Treating moderate-to-severe atopic dermatitis in children and adolescents: Insights from the experts

touch™ IMMUNOLOGY

Disclaimer

- *Unapproved products or unapproved uses of approved products may be discussed by the faculty; these situations may reflect the approval status in one or more jurisdictions*
- *The presenting faculty have been advised by USF Health and touchIME to ensure that they disclose any such references made to unlabelled or unapproved use*
- *No endorsement by USF Health and touchIME of any unapproved products or unapproved uses is either made or implied by mention of these products or uses in USF Health and touchIME activities*
- *USF Health and touchIME accept no responsibility for errors or omissions*

touch™ IMMUNOLOGY

A conversation between:

Dr Benjamin Ungar
Mount Sinai, New York,
NY, USA

Prof. Dr. med. Diamant Thaçi
University of Lübeck,
Lübeck, Germany

touch™ IMMUNOLOGY

Understanding and assessing disease severity in children and adolescents with atopic dermatitis

Dr Benjamin Ungar

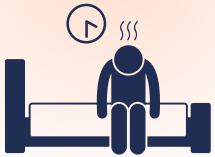
Mount Sinai, New York, NY, USA

touch™ IMMUNOLOGY

Symptom burden in paediatric populations with AD

CHRONIC PRURITUS[1–3]

SLEEP DISTURBANCE[1,2]



- IMPAIRED QOL[1]
- COGNITIVE IMPAIRMENT[1]
- PSYCHOLOGICAL STRESS[1]
- IMPAIRED FAMILY RELATIONSHIPS[1,2]
- POOR SELF-ESTEEM[2]
- POOR SCHOOL PERFORMANCE[2]
- EMOTIONAL/ BEHAVIOURAL ISSUES[3]
- BURDENSOME TREATMENT (TIME/EXPENSE)[2]

Symptom burden is particularly significant for patients with chronic hand dermatitis[4]

AD, atopic dermatitis; QoL, quality of life.

1. Cameron S, et al. *Allergy.* 2024;26–36; 2. Lyons JJ, et al. *Immunol Allergy Clin North Am.* 2015;35:161–83;
3. Drucker AM, et al. *J Investig Dermatol.* 2017;137:26e30; 4. Fowler JF, et al. *J Am Acad Dermatol.* 2006;54:448–57.

touch™ IMMUNOLOGY

Considerations for the selection of systemic therapy for children and adolescents with moderate-to-severe atopic dermatitis

Dr Benjamin Ungar

Mount Sinai, New York, NY, USA

touch™ IMMUNOLOGY

Approved systemic therapies in moderate–severe AD

FDA

Monoclonal antibody

Dupilumab (anti-IL-4Rα)[1]
- Adult and paediatric patients aged ≥6 months

Tralokinumab (anti-IL-13)[2]
- Adult and paediatric patients aged ≥12 years

JAK inhibitor

Abrocitinib[6]
- Adult and paediatric patients aged ≥12 years

Upadacitinib[7]
- Adult and paediatric patients aged ≥12 years

EMA

Monoclonal antibody

Dupilumab (anti-IL-4Rα)[3]
- Adult and paediatric patients aged ≥12 years
- Children aged 6 months–11 years with severe AD

Lebrikizumab (anti-IL-13)[4]
- Adult and paediatric patients aged ≥12 years

Tralokinumab (anti-IL-13)[5]
- Adult and paediatric patients aged ≥12 years

JAK inhibitor

Abrocitinib[8]
- Adult and paediatric patients aged ≥12 years

Baricitinib[9]
- Adult and paediatric patients aged ≥2 years

Upadacitinib[10]
- Adult and paediatric patients aged ≥12 years

Agents used off-label for systemic therapy in paediatric patients with severe AD include methotrexate and cyclosporin A[11]

AD, atopic dermatitis; EMA, European Medicines Agency; FDA, US Food and Drug Administration; IL, interleukin; IL-4Ra, IL-4 receptor alpha; JAK, Janus kinase; pts, patients.

1. FDA. Dupilumab PI. 2024; 2. FDA. Tralokinumab PI. 2024; 3. EMA. Dupilumab SmPC. 2024; 4. EMA. Lebrikizumab. Summary of opinion. 2023. Available at: https://bit.ly/3WBCrkF (accessed 16 August 2024); 5. EMA. Tralokinumab SmPC. 2023; 6. FDA. Abrocitinib PI. 2023; 7. FDA. Upadacitinib PI. 2024; 8. EMA. Abrocitinib SmPC. 2024; 9. EMA. Baricitinib SmPC. 2024; 10. EMA. Upadacitinib SmPC. 2024; 11. Lockhart MK, Siegfried EC. *Dermatol Clin*. 2022;40:137–43.

All PIs available at: www.accessdata.fda.gov/scripts/cder/daf/index.cfm. All SmPCs available at: www.ema.europa.eu/en/medicines; all URLs accessed 10 July–28 August 2024.

Practical management of side effects of systemic treatments for moderate-to-severe atopic dermatitis

Dr Benjamin Ungar

Mount Sinai, New York, NY, USA

touch™ IMMUNOLOGY

Systemic therapies in paediatric AD: Notable side effects

Biologics[1]

Dupilumab

1. Conjunctivitis
2. Injection-site reactions

Lebrikizumab

Tralokinumab

JAK inhibitors[1]

Abrocitinib

1. Nausea
2. Acne (less than with upadacitinib)
3. ↑ upper respiratory tract & herpetic infections
4. Headache

Baricitinib

1. Headache
2. ↑ upper respiratory and herpes simplex infections

Upadacitinib

1. Acne
2. Nasopharyngitis, ↑ upper respiratory tract and herpetic infections
3. Headache

Abnormal haematologic counts, ↑ lipids & creatine phosphokinase levels[1]*
Boxed warning[1] and PRAC recommendation[2] for JAK inhibitor agent class for theoretical risk of malignancy, cardiovascular disease, emboli, and serious infections

Biologics are not associated with an increase in AEs/SAEs leading to discontinuation vs topical therapy alone[3]

The risk–benefit profile of **JAK inhibitors** should be considered when selecting an agent in clinical practice[3]

*Not clinically significant.
AD, atopic dermatitis; AE, adverse event; JAK, Janus kinase; PRAC, Pharmacovigilance Risk Assessment Committee; SAE, serious AE.
1. Butala S, Paller AS. *J Allergy Clin Immunol.* 2023;151:681–5; 2. EMA. 2023. Available at: https://shorturl.at/uXLcC (accessed 7 August 2024);
3. Chu DK, et al. *Ann Allergy Asthma Immunol.* 2024;132:274–312.

touch™ IMMUNOLOGY

Long-term data: Systematic review and updates from EADV 2023

Long-term efficacy and safety data with systemic therapies for atopic dermatitis

Trial	Agent(s)	Outcomes	Conclusions
Systematic review of 33 publications on biologics and JAK inhibitors[1]	**Biologics:** Dupilumab Tralokinumab **JAK inhibitors:** Upadacitinib Baricitinib	**Efficacy (48–60 weeks)** • **Dupilumab** and **upadacitinib** achieved clinically superior efficacy outcomes (EASI 75 and vIGA-AD 0/1) • **Tralokinumab** data also highly satisfactory **Safety** • **Dupilumab (52-week treatment); tralokinumab (36-week maintenance)** showed the lowest risk of AEs; most discontinuations due to AD flares	Systematic review results like these may help inform treatment guidelines
Phase III Measure Up 1 study[2] Adults and adolescents aged ≥12 years with moderate-to-severe AD	**Upadacitinib (15 mg / 30 mg)** vs placebo Long-term efficacy and safety	Efficacy of both doses was consistently maintained for: • **Skin clearance** (EASI 75; EASI 90; vIGA-AD 0/1) and • **Symptom control** (WI-NRS 0/1) from week 16 **through week 140** **Safety consistent with the known upadacitinib safety profile, with no new safety signals observed**	Upadacitinib sustained skin clearance and itch with a consistent safety profile across 140 weeks

EASI, Eczema Area and Severity Index; JAK, Janus kinase; vIGA-AD, Validated Investigator Global Assessment for Atopic Dermatitis; WI-NRS, Worst Itch Numerical Rating Scale.

1. Ayen-Rodriguez A, et al. *Life.* 2022;12:1159; 2. Silverberg JI, et al. *Br J Dermatol.* 2024;190(Suppl.2):ii8.

touch™ IMMUNOLOGY

Latest data: Updates from AAD 2024 and AAAAI 2024

Long-term data for symptom improvement and disease control with systemic biological therapies

Trial	Agent	Outcomes	Conclusions
Phase III LIBERTY AD PED-OLE[1] Children and adolescents aged 0.5–17 yrs (N=763)	**Dupilumab** 300 mg Q4W (<60 kg) or 200/300 mg Q2W (≥60 kg)	**Weeks 4, 16, 28, 40 and 52** **EASI <7 maintained** in **≥4 of 5 timepoints** in most patients across ages (years): • 0.5–5, **63%** • 6–11, **58%** • 12–17, **50%**	Most patients achieved sustained and consistent improvements in signs and area affected by AD during 1 year of treatment with dupilumab
Phase III extension[2] Adults and adolescents with moderate-to-severe AD; week 16 responders (ADvocate1/2)	**Lebrikizumab** vs placebo	**At week 52** • EASI 75: **80%**; ≥4-point improvement in NRS: **84%** **Continuous maintenance of composite endpoint (EASI ≤7 or NRS ≤4) for 36 wks after Q2W to Q4W switch** **At week 52** **91%** of pts on Q4W regimen continued to maintain EASI ≤7 or NRS ≤4	Patients with moderate-to-severe AD switching to Q4W after Q2W induction maintain a response at week 52

AD, atopic dermatitis; EASI, Eczema Area and Severity Index; NRS, pruritus Numeric Rating Scale; POEM, Patient-Oriented Eczema Measure; Q2W, every 2 weeks; Q4W, every 4 weeks.

1. Siegfried E, et al. *J Am Acad Dermatol.* 2024;91(Suppl.):AB188; 2. Stein Gold L, et al. *J Am Acad Dermatol.* 2024;91(Suppl.):AB58.

touch™ IMMUNOLOGY