International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

ARTICLE TITLE	TARGETED BIOLOGICS IN CHILDHOOD ATOPIC DERMATITIS: A COMPREHENSIVE REVIEW OF IMPACT AND INNOVATION
DOI	https://doi.org/10.31435/ijitss.4(48).2025.4018
RECEIVED	02 October 2025
ACCEPTED	12 December 2025
PUBLISHED	24 December 2025
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

TARGETED BIOLOGICS IN CHILDHOOD ATOPIC DERMATITIS: A COMPREHENSIVE REVIEW OF IMPACT AND INNOVATION

Darya Lazitskaya *(Corresponding Author, Email: datskayalo@gmail.com)*
MD; Międzyleski Specialist Hospital in Warsaw, Warsaw, Poland
ORCID ID: 0009-0007-8680-8826

Dmytro Kowalczuk
MD; Międzyleski Specialist Hospital in Warsaw, Warsaw, Poland
ORCID ID: 0009-0004-1433-5052

Mykola Sobchynskyi
MD; Międzyleski Specialist Hospital in Warsaw, Warsaw, Poland
ORCID ID: 0009-0008-1804-1114

Andrzej Myrny
MD; University Clinical Center of the Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0006-5592-259X

Wiktoria Kasianik
MD; Mazovian Rehabilitation Center STOCER Ltd., Saint Anna Trauma Surgery Hospital, Warsaw, Poland
ORCID ID: 0009-0004-1540-5227

Kamil Turlej
MD; University Clinical Center of the Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0008-2919-284X

Valeryia Milasheuskaya
MD; Wroclaw Medical University, Wrocław, Poland
ORCID ID: 0009-0006-4126-2375

Iga Kiełbaszewska
MD; Independent Public Healthcare Center in Hajnówka, Hajnówka, Poland
ORCID ID: 0009-0004-9892-4769

Natalia Surosz
MD; Międzyleski Specialist Hospital in Warsaw, Warsaw, Poland
ORCID ID: 0009-0005-1939-151X

Katsiaryna Miraniuk
MD; Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0006-1406-9756

Dawid Wiczkowski
MD; Independent Public Specialist Western Hospital named after St. John Paul II, Grodzisk Mazowiecki, Poland
ORCID ID: 0009-0004-7050-9598

ABSTRACT

Atopic dermatitis (AD) is a prevalent chronic inflammatory skin disease in children that significantly impairs their quality of life and can be linked to other allergic disorders. Current treatments for paediatric AD are not always effective, but biologics hold promise as they work on the key factors behind inflammation.

Dupilumab, a fully human monoclonal antibody that inhibits IL-4 and IL-13 signalling by binding to the IL-4 Rα subunit, has shown good efficacy and an acceptable safety profile in treating infants and children with moderate-to-severe AD. It is now registered for the treatment of moderate-to-severe AD in paediatric patients, including young children and infants as young as six months in some regions.

Researchers are continuing to look at how safe and effective dupilumab is for children of different ages with atopic dermatitis, and whether starting treatment early can change how the disease develops over time. Other biologic treatments such as tralokinumab (which blocks IL-13), lebrikizumab, nemolizumab, tezepelumab, and JAK inhibitors are also being studied, and some have already been approved for use in children. Together, these therapies are expanding the options available for managing paediatric AD. In this review, we highlight the latest evidence on biologics in children, focusing on how they work, how well they control disease, and what is known about their safety, to help support treatment decisions in practice.

Aim of Study: We aim to review current understanding of atopic dermatitis and the latest developments in targeted therapies, including biologics and small-molecule inhibitors, based on clinical trial findings.

KEYWORDS

Atopic Dermatitis, Dupilumab, Infant, Child, Treatment

CITATION

Darya Lazitskaya, Dmytro Kowalczuk, Mykola Sobchynskyi, Andrzej Myrny, Wiktoria Kasianik, Kamil Turlej, Valeryia Milasheuskaya, Iga Kiełbaszewska, Natalia Surosz, Katsiaryna Miraniuk, Dawid Wiczkowski. (2025). Targeted Biologics in Childhood Atopic Dermatitis: A Comprehensive Review of Impact and Innovation. *International Journal of Innovative Technologies in Social Science*. 4(48). doi: 10.31435/ijitss.4(48).2025.4018

1. Introduction

Atopic dermatitis (AD) is an inflammatory skin condition that usually causes dry, itchy, eczema-like rashes and can have a major impact on a child's quality of life. (Michael et al., 2024). Beyond the physical symptoms, AD places a considerable burden on mental health and overall well-being (Barbara et al., 2003). Sometimes standard therapies can't manage symptoms (Riccardo et al, 2020). When this happens, biologic therapies can provide new options. Dupilumab, a fully human monoclonal antibody that specifically binds to the IL-4 Rα subunit, inhibiting IL-4 and IL-13 signalling and blocking the occurrence of type 2 inflammatory response, has shown good efficacy and good safety profile in treating infants and children with moderate-to-severe AD (Mingyue et al, 2024). Other biologic agents are either under investigation or have recently been approved for paediatric AD. (Lisa, 2023). In this report we examine current studies on biologic treatments for paediatric atopic dermatitis, focusing on their mechanisms, benefits, and safety profile.

2. Materials and Methods

A search of the PubMed and Google Scholar databases was conducted using relevant keywords to find available studies published up to April 25, 2025.A preliminary selection of titles and abstracts was made, followed by a full-text review of the relevant publications.

3. Results

3.1. Epidemiology

Prevalence of atopic dermatitis (AD) has remarkably increased in the last decades, with over 30% of the population affected by one or more allergic disorders (Riccardo et al, 2020). Describing its incidence and prevalence is challenging due to substantial variation in diagnostic criteria used for its identification, fluctuating course, and geographical differences (Alexis et al, 2020).

In a recent cross-sectional study on the epidemiology of AD in children aged 6 to 11 years (Alexis et al, 2020), the 1-year diagnosed AD prevalence estimates worldwide included:

- United States, 10.0%
- Canada, 13.3%
- the EU5 Countries, 15.5%
- Japan, 10.3%
- all countries studied, 12.2%

Overall, 10–20% of children and 3–7% of adults in developed countries have AD. Based on a US study, 58% have mild disease, 35% moderate and 7% severe, with adolescents and adults more often moderate-to-severe (Barbara et al, 2003). It has been noted that AD is more prevalent in young children and has been linked to a variety of other allergy disorders (Barbara et al, 2003). Comorbidities that were more prevalent in the AD population than in the non-AD population included asthma (12 vs 4%; age-adjusted prevalence ratio, 3.0 [95% CI 1.8–4.9]; $p < 0.001$) and food allergy (8 vs 2%; 3.7 [1.5–9.2]; $p = 0.005$). Previous studies have also reported correlations between AD and several comorbidities, including asthma, allergic rhinitis, food allergy, and mental health disorders including attention deficit disorder/attention deficit hyperactivity disorder (ADD/ADHD), autism, and depression (Bylund et al, 2020; Silverberg, 2017).

3.2 Pathophysiology

Atopic dermatitis (AD) has a complex pathophysiology. At the heart of AD is an immune response dominated by type 2 inflammation. Cytokines produced by Th2 cells, such as IL-4, IL-13, and IL-31, along with IL-22 and the skin-derived cytokine TSLP, play major roles in driving the disease (Camille et al., 2024). Among these, IL-4 and IL-13 are particularly important, as they trigger many of the inflammatory changes seen in AD (Gandhi et al., 2016; Le-Floc'h et al., 2020). These molecules influence the skin and immune system in several ways, including:

- Promoting increased production of immunoglobulin E (IgE), which is often elevated in AD patients.
- Up regulating chemokines that attract inflammatory cells to the skin, thus perpetuating the inflammatory cycle.
- Disrupting the skin's barrier function by reducing the expression of essential epidermal proteins such as filaggrin (FLG) and loricrin (LOR). (Gandhi et al, 2017)

IL-31 is another key Th2 cytokine that plays an important role in mediating pruritus, a hallmark symptom of AD1 (Oetjen et al, 2017). TSLP also drives the inflammatory process by activating dendritic cells to release type 2 cytokines like IL-4, IL-5, and IL-13 (Indra, 2013). During flare-ups, there is an increased expression of lymphocytes Th2 and Th22 and their cytokines IL-4, IL-13, and IL-22, as well as dendritic cells (DCs) (Barbara et al, 2003).

Environmental factors such as emotions, sweating, and physical exercise, alongside microbiological factors, particularly skin colonisation with Staphylococcus aureus, are important in AD flare-ups. Staphylococcus aureus has been found to colonise AD skin lesions in up to 90% of patients and can contribute to disease exacerbations. Skin microbiomedysbiosis and the role of Staphylococcus aureus in atopic dermatitis have been reviewed in studies (Lawrence, 2022; Barbara et al, 2003).

3.3 Diagnosis

The diagnosis of atopic dermatitis (AD) is based on clinical assessment. There are no objective diagnostic tests or accepted biomarkers for AD (Alexis et al, 2020), so diagnosis relies on the characteristic morphology, distribution of skin lesions and history of pruritus and atopy. Several scales are used to assess atopic dermatitis (AD) (Lawrence, 2022). These scales evaluate aspects such as disease extent and lesion severity. For instance, EASI is a validated scale utilising a 7-point assessment of disease extent in 4 defined body regions and a 4-point severity scale for 4 clinical signs. EASI evaluates both the extent of eczema and lesion severity. SCORAD is a clinically validated scale that assesses disease extent based on the rule of 9s, and intensity based on 6 clinical signs rated on a 4-point scale, plus patient-reported pruritus and sleep loss.

SCORAD evaluates both BSA and lesion severity. The IGA is a 4 or 5-point scale of global disease severity based on the morphological appearance of lesions. The POEM is a validated score assessing 7 symptoms over the preceding 7 days (Charman et al, 2013; Leshem et al, 2019). EASI-75, IGA 0/1, and SCORAD-50 are used as measures of treatment effectiveness (Sneha et al, 2023).

When diagnosing atopic dermatitis, it's important to exclude infections and rashes such as impetigo, molluscum contagiosum, tinea corporis, and viral exanthems (Eichenfield et al., 2013). Distinguishing AD from it can be especially difficult, because these infections can be present at the same time and worsen the symptoms of AD. (Frazier et al, 2020).

However, several well-designed US caregiver-centred surveys have reported prevalence estimates of 11–13% for healthcare-diagnosed eczema in the US. In the US primary care setting, one cross-sectional survey study reported an AD prevalence of 24% among paediatric patients aged 0–5 years (Drucker et al, 2016; Chung et al, 2018).

3.4 Treatment

Treatment for atopic dermatitis (AD) takes a broad approach. The goal is to calm inflammation, help the skin heal and retain moisture, ease symptoms like itching and dryness, and improve overall quality of life for the patient (Barbara et al, 2003). Topical steroids are the first-line treatment in most cases (Sneha et al, 2023). However, about one-third of patients require systemic treatment (Riccardo et al, 2020).

Topical Therapies: Intensive skincare, including the proactive use of topical glucocorticosteroids (TCS) and topical calcineurin inhibitors (TCIs), forms a cornerstone of AD management. Emollients are a crucial part of basic AD management and should be implemented in all patients at all levels of disease severity (Boguniewicz et al, 2017). They help to repair the epidermal barrier and should be used regularly, at least twice daily and after washing, ideally within five minutes (Lansang et al, 2019). A US survey indicated that many children presenting to primary care use skincare practices that may be detrimental to the skin barrier, highlighting the need for guidance on appropriate practices (Al-Naqeeb et al, 2019).

Topical Corticosteroids (TCS) are a mainstay of anti-inflammatory treatment for AD and are used to treat acute flares and for maintenance in some cases. Low-to-medium potency TCS are used for mild acute flares, while medium-to-high potency TCS are used for moderate to severe flares, with lower potency options for sensitive areas. For maintenance, TCS can be used (Lawrence, 2022). Inadequate response to TCS may indicate the need to step up therapy (Boguniewicz et al, 2017). It's important to note that some caregivers and physicians may have a fear of steroid therapy, which could impact treatment success (Barbara et al, 2003). Fluocinoloneacetonide, fluticasone propionate, desonide, and hydrocortisone butyrate are the only TCS that are FDA-approved for infants aged three months and older (Huang et al, 2017).

Topical Calcineurin Inhibitors (TCI) such as tacrolimus and pimecrolimus are also used as anti-inflammatory agents. They can be used for acute treatment and for maintenance therapy and prevention of flares. TCI represent a breakthrough in AD treatment (Barbara et al, 2003).

Topical Phosphodiesterase-4 (PDE-4) Inhibitors like crisaborole 2% are another steroid-free option approved for mild to moderate AD in patients as young as three months(Al-Naqeeb et al, 2019). Crisaborole inhibits PDE-4, an intracellular enzyme involved in the synthesis of pro-inflammatory cytokines (Barbara et al, 2003). Studies have shown its efficacy and safety in infants and children, with a mean percentage change in EASI score of -57.5% observed in one study of infants. The FDA extended the indication of crisaborole to include infants as young as 3 months in March 2020. Crisaborole is the only FDA-approved topical PDE4 inhibitor for paediatric AD (Alexis et al, 2020).

Topical Janus Kinase (JAK) Inhibitors such as ruxolitinib are being developed. Ruxolitinib cream (a JAK1/2 inhibitor) has shown efficacy and safety in phase 3 trials for mild to moderate AD in patients aged 12 years and older, leading to EASI-75 in over half of patients after 8 weeks. It also improved pruritus 17. Delgocitinib (pan-JAK) is another topical JAK inhibitor available in Japan for mild-to-moderate AD. (Silverberg et al, 2021; Silverberg, 2019; Silverberg et al, 2020)

Phototherapy can be considered in selected cases of moderate to severe AD. Treatment guidelines for AD often follow a step-care approach, where phototherapy can be a step-up option for patients with inadequate response to topical treatments. In particularly severe, recurrent cases of AD, phototherapy is mentioned as a first-line treatment option in selected cases, alongside dupilumab and cyclosporin A. While phototherapy is a valuable tool, it might not always be sufficient for managing moderate to severe AD, necessitating the consideration of systemic therapies, including newer biologics.

3.5 Systemic therapies

Systemic therapies are recommended for moderate to severe AD when topical therapies are not enough (Wollenberg et al, 2018).

Several conventional systemic immunosuppressants are used in the treatment of AD:

Cyclosporine A (CsA) was effective in some patients with moderate to severe AD. In cases of severe AD (SCORAD ≥ 50), CsA is considered a first-line treatment option alongside dupilumab and phototherapy in selected cases (Sarıcaoğlu et al, 2018).

Methotrexate (MTX) may be considered off-label for severe AD. However, it is listed as a second-line treatment for severe AD (SCORAD ≥ 50) (Taieb et al, 2018).

Mycophenolatemofetil and azathioprine are also used off-label as systemic non-steroidal immunosuppressants (NSISS) for severe AD that has not responded to topical therapy. Similar to methotrexate, robust evidence from large, well-designed, randomised controlled trials, particularly in children, is lacking to definitively support their use. Azathioprine is also considered a second-line treatment for severe AD (SCORAD ≥ 50).

Systemic corticosteroids (CS) are generally not recommended for routine AD treatment due to their unfavourable risk-benefit profile and the likelihood of disease relapse after cessation. Despite this, they are still used in clinical practice. In the United States, systemic corticosteroids are licensed for the indication of AD (Alexander et al, 2017). Systemic glucocorticosteroids (GCS) may be used for short durations (up to 14 days) and/or local GCS daily all over the skin (possibly for several days under a dressing) in the treatment of severe exacerbations (Klasa et al, 2017).

It is important to note that, with the exception of cyclosporine A (in some regions) and systemic corticosteroids (in the US), many NSISS are frequently prescribed off-label for AD, especially in the paediatric population (Barbara et al, 2003).

Systemic and Topic Janus Kinase (JAK) inhibitors are novel oral treatments for moderate-to-severe atopic dermatitis (AD). These small molecules primarily target the JAK-STAT signalling pathway, which plays a key role in AD by transmitting signals from inflammatory cytokines like IL-4, IL-13, and IL-31. By blocking the phosphorylation of JAK proteins, these inhibitors interrupt the downstream signalling cascade, leading to a reduction in inflammation and itch observed in clinical trials. (Camille et al, 2024).

Several systemic JAK inhibitors are approved for AD (Sneha et al, 2023). These include:

• Abrocitinib is an oral JAK1 inhibitor. It was granted Breakthrough Therapy designation by the FDA for moderate-to-severe AD in patients aged 12 years and older. Results from Phase 3 trials (JADE MONO-1 and JADE MONO-2) in patients aged 12 years and older with moderate-to-severe AD showed improvements in Investigator Global Assessment (IGA) and Eczema Area and Severity Index (EASI)-75 outcomes compared with placebo for both tested doses of abrocitinib (Simpson et al, 2020).

• Upadacitinibis JAK1 inhibitor, approved by the FDA and EMA, demonstrated better efficacy than placebo in Phase IIB studies in adults and is undergoing evaluation in younger patients. A trial comparing upadacitinib and dupilumab noted higher rates of certain adverse events, including acne, serious infections, eczema herpeticum, and herpes zoster, with upadacitinib (Guttman-Yassky et al, 2019).

• Baricitinib (JAK1/JAK2 inhibitor), approved in Europe for AD and FDA-approved for alopecia areata. Studies showed that over 50% of patients receiving baricitinib 4mg daily achieved primary endpoints of IGA 0/1 and EASI-75 at week 16 compared to placebo (Radi et al, 2021).

• Delgocitinib is pan-JAK inhibitor1 and a JAK/TYK2 inhibitor, it blocks multiple signalling pathways involved in inflammation.Delgocitinib was initially developed and approved in Japan as an ointment formulation for patients with AD aged 16 years and older. The efficacy and safety of delgocitinib ointment are being evaluated in pediatric patients with AD in Japan. A phase 2 clinical study in 103 Japanese patients aged 2 to 15 years with moderate to severe AD investigated its use. Patients were randomized to receive delgocitinib ointment in 0.25% or 0.5% concentrations, or vehicle ointment, twice daily for 4 weeks. The study showed that a higher proportion of patients treated with delgocitinib achieved a modified EASI-75 score compared to the placebo group (38.2% in the 0.25% group and 50.0% in the 0.5% group vs. 8.6% in the placebo group). Additionally, more patients treated with delgocitinib ointment achieved an Investigator's Global Assessment (IGA) score of clear or almost clear compared to those treated with vehicle at the end of the treatment period (Nakagawa et al, 2019).

Compared to biologics, systemic JAK inhibitors offer the advantage of oral administration, providing greater dosing flexibility and ease of use, including being easy to stop and start without refrigeration. They also tend to offer a more rapid improvement in AD signs and symptoms, particularly pruritus, likely due to broader immune suppressio. They have a shorter half-life and rapid clearance], and do not pose a risk of anti-drug antibody development. However, targeting a broader range of pathways means greater safety risks compared to biologics.

3.6 Biologics

Needs and challenges associated with conventional systemic therapies directly leads to the emergence and increasing importance of biologic therapies in AD. The first biologic approved for AD in both adults and, subsequently, in the paediatric population was duplimumab.

Dupilumab is a fully human IgG4 monoclonal antibody that targets the interleukin-4 receptor alpha subunit (IL-4Rα) (Riccardo et al, 2020). Its blocking the signal transduction pathways activated by both IL-4 and IL-13 (Hamilton et al, 2015). These two interleukins are key factors in type 2 inflammation, including IgE-mediated allergic inflammation. By binding to the IL-4Rα subunit, which is shared by both the IL-4 and IL-13 receptors, dupilumab inhibits the inflammatory cascade mediated by these two cytokines, thereby hindering the development and progression of Th2-mediated pathologies1. (Wollenberg et al, 2020; Halling et al, 2020).

Dupilumab is the first biologic therapy approved by the FDA for the treatment of moderate-to-severe atopic dermatitis (AD) in patients 6 years and older, and subsequently for children as young as 6 months. In the EU, it is approved for severe AD in children aged 6-11 years. The 600/300 mg dosing scheme is indicated for asthma patients dependent on oral corticosteroids or with co-morbid moderate-to-severe AD for which dupilumab is indicated (Amy, 2024; Barbara et al, 2003).

Age Group	Study/Trial	Key Findings	Adverse Events
Infants & Young Children (6 months–5 years)	LIBERTY AD PED-OLE (Phase 3 open-label extension)	Long-term safety profile acceptable; sustained efficacy up to 1 year; by week 52 many achieved IGA 0/1 and ≥50%, 75%, or 90% EASI improvement.	Nasopharyngitis, cough, pyrexia; injection site reactions; conjunctivitis; transient eosinophilia.
Children (6–11 years)	R668-AD-1412, LIBERTY AD PEDS (AD-1652), LIBERTY AD PED-OLE	Significant efficacy with dupilumab ± TCS; improved EASI, CDLQI, and NRS after 52 weeks; effective even with comorbid asthma/allergic rhinitis.	Injection site reactions; conjunctivitis; occasional facial redness/dermatitis; generally safe.
Adolescents (12–17 years)	LIBERTY AD ADOL (Phase 3, monotherapy)	Sustained benefit with continued therapy; EASI and NRS improvement at 1 year; confirmed by real-world studies.	Injection site reactions; conjunctivitis; occasional paradoxical eruptions (psoriasiform, facial).
All pediatric groups	Multiple RCTs & real-world studies	Demonstrated considerable short- and mid-term efficacy and safety; long-term data accumulating with consistent profile.	Ocular surface disease (DAOSD) in some; rare treatment discontinuation due to adverse events.

Clinical trials and real-world studies have demonstrated a considerable short and mid-term efficacy and safety profile for dupilumab. The most frequently reported treatment-emergent adverse events (TEAEs) in children aged 6 months to 5 years were nasopharyngitis, cough, and pyrexia. Other common adverse events reported across different age groups include injection site reactions and conjunctivitis. Dupilumab can temporarily induce eosinophilia, especially in the initial weeks of treatment, but this has generally not been clinically relevant or requiring intervention.Serious Adverse Events: Serious TEAEs leading to treatment discontinuation have been infrequent.Dupilumab-associated ocular surface disease (DAOSD) is a frequently reported side effect in adult AD patients. Symptoms may be more difficult to recognise in infants and preschoolers. Dupilumab treatment is associated with a decrease in the number and function of conjunctival goblet cells in adult AD patients.Some patients on dupilumab have developed paradoxical eruptions such as facial redness/dermatitis, and psoriasiform eruptions. Long-term safety data in children, adolescents, and adults have been accumulating and generally show a consistent safety profile. Laboratory safety analysis suggests that routine laboratory testing is not typically needed for patients using dupilumab for moderate-to-severe A (Safety et al, 2020; [57]; Wollenberg et al, 2018).

There is a continuous need for the development of additional monoclonal antibodies to increase the probability of achieving disease control in AD patients (Thanaporn et al, 2020). Ongoing and future research efforts are focused on several key areas. Investigations are underway to understand the long-term effects of dupilumab treatment, especially in young children. The impact of inhibiting IL-4/IL-13 signalling on associated comorbidities like asthma, allergic rhinitis, and food allergy in paediatric AD patients has not yet been fully investigated. Furthermore, studies are exploring the potential for early intervention with dupilumab in infants and young children to potentially modify the course of AD and potentially reduce the risk or severity of developing other atopic disorders (Alexis et al, 2020).

IL-13 is recognised as a principal driver of inflammation in AD. Tralokinumab is a monoclonal antibody that specifically targets and inhibits IL-13 signalling, revealed through structural characterisation to inhibit binding to IL-13Rα1 and IL-13Rα23. Tralokinumab is registered for the treatment of moderate-to-severe AD in adolescents . Phase 3 trials in adults and adolescents have been completed, with a long-term safety and efficacy Phase 3 trial for previous participants currently underway. Efficacy and safety data from Phase 3 trials (ECZTRA 1) showed improvements in various AD severity scores.Studies indicate it normalises type 2 inflammation and increases skin microbial diversity (Popovic et al, 2017).

Lebrikizumab is another humanised IgG4κ monoclonal antibody,lebrikizumab also specifically inhibits IL-13 activity, described as a high-affinity IL-13 inhibitor. Two recent Phase III trials (Measure Up 1 and Measure Up 2) have shown clinical efficacy. Skin clearance and pruritus has been improved.. Common adverse events were observed in a Phase 2b trial.

TSLP is an epidermal cytokine involved in activating inflammatory pathways in AD. Tezepelumabis a fully human IgG2λ monoclonal antibody that binds to TSLP. It is being evaluated in Phase 2b clinical trials in adults with moderate-to-severe AD (Simpson et al, 2019).

OX40 is a receptor implicated in T cell responses and inflammation.ISB 830 / GBR 830 / Telazorlimabis a humanised IgG1 anti-OX40 monoclonal antibody. Phase 2a trials have been conducted. A Phase 2b trial is ongoing. Studies have shown it improves skin gene signatures and clinical scores. (Camille et al, 2024).

IL-22 is linked to epidermal abnormalities and barrier defects in AD. Fezakinumab (ILV-094) is a human IgG1λ anti-IL-22 monoclonal antibody. A Phase 2a study in moderate-to-severe AD showed potential, with patients with higher baseline IL-22 levels showing significant improvement (Thanaporn et al, 2020).

Targeting IL-12/IL-23 and IL-17Aare associated with TH1 and TH17 inflammation. Ustekinumab is an IL-12/IL-23 p40 antagonist. While approved for paediatric psoriasis, a Phase II study in adults with AD did not show significant clinical improvement, although it did demonstrate notable transcriptomic changes.Secukinumab is a monoclonal antibody targeting IL-17A. Also approved for pediatric psoriasis, Phase II studies have been completed in AD. (Rerknimitr et al, 2017).

IgE is central to allergic immune responses. Omalizumab is an anti-IgE monoclonal antibody. While widely used for other allergic conditions, sources state there are no satisfactory treatment effects in patients with AD in general. However, a Phase 4 trial in children with severe AD found that it significantly reduced disease severity and the need for topical steroids. It has also been used as a pretreatment to reduce risks during oral immunotherapy for food allergy. Notably, omalizumab (along with dupilumab and tralokinumab) is a biologic that may be maintained during surgical scenarios (Rerknimitr et al, 2017).

Ligelizumab is another anti-IgE monoclonal antibody with greater affinity for IgE than omalizumab. A Phase II randomised controlled trial was completed in 2013, but no results have been posted (Thanaporn et al, 2020).

Biologic	Target / Mechanism	Pediatric approval / status	Key trials / findings	Common AEs / Notes
Tralokinumab	IL-13 neutralising monoclonal antibody	Registered for adolescents (per report)	Phase 3 trials (ECZTRA series) completed in adults/adolescents; showed improvements in AD severity and increased skin microbial diversity.	Generally well tolerated; trial-specific AEs reported in literature.
Lebrikizumab	High-affinity IL-13 inhibitor (IgG4κ)	Under investigation; Phase III adult trials (Measure Up 1 & 2) positive	Phase III Measure Up 1 & 2 showed clinical efficacy (skin clearance, pruritus improvement).	Common AEs observed in Phase 2b; safety profile under continued evaluation.
Tezepelumab	Anti-TSLP (thymic stromal lymphopoietin) monoclonal antibody	Under investigation (phase 2 trials in adults mentioned)	Randomized phase 2a trial in adults showed activity in moderate-to-severe AD (Simpson et al., 2019).	Safety being evaluated in ongoing trials.
ISB-830 / GBR-830 (anti-OX40)	Anti-OX40 (modulates T-cell responses)	Investigational (Phase 2a done; Phase 2b ongoing)	Phase 2a trials improved skin gene signatures and clinical scores; Phase 2b ongoing.	Early-stage data; longer-term safety and efficacy pending.
Fezakinumab (ILV-094)	Anti-IL-22 monoclonal antibody	Investigational (Phase 2a in adults)	Phase 2a showed potential; patients with higher baseline IL-22 had greater benefit.	Data limited; biomarker-selected populations may respond better.
Omalizumab	Anti-IgE monoclonal antibody	Approved for other allergic conditions in children; mixed results in AD	Generally no strong effect in AD overall; a Phase 4 trial in children with severe AD showed reduced disease severity and topical steroid use.	Well-known safety profile from allergy use; variable efficacy in AD.
Ligelizumab	Anti-IgE monoclonal antibody (higher affinity than omalizumab)	Investigational; Phase II trial completed (2013) but no posted results in report	Phase II RCT completed; results not posted (per report).	Development ongoing in other allergic indications.
Ustekinumab	Anti-IL-12/IL-23 (p40) antagonist	Approved for pediatric psoriasis; AD trial in adults not showing significant clinical improvement	Phase II study in adults with AD did not show significant clinical improvement but showed transcriptomic changes.	Used in pediatric psoriasis; limited role in AD per report.
Secukinumab	Anti-IL-17A monoclonal antibody	Approved for pediatric psoriasis; Phase II studies in AD completed	Phase II studies in AD completed; efficacy in AD unclear per report.	Primarily used for psoriasis; limited AD evidence.

The landscape of targeted therapies for AD, including the various biologics discussed above, is continuously expanding, holding promise for improved and potentially more personalised treatment options that move beyond conventional systemic therapies. Further research, particularly in diverse pediatric populations and regarding the long-term implications and practical implementation of these agents in younger children, is crucial. Psychological challenges related to the long-term subcutaneous administration of biologics in infants and preschoolers also necessitate attention and support.

4. Conclusions

Biologics represent a breakthrough for moderate-to-severe AD. Dupilumab, the first biologic approved, targeting the IL-4Rα subunit to inhibit both IL-4 and IL-13 signalling, has demonstrated significant efficacy in improving clinical signs. It reducing pruritus and improving quality of life across adults, adolescents, children 6-11 years, and even children as young as 6 months. It shows an excellent safety profile. Also do no increases risk of systemic infections. Targeted small molecule inhibitors offer another class of treatment. Abrocitinib (JAK1) and upadacitinib (JAK1) have shown high efficacy in clinical trials. Overall, biological therapeutics and JAK inhibitors has improved treatment options for patients with moderate-to-severe AD. They offer effective strategies and provide the potential for better disease control and improved quality of life.

Author's Contribution:
Conceptualization: Darya Lazitskaya, Dmytro Kowalczuk
Methodology:MykolaSobchynskyi, KatsiarynaMiraniuk
Formal analysis: Natalia Surosz, DawidWiczkowski, KamilTurlej
Investigation: IgaKiełbaszewska, AndrzejMyrny, WiktoriaKasianik
Writing-rough preparation: ValeryiaMilasheuskaya, DmytroKowalczuk, Natalia Surosz
Writing-review and editing: Darya Lazitskaya, Dmytro Kowalczuk
Supervision: Darya Lazitskaya, Dmytro Kowalczuk

All authors have read and agreed with the published version of the manuscript.

Funding Statement: The authors did not receive special funding.
Institutional Review Board Statement: Not applicable.
Informed Consent Statement: Not applicable.
Data Availability Statement: Not applicable.
Conflict of Interest Statement: The authors declare no conflict of interest.

REFERENCES

1. Al-Naqeeb J, Danner S, Fagnan LJ, et al. The burden of child-hood atopic dermatitis in the primary care setting: a report from the Meta-LARC Consortium. J Am Board Fam Med. 2019;32(2):191–200. https:// doi.org/ 10.3122/ jabfm. 2019. 02. 180225.
2. Alexander T, Maxim E, Cardwell LA, Chawla A, Feldman SR. Prescriptions for atopic dermatitis: oral corticosteroids remain commonplace. J Dermatolog Treat. 2018;29(3):238–40. doi: 10.1080/09546634.2017.1365112
3. Alexis Tracy, SafiyyahBhatti, Lawrence F. Eichenfield. Update on Pediatric Atopic Dermatitis, Cutis. 2020 Sep;106(3):143-146. DOI: 10.12788/cutis.0077
4. Amy S. Palle, Elaine C. Siegfried, Eric L. Simpson, Michael J. Cork, Robert Sidbury, Iris H. Chen, Faisal A. Khokha, Jing Xiao, Ariane DubostBrama, Ashish Bansal. Dupilumab Safety and Efficacy up to 1 Year in Children Aged 6 Months to 5 Years with Atopic Dermatitis: Results from a Phase 3 OpenLabel Extension Study. American Journal of Clinical Dermatology (2024) 25:655–668. https://doi.org/10.1007/s40257-024-00859-y
5. Annie George, Rafael Paolo Lansang, BHS, PerlaLansang and Melinda Gooderham. A Practical Guide to Using Biologics in Pediatric Dermatology. Journal of Cutaneous Medicine and Surgery 2024, Vol. 28(1) 59–67. DOI:10.1177/12034754231222415 jcms.sagepub.com
6. Bao L, Zhang H, Chan LS. The involvement of the JAK-STAT signaling pathway in chronic inflammatory skin disease atopic dermatitis.JAKSTAT. 2013;2(3):e24137. https:// doi.org/ 10.4161/ jkst. 24137.
7. Barbara Klasa, Ewa Cichocka-Jarosz. ATOPIC DERMATITIS – CURRENT STATE OF RESEARCH ON BIOLOGICAL TREATMENT. Journal of Mother and Child 24(1) 2020 53-66. doi: 10.34763/jmotherandchild.2020241.2003.0000010

8. Barrett J. Fda approves dupilumab for atopic dermatitis in children. drug topics; 2020 Available from: https://www.drugtopics.com/autoimmune-diseases/fda-approves-dupilumab-atopic-dermatitis-children [2020, May 27].
9. Beck LA, Thaçi D, Hamilton Jd, Graham nM, Bieber t, rocklin r, et al. dupilumab treatment in adults with moderate-to-severe atopic dermatitis. nengl J Med 2014;371:130–9.
10. Bin L, Leung DY. Genetic and epigenetic studies of atopic der-matitis. Allergy Asthma ClinImmunol. 2016;12:52. https:// doi.org/ 10.1186/ s13223- 016- 0158-5.
11. Boguniewicz M, Fonacier L, Guttman-Yassky E, Ong PY, Silver-berg J, Farrar JR. Atopic dermatitis yardstick: Practical recom-mendations for an evolving therapeutic landscape. Ann Allergy Asthma Immunol. 2018;120(1):10-22.e2. https:// doi.org/ 10.1016/j. anai. 2017. 10. 039.
12. Bylund S, von Kobyletzki LB, Svalstedt M, Svensson A. Preva-lence and incidence of atopic dermatitis: a systematic review. ActaDermVenereol. 2020;100(12):adv00160. https:// doi.org/ 10.2340/ 00015 555- 3510.
13. Camille Rothenberg-Lausell, Jonathan Bar, Dante Dahabreh, Yael Renert-Yuval, Ester Del Duca and Emma Guttman-Yassky. Biologic and small-molecule therapy for treating moderate to severe atopic dermatitis: Mechanistic considerations. J Allergy ClinImmunol. 2024 Jul;154(1):20-30. DOI: 10.1016/j.jaci.2024.04.009
14. Zhou B, Peng C, Cao Q, Wang J, Chen X, Li J. Dupilumab therapy in children aged 2-12 years with uncontrolled moderate-to-severe atopic dermatitis: a Chinese real-world study. J EurAcadDermatolVenereol. 2023;38(1):e35–e38. doi:10.1111/jdv.19409
15. Chung J, Simpson EL. The socioeconomics of atopic dermatitis.Ann Allergy Asthma Immunol. 2019;122(4):360–6. https:// doi.org/ 10.1016/j. anai. 2018. 12. 017.
16. Cork MJ, Danby SG, Ogg GS. Atopic dermatitis epidemiol-ogy and unmet need in the United Kingdom.J Dermatol Treat. 2019;8:801–9. https:// doi.org/ 10.1080/ 09546 634. 2019. 16551 37.
17. Cork MJ, Thaçi D, Eichenfield LF, et al. Dupilumab in adolescents with uncontrolled moderate-to-severe atopic dermatitis: results from a phase IIa open-label trial and subsequent phase III open-label extension. Br J Dermatol. 2020;182:85-96.
18. Drucker AM, Wang AR, Li WQ, Sevetson E, Block JK, Qureshi AA. The burden of atopic dermatitis: summary of a report for the National Eczema Association. J InvestigDermatol. 2017;137(1):26–30. https:// doi.org/ 10.1016/j. jid. 2016. 07. 012.
19. Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. J Am AcadDermatol. 2014;70(2):338–51. https:// doi.org/ 10.1016/j. jaad. 2013. 10. 010.
20. European Medicines Agency (EMA). DUPIXENT® (dupilumab). Summary of opinion (post-authorisation).2023. https:// www.ema. europa. eu/ en/ documents/ smop/ chmp- post- authorisat ion- summa ry- posit ive- opini on-dupixent- ii- 60_ en. pdf. Accessed 27 Feb 2023.
21. Frazier W, Bhardwaj N. Atopic dermatitis: diagnosis and treatment. Am Fam Physician. 2020;101(10):590–8.
22. Futamura M, Leshem YA, Thomas KS, Nankervis H, Williams HC, Simpson EL. A systematic review of Investigator Global Assessment (IGA) in atopic dermatitis (AD) trials: many options, no standards. J Am AcadDermatol. 2016;74(2):288–94. https:// doi.org/10.1016/j.jaad.2015.09.062.
23. Thaçi D, Simpson EL, Beck LA, Bieber T, Blauvelt A, Papp K, et al. Efficacy and safety of dupilumab in adults with moderate-to-severe atopic dermatitis inadequately controlled by topical treatments: a randomised, placebo-controlled, dose-ranging phase 2b trial. Lancet 2016;387:40–52.
24. Wollenberg A, Beck LA, Blauvelt A, Simpson EL, Chen Z, Chen Q, et al. Laboratory safety of dupilumab in moderate-to-severe atopic dermatitis: results from three phase III trials (LIBERTY AD SOLO 1, LIBERTY AD SOLO 2, LIBERTY AD CHRONOS). Br J Dermatol. 2020;182(5): 1120–35. [PubMed: 31407311]
25. Guttman-Yassky E, Thaçi D, Pangan AL, Hong HC, Papp KA, Reich K, et al. Upadacitinib in adults with moderate to severe atopic dermatitis: 16-week results from a randomized, placebocontrolled trial. J Allergy ClinImmunol. 2020;145(3):877–84. doi: 10.1016/j.jaci.2019.11.025.
26. Halling AS, Loft ND, Silverberg JI, Guttman-Yassky E, Thyssen JP. Real-world evidence of dupilumab efficacy and risk of adverse events: a systematic review and meta-analysis. J Am AcadDermatol. 2020.
27. Le-Floc'h A, Allinne J, Nagashima K, Scott G, Birchard D, Asrat S, et al. Dual blockade of IL-4 and IL-13 with dupilumab, an IL-4Rα antibody, is required to broadly inhibit type 2 inflamma-tion. Allergy. 2020;75(5):1188–204. https:// doi.org/ 10.1111/ all. 14151.
28. Nakagawa H, Nemoto O, Igarashi A, et al. Phase 2 clinical study of delgocitinib ointment in pediatric patients with atopic dermatitis. J Allergy ClinImmunol. 2019;144:1575-1583.
29. Paller AS, Simpson EL, Siegfried EC, Cork MJ, Wollenberg A, Arkwright PD, et al. Dupilumab in children aged 6 months to younger than 6 years with uncontrolled atopic dermatitis: a randomised, double-blind, placebo-controlled, phase 3 trial. Lan-cet. 2022;400(10356):908–19. https:// doi.org/ 10.1016/ S0140- 6736(22) 01539-2.
30. Patruno C, Fabbrocini G, Lauletta G, et al. A 52-week multicenter retrospective real-world study on effectiveness and safety of dupilumab in children with atopic dermatitis aged from 6 to 11 years. J Dermatol Treatment. 2023;34(1):2246602. doi:10.1080/09546634.2023.2246602

31. Popovic B, Breed J, Rees DG, Gardener MJ, Vinall LM, Kemp B, et al. Structural Characterisation Reveals Mechanism of IL-13-Neutralising Monoclonal Antibody Tralokinumab as Inhibition of Binding to IL-13Rα1 and IL-13Rα2. J Mol Biol. 2017;429(2):208–19. [PubMed: 27956146]
32. Radi G, Simonetti O, Rizzetto G, Diotallevi F, Molinelli E, Offidani A. Baricitinib: The First Jak Inhibitor Approved in Europe for the Treatment of Moderate to Severe Atopic Dermatitis in Adult Patients. Healthcare (Basel). 2021;9(11)
33. Riccardo Castagnoli, Maria de Filippo, Martina Votto, AlessiaMarseglia, LorenzaMontagna, Gian Luigi Marseglia, Amelia Licari. An update on biological therapies for pediatric allergic diseases. Minerva Pediatrica 2020 October;72(5):364-71. DOI: 10.23736/S0026-4946.20.05993-9
34. Safety, pharmacokinetics and efficacy of dupilumab in patients ≥6 months to <6 Years With Moderate-to-Severe Atopic Dermatitis (liberty AD preschool). Clinical Trials; 2017 [InterneAvailable from: https://clinicaltrials.gov/ct2/show/NCT03346434 [2020, Jan 19]
35. Sarıcaoğlu H, Yazici S, Zorlu Ö, BülbülBaşkan E, Aydoğan K. Cyclosporine-A for severe childhood atopic dermatitis: clinical experience on efficacy and safety profile. Turk J Med Sci. 2018;48(5):933–8. doi: 10.3906/sag-1711-7
36. Silverberg JI, Barbarot S, Gadkari A, et al. Epidemiology of atopic dermatitis in children aged 6–11 years: a cross-sectional study in the United States (US), Canada, Europe, and Japan. Paper presented at: American Academy of Dermatology Annual Meeting; March 20-24, 2020; Denver, CO.
37. Silverberg JI, Guttman-Yassky E, Thaçi D, Irvine AD, Stein Gold L, Blauvelt A, et al. Two phase 3 trials of lebrikizumab for moderate-to-severe atopic dermatitis.N Engl J Med 2023;388:1080-91.
38. Simpson E L, Pallera S, Siegfried E C, Boguniewicz M, Sher L, Gooderham MJ, et al. Efficacy and Safety of Dupilumab in adolescents With Uncontrolled Moderate to Severe atopic dermatitis: a Phase 3 randomized clinical trial. JaMadermatol 2019;156:44–56.
39. Simpson EL, PalleraS, Siegfried EC, Boguniewicz M, Sher L, Gooderham MJ, et al. Efficacy and Safety of Dupilumab in adolescents With Uncontrolled Moderate to Severe atopic dermatitis: a Phase 3 randomized clinical trial. JaMadermatol 2019;156:44–56.
40. Simpson EL, Parnes JR, She D, Crouch S, Rees W, Mo M, et al. Tezepelumab, an anti-thymic stromal lymphopoietin monoclonal antibody, in the treatment of moderate to severe atopic dermatitis: a randomized phase 2a clinical trial. J Am AcadDermatol 2019;80:1013-21.
41. Simpson EL, Sinclair R, Forman S, et al. 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. Lancet. 2020;396:255-266.
42. Sneha Butala, Leslie Castelo-Soccio, Rishi Seshadri, Eric L. Simpson, John J O'Shea, Thomas Bieber, Amy S. Paller, MS, MD. Biologic versus small molecule therapy for treating moderate to severe atopic dermatitis: clinical considerations. J Allergy ClinImmunolPract. 2023 May ; 11(5): 1361–1373. doi:10.1016/j.jaip.2023.03.011
43. Study to assess the long-term safety of dupilumab administered in participants ≥6 months to<18 Years of Age With Atopic Dermatitis (AD) ClinicalTrials.gov ID NCT02612454
44. Taieb Y, Baum S, Ben Amitai D, Barzilai A, Greenberger S. The use of methotrexate for treating childhood atopic dermatitis: A multicenter retrospective study. J Dermatolog Treat. 2019;30(3):240– 4. doi: 10.1080/09546634.2018.1508816
45. Thanaporn Ratchataswan, MDA, Tina M. Banzon, MDA,E, Jacob P. Thyssen, MD, PhD, DmSciB, Stephan Weidinger, MD, PhD, MaHMC, Emma Guttman-Yassky, MD, PhDD, Wanda Phipatanakul, MD, MSA,E. Biologics for Treatment of Atopic Dermatitis: Current Status and Future Prospect. J Allergy ClinImmunolPract. 2021 March ; 9(3): 1053–1065. doi:10.1016/j.jaip.2020.11.034