17. Apremilast, an Oral Phosphodiesterase 4 Inhibitor, Is Associated With Long-term (52-Week) Improvement in Swollen and Tender Joint Counts in Patients With Psoriatic Arthritis: Results From Three Phase 3, Randomized, Controlled Trials.

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Background/Purpose: Apremilast, an oral phosphodiesterase 4 inhibitor, works intracellularly to modulate inflammatory mediators. The PALACE 1, 2, and 3 trials compared the efficacy and safety of apremilast with placebo in patients with active psoriatic arthritis (PsA) despite prior conventional DMARDs and/or biologics.

Methods: Patients were randomized 1:1:1 to placebo, apremilast 20 mg BID (APR20), or apremilast 30 mg BID (APR30) stratified by baseline DMARD use (yes/no). Patients whose swollen and tender joint counts (SJC/TJC) had not improved by ≥20% were considered non-responders at Week 16 and were required to be re-randomized (1:1) to APR20 or APR30 if initially randomized to placebo, or continued on their initial apremilast dose. At Week 24, all remaining placebo patients were re-randomized to APR20 or APR30. Patients taking concurrent DMARDs were allowed to continue stable doses (methotrexate, sulfasalazine, leflunomide, or a combination). Given the relative weighting of SJC/TJC in the ACR20 composite index and their clinical importance, we examined these measures across the 3 trials.

Results: Apremilast resulted in statistically significant and clinically meaningful improvements in ACR20 response (primary endpoint) in all 3 PALACE trials. Median percent reductions (improvements) in SJC/TJC in the intent-to-treat population were statistically significant vs. placebo at Week 16 in all 3 trials. SJCs were (placebo, APR20, APR30, respectively): -16.7%, -39.1% (P=0.0060), -50.0% (P<0.0001) (PALACE 1); -33.3%, -50.0% (P=0.0028), -53.9% (P=0.0008) (PALACE 2); and -20.0%, -34.9% (P=0.0393), -50.0% (P=0.0022) (PALACE 3); TJCs were: -9.0%, -24.2% (P=0.0007), -43.2% (P<0.0001) (PALACE 1); -8.7%, -36.2% (P<0.0001), -33.3% (P=0.0031) (PALACE 2); and -7.7%, -29.3% (P=0.0001), -42.9% (P<0.0001) (PALACE 3). In patients receiving apremilast from baseline, improvements in SJC/TJC were observed at Week 52, with SJC improvements with APR20 and APR30 of -78.8 and -77.8% (PALACE 1), -87.5% and -87.5% (PALACE 2), and -80.0% and -79.2% (PALACE 3), and TJC improvements of -69.2% and -62.5% (PALACE 1), -58.3% and 63.1% (PALACE 2), and -66.7% and -70.0% (PALACE 3), respectively. The most common adverse events reported in patients treated with apremilast for up to 24 weeks (PALACE 1-3, pooled) were diarrhea (12.2%), nausea (10.1%), and headache (8.0%). The safety profile of apremilast through 52 weeks was similar to that observed with apremilast for up to 24 weeks of treatment.

Conclusion: Over 52 weeks, apremilast continued to demonstrate efficacy in the treatment of PsA, including clinically meaningful improvements in SJC/TJC. Apremilast demonstrated an acceptable safety profile and was generally well-tolerated through 52 weeks.