16. ***Apremilast, an Oral Phosphodiesterase 4 Inhibitor, Is Associated With Long-term (104-Week) Improvement in Fatigue in Patients With Psoriatic Arthritis: Pooled Results From 3 Phase III, Randomized, Controlled Trials.***

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Fatigue commonly affects individuals with psoriatic arthritis (PsA) and is associated with decreased quality of life and loss of work productivity. The PALACE 1 (NCT01172938), 2 (NCT01212757), and 3 (NCT01212770) studies compared the efficacy and safety of apremilast (APR), including fatigue level, with placebo in patients with active PsA despite prior conventional disease-modifying anti-rheumatic drugs (DMARDs) and/or biologics. We report data over 104 weeks from a pooled analysis of PALACE 1-3.
Patients were randomized (1:1:1) to receive placebo, APR 30 mg BID (APR30), or APR 20 mg BID (APR20) stratified by baseline DMARD use (yes/no). The placebo-controlled phase continued to Week 24, with an early escape option at Week 16. At Week 24, all remaining placebo patients were re-randomized to APR30 or APR20. Double-blind APR treatment continued to Week 52; patients could then continue to receive open-label APR up to an additional 4 years. Fatigue was assessed using FACIT-F version 4 scores (FACIT-F range: 0-52; lower scores denote higher levels of fatigue; minimal clinically important differences [MCID]: ≥3.56) and SF-36 Vitality domain (SF-36 VT) scores (MCID: ≥2.5).
Baseline mean FACIT-F (range: 29.4-30.9) and SF-36 VT (range: 40.6-40.8; norm-based) scores among the treatment groups were below population norms (i.e., FACIT-F: 40.1-43.6; SF-36 VT: 50.0). At Week 16, with APR30 treatment, significantly greater improvement in FACIT-F (APR30: 3.45, P<0.0001; APR20: 1.47) and SF-36 VT (APR30: 3.06, P=0.0006; APR20: 1.59) scores were observed compared with placebo (1.14 and 1.20, respectively). Long-term improvements in FACIT-F scores were observed in APR30 patients at Weeks 52 and 104 (mean change: 4.8 and 5.6, respectively). At Week 104, improvement in fatigue was maintained with a mean FACIT-F of 35.0, and 50.9% of patients receiving APR30 reported a clinically meaningful improvement. Similarly, improvements in SF-36 VT scores were observed in APR30 patients at Weeks 52 and 104 (mean change: 4.7 and 5.6, respectively). At Week 104, with APR30 treatment, mean SF-36 VT score was 46.5, and 61.7% of patients achieved the SF-36v2 VT MCID. Over 104 weeks, most adverse events were mild to moderate in severity; in general, no increase was seen in the incidence or severity of adverse events with longer term exposure.
APR-treated patients experienced improvements in fatigue, as measured by FACIT-F and SF-36 VT scores. Over 104 weeks, clinically meaningful improvements were maintained. APR demonstrated an acceptable safety profile and was generally well tolerated up to 104 weeks.

APR was effective in improving nail and scalp psoriasis and skin involvement, with maintenance of these improvements over time. The safety profile is consistent with the known safety profile for APR.