11. Laboratory Abnormalities in Patients With Psoriatic Arthritis Receiving Apremilast, an Oral Phosphodiesterase 4 Inhibitor: Pooled Safety Analysis of Three Phase 3, Randomized, Controlled Trials.

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Background: 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. The impact of apremilast on laboratory measurements was assessed in a pooled analysis of PALACE 1, 2, and 3.

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 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. The analysis comprises all data from the apremilast-exposure period (Weeks 0-≥52).

Results: 1,493 patients received ≥1 dose of study medication (placebo: n=495; APR20: n=501; APR30: n=497) and were included in the safety population. The apremilast-exposure period included 720 patients receiving APR20 (766.4 patient-years) and 721 receiving APR30 (769.0 patient-years). Marked abnormalities in clinical chemistry and hematology laboratory parameters were infrequent and comparable across treatment groups, with no meaningful treatment or dose effect noted during the apremilast-exposure periods (Weeks 0-≥24 and Weeks 0-≥52). All marked hematologic abnormalities occurred in a similar percentage of placebo and apremilast patients during the placebo-controlled phase (Weeks 0-24) with no significant changes in rate or severity during the Weeks 0-≥52 vs Weeks 0 to ≥24 apremilast-exposure period. During Weeks 0-≥52 (apremilast-exposure period), 1 patient (APR20) experienced platelets <75 x 109/L; the percentages of patients with hemoglobin <10.5 (male)/<8.5 (female) g/dL were 0.7% (5/712; APR20) and 0.8% (6/713; APR30). Overall, mean changes in clinical chemistry parameters were small and not clinically significant. ALT >3x ULN occurred in 1.1% (8/713; APR20) and 1.3% (9/713; APR30) of patients during Weeks 0-≥52 (apremilast-exposure period). Regardless of concomitant DMARD use, most of the marked abnormal laboratory changes were transient, did not recur despite continuation of study drug, did not lead to study discontinuation, and were not clinically significant requiring specific treatment.

Conclusion: Apremilast demonstrated an acceptable safety profile and was generally well-tolerated through 52 weeks. No clinically meaningful effects on laboratory parameters were noted. These data do not indicate a need for laboratory monitoring with apremilast.