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Atopic Dermatitis — Immunopathogenesis and Current Therapies

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Abstract. Atopic dermatitis affects around 204 million people and is the most common chronic inflammatory skin disease. Its pathogenesis is best described not as a linear sequence but as a self-reinforcing loop, in which impaired barrier function, microbial dysbiosis, keratinocyte alarmin release, adaptive type 2 polarization and neuronally mediated itch each sustain the others, with no single element upstream of the rest. Filaggrin loss-of-function variants establish barrier loss which admits allergens and lets Staphylococcus aureus dominate the lesional flora. Injured keratinocytes release TSLP, IL-25 and IL-33, which drive group 2 innate lymphoid cells and Th2 cells to produce IL-4, IL-13 and IL-31. IL-31 then acts on sensory neurons, and scratching it provokes damage to the barrier again. This review traces that circuit and the therapies now aimed at it. Treatment has moved from systemic immunosuppressants, which suppress the adaptive response as a whole, to antibodies against IL-4Rα, IL-13 and the IL-31 receptor which have each produced substantial benefit in phase 3 trials, as have JAK inhibitors acting intracellularly on several of these signals at once. However, none has produced it in all patients. Which agent suits which patient is still decided empirically, because the endotypes defined in molecular studies have no counterpart in the trial literature. Rocatinlimab, an antibody against the costimulatory receptor OX40, was halted from development after cases of Kaposi's sarcoma, so the search for a therapy that acts on the cells sustaining the disease rather than the signals they release is not yet settled.

Keywords: skin barrier, type 2 inflammation, interleukin-31, JAK inhibitors, endotypes

1. Introduction

Atopic dermatitis (AD) is a chronic, relapsing, intensely pruritic inflammatory skin disease characterized by dry and eczematous skin. It is the most common chronic inflammatory skin disorder, with a worldwide prevalence of 2.6% (4% in children and 2% in adults), affecting an estimated ~204 million people (~103 million children and ~101 million adults). There is variation by sex, with females being slightly more likely to suffer from AD, and by geography. However, epidemiological data are lacking for a large fraction of countries, so global estimates carry uncertainty [1].

AD usually begins in childhood, with symptoms typically emerging within the first 5 years, and a substantial fraction persists into adulthood or arises in adulthood. In a proportion of children, AD

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progresses into other atopic conditions, namely asthma, and allergic conditions such as food allergy and allergic rhinitis. This is known as the 'atopic march' [2]. The filaggrin gene (FLG) is central to this process as it encodes a key structural protein of the stratum corneum, and common loss-of-function mutations cause defective epidermal barriers which are a major predisposing factor of AD. These variants also show a highly significant association with asthma occurring in the context of AD, and impaired barrier function is thought to predispose to epicutaneous allergen sensitization and the subsequent development of the atopic march [3].

Epidermal barrier dysfunction and immune dysregulation dominated by type 2 inflammation are the two interdependent processes that lead to the pathogenesis of AD. However, other immune responses and cytokine pathways are likely also involved. Progress in defining these immune pathways has driven a shift in management from broad-spectrum immunosuppression toward therapies directed at specific molecular mediators of the disease [2].

The consequences of the disease are not confined to the skin. Persistent pruritus disturbs sleep and impairs quality of life. When disease is severe or widespread, when optimized topical therapy fails to control it, or when the impairment is substantial, treatment moves to phototherapy or a systemic agent [4]. Management is therefore a matter of matching the intensity of intervention to disease severity, in a condition that is controlled rather than cured.

For most of its history that matching was done with agents that suppressed inflammation indiscriminately. Topical corticosteroids and calcineurin inhibitors, and the oral immunosuppressants, act broadly rather than on any defined mediator, and their use has been limited as much by cumulative toxicity as by efficacy. The position changed when the clinical efficacy of dupilumab, an IL-4 receptor antagonist, supplied conclusive proof of the importance of the type 2 immune pathway in AD [2]. That result converted a mechanistic hypothesis into a validated therapeutic target and established the pattern that has organized the field since, in which a pathway implicated by translational study is tested by a molecule directed against it.

A decade of that pattern has produced agents against IL-13, against the IL-31 receptor, against the Janus kinases that transduce these signals intracellularly, and most recently against the OX40 costimulatory axis. The resulting range of options is genuinely new, but it has arrived faster than the evidence needed to choose between them. Direct comparisons are scarce, safety data are unevenly distributed across the classes, and treatment is still delivered through a one-size-fits-all approach despite endotypes that differ by age, chronicity, ethnicity, filaggrin status and IgE level [5].

This review sets out the immunopathogenesis of AD and the therapies now available against it, with the two treated as a single argument rather than as separate surveys.

2. Immunopathogenesis

2.1. Epidermal barrier dysfunction

The epidermal barrier is the first line of defense compromised in AD. Filaggrin is a key protein that facilitates terminal differentiation of the epidermis and formation of the skin barrier. It aggregates keratins to form corneocytes, which are then cross-linked with transglutaminases to form the cornified cell envelope (CCE). This is part of the outermost epidermal layer, the stratum corneum, which is needed for mechanical protection, moisture retention, and antimicrobial defense. A primary epithelial barrier defect was established by the finding that two independent loss-of-function variants in FLG, R501X and 2282del4, which are carried by approximately 9% of people of European origin, are very strong predisposing factors for AD. These same variants are also significantly associated with asthma occurring in the context of AD, linking the cutaneous barrier

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defect to the wider atopic phenotype and atopic march [3]. This barrier defect is stage (1) of the cycle shown in Figure 1.

However, the barrier defect is not purely genetic. Filaggrin expression is significantly reduced in acute AD skin even in patients who do not carry FLG mutations, and keratinocytes differentiated in the presence of IL-4 and IL-13 show markedly reduced filaggrin expression. AD therefore involves an acquired defect in filaggrin expression that is modulated by the atopic inflammatory response, such that the type 2 immune milieu itself contributes to barrier impairment, providing a rationale for the idea that neutralizing IL-4 and IL-13 could improve barrier integrity. Barrier dysfunction is thus both a cause and a consequence of inflammation [6].

2.2. Innate immune activation: keratinocyte alarmins and ILC2s

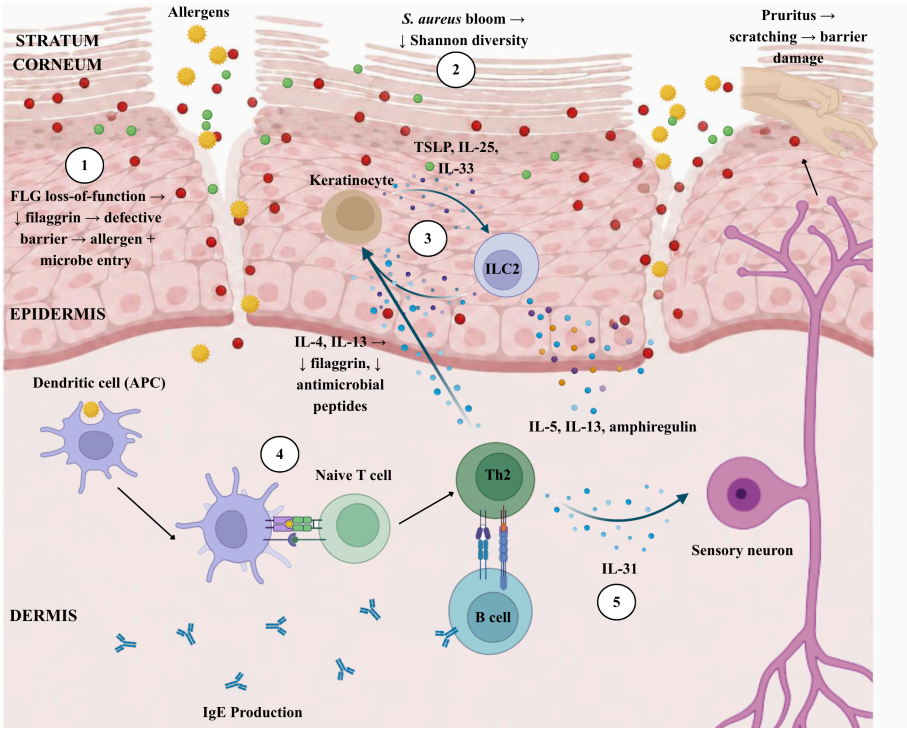


Figure 1. Immunopathogenesis of atopic dermatitis as a self-reinforcing cycle. Circled numerals mark the order in which the cascade is described, but they indicate narrative sequence, not strict temporal precedence, since the loop has no single origin. Because these limbs return to earlier stages, no element is upstream of all others. Constructed from references Created with BioRender

In addition to admitting allergens and microbes, a defective barrier also initiates the innate immune response that seeds type 2 inflammation. Group 2 innate lymphoid cells (ILC2s) express skin-homing receptors (CLA, CCR10 and CCR4), infiltrate the skin after allergen exposure, and are enriched in lesional skin from AD patients by TSLP (thymic stromal lymphopoietin) dependent recruitment, where they release type 2 cytokines IL-5 and IL-13. Because ILC2s generate these cytokines without antigen-specific priming, they provide an early, innate source of type 2 mediators that precedes and primes the adaptive response. Their activation is driven predominantly by the epithelial alarmins IL-25, IL-33 and TSLP, as they express IL-17RB (IL-25 receptor), ST2 (IL-33 receptor) and TSLPR (TSLP receptor), which are upregulated on activation, causing a positive feedback loop that amplifies the immune response. This ILC2 proliferation and activation can be

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suppressed by the interaction of KLRG1(killer cell lectin-like receptor G1) with E-cadherin, reducing IL-5 and IL-13 release [7]. The relationships between barrier failure, alarmin release and ILC2 activation are shown in Figure 1. First, loss-of-function mutation in the filaggrin gene (FLG) reduces filaggrin and produces a defective stratum corneum, admitting allergens and microbes. The altered surface favors a Staphylococcus aureus bloom with a fall in Shannon diversity. Stressed keratinocytes release the alarmins TSLP, IL-25 and IL-33, which activate group 2 innate lymphoid cells (ILC2) to secrete IL-5, IL-13 and amphiregulin without antigen-specific priming. Dendritic cells acting as antigen-presenting cells prime naive T cells toward a Th2 phenotype, and Th2 cells interact with B cells to drive IgE production. Th2-derived IL-31 acts on its receptor on sensory neurons to evoke pruritus [3, 6-10].

Biopsies from AD patients show ST2, IL-17BR and TSLPR upregulation in ILC2s, causing significant release of type 2 cytokines and amphiregulin in response to IL-33. They also show elevated KLRG1 expression, which may improve the suppression of ILC2-mediated type 2 cytokine-driven inflammatory response via E-cadherin binding, however, in AD, E-cadherin is downregulated due to filaggrin insufficiency, thus preventing the inhibition [7].

2.3. Adaptive type 2 immunity: Th2 cells, IL-4/IL-13, and IgE

The innate type 2 signal is captured and amplified by an adaptive response built around Th2 lymphocytes, and the two cytokines at its core are IL-4 and IL-13. Skin-homing T cells, identified by cutaneous lymphocyte antigen (CLA), traffic to the epidermis and, on activation, release the Th2 mediators IL-4, IL-5, IL-13 and IL-31. IL-4 and IL-13 are the central effectors, as they downregulate terminal-differentiation genes and tight-junction components such as claudins, feeding directly back onto the barrier defect. This Th2 tilt is mirrored systemically in the extrinsic AD endotype, which is defined by raised total and allergen-specific IgE, higher eosinophil counts, and a personal or family history of atopy [2].

High-resolution transcriptomics have clarified which of these cytokines dominates the lesion. RNA-sequencing comparison of AD and psoriasis skin showed IL-13 as the transcript that most sharply set AD lesions apart, whereas IL-4 messenger RNA was detectable in only about 40% of lesional samples and then only at very low levels [8]. At the tissue level, AD behaves as an IL-13-driven rather than IL-4-driven disease. Mechanistically, IL-4 and IL-13 signal through shared receptor complexes assembled around the IL-4Rα chain, which is why an antibody against IL-4Rα, like dupilumab, neutralizes both cytokines at once, whereas agents directed at IL-13 itself block only that arm. Downstream of the receptor, both cytokines transmit through the JAK-STAT pathway, which in AD drives Th2 polarization, suppresses antimicrobial peptides and disrupts the barrier, so the same signal can be interrupted at the receptor or inside the cell [2]. Figure 2 shows where each of these agents intercepts the pathway, from the receptor to the kinases inside the cell. Costimulation is addressed at either end of the OX40/OX40L axis: rocatinlimab binds OX40 on activated T cells, amlitelimab the ligand on dendritic cells. Conventional immunosuppressants (calcineurin inhibitors such as cyclosporine, corticosteroids, methotrexate, azathioprine and mycophenolate mofetil) suppress the Th2 cell broadly rather than at a defined mediator. Downstream, dupilumab blocks the shared IL-4 receptor alpha subunit and so interrupts IL-4 and IL-13 signaling together, whereas tralokinumab and lebrikizumab act on IL-13 alone: tralokinumab binds the cytokine with high affinity and neutralizes it, while lebrikizumab prevents assembly of the IL-4Ralpha/IL-13Ralpha1 heterodimeric signaling complex. Nemolizumab antagonizes the alpha subunit of the IL-31 receptor on sensory neurons. Janus kinases transduce these signals intracellularly and are inhibited with differing selectivity: abrocitinib and upadacitinib are JAK1-selective, ruxolitinib and baricitinib act

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on JAK1 and JAK2, and tofacitinib is non-selective. Crisaborole inhibits phosphodiesterase-4, preventing hydrolysis of cyclic AMP to 5'-AMP and thereby lowering type 2 cytokine output [4, 11-19].

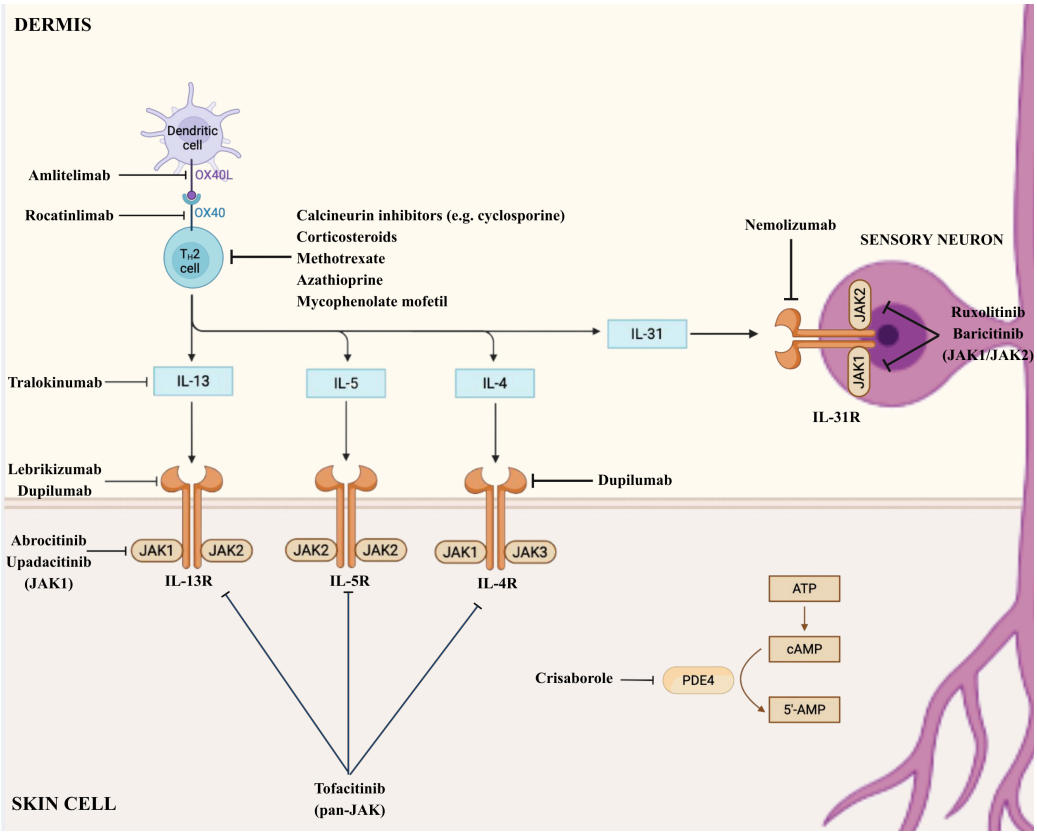


Figure 2. Molecular targets of current and emerging therapies for atopic dermatitis. Bar-headed lines denote inhibition. Created with BioRender

Type 2 immunity is dominant but not the only cause, as the immune map shifts with disease stage. Acute AD onset is marked by strong Th2 and Th22 (IL-22, S100 proteins) activation, and as lesions become chronic, these responses intensify, and the Th1 axis (IFN-γ, CXCL9, CXCL10) switches on in parallel. The relative weight of the Th22, Th17/IL-23 and Th1 axes varies by subtype, age and ancestry, and the disease extends beyond the visible lesion, with AD-specific inflammatory changes detectable in nonlesional skin and in circulating CLA+ T cells, demonstrating that moderate-to-severe AD is in part a systemic disease [2].

2.4. IL-31 and the neuroimmunology of itch

Pruritus is the defining symptom of AD, and it is not merely a by-product of skin inflammation but the output of a neuroimmune circuit that links the type 2 response directly to sensory nerves. The cytokine at its center is IL-31, which is produced predominantly by type 2 T cells, with only a minor contribution from mature dendritic cells. IL-31 is upregulated in lesional AD skin but not in psoriasis, marking it as a comparatively AD-specific pruritogen [9]. This neuroimmune limb appears as stage (5) in Figure 1.

The IL-31 receptor is a heterodimer of IL-31RA and the oncostatin-M receptor β chain (OSMRβ), and it is expressed on sensory neurons of the dorsal root ganglia, largely within the

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subpopulation of neurons that co-express the transient receptor potential channels TRPV1 (transient receptor potential vanilloid 1) and TRPA1 (transient receptor potential ankyrin 1). Functionally, IL-31 triggers calcium influx and ERK1/2 phosphorylation in these primary sensory neurons. Consistent with this, IL-31-induced itch is markedly reduced in TRPV1 and TRPA1-deficient mice, thus identifying these two channels as the conduits for IL-31-driven itch. This has an important clinical consequence. IL-31-driven itch depends on TRPV1 and TRPA1 rather than on the histamine pathway targeted by antihistamines and scratching provoked by IL-31 was unchanged in mast-cell-deficient and PAR-2 knockout mice, indicating that mast cell mediators such as histamine and tryptase are not required. This offers a mechanistic explanation for the limited benefit of antihistamines in the pruritus of AD, and it identifies the neuronal receptor as a target that also interrupts the itch-scratch cycle driving further barrier damage [9].

Evidence from patients supports the relevance of this axis. IL-31 is markedly increased in acute AD lesions and correlates with disease severity, and early trials of nemolizumab, a monoclonal antibody directed against IL-31RA, reduced pruritus, sleep disturbance and topical corticosteroid use. Targeting the neuronal receptor therefore relieves itch through a pathway distinct from conventional antipruritic therapy [2].

2.5. Endotype and phenotype heterogeneity

The mechanisms described so far do not operate identically in every patient. AD comprises distinct subtypes defined not only by clinical phenotype but by molecular endotype, differing with age, disease chronicity, ethnicity, filaggrin status and IgE level. The extrinsic phenotype accounts for approximately 80% of patients and features high total and allergen-specific serum IgE, eosinophilia, an atopic background and a greater rate of FLG mutation. The remaining 20% have intrinsic disease, with normal IgE levels, female predominance, later onset, preserved barrier function measured by transepidermal water loss and no other atopic background. Thus, beneath a clinical label lies a highly heterogeneous spectrum of biological and immunological endotypes [5].

Ethnicity and age define further endotypes with direct therapeutic implications. Han Chinese patients show robust Th2 activation together with Th17/IL-23 and Th17/Th22 marker upregulation, and greater lesional Th17 expression with lower Th1 markers than European American patients, establishing a blended Th17/Th2 endotype across Asian patients that may respond to agents developed for psoriasis. African American patients, in whom AD is particularly common and takes a treatment-resistant lichenified form, show Th1/Th17 attenuation with predominant Th2/Th22 skewing and a low prevalence of FLG loss-of-function mutations. Age contributes similarly, as skin-homing Th1 development is suppressed and delayed in children with AD relative to adults. This heterogeneity is the argument against a one-size-fits-all approach and the basis for matching therapy to endotype [5].

2.6. Microbiome dysbiosis

The final element of the pathogenic loop lies on the skin surface, where barriers and immune dysfunction reshape the resident microbial community. Sequencing of the bacterial 16S ribosomal RNA gene in children with moderate-to-severe AD, sampled at baseline, during flare and after treatment, showed that disease severity correlates inversely with Shannon diversity, a measure combining the richness and evenness of a community. Diversity fell markedly during flares at the antecubital and popliteal creases, and the collapse was driven largely by staphylococcal expansion, with S. aureus reaching 65% of sequences in flares from untreated patients compared with 15% in

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intermittently treated patients. Representation of the commensal S. epidermidis also rose during flares, indicating a shift not confined to the recognized pathogen [10]. Figure 1 places this dysbiosis within the wider cycle, where the loss of antimicrobial peptides driven by IL-4 and IL-13 returns to favor staphylococcal overgrowth.

Two observations establish this dysbiosis as an integral part of disease activity rather than simple secondary infection. When S. aureus sequences were computationally subtracted and the remaining counts renormalized, the reduction in diversity during untreated flares remained significant, showing a broader ecological shift than overgrowth of a single organism. The changes are also dynamic, as intermittent treatment was associated with greater diversity and increases in Streptococcus, Propionibacterium and Corynebacterium followed therapy, with diversification preceding clinical improvement [10].

The relationship is bidirectional. Th2 polarization facilitates S. aureus binding and colonization, while IL-4 and IL-13 suppress cutaneous antimicrobial peptide production, leaving AD skin predisposed to infection that further aggravates inflammation and barrier defects. Microbial dysbiosis is therefore both a consequence of the preceding abnormalities and a driver that sustains them, showing the self-reinforcing loop [2].

3. Current therapies

3.1. Topical therapy

Topical therapy remains the foundation of AD management, acting directly on the barrier and inflammatory events described above. Corticosteroids and calcineurin inhibitors carry the longest clinical record, and both suppress cutaneous inflammation broadly rather than targeting any single mediator of the type 2 axis. Newer nonsteroidal agents were appraised alongside them when a multidisciplinary workgroup graded the evidence for adult topical management using formal certainty-of-evidence methods. That appraisal produced strong recommendations for moisturizers, corticosteroids, calcineurin inhibitors and the topical phosphodiesterase-4 (PDE4) and Janus kinase (JAK) inhibitors, and recommended against topical antimicrobials, antiseptics and antihistamines [11]. Figure 2 sets out where each of the agents discussed in this section acts.

Nonsteroidal alternatives extend that principle to patients in whom steroid or calcineurin inhibitor use is unsuitable. Crisaborole, a topical PDE4 inhibitor, raises intracellular cyclic AMP and lowers the production of type 2 cytokines. Two identical trials randomized 1016 patients aged 2 to 79 years to twice-daily crisaborole and 506 to vehicle for 28 days, and success on the static global assessment was reached by 32.1% against 21.7%. Itch improved in three further studies, and adverse effects were largely confined to application-site stinging. The workgroup recommended it strongly on high-certainty evidence, the same grade it gave the corticosteroids, which places a nonsteroidal option on equal evidential footing for mild to moderate disease [11].

Topical JAK inhibition brings the intracellular strategy to the skin surface itself. Ruxolitinib 1.5% cream was approved in 2021 for short-term and non-continuous treatment of mild to moderate disease from twelve years of age. Two randomized trials found that 52.2% of treated patients reached a clear or almost clear assessment or a two-point improvement, against 11.1% on vehicle. Application is capped at 20% of body surface area and 60g per week to limit systemic absorption, since the class carries boxed warnings for serious infection, malignancy, major adverse cardiovascular events and thrombosis. The workgroup recommended it strongly on moderate-certainty evidence [11].

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3.2. Conventional systemic immunosuppressants

When topical therapy fails to control disease, treatment moves to agents that act systemically rather than only at the site of inflammation. The workgroup that graded topical management applied the same certainty-of-evidence methods to phototherapy and systemic therapy in adults, updating recommendations issued in 2014, before any biologic had been approved for the disease. Its eleven recommendations separate the two eras cleanly. Dupilumab, tralokinumab, abrocitinib, baricitinib and upadacitinib all carry strong recommendations resting on moderate-certainty evidence, whereas methotrexate, azathioprine and cyclosporine are recommended only conditionally on low-certainty evidence and mycophenolate mofetil on very low certainty. Phototherapy sits with the conditional group, its recommendation downgraded for imprecision and risk of bias across a literature dominated by narrowband ultraviolet B [4].

The regulatory and practical positions of these drugs reinforce that ranking. Every conventional immunosuppressant in the guideline is used off-label in AD, and each recommendation is qualified by a requirement for proper monitoring. Cyclosporine is effective from an initial 3 to 5 mg per kg daily but is generally limited to one year of use, azathioprine requires thiopurine methyltransferase genotyping or enzyme testing before initiation, and comorbidities or drug interactions can make either agent inappropriate for some patients. Systemic corticosteroids are the single intervention the workgroup recommends against, reserving them for acute severe flares and for short-term bridging to a corticosteroid-sparing therapy. By contrast, the biologics require no laboratory monitoring before or during treatment. The conventional agents are now reserved for refractory disease and for limited-term use, and the guideline grades none of them above a conditional recommendation [4].

3.3. Biologics targeting type 2 cytokines and IL-31

The adaptive type 2 axis was the first pathogenic node to yield a targeted systemic therapy. Dupilumab is a human monoclonal antibody directed against the alpha subunit of the IL-4 receptor, so it interrupts signaling by both IL-4 and IL-13 at their shared receptor rather than removing either cytokine individually. Two identically designed 16-week trials, SOLO 1 and SOLO 2, enrolled 671 and 708 patients. The primary endpoint was an Investigator Global Assessment (IGA) score of clear or almost clear with an improvement of at least two grades from baseline. Dupilumab reached it in 38% and 37% of patients on alternate-week and weekly dosing against 10% on placebo in SOLO 1, and in 36% on both schedules against 8% in SOLO 2. Pruritus, anxiety and depression scores and quality of life all improved alongside the skin, while injection-site reactions and conjunctivitis occurred more often than on placebo [12]. Table 1 summarizes the pivotal trial data for the biologics and oral JAK inhibitors discussed below.

Table 1. Pivotal trial data for biologics, oral JAK inhibitors and OX40-directed agents in AD. IGA 0/1, clear or almost clear on the Investigator's Global Assessment with at least a two-grade improvement; EASI-75, 75% improvement in the Eczema Area and Severity Index; PP-NRS4, four-point improvement in the Peak Pruritus Numeric Rating Scale; vIGA-AD, validated IGA for atopic dermatitis

Agent	Molecular target	Trial(s)	Randomized (n)	Endpoint timepoint	Primary efficacy outcomes	Notable adverse events	Ref
Dupilumab	IL-4Rα (shared IL-4/IL-13 receptor)	SOLO 1 / SOLO 2	671 / 708	16 wk	IGA 0/1: 38% (alternate-week) & 37% (weekly) vs 10%; 36% (both) vs 8%	Injection-site reactions, conjunctivitis	[12]

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Table 1. (continued)

Tralokinumab	IL-13 (neutralizes cytokine)	ECZTRA 1 / ECZTRA 2	802 / 794	16 wk (of 52)	IGA 0/1: 15.8% vs 7.1%; 22.2% vs 10.9%. EASI-75: 25.0% vs 12.7%; 33.2% vs 11.4%	Upper respiratory tract infection, conjunctivitis	[13]
Lebrikizumab	IL-13 (blocks IL-4Rα/IL-13Rα1 assembly)	ADvocate 1 / ADvocate 2	424 / 427	16 wk (of 52)	IGA 0/1: 43.1% vs 12.7%; 33.2% vs 10.8%. EASI-75: 58.8% & 52.1% vs 16.2% & 18.1%	Conjunctivitis	[14]
Nemolizumab	IL-31 receptor α subunit	ARCADIA 1 / ARCADIA 2	941 / 787	16 wk (of 48)	IGA 0/1: 36% vs 25%; 38% vs 26%. EASI-75: 44% vs 29%; 42% vs 30%. Itch relief from week 1	Worsening of atopic dermatitis (12% vs 11%; 7% vs 6%)	[15]
Abrocitinib	JAK1	JADE MONO-1	387	12 wk	IGA 0/1: 24% (100mg) & 44% (200mg) vs 8%. EASI-75: 40% & 63% vs 12%. PP-NRS4 at wk 2: 20% & 46% vs 3%	Nausea, nasopharyngitis, headache	[16]
Upadacitinib	JAK1	Measure Up 1 / Measure Up 2	847 / 836	16 wk	vIGA-AD 0/1: 48% (15mg) & 62% (30mg) vs 8%; 39% & 52% vs 5%. EASI-75: 70% & 80% vs 16%; 60% & 73% vs 13%	Acne, dose-related: 7% & 17% vs 2% (Measure Up 1)	[17]
Rocatinlimab	OX40 receptor (activated T cells)	ROCKET-IGNITE / ROCKET-HORIZON	769 / 726	24 wk	EASI-75: 42% (300mg) & 36% (150mg) vs 13%; 33% vs 14%. Rescue therapy imputed as non-response	Pyrexia, chills, aphthous ulcers	[18]
Amlitelimab	OX40 ligand (antigen-presenting cells)	SHORE; COAST 1 / COAST 2 (phase 3)	not reported in cited source	24 wk (SHORE)	SHORE vIGA-AD 0/1: 28.7% & 32.3% vs 16.8%. EASI-75: 48.1% & 46.8% vs 32.3%. COAST 2: not significant, 12-weekly cohort (EU analysis)	Kaposi's sarcoma: 2 cumulative cases	[19]

Blocking the shared receptor subunit is not the only way to reach this axis. Tralokinumab is a fully human IgG4 antibody that binds IL-13 with high affinity and neutralizes it specifically, leaving IL-4 signaling intact, and it was developed when dupilumab was the only licensed biologic for the

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disease. Two 52-week trials, ECZTRA 1 and ECZTRA 2, randomized 802 and 794 patients in a three-to-one ratio to 300 mg every two weeks or placebo. At week 16 a clear or almost clear score was reached by 15.8% against 7.1% in ECZTRA 1 and 22.2% against 10.9% in ECZTRA 2. EASI-75, an improvement of at least 75% in the Eczema Area and Severity Index (EASI), which scores the extent and severity of skin involvement, was reached by 25.0% against 12.7% and 33.2% against 11.4%. Conjunctivitis and upper respiratory tract infection were reported more often than on placebo, although most cases were mild [13].

IL-13 selectivity can be achieved at a second point in the same pathway. Lebrikizumab is a high-affinity IgG4 antibody against IL-13 that prevents formation of the IL-4Rα and IL-13Rα1 heterodimer, so it blocks assembly of the receptor complex rather than occupying it. Two identically designed 52-week trials, ADvocate1 and ADvocate2, randomized patients two-to-one to 250 mg every two weeks after a 500 mg loading dose, with results reported here for the 16-week induction period. An IGA response was reached by 43.1% of 283 patients against 12.7% of 141 on placebo in ADvocate1, and by 33.2% of 281 against 10.8% of 146 in ADvocate2. EASI-75 followed the same pattern, at 58.8% and 52.1% against 16.2% and 18.1%. Itch and its interference with sleep both improved, and conjunctivitis were more common than on placebo, as with the other agents in this class [14].

Nemolizumab approaches the disease from the itch pathway rather than the inflammatory one, antagonizing the alpha subunit of the IL-31 receptor. Two replicate trials, ARCADIA 1 and ARCADIA 2, assigned 1728 participants in a two-to-one ratio to 30 mg every four weeks or placebo, both on background topical corticosteroids with and without calcineurin inhibitors. Both met their coprimary endpoints at week 16, with an IGA response in 36% against 25% and 38% against 26% of participants, and EASI-75 in 44% against 29% and 42% against 30%. Itch relief appeared as early as the first week, and sleep had improved by week 16. That onset is faster than the skin clearance figures alone would suggest. Worsening of atopic dermatitis was the only event affecting more than 5% of participants, at rates close to placebo [15].

3.4. Oral JAK inhibitors

The cytokines driving AD converge on a few intracellular signaling routes, an alternative point of attack. IL-4, IL-13 and IL-31 all transmit through JAK pathways, so an oral JAK1 inhibitor interrupts several of the axes at once rather than neutralizing a single cytokine. Abrocitinib was tested as monotherapy in JADE MONO-1, which randomized 387 patients to 100 mg, 200 mg or placebo and met both coprimary endpoints at both doses by week 12. An IGA response was reached by 24% on 100 mg and 44% on 200 mg against 8% on placebo, and EASI-75 by 40% and 63% against 12%. Itch is reported separately on the peak pruritus numerical rating scale, where an improvement of four points from baseline counts as a response. The breadth of the mechanism is most visible there, with the four-point improvement already reported by 20% and 46% of treated patients in week 2, against 3% on placebo. Nausea was the most frequent event and was also dose-related, occurring in 9% and 20% of the two abrocitinib groups against 3% on placebo, followed by nasopharyngitis and headache [16].

Upadacitinib, also JAK1-selective, was assessed in two replicate trials, Measure Up 1 and Measure Up 2, enrolling 847 and 836 patients. An IGA response was reached by 48% on 15 mg and 62% on 30 mg against 8% on placebo in Measure Up 1, and by 39% and 52% against 5% in Measure Up 2. EASI-75 was achieved by 70% and 80% against 16% in the first trial, and by 60% and 73% against 13% in the second. Acne was the most frequent treatment-emergent event and was

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clearly dose-related, occurring in 7% and 17% of the two upadacitinib groups against 2% on placebo in Measure Up 1 [17]. Table 1 collects the trial data for both oral JAK inhibitors.

However, the Food and Drug Administration (FDA) applied class-wide warnings of increased risk of serious cardiac events, cancer, blood clots and death to JAK inhibitors. Those warnings drew largely from a rheumatoid arthritis trial in patients aged 50 years and over with a cardiovascular risk factor, randomized to tofacitinib or a tumor necrosis factor inhibitor, in which major adverse cardiovascular events and malignancy were more common on tofacitinib. That population differs substantially in baseline risk from most people starting systemic treatment for AD, and tofacitinib is a less selective inhibitor than the JAK1-preferential agents approved for this disease. The signals nonetheless warrant caution, since deaths and clotting events have been recorded in AD trials themselves, and vaccination against shingles before starting treatment is advised where practical. Both drugs are accordingly approved for patients in whom other systemic therapies have failed or are inadvisable [4].

3.5. Emerging pipeline: the OX40/OX40L pathway

Every therapy considered so far neutralizes a cytokine or blocks its signal, which addresses the inflammation present but not the cells that regenerate it. The OX40 receptor is a costimulatory molecule that appears only transiently on effector and memory T cells once they have been activated. Signaling through it supports the expansion of those cells, their output of inflammatory cytokines, and their differentiation into memory. In AD it expands the pathogenic T cell populations that perpetuate inflammation and generate the long-lived memory cells underlying chronicity. Blocking type 2 cytokines alone leaves those memory cells untouched, so depleting pathogenic OX40-positive T cells offers a route to rebalancing the T cell compartment rather than suppressing its output [18]. Both ends of this axis are shown at the top of Figure 2.

Rocatinlimab, an antibody against the receptor itself, was tested in two 24-week phase 3 trials, ROCKET-IGNITE and ROCKET-HORIZON, randomizing 769 and 726 adults across 19 countries each. Both met their coprimary endpoints. EASI-75 at week 24 was reached by 42% on 300 mg and 36% on 150 mg against 13% on placebo in IGNITE, and by 33% against 14% in HORIZON. Response rates were therefore lower than those recorded for the biologics and JAK inhibitors, although anyone who took rescue therapy counted as a non-responder from that point on. Pyrexia, chills and aphthous ulcers were the characteristic adverse events, mostly injection-related and concentrated after the first dose [18].

The pathway can also be addressed from the other side. Amlitelimab binds the OX40 ligand on antigen-presenting cells rather than the receptor on T cells and has reached phase 3. In SHORE, which allowed background topical therapy, validated IGA responses at week 24 were 28.7% and 32.3% on the two dosing schedules against 16.8% on placebo, and EASI-75 48.1% and 46.8% against 32.3%. Efficacy has varied across settings, however, with one of the two COAST trials meeting its endpoints while the other failed to show a significant benefit in the twelve-weekly cohort under the prespecified testing hierarchy. Whether depleting OX40-positive T cells or blocking the ligand carries the lower risk is the question the safety signals now pose, and the two formats have not been compared directly [19].

The pathway's status changed sharply after these trials were reported. Rocatinlimab development was halted after a safety review found two Kaposi's sarcoma cases, with one further case suspected, and the sponsor could not exclude a link to OX40 pathway modulation. Two cumulative cases have also been reported in the amlitelimab programme, both in patients with known risk factors. The most direct mechanistic support comes from human genetics, where an autosomal recessive loss-of-

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function mutation in OX40 was found in a young woman with childhood-onset classic disease, placing OX40 deficiency among the inborn errors of immunity that predispose to this herpesvirus-associated malignancy [19].

4. Discussion

The therapies that work in AD also test the model that explains it. The transcriptional dominance of IL-13 predicted that neutralizing that cytokine alone would be sufficient, and both antibodies directed at it met their endpoints in phase 3 [8, 13, 14]. The action of IL-31 on sensory neurons rather than through mast cell histamine predicted that blocking its receptor would relieve itch on a neuronal timescale, ahead of any change in the lesion, and nemolizumab reduced pruritus within the first week [9, 15]. Where a node of the loop has been targeted, the clinical result has followed the mechanism. This is the strongest evidence available that the sequence set out earlier is causal, and not merely a correlation with disease activity.

However, explaining why a drug works does not establish which drug to use, and the efficacy figures given cannot be read across trials, since they differ in duration, in background topical therapy and in how patients needing rescue treatment were counted. Head-to-head trials between systemic agents are almost entirely absent, so the comparison must be made indirectly [4, 20]. A living network meta-analysis pooling 97 trials and 24 679 patients placed high-dose upadacitinib and abrocitinib at the numerically highest relative efficacy among approved systemic treatments. Lebrikizumab and dupilumab differed by no important margin on the continuous measures, although dupilumab retained higher odds on the binary endpoints [20]. That ranking is not what practice follows. When the guideline workgroup was surveyed on their preferred first-line systemic agent, every member chose dupilumab, despite the JAK inhibitors ranking above it, because more than five years of clinical use have produced no major emergent safety concern [4]. Accumulated experience is being weighed against measured efficacy, and clinicians are currently giving it a greater weight.

Two problems limit what any such ranking can claim. The first is duration. The dupilumab trials reported at 16 weeks and abrocitinib monotherapy at week 12, against a disease that persists for decades [12, 16]. The two IL-13 antibodies ran for 52 weeks but re-randomized responders into maintenance arms after induction, so their long-term figures describe the maintenance of an achieved response, and not the trajectory of an unselected population [13, 14]. The network meta-analysis excluded these extension data and could draw no conclusion about long-term dosing strategies [20]. The second is who was enrolled. Every trial in Table 1 recruited adults, in several cases from 12 years of age, and none enrolled younger children [12-18]. This is a recognized limit on generalizability for a disease more common in children than in adults, and both guidelines confine themselves to adults with pediatric recommendations deferred to separate documents [4, 11, 20]. What the trial literature ranks, then, is the induction of response over three to six months in the group in which the disease is least common.

Efficacy and safety are also not known to the same standard. The efficacy figures come from trials designed to detect them, whereas the JAK safety warnings were extrapolated from a trial in a different disease that was not designed to answer this question at all. That study asked only whether tofacitinib was no worse than an established comparator, and its 1455 participants had rheumatoid arthritis, were aged 50 years or over and carried at least one cardiovascular risk factor [4]. A signal detected in that population over four years cannot be dismissed, but neither can it be transferred directly to a younger AD population taking a more selective drug.

The OX40 pathway raises a question the cytokine-directed therapies cannot answer. Each of them suppresses a signal and must be continued for that suppression to hold. The axis instead acts on the

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survival of pathogenic T cells and the maintenance of immune memory, so blocking it might alter the disease course rather than the current signal. Mid-stage trials of rocatinlimab and amlitelimab both suggested that some benefit could persist after treatment was withdrawn, which is what made the pathway the most credible candidate for that kind of effect. Kaposi's sarcoma cases have not refuted the rationale, but they have moved the question. The axis remains biologically credible, and what is now unresolved is whether the risk concentrates on identifiable hosts, whether prospective screening can reduce it, and whether the benefit is large enough to justify the monitoring that would be required [19].

A further limitation cuts across all of the above, since no trial described here selected patients on molecular grounds. The endotypes have no counterpart in trial literature. Patients with the intrinsic form, whose IgE is normal and whose barrier function is preserved, received the same interventions as the extrinsic majority, and their responses are pooled into the same summary figures [5]. Until stratified trials are done, every response rate quoted here describes an average patient who is known not to exist.

The epidemiological base on which these figures rest is narrower still. Data are lacking for 41.5% of countries worldwide, and most of what has been collected comes from Western Europe [1]. The endotype literature rests largely on comparisons between European American, Asian and African American cohorts rather than on population-representative sampling [5]. Prevalence estimates, endotype frequencies and response rates are therefore all drawn from a fraction of the affected population, which limits what can be claimed for the disease worldwide.

5. Conclusion

Atopic dermatitis has moved within two decades from a disease managed by broad suppression to one addressed by agents chosen against defined molecular targets. However, four problems remain open. Firstly, no current therapy produces durable remission after withdrawal, so treatment is indefinite. Also, no validated biomarker guides the choice between agents of comparable pooled efficacy. And furthermore, long-term safety data in children remain limited for the newest classes, and trial populations do not yet reflect the ancestral diversity of the patients who carry the disease.

The first of those problems briefly looked closer to solution than it now does. Rocatinlimab depletes activated T cells carrying OX40 rather than neutralizing the cytokines they release, and responses persisted through week 36 and, in some patients, after dosing stopped. The same pathway sustains CD4 and CD8 T cells that hold latent HHV-8 in check, so depleting them withdraw control on the virus as well as on the inflammation. Cases have now been reported on both agents, which makes it harder to attribute the risk to one antibody than to the pathway, and the case details that would settle it, including HHV-8 status, have not been released.

The other three problems are matters of evidence and not mechanism, and none is close to resolution. Safety in younger children rests on extrapolation, since no trial described here enrolled anyone below twelve years of age. The populations studied do not match the ancestral range of those who carry the disease. Pathogenesis is now described in enough detail to name a target, argue it from mechanism and confirm it in a trial, which the past two decades have done at four separate nodes now in clinical use. What it has not produced is a measurement made before treatment that identifies which of those nodes dominate in each patient, so drug choice still rests on trial and error among agents of comparable efficacy.

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References

[1] Tian, J., Zhang, D., Yang, Y., Huang, Y., Wang, L., Yao, X., & Lu, Q. (2023). Global epidemiology of atopic dermatitis: A comprehensive systematic analysis and modelling study. *British Journal of Dermatology, 190*(1), 55–61. https://doi.org/10.1093/bjd/ljad339

[2] Brunner, P. M., Guttman-Yassky, E., & Leung, D. Y. (2017). The immunology of atopic dermatitis and its reversibility with broad-spectrum and targeted therapies. *Journal of Allergy and Clinical Immunology, 139*(4S), S65–S76. https://doi.org/10.1016/j.jaci.2017.01.011

[3] Palmer, C. N., Irvine, A. D., Terron-Kwiatkowski, A., Zhao, Y., Liao, H., Lee, S. P., Goudie, D. R., Sandilands, A., Campbell, L. E., Smith, F. J., O'Regan, G. M., Watson, R. M., Cecil, J. E., Bale, S. J., Compton, J. G., DiGiovanna, J. J., Fleckman, P., Lewis-Jones, S., Arseculeratne, G., Sergeant, A., … McLean, W. H. (2006). Common loss-of-function variants of the epidermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis. *Nature Genetics, 38*(4), 441–446. https://doi.org/10.1038/ng1767

[4] Davis, D. M. R., Drucker, A. M., Alikhan, A., Bercovitch, L., Cohen, D. E., Darr, J. M., Eichenfield, L. F., Frazer-Green, L., Paller, A. S., Schwarzenberger, K., Silverberg, J. I., Singh, A. M., Wu, P. A., & Sidbury, R. (2024). Guidelines of care for the management of atopic dermatitis in adults with phototherapy and systemic therapies. *Journal of the American Academy of Dermatology, 90*(2), e43–e56. https://doi.org/10.1016/j.jaad.2023.08.102

[5] Czarnowicki, T., He, H., Krueger, J. G., & Guttman-Yassky, E. (2019). Atopic dermatitis endotypes and implications for targeted therapeutics. *Journal of Allergy and Clinical Immunology, 143*(1), 1–11. https://doi.org/10.1016/j.jaci.2018.10.032

[6] Howell, M. D., Kim, B. E., Gao, P., Grant, A. V., Boguniewicz, M., Debenedetto, A., Schneider, L., Beck, L. A., Barnes, K. C., & Leung, D. Y. (2007). Cytokine modulation of atopic dermatitis filaggrin skin expression. *Journal of Allergy and Clinical Immunology, 120*(1), 150–155. https://doi.org/10.1016/j.jaci.2007.04.031

[7] Salimi, M., Barlow, J. L., Saunders, S. P., Xue, L., Gutowska-Owsiak, D., Wang, X., Huang, L. C., Johnson, D., Scanlon, S. T., McKenzie, A. N., Fallon, P. G., & Ogg, G. S. (2013). A role for IL-25 and IL-33-driven type-2 innate lymphoid cells in atopic dermatitis. *Journal of Experimental Medicine, 210*(13), 2939–2950. https://doi.org/10.1084/jem.20130351

[8] Tsoi, L. C., Rodriguez, E., Degenhardt, F., Baurecht, H., Wehkamp, U., Volks, N., Szymczak, S., Swindell, W. R., Sarkar, M. K., Raja, K., Shao, S., Patrick, M., Gao, Y., Uppala, R., Perez White, B. E., Getsios, S., Harms, P. W., Maverakis, E., Elder, J. T., Franke, A., … Weidinger, S. (2019). Atopic dermatitis is an IL-13-dominant disease with greater molecular heterogeneity compared to psoriasis. *Journal of Investigative Dermatology, 139*(7), 1480–1489. https://doi.org/10.1016/j.jid.2018.12.018

[9] Cevikbas, F., Wang, X., Akiyama, T., Kempkes, C., Savinko, T., Antal, A., Kukova, G., Buhl, T., Ikoma, A., Buddenkotte, J., Soumelis, V., Feld, M., Alenius, H., Dillon, S. R., Carstens, E., Homey, B., Basbaum, A., & Steinhoff, M. (2014). A sensory neuron-expressed IL-31 receptor mediates T helper cell-dependent itch: Involvement of TRPV1 and TRPA1. *Journal of Allergy and Clinical Immunology, 133*(2), 448–460. https://doi.org/10.1016/j.jaci.2013.10.048

[10] Kong, H. H., Oh, J., Deming, C., Conlan, S., Grice, E. A., Beatson, M. A., Nomicos, E., Polley, E. C., Komarow, H. D., NISC Comparative Sequence Program, Murray, P. R., Turner, M. L., & Segre, J. A. (2012). Temporal shifts in the skin microbiome associated with disease flares and treatment in children with atopic dermatitis. *Genome Research, 22*(5), 850–859. https://doi.org/10.1101/gr.131029.111

[11] Sidbury, R., Alikhan, A., Bercovitch, L., Cohen, D. E., Darr, J. M., Drucker, A. M., Eichenfield, L. F., Frazer-Green, L., Paller, A. S., Schwarzenberger, K., Silverberg, J. I., Singh, A. M., Wu, P. A., & Davis, D. M. R. (2023). Guidelines of care for the management of atopic dermatitis in adults with topical therapies. *Journal of the American Academy of Dermatology, 89*(1), e1–e20. https://doi.org/10.1016/j.jaad.2022.12.029

[12] Simpson, E. L., Bieber, T., Guttman-Yassky, E., Beck, L. A., Blauvelt, A., Cork, M. J., Silverberg, J. I., Deleuran, M., Kataoka, Y., Lacour, J. P., Kingo, K., Worm, M., Poulin, Y., Wollenberg, A., Soo, Y., Graham, N. M., Pirozzi, G., Akinlade, B., Staudinger, H., Mastey, V., … SOLO 1 and SOLO 2 Investigators (2016). Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *New England Journal of Medicine, 375*(24), 2335–2348. https://doi.org/10.1056/NEJMoa1610020

[13] Wollenberg, A., Blauvelt, A., Guttman-Yassky, E., Worm, M., Lynde, C., Lacour, J. P., Spelman, L., Katoh, N., Saeki, H., Poulin, Y., Lesiak, A., Kircik, L., Cho, S. H., Herranz, P., Cork, M. J., Peris, K., Steffensen, L. A., Bang, B., Kuznetsova, A., Jensen, T. N., … ECZTRA 1 and ECZTRA 2 Study Investigators (2021). Tralokinumab for moderate-to-severe atopic dermatitis: results from two 52-week, randomized, double-blind, multicentre, placebo-

DOI: 10.54254/2753-8818/2026.36885

controlled phase III trials (ECZTRA 1 and ECZTRA 2). *British Journal of Dermatology, 184*(3), 437–449. https://doi.org/10.1111/bjd.19574

[14] Silverberg, J. I., Guttman-Yassky, E., Thaçi, D., Irvine, A. D., Stein Gold, L., Blauvelt, A., Simpson, E. L., Chu, C. Y., Liu, Z., Gontijo Lima, R., Pillai, S. G., Seneschal, J., … ADvocate1 and ADvocate2 Investigators (2023). Two phase 3 trials of lebrikizumab for moderate-to-severe atopic dermatitis. *New England Journal of Medicine, 388*(12), 1080–1091. https://doi.org/10.1056/NEJMoa2206714

[15] Silverberg, J. I., Wollenberg, A., Reich, A., Thaçi, D., Legat, F. J., Papp, K. A., Stein Gold, L., Bouaziz, J. D., Pink, A. E., Carrascosa, J. M., Rewerska, B., Szepietowski, J. C., Krasowska, D., Havlíčková, B., Kalowska, M., Magnolo, N., Pauser, S., Nami, N., Sauder, M. B., Jain, V., … ARCADIA 1 and ARCADIA 2 Study Investigators (2024). Nemolizumab with concomitant topical therapy in adolescents and adults with moderate-to-severe atopic dermatitis (ARCADIA 1 and ARCADIA 2): results from two replicate, double-blind, randomised controlled phase 3 trials. *The Lancet, 404*(10451), 445–460. https://doi.org/10.1016/S0140-6736(24)01203-0

[16] Simpson, E. L., Sinclair, R., Forman, S., Wollenberg, A., Aschoff, R., Cork, M., Bieber, T., Thyssen, J. P., Yosipovitch, G., Flohr, C., Magnolo, N., Maari, C., Feeney, C., Biswas, P., Tatulych, S., Valdez, H., & Rojo, R. (2020). Efficacy and safety of abrocitinib in adults and adolescents with moderate-to-severe atopic dermatitis (JADE MONO-1): A multicentre, double-blind, randomised, placebo-controlled, phase 3 trial. *The Lancet, 396*(10246), 255–266. https://doi.org/10.1016/S0140-6736(20)30732-7

[17] Guttman-Yassky, E., Teixeira, H. D., Simpson, E. L., Papp, K. A., Pangan, A. L., Blauvelt, A., Thaçi, D., Chu, C. Y., Hong, H. C., Katoh, N., Paller, A. S., Calimlim, B., Gu, Y., Hu, X., Liu, M., Yang, Y., Liu, J., Tenorio, A. R., Chu, A. D., & Irvine, A. D. (2021). Once-daily upadacitinib versus placebo in adolescents and adults with moderate-to-severe atopic dermatitis (Measure Up 1 and Measure Up 2): Results from two replicate double-blind, randomised controlled phase 3 trials. *The Lancet, 397*(10290), 2151–2168. https://doi.org/10.1016/S0140-6736(21)00588-2

[18] Guttman-Yassky, E., Kabashima, K., Worm, M., Luna, P. C., Hong, H. C., Chovatiya, R., Bernstein, J. A., Kern, J. S., Ehst, B. D., Magnolo, N., Herranz-Pinto, P., Stein Gold, L., Sofen, H., Pink, A. E., Esfandiari, E., Arai, T., Yang, Y., Shi, R., Barragan, C., Kricorian, G., … Bissonnette, R. (2026). Efficacy and safety of rocatinlimab for the treatment of moderate-to-severe atopic dermatitis in ROCKET-IGNITE and ROCKET-HORIZON: Two global, double-blind, placebo-controlled, randomised phase 3 clinical trials. *The Lancet, 407*(10523), 53–66. https://doi.org/10.1016/S0140-6736(25)01865-3

[19] Salek-Ardakani, S. (2026). Is Kaposi's sarcoma the end of the OX40/OX40L axis in atopic dermatitis? *Frontiers in Immunology, 17*, 1870289. https://doi.org/10.3389/fimmu.2026.1870289

[20] Drucker, A. M., Lam, M., Prieto-Merino, D., Malek, R., Ellis, A. G., Yiu, Z. Z. N., Rochwerg, B., Di Giorgio, S., Arents, B. W. M., Mohan, T., Burton, T., Spuls, P. I., Schmitt, J., & Flohr, C. (2024). Systemic immunomodulatory treatments for atopic dermatitis: Living systematic review and network meta-analysis update. *JAMA Dermatology, 160*(9), 936–944. https://doi.org/10.1001/jamadermatol.2024.2192