Lebrikizumab

We **recommend** lebrikizumab in AE patients who are candidates for systemic treatment.	↑↑	**100%** Evidence and consensus based, see Evidence Report

lebrikizumab: in licence for ≥ 12 years of age (with bodyweight ≥40kg);
dosage: initially 500 mg s.c. day 1 and 15 followed by 250 mg s.c. Q2W up to week 16-24
once clinical response is achieved, the recommended maintenance dose is 250 mg every Q4W. From week 24 onwards, generally Q4W

Certainty of evidence: Network meta-analysis from 2024[1, 2]:

Short term (up to 16 weeks) vs placebo (NMA medications used in clinical practice)

⊕⊕⊕⊕ HIGH for mean difference **POEM** -6.2 (-7.4, -5.1)
⊕⊕⊕◯ MODERATE for mean difference **EASI** -8.5 (-10.4, -6.5); **DLQI** -4.7 (-6.4, -2.8)
⊕⊕◯◯ LOW for mean difference **peak pruritus NRS** -2.1 (-2.6, -1.7)

For lebrikizumab versus other drugs, see Evidence Report

Mechanisms of action and efficacy

Lebrikizumab is a high-affinity humanized IgG4 mAb that binds specifically to soluble interleukin 13 and selectively prevents formation of the IL-13Rα1/IL-4Rα heterodimer receptor signaling complex.

In two identically designed randomised, double-blind, placebo-controlled monotherapy phase 3 studies (ADvocate1 and ADvocate2), adolescents (aged 12 years and older) and adult AE patients received either lebrikizumab at a dose of 250 mg Q2W (loading dose of 500 mg at baseline and week 2) or placebo.[3] After 16 weeks, 43.1% (lebrikizumab arm) vs. 12.7% (placebo arm) in ADvocate1 and 33.2% vs. 10.8% in Advocate2 achieved the primary endpoint of IGA score of 0 or 1 with a reduction of at least 2 points.[3] Patients who responded to lebrikizumab at the end of the 16-week induction period were re-randomized 2:2:1 to receive lebrikizumab 250 mg Q2W, Q4W or placebo (lebrikizumab withdrawal) for 36 additional weeks. After 52 weeks, an IGA of 0 or 1 with a ≥ 2-point improvement was maintained by 71.2% and 76.9% of patients treated with lebrikizumab Q2W or Q4W, respectively. In the lebrikizumab withdrawal arm only 47.9% maintained their response.[4] In a further placebo-controlled phase 3 study, in which the effect of lebrikizumab was investigated together with topical corticosteroids, the drug also proved to be clearly superior to placebo.[5]

Dosage: acute flare, short term, long term

The recommended dosage is an induction therapy of 500 mg at week 0 and week 2, followed by 250 mg Q2W until week 16. In patients with an initial partial response, 250 mg Q2W can be continued until week 24. Once a clinical response is achieved, the recommended maintenance dose of lebrikizumab is 250 mg Q4W.From week 24 onwards, Q4W is mandatory according to the drug approval.

Safety

Stein Gold et al. investigated the safety of lebrikizumab by analyzing data from eight phase 2 and phase 3 studies. Overall, the frequency of adverse events was comparable between patients receiving

lebrikizumab and those given a placebo. Conjunctivitis and AE were the most frequently reported events, with AE reported more frequently in the placebo groups then in the Q2W groups (18.4% versus 6.0%) and conjunctivitis reported more frequently in lebrikizumab in the Q2W groups than in the placebo groups (6.5% versus 1.8%). Nasopharyngitis, headache, allergic conjunctivitis, dry eye, and allergic rhinitis were reported more frequently in the lebrikizumab group.[6]

Simpson et al. reported injection site reactions (1.3%), herpes infection (3.8%), eosinophilia (3.2%) with no associated clinical symptoms, and conjunctivitis (9.6%) as adverse events in patients treated with lebrikizumab.[7]

Notably, based on the currently available clinical trial data lebrikizumab appears to have lower rates of ocular complications than dupilumab. 'Real world' comparisons, for instance through national registers, are still awaited.

Screening and monitoring

The guideline committee considers that biochemical or instrumental investigations are not required for screening or treatment monitoring. This is consistent with the manufacturer's information.

Combination with other treatments

We recommend combining Lebrikizumab, as any systemic treatment, with emollients and, whenever needed, topical anti-inflammatory treatment in AE patients.

References

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