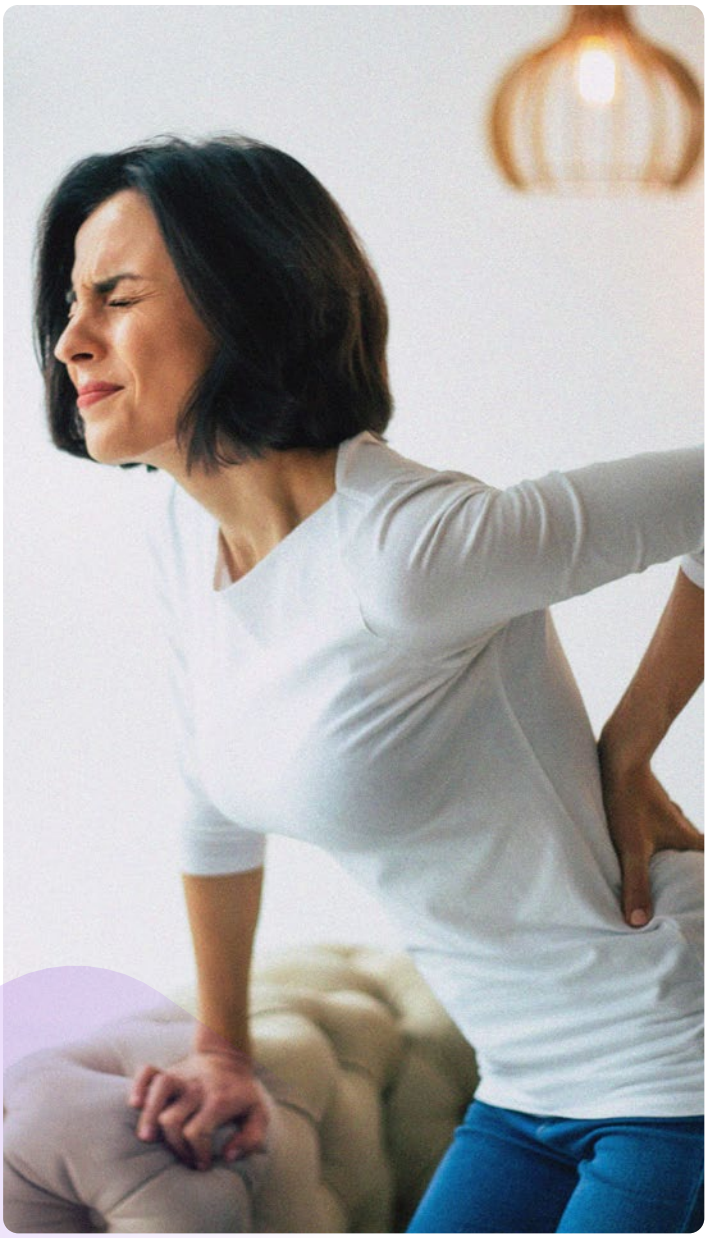
The study addressed limitations of the 2009 Assessment of SpondyloArthritis International Society (ASAS) criteria, which had shown sensitivity (83%) and specificity (84%) for a rheumatologist's diagnosis, adequate but insufficient given the high prevalence of chronic back pain. The CLASSIC study aimed for higher diagnostic precision, targeting ≥75% sensitivity and ≥90% specificity.

CLASSIC enrolled 1,015 patients from 61 centers across 27 countries, all presenting with undiagnosed back pain lasting at least 3 months and starting before the age of 45 years. Comprehensive diagnostic evaluations, including centralized imaging reviews, were conducted in five stages, with Stage 5 serving as the reference standard. Using advanced regression methods such as LASSO and multivariable logistic regression, investigators identified which clinical and imaging features best predicted a confirmed axSpA diagnosis.

The findings showed that MRI of the sacroiliac joints, particularly when both active and structural lesions were present, was the strongest independent predictor of axSpA, followed by radiographic sacroiliitis. Key clinical variables included HLA-B27 positivity, inflammatory back pain, inflammatory bowel disease, acute anterior uveitis, heel enthesitis, and elevated C-reactive protein.

After consensus review by ASAS and SPARTAN members, the final revised criteria achieved 79.5% sensitivity and 90.4% specificity, surpassing the predefined targets.

These updated ASAS-SPARTAN classification criteria represent a significant advance in identifying axSpA, emphasizing imaging findings and a streamlined set of clinical features to enhance diagnostic accuracy and consistency worldwide.



Study Defines Optimal Hydroxychloroquine Range for Lupus Safety

FINDINGS from a large international analysis, presented at the ACR Convergence 2025, have refined the therapeutic range for hydroxychloroquine (HCQ) in managing systemic lupus erythematosus (SLE).[6]

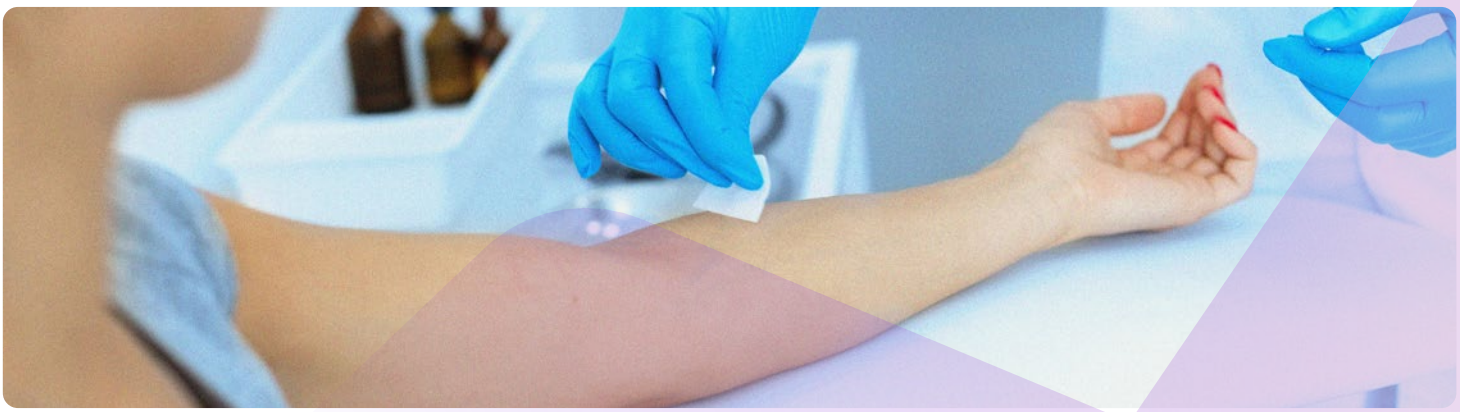
Current guidelines recommend an HCQ dose of ≤5.0 mg/kg, yet prior data have shown up to six-times higher rates of SLE flares, often requiring hospitalization, among patients on this lower dose. Additionally, clinicians have lacked clear guidance on adjusting HCQ dosing in individuals with chronic kidney disease. This study aimed to establish blood level thresholds that balance efficacy and safety.

> **These results confirm and extend earlier findings that have previously defined a therapeutic HCQ range of 750–1,150 ng/mL**

Researchers analyzed pooled data from 1,842 patients with SLE across five cohorts and registries spanning North America, Europe, and Asia. HCQ blood levels at baseline were compared with subsequent HCQ-related toxicity, such as retinopathy, cardiomyopathy, and myopathy, and with disease activity measured by SLEDAI-2K scores. Using mixed regression models, the investigators identified that HCQ levels above 1,150 ng/mL were associated with a 1.9-fold higher risk of toxicity, primarily due to retinal damage. In contrast, levels below 750 ng/mL were linked to 1.4-fold higher odds of active disease, indicating insufficient therapeutic exposure.

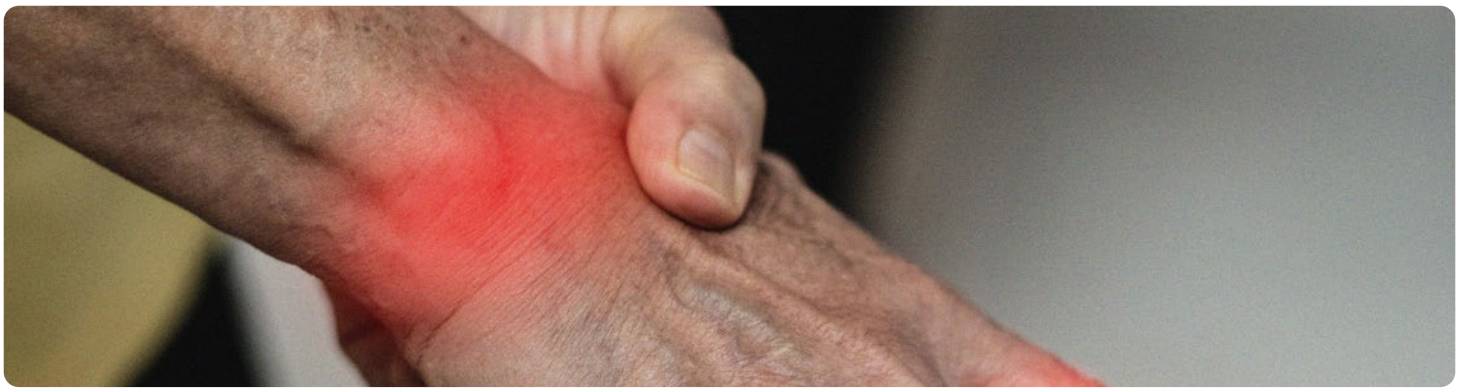
Among patients taking ≤5 mg/kg, nearly 52% had subtherapeutic levels (<750 ng/mL), while 18% had supratherapeutic levels (>1,150 ng/mL). Those with chronic kidney disease Stage ≥3 were particularly vulnerable, showing 2.3-fold higher odds of toxic or supratherapeutic levels, even when on guideline-recommended doses.

These results confirm and extend earlier findings that have previously defined a therapeutic HCQ range of 750–1,150 ng/mL that optimizes disease control while minimizing toxicity risk. The study emphasizes that routine HCQ blood level monitoring, rather than fixed weight-based dosing, could enable personalized treatment strategies for SLE, especially in patients with kidney impairment.



MAIT Cells Drive Inflammation and Joint Damage in Rheumatoid Arthritis

NEW research presented at the ACR Convergence 2025 identifies mucosal-associated invariant T (MAIT) cells as key contributors to inflammation and joint damage in rheumatoid arthritis (RA). The findings, from investigators at Paris University, France, and collaborating French research centers, highlight MAIT cells as both inflammatory effectors and potential therapeutic targets in RA.[7]



MAIT cells are innate-like T lymphocytes that recognize microbial metabolites and bridge the immune system and the microbiota. Previous studies have shown altered MAIT cell frequencies and function in autoimmune diseases, but their precise role in RA pathogenesis remained unclear.

In this study, researchers analyzed MAIT cells in blood and synovial fluid samples from 75 patients with RA and 42 healthy donors using flow cytometry and single-cell RNA sequencing. Additional experiments examined how MAIT cells interact with fibroblast-like synoviocytes *in vitro*, and how they affect arthritis severity in mouse models.

Circulating MAIT cells were markedly reduced in patients with RA compared with healthy donors (0.51% versus 2.7%; p<0.001) but displayed an activated and exhausted phenotype, producing high levels of IL-17 and granzyme B. In contrast, MAIT cells were enriched in the synovial fluid, particularly in early RA, and exhibited signatures of activation, exhaustion, and interferon pathway engagement. Computational analysis indicated that plasmacytoid dendritic cells and monocytes generate chemokine gradients that recruit MAIT cells into inflamed joints.

In co-culture experiments, activated MAIT cells stimulated fibroblast-like synoviocytes to increase the production of inflammatory cytokines (IL-1β, IL-6, IL-8, MCP-1) and matrix-degrading enzymes, amplifying joint inflammation. Importantly, in two arthritis mouse models, deletion of MR1, the molecule required for MAIT cell activation, or pharmacologic blockade with Ac-6-FP, significantly reduced arthritis severity and joint destruction.

These findings reveal that MAIT cells migrate from the blood to the joints, where they fuel local inflammation and tissue damage while also expressing IL-10, suggesting a complex role in immune regulation. Modulating MAIT cell activity or migration may offer a new therapeutic avenue for RA.

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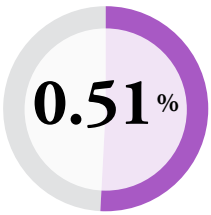

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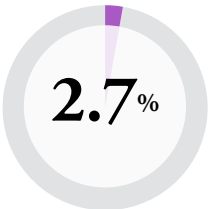

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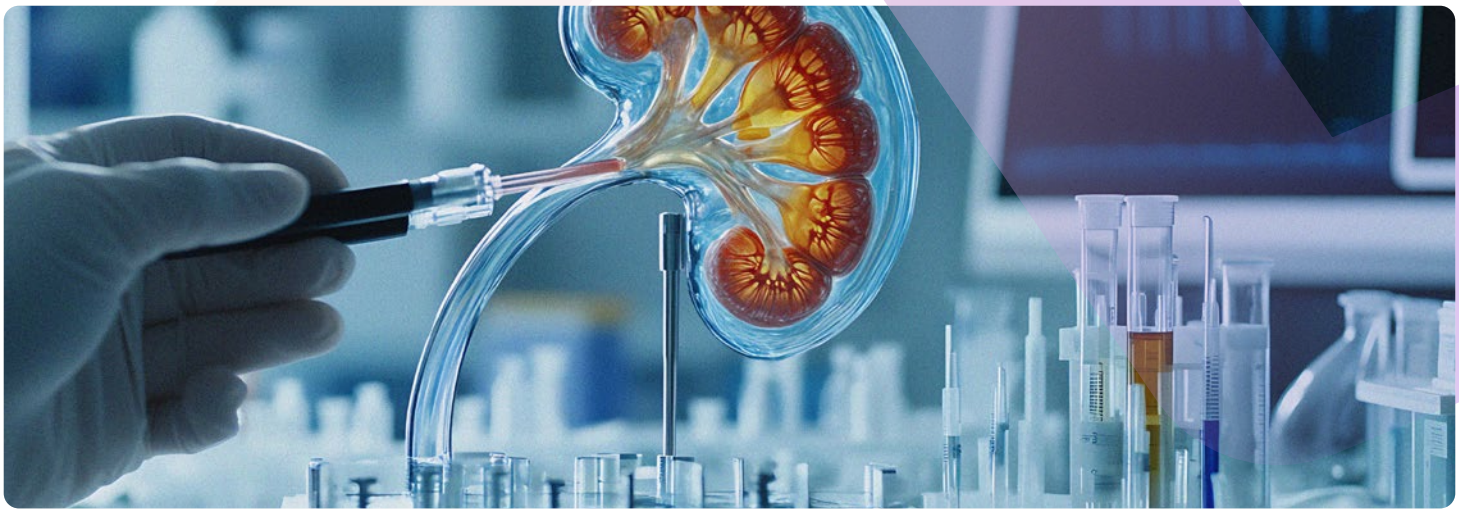

Urinary Tenascin C Predicts Kidney Function Loss in Lupus Nephritis

A GROUNDBREAKING study presented at the ACR Convergence 2025 identifies urinary Tenascin C as an important early predictor of kidney function loss in lupus nephritis (LN), offering a potential advance beyond traditional response markers such as proteinuria. Long-term predictors of renal decline remain limited in LN, despite kidney survival being a central therapeutic goal.[8]

Researchers followed 170 patients from the Accelerating Medicines Partnership cohort for up to 7.8 years. During this period, 31% experienced significant estimated glomerular filtration rate loss. Among more than 1,200 urinary proteins analyzed, Tenascin C measured at Month 3 demonstrated the strongest association with future kidney decline, with elevated levels persisting through Month 12. Other inflammatory and fibrosis-related markers, including CD163, CD206, FABP4, IL-6, and IGFBP-6, were also consistently linked to higher risk.

Single-cell RNA sequencing and spatial transcriptomics localized Tenascin C production to interstitial myofibroblasts, supporting its role in progressive renal fibrosis. Using these insights, the investigators developed an 11-protein urinary classifier capable of predicting long-term estimated glomerular filtration rate loss with high accuracy (area under the curve: 0.91 at 48 months). Notably, the model classified risk independently of proteinuria status at 1 year. It also revealed heterogeneity within response categories defined by the urine protein-to-creatinine ratio (UPCR): some UPCR responders had high-risk biomarker signatures, while some non-responders showed low-risk profiles, highlighting the limitations of relying solely on UPCR thresholds for clinical decision-making.

The study's findings demonstrate the potential for biomarker-driven risk assessment to personalize LN management, improve trial design, and identify patients who may benefit from early treatment intensification. By monitoring ongoing profibrotic and inflammatory activity that proteinuria may miss, urinary Tenascin C and related markers could help prevent irreversible kidney damage in high-risk individuals.

Checkpoint Inhibitor-Induced Arthritis Emerges as a Unique Cell-Driven Autoimmune Disease

A STUDY presented during the Plenary Session at the ACR Convergence 2025 provides important insight into the biology of inflammatory arthritis (IA) that emerges as an immune-related adverse event (irAE) after immune checkpoint inhibitor (ICI) therapy.[9]

Although this arthritis often resembles rheumatoid arthritis (RA) clinically, the study demonstrates that its underlying immunology is fundamentally different, and likely driven primarily by autoreactive T cells rather than autoantibodies.

Investigators from Mayo Clinic, Rochester, Minnesota, USA, analyzed immune profiles from 163 participants, including patients with IA irAEs, ICI-treated patients with cancer without irAEs, serology-matched RA controls, and healthy volunteers. Using flow cytometry, cytokine profiling, single-cell RNA sequencing, and functional *in vitro* assays, the team compared immune cell phenotypes, metabolic signatures, and autoreactivity across groups.

The findings revealed that IA irAEs represent a unique autoimmune phenotype, dominated by highly cytotoxic CD8+ T cells that are more activated than those seen in ICI-treated controls. These IA-associated CD8+ T cells expressed the highest levels of effector and cytotoxic molecules, alongside elevated metabolic activity. In contrast to RA, patients with IA irAEs did not show autoantibody elevations or expansion of atypical B cell populations. RA controls displayed increased CD4/CD8 ratios, reduced regulatory T cell frequencies, and robust autoantibody responses, none of which were present in the irAE group.

CD4+ T-cell alterations further distinguished IA irAEs from RA. Patients with irAEs exhibited a striking shift toward a CXCR3-CCR6- T cell phenotype, alongside reductions in the CXCR3+CCR6+ subset, suggesting a reprogramming of T helper cell pathways in response to ICI exposure.

Cytokine patterns also supported a T cell-centered mechanism. Patients with IA and irAEs showed elevated plasma IL-6, IL-12, and Type I IFN signatures, with *in vitro* experiments demonstrating that this cytokine combination promotes cytotoxic gene expression in T cells. Blocking IL-6 receptors, IL-12 or IFN-α pathways reversed these cytotoxic and metabolic phenotypes, indicating potential therapeutic targets.

“Cytokine patterns also supported a T cell-centered mechanism. Patients with IA and irAEs showed elevated plasma IL-6, IL-12, and Type I IFN signatures”

Together, the data suggest that inflammatory arthritis irAEs are not simply ICI-triggered RA, but rather a distinct autoimmune condition characterized by T cell hyperactivation, metabolic reprogramming, and cytokine-driven cytotoxicity, yet largely independent of traditional autoantibody mechanisms.

This work provides a more refined understanding of checkpoint inhibitor-associated arthritis and highlights pathways that may guide future treatment strategies for affected patients.

Many High-Risk Women with Osteoporosis Remain Undertreated

MORE than 85% of postmenopausal women in the USA with high or very high fracture risk remain untreated, according to a new retrospective cohort study presented at the ACR Convergence 2025. Among those who did receive therapy, more than half were treated with oral bisphosphonates, despite these not being recommended for women at very high risk in current guidelines. Only around 5% of treated women received anabolic therapies, the most effective initial treatment.[10]

Data from the Optum Market Clarity Bone database (Optum®, Eden Prairie, Minnesota, USA) were analyzed to identify women aged 55 years or older with osteoporosis, a prior fracture, or earlier osteoporosis therapy between 2016–2023. To be eligible, women were required to have at least 455 days of continuous insurance coverage and to have complete data on BMI and race. Those with Paget's disease or metastatic cancer were excluded.

The study identified 41,597 women treated for postmenopausal osteoporosis. Just over half met the criteria for very high fracture risk. Among these women, 12.6% had experienced a recent fracture within the previous year, fewer than 1% had a bone mineral density T-score of −3.0 or below, and more than 38% had a FRAX® score (University of Sheffield, UK) indicating very high risk. A further 21% were classified as high risk, and around 27% as low risk.

> **More than 85% of postmenopausal women in the USA with high or very high fracture risk remain untreated**

Oral bisphosphonates were the most frequently used medications across all patients. More than 56% of treated women received this therapy. Denosumab was prescribed for 23% and zoledronic acid for nearly 16% of participants. Despite guideline recommendations, only around 5% of treated women and 5.7% of those at very high risk received anabolic therapies, which are considered the most efficient initial treatment option for this group.

The analysis also included 318,140 untreated women (mean age: 74 years), 37% of whom had very high fracture risk and 47% high risk, with a further 15.9% classified as low risk. These findings indicate that a substantial proportion of women who could benefit from treatment remained untreated.

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