# This Week in Rheumatology

# **Drugs and Pharmacology**

Recent research highlights critical safety considerations for biologics and JAK inhibitors (JAKi) in inflammatory and autoimmune diseases. A review by Moreau et al. underscores the need for vigilant monitoring of JAKi side effects, particularly infections, cardiovascular events, and malignancies, with heightened risks in older patients, smokers, and those with pre-existing cardiovascular or cancer risk factors. Preventive strategies—such as screening, vaccination, and prophylaxis—are emphasized to mitigate these risks. Meanwhile, a meta-analysis by Isufi et al. provides reassuring data on biologics in patients with a history of cancer, showing no increased risk of new or recurrent malignancies with TNF-alpha inhibitors, IL-12/23 inhibitors, or vedolizumab compared to conventional therapies. However, individualized risk assessment remains crucial, especially for newer biologics where data are limited. Together, these studies underscore the importance of balancing efficacy with tailored safety protocols in clinical practice.

#### References

- Safety profile of JAK inhibitors in inflammatory or autoimmune diseases. by Moreau J, Chikhoune L, Poggi C, Stabler S, Letarouilly JG, Hachulla E, Launay D. La Revue de medecine interne. PMID: 40562664
- Risk of new or recurrent cancer during treatment with biologics in patients with immune-mediated inflammatory diseases and previous cancer: a metaanalysis. by Isufi D, Schwarz CW, Jensen MB, Seidelin J, Skov L, Loft N. Clinical and experimental medicine. PMID: 40560239

#### Exercise and Rehabilitation

Recent studies highlight the growing role of digital and supervised exercise interventions in improving outcomes for chronic musculoskeletal conditions. A randomized controlled trial on fibromyalgia (Zhang et al., 2024) demonstrated that combining remote-supervised exercise (via web-based therapist guidance) with pregabalin/duloxetine significantly reduced pain (BPI scores), improved sleep, and enhanced quality of life over 3 months compared to unsupervised exercise, underscoring the value of structured, long-term supervision. Meanwhile, a narrative review on rheumatoid arthritis (Fedorchenko et al., 2024) emphasized multimodal rehabilitation—walking (notably high-intensity intervals), aquatic therapy, and yoga—for reducing disease activity (DAS28), pain, and fatigue while boosting mobility and mental health. Wearable tech and EULAR/ACR guidelines were noted as key tools for personalizing regimens, though adherence barriers persist. Complementing these, a meta-analysis (Zhang et al., 2024) found digital

health interventions (e.g., activity trackers, web/phone apps) effectively reduced sedentary behavior in chronic disease patients (e.g., arthritis, diabetes), with small but significant decreases in sitting time (-30.8 min/day) and SB proportion (-4.65%), particularly in younger cohorts. Together, these studies advocate for integrating technology-enhanced, supervised exercise and tailored PA into chronic disease management, balancing efficacy with patient-centered adaptability.

#### References

- The Effect of a Remote Network Technology Supervised Exercise Program
   Combined With Drug Treatment for Fibromyalgia: Randomized, Single-Blind,
   Controlled Trial. by Zhang C, Zhang P, Zhao Y, Liu Y, Hu Y, Zhu Z, Xiao H.
   Journal of medical Internet research. PMID: 40570164
- Physical activity of older patients with rheumatoid arthritis. by Fedorchenko Y, Zimba O, Qumar AB, Yessirkepov M, Kocyigit BF. Rheumatology international. PMID: 40560403
- Effectiveness of Digital Health Interventions on Sedentary Behavior Among Patients With Chronic Diseases: Systematic Review and Meta-Analysis. by Zhang Y, Ngai FW, Yang Q, Xie YJ. JMIR mHealth and uHealth. PMID: 40554804

# **Immunology**

A systematic review and meta-analysis by Chen et al. (2024) highlights the clinical significance of inflammageing biomarkers—CRP/Hs-CRP, IL-6, and TNF-alpha—in middle-aged and older adults. Elevated CRP/Hs-CRP and IL-6 were strongly associated with a 1.54- and 1.47-fold increased risk of all-cause mortality, respectively (p=0.001), while elevated CRP/Hs-CRP also correlated with a 1.48-fold higher odds of depression (p<0.001). However, evidence linking these biomarkers to hospitalization, readmission, or anxiety remains limited. The authors propose integrating biomarker monitoring into chronic disease management to mitigate mortality and depression risks, emphasizing precision care strategies. These findings underscore the potential of inflammageing biomarkers as predictive tools for adverse outcomes in aging populations.

#### References

 Association between the inflammageing biomarkers and clinical outcomes amongst the community-dwelling middle-aged and older adults: A systematic review and meta-analysis. by Chen D, Tam WWS, Zhang J, Lu J, Wu VX.
Ageing research reviews. PMID: 40562315

## **Osteoarthritis**

Recent research highlights key advances and uncertainties in osteoarthritis (OA) management. Exercise therapy for knee OA shows reduced certainty in effectiveness, with unclear mechanisms and optimal dosing, though remote delivery remains viable (Haber et al., 2025). Surgical options like microfracture (MF) and arthroscopic debridement (AD) for small cartilage lesions (<2 cm²) yield

comparable 2-year outcomes, challenging MF's dominance (Randsborg et al., 2024). Agricultural activities are newly linked to increased arthritis risk in middle-aged/elderly populations, suggesting occupational screening value (Wang et al., 2024). Diagnostic accuracy for thumb OA varies, with physical exams (e.g., adduction test) outperforming history-taking, though evidence quality is mixed (He et al., 2024). Frailty intensifies the pain-radiographic severity correlation in knee OA, underscoring its role in personalized care (Halliwell et al., 2024). Platelet-rich plasma (PRP) protocols show stage-dependent efficacy: leukocyte-rich PRP suits early OA (anti-inflammatory), while leukocyte-poor PRP excels in advanced disease (tissue repair) (Yu et al., 2024). Photobiomodulation (790 nm laser) significantly reduces pain and improves function versus sham/control (Dos Santos Maciel et al., 2024).

#### References

- Recent highlights and uncertainties in exercise management of knee osteoarthritis. by Haber T, Lawford BJ, Bennell K, Holden M, White DK, Hinman RS. Journal of physiotherapy. PMID: 40579310
- Microfracture Versus Arthroscopic Debridement for the Treatment of Symptomatic Cartilage Lesions of the Knee: 2-Year Results From a Multicenter Double-Blinded Randomized Controlled Trial. by Randsborg PH, Aae TF, Visnes H, Birkenes T, Benth JS, Lian OB, Hanvold HA, Aroen A. The American journal of sports medicine. PMID: 40570306
- The association between agricultural activities and arthritis in middle-aged and elderly people: Findings from a cohort study based on CHARLS. by Wang X, Zou G, Zhang W, Zhang Y, Zheng R, Li S. PloS one. PMID: 40569900
- Diagnostic accuracy of history taking, physical examination, and auxiliary examination for thumb osteoarthritis: a systematic review. by He Y, Krastman P, Bierma-Zeinstra SMA, Kraan G, Mathijssen NM, Runhaar J. Annals of medicine. PMID: 40569761
- The relation between radiographic knee osteoarthritis severity and pain is stronger among more frail people. by Halliwell C, Rayner SE, Waghorn J, Feltmate B, Moyer R, O'Brien MW. Clinical rheumatology. PMID: 40569498
- The efficacy of platelet-rich plasma preparation protocols in the treatment of osteoarthritis: a network meta-analysis of randomized controlled trials. by Yu D, Zhao J, Zhao K. Journal of orthopaedic surgery and research. PMID: 40551225
- Effect Of Photobiomodulation (Low-Level Laser Therapy) In Patients With Knee Osteoarthritis: A Randomized Controlled Trial. by Dos Santos Maciel T, Correa Lima Chamy N, Dos Santos Maciel M, Pasqual Marques A. Lasers in medical science. PMID: 40545487

### Other Rheumatic Diseases

Recent studies highlight key prognostic factors and clinical challenges in rheumatic diseases. In anti-aminoacyl-tRNA synthetase (anti-ARS) antibody-positive interstitial lung disease (ILD), a longitudinal study of 131 patients found 5-and 10-year mortality rates of 15% and 28%, respectively, with pulmonary events occurring in 24% by decade's end. Poor outcomes were linked to anti-PL-7

antibodies, dysphagia, usual interstitial pneumonia (UIP) pattern, and reduced DLCO%, underscoring the need for comprehensive risk stratification (Yamaguchi et al., Clin Rheumatol). Meanwhile, mitochondrial pathology in non-IBM inflammatory myopathies (e.g., polymyositis) correlated with treatment resistance and worse functional outcomes, including progression to IBM in some cases, suggesting mitochondrial dysfunction as a biomarker for disease severity (Lauletta et al., J Neurol). On the therapeutic front, a Danish cohort study revealed a modestly elevated risk of serious bacterial infections (IRR 1.11) in the year after initiating biologics for IBD or IRD, peaking in the first three months and driven by comorbidities, older age, and corticosteroid use—with anakinra posing the highest risk in IRD (Platz et al., Ann Med). Together, these findings emphasize the importance of tailored monitoring for pulmonary, muscular, and infectious complications in rheumatic disease management.

### **References**

- Long-term clinical prognosis of anti-aminoacyl-tRNA synthetase antibodies and interstitial lung disease. by Yamaguchi K, Sullivan DI, Khushboo S, Saygin D, Laverde SM, Moghadam-Kia S, Ascherman DP, Oddis CV, Aggarwal R. Clinical rheumatology. PMID: 40571884
- Mitochondrial pathology in inflammatory myopathies: a marker of worse clinical outcome. by Lauletta A, Bosco L, Merlonghi G, Falzone YM, Cheli M, Bencivenga RP, Zoppi D, Ceccanti M, Kleefeld F, Leonard-Louis S, Stenzel W, Benveniste O, Maggi L, Previtali SC, Garibaldi M. Journal of neurology. PMID: 40569469
- Risk of serious bacterial infections in inflammatory rheumatic or bowel disease patients during biological therapies: nationwide Danish cohort study. by Platz ECH, Laugesen GE, Ostergaard AA, Byg KE, Petersen I, Johansen IS. Annals of medicine. PMID: 40560844

#### **Psoriatic Arthritis**

Recent studies highlight critical challenges and treatment strategies in psoriatic arthritis (PsA). A retrospective analysis by Cui et al. (Clin Rheumatol) revealed significant diagnostic delays, particularly in dermatology clinics (median 45.5 vs. 16.5 months in rheumatology), with axial PsA patients facing the longest delays (57 months). Strikingly, 30% of dermatology-cohort patients waited >6 years for diagnosis, underscoring the need for improved interdisciplinary awareness. Meanwhile, van Es et al. (RMD Open) compared TNFi discontinuation strategies in PsA, finding no overall difference in drug retention between cycling (TNFi→TNFi) and swapping (TNFi→IL-17i). However, men fared worse with swapping, suggesting personalized approaches post-TNFi failure. While axSpA patients benefited from cycling, PsA outcomes were strategy-neutral, emphasizing disease-specific management.

#### References

 Diagnostic delay in patients with psoriatic arthritis from dermatology and rheumatology clinics: a medical record review study. by Cui R, Chen M, Tao YL, Li X, Ding YF, Deng H, Dai SM. Clinical rheumatology. PMID: 40571883  Cycle versus swap strategy after TNFi discontinuation in psoriatic arthritis and axial spondyloarthritis: a quasi-experimental study. by van Es I,
Vriezekolk JE, den Broeder N, de Beijer L, den Broeder AA, van Herwaarden N, Mahler E, Leijten EFA. RMD open. PMID: 40562682

### **Rheumatoid Arthritis**

Recent studies highlight novel approaches to predicting treatment response and managing complications in rheumatoid arthritis (RA). A phase 3 trial (PreCePra) demonstrated that functional MRI (fMRI)-measured CNS pain activation predicts TNF inhibitor efficacy: patients with high baseline CNS activation had significantly better response to certolizumab pegol (57% achieved low disease activity) versus placebo (26%; p=0.0017), suggesting fMRI could stratify candidates for biologic therapy (Hess et al., Lancet Rheumatol). Meanwhile, lung ultrasound (LUS) outperformed clinical scores for interstitial lung disease (ILD) screening in RA, with ≥5 B-lines showing 87% sensitivity and 74% specificity versus HRCT (AUC 0.86). A composite clinical score (including age, RF/anti-CCP status, and crackles) improved outcomes when combined with LUS (Edith et al., Clin Rheumatol). On the therapeutic front, a Chinese registry study (CERTAIN) found integrative medicine (IM) combining conventional and Chinese therapies accelerated glucocorticoid (GC) discontinuation (40.8% vs. 16.1% with Western medicine alone; HR=2.175), particularly in younger patients on lower GC doses (Yao et al., Chin J Integr Med). Together, these advances underscore precision tools for treatment selection and multidisciplinary strategies to reduce GC dependence.

#### References

- Disease-associated brain activation predicts clinical response to TNF inhibition in rheumatoid arthritis (PreCePra): a randomised, multicentre, double-blind, placebo-controlled phase 3 study. by Hess A, Tascilar K, Schenker HM, Konerth L, Schonau V, Sergeeva M, Kreitz S, Prade J, Strobelt S, Selvakumar M, Kleyer A, Englbrecht M, Hueber AJ, Zaiss MM, Feist E, Burmester GR, Voll RE, Finzel S, Baerwald C, Rosch J, Behrens F, Koehm M, da Silva JAP, Damjanov N, Dorfler A, Schett G, Rech J. The Lancet. Rheumatology. PMID: 40570879
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- Glucocorticoid Discontinuation in Patients with Rheumatoid Arthritis under Background of Chinese Medicine: Challenges and Potentials Coexist. by Yao CH, Zhang C, Song MG, Xia CM, Chang T, Ma XL, Liu WX, Liu ZX, Liu JM, Tang XP, Liu Y, Liu J, Peng JY, He DY, Huang QC, Gao ML, Yu JP, Liu W, Zhang JY, Zhu YL, Hou XJ, Wang HD, Fang YF, Wang Y, Su Y, Tian XP, Lyu AP, Gong X, Jiang Q. Chinese journal of integrative medicine. PMID: 40553362

# **Systemic Lupus Erythematosus**

Recent research on systemic lupus erythematosus (SLE) highlights innovative

therapeutic approaches and sex-specific disease patterns. A Bayesian analysis leveraging adult data supported the FDA's approval of intravenous belimumab for childhood-onset SLE (cSLE), demonstrating efficacy in pediatric patients when adult trial results were incorporated with a 55% weight, alongside consistent pharmacokinetics and safety (Pottackal et al., *Lupus*). Meanwhile, a scoping review (Albrecht et al., *Rheumatol Int*) underscores stark sex differences: men exhibit later onset, higher rates of nephritis, cardiovascular damage, and severe infections, while women more frequently present with Ro/SSA autoantibodies, photosensitivity, and osteoporosis, with treatment disparities (e.g., more cyclophosphamide in men). Notably, CAR-T cell therapy emerges as a transformative option for refractory SLE, showing durable remission in early trials, though challenges like toxicity and antigen escape persist (Nie et al., *Curr Opin Immunol*). Together, these advances underscore progress in precision therapeutics and the need for sex-tailored management in SLE.

#### References

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- Sex- and gender-related differences in systemic lupus erythematosus: a scoping review. by Albrecht K, Troll W, Callhoff J, Strangfeld A, Ohrndorf S, Mucke J. Rheumatology international. PMID: 40576834
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