secondary endpoints were PASI 75 and ACR 50 responses, change from baseline in HAQ-DI, and improvement in enthesitis (Leeds enthesitis index) and dactylitis score (by a 0–3 scoring system) at wk24; and ACR 20 response at wk16. Other secondary endpoints included change from baseline in SF-36 and proportion of pts achieving Minimal Disease Activity (MDA). Through wk24, efficacy analyses were performed in a modified Intent-to-Treat (mITT) population. Pts who met treatment failure criteria, early escaped or had missing data at wk24, were considered non-responders for ACR and MDA endpoints at wk24.

Results: 149 pts were randomized to receive study agent (PBO: 49, GUS: 100). Baseline demographics and ACR component measures were generally similar between the two groups. Four [8.2%] pts in PBO and 9 [9.0%] pts in GUS were previously exposed to TNF α agents. The study met its primary and all secondary endpoints. Significantly more GUS pts achieved ACR 20/50/70 responses and PASI 75/90/100 responses at wk24 (Table 1). Significant treatment effect on ACR20 response was observed as early as wk4 (21% vs 0, $p<0.001$), and the effect increased over time reaching the maximum by wk16 (60.0% vs. 16.3%, $p<0.001$) vs. PBO. Results for other secondary efficacy endpoints are summarized in Table 1.

Through wk24, proportions of pts with ≥ 1 AE were comparable between the two groups (PBO: 32.7%; GUS: 36.0%, respectively). Infections were the most common AEs (PBO: 20.4%; GUS: 17.0%, respectively). Two pts had SAEs (knee injury, $n=1$; myocardial infarction, $n=1$). There were no serious infections, malignancies, or deaths through wk24.

Efficacy Endpoints	PBO	GUS	p-value
ACR 20	18.4%	58.0%	$p<0.001$
ACR 50	10.2%	34.0%	$p=0.002$
ACR 70	2.0%	14.0%	$p=0.023$ (post hoc)
PASI 75	12.5%	78.6%	$p<0.001$
PASI 90	6.3%	66.3%	$p<0.001$
PASI 100	6.3%	39.8%	$p<0.001$
Mean (SD) change from BL in HAQ-DI score	-0.06 (0.53)	-0.42 (0.51)	$p<0.001$
Median % change from BL in LEI ^b	-33.33%	-100.00%	$p=0.009$
% of pts with unresolved enthesitis ^b	71.0%	43.4%	$p=0.012$
Median % change from BL in dactylitis ^c	-33.33%	-100.00%	$p<0.001$
% of pts with unresolved dactylitis ^c	82.6%	44.8%	$p<0.001$
Mean (SD) change from BL in SF-36 PCS score	0.46 (6.51)	6.59 (7.47)	$p<0.001$
Mean (SD) change from BL in SF-36 MCS score	0.42 (6.74)	4.95 (9.06)	$p=0.002$
% of pts achieving Minimal Disease Activity	2.0%	23.0%	$p=0.001$
Mean (SD) change from BL in PASDAS	-0.49 (1.33)	-2.50 (1.59)	$p<0.001$
Mean (SD) change from BL in GRACE Index	-0.35 (1.39)	-2.73 (1.76)	$p<0.001$
Mean (SD) change from BL in mCPDAI	-0.8 (2.26)	-3.9 (2.79)	$p<0.001$
Mean (SD) change from BL in DAPSA	-4.97 (20.11)	-23.08 (20.21)	$p<0.001$

*All pts randomized into the study, received at least 1 administration of study treatment (GUS or PBO), and were analyzed according to their assigned treatment group regardless of their actual treatment received; ^bAmong the pts with enthesitis at baseline (PBO: $N=31$; GUS: $N=76$); ^cAmong the pts with dactylitis at baseline (PBO: $N=23$; GUS: $N=58$); LEI: Leeds Enthesitis Index; PCS: Physical Component Score, MCS: Mental Component Score, PASDAS: Psoriatic Arthritis Disease Activity Score, GRACE: GRAPPA Composite score, mCPDAI: modified Composite Psoriatic Disease Activity Index, DAPSA: Disease Activity Index for Psoriatic Arthritis, BL: Baseline

Conclusions: In pts with active PsA and $\geq 3\%$ BSA of psoriasis, GUS demonstrated significant improvement on joint symptoms, physical function, psoriasis, enthesitis, dactylitis and quality of life. GUS was well tolerated with no unexpected safety findings in this population.

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OP0219 **EARLY ONSET OF EFFICACY WITH APREMILAST MONOTHERAPY IN BIOLOGIC-NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: A PHASE 3B, RANDOMIZED, CONTROLLED TRIAL**

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Background: ACTIVE is the first apremilast (APR) trial to evaluate time to onset of efficacy beginning at Wk 2 in biologic-naïve psoriatic arthritis (PsA) patients (pts) who may have had exposure to 1 prior conventional DMARD.

Objectives: Report the study results through Wk 52.

Methods: Pts were randomized (1:1) to APR 30 mg BID or placebo (PBO). Pts were eligible for early escape (investigator discretion) at Wk 16. At Wk 24, all pts entered active treatment with APR. The primary endpoint was ACR20 response at Wk 16. Other assessments included changes in DAS-28 (CRP), SJC, TJC, HAQ-DI, morning stiffness duration/severity, and enthesitis, as measured by the Gladman Enthesitis Index (GEI; 0=no enthesitis, 6=all 6 sites active). Along with collection of safety data, tolerability adverse events (AEs) of diarrhea were further characterized.

Results: 219 pts were randomized (APR: $n=110$; PBO: $n=109$); overall, 160/180 (88.9%) pts receiving APR completed Wk 52. Separation in the proportion of ACR20 responders to APR vs PBO was noted at Wk 2 (16.4% vs 6.4%; $P=0.0252$), the first post-baseline (BL) visit. Early onset of response to APR was observed across clinical assessments, with improvements in DAS-28 (CRP), SJC, HAQ-DI, enthesitis, and morning stiffness severity (Table). At Wk 16, significant ACR20 response rates were observed with APR vs PBO (38.2% vs 20.2%; $P<0.005$), with similar rates for the subset of pts with use of 1 prior non-biologic DMARD (39.2% vs 20.5%; $P<0.05$), which comprises 69% of study pts. Significant reductions in PsA disease activity/manifestations vs PBO were also demonstrated by changes in DAS-28 (CRP) ($P<0.0001$), SJC, and HAQ-DI ($P=0.0229$), and improvements in morning stiffness severity and GEI score ($P=0.0014$). With continued APR exposure, the Wk 52 ACR20/ACR50/ACR70 response rates were 63.3%/32.4%/14.0%, and percent change in SJC was -74.5%. Among APR pts with BL enthesitis, 62.8% reached a GEI score of 0. Overall incidence of AEs in the PBO-controlled period was generally similar between APR and PBO. The most commonly reported AEs ($\geq 5\%$ of pts) with APR vs PBO were nasopharyngitis (8.3% vs 6.4%), nausea (8.3% vs 1.8%), headache (7.3% vs 3.7%), hypertension (6.4% vs 6.4%), and diarrhea (pt or investigator reported) (14.7% vs 11.0%); using a protocol-defined characterization of diarrhea (≥ 2 watery/liquid stools/day), overall incidence was lower for APR and PBO (11.0% and 8.3%). Serious AEs were lower with APR vs PBO (2.8% vs 4.6%). No opportunistic infections, reactivations of TB, or cases of marked depression were seen. In general, no increase was seen in AE incidence/severity with longer-term exposure to APR.

	Wk 2		Wk 16		Wk 52
	APR $n=110$	PBO $n=109$	APR $n=110$	PBO $n=109$	APR $n=171$
ACR20, n/m (%)	18/110 (16.4)*	7/109 (6.4)	42/110 (38.2)†	22/109 (20.2)	107/169 (63.3)
DAS-28 (CRP), mean change	-0.59* (16.4)*	-0.31 (6.4)	-1.07* (38.2)†	-0.39 (20.2)	-1.58 (63.3)
SJC, mean % change	-27.7 (16.4)*	-17.5 (6.4)	-46.4* (38.2)†	4.2 (20.2)	-74.5 (63.3)
HAQ-DI score (0-3), mean change	-0.13* (16.4)*	-0.05 (6.4)	-0.21* (38.2)†	-0.06 (20.2)	-0.36 (63.3)
HAQ-DI MCID ≥ 0.30 , n/m (%)	24/110 (21.8)	13/109 (11.9)	39/110 (35.5)	30/109 (27.5)	78/171 (45.6)
SF-36v2 PF score, mean change	NA	NA	2.43‡	-1.04	5.5
Improvement in morning stiffness severity, n/m (%)	47/110 (42.7)‡	23/109 (21.1)	51/110 (46.4)‡	28/109 (25.7)	98/171 (57.3)
GEI score (0-6), mean change*	-1.1*	-0.4	-1.5‡	-0.4	-1.5

Full analysis set was used for Wk 2 and Wk 16; for response parameters, pts without sufficient data (observed and imputed) for the determination of response status were categorized as non-responders. Wk 52 analyses were data as observed among all pts who received apremilast, regardless of when apremilast treatment started (BL, Wk 16 or Wk 24); actual number of pts may vary for each end point depending on availability of data.

*Evaluated in pts with enthesitis at BL (GEI >0).

† $P<0.05$; ‡ $P<0.005$; § $P<0.0001$ vs PBO; based on a mixed-effects model for repeated measures for continuous parameters and a Cochran-Mantel-Haenszel test for binary parameters.

APR=apremilast 30 mg BID; PBO=placebo; ACR20=20% improvement in American College of Rheumatology response criteria; n/m=number of responders/number of pts with sufficient data for evaluation; DAS-28 (CRP)=28-joint count Disease Activity Score (C-reactive protein); SJC=swollen joint count; HAQ-DI=Health Assessment Questionnaire-Disability Index; MCID=minimal clinically important differences; SF-36v2 PF=36-item Short-Form Health Survey version 2 Physical Functioning domain; NA=not assessed at time point; GEI=Gladman Enthesitis Index; pts=patients; BL=baseline.

Conclusions: In biologic-naïve pts treated with APR, onset of effect was observed starting at Wk 2 across PsA manifestations, including morning stiffness severity and enthesitis, with sustained improvements through Wk 52. AEs were consistent with those reported for other APR phase 3 PsA and psoriasis studies.

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