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Atopic Dermatitis and Psoriasis: Therapeutic Strategies, Clinical Guidelines, and Treatment Approaches

A closer look at challenges, ongoing clinical trials, and real-world efficacy studies

Therapeutic management of atopic dermatitis (AD)

AD[1]

Common skin disease, affecting 25% of children and 7% of adults

Multifactorial pathogenesis, including skin barrier dysfunction, inflammation, and dysbiosis

Characterised by lichenification and pruritus of the skin

AD impacts the quality of life of both patients and family members

Therapeutic options for the treatment of AD[2,3]

Topical first-line agents
- Topical corticosteroids (CS)
- Calcineurin inhibitors

Phosphodiesterase-4 (PDE4) inhibitors
- Crisaborole 2% ointment
- Difamilast
- Roflumilast

Aryl hydrocarbon receptor agonist
- Tapinarof

Janus kinase (JAK) inhibitors
- Topical ruxolitinib
- Delgocitinib

Oral JAK inhibitors
- Upadacitinib
- Abrocitinib
- Baricitinib

Biologics
- Dupilumab
- Tralokinumab
- Lebrikizumab
- Nemolizumab
- Benralizumab

Other experimental agents[2]

Microbial
- Omiganan (antimicrobial peptide)
- *Roseomonas mucosa*
- Targeted microbiome transplant lotion containing *Staphylococcus hominis*

Orals
- SCD-044
- RPT193

Injectables
Anti-OX40 and anti-OX40L antibodies

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Guidelines and treatment approaches for AD

Treat-to-target strategy for the management of patients with AD[4]

- **Self-reported Patient Global Assessment of disease severity**
- **Time-points for the assessment of disease control: 3 and 6 months**

Treatment thresholds

- Eczema Area and Severity Index (EASI)
- SCORing AD
- Peak Pruritus Numerical Rating Scale (PP-NRS)
- Dermatology Life Quality Index
- Patient-Oriented Eczema Measure

Systematic review on the evidence of methotrexate (MTX) dosing regimens used for treating AD[5]

Five randomised controlled trials (RCTs) and 21 guidelines were included

RCTs compared MTX with other treatments but not different MTX dosing regimens

Start dose: 7.5–15 mg/week Maintenance dose: 14.5–25 mg/week

All trials showed improved AD signs and symptoms despite varying doses

Guidelines recommended test dose and folic acid supplementation

Systematic review on efficacy and safety of low-dose cyclosporine (Cs) A relative to immunomodulatory drugs used in AD[6]

Five RCTs comparing low-dose CsA (<4 mg/kg) with high-dose CsA (>4 mg/kg) and other treatments

Low-dose CsA showed non-inferior efficacy compared to high-dose CsA and other treatments

No significant difference in the occurrence of adverse events (AEs) between the low-dose CsA and other treatments

Therapeutic management of psoriasis (PSO)

PSO[7,8]

- Chronic, immune-mediated inflammatory disease with systemic involvement
- Worldwide prevalence of 1–3%

Therapeutic options for the treatment of PSO[9]

Topical therapy

- CS
- Vitamin D3 analogues
- Combination products: Calcipotriol and betamethasone dipropionate

Systemic therapy

- Phototherapy
- Acitretin
- MTX
- Cs
- Biologic therapy

Challenges in treating paediatric PSO[10]

- Accurate diagnosis of PSO
- Lack of supporting data for safe and long-term use of medication
- Comorbid health risks
- Potential impact of immunisation
- Individualisation of treatment dosages
- Economic barriers to recommended treatments
- Psychological burden of disease

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Newer therapies and current/ongoing clinical trials

Abrocitinib[11]

JAK1 selective inhibitor approved for the treatment of moderate-to-severe AD

Reduction of itch and skin clearance with abrocitinib

Abrocitinib monotherapy in phase 3 studies of patients aged ≥12 years
- JADE MONO-1 [NCT03349060]
- JADE MONO-2 [NCT03575871]

Topical medications in phase 3 studies of patients
- JADE COMPARE [NCT03720470] aged >18 years
- JADE TEEN [NCT03796676] aged 12 to <18 years

JADE EXTEND (NCT03422822)
- An ongoing, phase 3, long-term extension study of oral abrocitinib
- Participants: Adult (>18 years of age) and adolescent (12 to <18 years of age) patients with moderate-to-severe AD
- Dosage: 200 mg or 100 mg once daily

Results of JADE EXTEND trial
- 70% of patients received abrocitinib for >36 weeks
- 45% of patients received abrocitinib for >48 weeks
- Treatment-emergent AEs (TEAEs)
  - Nasopharyngitis
  - AD
  - Nausea
  - Upper respiratory tract infections
- Treatment with abrocitinib resulted in clinically relevant skin and pruritus improvement
- Tolerable and consistent safety profile

Lebrikizumab[12]

Anti-interleukin-13 monoclonal antibody for treatment of moderate-to-severe AD

Lebrikizumab monotherapy in phase 3 studies ADvocate 1 (NCT04146363) and ADvocate 2 (NCT04178967)

- Participants: Adult and adolescent patients (12 years or older) with moderate-to-severe AD
- Dosage: 500 mg loading dose at baseline and week 2 followed by 250 mg every 2 weeks
- Higher percentage of patients receiving lebrikizumab achieved an EASI 75 response and Investigator Global Assessment score of 0 (clear) or 1 (almost clear) at week 16
- Favourable safety and tolerability profiles

Upadacitinib[13]

Oral selective-JAK1 inhibitor for treatment of moderate-to-severe AD

Upadacitinib monotherapy in phase 3 studies Measure Up 1 (NCT03569293) and Measure Up 2 (NCT03607422)

- Dosage: 15 mg, 30 mg
- Significant decrease in EASI scores, and pruritus NRS scores
- 30 mg dose was more effective than the 15 mg dose for patients with moderate-to-severe AD
- Patients treated with upadacitinib experienced a higher incidence of mild and tolerated AEs but no significant serious AEs

Benvitimod[14]

Topical drug, approved for mild-to-moderate PSO

Meta-analysis of six RCTs evaluating the efficacy of 1.0% benvitimod with a total of 1,925 patients

Patients after treatment with benvitimod for 12 weeks achieved:
- Physician global assessment score of 0 or 1
- Psoriasis area and severity index (PASI) 75
- PASI 90
- Body surface area reduction

Significant benefits for patients who received benvitimod
- PP-NRS score
- >4-point decrease in PP-NRS score
- Dermatology Life Quality Index score

Significantly higher incidence of AEs was recorded in the benvitimod group but the risk was non-significant for serious AEs

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Safety and efficacy of current treatment approaches

JAK inhibitors[3]

Delgocitinib

- Three major randomised phase 3 trials of topical delgocitinib for AD
  - JapicCTI-173554
  - JapicCTI-173555
  - JapicCTI-184064
- AEs related to the drug were mostly mild

Ruxolitinib

- In 631 patients who were a part of Topical Ruxolitinib Evaluation in Atopic Dermatitis (TRuE-AD) 1 and 618 in TRuE-AD 2 trials
- Most common treatment-related AE was:
  - Burning sensation at the application site that was mainly associated with the vehicle (4.4%) rather than the drug
- No serious AEs

PDE4 inhibitors[3]

Crisaborole 2% ointment

- Local pain, burning, and stinging were the common AEs in two 28-day, randomised, double-blind, and vehicle-controlled trials (AD-301: NCT02118766, AD-302: NCT02118792)

Difamilast

- No serious AEs were reported in phase 3 study

Aryl hydrocarbon receptor agonists[3]

Tapinarof

- In a randomised, multicentre, phase 2b, double-blind, and vehicle-controlled study (NCT02564055)
  - 51% of patients reported TEAEs, varying from mild to moderate in intensity
  - Nasopharyngitis was a frequently reported TEAEs

Real-world data on the effectiveness of PSO treatment[15]

- Data from the Psoriasis Standardised Diagnosis and Treatment Center, Southeast China was analysed
- PASI 50/90 criteria were used to assess the treatment response
- Study participants
  - First-time patients with PSO diagnosis (n = 46)
  - Patients with previous PSO diagnosis (n = 361)
- Proportion of patients who achieved treatment response
  - First-time diagnosed patients: 76.1%
  - Patients with previously diagnosed PSO: 62.6%

'As needed' biologic therapy in PSO[16]

- Continuous use of biologics for treatment of PSO can elevate the risk of infections, drug AEs, and economic burden
- 'As needed' is an approach for the biologic therapy where the person takes medication at the first sign of PSO recurrence
- A multistakeholder mixed-methods study suggests that this approach can help reduce the treatment burden, facilitating patient-led ownership of care

Key messages

- Topical and systemic therapies have revolutionised the landscape of AD therapy, enhancing personalised decision-making based on patient characteristics, thereby making clinicians' lives easier
- Medications approved for adult PSO lack data and labelling to support their safe and effective use in paediatric patients with PSO
- Real-world study indicates unmet needs in PSO treatment and management in people with a history of PSO

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