SUSTAINED IMPROVEMENTS WITH UP TO 104 WEEKS OF APREMILAST MONOTHERAPY IN BIOLOGIC-NAIVE 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-naive subjects with psoriatic arthritis (PsA) who never 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 of –0.37 at Week 104. Safety findings for the APR-exposure period were consistent with previous reports. The most commonly reported AEs (>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 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.

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=–20%/50%/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 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-naive 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 IFEKIZUMAB 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 studies1,2 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, TNF-experience 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. IXEQ4W 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

Abstract AB0944

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

ACR20/50/70=–20%/50%/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 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-naive 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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Scientific Abstracts

secukinumab efficacy in patients with active psoriatic arthritis: pooled analysis of four phase 3 trials by prior anti-TNF therapy and concomitant methotrexate use

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Background: Secukinumab has demonstrated rapid, significant and sustained improvement in the signs and symptoms of psoriatic arthritis (PsA) in multiple Phase 3 studies.1,2

Objectives: To report pooled efficacy results for secukinumab versus placebo at Week (Wk) 16 in PsA patients (pts) by previous anti-TNF therapy and with or without concomitant methotrexate (MTX) use from four Phase 3 studies: FUTURE 2, FUTURE 3, FUTURE 4 and FUTURE 5.

Methods: Overall, 397, 414, 341, and 996 pts with active PsA were randomised to receive subcutaneous (s.c.) 300 mg and 150 mg administered at baseline (BL) with loading doses at Wks 1, 2, and 3, followed by maintenance doses every 4 wks (q4w) starting at Wk 4. Data collected up to Wk 16 were pooled. Assessments included ACR20/50/70, DAS28-28 CRP, PASI 75/90, SF-36 PCS, HAQ-DI, and resolution of dactylitis, and enthesis.

Results: A total of 2049 pts were included in the analysis, of which 461, 572, 335, and 681 pts received secukinumab 300 mg, 150 mg, 150 mg without load and placebo, respectively. Improvements were observed with secukinumab vs placebo for all endpoints at Wk 16 in both anti-TNF-naive and anti–TNF-IR pts and in pts with and without concomitant MTX use. Higher ACR and PASI responses and greater improvement of disease activity were observed in anti–TNF-IR pts compared to anti–TNF-IR pts. Secukinumab 300 mg provided numerically higher ACR and PASI responses compared to the 150 mg dose particularly for anti–TNF-IR pts in pts with no concomitant MTX use. Earlier responses were observed with secukinumab with load compared to without load primarily across ACR, DAS28-28 CRP and PASI endpoints.

Conclusions: Secukinumab provided improvements in the signs and symptoms of active PsA regardless of previous anti-TNF therapy or concomitant MTX use. Higher response rates were generally observed in anti–TNF-naive pts compared to anti–TNF-IR pts. Secukinumab 300 mg was associated with higher responses compared to 150 mg particularly in anti–TNF-IR pts and in pts with no concomitant MTX use.

REFERENCES:


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