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Tralokinumab

Updated: January 23, 2023.

OVERVIEW

Introduction

Tralokinumab is a human monoclonal antibody to IL-13 which is used to treat atopic dermatitis. Tralokinumab is generally well tolerated and has not been linked to elevations in serum aminotransferase levels during therapy or to instances of clinically apparent liver injury.

Background

Tralokinumab (tral' oh kin' ue mab) is a human monoclonal IgG4 antibody directed against IL-13, a major mediator of chronic inflammation and which is over-expressed and a dominant cytokine in lesional skin cells in atopic dermatitis. Tralokinumab has been assessed in several chronic inflammatory diseases, including asthma, chronic bronchitis, idiopathic pulmonary fibrosis, and ulcerative colitis, and while demonstrating little positive benefit in these conditions, was found to be well tolerated with adverse event rates similar to those with placebo. In contrast, preregistration randomized, placebo controlled trials of tralokinumab in patient with moderate-to-severe atopic dermatitis demonstrated significant response rates with tralokinumab alone as well as in combination with topical corticosteroids. Clinical responses were generally maintained with long term therapy. Tralokinumab was approved in the United States in 2021 for adults with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies. Tralokinumab is available in single dose pre-filled syringes of 150 mg in 1 mL under the brand name Adbry. The recommended regimen is an initial dose of 600 mg (4 syringes) subcutaneously followed by 300 mg (two syringes) every other week, which can be extended to every 4 weeks with long term use. Common side effects include mild local injection reactions, nasopharyngitis, fatigue, headache, arthralgia, skin rashes, conjunctivitis and eosinophilia. Uncommon, potentially severe adverse reactions include hypersensitivity reactions, keratitis, parasitic infections and risk of infection with viruses found in live attenuated vaccines.

Hepatotoxicity

Mild-to-moderate serum aminotransferase elevations arise in less than 1% of patients treated with tralokinumab, and such abnormalities are generally transient, asymptomatic, and rarely necessitate drug discontinuation. In most trials, serum ALT elevations occurred at similar rates in placebo recipients. In large, preregistration trials there were no instances of clinically apparent liver injury or severe hepatic adverse events attributed to tralokinumab. Since its approval and more general use, there have been no reports of clinically significant liver injury attributed to tralokinumab. Whether reactivation of hepatitis B might occur with tralokinumab therapy has yet to be reported. It has been associated with reactivation of herpes zoster.

Likelihood score: E (unlikely cause of clinically apparent acute liver injury).

Mechanism of Injury

The possible mechanisms of liver injury due to tralokinumab are unclear. Monoclonal antibodies and immunoglobulins are generally taken up and metabolized intracellularly to short peptides and amino acids. There is no evidence to suggest that inhibition of IL-13 signaling would trigger liver injury or autoimmune liver conditions.

Drug Class: Dermatologic Agents, Monoclonal Antibodies

Other Drugs for Atopic Dermatitis: Dupilumab

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Tralokinumab – Adbry®

DRUG CLASS

Dermatologic Agents, Atopic Dermatitis

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NO.	MOLECULAR FORMULA	STRUCTURE
Tralokinumab	1044515-88-9	Monoclonal Antibody	Not Available

ANNOTATED BIBLIOGRAPHY

References updated: 23 January 2023

FDA. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2022/761180Orig1s000IntegratedR.pdf

(Multidisciplinary FDA review of tralokinumab in support of its approval for use in atopic dermatitis mentions that two patients in trials of tralokinumab for atopic dermatitis developed elevations of ALT and jaundice, but neither was considered treatment related and liver enzymes overall remained within the normal range).

Danese S, Rudziński J, Brandt W, Dupas JL, Peyrin-Biroulet L, Bouhnik Y, Kleczkowski D, et al. Tralokinumab for moderate-to-severe UC: a randomised, double-blind, placebo-controlled, phase IIa study. Gut. 2015;64:243–9. PubMed PMID: 25304132.

(Among 111 patients with ulcerative colitis treated with tralokinumab or placebo subcutaneously every 2 weeks for 12 weeks, clinical response rates were similar [38% vs 33%] as were adverse event rates [75% vs 71%] and most severe adverse events were due to ulcerative colitis; no mention of ALT elevations or hepatotoxicity).

Russell RJ, Chachi L, FitzGerald JM, Backer V, Olivenstein R, Titlestad IL, Ulrik CS, et al; MESOS study investigators. Effect of tralokinumab, an interleukin-13 neutralising monoclonal antibody, on eosinophilic airway inflammation in uncontrolled moderate-to-severe asthma (MESOS): a multicentre, double-blind, randomised, placebo-controlled phase 2 trial. Lancet Respir Med. 2018;6:499–510. PubMed PMID: 29793857.

(Among 79 adults with moderate-to-severe asthma treated with tralokinumab [300 mg] or placebo subcutaneously every 2 week for 12 weeks, there were no differences in response rates between the two groups and adverse event rates were similar [85% vs 80%]).

Panettieri RA Jr, Sjöbring U, Péterffy A, Wessman P, Bowen K, Piper E, Colice G, Brightling CE. Tralokinumab for severe, uncontrolled asthma (STRATOS 1 and STRATOS 2): two randomised, double-blind, placebo-controlled, phase 3 clinical trials. Lancet Respir Med. 2018;6:511–525. PubMed PMID: 29792288.

(Among more than 2000 patients with severe, uncontrolled asthma treated with tralokinumab [300 mg] or placebo subcutaneously every 2 or 4 weeks for 52 weeks in two controlled trials, there were no differences in the annualized rates of asthma exacerbations between treatment groups and both total and severe adverse event rates were similar in all groups, although discontinuations for adverse events were more frequent with tralokinumab; no mention of ALT elevations or hepatotoxicity).

Silverberg JI, Toth D, Bieber T, Alexis AF, Elewski BE, Pink AE, Hijnen D, et al. ECZTRA 3 study investigators. Tralokinumab plus topical corticosteroids for the treatment of moderate-to-severe atopic dermatitis: results from the double-blind, randomized, multicentre, placebo-controlled phase III ECZTRA 3 trial. Br J Dermatol. 2021;184:450–463. PubMed PMID: 33000503.

(Among 380 adults with moderate-to-severe atopic dermatitis treated with as needed topical corticosteroids and either tralokinumab [300 mg] or placebo subcutaneously every 2 weeks for 16 weeks, with subsequent re-randomization and continuation for another 16 weeks, clinical response rates were higher with tralokinumab and increased with duration of therapy, while overall and severe adverse event rates were similar in both groups [71% vs 67%] and there were no noteworthy differences in laboratory values except for increases in eosinophils during early therapy with tralokinumab).

Wollenberg A, Blauvelt A, Guttman-Yassky E, Worm M, Lynde C, Lacour JP, Spelman L, et al. ECZTRA 1 and ECZTRA 2 study investigators. Tralokinumab for moderate-to-severe atopic dermatitis: results from two 52-week, randomized, double-blind, multicentre, placebo-controlled phase III trials (ECZTRA 1 and ECZTRA 2). Br J Dermatol. 2021;184:437–449. PubMed PMID: 33000465.

(Among 1596 adults with moderate-to-severe atopic dermatitis treated with tralokinumab [300 mg, after a loading dose of 600 mg] or placebo every two weeks for 16 weeks with re-randomization to 52 weeks in two controlled trials, clinical response rates at 16 weeks were higher with tralokinumab [16% and 22%] than placebo [7% and 11%], while total and severe adverse event rates were similar; no mention of ALT elevations or hepatotoxicity).

Duggan S. Tralokinumab: first approval. Drugs. 2021;81:1657–1663. PubMed PMID: 34406631.

(Review of the mechanism of action, history of development, pharmacology, clinical efficacy and safety of tralokinumab shortly after its approval for use in atopic dermatitis in the US mentions that total and severe adverse events were similar in tralokinumab- and placebo-treated groups and that most drug related adverse events were mild and transient including conjunctivity [5.4%], eosinophilia [1.3%] and injection site reactions [7.2%]; no mention of hepatotoxicity or ALT elevations).

Blauvelt A, Langley RG, Lacour JP, Toth D, Laquer V, Beissert S, Wollenberg A, et al. Long-term 2-year safety and efficacy of tralokinumab in adults with moderate-to-severe atopic dermatitis: Interim analysis of the ECZTEND open-label extension trial. J Am Acad Dermatol. 2022;87:815–824. PubMed PMID: 35863467.

(Among 345 patients with moderate-to-severe atopic dermatitis who had participated in controlled trials of tralokinumab and then continued in extension studies for at least 2 years, no new safety signals were seen; no mention of ALT elevations or hepatoxicity).

Simpson EL, Merola JF, Silverberg JI, Reich K, Warren RB, Staumont-Sallé D, Girolomoni G, et al. Safety of tralokinumab in adult patients with moderate-to-severe atopic dermatitis: pooled analysis of five randomized, double-blind, placebo-controlled phase II and phase III trials. Br J Dermatol. 2022;187(6):888–899. PubMed PMID: 36082590.

(In a pooled analysis of 2285 patients with atopic dermatitis in 5 randomized placebo-controlled trials of tralokinumab, adverse event rates were similar with the two groups [66% vs 67%], as were severe adverse events [2.1% vs 2.8%], and specific symptoms more frequent with tralokinumab included upper respiratory infections [16% vs 12%], conjunctivitis [5.4% vs 1.9%], injection site reactions [3.5% vs 0.3%], eosinophilia [22% vs 9%], but not ALT elevations above 3 times ULN [0.5% vs 0.6%]).