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# Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naive patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1

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**Citation**

Mease, P. J., Heijde, D. van der, Ritchlin, C. T., Okada, M., Cuchacovich, R. S., Shuler, C. L., … Gladman, D. D. (2017). Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naive patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1. *Annals Of The Rheumatic Diseases*, *76*(1), 79-87. doi:10.1136/annrheumdis-2016-209709

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EXTENDED REPORT

# Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naive patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1

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**Handling editor** Tore K Kvien

▶ Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/annrheumdis-2016-209709).

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Received 13 April 2016
Revised 21 July 2016
Accepted 25 July 2016
Published Online First 23 August 2016

**To cite:** Mease PJ, van der Heijde D, Ritchlin CT, *et al*. *Ann Rheum Dis* 2017;**76**:79–87.

## ABSTRACT

**Objective** To assess the safety and efficacy of ixekizumab, a monoclonal antibody that inhibits interleukin-17A, in a double-blind phase III trial enrolling patients with active psoriatic arthritis (PsA).

**Methods** Patients naive to biologic therapy with active PsA were randomised to subcutaneous injections of placebo (N=106), adalimumab 40 mg once every 2 weeks (active reference; N=101), ixekizumab 80 mg once every 2 weeks (IXEQ2W) (N=103), or ixekizumab 80 mg once every 4 weeks (IXEQ4W) (N=107). Both ixekizumab regimens included a 160-mg starting dose. The primary objective was to assess the superiority of IXEQ2W or IXEQ4W versus placebo as measured by the proportion of patients achieving an American College of Rheumatology 20 (ACR20) response at week 24.

**Results** Significantly more patients treated with ixekizumab achieved an ACR20 response with IXEQ2W (62.1%) or IXEQ4W (57.9%) than placebo (30.2%) ($p \leq 0.001$; non-responder imputation method). Disease activity and functional disability were significantly improved with both ixekizumab doses versus placebo at weeks 12 and 24, and there was significantly less progression of structural damage at week 24 ($p \leq 0.01$). Clearance of plaque psoriasis was greater with ixekizumab than placebo ($p \leq 0.001$). Efficacy results with adalimumab, the active reference arm, showed significant improvements versus placebo. Treatment-emergent adverse events were more frequent with ixekizumab (65.7–66.4%) and adalimumab (64.4%) than placebo (47.2%) ($p<0.05$).

**Conclusions** In biologic-naive patients with active PsA, ixekizumab treatment resulted in improvements in disease activity and physical function, as well as in the inhibition of structural damage progression. Overall, adverse events were more frequent in all active groups compared with placebo.

**Trial registration number** NCT01695239; EudraCT2011-002326-49; Results.

## INTRODUCTION

Psoriatic arthritis (PsA) is a chronic, systemic, immune-mediated, inflammatory arthritis commonly associated with plaque psoriasis, joint damage, dactylitis, enthesitis and axial involvement.[1 2] PsA can be progressive and destructive, resulting in physical deformities, impaired function, decreased quality of life and increased mortality.[3 4] The cytokine interleukin (IL)-17A promotes joint inflammation and damage by triggering the activation and trafficking of immune cells, inducing proinflammatory cytokines and chemokines, acting as a chemoattractant to neutrophils and monocytes, and stimulating release of matrix metalloproteases and receptor activator of nuclear factor kappa-B ligand, which contribute to cartilage and bone destruction, respectively.[5] Increased numbers of IL-17A-producing cells are present in the peripheral blood, synovial tissue and fluid, and skin plaques of patients with PsA;[6–11] the concentration of IL-17A-producing cells correlates with disease activity.[10] Based on these findings, specific inhibition of IL-17A represents an emerging targeted approach to PsA management.[12 13]

Ixekizumab, a recombinant, high-affinity, humanised, immunoglobulin G4κ monoclonal antibody selectively binds and neutralises IL-17A. The safety and efficacy of ixekizumab in patients with active PsA not previously treated with biologic agents are under investigation in a phase III study (SPIRIT-P1). Here we report the results from the 24-week, placebo-controlled and active-controlled, double-blind period of this study.

## METHODS

### Study design and patient population

The SPIRIT-P1 study (NCT01695239, EudraCT 2011-002326-49) is a 3-year, phase III, randomised, double-blind, placebo-controlled and active-controlled clinical trial comparing two regimens of ixekizumab and an active reference arm adalimumab (Humira; AbbVie) at the approved dose and regimen to treatment with placebo in patients not previously treated with biologic agents for plaque psoriasis or PsA. The double blind period of the study occurred in the first 24 weeks. Enrolled



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patients fulfilled the Classification Criteria for Psoriatic Arthritis (CASPAR);[14] had ≥3 of 68 tender joint count and ≥3 of 66 swollen joint count; and had either ≥1 PsA-related hand or foot joint erosion on centrally read X-rays or C reactive protein >6 mg/L. Further discussion of study design and patient population is included in the online supplementary material.

### Treatment and randomisation

Randomisation was performed centrally via an interactive voice response system based on a computer-generated randomisation code, with stratification by country and by prior/current/no use of conventional (non-biologic) disease-modifying antirheumatic drugs (cDMARDs). Patients were randomised at a 1:1:1:1 ratio to one of four treatment groups: ixekizumab 80 mg every 2 weeks (IXEQ2W), ixekizumab 80 mg every 4 weeks (IXEQ4W), adalimumab 40 mg Q2W, or placebo, all administered via subcutaneous injection (see online supplementary figure S1). Patients randomised to IXEQ4W or IXEQ2W were administered a starting dose of 160 mg given as two injections at week 0. Because the different randomised treatments used distinct schedules and distinguishable prefilled syringes, a double-dummy design with Q2W dosing was employed to conceal treatment allocation (see online supplementary figure S2).

Patients in all treatment groups with an inadequate response at week 16, distinguished by predefined tender and swollen joint count criteria (Inadequate Responders), were required to add or modify concomitant medications. The investigators, study personnel and patients were blinded to the Inadequate Response criteria. The Inadequate Response criteria are being applied in another ongoing and currently blinded study (SPIRIT-P2) in bDMARD-experienced patients with active PsA and thus, must remain blinded. Inadequate Responders remained on their originally assigned dose of ixekizumab or, if receiving adalimumab or placebo, were randomised again to IXEQ2W or IXEQ4W in a 1:1 ratio (see online supplementary figure S1). Inadequate Responders from the adalimumab treatment group received 8 weeks of placebo as a washout therapy prior to initiating ixekizumab treatment at week 24.

Patients already on stable doses of allowed cDMARDs, oral corticosteroids, opiates and/or non-steroidal anti-inflammatory drugs/cyclo-oxygenase-2 inhibitors continued these on study. Further discussion of treatment, concomitant medications and randomisation is provided in the online supplementary material.

### Study assessments

On scheduled study visits (weeks 1, 2, 4, 8, 12, 16, 20 and 24) during the double-blind treatment period, patients underwent assessments for safety and efficacy end points and were supplied with study medication if scheduled. Radiographic images of the hands and feet taken at the screening visit, week 16 and week 24 were assessed centrally by two expert readers who were blinded to treatment allocation, time point and patient data. The primary efficacy end point was the proportion of patients achieving an American College of Rheumatology (ACR) 20 response at week 24 versus placebo. Definitions of the ACR20, ACR50 and ACR70 responses used in the study are provided in the online supplementary material.[15]

Secondary end points included the proportion of patients achieving ACR50 or ACR70 responses; the proportion of patients achieving a 75%, 90% or 100% improvement in Psoriasis Area and Severity Index score (PASI 75, PASI 90 and PASI 100, respectively);[16 17] percentage of psoriasis-affected body surface area (BSA); change from baseline in the Health Assessment Questionnaire-Disability Index (HAQ-DI);[18 19] change from baseline in the van der Heijde modified total Sharp score (mTSS, a measure of structural disease progression based on radiographic assessment of bone erosions and joint space narrowing in the hands and feet);[20] and change from baseline in 28-joint Disease Activity Score using C reactive protein (DAS28-CRP) versus placebo.[21] Additional secondary end points for patients affected at baseline were enthesitis (inflammation of tendon and ligament insertions, as assessed by the presence or absence of tenderness at the six sites of the Leeds Enthesitis Index (LEI)),[22] dactylitis (swelling of the whole digit, with assessment of the number of all 20 digits that are affected, according to the Leeds Dactylitis Index-Basic (LDI-B)),[23 24] the Itch Numeric Rating Scale (itch NRS)[25] and a modified version of the Nail Psoriasis Severity Index (NAPSI),[26] which assessed fingernails only.

Safety evaluations included adverse event (AE) reporting, vital signs, physical exam findings, concomitant medications, ECG, and drug immunogenicity, haematology and laboratory evaluations. AEs of special interest included cytopenias, liver function test changes/enzyme elevations, infections, injection site reactions, hypersensitivity, cerebrocardiovascular events, malignancies, *Pneumocystis* pneumonia/interstitial lung disease, depression and Crohn's disease/ulcerative colitis.

### Statistical analyses

Efficacy analyses were conducted on the intent-to-treat population (all randomised patients). Primary analyses of categorical variables were based on a logistic regression analysis with treatment, geographical region and baseline cDMARD experience in the model. Missing data were imputed using a non-responder imputation method, in which patients who were Inadequate Responders, or who discontinued treatment before week 24, were defined as non-responders. The primary analyses for all continuous variables were based on mixed-effects models for repeated measures with treatment, geographical region, baseline score, baseline cDMARD experience, visit and the interaction of treatment-by-visit in the model. To control the overall type I error rate at a two-sided $\alpha$ level of 0.05, a multiplicity-controlled analysis was used for the primary end point and the six predetermined secondary end points. If the week 24 ACR20 primary efficacy analysis was significant for one or both ixekizumab doses, the secondary analyses were considered in the following sequence: week 24 HAQ-DI, week 24 mTSS, week 12 ACR20, week 12 PASI 75, week 12 LEI and week 12 itch NRS. All other secondary end points were assessed at a significance level of $p<0.05$ with no adjustment for multiplicity. Safety analyses were conducted on the safety population (all patients who took at least one dose of study medication). Fisher's exact test was used for categorical safety data. Continuous safety variables used analysis of covariance (ANCOVA) with treatment and baseline value in the model. Details of additional statistical methods are provided in the online supplementary material.

The adalimumab 40 mg Q2W treatment arm served as active reference for comparison with placebo. The study was not powered to test equivalence or non-inferiority of ixekizumab versus adalimumab.

## RESULTS

### Patient population

Of 719 patients screened, 417 were randomised (see online supplementary figure S3). The mean age was 49.5 years, 46.0% were male, 85.3% were cDMARD-experienced, 64% were currently using cDMARDs and 54.2% reported current methotrexate use. For those taking methotrexate at baseline, the average



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methotrexate dose was 15.8±5.04 mg/week (mean±SD). Overall, 69.5% had psoriasis involving ≥3% of BSA, 58% had enthesitis and 37.6% had dactylitis at baseline (table 1).

Of the 382 patients completing the 24-week double-blind period, 57 were Inadequate Responders (11 IXEQ4W, 10 IXEQ2W, 9 adalimumab, 27 placebo) and received rescue medication from week 16 through week 24. A numerically greater percentage of patients in the IXEQ4W (90.7%), IXEQ2W (94.2%) and adalimumab (96%) groups than in the placebo group (85.8%) completed the 24 weeks.

**Table 1** Baseline characteristics of the patients according to treatment group

| | Placebo N=106 | IXEQ4W N=107 | IXEQ2W N=103 | Adalimumab 40 mg Q2W* N=101 | Total N=417 |
|---|---|---|---|---|---|
| Age (years), mean (SD) | 50.6 (12.3) | 49.1 (10.1) | 49.8 (12.6) | 48.6 (12.4) | 49.5 (11.9) |
| Male, n (%) | 48 (45.3) | 45 (42.1) | 48 (46.6) | 51 (50.5) | 192 (46.0) |
| Weight (kg), mean (SD) | 83.8 (19.6) | 85.5 (23.0) | 81.6 (17.5) | 91.6 (21.9)† | 85.6 (20.9) |
| BMI (kg/m$^2$), mean (SD) | 29.2 (6.3) | 30.2 (8.4) | 28.6 (6.6) | 32.1 (11.4)‡ | 30 (8.5) |
| Race, n (%) | | | | | |
| White | 99 (93.4) | 102 (95.3) | 96 (93.2) | 95 (94.1) | 392 (94.0) |
| Asian | 5 (4.7) | 2 (1.9) | 5 (4.9) | 3 (3.0) | 15 (3.6) |
| American Indian or Alaska native | 2 (1.9) | 2 (1.9) | 2 (1.9) | 3 (3.0) | 9 (2.2) |
| Other | 0 | 1 (0.9) | 0 | 0 | 1 (0.2) |
| Time since psoriatic arthritis diagnosis (years), mean (SD) | 6.3 (6.9) | 6.2 (6.4) | 7.2 (8.0) | 6.9 (7.5) | 6.7 (7.2) |
| Time since psoriasis diagnosis (years), mean (SD) | 16.0 (13.8) | 16.5 (13.8) | 17.0 (14.0) | 15.7 (12.7) | 16.3 (13.5) |
| Background cDMARD therapy, n (%) | | | | | |
| Naïve | 13 (12.3) | 17 (15.9) | 17 (16.5) | 14 (13.9) | 61 (14.6) |
| Past use | 24 (22.6) | 22 (20.6) | 23 (22.3) | 20 (19.8) | 89 (21.3) |
| Current use | 69 (65.1) | 68 (63.6) | 63 (61.2) | 67 (66.3) | 267 (64.0) |
| Methotrexate current use, n (%) | 59 (55.7) | 57 (53.3) | 53 (51.5) | 57 (56.4) | 226 (54.2) |
| Patients with specific disease characteristics, n (%) | | | | | |
| Current psoriasis§ | 102 (96.2) | 100 (93.5) | 95 (92.2) | 97 (96.0) | 394 (94.5) |
| Psoriasis BSA ≥3%¶ | 67 (67.7) | 73 (73.0) | 59 (64.8) | 68 (72.3) | 267 (69.5) |
| Fingernail psoriasis§ | 74 (69.8) | 70 (65.4) | 74 (71.8) | 71 (70.3) | 289 (69.3) |
| Dactylitis§ | 39 (36.8) | 54 (50.5) | 41 (39.8) | 23 (22.8)‡ | 157 (37.6) |
| Enthesitis§ | 57 (53.8) | 70 (65.4) | 59 (57.3) | 56 (55.4) | 242 (58.0) |
| Baseline disease and quality of life scores, mean (SD) | | | | | |
| Tender joint count (68 joints) | 19.2 (13.0) | 20.5 (13.7) | 21.5 (14.1) | 19.3 (13.0) | 20.1 (13.4) |
| Swollen joint count (66 joints) | 10.6 (7.3) | 11.4 (8.2) | 12.1 (7.2) | 9.9 (6.5) | 11.0 (7.4) |
| HAQ-DI | 1.2 (0.60) | 1.2 (0.54) | 1.2 (0.57) | 1.1 (0.59) | 1.2 (0.58) |
| Patient-reported pain VAS 0–100 | 58.5 (23.0) | 60.1 (19.4) | 58.4 (21.7) | 58.7 (19.7) | 58.9 (20.9) |
| Patient-assessed global disease activity VAS 0–100 | 61.1 (22.7) | 62.7 (19.1) | 62.5 (19.9) | 59.1 (19.1) | 61.4 (20.2) |
| Physician-assessed global disease activity VAS 0–100 | 55.9 (19.3) | 57.6 (18.7) | 58.5 (19.0) | 55.4 (18.7) | 56.9 (18.9) |
| CRP (mg/L) | 15.1 (23.6) | 12.8 (16.4) | 15.1 (25.9) | 13.2 (19.1) | 14.1 (21.5) |
| mTSS | 17.6 (28.6) | 19.2 (32.7) | 15.2 (28.9) | 15.9 (27.4) | 17.0 (29.4) |
| DAS28-CRP | 4.9 (1.0) | 5.0 (1.0) | 5.0 (1.1) | 4.9 (1.0) | 4.9 (1.0) |
| LEI** | 2.9 (1.7) | 2.7 (1.6) | 3.1 (1.8) | 3.0 (1.6) | 2.9 (1.7) |
| LDI-B†† | 46.2 (65.5) | 58.1 (96.7) | 40.6 (54.6) | 93.9 (111.9)‡ | 55.8 (83.6) |
| LDI-B‡‡ | 62.7 (69.3) | 73.0 (103.4) | 64.0 (56.6) | 119.9 (113.5)‡ | 75.9 (89.4) |
| % Psoriasis BSA involved¶ | 14.4 (20.2) | 15.1 (16.3) | 12.0 (15.6) | 14.8 (19.2) | 14.1 (17.9) |
| PASI total score¶ | 6.2 (7.5) | 6.9 (6.6) | 6.0 (7.0) | 5.5 (6.5) | 6.1 (6.9) |
| NAPSI§§ | 19.8 (17.2) | 21.3 (18.9) | 25.0 (21.2) | 20.9 (17.5) | 21.8 (18.8) |
| SF-36 PCS | 34.0 (8.3) | 32.4 (10.1) | 34.2 (8.7) | 33.9 (8.8) | 33.6 (9.0) |

*The adalimumab 40 mg Q2W treatment arm served as active reference for comparison with placebo. The study was not powered to test equivalence or non-inferiority of ixekizumab versus adalimumab.
†p≤0.01 vs placebo.
‡p<0.05 vs placebo.
§Presence or absence, as qualitatively assessed by the investigator.
¶Evaluated in patients with psoriasis, as qualitatively assessed by the investigator, at baseline.
**Evaluated in patients with enthesitis, as qualitatively assessed by the investigator, at baseline.
††Evaluated in patients with dactylitis, as qualitatively assessed by the investigator, at baseline.
‡‡Evaluated in patients with baseline LDI-B score >0; post hoc analysis.
§§Evaluated in patients with fingernail psoriasis, as qualitatively assessed by the investigator, at baseline.
BMI, body mass index; BSA, body surface area; cDMARD, conventional disease-modifying antirheumatic drug; CRP, C reactive protein; DAS28-CRP, 28-joint Disease Activity Score using C reactive protein; HAQ-DI, Health Assessment Questionnaire-Disability Index; IXEQ2W, 80 mg ixekizumab once every 2 weeks; IXEQ4W, 80 mg ixekizumab once every 4 weeks; LDI-B, Leeds Dactylitis Index-Basic; LEI, Leeds Enthesitis Index; mTSS, van der Heijde modified total Sharp score; NAPSI, Nail Psoriasis Severity Index; PASI, Psoriasis Area and Severity Index; Q2W, every 2 weeks; SF-36 PCS, Short Form (36 Items) Health Survey Physical Component Score; VAS, visual analogue scale.



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**Table 2** Comparison of efficacy during the 24 weeks of placebo-controlled therapy

| | Placebo | | IXEQ4W | | IXEQ2W | | Adalimumab 40 mg Q2W* | |
|---|---|---|---|---|---|---|---|---|
| | 12 weeks | 24 weeks | 12 weeks | 24 weeks | 12 weeks | 24 weeks | 12 weeks | 24 weeks |
| *Responder rate:* | | | | | | | | |
| | N=106 | | N=107 | | N=103 | | N=101 | |
| ACR20, % | 31.1 | 30.2 | 57.0† | 57.9† | 60.2† | 62.1† | 51.5‡ | 57.4† |
| ACR50, % | 4.7 | 15.1 | 33.6† | 40.2† | 39.8† | 46.6† | 29.7† | 38.6† |
| ACR70, % | 0 | 5.7 | 15.0 | 23.4† | 16.5 | 34.0† | 17.8 | 25.7† |
| | N=92 | | N=100 | | N=90 | | N=89 | |
| HAQ-DI MCID, %§ | 29.3 | 26.1 | 49.0‡ | 49.0† | 64.4† | 57.8† | 49.4‡ | 49.4† |
| | N=28 | | N=39 | | N=26 | | N=18 | |
| LDI-B (0), %¶,** | 53.6 | 25.0 | 74.4 | 79.5† | 69.2 | 76.9† | 61.1 | 77.8† |
| | N=57 | | N=68 | | N=57 | | N=54 | |
| LEI (0), %¶,†† | 28.1 | 19.3 | 27.9 | 42.6‡ | 47.4‡‡ | 38.6§§ | 35.2 | 33.3 |
| | N=67 | | N=73 | | N=59 | | N=68 | |
| PASI 75, %¶¶ | 7.5 | 10.4 | 75.3† | 71.2† | 69.5† | 79.7† | 33.8† | 54.4† |
| PASI 90, %¶¶ | 1.5 | 6.0 | 52.1† | 56.2† | 57.6† | 67.8† | 22.1‡ | 36.8† |
| PASI 100, %¶¶ | 1.5 | 3.0 | 31.5† | 42.5† | 40.7† | 52.5† | 14.7§§ | 23.5‡ |
| | N=41 | | N=52 | | N=41 | | N=37 | |
| sPGA (0, 1), %*** | 7.3 | 17.1 | 75.0† | 65.4† | 80.5† | 73.2† | 45.9† | 62.2† |
| sPGA (0), %*** | 2.4 | 2.4 | 30.8‡ | 38.5‡ | 36.6‡ | 39.0‡ | 10.8 | 18.9‡‡ |
| | N=74 | | N=70 | | N=74 | | N=71 | |
| NAPSI (0), %††† | 8.1 | 18.9 | 20.0‡‡ | 25.7 | 27.0‡ | 36.5§§ | 19.7‡‡ | 39.4‡ |
| *LS mean change from baseline (SE):* | | | | | | | | |
| | N=106 | | N=107 | | N=103 | | N=101 | |
| DAS28-CRP | −0.57 (0.11) | −0.84 (0.13) | −1.63 (0.11)† | −1.96 (0.12)† | −1.67 (0.11)† | −2.04 (0.12)† | −1.57 (0.12)† | −1.74 (0.12)† |
| | N=106 | | N=107 | | N=103 | | N=101 | |
| HAQ-DI | −0.13 (0.05) | −0.18 (0.05) | −0.37 (0.05)† | −0.44 (0.05)† | −0.47 (0.05)† | −0.50 (0.05)† | −0.35 (0.05)† | −0.37 (0.05)‡ |
| | N=106 | | N=107 | | N=103 | | N=101 | |
| SF-36 PCS | 2.3 (0.8) | 2.9 (1.0) | 5.8 (0.8)† | 7.5 (0.9)† | 7.6 (0.8)† | 8.2 (0.9)† | 5.7 (0.8)† | 6.8 (0.9)‡ |
| | N=28 | | N=39 | | N=26 | | N=18 | |
| LDI-B¶,** | −36.3 (10.3) | −33.7 (9.7) | −72.8 (8.8) † | −75.4 (8.1)† | −63.9 (10.6)‡‡ | −66.1 (9.8)‡ | −62.1 (11.9) | −76.0 (10.9)† |
| | N=57 | | N=70 | | N=59 | | N=56 | |
| LEI‡‡‡ | −0.8 (0.24) | −0.8 (0.26) | −0.9 (0.21) | −1.3 (0.21) | −1.5 (0.24)‡‡ | −1.4 (0.24) | −0.8 (0.24) | −0.9 (0.23) |
| | N=102 | | N=100 | | N=95 | | N=97 | |
| % BSA§§§ | −1.6 (1.2) | −2.7 (1.4) | −10.4 (1.2)† | −12.0 (1.3)† | −8.8 (1.2)† | −10.6 (1.4)† | −7.7 (1.2)† | −9.5 (1.4)† |
| | N=74 | | N=70 | | N=74 | | N=71 | |
| NAPSI††† | −1.1 (1.4) | −2.4 (1.7) | −8.4 (1.5)† | −14.0 (1.5)† | −7.7 (1.4)† | −15.5 (1.5)† | −6.8 (1.4)‡ | −10.7 (1.5)† |

*The adalimumab 40 mg Q2W treatment arm served as active reference for comparison with placebo. The study was not powered to test equivalence or non-inferiority of ixekizumab versus adalimumab.
†p≤0.001 vs placebo.
‡p≤0.01 vs placebo.
§Data reported for patients with a baseline HAQ-DI score ≥0.35. The MCID for HAQ-DI is an improvement from baseline ≥0.35.
¶Post hoc analysis.
**Data are reported for patients with dactylitis, as qualitatively assessed by the investigator, at baseline and baseline LDI-B score >0.
††Data are reported for patients with enthesitis, as qualitatively assessed by the investigator, at baseline and baseline LEI score >0.
‡‡p<0.05 vs placebo.
§§p≤0.025 vs placebo.
¶¶Data are reported for patients with baseline psoriatic lesion(s) involving ≥3% BSA.
***Data are reported for patients with sPGA ≥3 at baseline.
†††Data are reported for patients with fingernail psoriasis, as qualitatively assessed by the investigator, at baseline.
‡‡‡Data are reported for patients with enthesitis, as qualitatively assessed by the investigator, at baseline.
§§§Data are reported for patients with psoriasis, as qualitatively assessed by the investigator, at baseline.
ACR20/50/70, 20/50/70% American College of Rheumatology response; BSA, body surface area; DAS28-CRP, 28-joint Disease Activity Score using C reactive protein; HAQ-DI, Health Assessment Questionnaire-Disability Index; IXEQ2W, 80 mg ixekizumab once every 2 weeks; IXEQ4W, 80 mg ixekizumab once every 4 weeks; LDI-B, Leeds Dactylitis Index-Basic; LEI, Leeds Enthesitis Index; LS, least squares; MCID, minimal clinically important difference; NAPSI, Nail Psoriasis Severity Index; PASI 75/90/100, Psoriasis Area and Severity Index Improvement Response for 75/90/100%; Q2W, every 2 weeks; SF-36 PCS, Short Form (36 Items) Health Survey Physical Component Score; sPGA, static Physician Global Assessment of psoriasis.

## Efficacy results

Table 2 summarises the outcomes of efficacy end points at 12 weeks and 24 weeks. The primary efficacy end point of ACR20 response at week 24 was met with both IXEQ4W (57.9%) and IXEQ2W (62.1%); response rates in both ixekizumab groups were significantly greater than in the placebo group (30.2%) (p≤0.001) (figure 1A). The adalimumab group (active reference) also had a significantly greater ACR20 response at week 24 (57.4%) compared with placebo (p≤0.001). Despite the adalimumab group having a statistically higher baseline weight and



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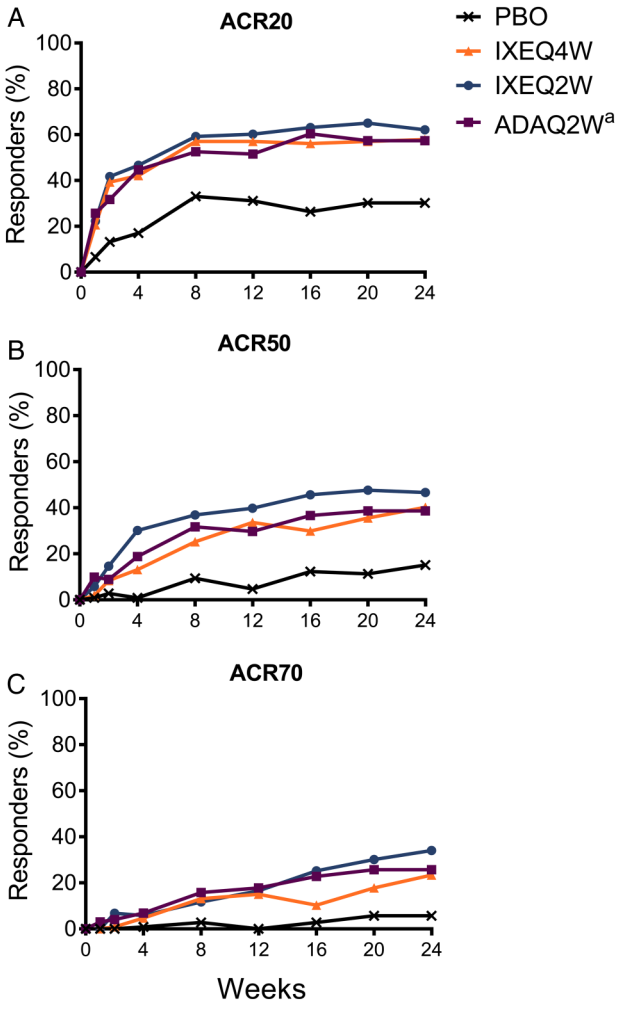


**Figure 1** Time course of ACR responses. The percentages of patients achieving ACR20 (A), ACR50 (B) and ACR70 (C) are shown. Patients with inadequate responses to treatment at week 16 or missing data were analysed as non-response up to week 24. [a]Active reference arm for comparison with placebo. The study was not powered to test equivalence or non-inferiority of ixekizumab versus adalimumab. ACR20/50/70, 20/50/70% American College of Rheumatology response; ADAQ2W, 40 mg adalimumab once every 2 weeks; IXEQ2W, 80 mg ixekizumab once every 2 weeks; IXEQ4W, 80 mg ixekizumab once every 4 weeks; PBO, placebo; Q2W, once every 2 weeks.

body mass index (BMI) compared with the placebo group (table 1), a Cochran-Armitage trend test within the adalimumab group demonstrated no effect of weight or BMI on the ACR20 response at week 24 (data not shown). The ACR20 response at 12 weeks, tested as a secondary end point, was also significantly greater in patients randomised to IXEQ4W (57%) and IXEQ2W (60.2%) versus placebo (31.1%) ($p \leq 0.001$). ACR20 response rates for both ixekizumab groups and the adalimumab group were significantly greater than the placebo group as early as week 1 ($p \leq 0.01$), and the differences were maintained throughout the 24-week period ($p \leq 0.01$). The treatment responses on ixekizumab were significantly greater than those on placebo as early as week 4 for ACR50 and week 8 for ACR70 and persisted through week 24 ($p < 0.05$) (figure 1B, C). Mean reductions in each component of the ACR core set are presented in online supplementary figure S4 and table S1.

Mean reductions in the level of disease activity observed with the DAS28-CRP at week 24 were −0.84 with placebo and −1.96, −2.04 and −1.74 in the IXEQ4W, IXEQ2W and adalimumab groups (all $p \leq 0.001$), respectively (table 2 and see online supplementary figure S5A). At week 24, improvements from baseline in physical function, measured by HAQ-DI, were significantly greater in patients receiving IXEQ4W (−0.44), IXEQ2W (−0.50) and adalimumab (−0.37) than in those receiving placebo (−0.18) ($p \leq 0.01$) (table 2 and see online supplementary figure S4F). For patients with HAQ-DI ≥0.35 at baseline, a greater percentage of patients achieved the minimal clinically important difference in HAQ-DI (improvement ≥0.35 from baseline)[27] at week 24 in the IXEQ4W (49.0%), IXEQ2W (57.8%) and adalimumab (49.4%) groups compared with the placebo group (26.1%) ($p \leq 0.001$) (table 2). The improvement from baseline in Short Form (36 Items) Health Survey Physical Component Score was also significantly greater at week 24 for patients receiving IXEQ4W (7.5), IXEQ2W (8.2) and adalimumab (6.8) compared with those receiving placebo (2.9) ($p \leq 0.01$) (table 2).

Progression of structural damage, measured by changes from baseline in mTSS at week 24, was significantly less in the IXEQ4W (0.17), IXEQ2W (0.08) and adalimumab (0.10) groups than in the placebo group (0.49) ($p \leq 0.01$) (table 3). Significantly greater percentages of patients in the ixekizumab groups and adalimumab group at week 24 experienced no structural progression as defined by thresholds of ≤0.5 or ≤0.95 compared with the placebo group (table 3).

For patients with dactylitis and LDI-B >0 at baseline, significantly greater improvements in mean LDI-B scores at week 24 (post hoc analysis) were observed for the IXEQ4W, IXEQ2W and adalimumab groups compared with the placebo group ($p \leq 0.01$) (table 2 and see online supplementary figure S5B), and complete resolution of dactylitis symptoms (LDI-B=0) at week 24 (post hoc analysis) occurred at a greater rate in the IXEQ4W (80%), IXEQ2W (77%) and adalimumab (78%) groups than in the placebo group (25%) ($p \leq 0.001$) (table 2 and see online supplementary figure S6A). For patients with enthesitis at baseline, the reduction in LEI score at week 12 was greater only in the IXEQ2W group than in the placebo group ($p=0.038$); the change did not reach the significance threshold ($p<0.025$) based on the multiplicity-controlled analysis. At week 24, reductions in LEI score were numerically greater in both ixekizumab groups than in the placebo group (IXEQ4W, −1.3 $p=0.151$; IXEQ2W, −1.4 $p=0.099$; placebo, −0.8) but did not meet statistical significance (table 2 and see online supplementary figure S5C). Among patients with LEI>0 at baseline, complete resolution of enthesitis symptoms (LEI=0) at week 24 (post hoc analysis) occurred at a greater rate with IXEQ4W (43%) and IXEQ2W (39%) than with placebo (19%) ($p<0.05$) (table 2 and see online supplementary figure S6B).

Among patients with psoriasis at baseline affecting ≥3% BSA, a significantly greater percentage of patients achieved PASI 75 at week 12 for the IXEQ4W (75.3%), IXEQ2W (69.5%) and adalimumab (33.8%) groups compared with the placebo group (7.5%) ($p<0.001$) (table 2 and figure 2A). Significantly greater PASI responses compared with placebo were observed as early as week 4 for PASI 75 and PASI 90, and week 8 for PASI 100 ($p \leq 0.01$) (figure 2). For patients with nail involvement at baseline, mean changes from baseline in the NAPSI score at week 24 were significantly greater for the IXEQ4W (−14.0), IXEQ2W (−15.5) and adalimumab (−10.7) groups than for the placebo group (−2.4) ($p \leq 0.001$) (table 2). At week 24, a significantly greater percentage of patients achieved complete resolution of nail psoriasis (NAPSI=0) in the IXEQ2W (36.5%) and adalimumab (39.4%) groups compared with the placebo group (18.9%) ($p<0.025$).



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**Table 3** Effect on structural disease progression

| | | Placebo N=106 | IXEQ4W N=107 | IXEQ2W N=103 | Adalimumab 40 mg Q2W* N=101 |
|---|---|---|---|---|---|
| LS mean change from baseline mTSS (SE)† | Week 16 | 0.36 (0.07) | 0.13 (0.07)‡ | 0.06 (0.07)§ | 0.12 (0.08)‡ |
| | Week 24 | 0.49 (0.09) | 0.17 (0.08)§ | 0.08 (0.08)¶ | 0.10 (0.09)¶ |
| Percentage of patients with change in mTSS at week 24 | ≤0 | 72.0 | 83.0 | 83.5 | 91.6¶ |
| | ≤0.5 | 77.4 | 89.0** | 94.8¶ | 95.8¶ |
| | ≤0.95 | 83.9 | 94.0‡ | 96.9§ | 95.8§ |

*The adalimumab 40 mg Q2W treatment arm served as active reference for comparison with placebo. The study was not powered to test equivalence or non-inferiority of ixekizumab versus adalimumab.
†Higher mTSS scores indicate more articular damage. The mean change from baseline at week 24 was assessed with a statistical significance threshold of p<0.025 in a hierarchical analysis; all other end points were assessed with a statistical significance threshold of p<0.05.
‡p≤0.025 vs placebo.
§p≤0.01 vs placebo.
¶p≤0.001 vs placebo.
**p<0.05 vs placebo.
IXEQ2W, 80 mg ixekizumab once every 2 weeks; IXEQ4W, 80 mg ixekizumab once every 4 weeks; LS, least squares; mTSS, van der Heijde modified total Sharp score; Q2W, every 2 weeks.

## Safety profile

A greater percentage of patients receiving ixekizumab (66%) and adalimumab (64%) reported at least one treatment-emergent AE compared with patients receiving placebo (47.2%). These were mostly mild or moderate, and the most common were injection site reaction, injection site erythema and nasopharyngitis (table 4).

Across all groups, 10 patients (2.4%) discontinued because of an AE. No deaths occurred. Injection site reactions were mostly mild in intensity and were more frequent in the ixekizumab groups than in the placebo group (see online supplementary table S2). No serious AEs (SAEs) of injection site reactions were reported, and four patients discontinued due to an AE of injection site reactions (two IXEQ2W, one adalimumab, one placebo). Reductions in neutrophils from normal levels, meeting the definition of National Cancer Institute Common Terminology Criteria for Adverse Events of grade 1 (lower limit of normal to 1500 cells/mm$^3$) and grade 2 (<1500–1000 cells/mm$^3$) neutropenia,[28] occurred in 6.2% and 4.8%, respectively, of the patients treated with ixekizumab (data not shown). One patient had grade 2 neutropenia on more than one assessment; no infection onset occurred within 14 days of any report of grade 2 neutropenia. There were no instances of grade 3 (<1000–500 cells/mm$^3$) or higher neutropenia, major cerebrocardiovascular events (cardiovascular death, myocardial infarction stroke, etc), interstitial lung disease/*Pneumocystis* pneumonia, Crohn's disease or ulcerative colitis in the ixekizumab-treated patients. Depression-related symptoms were reported in three patients in the ixekizumab groups; none were reported in the placebo group. One patient randomised to IXEQ2W discontinued from the study because of worsening of mild depression existing at baseline. No AEs of suicidal ideation or suicide attempt were reported. AEs of infection were similar in frequency between all treatment groups; the most commonly reported infections in the combined ixekizumab groups were nasopharyngitis, upper respiratory tract infection, bronchitis, conjunctivitis, oral herpes and pharyngitis (see online supplementary table S3). One patient treated with IXEQ2W experienced herpes zoster involving the eyelid, which was classified as a SAE. Four other SAEs of infection were gastroenteritis (IXEQ4W), oesophageal candidiasis (IXEQ2W), cellulitis (adalimumab) and mycoplasma pneumonia (adalimumab). All SAEs of infection resolved with treatment and did not lead to study discontinuation. One case of oral candidiasis (mild) was reported as an AE (IXEQ4W). There were no cases of invasive fungal disease or clinically active or reactivated tuberculosis. Mild or moderate hypersensitivity events, most commonly manifesting as rash or urticaria, were reported in seven patients in the ixekizumab groups; none were reported as serious. One patient treated with IXEQ4W discontinued the study due to rash. In the ixekizumab treatment groups, 11 patients had treatment-emergent anti-ixekizumab antibodies, and none had detectable neutralising antibodies; 72.7% (n=8/11) of these patients achieved an ACR20 response at week 24.

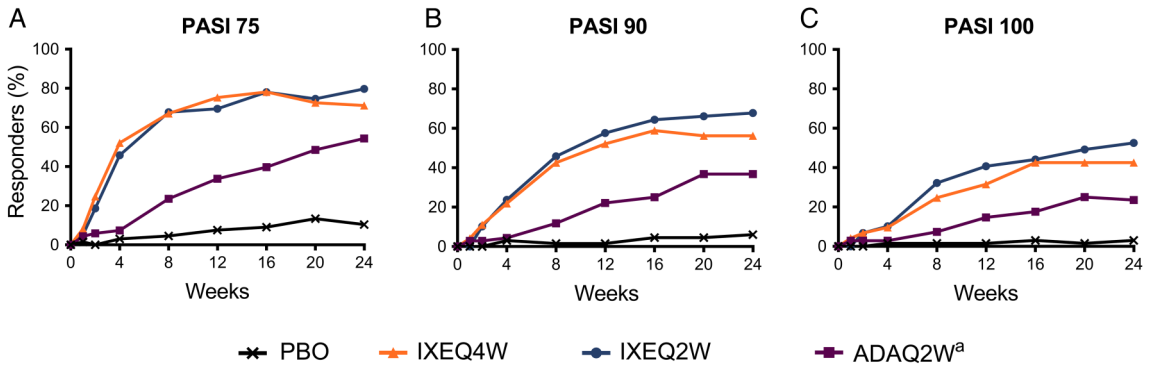


**Figure 2** Time course of PASI responses. The percentages of patients achieving PASI 75 (A), PASI 90 (B) and PASI 100 (C) are shown. PASI was measured in patients with baseline psoriatic lesion(s) involving ≥3% body surface area. Patients with inadequate responses to treatment at week 16 or missing data were analysed as non-response up to week 24. [a]Active reference arm for comparison with placebo. The study was not powered to test equivalence or non-inferiority of ixekizumab versus adalimumab. PASI 75/90/100, Psoriasis Area and Severity Index Improvement Response for 75/90/100%; IXEQ2W, 80 mg ixekizumab once every 2 weeks; IXEQ4W, 80 mg ixekizumab once every 4 weeks; Q2W, once every 2 weeks.



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**Table 4** Safety overview

| | Placebo (N=106) | IXEQ4W (N=107) | IXEQ2W (N=102) | Adalimumab 40 mg Q2W* (N=101) |
|---|---|---|---|---|
| TEAE, n (%) | 50 (47.2) | 71 (66.4)† | 67 (65.7)† | 65 (64.4)‡ |
| Mild | 27 (25.5) | 43 (40.2)§ | 41 (40.2)§ | 39 (38.6) |
| Moderate | 21 (19.8) | 24 (22.4) | 21 (20.6) | 25 (24.8) |
| Severe | 2 (1.9) | 4 (3.7) | 5 (4.9) | 1 (1.0) |
| Most frequent TEAEs¶, n (%) | | | | |
| Injection site reaction | 0 | 13 (12.1)** | 16 (15.7)** | 2 (2.0) |
| Injection site erythema | 0 | 7 (6.5)‡ | 13 (12.7)** | 2 (2.0) |
| Nasopharyngitis | 5 (4.7) | 7 (6.5) | 3 (2.9) | 7 (6.9) |
| Headache | 1 (0.9) | 4 (3.7) | 4 (3.9) | 3 (3.0) |
| Upper respiratory tract infection | 7 (6.6) | 5 (4.7) | 3 (2.9) | 5 (5.0) |
| ALT increased | 0 | 3 (2.8) | 4 (3.9) | 3 (3.0) |
| Diarrhoea | 3 (2.8) | 2 (1.9) | 5 (4.9) | 3 (3.0) |
| Muscle spasms | 1 (0.9) | 3 (2.8) | 4 (3.9) | 1 (1.0) |
| Bronchitis | 3 (2.8) | 3 (2.8) | 3 (2.9) | 4 (4.0) |
| AST increased | 0 | 2 (1.9) | 3 (2.9) | 2 (2.0) |
| Nausea | 2 (1.9) | 0 | 5 (4.9) | 4 (4.0) |
| Psoriatic arthropathy | 1 (0.9) | 3 (2.8) | 2 (2.0) | 3 (3.0) |
| Back pain | 0 | 2 (1.9) | 2 (2.0) | 3 (3.0) |
| Serious adverse events, n (%) | 2 (1.9) | 6 (5.6) | 3 (2.9) | 5 (5.0) |
| Serious infection, n (%) | 0 | 1 (0.9) | 2 (2.0) | 2 (2.0) |
| Discontinued due to AE, n (%) | 2 (1.9) | 2 (1.9) | 4 (3.9) | 2 (2.0) |
| AEs of special interest††, n (%) | 36 (34.0) | 52 (48.6)§ | 56 (54.9)† | 45 (44.6) |
| Infection | 27 (25.5) | 30 (28.0) | 24 (23.5) | 26 (25.7) |
| Any candida infection | 0 | 1 (0.9) | 1 (1.0) | 0 |
| Active or reactivated tuberculosis | 0 | 0 | 0 | 0 |
| Injection site reactions | 5 (4.7) | 26 (24.3)** | 27 (26.5)** | 6 (5.9) |
| Hepatic event | 7 (6.6) | 5 (4.7) | 9 (8.8) | 13 (12.9) |
| Allergic reaction/hypersensitivity | 3 (2.8) | 2 (1.9) | 5 (4.9) | 5 (5.0) |
| Cytopenia (all types) | 6 (5.7) | 1 (0.9) | 4 (3.9) | 4 (4.0) |
| Neutropenia | 0 | 0 | 1 (1.0) | 0 |
| Depression | 0 | 2 (1.9) | 1 (1.0) | 1 (1.0) |
| Cerebrocardiovascular event | 0 | 0 | 0 | 3 (3.0) |
| Malignancy | 1 (0.9) | 0 | 0 | 1 (1.0) |

*The adalimumab 40 mg Q2W treatment arm served as active reference for comparison with placebo. The study was not powered to test equivalence or non-inferiority of ixekizumab versus adalimumab.
†$p \leq 0.01$ vs placebo.
‡$p \leq 0.025$ vs placebo.
§$p < 0.05$ vs placebo.
¶Adverse events are listed according to the preferred term in MedDRA, V.17.1, and are events that occurred in ≥2.0% of the patients in the combined ixekizumab group.
**$p \leq 0.001$ vs placebo.
††Reported as adverse events and coded using MedDRA, V.17.1. Groups of adverse events of special interest are shown; adverse events of special interest not reported in any group included pneumocystis pneumonia, Crohn's disease/ulcerative colitis and interstitial lung disease.
AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; IXEQ2W, 80 mg ixekizumab once every 2 weeks; IXEQ4W, 80 mg ixekizumab once every 4 weeks; MedDRA, Medical Dictionary for Regulatory Activities; Q2W, once every 2 weeks; TEAE, treatment-emergent adverse event.

## DISCUSSION

In this phase III study, 80 mg of ixekizumab administered every 2 weeks or 4 weeks after a starting dose of 160 mg significantly improved signs and symptoms, including enthesitis and dactylitis, of PsA and patient-reported physical functioning, while also inhibiting bone destruction. Both ixekizumab dose regimens significantly reduced radiographic progression of joint damage when compared with placebo. A rapid therapeutic response was apparent as early as 1 week after beginning therapy. Moreover, nearly half of the patients with ≥3% affected BSA who were treated with ixekizumab achieved complete clearance of their psoriasis, a result consistent with earlier studies of ixekizumab in patients with moderate-to-severe psoriasis.[29 30]

A numerically greater proportion of patients receiving IXEQ2W achieved, for many end points, greater efficacy at week 24 compared with IXEQ4W. However, a formal comparison of the two ixekizumab treatments was not prespecified in the study design. Of note, the study was not intended to assess the effects of the 160 mg starting dose.

Patients treated with adalimumab, the active reference group, demonstrated significant efficacy compared with placebo across disease activity, functional outcome and radiographic endpoints. The inclusion of adalimumab, an active control, served as an internal reference arm to assess the relative efficacy of an approved and established treatment compared with placebo in the same study patient population as that for ixekizumab. The positive efficacy results for adalimumab further support the



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ability of SPIRIT-P1 to distinguish active treatments from placebo.

Within this manuscript, improvement in LDI-B is presented for two different baseline patient populations (see online supplementary table S4): (1) presence of dactylitis, based on a qualitative assessment conducted by the investigator (prespecified) or (2) presence of dactylitis, based on a qualitative assessment conducted by the investigator, and a baseline LDI-B score >0 (post hoc). Both assessments demonstrate a significant improvement in dactylitis with ixekizumab or adalimumab treatment versus placebo. However, the latter (post hoc) analysis uses a baseline population identified by applying a more objective measure (ie, based on a measurement of digit circumference and digit tenderness), which is intended to provide a clinically meaningful, yet more rigorous, estimation of the treatment effect.

The efficacy findings further highlight the role of IL-17A in the pathogenesis of PsA.[12 13 31]

The safety profile of ixekizumab was consistent with findings reported aligned with the safety profile in moderate-to-severe plaque psoriasis.[29 30] Other than findings related to mild-to-moderate, transient injection site reactions, most AEs occurred at similar rates to those observed with placebo. IL-17A can regulate neutrophil homoeostasis via several mediators of neutrophil production, trafficking and function, such as granulocyte colony-stimulating factor, growth-related oncogene-α and IL-8. Furthermore, IL-17A is integrally involved in host mucosal defences against *Candida albicans*,[32–34] which may contribute to the increased number of cases of candidiasis associated with IL-17A inhibition,[12 13 30] including the two reported in the current study. Treatment-emergent neutropenia was of grade 1 or 2. Observed infections occurred at similar rates in active treatment and placebo groups. No obvious correlation between ixekizumab dosing frequency and AEs was observed in this study.

The 24-week placebo controlled study duration was based on existing data and ethical considerations to minimise the duration of exposure to placebo treatment. An extension period of up to 3 years will permit longer-term safety and efficacy evaluations. Given that the current study was restricted to patients who were naive to biologic therapy, the results cannot be generalised to treatment of patients with a history of failed therapy or loss of efficacy to therapy or intolerance to anti-tumor necrosis factor (TNF) agents. Evaluation of ixekizumab in patients with PsA with previous experience with biologic therapy is currently under investigation in the SPIRIT-P2 clinical trial (NCT02349295; EudraCT 2011-002328-42).

In conclusion, 24 weeks of treatment with ixekizumab improved the key clinical domains of PsA. The safety findings were consistent with the current understanding of IL-17A inhibition and the clinical profile observed in previous ixekizumab studies in patients with moderate-to-severe psoriasis. The present findings support the view that IL-17A is a key cytokine in the pathogenesis of PsA and an important therapeutic target.

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**Acknowledgements** The authors thank David S Shrom, Suvajit Samanta and Stephanie M Krupski (Eli Lilly and Company, Indianapolis, Indiana, USA), and David Hartree, Molly R Nixon, Millie S Hollandbeck and Jennifer N Bodie (ClinGenuity, Cincinnati, Ohio, USA) for medical writing support and assistance with preparation and submission of this paper.

**Collaborators** The authors thank the SPIRIT-P1 study investigators (see online supplementary material for the full investigator list): N Barkham, L Bessette, R Blanco Alonso, EJ Box, M Brooks, R Burgos Vargas, V Chandran, R Dhar, A Fernandez Nebro, R Fleischmann, K Flint, J Forstot, F Galvan Villegas, F Garcia-Fructuoso, O Garmish, M Geneva-Popova, P Geusens, G Gladstein, H Goto, E Griep, R Harrell, A Hou, M Howell, A Kivitz, S Klein, A Kolczewska, M Korkosz, D Lopez Montilla, C Lue, Y Makino, JL Marenco de la Fuente, H Marzo-Ortega, P Mease, T Miyamura, E Mueller, L Myasoutova, F Navarro Sarabia, M Okada, A Ostor, K Papp, L Podrazilova, G Pulka, E-K Raussi, C Ritchlin, J Rosa, E Roussou, A Rychlewska-Hanczewska, K Sada, L Sedova, D Sikes, S Solomon, M Stack, M Stanislavchuk, K Suzuki, H Tahir, J Tälli, A Toncheva, A Turkiewicz, I Valter, S Vladeva, S Wolfe and N Zyablova.

**Contributors** PJM, CTR, CLS, DKB and DDG were involved in the conception and design of the clinical study; PJM, RSC, CLS and CHL were involved in the acquisition of the data; and all authors were involved in the analysis and interpretation of the data. All authors were involved in the drafting and revising of the manuscript. C-YL was involved in the statistical analysis.

**Funding** This study was funded and sponsored by Eli Lilly and Company.

**Competing interests** PJM reports grants and personal fees from Eli Lilly & Company during the conduct of the study. PJM also reports, outside the submitted work, grants, personal fees, and non-financial support from AbbVie, Amgen, Bristol Myers Squibb, Celgene, Crescendo, Genentech, Janssen, Pfizer and UCB Pharma; grants and personal fees from Merck and Novartis; and non-financial support from Corrona. DvdH reports personal fees from Eli Lilly & Company, during the conduct of the study. DvdH also reports personal fees from AbbVie, Amgen, AstraZeneca, Augurex, Bristol Myers Squibb, Celgene, Centocor, Chugai, Covagen, Daiichi, Galapagos, GlaxoSmithKline, Janssen, Merck, Novo Nordisk, Otsuka, Pfizer, Roche, Sanofi-Aventis, UCB Pharma and Vertex, outside the submitted work. DvdH is the director at Imaging Rheumatology BV. CTR reports personal fees from AbbVie, Amgen, Janssen, Novartis, UCB, Boerhinger Ingelheim, as well as grants from Amgen, outside the submitted work. MO reports grants and non-financial support from Eli Lilly & Company, during the conduct of this study. MO also reports non-financial support from Santen Pharmaceutical, Mitsubishi Tanabe Pharma, Pfizer and Abbott Japan, outside the submitted work. RSC and DKB were employees of Eli Lilly & Company, at the time this study was conducted. CLS, C-YL and CHL are employees of Eli Lilly & Company. DDG reports grants and personal fees from AbbVie, Amgen, Celgene, Janssen, Novartis, Pfizer and UCB, and personal fees from Eli Lilly & Company, outside the submitted work.

**Ethics approval** The protocol was approved by each site's institutional review board or ethics committee.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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Ann Rheum Dis: first published as 10.1136/annrheumdis-2016-209709 on 23 August 2016. Downloaded from http://ard.bmj.com/ on June 4, 2021 at Leids Universitair Medisch Centrum Walaeus Bibl./C1-Q64. Protected by copyright.

Annals of the Rheumatic Diseases

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# Ixekizumab: a new treatment option for people with PsA

Ixekizumab treatment resulted in improvements in disease activity and physical function in people with PsA.

## INTRODUCTION

Psoriatic arthritis (often shortened to PsA) is a chronic inflammatory disease that affects a person's joints, causing pain and disability. The disease often causes swelling of the fingers and toes. It gets its name from the link between this type of arthritis and a skin condition called psoriasis, which causes redness and scaling. PsA can be progressive and destructive. It can cause a reduction in people's quality of life and a risk of dying earlier than people without the disease.

Ixekizumab is a new drug being tested for PsA. It is a type of medicine known as a biologic disease-modifying antirheumatic drugs (bDMARD or biologic). It works by blocking a molecule called interleukin-17 (also called IL-17) that is involved in inflammation and the development of PsA and psoriasis.

## WHAT DID THE AUTHORS HOPE TO FIND?

Ixekizumab has already been studied in people with psoriasis, where it was found to be better than another biologic drug called etanercept (brand name Enbrel).[1,2] In this new study called SPIRIT-P1 the authors wanted to find out whether ixekizumab worked better than placebo (a dummy drug) in people with PsA, and if it could stop people getting damage in their joints.

## WHO WAS STUDIED?

SPIRIT-P1 looked at 417 people from different regions and countries all over the world. Everyone had PsA, rather than any other type of arthritis, and nobody had used any other biologic drug before. Of the people included in the study, most (70%) had psoriasis covering at least 3% of their body surface area.

## HOW WAS THE STUDY CONDUCTED?

This was a randomised, double-blind trial, which means that patients were assigned by chance to one of four treatment groups. Using chance in this way means that the groups are similar and allows the treatments to be compared objectively. The study lasted for 24 weeks. During this time neither the patients nor their doctors knew which group they were in. The four groups were: an ixekizumab injection every 2 weeks, an ixekizumab injection every 4 weeks, an adalimumab injection every 2 weeks, or placebo (a dummy drug). Anyone taking a stable dose of a conventional DMARD (for example, methotrexate) was allowed to carry on taking that drug as well for the whole of the study.

Everyone was tested to see how well the treatment worked for them (called an ACR response, which measures improvement according to the American College of Rheumatology criteria), as well as whether they had any structural joint damage, or improvements in their physical function. People who had swellings in their fingers or toes or psoriasis patches on their skin at the start of the study were also monitored for improvements in these symptoms.

## WHAT WERE THE MAIN FINDINGS?

The study found that after 24 weeks, significantly more patients treated with ixekizumab achieved a 20% improvement in their ACR response than people who were treated with placebo (30%). This response was detected as early as one week after the first injection. People's physical function was also significantly improved and there was less progression of structural damage, compared to people treated with placebo. Ixekizumab also delivered improvement in skin symptoms, and many people's finger and toe swellings cleared up completely. People treated with adalimumab also did much better than those who got placebo.

Side effects were reported in more people who took ixekizumab or adalimumab than placebo. These side effects were mostly mild or moderate and over 97% of people were able to carry on taking the drug. The most common side effects with ixekizumab were reactions or irritation where the injection was given, or nasopharyngitis (symptoms like a cold). Similar numbers of people in all groups got infections while they were in the study. There were no reports of serious complications such as cardiovascular events or cancers.

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## ARE THESE FINDINGS NEW?

Yes. This is the first study published specifically on ixekizumab for PsA. That means that the results are novel. SPIRIT-P1 is unique in terms of PsA studies because it included comparisons with adalimumab (an established treatment for PsA) as well as a placebo group.

## ARE THERE ANY LIMITATIONS?

This part of the study was only 24 weeks. This is because it would not be ethical to give people a placebo for longer than this. The study was also restricted to people who had not taken a biologic therapy before, which means that we cannot generalise the findings to people who have taken a biologic therapy and had no effect, or lost response after initially having a good response to a biologic therapy. Also, the way the study was designed means that it is not possible to demonstrate statistical differences between the two different ixekizumab groups (every 2 or 4 weeks) or to make any comparison between ixekizumab and adalimumab.

## WHAT DO THE AUTHORS PLAN ON DOING WITH THIS INFORMATION?

The study is carrying on with two groups of people (ixekizumab every 2 or 4 weeks). In total, SPIRIT-P1 will collect information for 3 years. More data from these groups at 52 weeks was already presented at the 2016 ACR and EULAR congresses. In addition, there is another study underway in people with PsA who have used biologic therapy before (SPIRIT-P2).

## WHAT DOES THIS MEAN FOR ME?

Ixekizumab is currently not approved for the treatment of PsA in the United States or Europe. However, the results highlighted in this article provide important information about the efficacy and safety of ixekizumab. This information will be needed for any potential approval of ixekizumab as a treatment option for people with PsA, and the drug may be available for you to try in the future.

If you live in Japan, ixekizumab is already approved for use in people with PsA, and so this study will provide useful information for you and your doctor about what to expect from treatment.

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Date prepared: September 2016

Summary based on research article published on: 23 August 2016

**From**: Mease, P. *et al*. Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naïve patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1. *Ann Rheum Dis* 2016;0:1–9. doi: 10.1136/annrheumdis-2016-209709.



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