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Abatacept

Updated: October 6, 2021.

OVERVIEW

Introduction

Abatacept is a recombinant fusion protein of the cell surface marker CTLA-4 and a fragment of immunoglobulin G that acts by interfering with T cell activation and is used to treat rheumatoid and psoriatic arthritis and juvenile idiopathic arthritis. Abatacept has been linked to a low rate of serum enzyme elevations during therapy, and to rare cases of idiosyncratic, clinically apparent liver injury with jaundice. Because abatacept is a potent inhibitor of lymphocyte function, it can cause reactivation of hepatitis B in susceptible patients.

Background

Abatacept (a bat' a sept) is a recombinant fusion protein that combines the extracellular domain of the cytotoxic T lymphocyte associated antigen-4 (CTLA-4) with the heavy chain fragment of immunoglobulin G. Abatacept blocks the actions of CTLA-4, which is important in the co-stimulatory pathway of activation of T cells. Blocking CTLA-4 inhibits maturation and activation of T cells, T cell proliferation and production of proinflammatory cytokines, such as tumor necrosis factor (TNF), interferon gamma and interleukin 2 and 6. Abatacept has been evaluated in several autoimmune inflammatory conditions, including rheumatoid and psoriatic arthritis, lupus erythematosus and inflammatory bowel disease. Abatacept was approved for use in the United States in 2005, and current formal indications include moderately severe rheumatoid and psoriatic arthritis in adults and juvenile idiopathic arthritis in children 2 years of age or above. Abatacept is available under the brand name Orencia as a lyophilized power for intravenous administration in single use vials of 250 mg and as a solution for subcutaneous administration in single use syringes of 50, 75, and 125 mg or in autoinjectors of 125 mg/mL. In adults, abatacept may be given subcutaneously or intravenously (at weeks 0, 2, 4 and then every 4 weeks) in doses based upon body weight ranging from 500 to 1000 mg. The dose in children is based upon body weight and given either intravenously or subcutaneously at weeks 0, 2, 4 and then every 4 weeks. Common side effects include infusion reactions of chills, fever and hypertension and nonspecific symptoms of headache, dizziness, nausea, back and body pain, nasopharyngitis, and rash. Acute hypersensitivity reactions occur in <1% of patients and anaphylaxis in <0.1%. Less common, but potentially severe side effects include an increased risk of infections and reactivation of tuberculosis and hepatitis B.

Hepatotoxicity

In prelicensure controlled trials, serum ALT elevations occurred in 2% to 3% of abatacept and a similar proportion of placebo treated subjects. The elevations were usually mild-to-moderate in severity, asymptomatic and self-limited in course. ALT elevations above 5 times the upper limit of normal (ULN) occurred <1% of abatacept recipients, and only rare patients had to stop therapy because of serum enzyme elevations. Clinically

apparent liver injury is not listed as a potential side effect in the product label for abatacept, but there has been at least one case report of acute liver injury with symptoms or jaundice attributed to abatacept: a case of severe acute hepatitis accompanied by ANA positivity and a response to corticosteroid therapy (Case 1). Thus, abatacept may precipitate an acute autoimmune hepatitis but this is quite rare.

Abatacept is a potent immunosuppressive agent and reactivation of hepatitis B in patients with ongoing or previous hepatitis B can occur. Reactivation is most frequent in patients with HBsAg in serum whether or not they have accompanying chronic hepatitis. Yet reactivation can also occur, although more rarely, in persons with resolved hepatitis B, who have anti-HBc but no HBsAg detectable in serum. With reactivation, serum levels of HBV DNA rise, followed by increases in serum ALT and AST and then symptoms and jaundice. The injury is hepatocellular and resembles acute hepatitis B. The onset of liver injury is usually after 3 to 12 monthly injections of the immunomodulatory agent in patients with HBsAg in serum. In patients with resolved hepatitis B, however, the time to reactivation is often much longer and may only arise after 1 to 10 or more years of immunosuppressive therapy. In studies from Taiwan, reactivation of hepatitis B attributed to abatacept were reported in up to 9% of treated subjects after 1 to more than 10 years of therapy, at a yearly rate of approximately 1 per 100 patients who had anti-HBc without HBsAg in serum. Reactivation was accompanied by ALT elevations in half and decompensation and death in a proportion. For these reasons, screening for hepatitis B markers is recommended before starting abatacept and regular monitoring for rises in HBV DNA levels during therapy is recommended for those with anti-HBc with or without HBsAg in serum. With evidence of reactivation (de novo appearance or rise in HBV DNA levels), antiviral therapy should be initiated using an agent with potent activity against HBV such as entecavir or tenofovir. The other option is prophylaxis with one of these antiviral agents.

Likelihood score: C (probable rare cause of clinically apparent liver injury including reactivation of hepatitis B in susceptible patients).

Mechanism of Injury

Abatacept is a recombinant human protein and as such is unlikely to be intrinsically hepatotoxic. Because it has immunomodulatory actions, it can cause reactivation of hepatitis B or induce an autoimmune liver reaction.

Outcome and Management

Abatacept has been linked to minor serum enzyme elevations and to rare instances of acute liver injury with jaundice. Discontinuation for serum enzyme elevations is rarely necessary, but should be done if the elevations are accompanied by symptoms or jaundice or for persistent ALT elevations of more than 5 times ULN. There is no information on cross sensitivity to liver injury between abatacept and other immunomodulatory cytokines. Reactivation of hepatitis B can occur with abatacept therapy and patients with preexisting HBsAg or anti-HBc without HBsAg should be given antiviral prophylaxis or monitored regularly for early evidence of reactivation, with prompt initiation of antiviral therapy using an agent with potent activity against HBV, such as entecavir or tenofovir.

Drug Class: Antirheumatic Agents

CASE REPORT

Case 1. Acute liver injury attributed to abatacept therapy.(1)

A 61 year old Japanese woman with Sjögren syndrome and rheumatoid arthritis developed epigastric pain and nausea after four infusions of abatacept. She had been treated previously with methotrexate, infliximab, adalimumab, tacrolimus and tocilizumab without a lasting response. She had no history of liver disease, drug allergies, risk factors for viral hepatitis or alcohol abuse. Physical examination showed jaundice and epigastric

tenderness. Laboratory tests show a total bilirubin of 15.2 mg/dL (12.1 mg/dL direct) with an ALT of 2217 U/L, AST 4310 U/L, alkaline phosphatase 1388 U/L and prothrombin time index 50%. Tests for hepatitis A, B (including HBV DNA) and C were negative, as were IgM antibodies to cytomegalovirus and Epstein Barr virus. The ANA was positive (1:1280), IgG was elevated (2,030 mg/dL) and rheumatoid factor was present (56.8 IU/mL), but SMA and AMA were negative. Over the next few weeks, she worsened with serum bilirubin rising to 24 mg/dL, prothrombin activity falling to 40% and appearance of hepatic encephalopathy and ascites. She was treated with high doses of methylprednisolone and plasma exchange. She was evaluated for emergency liver transplantation, but then began to improve spontaneously. Over the next several months, liver tests improved and were normal 6 months later.

Key Points

Medication:	Abatacept (500 mg, four intravenous infusions)
Pattern:	Mixed (R=4.6)
Severity:	4+ (jaundice, hospitalization, abnormal INR, hepatic coma)
Latency:	~6 weeks
Recovery:	~8 weeks
Other medications:	None concurrently

Comment

This case is an example of an acute hepatitis with a "mixed" pattern of serum enzyme elevations and severe course arising after 4 to 6 weeks of abatacept therapy of rheumatoid arthritis. Other common causes of acute liver injury were excluded. Tests for hepatitis B documented that the hepatitis was not due to reactivation. Autoimmune features were present, including high titers of ANA and elevations in IgG levels, but these might also have been present because of the underlying disease. Nonetheless, the course and outcome are most compatible with an autoimmune hepatitis induced by the immunomodulatory agent. This reaction must be quite rare.

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Abatacept – Orencia®

DRUG CLASS

Antirheumatic Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NO.	MOLECULAR FORMULA	STRUCTURE
Abatacept	332348-12-6	Recombinant Protein	Not Available

CITED REFERENCES

1. Iwanaga N, Origuchi T, Terada K, Ueki Y, Kamo Y, Kinoshita N, Yonemitsu N, et al. Rheumatoid arthritis complicated with severe liver injury during treatment with abatacept. Mod Rheumatol. 2014;24:874–6. PubMed PMID: 24611764.

ANNOTATED BIBLIOGRAPHY

References updated: 06 October 2021

Abbreviations: Anti-TNF, anti-tumor necrosis factor; DMARDs, disease modifying antirheumatic drugs; HBV, hepatitis B virus.

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").

Krensky AM, Azzi JR, Hafler DA. Immunosuppressants and tolerogens. 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. 637-53.

(Textbook of pharmacology and therapeutics).

Kremer JM, Westhovens R, Leon M, Di Giorgio E, Alten R, Steinfeld S, Russell A, et al. Treatment of rheumatoid arthritis by selective inhibition of T-cell activation with fusion protein CTLA4Ig. N Engl J Med. 2003;349:1907–15. PubMed PMID: 14614165.

(Among 339 patients with rheumatoid arthritis not responding adequately to methotrexate who were treated with 1 of 2 doses of abatacept or placebo for six months, response rates were 60% with higher doses of abatacept, 42% with lower doses, and 35% with placebo, while rates of adverse events were similar and no serious adverse event was attributed to drug; no mention of ALT elevations or hepatotoxicity).

Genovese MC, Becker JC, Schiff M, Luggen M, Sherrer Y, Kremer J, Birbara C, et al. Abatacept for rheumatoid arthritis refractory to tumor necrosis factor alpha inhibition. N Engl J Med. 2005;353:1114–23. PubMed PMID: 16162882.

(Among 389 patients with rheumatoid arthritis not responding to anti-TNF agents who were treated with abatacept or placebo for 6 months, clinical responses occurred with 50% of abatacept vs 20% of placebo recipients and overall rates of side effects were similar, although abatacept recipients were more likely to have infections [38% vs 32%] and acute infusion reactions [5% vs 3%]).

Abatacept (Orencia) for rheumatoid arthritis. Med Lett Drugs Ther. 2006;48(1229):17–8. PubMed PMID: 16498306.

(Concise review of the mechanism of action, efficacy, safety and costs of abatacept for rheumatoid arthritis; discussion of adverse events includes mention of increased rates of infections, especially when combined with anti-TNF agents).

Schiff M, Keiserman M, Codding C, Songcharoen S, Berman A, Nayiager S, Saldate C, et al. Efficacy and safety of abatacept or infliximab vs placebo in ATTEST: a phase III, multi-centre, randomised, double-blind, placebo-controlled study in patients with rheumatoid arthritis and an inadequate response to methotrexate. Ann Rheum Dis. 2008;67:1096–103. PubMed PMID: 18055472.

(Among 416 patients with rheumatoid arthritis not responding to methotrexate who were treated with abatacept, infliximab or placebo for 6 months, clinical responses were similar for abatacept and infliximab and side effect rates were similar).

Khraishi M, Russell A, Olszynski WP. Safety profile of abatacept in rheumatoid arthritis: a review. Clin Ther. 2010;32:1855–70. PubMed PMID: 21095481.

(Systematic review of the literature on safety of abatacept including analysis of 7 placebo controlled trials and 5 with long term follow up; no mention of ALT elevations of hepatotoxicity).

Ruperto N, Lovell DJ, Quartier P, Paz E, Rubio-Pérez N, Silva CA, Abud-Mendoza C, et al; Paediatric Rheumatology International Trials Organization and the Pediatric Rheumatology Collaborative Study Group. Long-term safety and efficacy of abatacept in children with juvenile idiopathic arthritis. Arthritis Rheum. 2010;62:1792–802. PubMed PMID: 20191582.

(Among 153 children with juvenile idiopathic arthritis treated with abatacept in a long term extension study, none developed a severe hepatic adverse reaction; no mention of ALT elevations).

Genovese MC, Covarrubias A, Leon G, Mysler E, Keiserman M, Valente R, Nash P, et al. Subcutaneous abatacept versus intravenous abatacept: a phase IIIb noninferiority study in patients with an inadequate response to methotrexate. Arthritis Rheum. 2011;63:2854–64. PubMed PMID: 21618201.

(Among 1457 patients with rheumatoid arthritis treated with either intravenous or subcutaneous abatacept for 6 months, both beneficial responses and adverse events were similar in the two groups; no mention of ALT elevations or hepatotoxicity).

Mease P, Genovese MC, Gladstein G, Kivitz AJ, Ritchlin C, Tak PP, Wollenhaupt J, et al. Abatacept in the treatment of patients with psoriatic arthritis: results of a six-month, multicenter, randomized, double-blind, placebo-controlled, phase II trial. Arthritis Rheum. 2011;63:939–48. PubMed PMID: 21128258.

(Among 170 patients with psoriatic arthritis treated with 1 of 3 doses of abatacept or placebo for 6 months, response rates were 33%, 48% and 42% in the abatacept and 19% in the placebo group, and side effects were slightly higher with high dose abatacept; no mention of ALT elevations or hepatotoxicity).

Drugs for rheumatoid arthritis. Treat Guidel Med Lett. 2012;10(117):37–44. PubMed PMID: 22538522.

(Concise review of therapy of rheumatoid arthritis mentions that abatacept can cause acute infusion reactions and probably increases the risk for serious infections, but not tuberculosis).

Grasland A, Sterpu R, Boussoukaya S, Mahe I. Autoimmune hepatitis induced by adalimumab with successful switch to abatacept. Eur J Clin Pharmacol. 2012;68:895–8. PubMed PMID: 22205272.

(35 year old woman with seronegative arthritis developed rise in ALT [from 18 to 266 U/L, ANA 1:80, SMA 1:320] two months after starting adalimumab, which fell to normal on stopping adalimumab and substituting prednisone; in follow up the liver injury did not recur on starting abatacept).

Sandborn WJ, Colombel JF, Sands BE, Rutgeerts P, Targan SR, Panaccione R, Bressler B, et al. Abatacept for Crohn's disease and ulcerative colitis. Gastroenterology. 2012;143:62–69.e4. PubMed PMID: 22504093.

(Pooled results from 4 controlled trials of abatacept in inflammatory bowel disease showing little evidence of efficacy and an increase in adverse events compared to placebo; no mention of ALT elevations or hepatotoxicity).

Germanidis G, Hytiroglou P, Zakalka M, Settas L. Reactivation of occult hepatitis B virus infection, following treatment of refractory rheumatoid arthritis with abatacept. J Hepatol. 2012;56:1420–1. PubMed PMID: 22127282.

(70 year old woman with long term refractory rheumatoid arthritis and anti-HBc without HBsAg in serum developed detectable HBV DNA [12,000 IU/mL] and low levels of HBsAg serum, with ALT levels rising to 10

times ULN, and with resolution of hepatitis and clearance of HBV DNA within 4 months of starting tenofovir therapy).

Kim PS, Ho GY, Prete PE, Furst DE. Safety and efficacy of abatacept in eight rheumatoid arthritis patients with chronic hepatitis B. Arthritis Care Res (Hoboken). 2012;64:1265–8. PubMed PMID: 22392695.

(Retrospective study of 8 patients with refractory rheumatoid arthritis who were treated with abatacept for 3-33 months who were known to be HBsAg positive, 4 received anti-HBV prophylaxis and all 4 responded to treatment and none had reactivation, whereas the 4 who did not receive prophylaxis had minimal response to treatment and all four had reactivation at 3-27 months, although none had hepatitis as antiviral therapy was evidently started promptly).

Weinblatt ME, Moreland LW, Westhovens R, Cohen RB, Kelly SM, Khan N, Pappu R, et al. Safety of abatacept administered intravenously in treatment of rheumatoid arthritis: integrated analyses of up to 8 years of treatment from the abatacept clinical trial program. J Rheumatol. 2013;40:787–97. PubMed PMID: 23588946.

(Analysis of pooled results from 8 clinical trials of intravenous abatacept including data on 3173 patients for up to 8 years of treatment found no increase in rates of adverse events with long term therapy; no mention of ALT elevations or hepatotoxicity).

Fanouriakis A, Vassilopoulos D, Repa A, Boumpas DT, Sidiropoulos P. Hepatitis B reactivation following treatment with abatacept in a patient with past hepatitis B virus infection. Rheumatology (Oxford). 2014;53:195–6. PubMed PMID: 23771951.

(68 year old woman with rheumatoid arthritis and anti-HBc without HBsAg in serum developed HBsAg 10 months after starting abatacept with high levels of HBV DNA [108 IU/mL] and brief period of ALT elevation after starting tenofovir, but ultimate clearance of HBV DNA and normal liver tests).

Westhovens R, Kremer JM, Emery P, Russell AS, Alten R, Barré E, Dougados M. Long-term safety and efficacy of abatacept in patients with rheumatoid arthritis and an inadequate response to methotrexate: a 7-year extended study. Clin Exp Rheumatol. 2014;32:553–62. PubMed PMID: 25005467.

(Analysis of long term open-label extension study of abatacept in 219 patients with psoriasis, of whom 114 were still receiving drug after 7 years, found sustained clinical benefits and no increase in rates of adverse events; no mention of ALT elevations or hepatotoxicity and no episodes of tuberculosis).

Takeuchi T, Matsubara T, Urata Y, Suematsu E, Ohta S, Honjo S, Abe T, et al; Japan Abatacept Study Group. Phase III, multicenter, open-label, long-term study of the safety of abatacept in Japanese patients with rheumatoid arthritis and an inadequate response to conventional or biologic disease-modifying antirheumatic drugs. Mod Rheumatol. 2014;24:744–53. PubMed PMID: 24754273.

(Among 217 Japanese patients with rheumatoid arthritis treated intravenously with abatacept for an average of 3 years, response rates ranged from 61-81% and were sustained; ALT elevations occurred in 11.5%, but none were considered serious; no mention of reactivation of hepatitis B and no patient developed tuberculosis).

Furie R, Nicholls K, Cheng TT, Houssiau F, Burgos-Vargas R, Chen SL, Hillson JL, et al. Efficacy and safety of abatacept in lupus nephritis: a twelve-month, randomized, double-blind study. Arthritis Rheumatol. 2014;66:379–89. PubMed PMID: 24504810.

(Among 298 patients with lupus nephritis treated with 2 doses of abatacept or placebo for 12 months, response rates were similar in all three groups, and adverse events were similar except for higher rates of infection with abatacept; no mention of ALT elevations or hepatotoxicity).

Iwanaga N, Origuchi T, Terada K, Ueki Y, Kamo Y, Kinoshita N, Yonemitsu N, et al. Rheumatoid arthritis complicated with severe liver injury during treatment with abatacept. Mod Rheumatol. 2014;24:874–6. PubMed PMID: 24611764.

(61 year old woman with Sjögren syndrome and rheumatoid arthritis developed nausea after 4 infusions of abatacept [bilirubin 15.2 mg/dL, ALT 2217 U/L, Alk P 1388 U/L, prothrombin activity 50%, ANA 1:1280], progressing to hepatic failure, treated with corticosteroids and plasma exchange, and ultimately resolving within 2 months of onset: Case 1).

Alten R, Kaine J, Keystone E, Nash P, Delaet I, Genovese MC. Long-term safety of subcutaneous abatacept in rheumatoid arthritis: integrated analysis of clinical trial data representing more than four years of treatment. Arthritis Rheumatol. 2014;66:1987–97. PubMed PMID: 24782324.

(Among 1879 patients with rheumatoid arthritis treated with subcutaneous abatacept for an average of 2.2 years in 5 clinical trials, serious adverse events included serious infections [1.8% per year], malignancy [1.3%], autoimmune conditions [1.4%], injection site reactions [1.7%], and 4 cases of tuberculosis, one fatal; ALT elevations occurred in 2.4% of patients, but there were no liver related serious adverse events).

Lovell DJ, Ruperto N, Mouy R, Paz E, Rubio-Pérez N, Silva CA, Abud-Mendoza C, et al; Pediatric Rheumatology Collaborative Study Group and the Paediatric Rheumatology International Trials Organisation. Long-term safety, efficacy, and quality of life in patients with juvenile idiopathic arthritis treated with intravenous abatacept for up to seven years. Arthritis Rheumatol. 2015;67:2759–70. PubMed PMID: 26097215.

(Among 153 children [ages 6-17 years] with juvenile idiopathic arthritis treated with abatacept in 43 centers for up 7 years, 30 [20%] had a serious adverse event [mostly infections and autoimmune events], but none were liver related; ALT elevations not mentioned).

Padovan M, Filippini M, Tincani A, Lanciano E, Bruschi E, Epis O, Garau P, et al. Safety of abatacept in rheumatoid arthritis with serological evidence of past or present hepatitis B virus infection. Arthritis Care Res (Hoboken). 2016;68:738–43. PubMed PMID: 26555747.

(Among 51 patients with rheumatoid arthritis and HBsAg and 21 with anti-HBc without HBsAg who were treated with abatacept for up to 4 years, none developed HBV reactivation or de novo HBsAg even though most [76%] did not receive antiviral prophylaxis).

Harigai M, Ishiguro N, Inokuma S, Mimori T, Ryu J, Takei S, Takeuchi T, et al. Postmarketing surveillance of the safety and effectiveness of abatacept in Japanese patients with rheumatoid arthritis. Mod Rheumatol. 2016;26(4):491–8. PubMed PMID: 26635183.

(Among 3882 Japanese patients wtih rheumatoid arthritis treated with abatacept for an average of 6 months, liver test abnormalities were reported in 0.75% and were considered serious in 0.05%, but no death was due to liver disease and there was no mention of hepatitis or reactivation of hepatitis B).

Talotta R, Atzeni F, Sarzi Puttini P. Reactivation of occult hepatitis B virus infection under treatment with abatacept: a case report. BMC Pharmacol Toxicol. 2016;17:17. PubMed PMID: 27098382.

(66 year old man with rheumatoid arthritis and anti-HBc without HBsAg or anti-HBs in serum developed detectable serum HBV DNA [326 IU/mL] 11 months after starting abatacept [750 mg each month] with minimal ALT elevations and no symptoms and was started on lamivudine when repeat HBV DNA was positive [1416 IU/mL], with subsequent lack of detectable HBV DNA and normal ALT levels).

Papalopoulos I, Fanouriakis A, Kougkas N, Flouri I, Sourvinos G, Bertsias G, Repa A, et al. Liver safety of non-tumour necrosis factor inhibitors in rheumatic patients with past hepatitis B virus infection: an observational, controlled, long-term study. Clin Exp Rheumatol. 2018;36:102–109. PubMed PMID: 28850029.

(Among 156 patients with inflammatory arthritidies and anti-HBc without HBsAg in serum who were treated with biologic DMARDs for an mean of 24 months, none of 85 receiving anti-TNF therapy developed reactivation of

hepatitis B compared to 2 of 71 receiving other biologics, including rituximab 1 of 32 on rituximab, 1 of 39 on abatacept and none of 30 on tocilizumab).

Watanabe T, Fukae J, Fukaya S, Sawamukai N, Isobe M, Matsuhashi M, Shimizu M, et al. Incidence and risk factors for reactivation from resolved hepatitis B virus in rheumatoid arthritis patients treated with biological disease-modifying antirheumatic drugs. Int J Rheum Dis. 2019;22:574–582. PubMed PMID: 30338649.

(Among 152 Japanese patients with rheumatoid arthritis and anti-HBc without HBsAg in serum who were treated with DMARDs for an average of 13 months, only 7 developed evidence of reactivation but none required antiviral therapy, HBV DNA remaining low or becoming undetectable and ALT remaining normal in all; reactivation occurring in 3 of 7 [43%] with vs 90% without anti-HBs at baseline and in 3 of 29 [10%] on abatacept, 2 of 17 [12%] infliximab, 1 of [4%] golimumab, 1 of 25 tocilizumab, but none on etanercept, adalimumab, or on methotrexate and steroids alone).

Cambier ML, Canestri A, Lependeven C, Peltier J, Mesnard L, Dahan K. Hepatitis B virus reactivation during belatacept treatment after kidney transplantation. Transpl Infect Dis. 2019;21:e13170. PubMed PMID: 31505095.

(47 year old man with HIV infection, end-stage renal disease and anti-HBc without HBsAg in serum, underwent kidney transplantation with long term belatacept, prednisone and mycophenolate as well as anti-HIV therapy with darunavir/R, etravirine and raltegravir and developed reactivation of HBV with an acute hepatitis, which responded to entecavir therapy with subsequent loss of HBV DNA).

Chen MH, Chen MH, Chou CT, Hou MC, Tsai CY, Huang YH. Low but long-lasting risk of reversal of seroconversion in patients with rheumatoid arthritis receiving immunosuppressive therapy. Clin Gastroenterol Hepatol. 2020;18:2573–2581.e1. PubMed PMID: 32205219.

(Among 1434 adults with rheumatoid arthritis treated between 2007 and 2018 at a single Taiwanese referral center, 925 initially had anti-HBc without HBsAg in serum among whom in follow up 17 developed HBsAg [2%], all with detectable HBV DNA in serum [>100,000 IU/mL in most], 8 with ALT elevations above 3 times ULN, 3 with hepatic decompensation and one died despite entecavir therapy once reactivation was detected; reactivation occurred in 16 of 473 [3.3%] who received a biologic agent for 10 to 105 [median=66] months including rituximab [n=9], adalimumab [n=2], abatacept [n=4] and etanercept [n=1] vs only 1 of 452 [0.2%] who received conventional DMARDs only).

Teraoka Y, Imamura M, Uchida T, Ohya K, Morio K, Fujino H, Ono A, et al. Abatacept treatment for patients with severe acute hepatitis caused by hepatitis B virus infection-Pilot study. J Viral Hepat. 2021;28:400–409. PubMed PMID: 33197288.

(Among 5 patients with severe acute hepatitis B treated with abatacept as well as with either entecavir or tenofovir, all had improvements in serum aminotransferase levels and hepatitis B markers and reportedly suffered on adverse reactions from therapy although the outcome in one case was not provided).

Chen MH, Lee IC, Chen MH, Hou MC, Tsai CY, Huang YH. Abatacept is second to rituximab at risk of HBsAg reverse seroconversion in patients with rheumatic disease. Ann Rheum Dis. 2021 Jun 29:annrheumdis-2021-220774. ePub ahead of print.

(Among 1937 patients with rheumatoid arthritis started on DMARDs therapy between 2003 and 2019, 489 had anti-HBc without HBsAg in serum, of whom 27 [5.5%] developed HBsAg and reactivation of hepatitis B during biologic DMARDs therapy, typically after 10 months to 15 years, the rate being highest for rituximab at 18 of 84 patients or 17 per 1000 person years [ptpy] and abatacept at 6 of 69 patients or 9 ptpy and lower for anti-TNF agents [etanercept 1, adalimumab 2] at 3 of 255 or 1 ptpy).