We could show DLQI-reduction and improvement in itch and skin dryness. Xerosis decreased gradually, objectified by SCH measurements. The initial pH-increase at day 7 could be attributed to the direct effect of the mineral water with acidity of 6.8. The disease-modifying effects of sulphur in mineral water include keratolytic, antimicrobial and immunomodulation properties.[5,8]

We demonstrated the positive effect of balneotherapy on disease severity, the PROs and functional skin physiology parameters in a time-dependent manner. Skin physiology changes reflect the dynamics of improved SC hydration and gradual normalization of surface pH. The patients' satisfaction together with clinical benefit revealed balneotherapy as effective and safe psoriasis treatment.

Acknowledgements

We thank the medical and logistics team at Dimina Specialized Hospital for physical and rehabilitation medicine, Voneshta Voda, Bulgaria for performing the medical care and balneotherapy procedures to the patients.

Conflicts of interests

None.

Funding source

This prospective study was supported by an unrestricted research grant provided by Laboratoires Pierre Fabre, Bulgaria.

R. Darlenski,[1,2,*] I. Bogdanov,[1] M. Kacheva,[1] D. Zheleva,[1] Z. Demerdjieva,[1] E. Hristakieva,[2] J.W. Fluhr,[3] N. Tsankov[1]

[1]Department of Dermatology and Venereology, Acibadem City Clinic Tokuda Hospital – Sofia, Sofia, Bulgaria, [2]Department of Dermatology and Venereology, Medical Faculty, Trakia University- Stara Zagora, Stara Zagora, Bulgaria, [3]Department of Dermatology and Allergology, Charité Universitätsmedizin, Berlin, Germany

*Correspondence: R. Darlenski. E-mail: darlenski@abv.bg

References

1 Damevska K, Franca K, Lotti T, Nikolovska S, Pollozhani N. Complementary and integrative therapies for psoriasis: looking forward. *Dermatol Ther* 2018; **31**: e12627.
2 Tsankov NK, Kamarashev JA. Spa therapy in Bulgaria. *Clin Dermatol* 1996; **14**: 675–678.
3 Huang A, Seite S, Adar T. The use of balneotherapy in dermatology. *Clin Dermatol* 2018; **36**: 363–368.
4 Zhu Q, Wu Y, Li Y *et al*. Positive effects of hydrogen-water bathing in patients of psoriasis and parapsoriasis en plaques. *Sci Rep* 2018; **8**: 8051.
5 Kazandjieva J, Grozdev I, Darlenski R, Tsankov N. Climatotherapy of psoriasis. *Clin Dermatol* 2008; **26**: 477–485.
6 Wollenberg A, Szepietowski J, Taieb A, Ring J. Corrigendum: Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I. *J Eur Acad Dermatol Venereol* 2019; **33**: 1436.
7 Baros DN, Gajanin VS, Gajanin RB, Zrnic B. Comparative analysis of success of psoriasis treatment with standard therapeutic modalities and balneotherapy. *Med Pregl* 2014; **67**: 154–160.
8 Gambichler T, Skrygan M. Expression of human beta-defensin-2 in psoriatic epidermis models treated with balneophototherapy. *J Eur Acad Dermatol Venereol* 2015; **29**: 169–173.

DOI: 10.1111/jdv.16908

Short- and long-term efficacy of fumaric acid esters or acitretin in combination with a 12-week course of PUVA in the treatment of palmoplantar pustulosis: results from a prospective randomized trial

Dear Editor,

Palmoplantar pustulosis (PPP) is a notoriously difficult-to-treat skin disease characterized by erythematous plaques and sterile pustules confined to the palms and/or soles. In severe or recalcitrant cases, systemic[1] psoralen plus ultraviolet A (PUVA) therapy alone or in combination with systemic retinoids (Re-PUVA)[2–4] was shown to be amongst the most effective treatment modalities for PPP. A small uncontrolled study has provided preliminary evidence that fumaric acid esters (FAE) might be also beneficial for subjects with PPP.[5]

In this prospective, randomized, assessor-blinded study, the safety and efficacy of FAE-PUVA was compared with Re-PUVA in patients with PPP. The results were analysed according to the intention-to-treat principle. The study was approved by the local ethics committee (clinicaltrials.gov identifier number: NCT00811005) and was divided into four phases: initial drug monotherapy phase (2 weeks), clearing phase (up to 12 weeks), maintenance phase (24 weeks) and follow-up phase (24 weeks). The total study duration thus extended over 62 weeks. At study inclusion, the patients were allocated according to a randomized sequence list to either FAE (up to a maximum daily dose of 720 mg dimethylfumarate) or acitretin (50 mg/day) treatment. After two weeks of monotherapy, PUVA treatment using a liquid formulation of oral 8-methoxypsoralen at a dose of 0.6 mg/kg one hour before irradiation was added thrice weekly for 12 weeks or until a ≥90% reduction of the baseline palmoplantar Pustulosis Area and Severity Index (ppPASI ≥90) was achieved (clearing phase). PUVA treatment was confined to affected palms and soles. In the maintenance phase, PUVA was

Table 1 Baseline characteristics of the study participants

No. of subjects	*n*	Fumaric acid esters	Acitretin
	21	11	10
Sex			
Female	15	10 (91%)	5 (50%)
Male	6	1 (9%)	5 (50%)
Median age, years (IQR)	49 (42–57)	52 (44–56)	49 (38–59)
Age by strata			
<40 years	5	2 (18%)	3 (30%)
40–60 years	11	7 (64%)	4 (40%)
>60 years	5	2 (18%)	3 (30%)
Skin phototype			
II	13	7 (64%)	6 (60%)
III	7	4 (36%)	3 (30%)
IV	1	0	1 (10%)
PPP, median years since diagnosis (IQR)	3 (1–9)	2 (1–9.5)	3 (2–6.8)
Median ppPASI at baseline	4.7 (2.8–9)	4.7 (2.7–9.1)	3.9 (3–7.7)
Current smoker	14	8 (73%)	6 (60%)
Autoimmune thyroiditis	4	3 (27%)	1 (10%)

IQR, interquartile range; PPP, palmoplantar pustulosis; ppPASI, palmoplantar Pustulosis Area and Severity Index.

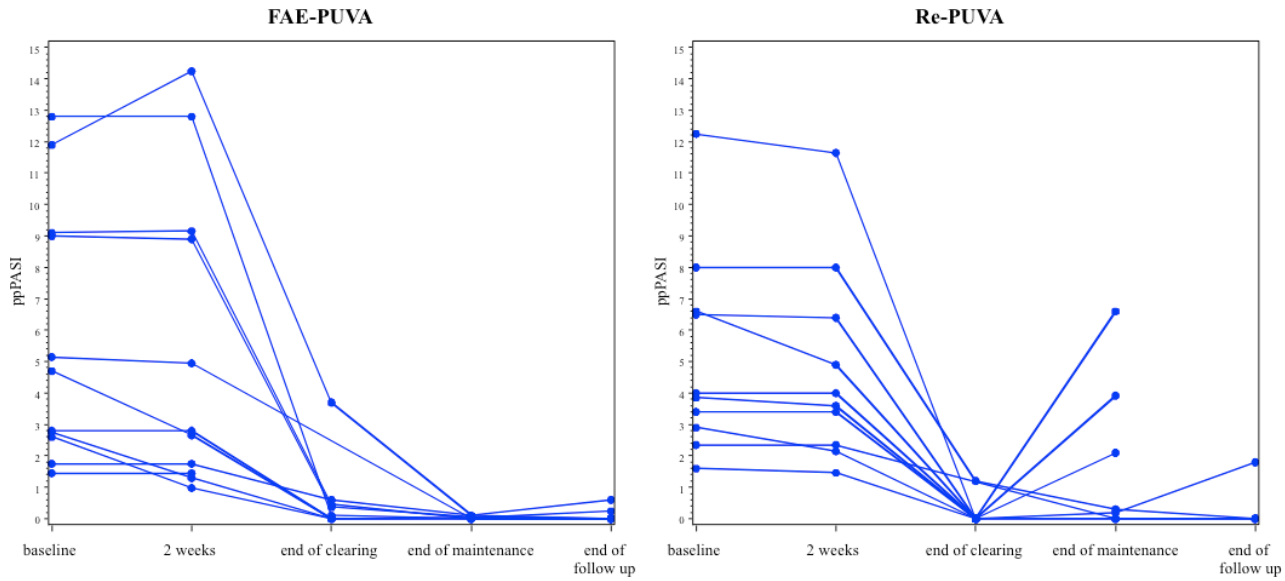

Figure 1 The course of individual palmoplantar Pustulosis Area and Severity Index (ppPASI) scores at baseline, after 2 weeks and at the end of the clearing, maintenance and follow-up phase in patients treated with FAE-PUVA and Re-PUVA

discontinued and the patients received half of the last FAE or acitretin dose for another 24 weeks or until significant relapse (ppPASI ≥50% of the baseline value) occurred. All patients with sustained remission at the end of the maintenance phase were followed for another 24 weeks without any treatment (follow-up phase).

A total 21 patients with chronic PPP were included into the study; of these, 11 patients were allocated to FAE-PUVA and 10 patients to Re-PUVA, respectively (Table 1). Despite randomized allocation, there was a much higher proportion of females in the FAE-PUVA group as compared to the Re-PUVA study arm. It appears, however, unlikely that this may have confounded our results since no gender-related difference in treatment response has been reported for patients with PPP. At the end of clearing phase, 81.8% (9/11) of the patients in the FAE-PUVA group and 90% (9/10) of the patients in the Re-PUVA group achieved the primary endpoint of ppPASI ≥90 ($P = 0.593$). After

discontinuation of PUVA and another 24 weeks of maintenance treatment at a reduced drug dose, the ppPASI ≥90 rate in the FAE-PUVA arm was 90.9% (10/11) as opposed to 70% (7/10) in the Re-PUVA group ($P = 0.525$). During the ensuing follow-up period of 24 weeks, all patients (90.9%) in the FAE-PUVA group maintained a ppPASI ≥90 response whereas the ppPASI ≥90 rate in the Re-PUVA group dropped to 50% (5/10; $P = 0.038$). The course of the individual ppPASI scores in the two treatment arms is depicted in Fig. 1. In general, side-effects were only mild to moderate and transient in nature except in one patient who had to be withdrawn from the study at week 10 due to persistent FAE-induced nausea.

In conclusion, both FAE-PUVA and Re-PUVA appear to be highly effective and well tolerated in the short- and long-term management of PPP. There was a slightly more rapid clearing with Re-PUVA as compared to FAE-PUVA. However, this was compensated by a more sustained response to FAE maintenance treatment as evidenced by superior remission rates at the week 38 and week 62 follow-up. Thus, in combination with PUVA FAE appears as a viable alternative for PPP patients intolerant to acitretin. In addition, the results of our study indicate that the addition of a maintenance treatment might provide for extended long-term remissions. Finally, our study corroborates previous data indicating that FAE might be a useful agent for the treatment of PPP.

Conflict of interest

None reported.

Funding source

None reported.

Disclosure

Drs. AICHELBURG, PINKOWICZ, HOLZER, RADAKOVIC, SATOR and TANEW have nothing to disclose.

M.C. Aichelburg,[1,2,*,†] A. Pinkowicz,[1,†] G. Holzer,[1,2] S. Radakovic,[1] P.-G. Sator,[3] A. Tanew[1]

[1]Department of Dermatology, Medical University of Vienna, Vienna, Austria, [2]Department of Dermatology, Sozialmedizinisches Zentrum Ost-Donauspital, Vienna, Austria, [3]Department of Dermatology, Krankenhaus Hietzing, Vienna, Austria

*Correspondence: M.C. Aichelburg. E-mail: maximilian.aichelburg@meduniwien.ac.at

[†]These authors contributed equally to this study.

References

1 Murray D, Corbett MF, Warin AP. A controlled trial of photochemotherapy for persistent palmoplantar pustulosis. *Br J Dermatol* 1980; **102**: 659–663.

2 Lawrence CM, Marks J, Parker S, Shuster S. A comparison of PUVA-etretinate and PUVA-placebo for palmoplantar pustular psoriasis. *Br J Dermatol* 1984; **110**: 221–226.

3 Lassus A, Lauharanta J, Eskelinen A. The effect of etretinate compared with different regimens of PUVA in the treatment of persistent palmoplantar pustulosis. *Br J Dermatol* 1985; **112**: 455–459.

4 Rosen K, Mobacken H, Swanbeck G. PUVA, etretinate, and PUVA-etretinate therapy for pustulosis palmoplantaris. A placebo-controlled comparative trial. *Arch Dermatol* 1987; **123**: 885–889.

5 Ständer H, Stadelmann A, Luger T, Traupe H. Efficacy of fumaric acid ester monotherapy in psoriasis pustulosa palmoplantaris. *Br J Dermatol* 2003; **149**: 220–222.

DOI: 10.1111/jdv.16909

New insights into lichen planus pigmentosus associated with cicatricial alopecia

Dear Editor,

Lichen planus pigmentosus is a rare variant of classic lichen planus that most commonly affects Fitzpatrick skin phototype III to VI.[1,2] The coexistence of lichen planus pigmentosus and frontal fibrosing alopecia (FFA) was first described by Dlova.[3,4] In this work, we studied lichen planus pigmentosus in female patients with cicatricial alopecia and defined clinical, dermoscopic and histopathological features related to this diagnosis.

A cross-sectional study with patients with biopsy-confirmed cicatricial alopecia and dermoscopic features of lichen planus pigmentosus.[5,6] Patients with dermoscopy and histology features of melasma were excluded.[7] Patients underwent a 2 mm punch biopsy in the zygomatic region, where there were no clinically visible papules. Dermoscopy was performed using FotoFinder (Fotofinder Systems, Inc, Columbia, MD) and polarized light. Histology was undertaken using multiple horizontal sections of each specimen. Statistical analysis was performed with Student's *t*-test and Cramér's V.

A total of 16 patients ranging from 41 to 80 years old presented clinical and dermoscopic patterns of lichen planus pigmentosus associated with biopsy conformed cicatricial alopecia,[5,6] All of them underwent facial biopsy at the zygomatic area. Of all patients, 4 (25%) had phototype IV, 5 (31%) had phototype V, 7 (44%) had phototype VI; 8 (50%) presented FFA and 8 (50%) had fibrosing alopecia in a pattern distribution (FAPD). The diagnosis of FAPD was based on Teixeira *et al*'s criteria.[8] Twelve patients of the total (75%) had facial papules on the forehead and temporal areas.[9]

Brown to grey–blue asymmetric perifollicular hyperpigmentation was the most common dermoscopic finding of facial lichen planus pigmentosus and is strongly associated with the presence

