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HAc40 is a novel microbiome modulator, effective on atopic dermatitis in children: data from two pilot vehicle-controlled trials

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Microbial balance is fundamental to healthy skin and changes in this ecosystem may lead to several diseases.[1] Atopic dermatitis (AD) is associated with altered skin microbiome, prevalence of *S. aureus* colonization and secondary infections.[2,3] Due to prevalence of microbial resistance, antibiotics usage for treating AD has been discouraged[4] and several attempts have been conducted to restore a microbiome balance through skin bacteria replacement.[5]

AD course following antimicrobial therapy is linked to biofilm formation, that protects organisms from antibiotics and phagocytosis. Modifying skin microbiome at the biofilm level, seems to be a promising approach for AD treatment.[6]

A recently developed functional ingredient (Hyaluronic Acid combined with a fragment of Cutibacterium acnes bacterial wall, HAc40) has shown to sequestrate and inactivate S Aureustoxins, with a post-biotic action. Its role in restoring skin homeostasis was proved from preclinical investigations (unpublished data). LimpiAD® (AileensPharma) combines HAc40 in an emollient-based Medical Device and may represent a novel approach for fighting AD in its fundamental pathogenetic skin changes, i.e. microbiome alteration.

We present the results from two independent double-blinded, randomized studies comparing LimpiAD vehicle alone versus LimpiAD with HAc40 1% (L1) and 2.5% (L2.5) in paediatric patients with AD. Patients were Caucasian, aged 6 months-16 years with mild to moderate AD and pruritus (VAS>1). Exclusion criteria were any treatment or sun exposure (4 weeks before enrollment), any other relevant disease.

32 (L1) and 27 (L2.5) cases have been enrolled in the studies. Three cases were excluded from L1 because of lack of pruritus at baseline, and two from L2.5 because of lack of pruritus (one case) and different ethnicity in the other case. Analyses have been made on the intention to

treat group. Population in the two studies differed for baseline SCORAD values, with more severe dermatitis in L2.5 study.

A greater decrease in SCORAD (p=0.006 at T2 and 0.001 at T4), pruritus (0.052 at T4) and erythema (not significant) was registered in both studies in the treatment arm. Considering the two studies, in L1 a SCORAD reduction of 50% and 75% from baseline was measured in 80% and 53% out of 15 cases, compared with 14% and 17% out of 14 controls. Erythema decreased in both arms and the reduction was significant in the treatment arm.

As regards L2.5 study, 4 drop-outs at T2 in the vehicle group and 2 drop-outs at T4 for the treatment group were reported. However, SCORAD significantly decreased from baseline both at T2 and T4 in the treatment arm. A SCORAD reduction equal to 50% and 75% with respect to baseline were observed in 47% and 13% out of 15 cases, compared with 20% and 10% out of 10 controls, respectively. Pruritus significantly decreased only in the treatment arm at T4.

By comparing SCORAD and pruritus relative reduction (calculated as % of score variation from baseline), L2.5 showed a higher reduction with respect to L1 for both parameters at T4 (p=0.03 and p=0.003, respectively) showing how a higher concentration can improve the effect.

Overall, these data reported the effects of HAc40 on AD, resulting in clinically relevant decrements in SCORAD and pruritus as compared with the vehicle in both studies. By considering these findings and preclinical trials observations, we may deduce that microorganism control operated by HAc40 induces a prompt beneficial effect on pruritus, with a consequent rapid reduction in SCORAD values, which lately has been transferred also to the signs of the disease, as showed by erythema reduction. A larger population study and skin microbiome analysis are warranted in order to correlate the beneficial clinical effects with changes in microorganism population on the affected areas.

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Table 1: Effect of HAc40 (LimpiAD®) 1% and 2,5% on SCORAD, pruriturs and erythema in a peadiatric population with Atopic Dermatitis

		T0	T2	T4		T0	T2	T4
SCORAD	Vehicle (14)	8.1 (+ 6.1)	10.5 (+ 9.4)	10.9 (+ 9.6)	Vehicle (10)	25.8 (+ 10.7)	20.0 (+ 11.7)	16.9 (+ 11.7)
	LimpiAD 1% (15)	7.9 (+ 5.6)	5.5 (+4.2)*	2.5 (+2.1)*	LimpiAD 2.5% plus (15)	25.1 (+ 9.7)	17.0 (+7.7)*	14.5 (+10.5)*
SCORAD 50	Vehicle (14)	-	2 (14%)	2 (14%)	Vehicle (10)	-	1 (10%)	2 (20%)
	LimpiAD 1% (15)	-	4 (27%)	12 (80%)*	LimpiAD 2.5% plus (15)	-	4 (26%)	7 (47%)
SCORAD 75	Vehicle (14)	-	1 (7%)	1 (7%)	Vehicle (10)	-	0 (0%)	1 (10%)
	LimpiAD 1% (15)	-	0 (0%)	8 (53%)*	LimpiAD 2.5% plus (15)	-	2 (13%)	2 (13%)
Pruritus	Vehicle (14)	2.4 (+ 2.4)	2.6 (+ 3.1)	2.4 (+ 3.2)	Vehicle (10)	5.5 (+ 2.1)	5.3 (+ 2.1)	3.9 (+ 2.8)
	LimpiAD 1% (15)	2.3 (+ 1.5)	1.4 (+1.5)*	0.3 (+0.6)*	LimpiAD 2.5% plus (15)	4.0 (+ 1.5)	2.3 (+1.7)*	2.6 (2.4)*
Erythema	Vehicle (14)	1.2 (+ 0.6)	1.4 (+ 1.1)	0.9 (+ 0.9)	Vehicle (10)	1.7 (+ 0.5)	1.3 (+ 0.8)	1.1 (+ 0.7)
	LimpiAD 1% (15)	1.1 (+ 0.4)	0.9 (+ 0.7)	0.3 (+0.5)*	LimpiAD 2.5% plus (15)	1.7 (+ 0.5)	1.1 (+ 0.6)	0.8 (+ 0.7)

* Significant vs. baseline (P<0.05)