Objectives: To describe the long-term (5 year) efficacy and safety of APR monotherapy in DMARD-naïve subjects with active PsA from the phase 3 PALACE 4 study.

Methods: Subjects were randomised (1:1:1) to receive placebo, APR 30 mg BID (APR30), or APR 20 mg BID (APR20). At Week 16, subjects were eligible for early escape; placebo subjects were re-randomised to APR treatment, and APR subjects remained on their assigned dose. At Week 24, all subjects remaining on placebo were re-randomised to APR. Double-blind treatment continued to Week 52, with open-label APR treatment for up to 4 additional years.

Results: A total of 527 subjects were randomised and received ≥ 1 dose of placebo (n=176), APR30 (n=176), or APR20 (n=175). Among subjects randomised to APR30 at baseline, 45.5% (80/176) completed the Week 260 visit. At Week 52, modified ACR20, ACR50, and ACR70 responses were achieved by 58.0%, 29.8%, and 15.5% of subjects receiving APR30, respectively, regardless of when APR was started (baseline, Week 16, or Week 24). Rates of improvement in PsA signs and symptoms and physical function were sustained up to Week 260 with continued APR30 treatment, including reduction rates in SJC of 84.8% and in TJC of 76.4% (table 1). At Week 260, 65.8%, 39.0%, and 20.3% of subjects achieved a modified ACR20, ACR50, and ACR70 response, respectively, and 71.2% of APR30 subjects with baseline enthesitis achieved a MASES of 0; 95.1% with baseline dactylitis achieved a dactylitis count of 0. At Week 260, 52.9% of subjects achieved a HAQ-DI MCID ≥ 0.35 , 60.3% achieved a PASI-50 response, and 47.6% achieved a PASI-75 response (table 1). No new safety concerns were identified with APR up to 260 weeks. During Weeks>208 to $\leq$ 260, the most common adverse event (AEs) among APR30-exposed subjects was nasopharyngitis (6.9%). Serious AEs occurred in 5 APR30 subjects; serious infections were reported in 2 APR30 subjects (pelvic abscess and bacterial urinary tract infection), and no opportunistic infections were reported during Weeks>208 to $\leq$ 260.

Abstract AB0905 – Table 1

	Outcomes at Week 260
	APR30 n=119*
ACR20, n/m [§] (%)	77/117 (65.8)
ACR50, n/m [§] (%)	46/118 (39.0)
ACR70, n/m [§] (%)	24/118 (20.3)
SJC, mean % change	-84.8
TJC, mean % change	-76.4
MASES of 0, n/m (%) [‡]	47/66 (71.2)
Dactylitis count of 0, n/m (%) [‡]	58/61 (95.1)
HAQ-DI (0-3), mean change	-0.38
HAQ-DI MCID $\geq 0.35^{\dagger}$, n/m (%)	63/119 (52.9)
PASI-50, n/m (%) [¶]	38/63 (60.3)
PASI-75, n/m (%) [¶]	30/63 (47.6)

Conclusions: APR monotherapy demonstrated sustained response or improvements in PsA signs and symptoms, including SJC and TJC, enthesitis, dactylitis, physical function, and psoriasis in the population of subjects continuing treatment over 260 weeks. APR continued to demonstrate a favourable safety profile and was generally well tolerated.

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AB0906 IXEKIZUMAB IMPROVES FATIGUE IN A SUBSET OF PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is a chronic, systemic, inflammatory disease with both articular and extra-articular symptoms including joint pain, enthesitis, dactylitis, and fatigue. Fatigue is increasingly recognised as a priority symptom to patients and has been added to the PsA core set of outcomes for clinical trials.¹ The best instrument to assess fatigue has not yet been defined.

Objectives: To assess fatigue improvement following treatment with ixekizumab (IXE), an anti-interleukin (IL)-17A monoclonal antibody, relative to placebo (PBO) in PsA patients.

Methods: In two phase 3 randomised controlled trials, patients naïve to and experienced with biologic disease-modifying antirheumatic drugs (SPIRIT-P1, SPIRIT-P2, respectively) received subcutaneous PBO, ADA 40 mg every 2 weeks (SPIRIT-P1 only; reference arm), or IXE 80 mg every 2 weeks (Q2W) or every 4 weeks (Q4W) after a 160 mg starting dose for up to 24 weeks. At Week 16, all patients considered inadequate responders (IR) received rescue therapy. PBO and ADA patients were re-randomised (1:1) to Q2W or Q4W at Week 16 (IR) or Week 24; ADA patients underwent a washout prior to IXE treatment. Patients rated their worst level of fatigue during the past 24 hours at baseline, Week 4, 12, 16, 24, 32, and 52 on the 11-point Fatigue Severity Numeric Rating Scale (Fatigue NRS; not yet validated) where 0=no fatigue and 10=as bad as you can imagine. The minimal clinically important difference (MCID) was defined as an improvement ≥ 3 on the Fatigue NRS.

Results: At Week 24 significantly more patients in both studies achieved fatigue improvements ≥ 3 on the Fatigue NRS with both IXE doses versus PBO (table 1; NRI). When evaluating group level changes, statistically significant improvements on the Fatigue NRS were observed with both IXE doses versus PBO prior to Week 24 in both studies. At Week 24, significance was observed in the SPIRIT-P2 study only (table 1; MMRM). For patients who continued IXE treatment beyond Week 24, mean improvements on the Fatigue NRS persisted through Week 52 (table 1; MI).

Table 1

	SPIRIT-P1				SPIRIT-P2		
	PBO n=106	ADA n=101	Q4W n=107	Q2W n=103	PBO n=118	Q4W n=122	Q2W n=123
Baseline fatigue mean (SD)	5.37 (2.22)	5.45 (2.34)	5.76 (2.29)	5.52 (2.44)	5.9 (2.28)	5.9 (2.48)	6.0 (2.49)
Change from baseline at Week 24 ^a	-1.3 (0.25)	-1.5 (0.24)	-1.6 (0.24)	-1.9 (0.24)	-0.7 (0.37)	-2.0 (0.35)	-2.1 (0.34)
LS mean (SE)						**	**
Number (%) of patients achieving MCID at Week 24 ^{b,c}	19 (20.4)	28 (32.9)	35 (36.8)*	34 (40.5)*	6 (5.6)	33 (30.8)	36 (33.6)
Change from baseline at Week 52 ^d mean (SE)			-2.2 (0.28)	-2.3 (0.28)		-2.2 (0.24)	-2.2 (0.27)

^aMixed models repeated measures (MMRM) analysis was used to calculate change from baseline.

^bAnalysis of patients with Fatigue NRS ≥ 3 at baseline. SPIRIT-P1: PBO, n=93; ADA, n=85; Q4W, n=95; Q2W, n=84. SPIRIT-P2: PBO, n=108; Q4W, n=107; Q2W, n=107.

^cNonresponder imputation (NRI) was used to impute missing data based on logistic model.

^dMultiple imputation (MI) was used to impute missing data.

*p<0.05 vs PBO; **p<0.001 vs PBO.

Conclusions: In a subset of PsA patients, clinically meaningful improvements in fatigue level were observed following IXE treatment. Fatigue improvement persisted with up to 1 year of IXE treatment.

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