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Golimumab

Updated: February 10, 2017.

OVERVIEW

Introduction

Golimumab is a human monoclonal antibody to tumor necrosis factor (TNF) alpha that is used in the treatment of rheumatoid arthritis and ulcerative colitis. Golimumab has been linked to a low rate of serum enzyme elevations during therapy, but has not been linked to cases of idiosyncratic, clinically apparent liver injury with jaundice. Because golimumab is a potent inhibitor of TNF alpha, it is likely to cause reactivation of chronic hepatitis B in susceptible patients.

Background

Golimumab (goe lim' ue mab) is a human monoclonal immunoglobulin antibody to tumor necrosis factor (TNF) alpha, a proinflammatory cytokine that plays a role in cell injury, inflammation and tissue damage in inflammatory, autoimmune diseases. Golimumab is one of several monoclonal antibody inhibitors of TNF and has been shown to be effective in decreasing inflammation and improving symptoms in several autoimmune diseases, including rheumatoid arthritis and ulcerative colitis. Golimumab was approved for use in the United States for rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis in 2009, and the indications were broadened to include ulcerative colitis in 2013. Golimumab is available in liquid solution in single use, prefilled syringes of 50 and 100 mg under the brand name Simponi. Golimumab is given by subcutaneous injection and the regimen varies by indication. For inflammatory arthritidies the recommended dose is 50 mg once monthly. For ulcerative colitis, the recommendation is for an initial dose of 200 mg, followed by 100 mg at week 2 and then 100 mg every 4 weeks. Common side effects include injection site reactions, chills, fever, skin rash and fatigue. Less common but potentially severe side effects include hypersensitivity reactions and anaphylaxis, opportunistic infections, reactivation of tuberculosis or hepatitis B, congestive heart failure, lymphoma and other malignancies and demyelinating diseases.

Hepatotoxicity

In prelicensure controlled trials, serum ALT elevations occurred in up to 8% of golimumab vs 1% to 3% of placebo treated subjects. The elevations were usually mild-to-moderate in severity, asymptomatic, not accompanied by jaundice and self-limited in course. ALT elevations above 5 times the upper limit of normal (ULN) occurred in 1% to 3% of golimumab and in ~1% of placebo recipients, but only rare patients had to stop therapy because of serum enzyme elevations. There have been no published case reports of clinically apparent, acute liver injury with symptoms or jaundice attributed to golimumab, but experience with its use has been limited.

Nevertheless, golimumab is a potent TNF inhibitor, and virtually all TNF antagonists have been linked to cases of reactivation of hepatitis B, which can be severe and lead to acute liver failure and death or need for emergency liver transplantation. More than 100 cases of clinically apparent reactivation of hepatitis B have been attributed to TNF inhibitors such as infliximab, etanercept, adalimumab and certolizumab. Reactivation typically occurs in patients who are HBsAg carriers with inactive liver disease before treatment. The usual sequence of events is appearance of rising levels of HBV DNA in serum shortly after the anti-TNF therapy is started, followed by rise in levels of HBsAg and HBeAg. Between courses, when immune reconstitution begins, serum ALT and AST levels start to rise followed by symptoms and jaundice. The onset of liver injury is usually after 3 to 6 monthly injections of the TNF antagonist. Reactivation of hepatitis B tends to be severe and the mortality rate in jaundiced cases exceeds 10%. Liver histology demonstrates an acute hepatitis-like pattern with focal or confluent necrosis and prominent lymphocytic infiltrates of activated T cells, which is compatible with an immune mediated hepatic injury. There may also be evidence of an underlying chronic hepatitis or cirrhosis. Restarting the TNF inhibitor can result in recurrence of injury, although antiviral treatment usually blocks recurrence.

Reactivation of HBV can also occur in persons who have resolved hepatitis B (anti-HBc without HBsAg in serum) with reappearance of HBsAg in serum ("reverse seroconversion"). This form of reactivation is less common than classic reactivation (in an HBsAg carrier), yet tends to be more severe. Reverse seroconversion is rare in patients on anti-TNF therapy, occurring more frequently with rituximab or more rigorous forms of immunosuppression (myeloablation and hematopoietic cell transplantation). Reverse seroconversion has yet to be described as a result of golimumab therapy.

Because of the possibility of reactivation of hepatitis B with anti-TNF therapy, screening for markers of HBV infection before starting therapy is recommended. Patients with HBsAg in serum should receive prophylaxis with oral anti-HBV therapy. Patients with anti-HBc without HBsAg in serum should be monitored for evidence of reactivation and treated promptly with antiviral therapy if HBV DNA or HBsAg appear.

Finally, golimumab may reactivate other viral infections and acute hepatitis due to an opportunistic viral infection may occur.

Likelihood score: E* (unproven but suspected cause of clinically apparent liver injury).

Mechanism of Injury

The mechanism of liver injury in reactivation of hepatitis B appears to be a brisk immunological response to newly expressed viral antigens. Injury generally arises after anti-TNF therapy has stopped or between courses of treatment.

Outcome and Management

Guidelines for management of patients who are to receive golimumab recommend routine screening for hepatitis B before starting treatment. Screening should include tests for HBsAg and anti-HBc (and perhaps also anti-HBs as this may help in management). Prophylaxis with a potent oral, antiviral agent effective against hepatitis B is recommended for all persons who have HBsAg in serum and is suggested for those with anti-HBc without HBsAg. An alternative approach is careful monitoring for HBV DNA during therapy and prompt institution of antiviral therapy if levels rise. The choice of antiviral agents includes lamivudine, telbivudine, adefovir, tenofovir or entecavir. All are given once a day and are extremely well tolerated. Lamivudine is less expensive than the other agents, but is associated with a high rate of antiviral resistance particularly if given for more than 6 months. Tenofovir and entecavir are the most potent and have high barriers to antiviral resistance which is important if long term therapy is planned. However, there are no prospectively acquired controlled studies to support use of one of these agents over another. Finally, the appropriate duration of treatment is unclear. The typical recommendation is to continue antivirals for at least 6 months after stopping anti-TNF

therapy, but cases of reactivation following withdrawal of antiviral therapy (including fatal instances) have been described and some degree of monitoring during withdrawal of antiviral therapy is perhaps appropriate.

Drug Class: Antirheumatic Agents, Tumor Necrosis Factor Antagonists; Gastrointestinal Agents, Inflammatory Bowel Disease Agents, Monoclonal Antibodies

Other Drugs in the Subclass, Tumor Necrosis Factor Antagonists: Adalimumab, Certolizumab, Etanercept, Infliximab

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Golimumab – Simponi®

DRUG CLASS

Antirheumatic Agents

Gastrointestinal Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NO.	MOLECULAR FORMULA	STRUCTURE
Golimumab	476181-74-5	Monoclonal Antibody	Not Available

ANNOTATED BIBLIOGRAPHY

References updated: 10 February 2017

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 that "the biological immunosuppressants are largely free from hepatotoxicity, with the exception of the TNF alpha antagonists").

Chabner BA, Barnes J, Neal J, Olson E, Mujagiv H, Sequist L, Wilson W, et al. Targeted therapies: tyrosine kinase inhibitors, monoclonal antibodies, and cytokines. In, Brunton LL, Chabner BA, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 12th ed. New York: McGraw-Hill, 2011, pp. 1731-53.

(Textbook of pharmacology and therapeutics).

Kay J, Matteson EL, Dasgupta B, Nash P, Durez P, Hall S, Hsia EC, et al. Golimumab in patients with active rheumatoid arthritis despite treatment with methotrexate: a randomized, double-blind, placebo-controlled, dose-ranging study. Arthritis Rheum 2008; 58: 964-75. PubMed PMID: 18383539.

(Among 137 patients treated with methotrexate and golimumab in 4 different dose regimens compared to 34 given methotrexate alone, nausea occurred in 17% [vs 3% of controls], injection site reactions in 36% [vs 9%] and ALT elevations ≥2 times ULN in 8% [vs 3%]).

Inman RD, Davis JC Jr, Heijde Dv, Diekman L, Sieper J, Kim SI, Mack M, et al. Efficacy and safety of golimumab in patients with ankylosing spondylitis: results of a randomized, double-blind, placebo-controlled, phase III trial. Arthritis Rheum 2008; 58: 3402-12. PubMed PMID: 18975305.

(Among 356 patients with ankylosing spondylitis treated with golimumab or placebo for 14 weeks, transient ALT elevations occurred in 6% of golimumab and 2.6% of placebo recipients, and were ≥2 times baseline and ≥150 U/L in 3% vs 1.3%).

Emery P, Fleischmann RM, Moreland LW, Hsia EC, Strusberg I, Durez P, Nash P, et al. Golimumab, a human anti-tumor necrosis factor alpha monoclonal antibody, injected subcutaneously every four weeks in methotrexate-naive patients with active rheumatoid arthritis: twenty-four-week results of a phase III, multicenter, randomized, double-blind, placebo-controlled study of golimumab before methotrexate as first-line therapy for early-onset rheumatoid arthritis. Arthritis Rheum 2009; 60: 2272-83. PubMed PMID: 19644849.

(Among 637 patients with rheumatoid arthritis treated in a randomized controlled trial, responses at 24 weeks were slightly more frequent with the combination [38%] than methotrexate alone [29%] or golimumab alone [33%], but so were ALT elevations [4.4% and 6.3% vs 1.3% and 0%]).

Smolen JS, Kay J, Doyle MK, Landewé R, Matteson EL, Wollenhaupt J, Gaylis N, et al.; GO-AFTER study investigators. Golimumab in patients with active rheumatoid arthritis after treatment with tumour necrosis factor alpha inhibitors (GO-AFTER study): a multicentre, randomised, double-blind, placebo-controlled, phase III trial. Lancet 2009; 374 (9685): 210-21. PubMed PMID: 19560810.

(Among 461 patients with rheumatoid arthritis in a 14 week randomized controlled trial, 18% on placebo vs 35% and 38% on golimumab [50 or 100 mg monthly]; no mention of ALT elevations or hepatotoxicity).

Kavanaugh A, McInnes I, Mease P, Krueger GG, Gladman D, Gomez-Reino J, Papp K, et al. Golimumab, a new human tumor necrosis factor alpha antibody, administered every four weeks as a subcutaneous injection in psoriatic arthritis: Twenty-four-week efficacy and safety results of a randomized, placebo-controlled study. Arthritis Rheum 2009; 60: 976-86. PubMed PMID: 19333944.

(Among 456 patients with psoriatic arthritis treated in a randomized controlled trial for 24 weeks, response rates were 48% and 51% with 50 and 100 mg of golimumab vs 9% with placebo, and rates of adverse events were similar, marked ALT elevations occurring in 0-2% of golimumab- vs 3% of placebo recipients).

Keystone EC, Genovese MC, Klareskog L, Hsia EC, Hall ST, Miranda PC, Pazdur J, et al.; GO-FORWARD Study. Golimumab, a human antibody to tumour necrosis factor {alpha} given by monthly subcutaneous injections, in active rheumatoid arthritis despite methotrexate therapy: the GO-FORWARD Study. Ann Rheum Dis 2009; 68: 789-96. PubMed PMID: 19066176.

(Among 444 patients with rheumatoid arthritis in a randomized controlled trial, response rates at 14 weeks were 33% with methotrexate alone, 44% with golimumab alone and 56% with the combination, and adverse events were similar in all groups; ALT elevations were not mentioned).

Golimumab (simponi) for inflammatory arthritis. Med Lett Drugs Ther 2009; 51 (1316): 55-6. PubMed PMID: 19590489.

(Concise review of the mechanism of action, efficacy and safety of golimumab shortly after its approval for treatment of rheumatoid and psoriatic arthritis in the US).

Kremer J, Ritchlin C, Mendelsohn A, Baker D, Kim L, Xu Z, Han J, et al. Golimumab, a new human anti-tumor necrosis factor alpha antibody, administered intravenously in patients with active rheumatoid arthritis: Forty-eight-week efficacy and safety results of a phase III randomized, double-blind, placebo-controlled study. Arthritis Rheum 2010; 62: 917-28. PubMed PMID: 20131276.

(Among 444 patients treated with golimumab with or without methotrexate or placebo and methotrexate, infections were more frequent in those who received golimumab and side effects were more frequent in those who received golimumab and methotrexate; no mention of ALT elevations or hepatotoxicity).

McCluggage LK, Scholtz JM. Golimumab: a tumor necrosis factor alpha inhibitor for the treatment of rheumatoid arthritis. Ann Pharmacother 2010; 44: 135-44. PubMed PMID: 20118145.

(Review of the mechanism of action, pharmacology, clinical efficacy and safety of golimumab a fully humanized bivalent IgG1 monoclonal antibody to both soluble and transmembrane TNF; most common side effects are nausea and injection site reactions, serious adverse events include tuberculosis and lymphoma; no mention of ALT elevations or hepatotoxicity).

Keystone E, Genovese MC, Klareskog L, Hsia EC, Hall S, Miranda PC, Pazdur J, et al. Golimumab in patients with active rheumatoid arthritis despite methotrexate therapy: 52-week results of the GO-FORWARD study. Ann Rheum Dis 2010; 69: 1129-35. PubMed PMID: 20444749.

(Open label continuation of controlled trial of golimumab [Keystone 2009] showed that responses were sustained and adverse events did not increase; no mention of ALT elevations or hepatotoxicity).

Which TNF inhibitor for rheumatoid arthritis? Med Lett Drugs Ther 2010; 52 (1338): 38-9. PubMed PMID: 20467356.

(Discussion of the efficacy, safety and costs of the 5 TNF inhibitors approved for use in rheumatoid arthritis states that none have been shown to be more effective than any other and adverse effects are similar, although reactivation of tuberculosis may be less common with etanercept than infliximab).

Singh JA, Noorbaloochi S, Singh G. Golimumab for rheumatoid arthritis: a systematic review. J Rheumatol 2010; 37: 1096-104. PubMed PMID: 20436075.

(Systematic review of 4 controlled trials in 1231 patients treated with golimumab and 483 with placebo concluded that golimumab was more beneficial than placebo and adverse events rates were similar to those in controls; no mention of ALT elevations or hepatotoxicity).

Brunasso AM, Puntoni M, Gulia A, Massone C. Safety of anti-tumour necrosis factor agents in patients with chronic hepatitis C infection: a systematic review. Rheumatology (Oxford) 2011; 50: 1700-11. PubMed PMID: 21690185.

(Systematic review of 37 publications on 153 patients with hepatitis C who were treated with anti-TNF agents for an average of 12 months found only one instance of worsening during therapy and no evidence of increases in HCV RNA levels during treatment).

Smolen JS, Kay J, Landewé RB, Matteson EL, Gaylis N, Wollenhaupt J, Murphy FT, et al. Golimumab in patients with active rheumatoid arthritis who have previous experience with tumour necrosis factor inhibitors: results of a long-term extension of the randomised, double-blind, placebo-controlled GO-AFTER study through week 160. Ann Rheum Dis 2012; 71: 1671-9. PubMed PMID: 22459542.

(Among 459 patients with rheumatoid arthritis in a 24 week controlled trial of golimumab, 236 were continued on treatment for up to 160 weeks; listing of adverse events did not mention ALT elevations, hepatotoxicity or reactivation of hepatitis B).

Kavanaugh A, van der Heijde D, McInnes IB, Mease P, Krueger GG, Gladman DD, Gómez-Reino J, et al. Golimumab in psoriatic arthritis: one-year clinical efficacy, radiographic, and safety results from a phase III, randomized, placebo-controlled trial. Arthritis Rheum 2012; 64: 2504-17. PubMed PMID: 22378566.

(Open label continuation of controlled trial of golimumab for psoriatic arthritis found that clinical efficacy was maintained through 1 year and adverse events were similar to those reported earlier [Kavanaugh 2009], 3

patients discontinued therapy because of elevated ALT levels, but no new patients had "clinically meaningful" elevations in ALT since the previous report).

Aaltonen KJ, Virkki LM, Malmivaara A, Konttinen YT, Nordström DC, Blom M. Systematic review and meta-analysis of the efficacy and safety of existing TNF blocking agents in treatment of rheumatoid arthritis. PLoS One 2012; 7: e30275. PubMed PMID: 22272322.

(Systematic review of 26 controlled trials of anti-TNF agents for rheumatoid arthritis found similar rates of efficacy with different agents, but slightly lower rates of adverse events with etanercept, as measured by rates of discontinuation for adverse events [risk ratio=0.71]).

Braun J, Deodhar A, Inman RD, van der Heijde D, Mack M, Xu S, Hsu B. Golimumab administered subcutaneously every 4 weeks in ankylosing spondylitis: 104-week results of the GO-RAISE study. Ann Rheum Dis 2012; 71: 661-7. PubMed PMID: 22012970.

(Results of extended therapy with golimumab in patients enrolled in a previous controlled trial in ankylosing spondylitis [Inman 2009] found liver enzymes were more commonly elevated in those on 100 vs 50 mg of golimumab [5% vs 0.7%], no patient had concurrent elevation in ALT and bilirubin).

Emery P, Fleischmann RM, Doyle MK, Strusberg I, Durez P, Nash P, Amante E, et al. Golimumab, a human anti-tumor necrosis factor monoclonal antibody, injected subcutaneously every 4 weeks in patients with active rheumatoid arthritis who had never taken methotrexate: 1-year and 2-year clinical, radiologic, and physical function findings of a phase III, multicenter, randomized, double-blind, placebo-controlled study. Arthritis Care Res (Hoboken) 2013; 65: 1732-42. PubMed PMID: 23861303.

(Extended results of continuing golimumab in patients with rheumatoid arthritis enrolled in a controlled trial [Emery 2009] mentions serious adverse events of active tuberculosis in 11 patients, malignancies in 14; no mention of ALT elevations, hepatotoxicity or reactivation of hepatitis B).

Keystone EC, Genovese MC, Hall S, Miranda PC, Bae SC, Palmer W, Wu Z, et al. Golimumab in patients with active rheumatoid arthritis despite methotrexate therapy: results through 2 years of the GO-FORWARD study extension. J Rheumatol 2013; 40: 1097-103. PubMed PMID: 23678153.

(Further follow up on 392 patients with rheumatoid arthritis treated in a controlled trial of golimumab [Keystone 2009], who continued on either 50 or 100 mg of golimumab for 2 years mentions severe adverse events of serious infections [7%], tuberculosis [0.5%] and one patient who died of hepatic failure after "a complicated hospitalization including severe intra-abdominal hemorrhage following liver biopsy").

Kavanaugh A, McInnes IB, Mease PJ, Krueger GG, Gladman DD, van der Heijde D, Mudivarthy S, et al. Clinical efficacy, radiographic and safety findings through 2 years of golimumab treatment in patients with active psoriatic arthritis: results from a long-term extension of the randomised, placebo-controlled GO-REVEAL study. Ann Rheum Dis 2013; 72: 1777-85. PubMed PMID: 23161902.

(Further follow up on 394 patients with psoriatic arthritis [Kavanaugh 2009] who were continued on golimumab [50 or 100 mg monthly] for up to 2 years, among whom 5 discontinued therapy because of raised ALT levels and 4 for raised AST levels; no mention of clinically apparent liver injury or reactivation of hepatitis B).

Kay J, Fleischmann R, Keystone E, Hsia EC, Hsu B, Mack M, Goldstein N, et al. Golimumab 3-year safety update: an analysis of pooled data from the long-term extensions of randomised, double-blind, placebo-controlled trials conducted in patients with rheumatoid arthritis, psoriatic arthritis or ankylosing spondylitis. Ann Rheum Dis 2013 Dec 16. [Epub ahead of print] PubMed PMID: 24344160.

(Analysis of 3 year results from extension studies of 5 controlled trials of golimumab in inflammatory arthritis discusses long term adverse events of serious infections, tuberculosis, opportunistic infections, demyelination syndromes and lymphoma, but not ALT elevations, hepatotoxicity or reactivation of hepatitis B).

Sandborn WJ, Feagan BG, Marano C, Zhang H, Strauss R, Johanns J, Adedokun OJ, et al.; PURSUIT-Maintenance Study Group. Subcutaneous golimumab maintains clinical response in patients with moderate-to-severe ulcerative colitis. Gastroenterology 2014; 146: 96-109. PubMed PMID: 23770005.

(Among 464 patients with ulcerative colitis who achieved a clinical response during induction therapy and who were then treated with either 50 or 100 mg of golimumab or placebo, clinical responses were maintained in 47-50% of patients on golimumab vs 31% on placebo; 4 patients developed tuberculosis, 1 of whom died; no mention of ALT elevations or hepatotoxicity).

Sandborn WJ, Feagan BG, Marano C, Zhang H, Strauss R, Johanns J, Adedokun OJ, et al.; PURSUIT-SC Study Group. Subcutaneous golimumab induces clinical response and remission in patients with moderate-to-severe ulcerative colitis. Gastroenterology 2014; 146: 85-95. PubMed PMID: 23735746.

(Among 1064 adults with active ulcerative colitis given induction therapy, rates of response were 51-55% on golimumab vs 30% on placebo, and adverse events [through week 6] were similar; no mention of ALT elevations or hepatotoxicity).

Combe B, Dasgupta B, Louw I, Pal S, Wollenhaupt J, Zerbini CA, Beaulieu AD, et al.; GO-MORE Investigators. Efficacy and safety of golimumab as add-on therapy to disease-modifying antirheumatic drugs: results of the GO-MORE study. Ann Rheum Dis 2014; 73: 1477-86. PubMed PMID: 23740226.

(Among 3366 patients with rheumatoid arthritis treated with golimumab in an open label study, the most common clinically significant abnormal laboratory even was elevation in liver transaminases, but no specific rates given).

Golimumab (Simponi) for ulcerative colitis. Med Lett Drugs Ther 2014; 56 (1439): 25-6. PubMed PMID: 24691148.

(Concise review of the mechanism of action, efficacy, safety and costs of golimumab therapy of ulcerative colitis shortly after its approval for this indication in the US, mentions the risk of reactivation of tuberculosis and hepatitis B with all anti-TNF agents).

Bauer H, Luxembourger C, Gottenberg JE, Fournier S, Abravanel F, Cantagrel A, Chatelus E, et al.; Club Rhumatismes et Inflammation, a section of the French Society of Rheumatology. Outcome of hepatitis E virus infection in patients with inflammatory arthritides treated with immunosuppressants: a French retrospective multicenter study. Medicine (Baltimore) 2015; 94: e675. PubMed PMID: 25860212.

(Survey of French physicians treating patients with rheumatic diseases identified 23 patients who developed acute hepatitis E while being treated with immunosuppressive regimens [10 on anti-TNF, 4 rituximab, 2 abatacept, 2 tocilizumab and 16 receiving methotrexate, 4 leflunomide and 1 cyclosporine]; all recovered and cleared HEV RNA, some after reduction in immunosuppression and 5 with ribavirin therapy).

Di Bisceglie AM, Lok AS, Martin P, Terrault N, Perrillo RP, Hoofnagle JH. Recent US Food and Drug Administration warnings on hepatitis B reactivation with immune-suppressing and anticancer drugs: just the tip of the iceberg? Hepatology 2015; 61: 703-11. PubMed PMID: 25412906.

(Review of the pathogenesis, clinical course, treatment and prevention of HBV reactivation in patients receiving immunosuppressive or anticancer therapies, with particular focus on rituximab and ofatumumab).

Björnsson ES, Gunnarsson BI, Gröndal G, Jonasson JG, Einarsdottir R, Ludviksson BR, Gudbjörnsson B, Olafsson S. Risk of drug-induced liver injury from tumor necrosis factor antagonists. Clin Gastroenterol Hepatol 2015; 13: 602-8. PubMed PMID: 25131534.

(Among 11 cases of liver injury from anti-TNF agents identified over a 5 year period in Iceland, 9 were due to infliximab [among 1076 patients treated=1:120], 1 adalimumab [270 treated] and 1 etanercept [430 treated]; 8 women, 3 men; latency 1 to 6 months; 5 were jaundiced [peak bilirubin 0.6-7.6 mg/dL, ALT 169-1658 U/L, Alk P 71-916 U/L], 8 hepatocellular, 2 cholestatic and 1 mixed injury; 8 had ANA, 5 were treated with corticosteroids [only 1 long term], 8 were switched to another anti-TNF agent without recurrence).

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. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury enrolled in a US prospective study between 2004 and 2013, 6 cases [0.7%] were attributed to a tumor necrosis factor antagonist, including 3 to infliximab, 2 etanercept and 1 adalimumab, but none to certolizumab or golimumab).