

NEWS AND VIEWS

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Biologics as a therapeutic approach for a Th17-mediated severe dermatitis in skin barrier disorders

Carmen Riggioni^{1,2} | Montserrat Alvaro-Lozano^{1,2} | Laia Alsina^{1,2,3,4}¹Pediatric Allergy and Clinical Immunology Department, Hospital Sant Joan de Déu, Barcelona, Spain²Institut de Recerca Sant Joan de Déu, Barcelona, Spain³Clinical Immunology and Primary Immunodeficiencies Unit, Pediatric Allergy and Clinical Immunology Department, Hospital Sant Joan de Déu Barcelona Spain, Barcelona, Spain⁴Universitat de Barcelona, Barcelona, Spain**Correspondence:** Carmen Riggioni, Pediatric Allergy and Clinical Immunology Department, Hospital Sant Joan de Déu, Barcelona, Spain.
Email: criggioni@gmail.com**Keywords:** biologics, SAM-like syndrome, secukinumab, T helper 17

Biologics are a promising treatment for immune-mediated diseases in which the predominant pathogenic pathway is targeted. The use of biologics therapy for epidermal barrier function-impairing pathologies follows 3 strategies: tapering of T helper (Th) 2 responses; neutralization of non-type 2 pathways such as Th17; or blockade of acute phase reactions such as those driven by interleukin (IL)-6.¹ Initially, the treatment of eczematous disorders focused on the Th2 response without considering the key contribution of Th17 cells. However, recent work by Hernández-Martín et al² reports the successful treatment of a 9-month-old patient with severe dermatitis, allergies, and metabolic wasting (SAM)-like syndrome via targeting the Th17 pathway.

SAM syndrome (OMIM 615508) originates from bi-allelic mutations in desmoglein-1 or desmoplakin-encoding genes. This rare genetic condition results in high morbi-mortality and lacks an effective treatment. Although the genetic analysis of this 9-month-old patient was inconclusive, she presented with recurrent sepsis, failure to thrive, erythroderma, diffuse hyperkeratotic plaques, hypotrichosis, and onychodystrophy, thus matching the clinical characteristics of SAM syndrome.

Flow cytometry and viSNE (visualization of t-distributed stochastic neighbor embedding) analysis of blood revealed a single cluster of cells compatible with a Th17 phenotype (CD3⁺CD4⁺CCR4⁺CCR6⁺CXCR3⁺). This cluster displayed a 30-fold increase compared to control samples. Furthermore, IL-17-producing T cells and plasma levels of IL-17A were 67- and 38-fold higher than the control. The authors hypothesized that as an IL-17 excess may

induce keratinocyte-driven inflammation, IL-17A blockade with secukinumab would ameliorate the skin pathology.²

Secukinumab is a fully humanized IgG1 that specifically targets IL-17A. It acts as an IL-17A antagonist, thereby blocking its binding to the IL-17 receptor and inhibiting the release of proinflammatory cytokines and chemokines.³ In this case report, subcutaneous therapy with 75 mg of secukinumab was given once a week, for 4 weeks, followed by a monthly maintenance dose until 18 months of age. The treatment resulted in clinical improvement of the skin, adequate weight, and height gain, and a significant enhancement of life quality² (Figure 1).

These results are in agreement with a previous study in which secukinumab treatment reduced hyperkeratotic plaques in psoriasis, which are driven by IL-17A-dependent keratinocytes.⁴ They also position secukinumab as a therapeutic option for patients with SAM syndrome and similar severe hyperkeratotic skin conditions involving Th17 responses. Furthermore, a link with IL-17 has been reported in the pathogenesis of other chronic inflammatory and autoimmune skin diseases such as acne, hidradenitis suppurativa, alopecia areata, vitiligo, and bullous disease. This opens the possibility of targeting IL-17A to treat a wide range of skin disorders.⁵

In addition, Hernández-Martín's work² demonstrates the importance of looking beyond the well-established Th2 mechanisms when addressing severe dermatitis. The relatively underappreciated Th17 axis has emerged as a relevant therapeutic target for patients with skin barrier disorders. New insights into the immunological component of inborn conditions with dysregulated epithelial barriers are likely to identify novel and effective targeted approaches.

Abbreviations: IL, interleukin; SAM, severe dermatitis, allergies, and metabolic wasting syndrome; Th, T helper.

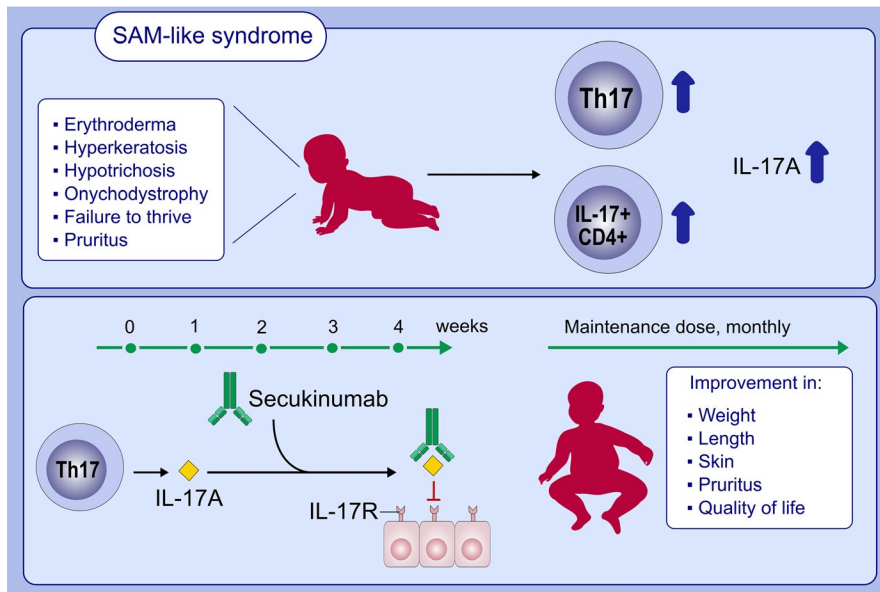


FIGURE 1 Peripheral blood of a 9-mo-old patient with SAM-like syndrome (erythroderma, diffuse hyperkeratotic plaques, hypotrichosis, onychodystrophy, failure to thrive, and pruritus) was evaluated by flow cytometry showing an increase in Th17 cells and IL-17A production. The patient was treated with secukinumab weekly, for 4 wks, followed by monthly maintenance until 18 mo of age. The treatment improved the patient's skin condition, growth, and quality of life. Th, T helper; IL, interleukin; R, Receptor; SAM, severe dermatitis, allergies, and metabolic wasting

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CONFLICTS OF INTEREST

Dr Riggioni, Dr Alvaro-Lozano and DrLaiaAlsina have nothing to disclose.

AUTHOR CONTRIBUTIONS

All authors contributed to the manuscript, revised and edited.

ORCID

Carmen Riggioni  <https://orcid.org/0000-0002-8745-0228>

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