Dear Editor, Psoriasis vulgaris is an immune-mediated disease, characterized by skin and systemic inflammation, that is associated with an increased risk of comorbidities such as cardiovascular disease. Although typically associated with moderate-to-severe psoriasis recent data suggest that increased vascular inflammation may occur in patients with milder psoriasis. It has been shown that systemic treatment of psoriasis leads to an improvement in cardiovascular-associated biomarkers, such as adiponectin levels.

Topical therapies containing corticosteroids and/or vitamin D₃ analogues are recommended for treating mild-to-moderate psoriasis, while patients with moderate-to-severe psoriasis are often treated with therapies that target systemic inflammation. However, topical treatments can also be used to treat more severe cases of psoriasis.

In the 12-week, phase III PSO-ABLE study in patients with mild-to-severe psoriasis, fixed combination calcipotriol (Cal) 50 μg g⁻¹ plus betamethasone dipropionate (BD) 0.5 mg g⁻¹ aerosol foam was significantly more efficacious than treatment with Cal/BD gel. In this analysis from PSO-ABLE, we assessed the proinflammatory psoriasis systemic biomarkers interleukin (IL)-17A and macrophage-derived chemokine/CCL22 (MDC), and the cardioprotective biomarker adiponectin, before and after treatment with Cal/BD aerosol foam in a subgroup of patients with the highest psoriasis severity. As these patients are at an increased risk of cardiovascular comorbidities, compared with more mildly affected patients, we hypothesized that any change in systemic biomarkers was most likely to be observed in this subgroup. Furthermore, we investigated the relationship between changes in IL-17A levels and the clinical efficacy of Cal/BD aerosol foam, as measured by the modified Psoriasis Area and Severity Index (mPASI; excluding the head).

From the primary PSO-ABLE patient population, of patients with available serum samples we selected the 50 patients with the highest psoriasis severity according to mPASI score at baseline and conducted post hoc serum sample analyses to compare changes in IL-17A, MDC and adiponectin levels between baseline and week 12. Blood samples for biomarker analysis were collected in vacutainers and serum was isolated after centrifugation. MDC and adiponectin were measured quantitatively using the HumanMAP® platform (Myriad RBM Inc., Austin, TX, U.S.A.). An ultrasensitive immune assay (Simoa®; Myriad RBM) was used to quantitatively measure IL-17A. Full inclusion and exclusion criteria are described elsewhere.

Of the 50 patients, 14 were women (28%) and 36 were men (72%). Mean age (± SD) of the subgroup was 56.0 ± 14.0 years, mean duration of psoriasis 18.6 ± 12.1 years and mean body surface area 12.6 ± 6.6. Baseline mPASI and levels of systemic biomarkers are described in Table 1. Significant improvement in mPASI was observed after 12 weeks of treatment with Cal/BD aerosol foam (P < 0.001) (Table 1). Mean levels of IL-17A and MDC decreased significantly from baseline to week 12 (P < 0.001); additionally, Cal/BD aerosol foam treatment led to significantly increased levels of adiponectin at week 12 (P = 0.03) (Table 1). Notably, there was a significant correlation between mPASI improvement and IL-17A levels (P = 0.04) (Fig. S1; see Supporting Information); no correlation was observed with the other two biomarkers assessed. No differences were detected between men and women.

The following biomarkers were also analysed and found to be statistically significantly different from baseline to week 12: IL-23, IL-16, kallikrein-5, MMP-3 and ICAM-1 (all P < 0.05). We found no significant changes for measurements in PARC, factor VII, IL-18, psaF, IL-12p40, endoglin, alpha-2-macroglobulin, IL-8, YCAM-1, IL-1RA, IgE, eotaxin-1, RANTES, VEGF, MIP-1-beta, SCF, ENRAGE, FRTN, ENA-78, TIMP-1, myoglobin, IGFBP1, HER-2, PAI-1, MCP-1, TNFRI and BDNF.

In support of other studies, this study demonstrates that the effects of topical treatment of psoriasis are not limited to reducing cutaneous manifestations, but can also significantly and positively influence systemic inflammatory and cardioprotective biomarker levels. However, Baran et al. recently examined the effect of topical treatment on cardiovascular biomarkers in psoriasis and failed to detect significant changes in adiponectin levels at end of study (week 2), possibly due to the short treatment duration. As the authors suggest, genetic or nutritional variations or methodological parameters in their study may have influenced this result.

The ability of immune cells to recirculate to and from the skin might explain how topical treatment of psoriasis can influence systemic immune function and systemic biomarker levels. Alternatively, this influence could be due to systemic absorption of topically applied agents (e.g. betamethasone). However, a previous study examining Cal/BD combination treatment efficacy demonstrated marginal exposure in 10% of...
patients and no detectable effects on the hypothalamus-pituitary axis, making significant systemic exposure unlikely.8

As this was a post hoc analysis of data from the PSO-ABLE study, which examined efficacy, it was not powered to assess changes in systemic biomarker levels. Additionally, as this analysis did not have a control group, we are unable to compare our results with those of other topical treatments or placebo. Despite these limitations, this exploratory study supports the hypothesis that effective topical treatment of psoriasis can affect systemic markers of inflammation. Prospective placebo-controlled studies are required to confirm these findings.

Acknowledgments

Medical writing support was provided by Mai Kurihara, PhD, of Mudskipper Business Limited.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher’s website:

Fig S1. Correlation between percentage change of modified Psoriasis Area and Severity Index vs. interleukin-17A from baseline to week 12.

Funding sources: this study was funded by LEO Pharma.

Conflicts of interest: the study was sponsored by LEO Pharma.

Table 1 Patient’s modified Psoriasis Area and Severity Index (mPASI) score and systemic biomarker levels

| Biomarker          | Baseline (mean ± SD) | Week 12 (mean ± SD) | P-value | Normal values* |
|--------------------|----------------------|---------------------|---------|----------------|
| mPASI              | 12.4 ± 4.0           | 3.7 ± 4.7           | < 0.001 | NA             |
| IL-17A (pg mL⁻¹)   | 0.92 ± 0.71          | 0.52 ± 0.41         | < 0.001 | 0.30 ± 0.59    |
| MDC (pg mL⁻¹)      | 745 ± 252            | 584 ± 210           | < 0.001 | 556 ± 135      |
| Adiponectin (µg mL⁻¹) | 4.57 ± 2.06        | 4.99 ± 2.74         | 0.03    | 5.56 ± 2.76    |

Data are presented as mean ± SD unless otherwise indicated. NA, not applicable; IL, interleukin; MDC, macrophage derived chemokine/ CCL22. *Based on samples from apparently healthy volunteers, with no questions asked other than age and sex.