Biologics (Rheumatology) Research Review™

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Issue 91 - 2025

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Abbreviations used in this issue:

BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; **bDMARD** = biologic disease-modifying antirheumatic drug; **CI** = confidence interval; **CRP** = C-reactive protein; **DAS28** = 28-joint Disease Activity Score; **eGFR** = estimated glomerular filtration rate; **ESR** = erythrocyte sedimentation rate; **IBD** = inflammatory bowel disease; **IL** = interleukin; **JAK** = Janus kinase; **LSM** = least squares mean; **MACE** = major adverse cardiovascular event; **MRI** = magnetic resonance imaging; **NSAID** = nonsteroidal anti-inflammatory drug; **PRO** = patient-reported outcome; **PsA** = psoriatic arthritis; **Q2W** = every 2 weeks; **RA** = rheumatoid arthritis; **RR** = relative risk; **SpA** = spondyloarthritis; **TNF** = tumour necrosis factor; **VAS** = visual analogue scale.

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Welcome to Issue 91 of Biologics Research Review.

In the multinational, randomised, placebo-controlled COAST-V study, patients with radiographic axial spondyloarthritis with structural lesions treated with ixekizumab demonstrated a decrease in erosions and increase in backfill at week 16, and the trend continued to week 52, suggesting a disease-modifying effect. According to the findings of a retrospective study, females and patients with the non-radiographic axial spondyloarthritis have a higher risk of discontinuing first-line biologic disease-modifying antirheumatic drug therapy. We conclude this issue with a pooled analysis investigating the long-term safety of bimekizumab in adult patients with axial spondyloarthritis or psoriatic arthritis.

We hope you find our selection for Biologics Research Review stimulating reading and we welcome your feedback. Furthermore, if you have discovered or been involved with what you think is significant global research, please let us know and we will consider it for inclusion next time.

Kind Regards,

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The effect of ixekizumab treatment on MRI sacroiliac joint structural lesions in patients with radiographic axial spondyloarthritis: Post-hoc analysis of a 52-week, randomised, placebo-controlled trial with an active reference arm

Authors: Maksymowych WP et al.

Summary: This *post-hoc* analysis of data from the 52-week, multinational, randomised, placebo-controlled COAST-V study examined the effect of ixekizumab 80 mg Q2W or Q4W, adalimumab 40 mg Q2W or placebo on MRI structural lesions in sacroiliac joints in 325 patients (mean age 41.5 years; 81% male) naive to biological DMARDs with radiographic axial spondyloarthritis (SpA). After 16 weeks, erosion decreased in ixekizumab Q2W recipients versus placebo recipients (LSM -0.91 vs 0.10; $p < 0.0001$) and ixekizumab Q4W recipients (LSM -0.57; $p = 0.0086$); adalimumab had a similar effect. Backfill increased from baseline to 16 weeks in patients receiving ixekizumab Q2W versus placebo (0.52 vs 0.04; $p = 0.0042$). Decreases in erosion differed between placebo and ixekizumab Q2W or Q4W recipients, with differences observed across sex, HLA-B27 status, and baseline bone marrow oedema score. Further changes occurred after 52 weeks in erosion and backfill, with both ixekizumab doses but these changes were largest with ixekizumab Q2W (mean erosion -1.50; mean backfill 0.76). In patients who switched from adalimumab to ixekizumab at 16 weeks, a decrease in erosion was also seen.

Comment: Incorporating MRI measures of damage (erosions indicate ongoing damage, backfill is bone "repair" or "scar formation") as well as inflammatory features (osteitis) makes sense. In this *post-hoc* analysis, 325 patients from the COAST-V ixekizumab study with available MRI scans were followed over 52 weeks and the scans scored using the Spondyloarthritis Research Consortium of Canada (SPARCC) method. Ixekizumab-treated patients demonstrated a decrease in erosions and increase in backfill at week 16, and the trend continued to week 52, suggesting a disease-modifying effect.

Reference: Lancet Rheumatol. 2025;7(5):E314-E322
Abstract

Impact of clinical subtype and sex on first-line biologic therapy discontinuation in axial spondyloarthritis

Authors: Remalante-Rayco P et al.

Summary: This retrospective cohort study sought to determine the effect of axial SpA subtype and sex on bDMARD discontinuation in 469 patients (64% discontinued first bDMARD). Discontinuation was associated with non-radiographic axial SpA (Nr-axial SpA; RR 1.80; 95% CI 1.26-2.59) and female sex (RR 1.49; 95% CI 1.081-2.045). Female patients with Nr-axial SpA had twice the discontinuation risk of male patients (HR 2.30; 95% CI 1.68-3.15; p < 0.001). Overall, bDMARD survival over 20 years was lower in females and Nr-axial SpA patients.

Comment: Increasingly we are recognising the different patterns of disease presentation and treatment response between genders. And the follow-on question is whether treatment cessation and switching are higher in females compared with males. In this retrospective study of patients with axial SpA, the authors sought to examine whether gender was an independent predictor of first bDMARD cessation. A worrying result, females with Nr-axial SpA had twice the discontinuation risk of males with Nr-axial SpA. Nr-axial SpA in females remains a treatment challenge.

Reference: Ann Rheum Dis. 2025;84(4):584-593
Abstract

Effect of bimekizumab on patient-reported outcomes and work productivity in patients with psoriatic arthritis: 1-year results from 2 phase III studies

Authors: Gladman DD et al.

Summary: This analysis provides 1-year follow-up data from the BE OPTIMAL (bDMARD-naive patients; n = 770) and BE COMPLETE (patients with inadequate response/intolerance to TNF inhibitors [TNF-IR]; n = 388) double-blind, placebo-controlled phase III trials and the open-label extension BE VITAL of subcutaneous bimekizumab in patients with active psoriatic arthritis (PsA). At 1 year, bimekizumab recipients had sustained mean improvements in patient-reported outcomes (PROs), including pain (bDMARD-naive -30.5 mm; TNF-IR -31.8 mm), fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue scale bDMARD-naive 5.3; TNF-IR 6.0), physical function (Health Assessment Questionnaire-Disability Index bDMARD-naive -0.34; TNF-IR -0.39), and health-related quality of life (HRQoL; 36-item Short Form Health Survey - physical bDMARD-naive 8.1; TNF-IR 8.4). Similar improvements were seen in placebo recipients who switched to bimekizumab at week 16. At week 52, overall work impairment improvements were sustained with bimekizumab, with similar trends in activity impairment, absenteeism and presenteeism.

Comment: Important takeaways from this bimekizumab PsA analysis, regardless of whether patients were TNF-experienced or biologic naive, sustained improvements in patient-reported symptoms, HRQoL, and work productivity were observed in bimekizumab-treated patients. Improvements in pain, fatigue, physical function and activity impairment were noted with reduced work absenteeism a useful measure within the suite of PROs used in this study

Reference: J Rheumatol. 2025;52(5):466-478
Abstract

Efficacy and safety of subcutaneous abatacept plus standard treatment for active idiopathic inflammatory myopathy: Phase 3 randomized controlled trial

Authors: Aggarwal R et al.

Summary: This 52-week, randomised, double-blind (24 weeks followed by open label), placebo-controlled phase III trial examined the use of subcutaneous abatacept and standard of care (SOC) in 148 patients with idiopathic inflammatory myopathy. After 24 weeks, improvement in the International Myositis Assessment and Clinical Studies definition of improvement (IMACS DOI) score was 56.0% with abatacept and 42.5% with placebo ($p = 0.083$), while at 52 weeks, the improvement was 69.8% (abatacept) and 69.0% (placebo/abatacept switch). The rate of IMACS DOI at 24 weeks was greater in those without dermatomyositis (57.1% vs 32.3%; $p = 0.040$) than those with dermatomyositis (55.0% vs 50.0%; $p = 0.679$).

Comment: A negative result in this abatacept refractory myositis trial. The proportion of patients who met improvement criteria was similar between abatacept and placebo groups. The inclusion criteria of treatment refractory inflammatory myopathy patients may well have contributed to the negative result, and the follow-up was short, 24 weeks, perhaps too short to observe relevant treatment effects in a cohort with refractory disease for the primary outcome. There was a placebo switch to active treatment at week 24 and an open-label phase, but this publication only reports the 24-week results. The authors note perhaps a greater benefit in non-dermatomyositis subtypes.

Reference: Arthritis Rheumatol. 2025;77(6):765-776
Abstract

Gender differences in clinical and prescribing characteristics of biologic and targeted synthetic drugs in naïve patients with rheumatoid arthritis: Data from BIOBADASER III registry

Authors: Vela-Casasempere P et al.

Summary: This Spanish, retrospective (2000-23) analysis of data from the BIOBADASER III registry (n = 3,384; 78.1% women) examined gender differences in the time course from rheumatoid arthritis (RA) diagnosis to initiation of first bDMARD or targeted synthetic DMARD (tsDMARD) and factors associated with earlier or later prescribing. Males had higher cardiovascular risk, and females more osteoporosis and Sjögren Syndrome, lower mean age (54.8 vs 57 years; $p < 0.001$), and longer disease duration (7.3 vs 6.7 years; $p = 0.031$). Females also had higher DAS28-ESR, but not DAS28-CRP scores, and higher subjective components of DAS28 and ESR, but lower CRP. After 2017 there was a difference between the sexes in disease duration (HR 0.9; 95% CI 0.81-0.99; $p = 0.026$). Later prescribing was associated with female sex, age, and treatment with conventional synthetic DMARDs (other than methotrexate), and earlier prescribing was associated with tobacco use, obesity and methotrexate or glucocorticoid use.

Comment: Gender differences in disease presentation, response to therapy and in prescription of medication have been increasingly recognised. The concerning results from this RA study of 3384 patients (78% female) showed female patients with longer disease duration at medication commencement and higher disease activity as measured by DAS28-ESR. Of note, females had higher subjective components of DAS28, and higher ESR, but lower CRP when compared with males. Female gender, and age were associated with later prescribing. One size does not fit all, as the authors note, discrepancies between subjective and objective measures of DAS28 raise the need for a research agenda to establish different cut-off points for men and women. We have seen similar results to this in the gender differences in BASDAI results. Time to think again.

Reference: Arthritis Res Ther. 2025;27(1):103
Abstract

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Comparative effects of biological and targeted synthetic DMARDs on incident chronic kidney disease in patients with rheumatoid arthritis

Authors: Nishimura N et al.

Summary: This Japanese, multicentre, cohort study assessed the comparative effects of biologic/targeted synthetic (b/ts)DMARDs (TNF inhibitor, cytotoxic T-lymphocyte-associated antigen-4-Ig [CTLA4-Ig], IL-6 receptor inhibitor, or JAK inhibitor) on the incidence of chronic kidney disease (CKD) in 2187 patients (3068 treatment courses; up to 11 years of follow-up) with RA who had a baseline eGFR of ≥60 mL/min/1.73 m^2. CKD occurred in 275 cases. Compared with CTLA4-Ig, TNF inhibitor recipients had a lower CKD incidence (HR 0.67; 95% CI 0.46-0.97; p = 0.04), whereas JAK inhibitor recipients had a higher incidence of CKD (HR 2.16; 95% CI 1.23-3.79; p = 0.01). The eGFR trajectory was greater in JAK inhibitor (-2.29 mL/min/1.73 m^2/year) than CTLA4-Ig recipients (-1.28 mL/min/1.73 m^2/year; p < 0.001).

Comment: Caution should be exercised in interpreting the results of this Japanese RA cohort examining the effect of RA treatment on progression of CKD. The authors report TNF inhibitor and abatacept treatment associated with reduced CKD incidence compared with JAK inhibitor therapy. Multiple propensity inverse probability weighting was used to adjust for confounders, but larger numbers are needed to be certain of the effect, and more description of background medications including over-the-counter NSAID consumption.

Reference: Rheumatology (Oxford) 2025;64(5):2395-2402
Abstract

Multi-domain effectiveness of guselkumab evaluated via composite indices through 1 year in patients with PsA and inadequate response to TNFi: Post hoc analysis of COSMOS

Authors: Gossec L et al.

Summary: This *post hoc* analysis of the randomised, placebo-controlled, phase IIIb COSMOS trial of guselkumab in 285 patients with active PsA and inadequate response to 1/2 TNF inhibitors evaluated composite indices including DAS28, the Disease Activity Index for Psoriatic Arthritis (DAPSA), Psoriatic Arthritis Response Criteria (PsARC), the Psoriatic Arthritis Disease Activity Score (PASDAS), the GRAPPA Composite score (GRACE), the modified Composite Psoriatic Disease Activity Index (mCPDAI), minimal disease activity (MDA), and very low disease activity (VLDA). At 24 weeks, more guselkumab than placebo recipients achieved composite index endpoints suggesting low disease activity (14.8-52.4% vs 3.1-28.1%) or remission (3.7-5.3% vs 0.012.1%). Among guselkumab recipients, low disease activity rates increased to 48 weeks (DAS28 47.8%; DAPSA 44.4%; mCPDAI, 40.2%; PASDAS 34.4%; GRACE 33.3%), while 27.0% achieved MDA and 64.0% had a PsARC response. In patients crossing over from placebo to guselkumab, 48-week response rates were similar to those of initial guselkumab recipients.

Comment: COSMOS was designed to examine PsA response with guselkumab in patients with inadequate response to 1 or 2 TNF inhibitors. This analysis used composite indices (DAPSA, PsARC, PASDAS, GRACE, mCPDAI, MDA) to assess outcomes over 24 and out to 48 weeks. Guselkumab was associated with improvement in all composite indices, 27% of patients achieved the MDA target in the treatment arm, an impressive result in this cohort of patients.

Reference: Rheumatology (Oxford) 2025;64(5):2565-2574
Abstract

Prevalence and incidence of uveitis in patients with spondyloarthritis: The impact of the biologics era. Data from the international ASAS-COMOSPA study

Authors: Maldonado-Ficco H et al.

Summary: The multinational retrospective ASAS-COMOSPA study assessed the prevalence of uveitis in 3984 patients with SpA, examined its association with geographical areas, and its incidence before and after (SpA onset after 2000) the biologic's era. The likelihood of uveitis increased over time, with a prevalence of 10.5% (95% CI 9.5-11.4) at time of diagnosis to 46.6% (95% CI 41.6-51.5) after 30 years. A higher risk of uveitis was associated with HLA-B27 positivity, a family history of uveitis, peripheral enthesitis, and IBD. Prevalence of uveitis was lower if SpA onset occurred after versus before the year 2000 (8.2% vs 25.5%; p < 0.01), as was incidence (2.8 vs 6.1 per 100 person-years).

Comment: How common is uveitis in SpA patients? This large retrospective study with 3984 patients across 22 countries sought to answer this question. The likelihood of presenting a first uveitis episode increased with disease duration, from a prevalence of 10.5% at the time of the SpA diagnosis to 46.6% after 30 years since the SpA diagnosis. HLA-B27 positivity, family history of uveitis, peripheral enthesitis, and IBD were associated with higher risk of uveitis.

Reference: Rheumatology (Oxford) 2025;64(5):2618-2624
Abstract

Independent commentary by Professor Paul Bird MD, PhD, GD MRI, FRACP

Paul Bird has extensive experience as a researcher and clinician. He is a rheumatologist in private practice and conjoint Professor at UNSW. Professor Bird completed his physician and rheumatology training in Sydney. Pursuing research alongside clinical medicine and patient care, he completed a PhD in 2005 examining MRI in rheumatoid arthritis, and a Graduate Diploma in MRI. He continues to undertake arthritis research with fellow Australian rheumatologists and with international colleagues. As a clinical researcher, he is the chief medical officer at Emeritus Clinical Research in Sydney and Melbourne, a trial centre undertaking phase 2,3 and 4 clinical trials.

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Effect of TNF-α blockers on reducing the risk of dementia in rheumatoid arthritis: A nationwide cohort study

Authors: Chen LF et al.

Summary: This population-based cohort study used data from the Taiwanese National Health Insurance Research Database to assess whether use of TNF-α inhibitors was associated with a reduced risk of dementia in 3987 RA patients using, and 20,689 RA patients not using, TNF-α inhibitors. Overall, no difference in dementia risk was initially identified; however, after adjusting for age, sex and comorbidities and when stratified by TNF-α inhibitor exposure, RA patients with longer-term use (>180 cumulative defined daily dose [cDDD]) had a lower risk of dementia (adjusted HR [aHR] 0.578; 95% CI 0.342-0.977). Higher cumulative doses (>1036 cDDD) were associated with a further reduction in dementia risk (aHR 0.387; 95% CI 0.188-0.793).

Comment: The premise of this study is based on previous reports (Sangha PS et al., Cureus 2020). A review in 2020 revealed an association between RA and risk of dementia, with some early evidence that biological therapies such as TNF inhibitors were associated with a lower risk of dementia. This Taiwanese study used the national medical database and included 3987 RA patients on TNF inhibitors and 20,689 RA patients not on TNF inhibitors as a comparison group. No difference in dementia risk was noted on initial analysis. Further analysis suggested higher cumulative doses of TNF inhibitor may be associated with a lower risk of dementia. An interesting concept, but too many confounders to be certain, more data are needed.

Reference: Clin Exp Rheumatol. 2025;43(5):931-938
Abstract

Long-term safety of bimekizumab in adult patients with axial spondyloarthritis or psoriatic arthritis: Pooled results from integrated phase IIb/III clinical studies

Authors: Mease PJ et al.

Summary: This pooled analysis used safety data from 6 phase IIb/III studies in patients with axial SpA (n = 848) and PsA (n = 1407) to assess the long-term safety profile of bimekizumab. Treatment-emergent adverse events (TEAEs) occurred at an exposure-adjusted incidence rate per 100 patient-years (EAIR/100 PY) of 136.9 in axial SpA and 139.6 in PsA. Overall, study discontinuations due to TEAEs in axial SpA and PsA patients was low (2.7/100 PY and 3.1/100 PY). The most frequent TEAEs were COVID-19 infection (7.8/100 PY and 8.8/100 PY), nasopharyngitis (8.2/100 PY and 7.7/100 PY) and upper respiratory tract infection (5.0/100 PY and 5.6/100 PY). The EAIR/100 PY of oral candidiasis was 3.7 in axial SpA and 4.2 in PsA, but the EAIR of discontinuation due to oral candidiasis was low (0.3/100 PY). EAIRs for IBD, uveitis, MACE and suicidal ideation/behaviour were low.

Comment: Encouraging safety data pooled from 6 studies of bimekizumab in axial SpA and PsA. Rates of IBD and uveitis were reassuringly very low and candidiasis occurred at rates of less than 5% across all groups, with most episodes mild to moderate. The EAIR of bimekizumab discontinuation due to oral candidiasis was also low.

Reference: RMD Open 2025;11(2):e005026
Abstract