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SUSTAINED IMPROVEMENTS WITH UP TO 104 WEEKS OF APREMILAST MONOTHERAPY IN BIOLOGIC-NAÏVE SUBJECTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS FROM A PHASE 3B, RANDOMISED, CONTROLLED TRIAL

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Background: ACTIVE is the first apremilast (APR) study to demonstrate onset of response to APR starting at Week 2 in biologic-naïve subjects with psoriatic arthritis (PsA) who may have had exposure to 1 prior conventional disease-modifying anti-rheumatic drug.

Objectives: To determine the efficacy and safety of APR through Week 104 in the ACTIVE study.

Methods: Subjects were randomised (1:1) to receive APR 30 mg BID or placebo (PBO) for 24 weeks; thereafter, all subjects received active treatment with APR. The long-term durability of APR treatment on various PsA manifestations was evaluated. Along with safety data, adverse events (AEs) of diarrhoea were further characterised.

Results: A total of 219 subjects were randomised (APR: n=110; PBO: n=109); 89% (142/160) of subjects entering year 2 of the study completed the Week 104 visit, and 64.8% (142/219) of randomised subjects completed the Week 104 visit, including 60.9% (67/110) of subjects randomised to APR at baseline. Early onset of response to APR was observed for ACR20 response and improvements in DAS-28 (CRP), HAQ-DI, enthesitis (in subjects with enthesitis at baseline), and morning stiffness severity. With continued APR exposure, the Week 104 ACR20 response rate was 62.9%; ACR50 and ACR70 response rates were 33.3% and 20.1%, respectively. Mean percent change in swollen joint count was -75.9%, and mean percent change in tender joint count was -68.3%. In all, 65.7% of APR subjects with baseline enthesitis reached a Gladman Enthesitis Index score of 0 (table 1). More than half of the APR subjects had improvements in morning stiffness severity. Sustained improvements in physical function were also observed, with a mean change of 5.9 in the SF-36v2 Physical Functioning score and a mean change in HAQ-DI score of -0.37 at Week 104. Safety findings for the APR-exposure period were consistent with previous reports. The most commonly reported AEs ($\geq 5\%$ of subjects) during the APR-exposure period were bronchitis (5.3%), headache (6.3%), hypertension (6.3%), nasopharyngitis (8.3%), upper respiratory tract infection (8.3%), nausea (8.7%), and diarrhoea (16.5%). New incidences of protocol-defined diarrhoea (≥ 2 watery/liquid stools/day) decreased during long-term APR exposure. Over the APR-exposure period, serious AEs occurred in 7.3% of subjects; 8.3% of subjects discontinued treatment due to an AE. No serious opportunistic infections, including tuberculosis reactivation, or cases of serious depression were seen.

	Week 52 APR 30 mg BID n=171	Week 104 APR 30 mg BID n=144
ACR20, n/m (%)	107/169 (63.3)	90/143 (62.9)
ACR50, n/m (%)	55/170 (32.4)	48/144 (33.3)
ACR70, n/m (%)	24/171 (14.0)	29/144 (20.1)
DAS-28 (CRP), mean change	-1.58	-1.66
Swollen joint count (0-76), mean % change	-74.5	-75.9
Tender joint count (0-78), mean % change	-65.6	-68.3
Gladman Enthesitis Index score (0-6)*, mean change	-1.5	-1.5
Gladman Enthesitis Index score=0*, n/m (%)	54/86 (62.8)	46/70 (65.7)
Improvement in morning stiffness severity, n/m (%)	98/171 (57.3)	79/144 (54.9)
SF-36v2 Physical Functioning score, mean change	5.5	5.9
HAQ-DI score (0-3), mean change	-0.36	-0.37
HAQ-DI MCID ≥ 0.30 , n/m (%)	78/171 (45.6)	68/144 (47.2)

Abstract AB0943 – Figure 1

Week 52 and Week 104 analyses were data as observed among all subjects who received APR, regardless of when APR treatment started (baseline, Week 16 or Week 24); actual number of subjects may vary for each end point depending on availability of data.

*Evaluated in subjects with enthesitis at baseline (Gladman Enthesitis Index score >0).

ACR20/50/70= $\geq 20\%/ \geq 50\%/ \geq 70\%$ improvement in modified American College of Rheumatology response criteria; n/m=number of responders/number of subjects with sufficient data for evaluation; DAS-28=28 joint count Disease Activity Score; CRP=C reactive protein; SF-36v2=36 item Short-Form Health Survey version 2; HAQ-DI=Health Assessment Questionnaire-Disability index; MCID=minimal clinically important differences.

Conclusions: In biologic-naïve subjects treated with APR, early onset of effect was observed across PsA manifestations, including morning stiffness severity and enthesitis, with sustained improvements through Week 104 in the subjects continuing APR therapy. AEs were consistent with those reported for other APR phase 3 PsA and psoriasis studies.

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EFFICACY AND SAFETY OF IXEKIZUMAB WHEN USED ALONE OR IN COMBINATION WITH CONVENTIONAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (CDMARDs) IN TNF-EXPERIENCED PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Registry studies^{1,2} suggest that cDMARDs do not improve TNFi efficacy in the treatment of psoriatic arthritis (PsA), but studies of novel biologics are warranted. In SPIRIT-P2, TNFi-experienced patients with active PsA were treated with ixekizumab (IXE), a high-affinity monoclonal antibody that selectively targets IL-17A.

Objectives: We conducted post-hoc analyses of SPIRIT-P2 data to investigate the efficacy and safety of IXE relative to placebo (PBO) when used alone or in combination with background MTX or cDMARDs in patients with PsA.

Methods: SPIRIT-P2 (NCT02349295) is a phase 3, multi-centre, randomised, double-blind, placebo-controlled trial of IXE in adults with active PsA and prior TNFi-inadequate response or intolerance. Patients were randomised 1:1:1 to receive PBO, 80 mg IXE either every 4 weeks (Q4W) or every 2 weeks (Q2W), after receiving a 160 mg initial IXE dose. Eligible established background cDMARD therapy was allowed in the double-blind treatment period (Week 0–24), but no changes were allowed unless for safety reasons or due to inadequate response at week 16. Efficacy and safety were assessed at week 24. Efficacy outcome measurements included ACR 20/50 responses, achievement of minimal disease activity (MDA), 28-joint disease activity score using CRP (DAS28-CRP), disease activity in psoriatic arthritis (DAPSA), and HAQ-DI. All comparisons were made relative to PBO by Fisher's exact test for categorical end points and analysis of covariance models for continuous end points.

Results: At baseline, 185 (51%) patients received background cDMARDs. Of these patients, 149 received background MTX. ACR20, ACR50, and MDA response rates were significantly higher in patients treated with IXE versus PBO regardless of background cDMARD use (table 1). Disease activity improved significantly with IXE versus PBO in each subgroup, as measured by DAS28-CRP and DAPSA. Likewise, physical function improved with IXE versus PBO as indicated by significantly more profound decreases in HAQ-DI with IXEQ4W with or without background cDMARDs, and with IXEQ2W monotherapy. HAQ-DI improvements were significantly more profound versus PBO in patients treated with IXEQ4W with or without background cDMARDs, and with IXEQ2W monotherapy. Among IXE treated patients, higher proportions of patients achieved HAQ-DI MCID in all subgroups versus PBO, but these were only significantly higher in patients treated with IXEQ4W or IXEQ2W monotherapy. Regardless of background cDMARD use, efficacy outcomes were significantly improved with both IXE groups versus PBO, except for HAQ-DI for IXEQ2W in combination with cDMARDs and HAQ-DI MCID in all background cDMARD subgroups. The proportions of patients who experienced ≥ 1 treatment emergent adverse events (AE), serious AEs (including serious infections), or discontinuations due to AEs were comparable to the overall trial population.³