

The use of ustekinumab and guselkumab in a pediatric psoriasis patient with active hepatitis B infection



Eingun James Song, MD, FAAD,^a Patrick Whitman, DO,^b and Jonmichael Samsel, BS^c
Mill Creek, Washington; Salem, Oregon; and Blacksburg, Virginia

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INTRODUCTION

While the majority of patients with psoriasis will be treated with topical agents, a significant number will still require escalation to systemic therapy. The choice of systemic therapy will often be dictated by the presence and absence of certain comorbidities. Comorbid active hepatitis B virus (HBV) infection remains therapeutically challenging given the potential for reactivation and subsequent liver damage with the use of biologic agents.¹ The likelihood of reactivation depends primarily on the phase of HBV infection and the mechanism of action of the biologic. Whereas the reactivation risk is relatively low in patients with occult or resolved HBV infection, the risk is significantly increased with active HBV infection. Because tumor necrosis factor- α plays an important role in anti-viral defense, the use of tumor necrosis factor- α inhibitors appears to pose the greatest risk for reactivation.² Several published studies with small sample sizes have shown the relative safety of ustekinumab in patients with HBV infection.^{3,4} There is even more limited data for the newer biologics given that these patients are generally excluded from clinical trials. A single case of a 48-year-old man with active HBV successfully treated with secukinumab has been reported.⁵ Herein, we report a pediatric psoriasis patient with active HBV treated successfully with guselkumab, an interleukin (IL)-23p19 inhibitor.

CASE REPORT

A 13-year-old girl presented to our dermatology clinic for severe widespread plaque psoriasis. The patient was adopted from Guatemala at 6 months of

Abbreviations used:

ALT:	alanine aminotransferase
AST:	aspartate aminotransferase
BSA:	body surface area
HBV:	hepatitis B virus
IGA:	investigator global assessment
IL:	interleukin

age, so any previous medical and family history was unknown. She was previously treated with ultra-potent topical steroids and methotrexate without sufficient improvement. At initial presentation, the patient had an affected body surface area (BSA) of 12% and a static investigator global assessment (IGA) score of 3. Affected areas included her scalp, forehead, ears, elbows, arms, abdomen, back, and knees.

The patient tested positive for hepatitis B surface antigen, hepatitis B core antibodies, and hepatitis B envelope antibodies, but negative for hepatitis B envelope antigen and hepatitis B surface antibodies. Her HBV DNA load was 3.4 IU/mL (log 10). Liver function tests (aspartate aminotransferase [AST], 24; alanine aminotransferase [ALT], 23) and α -fetoprotein were within the normal ranges. Given the absence of hepatitis B in the members of her adopted family, the patient most likely had congenitally acquired hepatitis B and was considered to be in a chronic inactive carrier state.

After consultation with a hepatologist, it was decided to initiate treatment with ustekinumab 45 mg, based on her weight of 160 lbs, along with entecavir 0.5 mg daily. Six weeks after her first dose of ustekinumab, she had a slight increase in her liver

From the North Sound Dermatology, Mill Creek,^a Silver Falls Dermatology, Salem,^b and Edward Via College of Osteopathic Medicine, Blacksburg.^c

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Correspondence to: Patrick Whitman, DO, Silver Falls Dermatology, 1793 13th St SE, Salem, OR 97302. E-mail: pwhitman@silverfallsderm.net.

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Table I. Body surface area and static investigator global assessment score*

Week(s)	Body surface area (%) [§]	Investigator global assessment [§]
0 [†]	12	3
4	7	3
16	7	3
28 [‡]	7	3
32	3	3
40	1	2
48	1	2

*5-point investigator global assessment score.

[†]First dose of ustekinumab administered.

[‡]First dose of guselkumab administered.

[§]Concomitant ultrapotent topical steroids were used.

enzymes (AST, 51; ALT, 77). Her viral load decreased to 2.4 IU/mL (log 10), and no abdominal pain, jaundice, itching or flu-like symptoms were reported or observed. At her 22-week follow-up with hepatology, her liver enzymes stabilized (AST, 36; ALT, 59), and her viral load decreased even further to 1.5 IU/mL (log 10).

At her 28-week follow-up with dermatology, the patient still had 7% BSA and an IGA 3, with significant involvement of her scalp, forehead, and ears. The patient was subsequently switched to guselkumab 100 mg, a selective IL-23p19 antagonist, given its favorable side effect profile and proven efficacy in inadequate ustekinumab responders.⁶ At her 4-week follow-up after her first injection with guselkumab, her BSA had decreased to 3% with an IGA 3. Of note, her forehead plaques had completely cleared. By week 12, the patient was down to 1% BSA with an IGA 2 (Table I). Her liver enzymes remained stable (AST, 26; ALT, 42), and viral load was now undetectable (Table II).

DISCUSSION

The safety profiles of biologics continue to improve in adult populations, prompting further consideration to be given to expanding their utility in the pediatric population. One area of concern is the reactivation of infectious processes such as HBV upon initiating treatment with immunosuppressing agents. Data mainly exists only for traditional therapies (cyclosporine, etanercept, adalimumab, infliximab, ustekinumab), whereas little is known of the risk involved with newer agents that target IL-23p19 like guselkumab.

Experimental models have shown tumor necrosis factor- α to play a critical role in HBV clearance in infected hepatocytes.⁷ IL-12 is important in activating a cellular immune response that targets intracellular

Table II. Laboratory parameters of interest*

Week(s)	AST (U/L)	ALT (U/L)	HBV DNA load (IU/mL [log 10])
0 [†]	24	23	3.4
6	51	77	2.4
22	36	59	1.5
28 [‡]	NR	NR	NR
40	26	42	<10 [§]

ALT, Alanine aminotransferase; AST, aspartate aminotransferase; HBV, hepatitis B virus; NR, not recorded.

*Concomitant entecavir 0.5 mg once daily.

[†]First dose of ustekinumab administered

[‡]First dose of guselkumab administered

[§]Quantifiable range for lab is >10 IU/mL

pathogens, and unnecessary inhibition may therefore increase the risk of viral reactivation.⁸ Agents such as guselkumab, which targets the p19 subunit specific to IL-23, avoid this interaction with IL-12 and may lower the risk of HBV reactivation. Duncan et al reported a single case of a 46-year-old man with isolated HBV core antibody positivity who was successfully treated with guselkumab.⁹ While larger studies are needed to further explore the safety profile of guselkumab in the treatment of pediatric patients with chronic HBV infection, the lack of hepatitis B reactivation and evident improvement of our 13-year-old patient with severe, recalcitrant plaque psoriasis suggests it may be an effective therapeutic option in this population. To our knowledge, this is the first reported case of the successful use of guselkumab in a pediatric psoriasis patient with active HBV.

Conflicts of interest

Dr. Song has been a consultant for Janssen and is a speaker for AbbVie, SUN pharma, UCB, Amgen, Novartis, and Eli Lilly. Authors Whitman and Samsel have no conflicts of interest to declare.

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