# IN BRIEF

## OSTEOARTHRITIS

### Sprifermin benefits maintained at 5 years

Structural benefits of treatment with intra-articular sprifermin for knee osteoarthritis were maintained 3.5–4 years post-treatment in the FORWARD trial, in which 378 (69%) patients completed 5-year follow-up. In those who had received sprifermin 100 µg every 6 months, the change from baseline in total femorotibial joint cartilage thickness seen at year 2 was sustained at year 5 with no new safety signals. Clinically relevant improvements in pain in the subgroup at risk of progression ($n = 161$) seen at year 3 were also maintained.

**ORIGINAL ARTICLE** Eckstein, F. et al. Long-term structural and symptomatic effects of intra-articular sprifermin in patients with knee osteoarthritis: 5-year results from the FORWARD study. *Ann. Rheum. Dis.* https://doi.org/10.1136/annrheumdis-2020-219181 (2021)

## RHEUMATOID ARTHRITIS

### Tapering csDMARDs leads to more RA flares

In a randomized, open-label study assessing tapering of conventional synthetic DMARDs (csDMARDs) in patients with rheumatoid arthritis (RA) in sustained clinical remission, 19 of 77 patients (25%) whose csDMARD treatment was reduced to half-dose had at least one disease flare, compared with 5 of 78 patients (6%) who continued stable-dose csDMARD therapy without tapering (risk difference 18%; 95% CI 7–29%). Significantly fewer flares occurred in the stable-dose group.

**ORIGINAL ARTICLE** Lillegraven, S. et al. Effect of half-dose vs stable-dose conventional synthetic disease-modifying antirheumatic drugs on disease flares in patients with rheumatoid arthritis in remission: the ARCTIC REWIND randomized clinical trial. *JAMA* **325**, 1755–1764 (2021)

## THERAPY

### NSAIDs not linked to worse COVID-19 outcomes

In contrast to anecdotal reports that pre-existing use of NSAIDs is linked to poor outcomes in patients with COVID-19, the findings of a prospective, multicentre cohort study found no increase in mortality or COVID-19 severity among NSAID users. The study included 72,179 patients across 255 health-care facilities in England, 4,211 (5.8%) of whom were taking systemic NSAIDs before they were admitted to hospital.

**ORIGINAL ARTICLE** Drake, T. M. et al. Non-steroidal anti-inflammatory drug use and outcomes of COVID-19 in the ISARIC Clinical Characterisation Protocol UK cohort: a matched, prospective cohort study. *Lancet* https://doi.org/10.1016/S2665-9913(21)00104-1 (2021)

## PSORIATIC ARTHRITIS

### Tildrakizumab shows promise in phase IIb study

The anti-IL-23p19 monoclonal antibody tildrakizumab improved skin and joint manifestations of psoriatic arthritis (PsA), but not dactylitis or enthesitis, in a 52-week phase IIb study. 391 patients with active PsA were randomly allocated to receive tildrakizumab 200 mg every 4 weeks, tildrakizumab 200 mg, 100 mg or 20 mg every 12 weeks or placebo; at week 24, those in the 20 mg or placebo groups were switched to tildrakizumab 200 mg every 12 weeks. Compared with the placebo group, more patients in the tildrakizumab groups achieved an ACR20 or ACR50 response, minimal disease activity and PASI 75, PASI 90 and PASI 100 responses at week 24; responses were maintained through week 52, and tildrakizumab was generally well tolerated.

**ORIGINAL ARTICLE** Mease, P. J. et al. Efficacy and safety of tildrakizumab in patients with active psoriatic arthritis: results of a randomised, double-blind, placebo-controlled, multiple-dose, 52-week phase IIb study. *Ann. Rheum. Dis.* https://doi.org/10.1136/annrheumdis-2020-219014 (2021)

Credit: Getty Images/molotovcoketail

## LUPUS NEPHRITIS

# Voclosporin improves outcomes in lupus nephritis

Lupus nephritis, a serious manifestation of systemic lupus erythematosus that can result in renal failure and the need for kidney transplantation, has historically been difficult to treat. The AURORA 1 study, in which the new-generation calcineurin inhibitor voclosporin was investigated in addition to standard care (mycophenolate mofetil and low-dose glucocorticoids) in lupus nephritis, has produced positive results, suggesting that this drug could be a useful addition to current lupus nephritis treatments.

"Early intervention and kidney response are linked to better long-term outcomes for lupus nephritis and prevent irreversible kidney damage," explains Robert Huizinga, corresponding author on the AURORA 1 study. "This study reports the phase III data on voclosporin and demonstrates its ability to achieve superior and faster complete renal response rates compared to standard of care alone — a significant advance in addressing this condition."

In AURORA 1, one of the largest lupus nephritis trials to date, 357 patients with active lupus nephritis were randomly assigned to receive either oral voclosporin or placebo in addition to standard care. The primary end point of complete renal response at 52 weeks was met in more of the patients treated with voclosporin (73 out of 179; 41%) than in those treated with placebo (40 out of 178; 23%). The time taken to achieve a 50% reduction in proteinuria was also shorter in those receiving voclosporin than in those receiving placebo.

Calcineurin inhibitors have been used to treat lupus nephritis for a long time, but concerns have been raised about infection risks associated with the use of these drugs. In contrast to the increased risk of serious infection reported in phase II studies of voclosporin, in the phase III AURORA 1 study, the safety profile was similar between those treated with voclosporin and those treated with placebo, allaying safety concerns for this new-generation calcineurin inhibitor.

Many new therapies for lupus nephritis are currently in development, but only voclosporin and belimumab have so far been approved by the FDA. "Our current drugs for lupus nephritis don't do a good job, so we have been excited to see the emergence of voclosporin and belimumab as add-on agents for lupus nephritis with similar efficacy profiles," comments Anne Davidson, an expert in lupus nephritis who was not involved in this study. "Issues of long-term safety, differences in responses among patients of different ethnicities, introducing voclosporin earlier or only in those with initial treatment failures, and overall long-term outcomes will need to be determined in further trials and observational studies to help determine the place for voclosporin in a treatment regime," she suggests.

Follow-up studies are underway that will hopefully address some of these unknown factors. "We are in the process of conducting an AURORA continuation study evaluating patients with up to 104 weeks of total treatment and we plan to share those results over the coming months," says Huizinga.

*Joanna Clarke*

**ORIGINAL ARTICLE** Rovin, B. H. et al. Efficacy and safety of voclosporin versus placebo for lupus nephritis (AURORA 1): a double-blind, randomised, multicentre, placebo-controlled, phase 3 trial. *Lancet* https://doi.org/10.1016/S0140-6736(21)00578-X (2021)