IN BRIEF

RISK FACTORS

HCQ use not protective against SARS-CoV-2

Patients receiving treatment with hydroxychloroquine (HCQ) for rheumatological conditions are not protected from SARS-CoV-2 infection, according to the results of a retrospective study of data from a US Veterans Health Administration database. During the study period (March–June 2020), the incidence of active infections did not differ between patients who received HCQ (31 of 10,703 (0.3%)) and those who did not (78 of 21,406 (0.4%)). The two groups also did not differ in rate of hospital admission, requirement of intensive care and mortality associated with SARS-CoV-2 infection.

ORIGINAL ARTICLE Gentry, C. A. et al. Long-term hydroxychloroquine use in patients with rheumatic conditions and development of SARS-CoV-2 infection: a retrospective cohort study. *Lancet Rheum.* https://doi.org/10.1016/S2665-9913(20)30305-2 (2020)

THERAPY

At-risk individuals willing to start interventions

The results of a Dutch survey reveal that individuals at increased risk of developing rheumatoid arthritis (seropositive individuals with arthralgia but not arthritis) or axial spondyloarthritis (axSpA; first-degree relatives of HLA-B27-positive patients with axSpA) are very willing to change their lifestyle and most are willing to initiate preventive medication. By contrast, most of the rheumatologists surveyed would not advise lifestyle changes (owing to lack of evidence) but seemed more willing than the at-risk individuals to start preventive medication, although the gap lessened when the perceived risk of disease was higher.

ORIGINAL ARTICLE van Boheemen, L. et al. Patients' and rheumatologists' perceptions on preventive intervention in rheumatoid arthritis and axial spondyloarthritis. *Arthritis Res. Ther.* **22**, 217 (2020)

EPIDEMIOLOGY

Multimorbidity worse in patients with RA

In a retrospective cohort study using data from a US commercial insurance database ($n = 277,782$), multimorbidity was more common in individuals with rheumatoid arthritis (RA) than in those without (OR 2.29; 95% CI 2.25–2.34). The burden of multimorbidity (total count of chronic conditions) was also higher in the RA group than in the non-RA group (ratio of conditions 1.68; 95% CI 1.66–1.70). Within an incident RA subcohort ($n = 61,124$), trajectory analyses revealed that chronic conditions accrued more rapidly in those with RA than in those without.

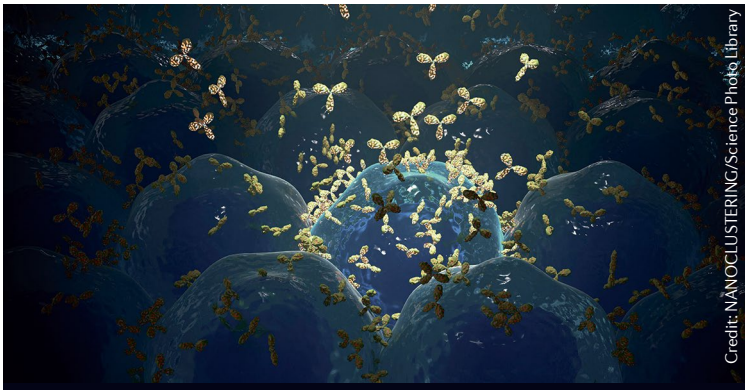
ORIGINAL ARTICLE England, B. R. et al. Burden and trajectory of multimorbidity in rheumatoid arthritis: a matched cohort study from 2006 to 2015. *Ann. Rheum. Dis.* https://doi.org/10.1136/annrheumdis-2020-218282 (2020)

RISK FACTORS

Depression linked to seronegative RA risk

An analysis of 195,358 women in the Nurses' Health Studies found 858 cases of incident rheumatoid arthritis (RA) (65% seropositive) during 3,087,556 person-years of follow-up. Compared with women without depression, women with depression (assessed ≥4 years before RA diagnosis) had an increased risk of incident seronegative RA (HR 1.63, 95% CI 1.27–2.09), but not of incident seropositive RA (HR 1.12, 95% CI 0.93–1.35). Regular use of antidepressants was strongly associated with subsequent seronegative RA (HR 1.75, 95% CI 1.32–2.32).

ORIGINAL ARTICLE Sparks, J. A. et al. Depression and subsequent risk for incident rheumatoid arthritis among women. *Arthritis Care Res.* https://doi.org/10.1002/ACR.24441 (2020)



SYSTEMIC LUPUS ERYTHEMATOSUS

IL-17 sustains plasma cells in SLE

Autoantibody production by long-lived plasma cells is one of the hallmarks of systemic lupus erythematosus (SLE), yet current immunotherapies for this condition often leave these long-lived B cells untouched. The pro-inflammatory environment in SLE is thought to aid the expansion and survival of long-lived plasma cells, but there has been uncertainty about the exact cytokines and mechanisms involved.

The results of a new study have revealed IL-17 as a candidate pro-survival factor for long-lived plasma cells in SLE. "Although there is compelling evidence that IL-17 promotes germinal centre B cell differentiation and antibody class switching in murine lupus, it has remained unclear whether IL-17 directly modulates autoreactive plasma cell function and promotes autoantibody responses during lupus development," states corresponding author Liwei Lu. "In this work, we uncovered a mechanistic link between IL-17 and long-lived plasma cells during nephritis development in SLE."

Lu and colleagues first established that circulating long-lived plasma cells from patients with active SLE expressed a high-affinity receptor for IL-17 and produced large quantities of autoantibodies. Patients with active SLE also had more T helper 17 (T_H17) cells than healthy individuals.

In an adoptive transfer model in which whole peripheral blood mononuclear cells (PBMCs) or T_H17 cell-depleted PBMCs from patients with SLE were transferred into lymphocyte-deficient mice, only the whole SLE PBMCs were able to induce autoantibody production, immune complex deposition and nephritis, suggesting an important role for T_H17 cells in these plasma-cell responses. Further investigations using mice deficient for IL-17 or IL-17 receptor revealed it was the production of IL-17 by the T_H17 cells that was necessary for the plasma cell response.

In vitro experiments on cells from mice with immunization-induced lupus to determine the underlying mechanism behind the effects of IL-17 on long-lived plasma cells uncovered a novel signalling pathway; IL-17 signalling caused the phosphorylation of p38, which in turn stabilized *Bcl2l1* mRNA (which encodes Bcl-xL) and promoted cell survival. Indeed, pre-treatment of plasma cells with an inhibitor of p38 abrogated IL-17-induced *Bcl2l1* transcript stabilization.

"In the future, we aim to further characterize the molecular network, and especially the pro-inflammatory cytokines, involved in maintaining the survival and function of long-lived plasma cells within the local inflammatory milieu of inflamed organs in SLE, which may provide new therapeutic strategies for targeting long-lived plasma cells in the treatment of SLE and other autoimmune diseases," says Lu.

Joanna Clarke

ORIGINAL ARTICLE Ma, K. et al. IL-17 sustains the plasma cell response via p38-mediated Bcl-xL RNA stability in lupus pathogenesis. *Cell. Mol. Immunol.* https://doi.org/10.1038/s41423-020-00540-4 (2020)