U.S. National Library of Medicine
National Center for Biotechnology Information

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-. Secukinumab. [Updated 2015 Aug 20].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Secukinumab

Updated: August 20, 2015.

OVERVIEW

Introduction

Secukinumab is a human monoclonal antibody to interleukin-17A which acts as an immunosuppressant agent and is used to treat moderate to severe plaque psoriasis. Secukinumab has not been linked to serum enzyme elevations during therapy or to instances of idiosyncratic acute liver injury.

Background

Secukinumab (sek" ue kin' ue mab) is a recombinant, human IgG1 monoclonal antibody to interleukin (IL)-17A, a cytokine involved in the release of proinflammatory mediators. The binding of the monoclonal antibody blocks the interaction of IL-17A with its receptor and thus decreases immune and inflammatory pathways. Secukinumab is considered an immunomodulatory agent and has been evaluated in several immune mediated diseases. In large clinical trials in severe plaque psoriasis, secukinumab was shown to be beneficial and was subsequently approved for this use in the United States in 2015. Secukinumab is available in single use vials, syringes and pens of 150 mg under the brand name Cosentyx. The typical dose is two 150 mg subcutaneous injections at weeks 0, 1, 2, 3 and 4 followed by every 4 weeks. Side effects are not common, but can include upper respiratory symptoms, nausea and diarrhea. Rare, but potentially severe adverse reactions include severe infections, reactivation of tuberculosis, exacerbation of Crohn disease and immediate hypersensitivity reactions.

Hepatotoxicity

In large premarketing clinical trials of secukinumab in more than 3000 patients with psoriasis, serum enzyme elevations during therapy were no more common than with placebo and there were no instances of clinically apparent liver injury attributed to its use. Since its approval there have been no reports of liver injury attributed to secukinumab therapy and no cases of reactivation of hepatitis B or autoimmune hepatitis, two possible hepatic complications of immunomodulatory monoclonal antibody therapy.

Mechanism of Injury

The mechanism by which secukinumab might cause liver injury is unknown. Secukinumab is a monoclonal antibody and, like other proteins, is metabolized into amino acids and is unlikely to have intrinsic toxicity. Because of its immunomodulatory activity, secukinumab might induce an autoimmune reaction against hepatocytes, but this has yet to be shown.

Outcome and Management

The hepatotoxicity of secukinumab has not been shown, but its mechanism of action suggests that it might result in some instances of autoimmune hepatitis and possibly reactivation of hepatitis B, which might call for therapy with agents active against HBV.

Other immunomodulatory biologic agents used to treat severe psoriasis include adalimumab, efalizumab, etanercept, golimumab, infliximab and ustekinumab.

Drug Class: Dermatologic Agents, Psoriasis Agents; Monoclonal Antibodies

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Secukinumab – Cosentyx®

DRUG CLASS

Dermatologic Agents, Psoriasis Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NO.	MOLECULAR FORMULA	STRUCTURE
Secukinumab	1229022-83-6	Monoclonal Antibody	Not Available

ANNOTATED BIBLIOGRAPHY

References updated: 20 August 2015

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; mentions rituximab and problems of reactivation of hepatitis B, but also states that "the biological immunosuppressants are largely free from hepatotoxicity, with the exception of the TNF alpha antagonists"; secukinumab not specifically mentioned).

Krensky AM, Vincenti F, Bennett WM. Immunomodulators. In, Brunton LL, Lazo JS, Parker KL, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 11th ed. New York: McGraw-Hill, 2006, pp. 1405-88.

(Textbook of pharmacology and therapeutics).

Efalizumab (Raptiva) for treatment of psoriasis. Med Lett Drugs Ther 2003; 45 (1171): 97-8. PubMed PMID: 14657802.

(Concise summary of efficacy, safety and costs of efalizumab shortly after its approval for use in psoriasis in the US; no mention of ALT elevations or hepatotoxicity).

Kaiser T, Moessner J, Patel K, McHutchison JG, Tillmann HL. Life threatening liver disease during treatment with monoclonal antibodies. BMJ 2009; 338: b508.

(66 year old man with psoriasis was treated with efalizumab [anti-CD11a] and then adalimumab [anti-TNF], and 11 days later developed jaundice and severe hepatitis [bilirubin 9.1 rising to 52 mg/dL, ALT 549 U/L, Alk P 131 U/L], with HBsAg being detected and slow but eventual recovery).

Aithal GP. Hepatotoxicity related to antirheumatic drugs. Nat Rev Rheumatol 2011; 7: 139-50. PubMed PMID: 21263458.

(Analysis of spontaneous adverse event reporting of progressive PMLE in the US between 2004-2010 identified 635 cases, with higher than expected number of cases from several immunosuppressive monoclonal antibodies including efalizumab [n=12], rituximab [124] and natalizumab [123]).

Papp KA, Langley RG, Sigurgeirsson B, Abe M, Baker DR, Konno P, Haemmerle S, et al. Efficacy and safety of secukinumab in the treatment of moderate-to-severe plaque psoriasis: a randomized, double-blind, placebo-controlled phase II dose-ranging study. Br J Dermatol 2013; 168: 412-21. PubMed PMID: 23106107.

(Among 125 patients with plaque psoriasis treated with one of four doses of secukinumab or placebo for 12 weeks, 1 patient was withdrawn from therapy after 9 days because of exacerbation of liver test abnormalities which were present at baseline, but few details were provided).

Rich P, Sigurgeirsson B, Thaci D, Ortonne JP, Paul C, Schopf RE, Morita A, et al. Secukinumab induction and maintenance therapy in moderate-to-severe plaque psoriasis: a randomized, double-blind, placebo-controlled, phase II regimen-finding study. Br J Dermatol 2013; 168: 402-11. PubMed PMID: 23362969.

(Among 404 adult patients with plaque psoriasis treated with one of 3 dose regimens of secukinumab or placebo, common side effects were nasopharyngitis, upper respiratory infections and diarrhea; and there were "no significant shifts in clinical chemistry… parameters").

Baeten D, Baraliakos X, Braun J, Sieper J, Emery P, van der Heijde D, McInnes I, et al. Anti-interleukin-17A monoclonal antibody secukinumab in treatment of ankylosing spondylitis: a randomised, double-blind, placebo-controlled trial. Lancet 2013; 382(9906): 1705-13. PubMed PMID: 24035250.

(Among 30 patients with ankylosing spondylitis treated with secukinumab or placebo, side effects included nasopharyngitis, respiratory infections and diarrhea; no mention of ALT elevations or hepatotoxicity).

McInnes IB, Sieper J, Braun J, Emery P, van der Heijde D, Isaacs JD, Dahmen G, et al. Efficacy and safety of secukinumab, a fully human anti-interleukin-17A monoclonal antibody, in patients with moderate-to-severe psoriatic arthritis: a 24-week, randomised, double-blind, placebo-controlled, phase II proof-of-concept trial. Ann Rheum Dis 2014; 73: 349-56. PubMed PMID: 23361084.

(Among 42 patients with psoriatic arthritis treated with 2 injections of secukinumab or placebo at 3 week intervals, side effects included headache, nausea, fatigue and dizziness; one patient had single, transient and mild ALT elevation 21 weeks after the last dose of secukinumab).

Genovese MC, Durez P, Richards HB, Supronik J, Dokoupilova E, Aelion JA, Lee SH, et al. One-year efficacy and safety results of secukinumab in patients with rheumatoid arthritis: phase II, dose-finding, double-blind, randomized, placebo-controlled study. J Rheumatol 2014; 41: 414-21. PubMed PMID: 24429175.

(Among 237 patients with rheumatoid arthritis treated with secukinumab or placebo for 20 weeks followed by open label therapy for up to 60 weeks, adverse events were mostly mild-to-moderate, 32% of patients had infections, and there were "no notable elevations in liver enzymes or total bilirubin").

Gisondi P, Dalle Vedove C, Girolomoni G. Efficacy and safety of secukinumab in chronic plaque psoriasis and psoriatic arthritis therapy. Dermatol Ther (Heidelb) 2014; 4: 1-9. PubMed PMID: 24452484.

(Review of the efficacy and safety of secukinumab in severe psoriasis mentions that the major adverse events of concern are infections, but that these are often mild and self-limited; no mention of ALT elevations or hepatotoxicity).

Langley RG, Elewski BE, Lebwohl M, Reich K, Griffiths CE, Papp K, Puig L, et al.; ERASURE Study Group; FIXTURE Study Group. Secukinumab in plaque psoriasis--results of two phase 3 trials. N Engl J Med 2014; 371: 326-38. PubMed PMID: 25007392.

(Among 1044 patients with plaque psoriasis treated with secukinumab or placebo in two large 52 week clinical trials, common side effects were nasopharyngitis, upper respiratory infection and diarrhea; no mention of ALT elevations or hepatotoxicity).

Paul C, Lacour JP, Tedremets L, Kreutzer K, Jazayeri S, Adams S, Guindon C, et al.; JUNCTURE study group. Efficacy, safety and usability of secukinumab administration by autoinjector/pen in psoriasis: a randomized, controlled trial (JUNCTURE). J Eur Acad Dermatol Venereol 2015; 29: 1082-90. PubMed PMID: 25243910.

(Among 182 patients with psoriasis treated with secukinumab [150 or 300 mg by autoinjector] or placebo for 12 weeks, adverse events included nasopharyngitis, headache and pruritus, whereas injection site reactions were uncommon; no mention of ALT elevations or hepatotoxicity).

Thaçi D, Humeniuk J, Frambach Y, Bissonnette R, Goodman JJ, Shevade S, Gong Y, et al.; STATURE study group. Secukinumab in psoriasis: randomized, controlled phase 3 trial results assessing the potential to improve treatment response in partial responders (STATURE). Br J Dermatol 2015 Mar 30. [Epub ahead of print] PubMed PMID: 25823958.

(Among 43 patients with psoriasis and only a partial response to secukinumab at 12 weeks who were treated with standard doses or more intensive therapy intravenously, response rates after 40 weeks were similar and no new adverse reactions were identified; no mention of ALT elevations or hepatotoxicity).

Nast A, Jacobs A, Rosumeck S, Werner RN. Efficacy and Safety of Systemic Long-Term Treatments for Moderate-to-Severe Psoriasis: A Systematic Review and Meta-Analysis. J Invest Dermatol 2015 Jun 5. [Epub ahead of print] PubMed PMID: 26046458.

(Systematic review of publications on the efficacy and safety of systemic therapies for psoriasis, states that there are not enough data for the selected safety outcomes for analysis of secukinumab).

McInnes IB, Mease PJ, Kirkham B, Kavanaugh A, Ritchlin CT, Rahman P, van der Heijde D, et al.; FUTURE 2 Study Group. Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2015 Jun 26. [Epub ahead of print] PubMed PMID: 26135703.

(Among 397 patients treated with 1 of 3 doses of secukinumab or placebo for at least 24 weeks, response rates were dose related and higher with secukinumab than with placebo and adverse events were largely mild-to-moderate in severity; no mention of ALT elevations or hepatotoxicity).

Drugs for psoriasis. Med Lett Drugs Ther 2015; 57 (1470): 81-4. PubMed PMID: 26035746.

(Concise summary of current options for therapy of psoriasis including topical agents, phototherapy, oral systemic drugs, and biologic agents including secukinumab, mentions that serious infections occurred in 1.2% of secukinumab treated patients; no mention of hepatotoxicity).

Secukinumab (Cosentyx) for psoriasis. Med Lett Drugs Ther 2015; 57 (1465): 45-7. PubMed PMID: 25853578.

(Concise summary of the mechanism of action, clinical efficacy, safety and costs of secukinumab shortly after its approval in the US mentions that urticarial and anaphylaxis have occurred with its use, but does not mention ALT elevations or hepatotoxicity).