12. Apremilast, an Oral Phosphodiesterase 4 Inhibitor, Is Associated With Long-term (52-Week) Improvements in Enthesitis and Dactylitis in Patients With Psoriatic Arthritis: Pooled Results From Three Phase III, Randomized, Controlled Trials.

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Background: The PALACE 1, 2, and 3 trials compared the efficacy and safety of apremilast (APR) with placebo in patients with active psoriatic arthritis (PsA) despite prior conventional disease-modifying antirheumatic drugs (DMARDs) and/or biologics.

Methods: Patients were randomized (1:1:1) to placebo, APR 30 mg BID (APR30), or APR 20 mg BID (APR20) stratified by baseline DMARD use (yes/no). Patients whose swollen and tender joint counts had not improved ≥20% at Week 16 were considered non-responders and were required to be re-randomized (1:1) to APR30 or APR20 if they were initially randomized to placebo, or continued on their initial APR dose. At Week 24, all remaining placebo patients were re-randomized to APR30 or APR20. The current analysis utilizes data from Weeks 0 to 52 pooled across PALACE 1-3.

Results: APR administration resulted in statistically significant and clinically meaningful improvements in ACR20 response at Week 16 (primary endpoint) in all 3 PALACE trials. In patients initially randomized to APR and with enthesitis (n=634) or dactylitis (n=428) at baseline, APR was associated with improvements in enthesitis and dactylitis severity over 52 weeks, as evidenced by reductions in Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) and dactylitis count. At Week 16, mean percent changes in MASES were -10.5% for placebo, -17.5% for APR30 (P=0.2435), and -14.6% for APR20 (P=0.5418) patients. In patients initially randomized to APR and completing 52 weeks, mean percent changes in MASES were -43.2% for APR30 and -43.6% for APR20 patients (baseline mean of 4.3 and 4.4, respectively). At Week 52, a MASES score of 0, indicating no pain at any of the entheses assessed, was achieved by 37.4% of APR30 and 41.4% of APR20 patients. At Week 16, mean percent changes in dactylitis count were -35.3% for placebo, -44.6% for APR30 (P=0.2682), and -38.4% for APR20 (P=0.7595) patients. At Week 52, mean percent changes in dactylitis count were -65.5% for APR30 and -71.2% for APR20 patients (baseline mean of 3.3 and 3.5, respectively). At Week 52, dactylitis counts decreased to 0 in 65.9% of APR30 and 66.9% of APR20 patients. The safety profile of APR through 52 weeks was similar to that observed with APR for up to 24 weeks of treatment (placebo-controlled period).

Conclusion: Over 52 weeks, APR demonstrated efficacy in the treatment of PsA, including improvements in enthesitis and dactylitis. APR demonstrated an acceptable safety profile and was generally well tolerated for ≥52 weeks.