Topical hypericin ointment photodynamic therapy is effective and safe in CTCL (FLASH study)

Additional cutaneous T-cell lymphoma (CTCL) therapies with better short/long term side effects are needed. Topical synthetic hypericin ointment 0.25% (SGX301) activated with external cool-white visible light is a novel, non-mutagenic photodynamic therapy. We conducted a randomized, placebo-controlled, observer-blinded multicenter Phase 3 trial evaluating its efficacy/safety in early stage IA-IIA CTCL across 37 U.S. sites. SGX301 was applied to 3 index lesions twice weekly, 18-24 hours prior to light therapy for a 6-week cycle for 3 treatment cycles. Cycle 1 (169 patients randomized 2:1 SGX301:placebo) and Cycle 2 (all received SGX301) were required; Cycle 3 (index and additional lesions treated with SGX301) was optional. Index lesion response rate (ILRR) and adverse events (AEs) were assessed 2 weeks after each cycle then monthly for 6 months. The trial primary endpoint was ILRR based on the Composite Assessment Index for Lesion Severity (CAILS) score with improvement ≥ 50% over baseline. After Cycle 1, ILRR for SGX301 vs placebo was 16% vs 4% ($p=0.04$). ILRR for subjects who received 2 cycles of SGX301 was 40% ($p<0.0001$) and after Cycle 3, 49% ($P<0.0001$). SGX301 was effective for both patch (42%, $p<0.0001$ after 2 cycles) and plaque (37%, $p=0.0009$) lesions. The most common AEs were Grade 1-2 local application site skin reactions (15% of subjects) and only 1% of subjects discontinued the study due to AEs. No drug-related serious AEs occurred and SGX310 was not found systemically. SGX301 is effective in early stage CTCL with a highly favorable safety profile.