

APPENDIX S1

MATERIALS AND METHODS

Study design

This prospective, randomized (1:1), controlled, open-label, non-interventional, dermatocosmetic study was conducted according to ICH-GCP, Declaration of Helsinki, and data protection regulations at the Center for Chronic Pruritus, Department of Dermatology, University Hospital Münster. All subjects gave written informed consent. The local ethics committee approved the trial (2007-452-f-S). The study is registered at the US National Institutes of Health (ClinicalTrials.gov) #NCT00663364.

Population and treatment

Subjects aged ≥ 18 years, with both chronic pruritus (>6 weeks) and clinical presence of dry skin, asking for dry skin treatment and willing to apply skin care, were eligible for this study. Subjects were excluded in case of participation in any other clinical study, in case of known allergy or sensitivity to any of the ingredients of the test products, if employed or otherwise related to the contract research organization or to the sponsor, if requiring topical steroids, or if they had history of cancer, active neoplastic disease or recent immunization (less than 10 days prior to use of the test product).

An independent nurse selected the lowest number from a randomization list, which allocates subjects to 1 of the 2 treatment groups: half of the subjects to receive Physiogel® Daily Moisture Therapy Body Lotion (N-palmitoylethanolamine (PEA)-free; "lotion") and the other half to receive Physiogel® Calming Relief A. I. Body Lotion (containing PEA (S1); "PEA lotion") (both from Stiefel Laboratories, Inc.). Both body lotions were lipid rich and similar in lipid composition. Subjects applied the emollients twice daily for 2 weeks without restriction regarding the treated skin areas (except for face and scalp). There were 3 study visits: baseline and treatment onset (V1), after 2 weeks (V2), and follow-up visit (V3) 2 weeks after the end of treatment. Adherence to treatment was assessed by weighing the tubes returned by the subjects.

Outcomes

Primary outcome variables were sensory symptoms (pruritus, stinging, related quality of life). Secondary variables were cosmetic acceptance of the emollients, patient-defined treatment benefit, dermatological symptoms (roughness, scaling, tightness) and a prurigo score.

Quality of life (QoL) was measured at Day 1 and after end of treatment with the 10-item questionnaire Dermatology Life Quality Index (DLQI); ranging from 0=no impairment to 30=maximum impairment (S2). Patient-defined treatment benefit was measured with the pruritus version of the Patient Benefit Index (PBI-P; ranging from 0=no benefit/not important to 4=helped very much/very important) (S3) at V1 and after end of treatment. Mean itch intensity in the preceding 4 (V1) or 2 weeks (all following visits),

was measured by visual analogue scale (100-mm VAS; ranging from 0=no itch to 10=worst imaginable itch). In addition, a percentage score was used to rate itch intensity changes (0%: no change; 100%: complete relief) at visit 2 and 3 compared with visit 1. Pruritus, stinging, and skin symptoms (roughness, scaling, tightness) were recorded at every visit in the patient documentation sheet via a standardized 5-point verbal rating scale (VRS; ranging from 1=not present to 5=very strong) questionnaire (S4). The following data were also documented on the same sheet: areas treated with lotion; whether twice-daily application of the lotion was sufficient and was followed or not, with reasons; cosmetic properties of the product (spreadability, absorption, smell, cosmetic acceptance (good, medium, bad)); presence of sleeping problems and their development during treatment; and side-effects. Prurigo score was documented at V1 and V2 for those subjects who showed scratch lesions at V1.

Data analysis

Trained personnel entered the data into Excel sheets. The data were checked for plausibility using algorithms, and implausible data were corrected or defined as missing. Analysis was performed for the per-protocol population (using all non-missing data for those subjects who had reported having applied the lotion on a regular basis) and where possible, for the intention-to-treat population with last-observation-carried-forward (LOCF; missing data at V2 were replaced by the subject's data at V1). Unless differently specified, only LOCF results are reported in this publication.

All data were analysed descriptively (number, percentage or mean, standard deviation (SD), minimum, maximum). The outcome parameters were tested for differences between the intervention groups using analysis of variance with repeated measures, *t*-test for independent samples, χ^2 test, Fisher exact test, or Freeman-Halton test, depending on test requirements (number of assessments, level of measurement, and number of cases). Significance level was defined as $p=0.05$ without correction for multiple testing. All analyses were conducted with SPSS 15.0.

SUPPLEMENTARY REFERENCES

1. Patel T, Yosipovitch G. Therapy of pruritus. *Expert Opin Pharmacother* 2010; 11: 1673–1682.
2. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI) – a simple practical measure for routine clinical use. *Clin Exp Dermatol* 1994; 19: 210–216.
3. Blome C, Augustin M, Siepmann D, Phan NQ, Rustenbach SJ, Ständer S. Measuring patient-relevant benefits in pruritus treatment: development and validation of a specific outcomes tool. *Br J Dermatol* 2009; 161: 1143–1148.
4. Phan NQ, Blome C, Fritz F, Gerss J, Reich A, Ebata T, et al. Assessment of pruritus intensity: prospective study on validity and reliability of the visual analogue scale, numerical rating scale and verbal rating scale in 471 patients with chronic pruritus. *Acta Derm Venereol* 2012; 92: 502–507.