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NLM Citation: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Omalizumab. [Updated 2020 Dec 28].
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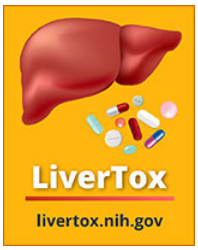

Omalizumab

Updated: December 28, 2020.

OVERVIEW

Introduction

Omalizumab is a monoclonal antibody to human immunoglobulin E (IgE), which leads to a decrease in IgE binding to mast cells and basophils and a reduction in allergic symptoms of asthma and seasonal rhinitis. Omalizumab therapy has not been associated with serum enzyme elevations during therapy and has yet to be implicated in cases of clinically apparent drug induced liver injury with jaundice.

Background

Omalizumab (oh" ma liz' ue mab) is a recombinant, human monoclonal antibody to IgE which binds avidly to circulating immunoglobulin E, preventing its attachment to high affinity receptors on mast cells and basophils. This receptor inhibition prevents the release of histamine and other mediators of the allergic immune response, reducing airway inflammation and spasm and alleviating symptoms of asthma and allergic rhinitis. Therapy with omalizumab has been shown to reduce the requirement for inhaled corticosteroids and lower the frequency of exacerbations of asthma and to decrease the severity and symptoms of chronic urticaria of unknown cause. Omalizumab was approved for use in the United States in 2003 for therapy of patients with severe and persistent asthma despite corticosteroid inhalation therapy. The indications were extended in 2014 to include chronic idiopathic urticaria and in later to include nasal polyps. Omalizumab has been evaluated in patients with seasonal rhinitis, but has yet to be approved for that use. Omalizumab is available in single use vials of 150 mg under the brand name Xolair. The recommended dose is 150 to 300 mg intravenously every 4 weeks or 225 to 375 mg every 2 weeks based upon body weight and IgE levels. Common side effects include injection site reactions, rash, diarrhea, nausea and vomiting, dizziness, fatigue and epistaxis. Rarely, omalizumab can cause serious acute anaphylaxis or anaphylactoid reactions (~0.1%) and should be given under close medical supervision.

Hepatotoxicity

In large clinical trials, omalizumab was not associated with changes in serum aminotransferase levels during therapy, and rates of most adverse reactions were similar in patients who received omalizumab or placebo. There have been no published reports of clinically apparent acute liver injury attributed to omalizumab therapy. Thus, liver injury from omalizumab must be rare, if it occurs at all.

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

Mechanism of Injury

Omalizumab is a human monoclonal antibody and is unlikely to be inherently hepatotoxic. While most recombinant proteins are metabolized by the liver, the metabolism leads largely to small peptides and amino acids which may be reused to synthesize proteins and are unlikely to be toxic or immunogenic. Omalizumab lowers serum levels of IgE, which seems to have no adverse effects on the liver and does not result in significant immunosuppression.

Drug Class: Antiasthmatic Agents, Monoclonal Antibodies

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Omalizumab – Xolair®

DRUG CLASS

Antiasthmatic Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NO.	MOLECULAR FORMULA	STRUCTURE
Omalizumab	242138-07-4	Monoclonal Antibody	Not Available

ANNOTATED BIBLIOGRAPHY

References updated: 20 December 2028

Zimmerman HJ. Drugs used to treat rheumatic and musculospastic disease. In, Zimmerman HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999, pp. 517-54.

(Expert review of hepatotoxicity published in 1999, well before the availability of most monoclonal antibody therapies).

Reuben A. Hepatotoxicity of immunosuppressive drugs. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2011, pp. 569-91.

(Review of hepatotoxicity of immunosuppressive agents; "the biological immuno-suppressants are largely free from hepatotoxicity, with the exception of the TNF alpha antagonists"; omalizumab is not specifically mentioned).

Barnes PJ. Pulmonary pharmacology. In, Brunton LL, Hilal-Dandan R, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 13th ed. New York: McGraw-Hill, 2018, pp. 727-48.

(Textbook of pharmacology and therapeutics).

Milgrom H, Fick RB Jr, Su JQ, Reimann JD, Bush RK, Watrous ML, Metzger WJ. Treatment of allergic asthma with monoclonal anti-IgE antibody. rhuMAb-E25 Study Group. N Engl J Med. 1999;341:1966–73. PubMed PMID: 10607813.

(In a controlled trial of omalizumab vs placebo for 20 weeks in 317 patients with asthma, side effects were similar between the two groups; no mention of ALT elevations or hepatotoxicity).

Casale TB, Condemi J, LaForce C, Nayak A, Rowe M, Watrous M, McAlary M, et al; Omalizumab Seasonal Allergic Rhinitis Trial Group. Effect of omalizumab on symptoms of seasonal allergic rhinitis: a randomized controlled trial. JAMA. 2001;286:2956–67. PubMed PMID: 11743836.

(A controlled trial of 3 doses of omalizumab versus placebo in 536 patients with allergic rhinitis reported no difference in adverse events between omalizumab and placebo therapy, and "there were no clinically significant alterations in laboratory values in either group").

Milgrom H, Berger W, Nayak A, Gupta N, Pollard S, McAlary M, Taylor AF, et al. Treatment of childhood asthma with anti-immunoglobulin E antibody(omalizumab). Pediatrics. 2001;108:E36. PubMed PMID: 11483846.

(Controlled trial of omalizumab versus placebo in 536 patients with asthma for 4 months found similar rates of adverse events in the two groups).

Berger W, Gupta N, McAlary M, Fowler-Taylor A. Evaluation of long-term safety of the anti-IgE antibody, omalizumab, in children with allergic asthma. Ann Allergy Asthma Immunol. 2003;91:182–8. PubMed PMID: 12952113.

(Among 225 children with asthma treated with omalizumab for up to 52 weeks, "There were no clinically significant changes... in laboratory safety tests").

Omalizumab (Xolair): an anti-IgE antibody for asthma. Med Lett Drugs Ther. 2003;45(1163):67–8. PubMed PMID: 12915804.

(Concise review of the efficacy and safety of omalizumab shortly after its approval for use in asthma in the US; no mention of ALT elevations or hepatotoxicity).

Ruffin CG, Busch BE. Omalizumab: a recombinant humanized anti-IgE antibody for allergic asthma. Am J Health Syst Pharm. 2004;61:1449–59. PubMed PMID: 15332692.

(Overview of the chemistry, mechanisms of action, pharmacology, efficacy and safety of omalizumab as therapy of asthma states that the rate of common adverse effects is similar between omalizumab and placebo treated patients; no mention of ALT elevations or hepatotoxicity).

Strunk RC, Bloomberg GR. Omalizumab for asthma. N Engl J Med. 2006;354:2689–95. PubMed PMID: 16790701.

(Review of the mechanism of action of omalizumab in asthma and studies of its efficacy and safety; no mention of ALT elevations or hepatotoxicity).

Antonicelli L, Stagnozzi G, Giuliodoro S, Abbruzzetti A, Massaccesi C. The safety of omalizumab therapy in a patient with severe persistent allergic asthma and hepatitis C. Ann Allergy Asthma Immunol. 2009;103:269–70. PubMed PMID: 19788028.

(Analysis of results from a single patient with chronic hepatitis C and severe asthma who received omalizumab for 19 months with a beneficial response and no change in serum ALT or HCV RNA levels).

Corren J, Casale TB, Lanier B, Buhl R, Holgate S, Jimenez P. Safety and tolerability of omalizumab. Clin Exp Allergy. 2009;39:788–97. PubMed PMID: 19302249.

(Review of the safety of omalizumab in 7500 patients controlled studies in asthma, allergic rhinitis and related conditions reported that overall and serious adverse event rates were similar between omalizumab and placebo groups, and that "There were no between-treatment-group differences ≥2% in the frequency of shifts from normal to abnormal in liver function tests").

Hanania NA, Alpan O, Hamilos DL, Condemi JJ, Reyes-Rivera I, Zhu J, Rosen KE, et al. Omalizumab in severe allergic asthma inadequately controlled with standard therapy: a randomized trial. Ann Intern Med. 2011;154:573–82. PubMed PMID: 21536936.

(Controlled trial of omalizumab versus placebo for 48 weeks in 850 patients with asthma found similar rates of serious adverse events and stated that "no clinically relevant abnormality of laboratory tests was observed").

Maurer M, Rosén K, Hsieh HJ, Saini S, Grattan C, Gimenéz-Arnau A, Agarwal S, et al. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. N Engl J Med. 2013;368:924–35. PubMed PMID: 23432142.

(Controlled trial of 3 doses of omalizumab versus placebo for 16 weeks in 323 patients with chronic urticaria stated that "the frequency of adverse events were similar across groups"; ALT elevations and hepatotoxicity were not mentioned).

Drugs for asthma and COPD. Treat Guidel Med Lett. 2013;11(132):75–86. PubMed PMID: 23896773.

(Concise summary of guidelines for therapy of asthma mentions that omalizumab is approved for use in severe, persistent asthma; no mention of ALT elevations or hepatotoxicity).

Tsabouri S, Tseretopoulou X, Priftis K, Ntzani EE. Omalizumab for the treatment of inadequately controlled allergic rhinitis: a systematic review and meta-analysis of randomized clinical trials. J Allergy Clin Immunol Pract. 2014;2:332–40.e1. PubMed PMID: 24811026.

(Systematic review of 11 controlled trials of omalizumab in 2870 patients with allergic rhinitis found no difference in rates of any adverse event between omalizumab and placebo; no specific discussion of ALT elevations or clinically apparent liver injury).

Chalasani N, Bonkovsky HL, Fontana R, Lee W, Stolz A, Talwalkar J, Reddy KR, et al; United States Drug Induced Liver Injury Network. Features and outcomes of 899 patients with drug-induced liver injury: The DILIN Prospective Study. Gastroenterology. 2015;148:1340–52.e7. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury enrolled in a US prospective study between 2004 and 2013, the only antiasthma drug implicated was montelukast [4 cases: 0.5%]).

Drugs for asthma. Med Lett Drugs Ther. 2017;59(1528):139–46. PubMed PMID: 28880849.

(Concise review of medications used for asthma including omalizumab side effects of which include injection site reactions, bruising and hypersensitivity reactions include anaphylaxis which can be life-threatening, for which reason it should be administered in a health care setting by medical staff training in treating anaphylaxis emergencies).

Chicharro P, Rodríguez-Jiménez P, de Argila D. Efficacy and safety of omalizumab in a patient with chronic spontaneous urticaria and active hepatitis B virus infection. Actas Dermosifiliogr. 2017;108:383–4. PubMed PMID: 27914623.

(56 year old woman with chronic urticaria and HBsAg in serum with HBV DNA 20,000 IU/mL but normal serum enzymes was treated with omalizumab, with rapid improvement in urticaria and no worsening of liver tests, HBV DNA falling to 627 IU/mL).

Menzella F, Galeone C, Formisano D, Castagnetti C, Ruggiero P, Simonazzi A, Zucchi L. Real-life efficacy of omalizumab after 9 years of follow-up. Allergy Asthma Immunol Res. 2017;9:368–72. PubMed PMID: 28497924.

(Among 8 adult patients with severe asthma with inadequate response to conventional therapy who were treated with omalizumab for 9 years, all had a sustained improvement in pulmonary function tests, decreased need for conventional medications and improved quality of life and there were "no changes in liver function parameters").

Di Bona D, Fiorino I, Taurino M, Frisenda F, Minenna E, Pasculli C, Kourtis G, et al. Long-term "real-life" safety of omalizumab in patients with severe uncontrolled asthma: A nine-year study. Respir Med. 2017;130:55–60. PubMed PMID: 29206634.

(Among 91 patients with severe persistent asthma treated with omalizumab for up to 9 years [mean 3.8 years], side effects included arthralgias, myalgias, fatigue, recurrent herpes labialis and urticaria, only 6 patients stopping therapy because of side effects; no mention of ALT elevations or hepatotoxicity).

Bhutani M, Yang WH, Hébert J, de Takacsy F, Stril JL. The real world effect of omalizumab add on therapy for patients with moderate to severe allergic asthma: The ASTERIX Observational study. PLoS One. 2017;12:e0183869. PubMed PMID: 28859150.

(Among 99 patients with severe persistent asthma treated with omalizumab for 52 weeks, asthma symptoms improved and 56 remained exacerbation free while adverse effects were usually mild, and of 9 severe adverse events only one was judged to be drug related [dizziness leading to discontinuation] and there were no reported liver related events).

Baan EJ, de Smet VA, Hoeve CE, Pacurariu AC, Sturkenboom MCJM, de Jongste JC, Janssens HM, et al. Exploratory study of signals for asthma drugs in children, using the eudraVigilance database of spontaneous reports. Drug Saf. 2020;43:7–16. PubMed PMID: 31617080.

(Review of the European drug adverse event vigilance database from 2011 to 2017 identified 21,364 reports in children and 172,035 for adults related to drugs for asthma, most commonly montelukast [n=2210], salbutamol [947] and omalizumab [690], some of which were considered new and not previously described; no discussion of liver related adverse events).

Gevaert P, Omachi TA, Corren J, Mullol J, Han J, Lee SE, Kaufman D, et al. Efficacy and safety of omalizumab in nasal polyposis: 2 randomized phase 3 trials. J Allergy Clin Immunol. 2020;146:595–605. PubMed PMID: 32524991.

(Among 265 patients with rhinosinusitis and nasal polyps enrolled in two randomized placebo controlled trials of omalizumab or placebo infusions every 4 weeks for 24 weeks, symptoms of nasal congestion and polyps improved with omalizumab therapy but not with placebo, while adverse event rates were similar in the two groups and there were no liver related severe adverse events; no mention of ALT elevations or hepatotoxicity).

Dekkers C, Alizadeh Aghdam M, Graaf M, Knulst AC, Meijer Y, van den Reek JMPA, Stadermann MB, Röckmann H. Safety and effectiveness of omalizumab for the treatment of chronic urticaria in pediatric patients. Pediatr Allergy Immunol. 2020 Dec 11. Epub ahead of print. PubMed PMID: 33305439.

(Among 38 children with chronic urticaria treated with omalizumab for up to two years, a clinical response was achieved in 76%, while only 12 children [32%] had mostly mild side effects, including headache, fatigue, injection site reactions, upper respiratory symptoms, arthralgias, hair loss and loss of concentration [which accounted for the only adverse event related discontinuation]; no mention of ALT elevations or hepatotoxicity).

Drugs for asthma. Med Lett Drugs Ther. 2020;62(1563):193–9. PubMed PMID: 33446622.

(Concise review of medications used for asthma including monoclonal antibodies to IgE, IL5, and the IL5 and IL4 receptors, which are used largely for eosinophilic asthma that has not responded adequately to conventional medications; mentions that zileuton and zafirlukast have been reported to cause life-threatening hepatic injury and that monitoring of liver tests during therapy is recommended whereas discussions of the other anti-asthma medications do not mention ALT elevations or hepatotoxicity).