With regards to infections in the use of dupilumab, this study echoed previous dupilumab trials because there was no increased overall risk of infections and a reduced risk of non-herpetic skin infections (56 [18%] of 315 participants in the placebo group and 12 [11%] of 110 and 26 [8%] of 315 participants in the two dupilumab dose groups). There is an increase in incidence of non-infectious conjunctivitis in patients on dupilumab (25 [8%] of 315 participants in the placebo group, 15 [14%] of 110 and 61 [19%] of 315 in the two dupilumab dose groups), which has been seen in previous trials. The authors suggest this complication might be unique to those with atopic dermatitis as similar conjunctivitis rates have not been seen in dupilumab use for other disease states.

This trial provides great promise for our ability to control atopic dermatitis. For patients with extensive, resistant disease, dupilumab is likely to be the first of many biologics that may offer safe and effective control of the disease. And for everyone else with atopic dermatitis, our growing understanding of the importance of adherence to the treatment and interventions to improve that adherence will offer a formidable way to improve outcomes with our existing treatments.

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JCS reports participation as the principal investigator of a single-patient open-label extension trial of dupilumab in adult patients at the clinical studies unit at her institution. SRF reports grants and personal fees as a consultant for Sanofi and Regeneron, outside of the area of work discussed here, and has a patent to improve patients' adherence to any self-administered treatment pending that has been commercialised by Wake Forest University School of Medicine.

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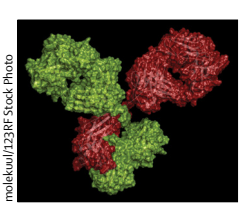
The switch to infliximab biosimilars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In *The Lancet*, Kristin Jørgensen and colleagues[1] report results from the NOR-SWITCH study, the first randomised non-inferiority trial of infliximab, showing that switching from originator to biosimilar does not lead to disease worsening, compromised safety, or increased immunogenicity in a group of patients in all the authorised therapeutic indications. In this 52-week phase 4 trial, 482 adult patients on stable treatment with infliximab originator were randomly assigned to either continued originator or switch to infliximab biosimilar treatment (CT-P13), using an unchanged dosing regimen. Patients with different disorders (32% had Crohn's disease, 19% had ulcerative colitis, 19% had spondyloarthritis, 16% had rheumatoid arthritis, 6% had psoriatic arthritis, and 7% had chronic plaque psoriasis) were included and pooled for analysis. The primary endpoint of disease worsening during the 52-week follow-up occurred similarly in patients in both groups (26% in the infliximab originator group and 30% in the CT-P13 group). The 95% CI of the adjusted treatment difference of –4·4% (–12·7 to 3·9) was within the predefined non-inferiority margin of 15%. Similarity between the treatment groups was also seen for changes in disease activity, safety, immunogenicity, and pharmacokinetic variables.

Although the study's design does not allow for conclusions on individual diseases, its results support the idea that infliximab originator can be replaced during treatment with a biosimilar. This switching has been one of the most controversial issues related to introduction of biosimilars and studies such as Jørgensen and colleagues', together with educational activities at different levels (eg, at the level of the European Commission)[2] are key to improve the acceptance of biosimilars by prescribing physicians, reimbursement decision makers, and patients.

Biosimilars are biological medicinal products that contain a highly similar version of the active substance of an original biological medicinal product (sometimes called a reference medicinal product) already authorised in the European Economic Area. For marketing authorisation, similarity to the reference medicinal

product in terms of quality characteristics, biological activity, safety, and efficacy based on a comprehensive comparability exercise needs to be established.[3] In the European Union (EU), the first biosimilar was authorised in 2006[4] and 28 new similar biological medicinal products for treatment of various conditions have since been approved.[5] In 2013, Remsima (Celltrion Healthcare, Budapest, Hungary), a biosimilar medicinal product to Remicade (Jansen Biologics, Leiden, Netherlands) containing infliximab (together with its duplicate [identical medicinal product marketed under different name] Inflectra; Hospira UK, Maidenhead, UK), was the first biosimilar monoclonal antibody to be authorised.[5] This authorisation followed the positive opinion of the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP).[6] The therapeutic indications granted and the dosing regimen are the same as those of Remicade, the first product containing infliximab authorised in the EU in August, 1999.

To support the authorisation of Remsima, the results of an extensive comparability exercise between reference medicinal product and biosimilar were presented,[6] and the major physicochemical characteristics and biological activities of Remsima were shown to be comparable to those of Remicade. The clinical data showing similarity between Remsima and Remicade consisted of two clinical trials: a comparative pharmacokinetic study in patients with ankylosing spondylarthritis and a comparative efficacy and safety study in patients with active rheumatoid arthritis.[6]

The totality of the data (including quality and comparability data) allowed for extrapolation to all indications of Remicade. The CHMP concluded that the benefit–risk balance of Remsima as a biosimilar product to Remicade was positive. The risk management plan agreed as part of the authorisation included close monitoring of adverse events and long-term efficacy data as part of the postmarketing setting through several patient registries and postauthorisation studies.[6] Since the approval of Remsima, four other antitumour necrosis factor biosimilar medicinal products have been authorised in the EU: Benepali (etanercept; Samsung Bioepis UK, Chertsey, UK),[7] Flixabi (infliximab; Samsung Bioepis UK, Chertsey, UK),[8] Amgevita (adalimumab; Amgen Europe, Breda, Netherlands),[9] and Solymbic (adalimumab; Amgen Europe, Breda, Netherlands)[10] and others are under evaluation.

Data showing interchangeability are not requested as part of the marketing authorisation in the EU, where the scope of the CHMP assessment is restricted to the evaluation of similarity and benefit–risk conclusions.[11] However, it is recognised that both the confirmation of efficacy and safety in other (extrapolated) indications and the potential effect of switching are important for patients, health-care professionals, and health-technology assessment bodies and payers.

As the number of new biosimilars being developed grows, new issues need to be addressed (eg, the clinical importance of differences in immunogenicity seen in laboratory tests and extrapolation to paediatric indications in the absence of paediatric-specific pharmaceutical forms), which are reported in the European Public Assessment Report for each biosimilar medicinal product.[7,8] The results of postauthorisation studies[12,13] to date have confirmed the conclusions on similarity and extrapolation at time of approval of infliximab biosimilars and did not provide any new information on differences in efficacy or safety. The revised European Crohn's Colitis Organisation position statement on the use of biosimilars for inflammatory bowel disease[14] and consequent inclusion of infliximab biosimilars as recommended treatment for inflammatory bowel disease[15] show how growing evidence and experience is leading to increased use of these safe, effective, and high-quality treatments giving patients access to medicines that have been approved with the same high standards as all other biological medicines. Results from studies such as the NOR-SWITCH trial support the concept that a switch from infliximab originator to biosimilar for non-medical reasons does not compromise the effectiveness or safety of treatment.

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New pathways of treatment for psoriatic arthritis

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Psoriatic arthritis occurs in up to 30% of patients with psoriasis.[1] The prevalence of psoriasis varies geographically, ranging between 1% and 3% of the population, depending on genetic variation.[2] Since the discovery of the cytokine interleukin 17A in 1993, and the subsequent discovery of one of the key cells that produce interleukin 17A and related cytokines, the T-helper-17 cell, in 2005,[3] this pathway has been a focus of research in the pathogenesis of psoriasis and closely related conditions, psoriatic arthritis and spondyloarthritis.[4] In *The Lancet*, Peter Nash and colleagues on behalf of the SPIRIT-P2 Study Group[5] provide further evidence for inhibition of interleukin 17A with ixekizumab in patients with psoriatic arthritis.

In SPIRIT-P2,[5] patients who had either inadequate response or adverse effects to previous biological therapy received placebo (n=118), ixekizumab (80 mg after a 160 mg starting dose) every 4 weeks (n=122), or ixekizumab (80 mg) every 2 weeks (n=123). More patients attained the primary endpoint of at least 20% improvement in the American College of Rheumatology response criteria (ACR-20) at week 24 with ixekizumab every 4 weeks (65 [53%] patients; effect size *vs* placebo 33·8% [95% CI 22·4–45·2]; p<0·0001) and ixekizumab every 2 weeks (59 [48%] patients; effect size *vs* placebo 28·5% [95% CI 17·1–39·8]; p<0·0001) than did patients with placebo (23 [20%] patients). There was also improvement with ixekizumab in clinical domains beyond inflammatory arthritis, including dactylitis in one dose group, psoriasis, nail disease, attainment of minimal disease activity, and measures of function and quality of life in both ixekizumab groups. Three (3%) patients with ixekizumab every 4 weeks, eight (7%) with ixekizumab every 2 weeks, and four (3%) with placebo had severe adverse events. Infections occurred in 47 (39%) patients with ixekizumab every 4 weeks, 47 (38%) with ixekizumab every 2 weeks, and 35 (30%) with placebo. There were three (2%) serious infections, all in patients in the ixekizumab every 2 weeks group.

This study lends support to the findings of SPIRIT-P1 trial,[6] in which patients with active psoriatic arthritis naive to biological therapy were treated with the same ixekizumab regimen versus placebo and the tumour necrosis factor (TNF) inhibitor, adalimumab. At 24 weeks, significant improvement was reported in ACR responses and measures of enthesitis, dactylitis, skin and nail disease, function, quality of life, and inhibition of progressive structural damage in all treatment groups compared with