Nemolizumab

Nemolizumab is currently not licensed for any indication worldwide. Therefore, we do not give a specific recommendation for the use in AE.

Mechanisms of action and efficacy

Nemolizumab is a humanized mAb targeting the IL-31 receptor alpha chain (IL-31RA), which was initially developed for the treatment of AE-related pruritus.

In a phase II, randomized, double-blind, placebo-controlled, 12-week trial, nemolizumab at monthly doses significantly improved pruritus.1

In a 2b study with nemolizumab 30mg dosing and TCS, there were significant improvements in signs and symptoms of AD - EASI scores, PP-NRS, sleep and DLQI score, which was confirmed in a post-hoc sub-analysis of the EASI ≥ 16 cohort.2,3

In a recently published 16-week, double-blind, phase III trial, Japanese patients with AE and moderate-to-severe pruritus received subcutaneous nemolizumab (60 mg) or placebo every 4 weeks until week 16, with concomitant topical agents.4 The primary end point was the mean percent change in the visual-analogue scale (VAS) score for pruritus from baseline to week 16. Secondary end points included the time course of change in the VAS score for pruritus up to week 4, EASI score, DLQI, Insomnia Severity Index, and safety. At week 16, the mean percent change in the VAS score was -42.8% in the nemolizumab group and -21.4% in the placebo group. The use of subcutaneous nemolizumab in addition to topical agents for atopic dermatitis resulted in a highly significant reduction in pruritus than placebo plus topical agents.

Dosage: acute flare, short term, long term

The first phase II study investigating nemolizumab published in 2017 investigated 0.1 mg/kg, 0.5 mg/kg, 2 mg/kg dosages administered every 4 weeks and 2 mg/kg dosage administered every 8 weeks. Results at 12 weeks found a significant, dose-dependent improvement in the primary outcome of pruritus for all groups that received nemolizumab every 4 weeks, as compared with placebo.5 In a two-part, phase II, randomized control trial published in 2018, Kabashima et al.6 compared three different nemolizumab dosages: 0.1 mg/kg, 0.5 mg/kg, 2 mg/kg administered every 4 weeks and 2 mg/kg administered every 8 weeks. All the parameters considered in the study showed an improvement and no evidence was found that the highest dosage was more effective than the lowest. Furthermore, the study showed that the positive outcomes obtained with Nemolizumab were maintained for up to 64 weeks.

In another 24-week, randomized, double-blind, multicenter study published in 2019 by Silverberg et al.2, three different nemolizumab dosages, 10 mg, 30 mg and 90 mg, were compared in an ethnically more diverse population. The drug was administered once every 4 weeks and nemolizumab 30 mg showed maximum dosage efficacy in improving EASI, IGA, and pruritus.

In the latest published study conducted in Japanese patients,4 the dosage tested was 60mg, administered every 4 weeks. At the reported dosage, nemolizumab showed a greater efficacy in reducing pruritus, compared to placebo plus topicals.
Safety

The most frequent adverse events related to the drug are reported to be injection-related reactions, musculoskeletal and connective tissue symptoms, upper respiratory tract infections, nasopharyngitis, peripheral oedema, and increased creatine phosphokinase.²

The authors conclude that longer and larger trials are necessary to determine whether nemolizumab has a durable effect and is safe for AE patients.²

Monitoring

No biochemical or instrumental exams are reported to be required for the monitoring of the therapy.

Combination with other treatments

According to the available study trials, the use of topical treatments such as emollients, corticosteroids and calcineurin inhibitors as a rescue therapy, in addition to nemolizumab, could have a synergistic effect in the treatment of AE and AE-related pruritus.
References