Other systemic treatment

Alitretinoin

Mechanisms of action and efficacy

Alitretinoin is a retinoid binding both retinoic acid (RAR) and retinoic X (RXR) receptors, thus delivering anti-inflammatory and anti-proliferative effects. It is licensed in some European countries for the treatment of chronic hand eczema irrespectively of its pathogenesis.

There is one large, multicenter randomized, placebo controlled clinical trial involving 1032 patients with chronic hand eczema, about one third of which were probably atopic hand eczema patients.[1] Improvement of eczema was seen in 75% of the patients. The patient group suffering from atopic hand eczema was not analyzed separately, and extrapalmar symptoms have not been assessed in this trial.

Six patients with AE and prominent hand involvement were treated with alitretinoin for twelve weeks in an uncontrolled, open label trial.[2] Both, palmar and extrapalmar lesions improved during the trial, as shown by the modified Total Lesion Symptom Score (mTLSS) hand eczema score and the SCORAD.

Dosage: acute flare, short term, long term

According to the mode of action, alitretinoin is suitable for long-term treatment. An alitretinoin treatment course should be planned for 3 to 6 months.

The dosage of alitretinoin is 10-30 mg per day.

Safety

As alitretinoin is highly teratogenic, all females of childbearing potential must adhere to a strict birth control programme*.*

Screening and monitoring

Before and during therapy: liver enzymes (aspartate aminotransferase (ASAT), aspartate aminotransferase (ALAT), gamma-glutamyl transpeptidase (GGT)), cholesterol, triglycerides, basal thyroid stimulating hormone (TSH), free thyroxine (fT4) peripheral blood levels; pregnancy test in women with childbearing potential.

Combination with other treatments

Concomitantly to alitretinoin, topical therapy with corticosteroids, calcineurininhibitors and emollients can be applied.

Special considerations

A retrospective analysis of children treated with alitretinoin because of hand eczema and other diagnoses including two severe AE patients, revealed that the response to alitretinoin was moderate in one subject, whereas the other patient failed to improve even after extending treatment to up to 11 months.[3]

Alitretinoin may be a treatment option for patients with chronic hand eczema and concommittant AE as in-label use, whereas there is no good rationale for its use in patients without chronic hand eczema.

Treatments under investigation

OX40-Inhibitors

OX40 and its ligand (OX40L) are co-stimulatory molecules involved in T-cell activation and survival, playing a key role in sustaining chronic inflammation in AE. The OX40–OX40L pathway enhances the proliferation of Th2 and Th22 cells, which are central to AE pathogenesis. Targeting this pathway offers a novel therapeutic approach aimed at modulating the immune response more upstream than current IL-4/IL-13 inhibitors. Early-phase trials of OX40 or OX40L inhibitors have shown promise in reducing inflammation and pruritus in moderate-to-severe AE.[4, 5] Recent clinical investigations have evaluated several OX-40/OX-40L inhibitors - telazorlimab, rocatinlimab, and amlitelimab - in adults with moderate-to-severe AE. In a phase 2a trial, telazorlimab (GBR 830/ISB 830) induced EASI-50 in 77% of patients by day 71 (compared to ~38% with placebo), with 23% achieving IGA 0/1. The treatment was well tolerated, with headache, mild infection, and myalgia among the most common adverse events.[6, 7] In a larger phase 2b study (NCT03568162), telazorlimab 300 mg or 600 mg every 2 weeks led to significantly greater EASI score reductions (−54.4% to −59.0%) versus placebo (−34.2% to −41.8%) at week 16, with favourable safety profiles.[8] Similarly, rocatinlimab (AMG 451/KHK 4083) demonstrated efficacy, with early-phase data showing a ~74% mean reduction in EASI by day 155, and the phase 2b STREAM-AD trial confirmed sustained EASI-75 rates and transcriptomic reversal of Th2/Th1/Th17/Th22 pathway activation, lasting well beyond treatment cessation.[9, 10] Lastly, amlitelimab (SAR445229/KY1005), targeting OX-40L, achieved ~80% mean EASI reduction at week 16 in its phase 2a trial (low-dose arm) versus ~49% with placebo. IGA 0/1 responses reached 44% versus 8% in placebo, with the most common side effects being headache and upper respiratory infections.[11, 12]
These results underscore the potential of OX40–pathway blockade as a novel, upstream immunomodulatory strategy in AE.

None of the OX40-Inhibitors is currently (November 2025) licensed for the treatment of AE in any country.

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