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POS1033

SAFETY OF IXEKIZUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS: AN INTEGRATED ANALYSIS OF 4 CLINICAL TRIALS

C. Sesin¹, G. Gallo², A. Gellett², A. Kronbergs², A. T. Sprabery², W. Xu², H. Patel², A. Deodhar³, B. Combe⁴, G. R. Burmester⁵, ¹Mount Sinai Medical Center, Miami Beach, United States of America; ²Eli Lilly and Company, Indianapolis, United States of America; ³Oregon Health & Science University, Portland, United States of America; ⁴Montpellier University, CHU Montpellier, Montpellier, France; ⁵Universitätsklinikum Charité, Berlin, Germany

Background: Patients with psoriatic arthritis (PsA) require long-term treatment, which may lead to adverse events (AEs). Ixekizumab, an interleukin-17A antagonist, is approved for the treatment of adults with active PsA.

Objectives: We report a summary of safety outcomes for patients enrolled in 4 PsA studies with up to 3 years of exposure to ixekizumab.

Methods: This integrated safety analysis included all patients with PsA who received at least 1 dose of ixekizumab (80mg every 2 or 4 weeks) in 4 clinical trials (NCT01695239, NCT02349295, NCT02584855, NCT03151551). Safety outcomes included treatment-emergent adverse events (TEAEs), serious AEs (SAEs), discontinuations due to AEs, deaths, and AEs of special interest.

Results: A total of 1401 patients were included in this safety analysis (51.5% female; mean age 49 years), with 2247.6 patient-years of exposure (Table 1). In all, 1131 patients (80.7%) reported ≥ 1 TEAE (exposure-adjusted incidence rate per 100 patient-years [IR] 50.3, 95% CI 47.5–53.3), mostly mild (32.9%) or moderate (39.7%) in severity. The most common TEAEs were nasopharyngitis (n=202, IR 9.0), upper respiratory infections (n=186, IR 8.3), and injection site reaction (n=156, IR 6.9). SAEs were reported by 134 patients (IR 6.0, 95% CI 5.0–7.1). 115 (8.2%) patients discontinued due to AEs (IR 5.1, 95% CI 4.3–6.1). Six deaths were reported (IR 0.3, 95% CI 0.1–0.6). Allergic reactions/hypersensitivity were reported in 102 patients (IR 4.5, 95% CI 3.7–5.5). Three cases were adjudicated as de novo inflammatory bowel disease (IR 0.13, 95% CI 0.04–0.41); 1 was ulcerative colitis (IR 0.04, 95% CI 0.01–0.32), 2 were Crohn's disease (IR

0.09, 95% CI 0.02–0.36). Major adverse cardiac events occurred in 12 patients (IR 0.5) and malignancies in 15 (IR 0.7), 9 of which were non-melanoma skin cancer. Opportunistic infections occurred in 40 (2.9%) patients (IR 1.8, 95% CI 1.3–2.4). Candidiasis occurred in 24 patients (oral: IR 0.7, 95% CI 0.4–1.2; oral fungal infection: IR 0.3, 95% CI 0.1–0.6; esophageal infection: IR 0.1, 95% CI 0.0–0.4). No active or reactive cases of tuberculosis were reported. Other opportunistic infections included hepatitis B (IR 0.0, 95% CI 0.0–0.3), herpes simplex (IR 1.8, 95% CI 1.3–2.5), and herpes zoster (IR 0.7, 95% CI 0.4–1.2).

Conclusion: The safety profile of ixekizumab across 4 clinical trials and up to 3 years of continuous treatment in patients with active PsA was consistent with the known safety profile reported in previous studies for psoriasis and PsA. No new safety events were found in this analysis.

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POS1034

RESPONSE TO SEQUENTIAL LINES OF BIOLOGICAL THERAPY IN PSORIATIC ARTHRITIS: A SINGLE CENTRE COHORT STUDY

A. Abdalla¹, A. Rambojun², L. C. Coates³, E. Korendowych¹, N. Mchugh², W. Tillett^{1,2}, ¹Royal National Hospital for Rheumatic Diseases, Rheumatology Department, Bath, United Kingdom; ²University of Bath, Department of Pharmacy and Pharmacology, Bath, United Kingdom; ³University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom

Background: Biologic interventions using highly specific immuno-modulatory biologic disease-modifying anti-rheumatic drugs (bDMARDs) represent a rapidly developing therapeutic approach to the treatment of Psoriatic Arthritis (PsA). However, despite high rates of response, adverse events, primary and secondary inefficacy are common, and multiple sequential lines of bDMARDs are often required. Data on drug persistence, as a surrogate for response, from national registries indicates switching has become accepted routine practice. One third of patients will fail or discontinue their first biologic with a significant proportion switching on to a 3rd biologic or higher.¹⁻⁴ Due to a lack of evidence on the response to sequential therapies, individual patients may not have further lines routinely funded after three bDMARDs in the UK. While limiting lines of therapy remains a UK concern, many countries with rationed healthcare systems follow the UK model of drug usage.

Objectives: To describe the response to sequential lines of bDMARD therapy prescribed in routine care in a UK single centre cohort.

Methods: A retrospective sample of patients with PsA who fulfilled CASPAR criteria and had received at least one bDMARD were taken from the Bath longitudinal cohort for inclusion in the study. Clinical and laboratory variables that constitute physician and patient-reported outcome measures were collected at baseline and after a median (range) follow-up of 3 months (2-5) into their respective therapy line in accordance with the National Institute for Health and Care Excellence (NICE) rules. The mean change with a 95% confidence interval (CI) was used to report the difference between the baseline and follow-up measures. All patients provided consent to use their data collected during routine care, and ethical approval by the local committee was granted.

Results: The patients mean age was 57.7 (SD 12.2) with a median (range) disease duration of 14.4 years (9.7 – 23.2). Data was available for 194 patients commencing 1st line bDMARD, 106 (2nd line), 93 (3rd line), 33 (4th line), 12 (5th line), and 9 (6th line and higher) from a total of 759 patients in the cohort. Mean tender and swollen joint count at baseline 1st bDMARD was 7 (SD 4.7) and 22 (SD 14.0), pain visual analogue scale 50 (SD 27.6) and PASI 1.3 (SD 2.2). Reasons for changing biological therapies include lack or loss of efficacy, intolerance, side effects, and comorbidities. Mean levels of joint disease at drug initiation did not diminish with subsequent lines of therapy. Clinical and patient

Pooled Ixekizumab (N=1401; Total Patient-Years=2247.6)					
	n (IR) 95% CI	Year 0–1 (n=1401) n (IR) 95% CI	Year 1–2 (n=946) n (IR) 95% CI	Year 2–3 (n=510) n (IR) 95% CI	Year ≥ 3 (n=89) n (IR) 95% CI
Total Patient-Years	2247.7	1207.3	689.8	347.7	2.9
Patients with ≥ 1 TEAE	1131 (50.3) 47.5–53.3	1050 (87.0) 81.9–92.4	496 (71.9) 65.9–78.5	234 (67.3) 59.2–76.5	6 (206.2) 92.6–458.9
SAEs	134 (6.0) 5.0–7.1	72 (6.0) 4.7–7.5	53 (7.7) 5.9–10.1	19 (5.5) 3.5–8.6	1 (34.4) 4.8–243.9
Discontinuations due to AEs	115 (5.1) 4.3–6.1	61 (5.1) 3.9–6.5	37 (5.4) 3.9–7.4	17 (4.9) 3.0–7.9	0 (0) 0.0–274.7
Hepatic reactions	112 (5.0) 4.1–6.0	80 (6.6) 5.3–8.3	32 (4.6) 3.3–6.6	14 (4.0) 2.4–6.8	0 (0) 0.0–274.7
Allergic reaction/hypersensitivity	102 (4.5) 3.7–5.5	83 (6.9) 5.5–8.5	23 (3.3) 2.2–5.0	5 (1.4) 0.6–3.5	0 (0) 0.0–274.7
Serious infection	28 (1.2) 0.9–1.8	18 (1.5) 0.9–2.4	9 (1.3) 0.7–2.5	3 (0.9) 0.3–2.7	0 (0) 0.0–274.7
Malignancies	15 (0.7) 0.4–1.1	4 (0.3) 0.1–0.9	8 (1.2) 0.6–2.3	4 (1.2) 0.4–3.1	0 (0) 0.0–274.7
Major adverse cardiac events	12 (0.5) 0.3–0.9	3 (0.2) 0.1–0.8	8 (1.2) 0.6–2.3	1 (0.3) 0.0–2.0	0 (0) 0.0–274.7
Inflammatory bowel disease	3 (0.1) 0.0–0.4	3 (0.2) 0.1–0.8	1 (0.1) 0.0–1.0	0 (0.0) 0.0–2.3	0 (0.0) 0.0–274.7
Ulcerative colitis	1 (0.0) 0.0–0.3	1 (0.1) 0.0–0.6	1 (0.1) 0.0–1.2	0 (0.0) 0.0–2.3	0 (0.0) 0.0–274.7
Crohn's disease	2 (0.1) 0.0–0.4	2 (0.2) 0.0–0.7	0 (0.0) 0.0–1.2	0 (0.0) 0.0–2.3	0 (0.0) 0.0–274.7

AE, adverse event; CI, confidence interval; IR, exposure-adjusted incidence rate per 100 patient-years; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

reported outcomes by line of therapy are reported in Figure 1. Clinical responses were greatest to first line bDMARD, however clinically relevant DAPSA improvements were seen up to 5th line. Absolute levels of psoriasis in the cohort were low, however improvement in PASI was achieved across all lines of therapy. Patient and Physician Global Assessments (1-5 on Likert scale) and the Pain Visual analogue score (VAS on 1-10 Likert scale) showed a similar trend with greatest improvement to first line treatment across all lines of therapy.

Conclusion: In this study we report the clinical response to sequential lines of bDMARD therapy for active PsA in routine clinical practice. Clinical response was greatest to the first line bDMARD but overall improvement in DAPSA, PASI or pain response did not appear to diminish up to 5th line. Further study in larger cohorts is required to confirm this finding and build on our understanding of clinical response to sequential lines of bDMARD therapy.

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Figure 1. Clinical and patient reported outcomes by line of therapy

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POS1035

UPADACITINIB AS MONOTHERAPY AND IN COMBINATION WITH NON-BIOLOGIC DMARDs FOR THE TREATMENT OF PSORIATIC ARTHRITIS: SUBGROUP ANALYSIS FROM TWO PHASE 3 TRIALS

P. Nash¹, P. Richette², L. Gossec³, A. Marchesoni⁴, C. T. Ritchlin⁵, K. Kato⁶, E. McDearmon-Blondell⁶, E. Lesser⁶, R. Mccaskill⁶, D. Feng⁶, J. Anderson⁶, E. Ruderman⁷. ¹School of Medicine, Griffith University, Brisbane, Australia; ²Service de Rhumatologie, Hôpital Lariboisière Centre Viggo Petersen and Inserm UMR1132 Bioscar, Université Paris Diderot UFR de Médecine, Paris, France; ³Sorbonne Université, Pitié Salpêtrière Hospital, Paris, France; ⁴ASST Gaetano, Pini-CTO, Milan, Italy; ⁵Allergy, Immunology and Rheumatology Division, Center for Musculoskeletal Medicine, University of Rochester Medical Center, Rochester, United States of America; ⁶AbbVie Inc., Rheumatology, North Chicago, United States of America; ⁷Northwestern University, Feinberg School of Medicine, Chicago, United States of America

Background: Approximately 40% of PsA patients (pts) on advanced therapy are on monotherapy.^{1,2} Upadacitinib (UPA) showed efficacy and safety in pts with active PsA in the Phase 3 SELECT-PsA 1 and SELECT-PsA 2 clinical trials.^{3,4}

Objectives: Assess efficacy and safety in subgroups of pts treated with UPA as monotherapy or in combination with non-biologic disease-modifying antirheumatic drugs (non-bDMARDs).

Methods: The SELECT-PsA program enrolled pts with prior inadequate response (IR) or intolerance to ≥ 1 non-bDMARD (N=1705) and prior IR or intolerance to ≥ 1 bDMARD (N=642). Data from both trials was integrated for pts receiving placebo (PBO), UPA 15mg once daily (QD) and UPA 30mg QD. Stable background treatment of ≤ 2 non-bDMARDs was permitted, but not required. Analysis includes UPA monotherapy vs combination therapy for endpoints: ACR20/50/70 responses and change from baseline in pain and HAQ-DI (Wk 12); Static Investigator Global Assessment of Psoriasis of 0 or 1 and at least a 2-point improvement from baseline and PASI75/90/100 responses (Wk 16); proportion of pts achieving resolution of enthesitis, dactylitis, and minimal disease activity (Wk 24). Binary outcomes, using the Cochran-Mantel-Haenszel-method and continuous outcomes, using mixed-effects model, were analyzed for repeated measures in the subgroups of UPA monotherapy and combination therapy. Point estimates and 95% confidence intervals (CIs) of PBO subtracted treatment effect were calculated. Treatment-emergent adverse events (TEAEs) were analyzed.

Results: Of 1916 pts, 574 (30%) received monotherapy and 1342 (70%) received combination therapy; 84% in combination therapy group received MTX +/- another non-bDMARD. Both UPA monotherapy and combination therapy led to improvements in efficacy vs PBO and across endpoints, for each dose, generally consistent point estimates of PBO subtracted treatment effect and associated overlapping CIs were observed (Figure 1). Generally, frequency of AEs and serious AEs, were comparable with UPA administered as monotherapy and combination therapy (Table 1). Frequency of AEs of serious infections and hepatic disorder were lower with monotherapy while frequency of AEs leading to discontinuation of study drug were lower with combination therapy. Most hepatic disorders were transient transaminase elevations.

Conclusion: In the SELECT PsA trials, efficacy and safety of UPA was generally consistent when administered as monotherapy or when given in combination with non-bDMARDs. Results from this analysis support the use of UPA with or without concomitant non-bDMARDs.

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POS1036

COLLAGEN TURNOVER MARKERS ARE ASSOCIATED WITH ACTIVE PSORIATIC ARTHRITIS AND DECREASE WITH GUSELKUMAB TREATMENT IN A PHASE-3 CLINICAL TRIAL

G. Schett¹, M. J. Loza², A. Palanichamy², O. Fitzgerald³, C. T. Ritchlin⁴, F. Barbaud², K. Sweet². ¹Friedrich Alexander University Erlangen-Nuremberg and