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Switching from a fumaric acid ester mixture to dimethylfumarate monotherapy in psoriasis

Editor

Psoriasis is a chronic inflammatory skin disorder with a significant disease burden. Whilst numerous treatments exist, development of effective and affordable therapies offering good patient outcomes remains desirable.

A mixture of fumaric acid esters (FAE) is commonly prescribed for oral treatment of moderate-to-severe plaque psoriasis in Germany. In other European countries (UK, Ireland, Italy and the Netherlands, among others), FAE have been imported or compounded by local pharmacies. Current international guidelines recommend FAE for the short- and long-term management of psoriasis.[1] Although the original formulation (Fumaderm®) contains a mixture of FAE, the main active ingredient is dimethylfumarate (DMF), an anti-inflammatory and immune-modulating agent with proven efficacy in psoriasis.[2] The monoethylfumarate salts within the FAE formulation have shown much lower biological activity both *in vitro* and *in vivo*.[3–5]

Dimethylfumarate (Skilarence®) was approved for use as monotherapy for the treatment of plaque psoriasis in June 2017. Its pivotal study was a phase III, double-blind, randomized, placebo-controlled, non-inferiority trial (BRIDGE, ClinicalTrials.gov NCT01726933), comparing the efficacy and safety of DMF versus the FAE mixture in patients with moderate-to-severe plaque psoriasis.[6] At week 16, DMF was superior to placebo ($P < 0.001$) and non-inferior to the FAE mixture ($P < 0.001$) in achieving Psoriasis Area and Severity Index 75, and superior to placebo in the percentage of patients who achieved 'clear' or 'almost clear' in the Physician's Global Assessment ($P < 0.001$). DMF also showed comparable results to the FAE mixture in quality of life improvement. Importantly, at a comparable dose, the safety profile of DMF was like that of the FAE mixture.[6]

So far, FAE have demonstrated a favourable long-term safety profile and good drug survival over time, alongside good levels of patient acceptability and satisfaction with treatment. Considering all preclinical and clinical evidence, it is reasonable to conceive that single-compound therapy with DMF will achieve comparable efficacy results, and at least similar tolerability, in patients with moderate-to-severe plaque psoriasis who undergo a straightforward 1 : 1 switch in terms of dosing.

In this context, phasing out of previous FAE treatment is not required, and treatment response will not be affected by the timing of the switch. This assumption is largely because DMF, the active ingredient in both formulations, is administered at identical doses in each tablet (30 or 120 mg). Benefits of switching include treatment with a therapy that is now licensed across Europe and requires less frequent monitoring (quarterly, rather than monthly) in patients with lymphocyte counts >1000/mL.[7,8] Whilst monitoring after DMF administration is still recommended, as for all other anti-psoriatic therapies, less frequent monitoring remains clinically meaningful as it reduces treatment burden for both patients and physicians, whilst still ensuring an appropriate safety margin.

Switching from the FAE mixture to DMF is common in clinical practice. For example, in the Netherlands, both the FAE mixture and DMF have been available alongside each other for some time and switching from the FAE mixture to DMF is feasible without loss of efficacy or side-effects. In addition, recently published results from a German prospective study in 40 patients who switched from the FAE mixture to an equivalent dose of DMF confirmed that a direct treatment switch is possible. Moreover, this study demonstrated that a direct switch offered the same clinical relief and did not require a washout period between therapies.[9] In summary, as clinical experience of switching grows, evidence indicates that switching to DMF is both feasible and effective.

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R.B. Warren,[1] J.N.W. Barker,[2] P. Van de Kerkhof,[3] K. Reich,[4,5,6] U. Mrowietz[7,*]

[1]Dermatology Centre, Salford Royal NHS Foundation Trust, Manchester NIHR Biomedical Research Centre, University of Manchester, Manchester, UK, [2]St John's Institute of Dermatology, King's College London, London, UK, [3]Department of Dermatology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, [4]Translational Research in Inflammatory Skin Diseases, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, [5]Skinflammation® Center, Hamburg, Germany, [6]Dermatologikum Berlin, Berlin,Germany, [7]Psoriasis-Center at the Department of Dermatology, University Medical Center Schleswig-Holstein, Kiel, Germany

*Correspondence: U. Mrowietz. E-mail: umrowietz@dermatology.uni-kiel.de

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Alternative hypothesis for mite identification with reference to 'Pyemotes ventricosus detection in a baby skin folds'

Editor

With reference to the letter to the Editor 'Pyemotes ventricosus detection in a baby skin folds', we here present an alternative hypothesis on mite's identification.[1] Indeed, polymorphic species have been described from the tarsonemid families Pyemotidae and Pygmephoridae, making both the differential diagnosis and the taxonomic identification a challenging matter.[2,3] According to an alternative hypothesis, the mite detected in the described case exhibits features of the *Pygmephoridae* family, superfamily *Pygmephoroidea* (Acari: Endostigmata), Tarsonemid taxa. These features include peculiar aspects of the gnathosoma, bifid and ophisthosoma, cylindric.[2,3] These (i.e. anterior and posterior extremities) appear narrowed and angle-shaped in recent *P. vetricosus* micrograph.[4] However, according to anatomical similarity, the closest species are some *Siteroptes (Siteroptoides)* species with *Pediculaster-like* phoretomorphs, including *S. Mesembrinae* and *S. Flechtmanni*.[5]

Pygmephoridae family includes about 30 genera and 350 species:[2,3,5] the majority feeds on fungi/plants and is usually phoretic on *Coleoptera* and *Diptera*. These species are commonly found on the soil, in the humus, in fallen leaves and in nests.[2,3,5] Species that belong to the *Pygmephoridae* family can potentially parasite humans: after bites, the penetration of allergens into the skin surface can occur, causing allergic reactions of immediate or delayed type.[6,7] This effect is supposed to be elicited by penetration of pyroglyphid mite antigen, with the same mechanism described for allergic skin reaction induced by *Dermatophagoides pteronyssinus* and *Dermatophagoides pharinae* from storage or domestic dust.[6–9] In particular, Pygmephorid mites (*Pygmephoridae, Tarsonemida*) were included in composition of house/bed dust mite population, especially in periods characterized by high humidity and temperature.[7]

The mite here presented was found in the central red bite punctum of an eczematiform lesion of the axilla. To date, there are no reports of a mite from the *Pygmephoridae* family detected on a baby skin. In addition, a mite showing this peculiar appearance in a KOH slide was never reported, thus the exact species of the presented mite has yet to be identified.

L. Tognetti,[1,2,*] E. Cinotti,[2] E. Pianigiani,[2] P. Rubegni[1]

[1]Department of Dermatology - Division of Medical, Surgical and Neuro-Sciences, University of Siena, Siena, Italy, [2]Department of Medical Biotechnologies, University of Siena, Siena, Italy

*Correspondence: L. Tognetti. E-mail: l.tognetti@student.unisi.it

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