Patients with systemic sclerosis effectively absorbed oral treprostinil diethanolamine, which produced a temporal association with improved cutaneous perfusion and temperature, according to study results. In a dual-center, open-label, phase 1 study, researchers evaluated 19 patients with systemic sclerosis (SSc; mean age, 48 years; 84.2% women; 89.5% Caucasian; 53% limited SSc). Eleven patients had an active digital ulcer at baseline.

Treprostinil diethanolamine sustained release (SR) was administered to patients with dose titration up to 4 mg twice daily.

Laser Doppler imaging quantified drug concentrations and perfusion, which were measured across 12 hours at 2 mg or 4 mg (or maximally tolerated) doses. Individual plasma concentration vs. time profiles using noncompartmental analysis methods determined pharmacokinetic parameters.

“Digital perfusion and skin temperature were modeled as a function of log-transformed drug concentration and other covariates by performing repeated measures analyses using random effects models,” the researchers wrote.

Sixteen patients completed the 8-week study. Approximately 3.6 hours after administration of treprostinil diethanolamine, peak plasma concentrations reached means of 1,176 pg/mL and 2,107 pg/mL for 2-mg and 4-mg doses, respectively. Overall exposure (AUC from 0 to 12 hours) was linear between doses and observed at 7,187 hr*pg/mL for 2-mg and 12,992 hr*pg/mL for 4-mg doses. Log-transformed plasma at the 4-mg dose had a positive association with perfusion (P=.015) and digital skin temperature (P=.013).

The most common adverse events were headache (89%), diarrhea (47%) and nausea (42%), which were similar to those seen with prostacyclin analogs. No serious adverse events or deaths were reported.

“Currently prostacyclin analogs are administered via intravenous or subcutaneous routes in [systemic sclerosis] patients with vascular complications,” the researchers concluded. “Our data show that oral SR formulation of treprostinil diethanolamine was effectively absorbed in patients with SSc, was associated with improved cutaneous perfusion and temperature with short-term treatment, and may provide a new therapeutic option for Raynaud’s phenomenon and peripheral vascular disease of SSc.”

Source: Helio