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The Role of OX40/OX40L Pathway Inhibition as a New Therapeutic Strategy for Atopic Dermatitis

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Resumo

A Dermatite Atópica é uma doença inflamatória cutânea, que afeta aproximadamente 15-20% das crianças e 2-10% dos adultos a nível mundial. A doença caracteriza-se pela presença de placas cutâneas exsudativas, liquenificadas e eritematosas, frequentemente associadas a xerose e prurido e cuja formação é desencadeada pela exposição a certos triggers endógenos ou ambientais, em indivíduos geneticamente predispostos.

A disrupção da barreira epidérmica e a desregulação imunológica constituem os pilares da doença, formando um ciclo vicioso em que a perda de integridade da barreira cutânea desencadeia uma resposta inflamatória exacerbada, enquanto a intensificação dessa resposta inflamatória agrava, por sua vez, a disfunção desta barreira. O OX40 e o OX40L são moléculas de checkpoint imunitário, que predominam, respetivamente, nas células T e nas células apresentadoras de antigénio e cuja interação potencia as respostas pró-inflamatórias das células T, fundamentais na fisiopatologia da dermatite atópica.

Apesar dos constantes avanços na abordagem terapêutica da dermatite atópica, ainda existe uma percentagem considerável de pacientes que não respondem às terapêuticas atualmente empregues na prática clínica, e um conjunto de unmet needs que ainda não foram colmatadas. Os inibidores da via OX40/OX40L representam uma abordagem inovadora no tratamento da dermatite atópica, ao modularem a atividade dos vários subgrupos de células T envolvidos na fisiopatologia da doença. O amlitelimab é um anticorpo monoclonal anti-OX40L que demonstrou eficácia clínica sustentada e um perfil de segurança favorável em dois estudos de fase 2a e 2b. O rocatinlimab e o telazorlimab são anticorpos direcionados ao OX40. O primeiro evidenciou resultados clínicos mais promissores num ensaio de fase 2b e, de acordo com os top-line results já divulgados, em quatro estudos de fase 3. Por outro lado, o telazorlimab apresentou resultados mais modestos e, até à data, não avançou para novos ensaios clínicos. O IMG-007 e o STAR-0310 são dois novos anticorpos anti-OX40, desenvolvidos através de modificações na região Fc, com o objetivo de prolongar a sua semi-vida e reduzir a citotoxicidade celular dependente de anticorpos. Estas alterações visam diminuir o potencial risco de efeitos adversos e possibilitar administrações terapêuticas com intervalos mais prolongados.

À luz dos ensaios clínicos atualmente disponíveis, esta nova abordagem terapêutica promete revolucionar o panorama de tratamento da dermatite atópica. Ainda assim, é premente o desenvolvimento de estudos comparativos diretos entre os diferentes inibidores da via OX40/OX40L, bem como entre estes e os fármacos já estabelecidos na prática clínica.

PALAVRAS-CHAVE: Dermatite Atópica, Anticorpos monoclonais, OX40, OX40-OX40L, Amlitelimab, Rocatinlimab, Telazorlimab, IMG-007, STAR-0310, Rocket Program

Abstract

Atopic Dermatitis is an inflammatory skin disease that affects approximately 15–20% of children and 2–10% of adults worldwide. It is characterized by exudative, lichenified, and erythematous plaques, typically associated with xerosis and pruritus, whose development is triggered by exposure to specific endogenous or environmental factors in genetically predisposed individuals.

Disruption of the epidermal barrier and immune dysregulation are the cornerstones of the disease, establishing a vicious cycle in which the loss of skin barrier integrity triggers an exacerbated inflammatory response, while the intensification of this inflammatory activity further aggravates epidermal barrier dysfunction. OX40 and OX40L are two immune checkpoint molecules, predominantly expressed on T cells and antigen-presenting cells, respectively, whose interaction enhances the pro-inflammatory responses of T cells, which are fundamental in the pathophysiology of atopic dermatitis.

Despite ongoing advances in the therapeutic approach to atopic dermatitis, a considerable proportion of patients remain unresponsive to treatments currently used in clinical practice, and several unmet needs have yet to be addressed. Inhibitors of the OX40/OX40L pathway represent an innovative therapeutic strategy by modulating the activity of the various T cell subsets involved in the disease. Amlitelimab is an anti-OX40L monoclonal antibody that has demonstrated sustained clinical efficacy and a favorable safety profile in two studies: a phase 2a and a phase 2b. Rocatinlimab and telazorlimab are two antibodies targeting OX40. The former has shown more promising clinical outcomes in a phase 2b clinical trial and, according to the top-line results already released, in four phase 3 studies. Telazorlimab, on the other hand, has shown more modest results and has not progressed to any recent phase 3 clinical trials. IMG-007 and STAR-0310 are two novel anti-OX40 antibodies developed through modifications to the Fc region, aiming to extend their half-life and reduce antibody-dependent cellular cytotoxicity, thereby minimizing the potential risk of adverse effects and enabling administration at longer dosing intervals.

In light of the currently available clinical trials, this new therapeutic option holds the potential to revolutionize the treatment landscape for atopic dermatitis. Nevertheless, there remains a pressing need for direct comparative studies between the various inhibitors of the OX40/OX40L pathway, as well as between these agents and the drugs already established in clinical practice.

Keywords: Atopic Dermatitis, Monoclonal Antibodies, OX40, OX40-OX40L, Amlitelimab, Rocatinlimab, Telazorlimab, IMG-007, STAR-0310, Rocket Program

List of Abbreviations

AD Atopic Dermatitis
ADCC Antibody-mediated cellular cytotoxicity
AEs Adverse Events
APCs Antigen-presenting cells
COVID-19 coronavirus 2019 disease
DLQI Dermatology Life Quality Index
EASI Eczema Area and Severity
HD High Dose
IGA Investigator's Global Assessment
IgE Immunoglobulin E
IL Interleukin
IV Intravenous
JAKi JAK inhibitors
LD Low Dose
LS Least-Squares
mRNA messenger Ribonucleic Acid
NRS Numerical Rating Scale
PK Pharmacokinetics
Q2W Once every 2 weeks
Q4W Once every 4 weeks
rIGA revised Investigator Global Assessment
SC Subcutaneous
SCORAD SCORing of Atopic Dermatitis
TARC Thymus and Activation-Regulated Chemokine
TCI Topical Calcineurin Inhibitors
TCS Topical Corticosteroids
TEAEs Treatment-emergent adverse events
Th T helper
vIGA validated Investigator's Global Assessment

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Introduction

Atopic dermatitis (AD) is a chronic and relapsing inflammatory skin disorder, affecting approximately 15–20% of children and 2–10% of adults worldwide.[1,2] The disease usually begins in childhood and may regress spontaneously, although 40% of patients continue to experience intermittent flares throughout their lives.[3]

A positive family history of atopy is present in 70% of individuals with AD. It represents the main risk factor for the disease, contributing to an increased susceptibility to other atopic conditions, such as food allergy, allergic rhinitis, or asthma.[4,5]

AD is characterized by erythematous, exudative, and lichenified skin plaques, typically associated with xerosis and pruritus. These lesions are triggered by exposure to specific endogenous or environmental factors in predisposed individuals.[6] Due to its chronic and fluctuating course, along with an increased risk of skin infections, sleep disturbances, and anxiety and depressive disorders, AD has a substantial impact on patient´s lives, as reflected by reduced scores on the Dermatology Life Quality Index (DLQI).[7]

The pathophysiology of AD involves multiple mechanisms, ranging from epidermal barrier dysfunction to immune dysregulation, primarily mediated by T helper (Th)2 and Th22 cells in acute lesions, as well as Th1 and Th17 cells in chronic lesions.[8]

The cornerstone of AD management involves identifying and avoiding individual triggers, along with daily skin moisturization. Topical therapy with corticosteroids or calcineurin inhibitors remains the first-line treatment for AD flare-ups. In cases refractory to topical treatment, alternative therapeutic approaches may be considered, including systemic corticosteroids, phototherapy, conventional immunosuppressants, or, more recently, systemic therapies that target specific immunological pathways. Advances in the elucidation of AD pathophysiology have driven the development of these targeted treatments, which act on selected cytokines, their respective receptors, or intracellular signaling pathways. Among these, JAK inhibitors (JAKi), interleukin (IL)-4, and IL-13 inhibitors have become the most widely used options in patients exhibiting an inadequate response to conventional therapies. [9,10]

Although these drugs are clinically more effective than conventional therapies, a considerable number of patients still fail to achieve a favorable clinical response. Moreover, their efficacy is not sustained, and AD symptoms frequently recur within days to weeks after treatment discontinuation. Additionally, they are associated with significant treatment-emergent adverse events (TEAEs), including opportunistic infections, rosacea, alopecia, and arthralgias.[11–14] It is therefore essential to develop drugs with alternative mechanisms of action and novel targets capable of addressing these unmet needs.

The OX40–OX40L pathway exerts a fundamental role in both the acute and chronic inflammatory processes of AD and represents a potential therapeutic target for the treatment of this disease.[15]

This narrative review will further explore this therapeutic strategy through the presentation and discussion of clinical trials that have either been published or are currently underway.

Objectives

The primary aim of this article is to review and summarize the current scientific literature on monoclonal antibodies targeting the OX40-OX40L pathway, in order to assess their safety, clinical efficacy, and potential therapeutic role in the treatment of AD.

Methods

A search was conducted for articles and clinical trials in databases such as PubMed, Google Scholar, ScienceDirect, Scopus, and ClinicalTrials.gov. A wide range of keywords, including 'atopic dermatitis', 'monoclonal antibodies', 'OX40-OX40L', 'amlitelimab', 'rocatinlimab', 'telazorlimab', 'IMG-007', 'STAR-0310' and 'Rocket Program' were used to refine the search for articles to be selected. The selection of articles was based on an analysis of their titles and reading of their abstracts, followed by a full reading of the articles selected. Inclusion criteria included articles published in English between 2012 and 2025 that addressed the role of the OX40-OX40L pathway in the pathophysiology of AD, as well as the inhibition of this pathway as a possible therapeutic strategy. Moreover, the reference lists of these articles were also analyzed to identify further relevant studies.

This narrative review covered a number of 42 articles and 16 clinical trials in clinicaltrials.gov.

Pathophysiology of AD and The Role of OX40/OX40L Pathway

The pathophysiology of AD is not yet fully understood; however, epidermal barrier disruption, immune dysregulation, and dysbiosis are recognized as key pillars of the disease.[16,17]

Alterations in intercellular lipids, tight junctions, and, most notably, structural proteins such as filaggrin (due to mutations in the *FLG* gene) underlie epidermal barrier dysfunction, resulting in increased skin permeability. Consequently, there is greater transepidermal water loss and enhanced penetration of external allergens and microbes, which contributes to the development of eczematous lesions and skin infections, further exacerbating barrier disruption.[17] Tissue damage resulting from epidermal dysfunction, along with increased exposure to specific external allergens, lead to an exaggerated release of epidermal-derived signaling molecules, including IL-25, IL-33, and thymic stromal lymphopoietin (TSLP). These cytokines activate antigen-presenting cells (APCs), which, upon interaction with naïve T cells, trigger a type 2 immune deviation, resulting in enhanced activation of Th2 cells expressing IL-4, IL-5, IL-13, and IL-31—key cytokines in the pathogenesis of AD and in promoting Immunoglobulin E (IgE) class switching. Simultaneously, these epidermis-derived cytokines stimulate group 2 innate lymphoid cells (ILC2s), which independently contribute to the type 2 inflammatory environment through the production of IL-5 and IL-13.[8,17] Although the pathophysiology of AD is primarily driven by Th2 cells; Th1, Th17, and Th22 subsets—and their respective cytokines—also play an important role in the development and perpetuation of the disease.[17]

The OX40/OX40L pathway plays a key role in the pathophysiology of AD, with the OX40 (TNFRSF4, CD134) receptor predominantly expressed on the surface of T cells and its ligand, OX40L (TNFSF4, CD252), on APCs.[18] Both T cells and APCs express on their surface a variety of molecules known as immune checkpoint molecules, which are activated during their interaction and are classified as either co-stimulatory or co-inhibitory, amplifying or attenuating T cell responses, respectively. The transmembrane glycoprotein OX40 and its ligand OX40L belong, respectively, to the tumor necrosis factor receptor superfamily (TNFRSF) and the tumor necrosis factor superfamily (TNFSF), functioning as co-stimulatory molecules.[8,19]

The OX40–OX40L pathway is initiated by the binding of APCs to naïve T cells, thereby promoting their differentiation into effector T cells. Following this interaction, OX40L is expressed on APCs within 24 hours, while OX40 is expressed on effector T cells between 1 and 5 days later, allowing subsequent interaction between the two molecules.[18,20] This interaction enhances effector T cell activity, promotes their proliferation, and extends their survival through activation of intracellular NF-κB1 and PI3K-PKB/Akt signaling pathways, which

drive cell division and upregulate anti-apoptotic protein production. On the other hand, this pathway facilitates the differentiation of effector T cells into quiescent memory T cells. Upon re-exposure to the same antigens, these memory cells become activated, rapidly expressing OX40 and subsequently binding to OX40L on APCs, thereby reinitiating their interaction. This mechanism illustrates how the OX40-OX40L pathway drives increased expansion and survival of the Th subsets implicated in the pathophysiology of AD, thereby amplifying and perpetuating the disease.[18]

Targeting the OX40/OX40L Pathway to Treat Atopic Dermatitis

Given the role of the OX40–OX40L pathway and its upstream mechanism of action, disruption of this interaction results in a reduced enhancement of T cell-mediated immune responses, including not only those driven by Th2 cells, but also by other Th cell subsets implicated in AD, such as Th1, Th17, and Th22. Consequently, novel pharmacological therapies have been developed to inhibit this pathway, primarily through monoclonal antibodies targeting one of these molecules. Four anti-OX40 antibodies (rocatinlimab, telazorlimab, IMG-007, and STAR-0310), along with one anti-OX40L antibody (amlitelimab), are currently being evaluated for the treatment of moderate-to-severe AD, with promising results reported to date.[8,21,22]

Amlitelimab

Amlitelimab (KY1005; SAR445229) is a non-depleting, human IgG4 monoclonal antibody, that targets OX40L expressed on APCs, thereby inhibiting its binding to OX40 on T cells.[18,20]

A Phase 1 randomized, double-blind, placebo-controlled study (NCT03161288) involving 64 healthy participants assessed the safety, tolerability, immunogenicity, and pharmacokinetics (PK) of amlitelimab. Participants were allocated into eight cohorts, each comprising six individuals receiving an intravenous (IV) dose of KY1005, and two receiving a placebo. In the first three cohorts, single doses of KY1005 were administered at 0.006, 0.018, and 0.05 mg/kg. In the remaining five cohorts, participants received multiple doses, beginning with an initial dose of 0.15, 0.45, 1.35, 4, or 12 mg/kg, respectively, followed by two maintenance doses at Weeks 4 and 8, each at 50% of the initial one. No serious TEAEs were observed, and all adverse events (AEs) were self-resolving, with headaches being the most frequently reported. KY1005 therefore demonstrated a favorable safety and tolerability profile.[8,23]

A Phase 2a multicenter, randomized, double-blind, parallel-group trial (NCT03754309) involving 88 participants, was conducted to evaluate the efficacy, safety, and tolerability of amlitelimab in adults with moderate-to-severe AD. Patients were randomly assigned (1:1:1) to receive IV administration of either a low dose (LD) of amlitelimab (200 mg loading dose followed

by a 100 mg maintenance dose); a high dose (HD) of amlitelimab (500 mg loading dose followed by a 250 mg maintenance dose); or a placebo, every 4 weeks (Q4W) at Weeks 0, 4, 8, and 12. The percentage change in the Eczema Area and Severity Index (EASI) and the incidence of TEAEs at Week 16 constituted the primary endpoints of the study. At Week 16, the mean percentage change in EASI from baseline was −80.12% in the LD group and −69.97% in the HD group, versus −49.4% in the placebo group ($p = 0.009$ and $p = 0.072$, respectively). The proportion of patients achieving EASI-75 (≥75% improvement from baseline in EASI score) was 59% in the LD arm, 52% in the HD arm, and 25% in the placebo arm. Additionally, at Week 16, 44% of patients in the LD group and 37% in the HD group achieved a score of 0 (clear skin) or 1 (almost clear skin) on the validated Investigator's Global Assessment (vIGA) scale, compared to 8% in the placebo group ($p < 0.001$ for both comparisons). Furthermore, 68% of individuals with a vIGA score of 0 or 1 at Week 16 sustained this response through Week 36—24 weeks after treatment discontinuation—while serum drug concentrations declined in parallel to levels below those considered pharmacologically active. Amlitelimab was overall well tolerated, with all TEAEs classified as mild to moderate. The most frequently reported TEAEs included headache, hyperhidrosis, pyrexia, upper respiratory tract infection, increased aspartate aminotransferase, and iron deficiency anemia.[8,18,24]

These findings were further supported by a Phase 2b randomized, double-blind, placebo-controlled trial (NCT05131477) involving 390 participants with moderate-to-severe AD over a 52-week study period. In Part 1 of the 24-week trial, patients were randomized (1:1:1:1:1) into five groups: one receiving placebo and four receiving subcutaneous (SC) administration of amlitelimab Q4W, with one of these treatment groups receiving a loading dose. The arms were as follows: (1) 250 mg Q4W with a 500 mg loading dose; (2) 250 mg Q4W; (3) 125 mg Q4W; (4) 62.5 mg Q4W; and (5) placebo, with the final dose administered at Week 20. Participants who attained a vIGA score of 0 or 1 and/or EASI-75 at Week 24 (clinical responders) proceeded to Part 2 of the study, where they were reallocated in a 3:1 ratio to either discontinue amlitelimab or continue the same dose Q4W up to Week 52. All dosage groups demonstrated an improvement in the percentage change in EASI at Week 16 (primary endpoint) and Week 24. At Week 16, the least-squares (LS) mean percent change in EASI was −29.4% in the placebo group. Compared to placebo, the LS mean percent differences in EASI were as follows: −32.1% in the 250 mg group with a loading dose ($p < 0.0001$); −27.3% in the 250 mg group ($p < 0.0001$); −22.2% in the 125 mg group ($p = 0.0002$); and −30.2% in the 62.5 mg group ($p < 0.0001$). Moreover, a higher proportion of patients receiving amlitelimab achieved EASI-75 and a vIGA score of 0 or 1 at Weeks 16 and 24 (secondary endpoints), compared to those receiving a placebo. At Week 52, 71.9% and 69% of participants who continued receiving their assigned dose of amlitelimab Q4W

(pooled arms) maintained a vIGA score of 0 or 1 and EASI-75, respectively. Patients who discontinued treatment showed similar results, with 57% maintaining a vIGA score of 0 or 1 and 61.6% sustaining EASI-75 - 28 weeks after the last dose of amlitelimab was administered. Patients treated with amlitelimab exhibited a reduction in serum levels of biomarkers associated with AD, up to Week 52, including total IgE, IL-13, IL-17A, IL-22, and IL-31, in both those who continued treatment and those who discontinued it. Amlitelimab exhibited a favorable safety profile, with no significant life-threatening AEs reported. The most commonly documented events were nasopharyngitis, upper respiratory tract infection, coronavirus disease 2019 (COVID-19), and headache.[25]

Currently, eight clinical trials involving amlitelimab are ongoing as part of the OCEANA Clinical Program, as detailed in Table II.

Rocatinlimab

Rocatinlimab (KHK4083/AMG 451) is a non-fucosylated, human IgG1 monoclonal antibody, that binds to OX40 on activated T cells, thereby blocking the clonal expansion of these cells and suppressing inflammation mediated by Th1, Th2, Th17, and Th22 cells.[18,26]

A Phase 1 single-center, open-label, repeated-dose study (NCT03096223) evaluated the safety and tolerability of KHK4083 in 22 patients with moderate-to-severe AD. Patients received IV administrations of 10 mg/kg of KHK4083 once every two weeks (Q2W) for 6 weeks (a total of 3 infusions), followed by a 16-week follow-up period. TEAEs were observed in 17 patients (77.3%), all of which were classified as mild or moderate in severity. The majority were related to infusion reactions, including pyrexia, chills, and malaise. One of the study's exploratory objectives was to assess the clinical efficacy of KHK4083, having recorded a 74.12 ± 20.53% reduction in EASI from baseline, and a vIGA score of 0 or 1 in 35% of patients at Week 22. The results indicated that rocatinlimab demonstrated a good safety profile and clinical efficacy, which were maintained for 16 weeks after treatment discontinuation.[27]

Subsequently, the Phase 2b, multicenter, randomized, double-blind, placebo-controlled trial (NCT03703102) assessed the efficacy of rocatinlimab, for which the primary endpoint was the percentage change in EASI score from baseline to Week 16. A total of 274 participants with moderate-to-severe AD were randomized into five groups (1:1:1:1:1), four of which received rocatinlimab SC (150 mg Q4W, 600 mg Q4W, 300 mg Q2W, or 600 mg Q2W), while one group received placebo SC, until Week 16. At Week 18, active treatment was extended until Week 36, followed by a 20-week follow-up period without active treatment, lasting until Week 56. The results demonstrated that all rocatinlimab treatment groups showed a significantly higher LS mean percentage reduction in the EASI score from baseline to Week 16 compared to placebo,

which exhibited a 15% decrease. Among the treatment groups, participants who received 150 mg of rocatinlimab Q4W experienced a 48.3% reduction in the EASI score, while those on 600 mg showed a 49.7% decrease. In the groups receiving rocatinlimab Q2W, the 300 mg group had a 61.1% decrease, and the 600 mg group experienced a 57.4% reduction (all $p < 0.001$). In all secondary outcomes (Table III), the treatment groups outperformed placebo. The clinical efficacy of rocatinlimab was sustained across all treatment groups through Week 36, with the 300 mg Q2W regimen standing out. Furthermore, among patients in the treatment groups who achieved EASI-75 at Week 36, 73-96% maintained their response without relapse through Week 56. It is also worth noting that there was a significant decrease in serum concentrations of Thymus and Activation-Regulated Chemokine (TARC), IgE, and IL-22 - key biomarkers in AD - through Week 16. These levels remained low throughout the remainder of the study in most participants in the treatment groups. TEAEs were similar across all rocatinlimab treatment groups, with the most common being pyrexia, nasopharyngitis, chills, headache, aphthous ulcers, and nausea. Serious AEs occurred in 2% to 6% of patients in the rocatinlimab-treated groups, compared with 1.8% in the placebo group. There were no reports of serious hypersensitivity reactions or deaths.[28]

ROCKET is a program of eight Phase 3 clinical trials designed to establish the safety, tolerability, and efficacy profile of rocatinlimab, as well as the most appropriate dosing regimens and their durability, in patients with moderate-to-severe AD.[29] Currently, top-line results from four clinical trials have been presented, with only the full disclosure of results pending, while the remaining studies are still in the development or recruitment phases.

ROCKET-HORIZON (NCT05651711) is a Phase 3, randomized, double-blind, placebo-controlled, parallel-assignment clinical trial, that included 726 participants, randomized to receive rocatinlimab at a dose of Q4W for 24 weeks, with a loading dose at Week 2, or a placebo with the same dosing schedule. The primary endpoints were defined as achieving a vIGA score of 0 or 1 with a ≥2-point reduction from baseline, as well as the percentage of patients achieving EASI-75 at Week 24.[29–32] The top-line results already released revealed that 32.8% of patients in the treatment group reached EASI-75 at Week 24, compared to 13.7% in the placebo group (a 19.1% difference, $p < 0.001$).[29,31,32] At the same time, 19.3% of participants in the treatment group achieved a vIGA score of 0 or 1 with a ≥2-point reduction from baseline, compared to 6.6% of patients in the placebo group, representing a 12.8% difference ($p < 0.001$). The trial also yielded remarkable results in the revised Investigator's Global Assessment (rIGA), an efficacy criterion that adopts a stricter definition of 1 (almost clear) compared to vIGA. At Week 24, 16.4% of patients treated with rocatinlimab achieved a rIGA score of 0 or 1, versus 4.9% in the placebo group, a difference of 11.5% ($p < 0.001$).[29,31] TEAEs were more prevalent in

the group receiving rocatinlimab, with the most common being pyrexia, nasopharyngitis, chills, headaches, aphthous ulcers, and nausea. [32]

ROCKET-IGNITE (NCT05398445) is a Phase 3, 24-week, randomized, double-blind, placebo-controlled study, involving 769 adults with moderate-to-severe AD. Patients were randomized to receive either high- or low-dose rocatinlimab Q4W for 24 weeks, with an additional loading dose at Week 2; or a placebo at the same intervals. The primary endpoints are consistent with those of ROCKET-HORIZON.[32–34] In the HD group of rocatinlimab, 42.3% of patients achieved a ≥75% reduction in EASI at Week 24, representing a 29.5% greater reduction compared to placebo ($p < 0.001$). In the LD group, 36.3% of participants achieved EASI-75, showing a 23.4% difference compared to placebo ($p < 0.001$). Furthermore, 22.7% of patients in the HD group achieved a rIGA score of 0 or 1, a 14.4% difference vs. placebo ($p < 0.001$), while 16.3% of patients in the LD group attained this same score, an 8.0% difference vs. placebo ($p = 0.01$). Rocatinlimab exhibited a safety profile similar to that observed in previous trials, with TEAEs occurring more frequently in the treatment groups, and including pyrexia, chills, and headaches.[35]

ROCKET-SHUTTLE (NCT05724199) is a Phase 3, 24-week, randomized, double-blind, placebo-controlled clinical trial, involving 746 participants. Patients were allocated (1:1:1) to receive either high- or low-dose rocatinlimab Q4W for 24 weeks, with an additional loading dose at Week 2; or a placebo administered at the same dosing schedule. All groups also received a dose of topical corticosteroids (TCS) or topical calcineurin inhibitors (TCI). This study was conducted to assess the safety and efficacy of rocatinlimab in combination with topical TCS/TCI, using the same primary endpoints as ROCKET-HORIZON and ROCKET-IGNITE.[36,37] At Week 24, 26.1% and 23.3% of patients in the HD group achieved a vIGA and rIGA score of 0/1, respectively, while 25.8% and 22.7% in the LD group achieved these endpoints, with the difference in all these groups ranging from 10.9% to 13.8% compared to placebo ($p \leq 0.002$). Additionally, 52.3% of the HD group achieved EASI-75, a 28.7% difference vs. placebo, while in the LD group, 54.1% of patients reached EASI-75, a 30.4% difference vs. placebo (both $p < 0.001$).[35]

ROCKET-VOYAGER (NCT05899816) is a Phase 3, 24-week, randomized, double-blind, placebo-controlled study, involving 221 participants, and designed to explore the potential impact of rocatinlimab on the immune response to tetanus and meningococcal vaccines, compared to placebo. Patients received either rocatinlimab or placebo Q4W, with the primary endpoint being the number of participants with a positive anti-tetanus/anti-meningococcal response at Week 24. [38] The top-line results indicated that rocatinlimab did not affect responses to these vaccines. [35]

The remaining ongoing clinical trials in the ROCKET program are listed in Table V.

Telazorlimab

Telazorlimab (GBR 830/ISB 830) is a humanized IgG1 monoclonal antibody that targets OX40 on T cells, thereby blocking its interaction with OX40L and interrupting this signaling pathway. [18,26]

Three phase 1 studies were carried out to evaluate the immunogenicity and PK of telazorlimab. One of these was a single ascending dose trial in healthy participants, in which GBR 830 was administered via IV infusion at doses of 0.3, 1, 3, and 10 mg/kg. The study demonstrated that the drug was well tolerated, showed a comparable PK profile between healthy individuals and patients with AD, and exhibited high bioavailability, a prolonged half-life, and no evidence of target-mediated drug disposition.[39]

Telazorlimab was the first monoclonal antibody targeting the OX40-OX40L pathway to be included in a Phase 2a study (NCT02683928). In this randomized, double-blind, placebo-controlled, repeated-dose trial, 62 participants with moderate-to-severe AD were randomized in a 3:1 ratio to receive either 10 mg/kg of GBR 830 or placebo, both administered intravenously on Days 1 and 29. The study demonstrated that the administration of two doses of GBR 830, 4 weeks apart, was safe and well tolerated. Most TEAEs were mild or moderate in severity, with headache, AD exacerbation, nasopharyngitis, and upper respiratory tract infection being the most commonly reported. Participants treated with GBR 830 experienced significant reductions from baseline in epidermal thickness, observed on Day 29 ($p < 0.01$) and Day 71 ($p < 0.001$), whereas no marked changes were detected in the placebo group. Similarly, the study revealed that GBR 830 induced a significant decrease in the expression of messenger ribonucleic acid (mRNA) markers associated with the Th1, Th2, Th17, and Th22 subtypes. The drug demonstrated favorable clinical efficacy, with a higher percentage of participants achieving EASI-50 in the treatment group (76.9%) compared to the placebo group (37.5%) on Day 71. [40]

A Phase 2b randomized, double-blind, placebo-controlled, parallel-group, 2-part trial (NCT03568162) was subsequently conducted to further investigate the safety and efficacy of telazorlimab in adults with moderate-to-severe AD. The primary endpoint was the percentage change in EASI from baseline at Week 16. In Part 1, 313 participants were randomly assigned (1:1:1:1) to receive either placebo or one of three telazorlimab SC regimens for 16 weeks: (1) 150 mg loading dose followed by 75 mg Q4W, (2) 600 mg loading dose succeeded by 300 mg Q4W, or (3) 600 mg loading dose followed by 300 mg Q2W. This was followed by a 38-week open-label period, during which all participants received 300 mg of telazorlimab Q2W and a subsequent 12-week treatment-free period. In Part 2, 149 different patients were randomized (1:1) to receive either a 1200 mg loading dose of telazorlimab SC, succeeded by 600 mg Q2W for 16 weeks; or a placebo with the same administration schedule. This was also followed by a

38-week open-label period, in which all patients received 600 mg of telazorlimab Q2W accompanied by a subsequent 12-week follow-up period. At Week 16, the LS mean percentage change from baseline in EASI was superior in the 300 mg Q2W (Part 1) and the 600 mg Q2W (Part 2) arms, when compared to placebo (-54.4% vs. -34.2% in Part 1 and -59% vs. -41.8% in Part 2, respectively, with p = 0.008 in both). This clinical improvement was sustained in both treatment groups during the open-label period and up to Week 66, 12 weeks after treatment discontinuation. On the other hand, 23.7% of patients in the 300 mg Q2W group and 25.3% in the 600 mg Q2W group reached EASI-75, compared to 11.3% and 18.9% in the placebo groups of Part 1 and Part 2, respectively. Telazorlimab was considered safe and well tolerated, with most TEAEs being of mild to moderate severity. The most commonly reported events were AD exacerbation, nasopharyngitis, upper respiratory tract infections, and headache, occurring with comparable frequency in both the treatment and placebo groups.[41]

Currently, there are no new clinical trials evaluating telazorlimab for the treatment of AD. However, a new monoclonal antibody (STAR-0310), derived from telazorlimab, has recently been developed to enhance its pharmacological and therapeutic properties.

STAR-0310

STAR-0310 is a monoclonal antibody developed to target the OX40 receptor. It was designed from an affinity-matured version of telazorlimab, incorporating YTE technology to extend its half-life and reduce its potential to induce antibody-dependent cellular cytotoxicity (ADCC). A Phase 1a randomized, double-blind, placebo-controlled, single ascending dose trial will evaluate the safety, tolerability, immunogenicity, and PK of STAR-0310 in 40 healthy participants. Initial results are expected to be released in the third quarter of 2025.[22,42]

IMG-007

IMG-007 is a novel humanized, anti-OX40 IgG1 monoclonal antibody, developed to effectively inhibit the OX40-OX40L signaling pathway and modulate ADCC activity, without depleting T cells.[21]

A Phase 1, randomized, double-blind, placebo-controlled trial (NCT06304740) was conducted to evaluate the safety and PK profile of a single SC dose of IMG-007 in healthy volunteers. Overall, IMG-007 SC demonstrated a favorable safety profile, with injection site reactions being the most commonly reported TEAEs, occurring more frequently in the placebo arm (75%) compared to the IMG-007 arm (25%). This favorable safety profile aligns with the suppression of ADCC function. Additionally, it was inferred that a single SC dose of IMG-007 had a mean terminal half-life of 34.7 days. [21]

Complementing the Phase 1 trial, a Phase 2a, open-label study (NCT05984784)

was conducted to assess the efficacy and safety of IMG-007. Eligible patients received three 300 mg IV infusions of IMG-007 Q2W (on Days 1, Week 2, and Week 4) and were followed up until Week 24. By Week 16, the interim results showed a mean percentage change in EASI of 77%, and 54% of patients achieved EASI-75. Additionally, sustained inhibition of serum markers associated with Th1, Th2, and Th17 cells was observed and maintained throughout the 24-week follow-up period. IMG-007 was well tolerated, and exhibited a favorable safety profile, with no serious AEs or treatment-related AEs recorded, including pyrexia or chills- effects commonly associated with monoclonal antibody therapies. [21,43]

A phase 2b clinical trial is scheduled to begin in the first quarter of 2025. [21]

Discussion

Given its heterogeneous pathophysiology and unpredictable clinical course, AD continues to pose a therapeutic challenge for clinicians, and significantly impacts patient´s quality of life. Approximately 75% of patients with AD report dissatisfaction with current therapeutic approaches, mainly due to the frequent recurrence of flare-ups, the need for periodic pharmacological adjustments, and the slow onset of efficacy associated with recent biological agents.[44] These limitations highlight the need for novel therapeutic strategies targeting alternative pathogenic pathways.

Inhibiting the OX40/OX40L pathway represents an innovative approach to treating AD by modulating the activity of the various T cell subsets involved in the disease. The initial clinical trials with anti-OX40L (amlitelimab) and anti-OX40 antibodies (rocatinlimab, telazorlimab, IMG-007, and STAR-0310) have yielded promising results.

In two Phase 2 trials, amlitelimab demonstrated significant and sustained clinical efficacy in treating patients with moderate-to-severe AD. The percentage change in EASI from baseline to Week 16 ranged from -69.97% to -80.12%, and -51.6% to -61.5%, depending on the study.[24,25] The Phase 3 clinical trials of the Oceana Program will provide further insights into the long-term efficacy and safety of amlitelimab.[47-54]

Rocatinlimab exhibited rapid and sustained clinical efficacy in a Phase 2b clinical trial. The drug achieved a percentage change in EASI ranging from -48.3% to -61.6% from baseline to Week 16, with the 300 mg Q2W dose showing the most favorable results.[28] Nevertheless, Q4W administration may offer a more practical dosing regimen and improve patient adherence. The top-line results released so far from the ROCKET Program support the hypothesis that rocatinlimab is both an effective and safe treatment for AD. [29-38] The release of full results and the completion of the remaining clinical trials of the ongoing program are awaited. [55-58]

Telazorlimab was the first anti-OX40 monoclonal antibody to demonstrate promising results in the treatment of AD, which led to the initiation of further studies. In the Phase 2b trial, it was concluded that two higher-dose regimens of telazorlimab (300 mg and 600 mg Q2W, following an initial loading dose) resulted in a greater reduction in EASI after 16 weeks of treatment, compared to placebo. However, treatment with telazorlimab showed more limited clinical efficacy, with no significant proportion of patients achieving EASI-75.[41]

Two new anti-OX40 monoclonal antibodies (STAR-0310 and IMG-007) were developed through bioengineering modifications to the Fc region, aimed at extending their half-life and silencing ADCC, thereby reducing the potential risk of adverse effects.[45,46] STAR-0310, developed from telazorlimab, was recently included in a Phase 1a study.[42] Treatment with IMG-007

resulted in a mean percentage change in EASI of 77% and an EASI-75 response of 54% both at Week 16 in patients receiving three 300 mg Q2W doses.[43] IMG-007 exhibited a half-life of 34.7 days, while STAR-0310 had a half-life of 26 days, both significantly longer than the typical half-life of other IgG1 antibodies, which is around 10-14 days.[21,22] Both drugs could play a significant role in the treatment of AD, due to their prolonged half-life and reduced ADCC activity, potentially enabling safer dosing regimens with longer intervals.

The clinical efficacy of all OX40/OX40L pathway inhibitors was sustained over time, with effects lasting from 3 to 9 months after the last administered dose, accompanied by a decrease in the serum concentration of the drug to levels below those considered pharmacologically active. Simultaneously, there was a prolonged decrease in serum biomarkers associated with the Th1, Th2, Th17, and Th22 subsets, which may indicate the induction of a disease-modifying effect by these antibodies.[24,25,28,41] Thus, while the biologics currently used to treat AD require administration every two weeks, antibodies targeting the OX40-OX40L pathway could potentially be administered at more extended intervals, improving adherence and reducing the treatment burden, thereby addressing a significant unmet need in AD.[9]

All OX40/OX40L pathway inhibitors presented a favorable safety profile, with no major AEs reported. The most common TEAEs were pyrexia and chills.[23-25,27-38,40-43] The adverse effects associated with the administration of monoclonal antibodies are often linked to their immunomodulatory action, which may predispose patients to the development of infections. However, as OX40 is primarily expressed on effector T cells, inhibiting the OX40-OX40L pathway helps preserve the homeostasis of naïve and resting memory T cells, thereby avoiding generalized immunosuppression and reducing the risk of infections associated with these antibodies.[26] Furthermore, the biologic agents currently employed in the therapeutic management of AD specifically target the Th2 immune pathway, which can result in a shift towards Th1 or Th17- mediated inflammation, contributing to some of their adverse effects, such as rosacea, alopecia, psoriasis, or arthralgia. In contrast, inhibitors of the OX40/OX40L pathway modulate the response of all Th cell subsets due to their upstream mechanism of action, providing more comprehensive control of AD and a lower risk of adverse reactions associated with a preferential deviation towards a particular immune pathway.[18,26]

Nevertheless, we must await the full results of the Phase 3 studies, which will establish the long-term efficacy and clinical safety of these agents. Head-to-head studies between the different inhibitors of the OX40/OX40L pathway, as well as comparisons with the drugs already established in clinical practice, are essential to define the most appropriate dosing regimens and enable a more effective and personalized approach to the treatment of AD.

Conclusion

Despite continuous advancements in the development of new treatments for AD, a significant proportion of patients remain unresponsive to therapies currently used in clinical practice. Monoclonal antibodies inhibiting the OX40/OX40L pathway, particularly amlitelimab and rocatinlimab, have emerged as promising therapeutic options in the AD treatment landscape, primarily due to their potential disease-modifying effects. We now await the results of Phase 3 clinical trials, along with trials for two new anti-OX40 antibodies (IMG-007 and STAR-0310), to confirm their long-term therapeutic success. Nonetheless, based on current clinical trial outcomes, these novel therapeutic approaches hold the potential to revolutionize the management of AD, offering renewed hope for sustained disease control and significant improvements in patient´s quality of life.

Appendix

Tables

Table I: Completed clinical trials investigating Amlitelimab for the treatment of Atopic Dermatitis

Trial	Phase	Study Design	Endpoints	Main Results	Main Adverse Events
NCT03161288 [23]	1	Single-center, double-blind, randomized, placebo-controlled trial. N= 64 participants Subjects were randomized to amlitelimab or placebo (6:2) across 8 cohorts.	**Primary**: Safety and tolerability of amlitelimab.	Amlitelimab was well-tolerated, with no serious AEs reported.	Mild headache was the most common. All events were self-resolving and of mild to moderate severity.
NCT03754309 [24]	2a	Multicenter, double-blind, randomized (1:1:1), placebo controlled, parallel-group trial N=88 participants **LD**: Amlitelimab 200 mg loading dose + 100 mg maintenance dose Q4W **HD**: Amlitelimab 500 mg loading dose + 250 mg maintenance dose Q4W **Placebo**	**Primary**: - Percentage change in EASI from baseline to Week 16 - Incidence of TEAEs **Secondary**: - Percentage of patients achieving EASI-50, EASI-75 and EASI-90 - Percentage of patients with a vIGA score of 0/1 at Week 16 - Change in SCORing of Atopic Dermatitis (SCORAD) Index, affected Body Surface Area (BSA), change in DLQI, change in Numerical Rating Scale (NRS) for pruritus, etc.	• **LS mean percentage change in EASI** from baseline to Week 16: **LD**: − 80.1%; **HD**: − 70.0% vs. **Placebo**: − 49.4% • **EASI-75** at Week 16: **LD:** 59%; **HD**: 52% vs. **Placebo**: 25% • Percentage of patients with a **vIGA** score of 0/1 at Week 16: **LD:** 44%; **HD:** 37% vs. **Placebo:** 8%	Most frequent TEAEs: Headache, upper respiratory tract infection, hyperhidrosis, pyrexia, increased aspartate aminotransferase and iron deficiency anemia.

NCT05131477 [25]	2b	Multicenter, 2-part, double-blind, randomized, placebo-controlled trial N= 390 participants **Part 1 (24 weeks):** Randomization 1:1:1:1:1 - Amlitelimab SC 250 mg Q4W, 125 mg Q4W or 62.5 mg Q4W without loading dose or 250 mg Q4W with 500 mg loading dose; - Placebo **Part 2 (28 weeks):** Re-randomization 3:1 (clinical responders) - Continuation of their dosing regimen before Week 24 or - Withdrawn from amlitelimab	**Primary**: - Percentage change in EASI from baseline to Week 16 **Secondary**: **Part 1:** - Percentage change in EASI from baseline to week 24 - EASI-75 response at Weeks 16 and 24 - Percentage of patients with vIGA score of 0/1 at Weeks 16 and 24 **Part 2:** - vIGA score of 0/1 and EASI-75 responses at Week 52 in clinical responders of part 1	• Difference from placebo in **LS mean percentage change in EASI** from baseline to Week 16: - **250 mg with 500mg of loading dose**: - 32.1% ($p < 0.0001$) - **250 mg**: − 27.3% ($p < 0.0001$) - **125 mg**: − 22.2% ($p = 0.0002$) - **62.5 mg**: − 30.2% ($p < 0.0001$) • Higher percentage of patients achieving **vIGA** score of 0/1 at Week 16 and Week 24 in amlitelimab groups vs. placebo. • Higher percentage of patients achieving **EASI-75** at Week 16 and Week 24 in amlitelimab groups vs. placebo. • Similar percentage of clinical responders achieving vIGA score of 0/1 and EASI-75 at Week 52 in pooled amlitelimab groups vs. withdrawn group (71.9% and 69%) vs. (57% vs. 61.6%).	Most frequent TEAEs: nasopharyngitis, COVID-19, headache.

AEs-Adverse Events; LD-Low Dose; Q4W-Once every 4 weeks; HD-High Dose; EASI-Eczema Area and Severity; TEAEs-Treatment-emergent adverse events; vIGA-validated Investigator's Global Assessment; SCORAD- SCORing of Atopic Dermatitis; BSA-Body Surface Area; DLQI-Dermatology Life Quality Index; NRS- Numerical Rating Scale; LS-Least-Squares; SC-Subcutaneous.

Table II: Ongoing Oceana Program clinical trials investigating Amlitelimab for the treatment of Atopic Dermatitis

ClinicalTrials.gov identifier	Title	Phase	Study Design	Primary Endpoint	Status	Estimated study completion date
NCT06130566[47]	COAST-1	3	Multinational, multicenter, randomized, double-blind, placebo-controlled, parallel-group, 3-arm study. 420 participants (estimated).	Percentage of patients reaching EASI-75 and vIGA score of 0/1 with ≥2-point reduction in IGA, at Week 24.	Recruiting	2025-11-14
NCT06181435 [48]	COAST-2	3	Multinational, multicenter, randomized, double-blind, placebo-controlled, parallel-group, 3-arm study. 420 participants (estimated).	Percentage of patients reaching EASI-75 and vIGA score of 0/1 with ≥2-point reduction in IGA, at Week 24.	Recruiting	2026-02-03
NCT06224348 [49]	SHORE	3	Multinational, multicenter, randomized, double-blind, placebo-controlled, parallel-group, 3-arm study. 496 participants (estimated).	Percentage of patients reaching EASI-75 and vIGA score of 0/1 with ≥2-point reduction in IGA, at Week 24.	Recruiting	2026-01-21
NCT06407934 [50]	ESTUARY	3	Multinational, multicenter, randomized, double-blind, placebo-controlled, parallel-group study. 961 participants (estimated), responders from the parent trials (COAST-1, COAST-2, or SHORE).	Proportion of participants who maintain clinical response (vIGA score of 0/1 and/or EASI-75) at Week 48 compared to treatment withdrawal.	Recruiting	2027-01-05
NCT06241118 [51]	AQUA	3	Multinational, multicenter, randomized, double-blind, placebo-controlled, parallel-group, 3-arm study. 249 participants (estimated) who have had inadequate response to prior biologic or oral JAKi therapy.	Percentage of patients reaching EASI-75 and vIGA score of 0/1 with ≥2-point reduction, at Week 36. Percentage change in the weekly average of daily sleep disturbance NRS.	Recruiting	2026-06-30
NCT05769777 [52]	ATLANTIS	2	Open-label, single-group, 1-arm, long-term safety study. 901 participants (estimated).	Percentage of patients who experienced TEAEs from baseline through Week 176.	Recruiting	2028-10-09
NCT05492578 [53]	RIVER-AD	2/3	Open-label, single-group, long-term safety study. 1310 participants (estimated) who have previously been enrolled in an amlitelimab Oceana Program clinical trial.	Percentage of patients who experienced TEAEs from baseline through Week 332.	Recruiting	2028-12-29
NCT06015308 [54]	HYDRO	2	Multicenter, randomized, double-blind, placebo-controlled, 2-arm study. 215 participants (estimated).	Percentage of patients with positive tetanus and pneumococcal vaccine response at Week 16.	Recruiting	2026-02-27

vIGA-validated Investigator's Global Assessment; IGA-Investigator's Global Assessment; JAKi-JAK inhibitors; NRS-Numerical Rating Scale; TEAEs-Treatment-emergent adverse events.

Table III: Completed clinical trials investigating Rocatinlimab for the treatment of Atopic Dermatitis

Trial	Phase	Study Design	Endpoints	Main Results	Main Adverse Events
NCT03096223 [27]	1	Single-center, open-label, repeated-dose study N= 22 participants 10 mg/kg IV Q2W, during 6 weeks (total of 3 infusions) + 16 weeks of follow-up	**Primary**: Safety and tolerability of rocatinlimab (Incidence of TEAEs up to Week 22) **Secondary**: Clinical efficacy and pharmacodynamics of rocatinlimab	• Good safety and tolerability profile. • **EASI** change from baseline in percentage (mean ± SD): - 74.12 ± 20.53% at Week 22. • Percentage of patients achieving **vIGA** 0/1: 35% at Week 22.	• Mild or moderate TEAEs, mostly due to infusion reactions: pyrexia, chills, and malaise.
NCT03703102 [28]	2b	Multicenter, randomized, double-blind, parallel-group, placebo-controlled study N=274 participants Randomized 1:1:1:1:1 to: • Rocatinlimab 150 mg SC Q4W • Rocatinlimab 600 mg SC Q4W • Rocatinlimab 300 mg SC Q2W • Rocatinlimab 600 mg SC Q2W • Placebo	**Primary**: - Percentage change in EASI from baseline to Week 16 **Secondary**: - Achievement of EASI-50, EASI-75, EASI-90 at Week 16 - Achievement of rIGA/vIGA score of 0 or 1 with ≥2-point reduction from baseline at Week 16 - Percentage change from baseline in SCORAD - Change from baseline in DLQI - Percentage change from baseline in pruritus NRS score - Percentage change from baseline in sleep disturbance NRS score	• **LS mean change in EASI** from baseline to Week 16: - **150 mg Q4W**: −48.3% - **600 mg Q4W**: −49.7% - **300 mg Q2W**: −61.1% - **600 mg Q2W**: −57.4% vs. **Placebo**: −15.0% (all $p < 0.001$) • Rocatinlimab outperformed placebo in all secondary outcomes, with the 300 mg Q2W dose showing the greatest results at Week 16. • Among rocatinlimab-treated patients who achieved EASI-75 at Week 36, 73–96% remained relapse-free at Week 56 after treatment discontinuation. • Decreased serum concentrations of TARC, IgE, and IL-22 in the rocatinlimab groups throughout the study.	• Most frequent TEAEs: pyrexia, chills, headache, aphthous ulcer, and nausea. • Serious adverse events occurred in 2–6% of rocatinlimab patients and 1.8% of the placebo group.

IV-Intravenous; Q2W-Once every 2 weeks; TEAEs-Treatment-emergent adverse events; EASI-Eczema Area and Severity; vIGA-validated Investigator's Global Assessment; SC-Subcutaneous; Q4W-Once every 4 weeks; rIGA-revised Investigator Global Assessment; SCORAD-SCORing of Atopic Dermatitis; DLQI-Dermatology Life Quality Index; NRS-Numerical Rating Scale; LS-Least-Squares; TARC-Thymus and Activation-Regulated Chemokine; IgE-Immunoglobulin E; IL-Interleukin.

Table IV: Top-line results from ROCKET Program clinical trials investigating Rocatinlimab for the treatment of Atopic Dermatitis

Trial	Phase	Study Design	Endpoints	Main Results	Main Adverse Events
HORIZON (NCT05651711)[29–32]	3	Randomized, double-blind, placebo-controlled, parallel assignment study N=726 participants - **Rocatinlimab arm**: dose of rocatinlimab SC Q4W + loading dose at Week 2 - **Placebo arm**: dose of placebo SC Q4W + loading dose at Week 2	**Primary**: - Achievement of vIGA/rIGA score of 0 or 1 with ≥2-point reduction from baseline at Week 24 - Achievement of EASI-75 at Week 24	• **EASI-75** at Week 24: **Rocatinlimab group:** 32.8% vs. **Placebo:** 13.7% (19.1% difference, p<0.001). • **vIGA 0/1** in 19.3% of the rocatinlimab group vs. 6.6% in the placebo group (12.8% difference, p<0.001). **rIGA 0/1** in 16.4% of the rocatinlimab group vs. 4.9% in the placebo group (11.5% difference, p<0.001).	- TEAEs were more common in the rocatinlimab group. - Most frequent: pyrexia, nasopharyngitis, chills, headache, aphthous ulcer, and nausea.
IGNITE (NCT05398445)[32-35]	3	Randomized, double-blind, placebo-controlled study N=769 participants - **Arm 1**: HD of rocatinlimab SC Q4W + loading dose at Week 2 - **Arm 2**: LD of rocatinlimab SC Q4W + loading dose at Week 2 -**Placebo** SC Q4W + loading dose at Week 2	**Primary**: - Achievement of vIGA score of 0/1 with ≥2-point reduction from baseline at Week 24 - Achievement of EASI-75 at Week 24	• **rIGA** score of 0/1 in 22.7% of the HD group and 16.3% of the LD group (14.4% and 8% difference from placebo, respectively, p≤0.01). • **EASI-75** at Week 24: **HD group:** 42.3% **LD group:** 36.3% (29.5% and 23.4% difference from placebo, respectively, p<0.001)	- Most frequent TEAEs: pyrexia, chills, and headache.
SHUTTLE (NCT05724199) [35-37]	3	Randomized, double-blind, placebo-controlled study N=746 participants - **Rocatinlimab HD** Q4W + TCS/TCI + loading dose at Week 2 - **Rocatinlimab LD** Q4W + TCS/TCI + loading dose at Week 2 - **Placebo** Q4W + TCS/TCI + loading dose at Week 2	**Primary**: - Achievement of rIGA/vIGA score of 0 or 1 with ≥2-point reduction from baseline at Week 24 - Achievement of EASI-75 at Week 24	• **vIGA** score of 0/1 in 26.1% of the HD group and 25.8% of the LD group. • **rIGA** score of 0/1 in 23.3% of the HD group and 22.7% of the LD group. **EASI-75** at Week 24: **HD group:** 52.3% **LD group:** 54.1% (28.7% and 30.4% difference from placebo, respectively, p<0.001).	Ø

VOYAGER (NCT05899816) [38]	3	Randomized, double-blind, placebo-controlled study N=221 participants -**Rocatinlimab** Q4W for 24 weeks + loading dose at Week 2 -**Placebo** Q4W for 24 weeks + loading dose at Week 2	**Primary:** - Number of participants with a positive anti-tetanus response from Week 20 to Week 24 - Number of participants with a positive anti-meningococcal response from Week 20 to Week 24	Rocatinlimab does not interfere with responses to tetanus and meningococcal vaccinations.	Ø

SC-Subcutaneous; Q4W-Once every 4 weeks; vIGA-validated Investigator's Global Assessment; rIGA-revised Investigator Global Assessment; EASI-Eczema Area and Severity; TEAEs-Treatment-emergent adverse events; HD-High Dose; LD-Low Dose; TCS-Topical Corticosteroids; TCI-Topical Calcineurin Inhibitors.

Table V: Ongoing ROCKET Program clinical trials investigating Rocatinlimab for the treatment of Atopic Dermatitis

ClinicalTrials.gov identifier	Title	Phase	Study Design	Primary Endpoint	Status	Estimated study completion date
NCT05633355 [55]	ROCKET-ORBIT	3	Open-label, 52-week, non-randomized, single-group assignment study. 187 participants between 12-17 years old.	Number of participants with treatment-emergent serious AEs up to Week 52	Active, not recruiting	2025-07-28
NCT05704738 [56]	ROCKET-ASTRO	3	Double-blind, 52-week, re-randomized, sequential assignment, placebo-controlled study. 532 participants between 12-17 years old.	Percentage of patients achieving EASI-75 at Week 24; vIGA score of 0/1 with ≥2-point reduction at Week 24	Active, not recruiting	2025-11-27
NCT06224192 [57]	ROCKET-OUTPOST	3	Open-label, 52-week, randomized, performance study. 151 participants.	Proportion of full-dose self-administered rocatinlimab injections among attempted home-use injections up to Week 16	Active, not recruiting	2026-03-11
NCT05882877 [58]	ROCKET-ASCEND	3	Double-blind, 116-week, randomized, parallel assignment, placebo-controlled study. 2200 participants (estimated) who have completed a parent study within the ROCKET program.	Number of participants with TEAEs	Recruiting	2027-05-14

AEs-Adverse Events; EASI-Eczema Area and Severity; vIGA-validated Investigator's Global Assessment; TEAEs-Treatment-emergent adverse events.

Table VI: Completed clinical trials investigating Telazorlimab for the treatment of Atopic Dermatitis

Trial	Phase	Study Design	Endpoints	Main Results	Main Adverse Events
NCT02683928 [40]	2a	Double-blind, randomized, placebo-controlled, exploratory study. N=62 participants 10 mg/kg IV infusions of GBR 830 or placebo on Day 1 and Day 29.	**Primary**: Incidence of TEAEs and changes from baseline in epidermal hyperplasia and active AD mRNA expression signature **Secondary**: • Percentage improvement from baseline in IGA and EASI scores • EASI-50 and EASI-75 responses • Achievement of IGA score of 0 or 1 • Pruritus NRS and DLQI changes from baseline	• Significant reductions **in epidermal thickness** from baseline on Day 29 ($P < 0.01$) and Day 71 ($P < 0.001$) in the GBR 830 group with no significant changes in the placebo group. • Significant reduction in mRNA expression of biomarkers associated with Th1, Th2, Th17 and Th22 subtypes. • On Day 71, a higher percentage of patients in the GBR 830 group achieved **EASI-50** (76.9%) compared to placebo (37.5%).	Most frequent TEAEs: headache, exacerbation of AD, nasopharyngitis, and upper respiratory tract infection.
NCT03568162 [41]	2b	Double-blind, randomized, placebo-controlled, parallel-group, 2-part study **Part 1:** 313 subjects randomized (1:1:1:1): (1) Loading dose of 150 mg and 75 mg Q4W of telazorlimab; (2) Loading dose of 600 mg and 300 mg Q4W of telazorlimab; (3) Loading dose of 600 mg and 300 mg Q2W of telazorlimab; (4) Placebo **Part 2:** 149 subjects randomized 1:1: (1) Loading dose of 1200 mg and 600 mg Q2W of telazorlimab; (2) Placebo	**Primary:** Percentage change from baseline in EASI, at Week 16. **Secondary:** • Proportion of subjects achieving EASI-75 and EASI-50 • IGA score of 0 or 1 with ≥2-point reduction from baseline • Pruritus NRS score improvement ≥4	•**LS mean percentage change in EASI** from baseline to Week 16: **300 mg Q2W** (part 1): -54.4% vs. **Placebo** -34.2% ($p = 0.008$) **600 mg Q2W** (part 2): -59% vs. **Placebo** -41.8% ($p = 0.008$) • Achievement of **EASI-75**, at Week 16, in 300mg Q2W of telazorlimab SC group vs.placebo: 23.7% vs. 11.3%. • Achievement of **EASI-75**, at Week 16, in 600 mg Q2W of telazorlimab SC group vs.placebo: 25.3% vs. 18.9%.	The frequency of TEAEs was similar between telazorlimab and placebo arms. Most frequent TEAEs: exacerbation of AD, nasopharyngitis, upper respiratory tract infection, and headache.

IV-Intravenous; TEAEs-Treatment-emergent adverse events; AD-Atopic Dermatitis; mRNA-messenger Ribonucleic Acid; IGA-Investigator's Global Assessment; EASI-Eczema Area and Severity; NRS-Numerical Rating Scale; DLQI-Dermatology Life Quality Index; Th-T helper; Q4W-Once every 4 weeks; Q2W-Once every 2 weeks; LS-Least-Squares; SC-Subcutaneous.

Table VII: Completed clinical trials investigating IMG-007 for the treatment of Atopic Dermatitis

Trial	Phase	Study Design	Endpoints	Main Results	Main Adverse Events
NCT06304740 [21,42]	1a	Double-blind, randomized, placebo-controlled study. N=16 participants Three sequential dose cohorts, each receiving escalating doses of IMG-007 SC or placebo SC.	**Primary**: Safety and tolerability of IMG-007 (Incidence of TEAEs) **Secondary**: PK of IMG-007	• Good safety and tolerability profile. • A single SC dose of IMG-007 showed a **mean terminal half-life** of 34.7 days (longer than other anti-OX40/OX40L monoclonal antibodies).	• Most frequent TEAEs: injection site reactions. • TEAEs were more frequent in the placebo arm (75%) than in the IMG-007 arm (25%).
NCT05984784 [21,43]	2a	Open-label study. N=13 participants Patients received 300 mg of IMG-007 IV at baseline, Week 2, and Week 4, followed by a 24-week follow-up period.	**Primary:** Safety and tolerability of IMG-007 (Incidence of TEAEs) **Secondary:** • Percentage change from baseline in EASI over time • PK of IMG-007	• Mean reduction in **EASI** of 77% from baseline to Week 16 and **EASI-75** response of 54% at Week 16. • Inhibition of serum markers of Th1, Th2 and Th17 cells was sustained during the 24-week follow-up period.	No serious adverse events or treatment-related AEs.

SC-Subcutaneous; TEAEs-Treatment-emergent adverse events; PK-Pharmacokinetics; IV-Intravenous; EASI-Eczema Area and Severity; Th-T helper; AEs-Adverse Events.

References

1. Nutten S. Atopic dermatitis: global epidemiology and risk factors. Ann Nutr Metab. 2015;66(Suppl 1):8-16. doi:10.1159/000370220.

2. Barbarot S, Auziere S, Gadkari A, et al. Epidemiology of atopic dermatitis in adults: Results from an international survey. *Allergy*. 2018;73(6):1284-1293. doi:10.1111/all.13401.

3. Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J. Atopic dermatitis. In: Harrison's Principles of Internal Medicine. 20th ed. Vol 1. New York: McGraw-Hill Education; 2018.

4. Davidson WF, Leung DYM, Beck LA, et al. Report from the National Institute of Allergy and Infectious Diseases workshop on "Atopic dermatitis and the atopic march: Mechanisms and interventions." *J Allergy Clin Immunol*. 2019;143(3):894-913. doi:10.1016/j.jaci.2019.01.003.

5. Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis. *J Am Acad Dermatol*. 2014;70(2):338-351. doi:10.1016/j.jaad.2013.10.010.

6. Torres T, Ferreira EO, Gonçalo M, Mendes-Bastos P, Selores M, Filipe P. Update on atopic dermatitis. *Acta Med Port*. 2019;32(9):606-613. doi:10.20344/amp.11963.

7. Lifschitz C. The impact of atopic dermatitis on quality of life. *Ann Nutr Metab*. 2015;66(Suppl 1):34-40. doi:10.1159/000370226.

8. Lé AM, Torres T. OX40-OX40L inhibition for the treatment of atopic dermatitis—focus on rocatinlimab and amlitelimab. *Pharmaceutics*. 2022;14(12). doi:10.3390/pharmaceutics14122753.

9. Alvarenga JM, Bieber T, Torres T. Emerging biologic therapies for the treatment of atopic dermatitis. *Drugs*. 2024;84(11):1379. doi:10.1007/s40265-024-02095-4.

10. UpToDate (Internet). Waltham, MA: UpToDate, Inc.; Treatment of atopic dermatitis (eczema); available from: https://www.uptodate.com/contents/treatment-of-atopic-dermatitiseczema?search=dermatite%20atopica&source=search_result&selectedTitle=3%7E150&usage_type=default&display_rank=1#H903644714. Last accessed 2024/12/23.

11. Guttman-Yassky E, Silverberg JI, Thaçi D, et al. Upadacitinib treatment withdrawal and retreatment in patients with moderate-to-severe atopic dermatitis: results from a phase 2b, randomized, controlled trial. *J Eur Acad Dermatol Venereol*. 2023;37(12):2558-2568. doi:10.1111/jdv.19391.

12. Blauvelt A, Silverberg JI, Lynde CW, et al. Abrocitinib induction, randomized withdrawal, and retreatment in patients with moderate-to-severe atopic dermatitis: results from the JAK1 atopic dermatitis efficacy and safety (JADE) REGIMEN phase 3 trial. *J Am Acad Dermatol*. 2022;86(1):104-112. doi:10.1016/j.jaad.2021.05.075.

13. Wollenberg A, Blauvelt A, Guttman-Yassky E, et al. Tralokinumab for moderate-to-severe atopic dermatitis: results from two 52-week, randomized, double-blind,

multicentre, placebo-controlled phase III trials (ECZTRA 1 and ECZTRA 2). *Br J Dermatol*. 2021;184:386-387. doi:10.1111/bjd.19574.

14. Worm M, Simpson EL, Thaçi D, et al. Efficacy and safety of multiple dupilumab dose regimens after initial successful treatment in patients with atopic dermatitis: a randomized clinical trial. *JAMA Dermatol*. 2019;155(12):1375-1383. doi:10.1001/jamadermatol.2019.3617.

15. Abdelhalim A, Orhan M, Mohamed Y, et al. A narrative review of the OX40-OX40L pathway as a potential therapeutic target in atopic dermatitis: focus on rocatinlimab and amlitelimab. *Dermatol Ther (Heidelb)*. 2024;14(12):3197. doi:10.1007/s13555-024-01308-8.

16. Malik K, Heitmiller KD, Czarnowicki T. An Update on the Pathophysiology of Atopic Dermatitis. *Dermatol Clin*. 2017;35(3):317-326. doi:10.1016/j.det.2017.02.006

17. Kim J, Kim BE, Leung DYM. Pathophysiology of atopic dermatitis: clinical implications. *Allergy Asthma Proc*. 2019;40(2):84. doi:10.2500/AAP.2019.40.4202.

18. Sadrolashrafi K, Guo L, Kikuchi R, et al. An OX-Tra'Ordinary tale: the role of OX40 and OX40L in atopic dermatitis. *Cells.* 2024;13(7). doi:10.3390/cells13070587.

19. Furue M, Furue M. OX40L–OX40 signaling in atopic dermatitis. *J Clin Med.* 2021;10(12). doi:10.3390/jcm10122578.

20. Guttman-Yassky E, Croft M, Geng B, et al. The role of OX40 ligand/OX40 axis signalling in atopic dermatitis. *British Journal of Dermatology*. Published online June 5, 2024. doi:10.1093/bjd/ljae230

21. GlobeNewswire (Internet). Inmagene reports positive topline results of IMG-007, a nondepleting anti-OX40 monoclonal antibody with an extended half-life for the treatment of atopic dermatitis. Available from: https://www.globenewswire.com/news-release/2025/01/09/3007096/0/en/Inmagene-Reports-Positive-Topline-Results-of-IMG-007-a-Nondepleting-Anti-OX40-Monoclonal-Antibody-with-an-Extended-Half-Life-for-the-Treatment-of-Atopic-Dermatitis.html. Last accessed 2025/03/01.

22. Astria Therapeutics (Internet). Astria Therapeutics announces exclusive worldwide license agreement with Ichnos Sciences for OX40 portfolio. Available from: https://ir.astriatx.com/news-releases/news-release-details/astria-therapeutics-announces-exclusive-worldwide-license. Last accessed 2025/03/14.

23. Saghari M, Gal P, Gilbert S, et al. OX40L inhibition suppresses KLH-driven immune responses in healthy volunteers: a randomized controlled trial demonstrating proof-of-pharmacology for KY1005. Clin Pharmacol Ther. 2022;111. doi:10.1002/cpt.2539.

24. Weidinger S, Bieber T, Cork MJ, et al. Safety and efficacy of amlitelimab, a fully human nondepleting, noncytotoxic anti-OX40 ligand monoclonal antibody, in atopic dermatitis: results of a phase IIa randomized placebo-controlled trial. *Br J Dermatol.* 2023;189(5):531-539. doi:10.1093/bjd/ljad240.

25. Weidinger S, Blauvelt A, Papp KA, Reich A, Lee CH. Phase 2b randomized clinical trial of amlitelimab, an anti-OX40 ligand antibody, in patients with moderate-to-severe atopic dermatitis. *J Allergy Clin Immunol*. 2024. doi:10.1016/j.jaci.2024.10.031.

26. Croft M, Esfandiari E, Chong C, et al. OX40 in the pathogenesis of atopic dermatitis—a new therapeutic target. *Am J Clin Dermatol*. 2024;25(3):447-461. doi:10.1007/s40257-023-00838-9.

27. Nakagawa H, Iizuka H, Nemoto O, et al. Safety, tolerability and efficacy of repeated intravenous infusions of KHK4083, a fully human anti-OX40 monoclonal antibody, in Japanese patients with moderate to severe atopic dermatitis. *J Dermatol Sci*. 2020;99(2):82-89. doi:10.1016/j.jdermsci.2020.06.005.

28. Guttman-Yassky E, Simpson EL, Reich K, et al. An anti-OX40 antibody to treat moderate-to-severe atopic dermatitis: a multicentre, double-blind, placebo-controlled phase 2b study. *Lancet*. 2023;401(10372):204-214. doi:10.1016/S0140-6736(22)02037-2.

29. PR Newswire (Internet). Kyowa Kirin announces top-line data from rocatinlimab Phase 3 ROCKET HORIZON trial for adults with moderate to severe atopic dermatitis. Available from: https://www.prnewswire.com/news-releases/kyowa-kirin-announces-top-line-data-from-rocatinlimab-phase-3-rocket-horizon-trial-for-adults-with-moderate-to-severe-atopic-dermatitis-302258420.html. Last accessed 2025/02/14.

30. ClinicalTrials.gov (Internet). Study Details | A study assessing rocatinlimab (AMG 451) monotherapy in moderate-to-severe atopic dermatitis (AD) (ROCKET-Horizon). Available from: https://clinicaltrials.gov/study/NCT05651711?cond=Atopic%20Dermatitis&intr=rocatinlimab&rank=5#study-plan. Last accessed 2025/02/14.

31. MPR (Internet). HORIZON: Rocatinlimab effective in adults with atopic dermatitis. Available from: https://www.empr.com/news/horizon-rocatinlimab-effective-in-adults-with-atopic-dermatitis/. Last accessed 2025/02/14.

32. National Institute for Health and Care Research (NIHR) (Internet). Rocatinlimab for moderate-to-severe atopic dermatitis in adults and adolescents: Licensing and market availability plans. Currently in phase III clinical trials. Available from: https://io.nihr.ac.uk/wp-content/uploads/2025/01/36878-Rocatinlimab-for-Atopic-Dermatitis-V1.0-JAN2025-NON-CONF.pdf. Last accessed 2025/05/26.

33. Health Research Authority (Internet). A Phase 3 study of rocatinlimab monotherapy in atopic dermatitis (AD) (ROCKET-Ignite). Available from: https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/a-phase-3-study-of-rocatinlimab-monotherapy-in-atopic-dermatitis-ad-rocket-ignite/. Last accessed 2025/02/19.

34. ClinicalTrials.gov (Internet). Study Details | A study evaluating rocatinlimab in moderate-to-severe atopic dermatitis (ROCKET-IGNITE). Available from: https://clinicaltrials.gov/study/NCT05398445?cond=Atopic%20Dermatitis&intr=rocatinlimab&rank=6. Last accessed 2025/02/19.

35. Amgen (Internet). Amgen and Kyowa Kirin provide top-line results from rocatinlimab Phase 3 IGNITE study in adults with moderate to severe atopic dermatitis. Available

from: https://www.amgen.com/newsroom/press-releases/2025/03/amgen-and-kyowa-kirin-provide-top-line-results-from-rocatinlimab-phase-3-ignite-study-in-adults-with-moderate-to-severe-atopic-dermatitis. Last accessed 2025/03/15.

36. ClinicalTrials.gov (Internet). Study Details | A study assessing rocatinlimab in combination with topical corticosteroid and/or topical calcineurin inhibitors in adult participants with moderate-to-severe atopic dermatitis (AD). Available from: https://clinicaltrials.gov/study/NCT05724199?cond=Atopic%20Dermatitis&intr=rocatinlimab&rank=7. Last accessed 2025/02/19.

37. Health Research Authority (Internet). A Phase 3 study of rocatinlimab, corticosteroids and/or calcineurin inhibitors in AD (ROCKET-Shuttle). Available from: https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/a-phase-3-study-of-roctinlimab-corticosteroids-andor-calcineurin-inhibitors-in-ad-rocket-shuttle/. Last accessed 2025/02/19.

38. ClinicalTrials.gov (Internet). Study Details | A study assessing rocatinlimab on vaccine antibody response in moderate-to-severe atopic dermatitis (AD) (ROCKET – VOYAGER). Available from: https://clinicaltrials.gov/study/NCT05899816?cond=rocatinlimab&intr=nct05899816&rank=1. Last accessed 2025/03/16.

39. Gudi G, Vinu CA, Sunitha GN, et al. Clinical pharmacokinetics and immunogenicity of GBR 830, a first-in-class humanized monoclonal antibody inhibiting OX40 to treat atopic dermatitis

40. Guttman-Yassky E, Pavel AB, Zhou L, et al. GBR 830, an anti-OX40, improves skin gene signatures and clinical scores in patients with atopic dermatitis. *J Allergy Clin Immunol*. 2019;144(2):482-493.e7. doi:10.1016/j.jaci.2018.11.053

41. Rewerska B, Sher LD, Alpizar S, et al. Phase 2b randomized trial of OX40 inhibitor telazorlimab for moderate-to-severe atopic dermatitis. *J Allergy Clin Immunol Glob*. 2024;3(1). doi:10.1016/j.jacig.2023.100195

42. Business Wire (Internet). San Francisco: Business Wire; 2025. Astria Therapeutics Announces Initiation of Phase 1a Trial of STAR-0310, a Potential Best-in-Class Monoclonal Antibody OX40 Antagonist for the Treatment of Atopic Dermatitis. Available at: https://www.businesswire.com/news/home/20250123072294/en/Astria-Therapeutics-Announces-Initiation-of-Phase-1a-Trial-of-STAR-0310-a-Potential-Best-in-Class-Monoclonal-Antibody-OX40-Antagonist-for-the-Treatment-of-Atopic-Dermatitis. Last accessed 2025/03/14.

43. Shen Y, Lin Z, Guo C, Nair A, Lu Y, Silverberg JI. IMG-007, a nondepleting OX40 monoclonal antibody with an extended half-life, improves skin lesions in adults with moderate-to-severe atopic dermatitis: interim results from a phase 2a trial. *Br J Dermatol*. 2024;191(Suppl 2):e76. doi:10.1093/bjd/ljae266.076.

44. Augustin M, Costanzo A, Pink A, et al. Real-world treatment patterns and treatment benefits among adult patients with atopic dermatitis: results from the Atopic Dermatitis Patient Satisfaction and Unmet Need Survey. *Acta Derm Venereol*. 2022;102:adv3932. doi:10.2340/actadv.v102.3932.

45. Clinical Trials Arena (Internet). London: Netwise Publishing Ltd; 2025. Available at: https://www.clinicaltrialsarena.com/news/inmagene-study-kickstart-proof-of-concept-img007/. Last accessed 2025/04/14.

46. Biris N, Macoin J, Carretero L, Perez C, Zhao C. Development and characterization of STAR-0310: a novel OX40 antagonistic monoclonal antibody. Cells. 2024;13(7):0587. doi:10.3390/cells13070587.

47. ClinicalTrials.gov (Internet). Study Details | A Study to Evaluate the Efficacy and Safety of Subcutaneous Amlitelimab Monotherapy Compared With Placebo in Participants Aged 12 Years and Older With Moderate-to-severe Atopic Dermatitis. [Internet]. Available from:https://clinicaltrials.gov/study/NCT06130566?cond=Atopic%20Dermatitis&intr=amlitelimab&rank=2. Last accessed 2025/04/14.

48. ClinicalTrials.gov (Internet). Study Details | A Study to Evaluate the Efficacy and Safety of Subcutaneous Amlitelimab Monotherapy Compared With Placebo in Participants Aged 12 Years and Older With Moderate-to-severe Atopic Dermatitis (COAST 2). [Internet]. Available from: https://clinicaltrials.gov/study/NCT06181435?cond=Atopic%20Dermatitis&intr=amlitelimab&rank=3. Last accessed 2025/04/14.

49. ClinicalTrials.gov (Internet). Study Details | A Study to Evaluate the Efficacy and Safety of Subcutaneous Amlitelimab in Participants Aged 12 Years and Older With Moderate-to-severe Atopic Dermatitis on Background Topical Corticosteroids. [Internet]. Available from:https://clinicaltrials.gov/study/NCT06224348?cond=Atopic%20Dermatitis&intr=amlitelimab&rank=7. Last accessed 2025/04/14.

50. ClinicalTrials.gov (Internet). Study Details | A Study to Evaluate the Treatment Response and Safety of Two Dose Regimens of Subcutaneous Amlitelimab Monotherapy Compared With Treatment Withdrawal in Participants Aged 12 Years and Older With Moderate-to-severe Atopic Dermatitis. [Internet]. Available from: https://clinicaltrials.gov/study/NCT06407934?cond=Atopic%20Dermatitis&intr=amlitelimab&rank=4. Last accessed 2025/04/14.

51. ClinicalTrials.gov (Internet). Study Details | A Study to Evaluate the Efficacy and Safety of Subcutaneous Amlitelimab on Background Topical Corticosteroids Therapy in Participants Aged 12 Years and Older With Moderate-to-severe AD Who Have Had an Inadequate Response to Prior Biologic Therapy or an Oral JAK Inhibitor. Available from: https://clinicaltrials.gov/study/NCT06241118?cond=Atopic%20Dermatitis&intr=amlitelimab&rank=9. Last accessed 2025/04/14.

52. ClinicalTrials.gov (Internet). Study Details | Open Label, Long-term Study Evaluating Safety and Efficacy of Subcutaneous Amlitelimab in Participants Aged 12 Years and Older With Moderate to Severe Atopic Dermatitis. Available from: https://clinicaltrials.gov/study/NCT05769777?cond=Atopic%20Dermatitis&intr=amlitelimab&rank=1. Last accessed 2025/04/14.

53. ClinicalTrials.gov (Internet). Study Details | Long-Term Safety and Efficacy Evaluation of Amlitelimab in Participants of Previous Amlitelimab Moderate to Severe Atopic Dermatitis Clinical Trials. Available from:

https://clinicaltrials.gov/study/NCT05492578?cond=Atopic%20Dermatitis&intr=amlitelimab&rank=8. Last accessed 2025/04/14.

54. ClinicalTrials.gov (Internet). Study Details | A Study to Investigate Vaccine Responses in Subcutaneous Amlitelimab Treated Atopic Dermatitis Participants Aged 18 Years and Older Compared With Placebo. Available from: https://clinicaltrials.gov/study/NCT06015308?cond=Atopic%20Dermatitis&intr=amlitelimab&rank=5. Last accessed 2025/04/14.

55. ClinicalTrials.gov (Internet). Study Details | A Study to Assess the Safety, Tolerability, and Efficacy of Rocatinlimab in Adolescent Participants With Moderate-to-severe Atopic Dermatitis (AD). Available from: https://clinicaltrials.gov/study/NCT05633355?cond=Atopic%20Dermatitis&intr=rocatinlimab&rank=2. Last accessed 2025/02/19.

56. ClinicalTrials.gov (Internet). Study Details | A Study to Evaluate Rocatinlimab (AMG 451) in Adolescent Participants With Moderate-to-severe Atopic Dermatitis (AD). Available from: https://clinicaltrials.gov/study/NCT05704738?cond=Atopic%20Dermatitis&intr=AMG%20451&rank=4#study-plan. Last accessed 2025/02/19.

57. ClinicalTrials.gov (Internet). Study Details | A Study With Self-administered Rocatinlimab in Adolescent and Adult Participants With Moderate-to-severe AD. Available from: https://clinicaltrials.gov/study/NCT06224192?cond=Atopic%20Dermatitis&intr=AMG%20451&rank=5#study-plan. Last accessed 2025/02/19.

58. ClinicalTrials.gov (Internet). Study Details | A Study to Assess Long-term Safety, Tolerability, and Efficacy of Rocatinlimab in Adult and Adolescent Participants With Moderate-to-severe Atopic Dermatitis (AD). Available from: https://clinicaltrials.gov/study/NCT05882877?cond=Atopic%20Dermatitis&intr=rocatinlimab&rank=8 Last accessed April 14, 2025.

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