Atopic dermatitis

The challenge

Atopic dermatitis (AD) is characterized by a complex pathophysiology with a wide spectrum of phenotypes. This high diversity makes mechanistic in silico approaches particularly adapted for guiding clinical development.

In the context of the bacterial lysate OM-85's development to treat atopic dermatitis, [1] OM Pharma wanted to conduct an in silico exploration of the immune mechanisms driving the treatment response in order to characterize the best responders.

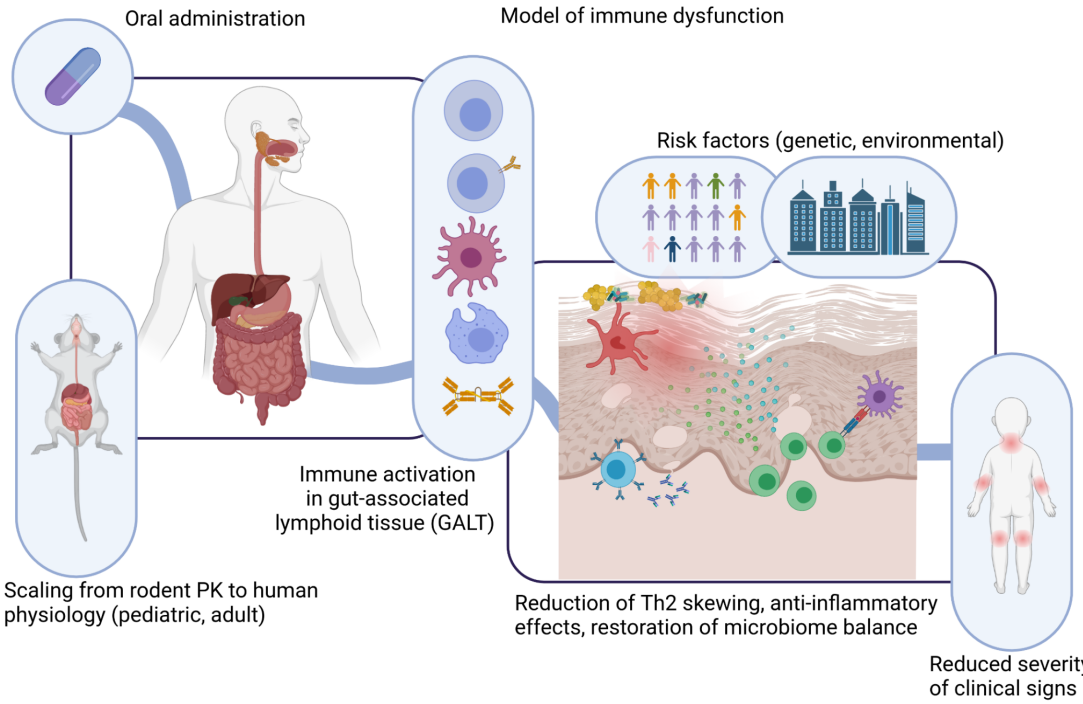
The solution

Background

Nova has built a mechanistic model of AD representing the interplay between the skin barrier and the immune system in a pediatric population. It describes the key pathways and biomarkers influencing disease course, including the mechanisms driving the immune response dysregulation, the loss of skin barrier integrity and the perturbation of the skin microbiome.

How nova approached the challenge

The model integrates a wide spectrum of AD endotypes and phenotypes for which the model successfully reproduced patient responses to standards of care (emollient, topical corticosteroids, and topical calcineurin inhibitors) as well as to OM-85 [2], the investigational treatment. For this, the model was enriched with data on OM-85 ADME (absorption, distribution, metabolism, and excretion) and mechanism of action (immune modulation and gut-skin axis).



Schematic of atopic dermatitis mechanism implemented in the model including mechanism of action of OM-85, allergen/pathogen-induced inflammation, skin barrier dysregulation and regulatory immune responses. Oral administration of the bacterial lysate exposes the gut-associated mucosal immune system (GALT) to the antigenic stimulus of the product which activates the migration of circulating immune components to the skin barrier.
Figure created with biorender.com.

Nova applied its **jinkō** in silico clinical trial platform to explore patient response to OM-85 to identify key markers of the immune response predictive of the treatment efficacy and their impact on clinical trial eligibility and sample size. For this, clinical scores commonly used in AD management (SCORAD and EASI) were used to evaluate the efficacy of the treatment.

The **outcome**

A subset of key immunological markers among the full set of thirteen represented in the model was identified as predictive of response to OM-85. When using threshold levels for the key markers as eligibility criteria in an in silico clinical trial setting, enrolling predicted best responders above the median increased the average clinical efficacy by 85% while reducing the sample size by 52%. A more selective enrollment rule appeared as a less optimal option, associated with a low gain and a notable reduction of the sample size. This set of selected patients exhibits a prolonged efficacy of the treatment.

To summarize, this in silico approach suggested key information for the design points of future clinical trials for pediatric AD, including the selection of clinical trial study populations, leading the way for optimal clinical development programs.

References

[1] OM-85 bacterial extract is being currently investigated for children with moderate AD in a Phase 2a trial, https://www.clinicaltrials.gov/ct2/show/NCT05222516

[2] Bodemer C, Guillet G, Cambazard F, Boralevi F, Ballarini S, Milliet C, Bertuccio P, La Vecchia C, Bach JF, de Prost Y. Adjuvant treatment with the bacterial lysate (OM-85) improves management of atopic dermatitis: A randomized study. PLoS One. 2017 Mar 23;12(3):e0161555. doi: 10.1371/journal.pone.0161555. PMID: 28333952; PMCID: PMC5363804.