



Advances in the treatment of severe atopic dermatitis

Information for
healthcare professionals

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Atopic dermatitis

Atopic dermatitis or atopic eczema is a very common skin condition that affects approximately 1 in 5 children and 1 in 10 adults in the UK.

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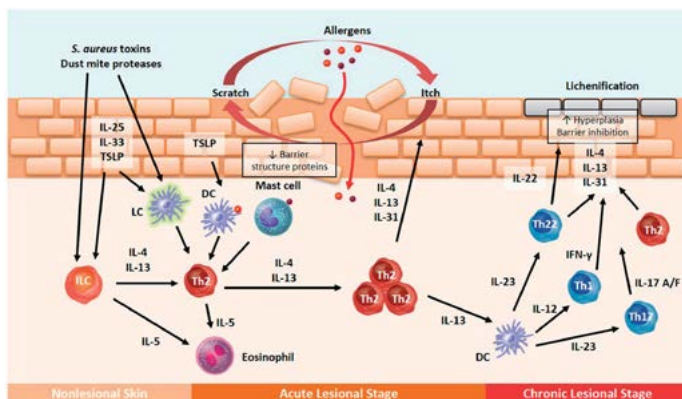
It is an inflammatory condition of the skin characterised by dry skin, intense itching, erythema (redness of the skin) and lichenification (thickening of the skin), and can have a significant impact on physical, psychological and social well-being and dramatically impair quality of life.

For the majority of individuals with atopic eczema, standard therapy with topical treatment will help alleviate symptoms however individuals whose eczema symptoms cannot be controlled using

standard topical therapy are often managed with systemic immunosuppressive medication such as cyclosporine or methotrexate, which can have debilitating side effects, therefore newer therapies such as monoclonal antibodies and JAK inhibitors could be life changing for these individuals.

Atopic dermatitis has a very complex pathophysiology, it is thought that a dysregulated TH2 immune response triggering production of inflammatory chemical mediators including histamine, eosinophils and cytokines IL4, IL13, TSLP, IL17, IL22, IL31, promote chronic inflammation in the skin, as well as itch and barrier impairment, and for some individuals there is a genetically determined filaggrin gene mutation causing a disrupted or faulty epidermal barrier, all leading to skin inflammation and allowing penetration of microbes, irritants and allergens into the dermis.

Immune response in eczema



Michael J. Cork, Simon G. Danby & Graham S. Ogg (2019): Atopic dermatitis epidemiology and unmet need in the United Kingdom, *Journal of Dermatological Treatment*, DOI: 10.1080/09546634.2019.1655137 To link to this article: <https://doi.org/10.1080/09546634.2019.1655137>

Biologic therapy

Biologics are designed to work by blocking or inhibiting specific chemical mediators or cytokines such as interleukins (IL) in the immune system from mounting an allergic response and causing inflammation. Biologic therapies have been designed to target specific interleukins (IL) depending on the type of allergic response and this is what makes the treatment effective at controlling the inflammatory process and reducing the potential for systemic side effects. In atopic eczema treatments have been designed to target cytokine messengers such as IL 4, IL 13, IL31 all of which have been found to be present in the inflammatory process. Dependant on what type of eczema your patient has will determine which IL (interleukin) to target and which treatment they will receive.

Treatment pathways

Biologic therapies are usually offered as a 5th line treatment option under specialist dermatology supervision (see NICE guidelines) for patients with moderate - severe atopic eczema where standard systemic therapies such as cyclosporine or methotrexate have failed to improve the symptoms or where systemic treatments are not suitable or contraindicated.

The use of biologic therapies is closely monitored by the dermatologist and will usually be continued if there is an improvement in symptom severity or psychosocial reporting and no serious side effects, however if there is no significance improvement after 16 weeks as per NICE guidelines then the biologic therapy will stop and different therapy will be sought.

Tools used to score improvement in eczema severity include;

- Eczema Area and Severity Index (EASI): www.easiscore.com
- Patient Orientated Eczema Measure (Poem): www.nottingham.ac.uk/research/groups/cebd/resources/poem.aspx
- SCORing Atopic Dermatitis (SCORAD): dermnetnz.org/topics/scorad

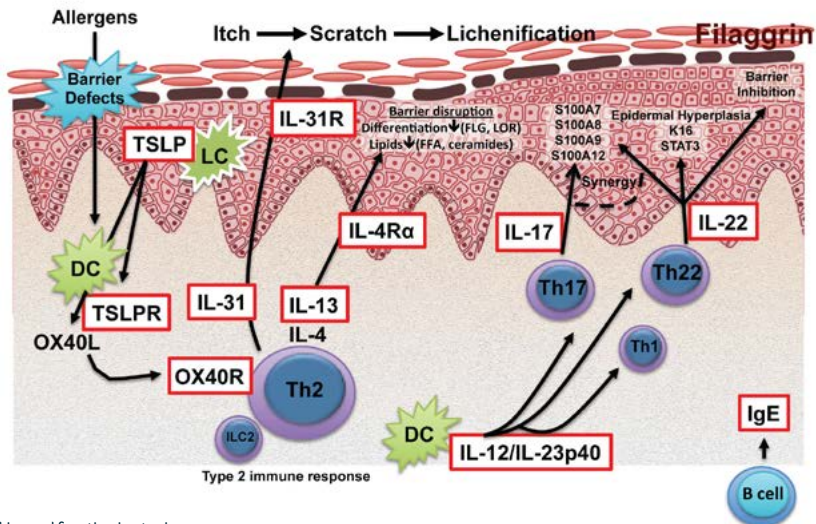
Monoclonal antibody therapy

Monoclonal antibody therapies work by blocking or inhibiting type 2 cytokine pathways and reducing the inflammatory process. Due to the complex pathophysiology of atopic eczema, monoclonal antibody therapies are designed to target various inflammatory pathways and block the effects of key cytokines or chemical messengers in the immune system.

Some key chemical messengers that are of interest in the development of therapies include Interleukins (IL4) (IL13) and (IL31), targeted as important inflammatory mediators in the development of atopic eczema.

Overexpression of IL4 induces skin inflammation and itch, IL13 has central role in inducing inflammation, itch and reducing skin barrier integrity and the IL31 receptor promotes itch and inflammation. Research has shown that targeting these key cytokines can not only improve symptoms and improve quality of life for individuals with atopic eczema, but has also been shown to have a therapeutic effect on other atopic disease co morbidities including atopic asthma.

Interleukins and function in atopic eczema



Interleukins and function in atopic eczema

Brunner, Guttman Yassaky, Leung (2017) The immunology of atopic dermatitis and its reversibility with broad-spectrum and targeted therapies. *Journal of Allergy & Clinical Immunology* Vol 139 (4)

Small molecule drugs or JAK inhibitors

JAK inhibitors (Janus Kinase Inhibitor) belong to the group of biologic medications commonly known as DMARDS (Disease Modifying Anti Rheumatic Drugs). JAK inhibitors work by inhibiting or closing off the inflammatory messengers that activate the symptoms of eczema. They do this by targeting the key messengers called cytokines in the immune system. Cytokines work to regulate the immune system and reduce inflammation, however in atopic eczema, some of these cytokines overproduce and this causes an increase in inflammation and itch. JAK inhibitors work by blocking these cytokines from sending the signal to the cells in the immune system to help reduce itch and inflammation.

A range of these medications for oral (tablet) and topical (cream) based formulations are currently being

investigated and going through rigorous testing for use in eczema (atopic dermatitis) to see if they can improve or control symptoms. It is important to note that any patient starting on biologics will need long term monitoring. Clinicians must be vigilant and record and report any changes in a person health status while they are taking the medication.

One JAK 1 inhibitor, has been approved for use in adults within the UK for severe atopic dermatitis and is an oral medication. There are other JAK inhibitors in the development phase (phase 111) both oral and topical that are not yet licensed. It is thought that oral JAK inhibitors may become approved for moderate to severe atopic dermatitis and topical JAK inhibitors may be licensed for mild, moderate or severe atopic dermatitis.

Presentations of eczema



Papules and nodules



Infected eczema



Localised erythema

Photo credit: <https://dftbskindeep.com>



Useful information:

Biologic therapy and eczema management

Vaccination and biologic therapies

It is important that patients receive the COVID-19 vaccine, annual flu vaccine and pneumococcal vaccine. The patient should be flagged on the GP system and their medical records updated to state they are on immunosuppressive medication.

What are the common side effects of biologic therapies?

As with all medication, there can be side effects. The most common side effects include a mild reaction around injection site (swelling, redness, itching and bruising), red eyes, conjunctivitis, eczema around the eyes, headache, sore throat and herpes.

What are the red flags or side effects that may require specialist care?

Infection – Due to the action of the biologic medication to suppress the immune system, there is an increased risk of infection especially herpes. It is recommended that patients reporting with symptoms of infection should have an immediate consultation.

Eye symptoms – For any new reported eye symptoms, contact the dermatology department for advice. Severe eye symptoms, including severe itch, watering, conjunctival redness, pain, photophobia or loss of vision, will require an urgent referral to ophthalmology.

Musculoskeletal symptoms – arthralgia and joint stiffness is rare, but if this occurs, advise the patient to contact their dermatology department and, if required, arrange a review with the rheumatology department.

Asthma – biologic therapy given for eczema can also have a beneficial effect on asthma and many patients find they can reduce or even cease taking their asthma medication whilst on the biologic therapy. You must note that, if the biologic therapy is stopped or reduced, there may be an impact on the patient's asthma control. The patient should be educated to be aware of this effect and an action plan agreed with their GP or respiratory team.

Pregnancy – The GP must inform the dermatology department for urgent review and follow up if the patient who is receiving biologic therapy or has recently stopped therapy within 12 weeks of becoming pregnant.

Severe allergic reactions including anaphylaxis are possible with biologic therapies, but very rare. If a severe allergic reaction occurs, advise your patient to dial 999 or immediately go to the nearest accident and emergency department.

Are topical treatments, including regular emollient use, still required when on biologic therapy?

Yes – biologic therapies have been designed to be taken alongside standard treatment and the continued use of topical treatment, especially emollient therapy, is recommended even when the skin is good. Research has shown that for up to 76% of individuals on biologic therapy, they have had a reduction in the severity of their symptoms and have been able to reduce the frequency of their regular medication.

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Call: 01322 619898

Webchat: allergyuk.org

Email: info@allergyuk.org



Planwell House • Lefa Business Park • Edgington Way • Sidcup • Kent • DA14 5BH
Tel: 01322 619898 • Fax: 01322 470330

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