The use of interleukin 23 inhibitors in patients with chronic hepatitis B infection: A case series

Peter Yi Ch'en, BS,[a] Sterling Farrer, DO,[b] Lauren Miranda-Cacdac, BA,[c] and Eingun James Song, MD, FAAD[d]

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INTRODUCTION

Although topical therapies remain the mainstay of psoriasis treatment, escalation to systemic therapies is often required for severe or recalcitrant cases. Because of the immunosuppressive nature of some of these medications, patients with chronic infections pose a therapeutic challenge. Chronic hepatitis B virus (HBV) infection is of particular interest because the use of certain biologics can increase the risk of viral reactivation and consequent liver damage. In particular, the use of tumor necrosis factor-alfa (TNF-α) blockers for plaque psoriasis has been widely observed to increase the likelihood of chronic HBV reactivation.[1] There is substantial evidence that TNF-α plays a role in suppressing viral replication, and thus its downregulation may lead to HBV reactivation.[2] However, newer biologic agents that are more targeted may be safer to use in patients with psoriasis and chronic HBV. There are limited data regarding the treatment of this population because chronic HBV is generally an exclusion criterion in clinical trials. There have been several cohort studies that have suggested interleukin 17 (IL-17) inhibitors have a lower risk of HBV reactivation than TNF-α inhibitors.[3,4] We have previously reported the successful treatment of plaque psoriasis in a 13-year-old woman with chronic HBV using guselkumab, an IL-23p19 inhibitor.[5] Here, we report the successful treatment of 3 patients with plaque psoriasis and chronic HBV using 3 different IL-23p19 inhibitors—risankizumab, guselkumab, and tildrakizumab. Baseline demographics and treatment history of each patient is presented in Table I.

Abbreviations used:

ALT:	alanine aminotransferase
AST:	aspartate aminotransferase
BSA:	body surface area
HBV:	hepatitis B virus
IL:	interleukin
PGA:	physician global assessment
TNF-α:	tumor necrosis factor-alfa

CASE 1—GUSELKUMAB

A 14-year-old Guatemalan woman presented to our dermatology clinic with severe generalized plaque psoriasis primarily involving her scalp, forehead, elbows, abdomen, and shins. She was previously treated with ultrapotent topical steroids, methotrexate, and ustekinumab without sufficient improvement.

At the initial presentation, she had an affected total body surface area (BSA) of 7% and a physician global assessment (PGA) score of 3. She had tested positive for hepatitis B surface antigen and hepatitis B core IgG antibody in the past. Her HBV DNA load at baseline was 1.5 IU/mL (log10). Baseline liver function tests results showed normal aspartate aminotransferase (AST), 36 and elevated alanine aminotransferase (ALT), 59. Given the laboratory test results, she was considered to be in a chronic inactive carrier state for HBV.

From the Albert Einstein College of Medicine, Bronx, New York[a]; Silver Falls Dermatology, Salem, Oregon[b]; A.T. Still University-School of Osteopathic Medicine in Arizona, Mesa, Arizona[c]; and North Sound Dermatology, Mill Creek, Washington.[d]

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Correspondence to: Peter Ch'en, BS, Albert Einstein College of Medicine, 1945 Eastchester Road, Apt 16H, Bronx, NY10461. E-mail: peter.chen@einsteinmed.edu.

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Table I. Demographics and treatment history

Variable	Case 1	Case 2	Case 3
Age (y) at initial visit	14	49	62
Sex	F	M	M
Fitzpatrick skin type	5	4	4
IL-23p19 inhibitor	Guselkumab	Risankizumab	Tildrakizumab
Past treatments	- Ustekinumab - Methotrexate - Clobetasol 0.05% spray - Desonide 0.05% cream	- Clobetasol 0.05% cream, and solution - Ketoconazole 2% shampoo - Phototherapy	-Triamcinolone acetonide 0.1% cream
Baseline: BSA/PGA	7%/3	6%/4	50%/4
Posttreatment: BSA/PGA	2%/2	0%/0	0%/0
Wks on Treatment	39 wks	72 wks	62 wks

BSA, Body surface area; *PGA*, physician global assessment.

Table II. Guselkumab laboratory parameters of interest

Wk(s)	AST (IU/L)	ALT (IU/L)	HbsAg	Anti-HBs	Anti-HBc Total	Anti-HBc, IgM	HBV DNA log10 (IU/mL)
(−) 53[†]	24	23	Positive	N/A	Positive	N/A	3.4
(−) 26[†]	51	77	N/A	N/A	N/A	N/A	3.4
0	36	59	N/A	N/A	N/A	N/A	1.5
11	26	42	Positive	N/A	N/A	N/A	Not detectable
42*	80	71	Positive	N/A	N/A	N/A	2.5
114*	23	40	N/A	N/A	N/A	N/A	Not detectable

ALT, Alanine aminotransferase; *AST*, aspartate aminotransferase; *anti-HBs*, hepatitis B surface antibody; *anti-HBc Total*, hepatitis B core antibody total; *anti-HBc, IgM*, hepatitis B core IgM antibody; *HBV*, hepatitis B virus; *HbsAg*, hepatitis B surface antigen; *IgM*, immunoglobulin M.

*Postguselkumab treatment.

[†](−) denotes weeks before the start of guselkumab treatment.

Despite 28 weeks of ustekinumab therapy, the patient still had 3% BSA/PGA 3 with residual plaques on the scalp and forehead. Because the only other biologic that was approved for her age at the time of treatment was etanercept, the decision was made to use off-label guselkumab with concurrent entecavir 0.5 mg daily.

After 36 weeks on guselkumab, her BSA was 2% with a PGA of 2. She continued to have low-grade transaminitis (ALT, 71 and AST, 80) but her HBV DNA load remained low. Guselkumab treatment was stopped at 39 weeks because of limited improvement and she switched to ixekizumab, which she eventually achieved PGA 0 on. Refer to Table II for laboratory test results.

CASE 2—RISANKIZUMAB

A 49-year-old Chinese man presented to our dermatology clinic with severe generalized plaque psoriasis, affecting the scalp, elbows, arms, abdomen, and knees. He was previously treated with ketoconazole shampoo, ultrapotent topical steroids, and phototherapy without satisfactory improvement.

At the initial presentation, the BSA was 6% with a PGA score of 4.

He tested positive for hepatitis B surface antigen and total hepatitis B core IgG antibody. He tested negative for hepatitis B surface antibodies and had an undetectable viral load. Liver function tests were mildly increased (AST, 65 and ALT, 92), which was attributed to nonalcoholic fatty liver disease. After consultation with his gastroenterologist, he was started on risankizumab 150 mg subcutaneously every 12 weeks after the induction dose and concurrent entecavir 0.5 mg daily.

After 28 weeks of treatment with risankizumab monotherapy, the patient had achieved PGA 0. Laboratory test results at the 70-week mark remained normal, with an undetectable HBV DNA level. Refer to Table III for laboratory test results.

CASE 3—TILDRAKIZUMAB

A 62-year-old Vietnamese man presented to our dermatology clinic with severe widespread plaque psoriasis primarily on the arms, legs, and trunk. He was previously treated with topical steroids without

Table III. Risankizumab laboratory parameters of interest

Wk(s)	AST (IU/L)	ALT (IU/L)	HbsAg	Anti-HBs	Anti-HBc total	Anti-HBc, IgM	HBV log10 DNA (IU/mL)
0	65	92	Positive	Negative	Positive	Negative	N/A
70	35	56	N/A	N/A	N/A	N/A	Not detected

ALT, Alanine aminotransferase; *AST*, aspartate aminotransferase; *anti-HBs*, hepatitis B surface antibody; *anti-HBc total*, hepatitis B core antibody total; *anti-HBc, IgM*, hepatitis B core IgM antibody; *HbsAg*, hepatitis B surface antigen; *HBV*, hepatitis B virus.

Table IV. Tildrakizumab laboratory parameters of interest

Wk(s)	AST (IU/L)	ALT (IU/L)	HbsAg	Anti-HBs	Anti-HBc total	Anti-HBc, IgM	HBV DNA log10 (IU/mL)
0	19	17	Positive	Negative	Positive	N/A	1.301
46	21	22	Positive	Negative	Positive	Negative	Not detected

ALT, Alanine aminotransferase; *AST*, aspartate aminotransferase; *anti-HBs*, hepatitis B surface antibody; *anti-HBc total*, hepatitis B core antibody total; *anti-HBc, IgM*, hepatitis B core IgM antibody; *HbsAg*, hepatitis B surface antigen; *HBV*, hepatitis B virus.

satisfactory improvement because phototherapy was not an option because of insurance limitations.

At the initial presentation, the patient had an affected BSA of 50% and a PGA score of 4.

His baseline laboratory test results were notable for positive hepatitis B surface antigen and total hepatitis B core IgG antibody. He tested negative for hepatitis B surface antibodies and his HBV DNA load was 1.301 IU/mL (log10). Liver function tests were normal (AST, 19 and ALT, 17). He was started on tildrakizumab 100 mg subcutaneously every 12 weeks after the induction dose and concurrent entecavir 0.5 mg daily.

At 17 weeks, the patient had achieved complete skin clearance which was maintained through 42 weeks. Laboratory test results at the 46-week mark remained within normal limits and his HBV viral load was undetectable. Refer to Table IV for laboratory test results.

DISCUSSION

Over 250 million people worldwide are infected with HBV.[6] Currently, there is a dearth of information regarding systemic immunosuppressant use in patients with chronic active hepatitis B infections. Most of the published literature has been on TNF-α and IL-12/IL-23 inhibitors. TNF-α is theorized to activate an antiviral pathway that causes degradation of covalently closed circular DNA in HBV-infected cells and therefore, blocking this pathway may lead to a higher HBV replication state and subsequent HBV reactivation.[7] Similarly, IL-12 is reported to play a role in the elimination of intracellular pathogens, such as HBV.[8]

Guselkumab, risankizumab, and tildrakizumab specifically target the p19 subunit that is found in IL-23, whereas ustekinumab targets the IL-12p40 subunit that is found on both IL-12 and IL-23. The usage of IL-23p19 inhibitors avoids the downregulation of the IL-12 pathway, which may decrease the likelihood of HBV reactivation.

The limitations of this study include a small sample size. Also, all 3 patients had chronic inactive hepatitis B, which is considered to be a relatively lower risk for reactivation. It is unknown how a patient with signs of more active disease, including higher viral load, positive hepatitis B envelope antigen, and high-grade transaminitis, would have responded to therapy. Larger studies are still required to further define the safety profile of these IL-23p19 inhibitors in patients with chronic HBV; however, the lack of HBV reactivation over a cumulative follow-up of 173 weeks with significant skin clearance in all 3 of our patients suggests that targeting this pathway is particularly attractive in this patient population.

The strength of this study is the diversity of the IL-23 inhibitors used as well as the exclusive skin color of the patient population. There is a paucity of publications that have studied the safety and efficacy of biologic therapy in patients with darker Fitzpatrick skin types; however, dedicated studies are now underway and will hopefully encourage further research in this area of need.

Conflicts of interest

None disclosed.

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