



Highlights from the European Alliance of Associations for Rheumatology (EULAR) 2026 Congress

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THE EUROPEAN Alliance of Associations for Rheumatology (EULAR) 2026 Congress was held in London, UK, from 3rd–6th June. The sessions spanned a broad array of clinical and basic science topics across rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), psoriatic arthritis, spondylarthritis, vasculitis, Sjögren's disease, myositis, juvenile idiopathic arthritis, systemic sclerosis, and osteoarthritis. This feature highlights some of the emerging concepts across rheumatology in 2026.

DECIPHERING IMMUNE TRENDS IN PRECLINICAL RHEUMATIC DISEASES

Multi-omic Approaches Reveal How Immune Cells Go Awry

Loss of B cell tolerance emerged as an early driver of systemic autoimmunity in both SLE and RA.¹ Bylinska et al.¹ profiled the pre-SLE continuum: autoantibody-negative controls, autoantibody-positive individuals, incomplete lupus erythematosus, and established SLE using 137-plex cellular Indexing of Transcriptomes and Epitopes by Sequencing. They reported a loss of inhibitory checkpoints in naïve B cells (leukocyte-associated Ig-like receptor 1 [LAIR1] down, cluster of differentiation [CD]83-high) early during the autoantibody-positive stage, but a slower transition to effector phenotype, with metabolic reprogramming and B cell receptor activation emerging in incomplete lupus erythematosus and SLE. In contrast, antigen-experienced memory, CD11c^{hi},

and CD24^{hi} subsets acquire mitochondrial and Type I interferon signature early in the antibody-positive stage and maintain these signatures throughout the pre-SLE to SLE continuum. This B cell shift is coupled to the myeloid compartment, which shows the largest transcriptional change of all: IL1B+ CD14+ monocytes show the largest transcriptional changes. As disease progresses, they lose TIMP1-CD63 pro-survival signalling to B cells and instead gain S100A9-mediated inflammatory signalling through the B cell receptor, alongside increased TNF and IL-6 signalling. T cell involvement is staged in parallel, with CD4 central memory cells marking the earliest transition, and CD4 and CD8 effector memory cells progressively engaging the activated B cell subsets.

In at-risk RA, Takada et al.² ran mass cytometry on 42 anti-cyclic citrullinated peptide (CCP)-positive individuals, 15 of whom converted to clinical disease within 2 years. Eight lymphocyte subsets were expanded relative to controls, but only

two predicted conversions. High baseline frequencies of CXCR5⁺-activated naïve B cells correlated with 47% RA-free survival at 1 year against 91% in the low group, and Ki-67⁺ proliferating peripheral helper T cells, at 53% versus 84%, with both curves separating inside the first year. The predictive unit, an activated naïve B cell population paired with a proliferating T-helper population, mirrors the naïve-B activation and effector-memory T cell engagement seen in pre-SLE.

Proteomics anchors the convergence at the soluble level. Pu et al.³ screened 2,920 plasma proteins in 46,687 UK Biobank participants with 606 incident RA cases over a median of 8.3 years; 1,520 proteins were associated with future onset. Mendelian randomisation nominated 11 proteins with genetic risk for causality, including TNF, IL1RN, CD40, human leukocyte antigen (HLA)-DRA, CD72, TNFRSF14, AIF1, RNASET2, ICAM3, CCL21, and ACRBP, four of them already drug targets. Two molecules recur across both diseases with hard, molecule-level support: TNF, monocyte-induced in pre-SLE and genetically causal in pre-RA, and CD72, lost as a B cell checkpoint in pre-SLE and flagged as a causal protein in pre-RA. The shared antigen-presentation pathway (HLA-DRA, CD40) reinforces the overlap, but rests on weaker, pathway-level evidence.

The Gut-Joint Axis

In the session 'Novel Insights into Pre-RA Mechanisms: What Happens Where and When?', Zaiss⁴ made the case that RA may begin in the gut, with anti-acetylated protein antibodies (AAPA) as the connecting thread. Drawing on the TIRx cohort, consisting of individuals who are AAPA-positive and have musculoskeletal symptoms but no clinical synovitis, he showed that AAPA significantly separated those who progressed to RA from those who did not, pointing to a diagnostic and possibly predictive role, while established disease was marked by high levels of tissue protein acetylation. To explain how this might arise, he turned to the collagen-induced arthritis model, where artificially acetylating gut *Escherichia coli* heightened its antigenicity, while intestinal acetylation, in turn, drove damage to the epithelial barrier. At the sites where acetylation occurred, myeloid cells gathered in the mucosal villi and CD11c⁺ cells presented to B cells, while the acetylated proteins themselves appeared to push those myeloid cells away from antigen presentation and towards an inflammatory effector role. Taken together, the data positioned gut protein acetylation as an upstream trigger of the autoantibody response that precedes joint disease.

“Advances in multi-omic profiling are uncovering the key immune cells and molecular pathways driving autoimmune rheumatic diseases long before clinical diagnosis”

Relevance to Practice

These studies demonstrate how advances in multi-omic profiling are uncovering the key immune cells and molecular pathways driving autoimmune rheumatic diseases long before clinical diagnosis. By defining the earliest stages of immune dysregulation, these approaches provide a valuable window of opportunity for disease interception before autoimmunity becomes tissue-centric and difficult to cure. This concept is already being translated into clinical practice through prevention trials, such as the ALTO trial, which showed that treatment with abatacept for 1 year delays arthritis progression for up to 4 years in individuals who are at very high risk of developing RA. Ongoing trials, including the ExIST trial, evaluating baricitinib in individuals at risk of inflammatory arthritis will determine whether targeting the JAK pathway can similarly delay arthritis onset in anti-CCP-positive individuals at moderate-to-high risk of disease.^{5,6}

BEYOND CD19: SEQUENTIAL B-LINEAGE TARGETING IN TREATMENT-REFRACTORY RHEUMATIC DISEASE

Relapse After CD19 CAR-T and Sequential BCMA-Directed Rescue

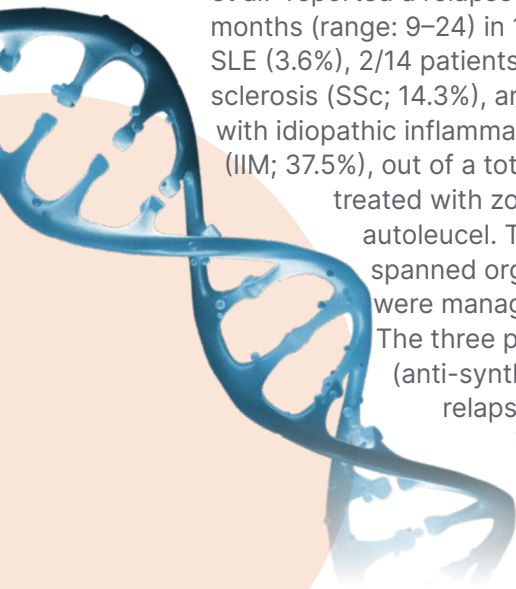
CD19 CAR-T cell therapy showed promise in inducing deep immune reset in patients with refractory SLE, but follow-up data presented at EULAR 2026 established that maintenance of long-term remission may not be a reality for all patients. Data presented by Wirsching et al.⁷ reported a relapse at a median of 13 months (range: 9–24) in 1/28 patients with SLE (3.6%), 2/14 patients with systemic sclerosis (SSc; 14.3%), and 3/8 patients with idiopathic inflammatory myopathies (IIM; 37.5%), out of a total of 50 patients treated with zorpcabtagene autoleucel. The six relapses spanned organ systems and were managed individually. The three patients with IIM (anti-synthetase, Jo1/PL7) relapsed with myositis, interstitial lung disease, or arthritis, and received,

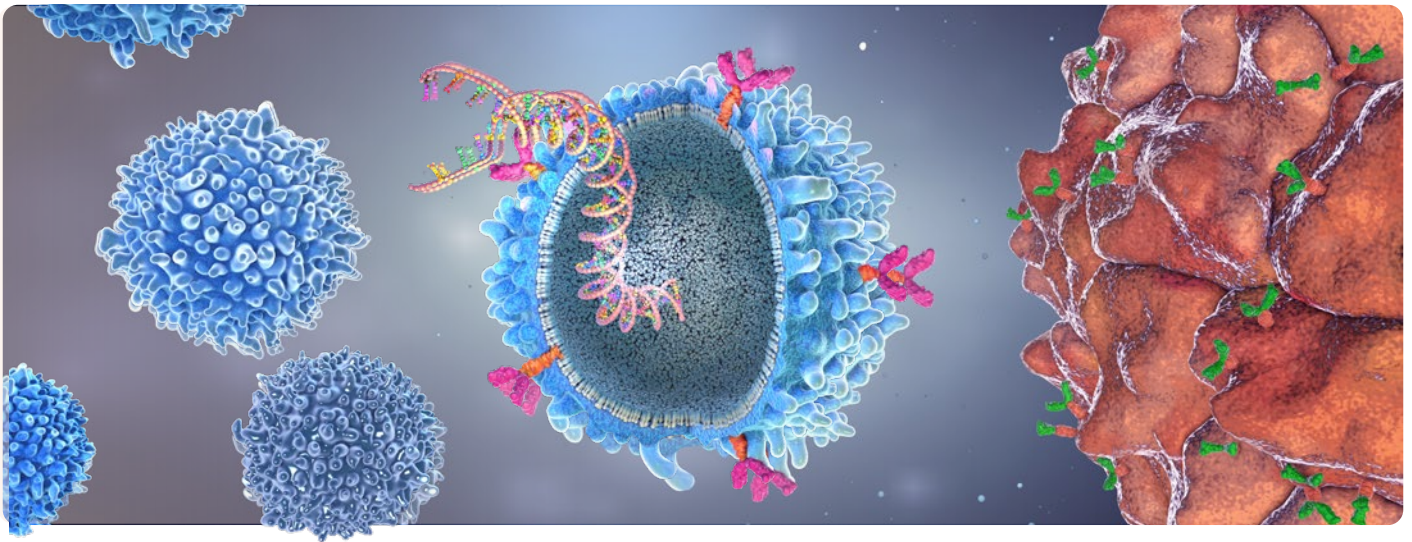
respectively, B cell maturation antigen (BCMA) CAR-T (idecabtagene vicleucel) with sustained remission, obinutuzumab plus nintedanib, and tofacitinib followed by BCMA CAR-T in the CARAMBA study. The patient with SLE (double-stranded DNA-positive) relapsed with transverse myelitis, arthritis, and skin disease. BCMA CAR-T cell therapy successfully cleared the neurological deficit, however, leaving behind residual cutaneous disease (despite double-stranded DNA seroconversion), which was cleared by anifrolumab. Both patients with SSc (Scl70-positive) relapsed with multi-organ disease and received the BCMA T cell engager teclistamab, with early improvement. Relapse after CD19 CAR-T is infrequent but real and late; IIM is the least durable setting, and BCMA-directed combinatorial therapy is the dominant rescue.

The rescue pattern points to the compartment CD19 leaves behind. CD19 CAR-T spares CD19-BCMA+ long-lived plasma cells, and the most systematic test of targeting them came from Boeltz et al.,⁸ who treated 16 patients with multidrug-resistant disease, eight with SSc, two with IIM, two with IgG4-related disease, two with RA, one with Sjögren's disease, and one with Graves' disease, with the CD3×BCMA T cell engager teclistamab in a named-patient programme. Clinical responses occurred in 15/16 patients, with seroconversion of autoantibodies that characteristically survive CD19 monotherapy, including anti-Sjögren's-syndrome-related antigen A, Scl-75/100, anti-CCP, rheumatoid factor, and Mi-2, alongside normalised IgG4. Nine patients reached drug-free remission (median: 11 months), though four progressed by a median of 5 months, and all 16 developed hypogammaglobulinaemia requiring Ig replacement.

Off-the-Shelf CAR-T Cell Therapy

Looking beyond autologous, single-target constructs, Shiff et al.⁹ presented FT839 (Fate Therapeutics, San Diego, California, USA), an off-the-shelf, induced pluripotent stem cell-derived dual-CAR-T cell designed to address three limitations of current CAR-T at once: single-antigen targeting, the need for conditioning chemotherapy, and per-patient manufacturing.





It expresses two CARs against the B cell lineage marker CD19 and the activation marker CD38, the latter spanning plasmablasts, plasma cells, and activated T and natural killer cells. FT839 is engineered with synthetic alloimmune defence receptor plus CD58 deletion to eliminate alloreactive immune cells and resist host rejection. In preclinical assays, FT839 eliminated CD19+ B cells, plasmablasts, plasma cells, and CD38+ activated CD4/CD8 T cells (>93–99%) while sparing resting CD38⁻ T cells. In HLA-mismatched cultures, FT839 demonstrated greater persistence than unmodified controls, consistent with the effects of its alioevation engineering (2.4×10^6 versus 1.3×10^4 cells; $p < 0.0001$). The data are preclinical, but FT839 is one example of the off-the-shelf, multi-target, conditioning-free CAR-T cell therapy.

“**CD19 CAR-T cell therapy showed promise in inducing deep immune reset in patients with refractory SLE**”

Relevance to Clinical Practice

While relapse following CD19 CAR-T therapy is uncommon, these findings show that sequential BCMA-directed therapies can successfully restore disease control in selected patients. Emerging off-the-shelf CAR-T platforms may also improve accessibility by reducing manufacturing delays and broadening immune-cell targeting. Although these approaches remain investigational, they represent an important step towards more personalised,

mechanism-based treatment for refractory rheumatic diseases.

AI IN RHEUMATOLOGY

Machine Learning Identifies Subgroups in JPsA From Multicentre Inception Cohorts

Shoop-Worrall et al.¹⁰ used machine learning to test whether juvenile psoriatic arthritis (JPsA) separates into distinct subgroups, pooling five multinational inception cohorts: CAPS, ICON, NPRD, ReACCh-Out, and CAPRI, including 3,282 children diagnosed with JPsA, enthesitis-related juvenile idiopathic arthritis, or undifferentiated juvenile idiopathic arthritis, between 2001–2023. Applying latent class analysis to active joint count, psoriasis, dactylitis, and nail involvement within the first 24 months of symptom onset, they consistently recovered three clusters: a low-burden low joint–psoriasis group, a high-burden psoriasis–dactylitis group, and an intermediate all features group. The psoriasis–dactylitis cluster was the most severely affected, with the highest enthesitis (70–83%), the greatest proportion reporting a family history of psoriasis (57–85%), and the worst patient-reported global, pain, and disability scores; these children were younger (median: 10–11 years) and more often female (65% versus 44%). The key methodological strength was testing the clusters across three case definitions: ILAR JPsA criteria, physician diagnosis, and CIASSification criteria for

Psoriatic ARthritis (CASPAR). The same broad phenotypes recurred under all three, supporting their robustness, but their proportions shifted markedly:

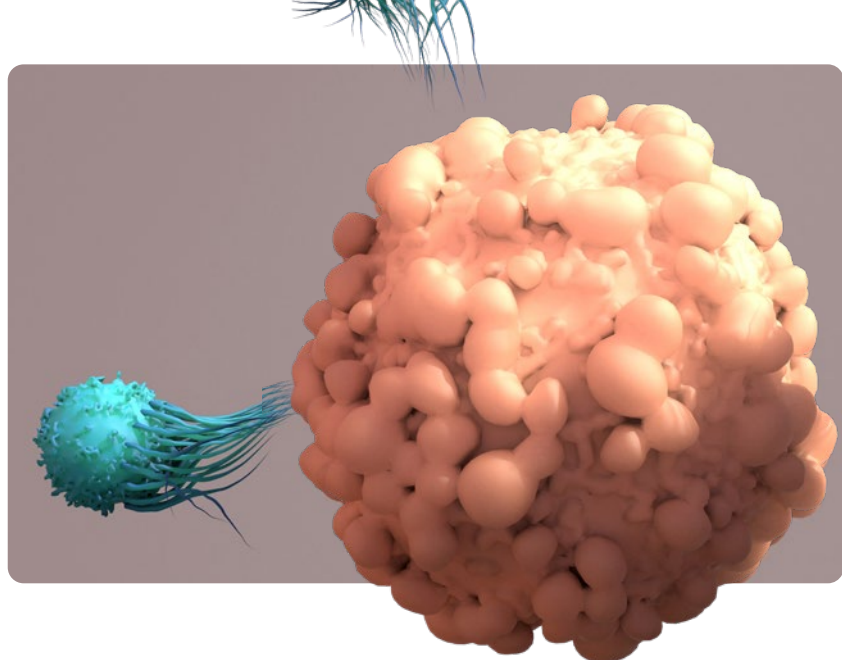
the low-burden group made up 26% under International League of Associations for Rheumatology (ILAR) criteria, yet 59% under physician diagnosis, and the CASPAR-defined population yielded an additional small high joint–dactylitis group not seen in the others. JPsA is therefore clinically heterogeneous, but how the subgroups are partitioned and how large each appears depends partly on the diagnostic definition applied.

Relevance to Clinical Practice

AI can identify clinically meaningful disease subgroups beyond conventional classification criteria. As machine learning becomes increasingly integrated into rheumatology, such approaches may improve patient stratification, prognostication, and treatment selection, supporting more personalised care and more efficient clinical trial design in JPsA.

CONCLUSION

Research presented at EULAR 2026 highlighted the rapid progress being made towards precision medicine in rheumatology. Advances in multi-omic technologies are improving our understanding of the earliest stages of autoimmune disease and identifying new opportunities for disease interception



before irreversible tissue damage occurs. At the same time, innovations in cellular therapies are expanding treatment options for patients with severe, treatment-refractory autoimmune diseases, while AI is helping to define clinically meaningful patient subgroups that may support more personalised care. Although many of these approaches remain investigational, together they demonstrate how technological advances are transforming both our understanding and management of rheumatic diseases. Continued clinical studies will be essential to determine how these discoveries can be translated into routine practice and ultimately improve outcomes for patients.

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