

## Nemolizumab

At the time of the voting process for this guideline update, nemolizumab was not licensed for any indication in the European Union. Therefore, there is currently no specific recommendation for the use in AE in this version of the guideline.

### 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. The drug is currently also approved for this treatment in Japan.

In two randomized, double-blind, placebo-controlled phase 3 trials (ARCADIA 1 and 2), a total of 1,728 adults and adolescents (aged  $\geq 12$  years) with moderate-to-severe AE and associated pruritus were enrolled. All participants had previously shown an inadequate response to TCS treatment. Patients received either 30 mg nemolizumab Q4W, with an initial loading dose of 60 mg, or placebo injections, alongside TCS and, in some cases, TCI. Randomization was conducted in a 2:1 ratio for nemolizumab versus placebo. At week 16, 44% (270/620) and 42% (220/522) of patients treated with nemolizumab achieved an EASI-75 response compared to 29% (93/321) and 30% (80/265) of patients receiving placebo. Similarly, the proportion of patients achieving IGA success (defined as an IGA score of 0 or 1 with a reduction of at least 2 points) was significantly higher in the nemolizumab groups than in the placebo groups. Significant benefits were also observed for secondary endpoints, with consistent improvements in pruritus and sleep disturbance.<sup>1</sup>

Patients who achieved a clinical response (IGA success or EASI-75) at week 16 were re-randomized (1:1:1) to receive nemolizumab 30 mg Q4W, nemolizumab 30 mg Q8W, or placebo for additional 32 weeks. During this period, additional topical anti-inflammatory therapy was also permitted. At week 48, a higher proportion of patients maintained IGA success in the nemolizumab Q4W (61.5%) and Q8W (60.4%) groups compared to the placebo group (49.7%). Similarly, EASI-75 response rates were higher in the nemolizumab Q4W (76.3%) and Q8W (75.7%) groups compared to placebo (63.9%).<sup>2</sup> **Dosage: acute flare, short term, long term**

Global phase III trials investigated the nemolizumab 30 mg Q4W dose administered up to week 16 with a loading dose of 60 mg at baseline and showed positive outcomes. After week 16, clinical responders did not show a clinical difference with the Q4W and Q8W maintenance regimen.<sup>1</sup>

### Safety

In the two mentioned phase 3 trials the frequency of adverse events was comparable between patients receiving nemolizumab and those given a placebo.<sup>1</sup>

The most common treatment-emergent adverse event was worsening of AE in 12% (75/616) participants in the nemolizumab group vs 11% (34/321) in the placebo group in ARCADIA 1; and 7% (37/519) vs 6% (15/263), respectively, in ARCADIA 2.

Asthma events occurred in both groups in both studies. However, it should be noted that more than 30% of all included patients reported pre-existing asthma.

In both studies, hypersensitivity reactions (urticaria) were noted. Non-serious and mild urticaria was reported in 1% and 2% patients receiving nemolizumab vs <1% patient receiving placebo in ARCADIA 1 and ARCADIA 2. Nemolizumab was not discontinued due to any of these events.<sup>1</sup>

### **Monitoring**

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

### **Combination with other treatments**

In phase 3 studies, nemolizumab was investigated with additional treatment with emollients, TCS or TCI therapy.

### **References**

- [1] Silverberg JI, Wollenberg A, Reich A, Thaçi D, Legat FJ, Papp KA, et al. Nemolizumab with concomitant topical therapy in adolescents and adults with moderate-to-severe atopic dermatitis (ARCADIA 1 and ARCADIA 2): results from two replicate, double-blind, randomised controlled phase 3 trials. *Lancet*. 2024;404; 445-460.
- [2] Silverberg JI, Wollenberg A, Legat FJ, Laquer VT, Armstrong AW, Herranz P, et al. 667- Maintenance of efficacy and safety with nemolizumab at week 48: results from two global phase 3 pivotal studies (ARCADIA-1 and ARCADIA-2) in patients with moderate-to-severe atopic dermatitis. *British Journal of Dermatology*. 2024;191; ljae266. 041.