Visible Light Activated Topical Hypericin Ointment in CTCL: FLASH Study Results

We conducted a randomized, placebo-controlled, observer-blinded multicenter Phase 3 trial evaluating the efficacy and safety of a novel photodynamic therapy, topical, 0.25% synthetic hypericin ointment (SGX301) activated with external cool-white visible light, in early-stage cutaneous T-cell lymphoma (CTCL, Stages IA-IIA). 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 (randomized to SGX301 vs placebo) and Cycle 2 (all received SGX301) were required; Cycle 3 (index and additional lesions treated with SGX301) was optional. Index lesion response (ILR) and adverse events (AEs) were assessed 2 weeks after each cycle and then monthly for 6 months. 169 patients were enrolled at 37 U.S. sites. The trial primary endpoint was ILR rate (RR, based on the Composite Assessment Index for Lesion Severity, CAILS, score). After Cycle 1, RRs for SGX301 vs placebo were 16% vs 4% ($p=0.04$). Cycle 2 RR for subjects who received 2 cycles of SGX301 was 40% ($p<0.0001$ vs Cycle 1 SGX301). Subjects who received 3 cycles of SGX301 had a RR of 49% ($p<0.0001$ vs Cycle 1 SGX301). No drug-related serious AEs were seen. 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 systemic absorption of hypericin was detected. The results of this study indicate that photodynamic treatment of early stage CTCL with SGX301 and external visible light is effective and well-tolerated