

Efficacy and Safety of Tildrakizumab in a Patient with Chronic HBV Infection

Luca Potestio , Ilaria Piscitelli, Gabriella Fabbrocini, Fabrizio Martora , Angelo Ruggiero , Matteo Megna*

Section of Dermatology, Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy

*These authors contributed equally to this work

Correspondence: Angelo Ruggiero, Section of Dermatology, Department of Clinical Medicine and Surgery, University of Naples Federico II, Via Pansini, 5, Naples, 80131, Italy, Tel +39 - 81 -7462457, Fax +39 - 81 - 7462442, Email Angeloruggiero1993@libero.it

Abstract: The introduction of biologic drugs revolutionized the management of moderate-to-severe forms of psoriasis. However, safety concerns still remain, particularly on patient affected by opportunistic infections. In this scenario, the safety of biologic drugs in patient with HBV infection is debated. Globally, screening for hepatitis before starting biological treatment is mandatory as well as a referral to an infectivologist and eventual prophylactic management should be evaluated case by case, also considering risk factors. On the one hand, the use of anti-Tumor Necrosis Factor seems to increase the risk of HBV reactivation, conversely, the use of recently approved classes of biologics [anti-interleukin (IL) 17 and anti-IL23] seems to have a lower risk of HBV reactivation. However, the evidence on the safety of anti-IL23 drugs in patients affected by HBV is scant, particularly for patients undergoing treatment with tildrakizumab. Herein, we report the first case of a female patient affected by moderate-to-severe psoriasis and with chronic HBV infection undergoing prophylaxis, successfully treated with tildrakizumab without reporting hepatitis reactivation. Even if limited, our case seems to confirm available evidence about the safety of anti-IL23, particularly tildrakizumab, on patients with chronic HBV infection undergoing prophylaxis.

Keywords: psoriasis, HBV infection, biologic therapy, anti-IL23, tildrakizumab

Introduction

Psoriasis is a chronic inflammatory skin condition affecting up to 3% of the worldwide population.¹ Despite the major knowledge on psoriasis pathogenesis led to the development of new effective and safe drugs, such as biologics and small molecules, the management of this condition may be still challenging.² Even if the introduction of biologics showed promising results in terms of effectiveness and safety, particularly for the most recently approved drug classes [anti-interleukins (IL) 17 and 23],^{3–5} several safety concerns still remain, particularly on the use of biologics in patients affected by chronic bacterial or viral infections.⁶

Hepatitis B is a type of viral hepatitis caused by the Hepatitis B virus (HBV).⁷ It can cause both acute and chronic infection and about 30% of worldwide population shows serological evidence of current or past infection.⁷

In this scenario, the immunomodulant nature of biologics makes patients with chronic infections a therapeutic challenge.⁸ Even if limited, data on the use of biologic drugs in patients affected by HBV are conflicting.⁸ On the one hand, the use of anti-“Tumor Necrosis Factor” α (anti-TNF α) seems to increase the risk of HBV reactivation,^{6,9} conversely, the use of recently approved classes of biologics anti-IL-17 and anti-IL-23 seems to have a lower risk of HBV reactivation.^{10–19}

The screening for hepatitis B is a routine measure before starting a treatment with biologics is recommended by current guidelines.²⁰ Patient with HBsAg positivity always require antiviral prophylaxis. A multidisciplinary approach, involving the infectivologist and/or hepatologist, in order to evaluate case by case an eventual prophylactic treatment is mandatory.^{21,22}

Tildrakizumab, a humanized monoclonal antibody specifically targeting the p19 subunit of IL-23, is the latest available anti-IL-23 on the Italian market.²³ Even if its effectiveness and safety have been widely reported in both clinical trials and real-life experiences,^{24–26} the safety of this drug in patients affected by HBV infection is lacking.

Case Report

Herein, we report the case of a 45-year-old female patient referring to our Clinic in August 2021 for a worsening of its psoriasis disease. Clinical examination showed the presence of erythematous-desquamative plaques on the trunk, upper and lower limbs. Globally, the patient had a Psoriasis Area Severity Index (PASI) of 15.6, a Body Surface Area (BSA) of 18%, and a Dermatology Life Quality Index (DLQI) of 22. We considered that she was suffering from plaque psoriasis for 10 years. Previous psoriasis treatment included topical therapies (corticosteroids, calcipotriol/betamethasone) and narrow-band ultraviolet B. Screening for comorbidities was negative, except for mild hypertension, not requiring oral medications.

Screening for biologic drug was performed due to psoriasis severity, the impact on the patient's quality of life as well as patient's refusal to conventional therapies for safety concerns. However, blood examination showed positive results for HBsAg and HBcAb while HBsAb was negative. Moreover, the patient revealed that she did not receive HBV vaccination. Thus, HBV-DNA quantitative test was performed showing a negative result. A diagnosis of chronic HBV infection was carried out. The patient denied having carried out transfusions as well as the use of injection drugs and the familiarity for HBV infection. Thus, the cause of HBV exposure remained unknown. Subsequently, the patient was referred to the infectiologist, who prescribed prophylaxis with entecavir 0.5 mg once daily for at least two weeks before starting biologic treatment, with anti-IL-17 or anti-IL-23 classes as preferred ones. Tildrakizumab was chosen, due to the lowest number of administrations required among biologics (1 s.c. injection every 12 weeks after the induction phase), according to the patient's requests and started at labeled dosage (100 mg at weeks 0, 4, and every 12 weeks thereafter). At 4-week follow-up, PASI100 (reduction of PASI of 100%) response was rapidly reached, with a complete skin clearance (Figure 1). Hepatitis B markers and transaminases were evaluated at week 4, 16, and 28, without showing signs of HBV reactivation.



Figure 1 Patient at baseline (A–D) and after 4 weeks (E–H) of treatment with tildrakizumab.

Discussion

The introduction of biologic drugs revolutionized the management of psoriasis.^{27–29} However, safety concerns may still remain, particularly on patient affected by chronic infections. In this scenario, the safety of biologic drugs in patient with HBV infection is debated. In particular, the use of anti-TNF α seems to increase the risk of HBV reactivation,^{6,9} while the use of recently anti-IL-17 and anti-IL-23 seems to have a lower risk of HBV reactivation.^{10–19}

Globally, screening for hepatitis before starting biological treatment is mandatory as well as a referral to an infectivologist and eventual prophylactic management should be evaluated case by case, also considering risk factors.^{20,21} Patients with a resolved HBV infection do not require specialist follow-up while prophylactic treatment is necessary in patient with HBsAg positivity.^{20,21} Of note, patients with HBcAb positivity and HBsAg negativity requires personalized management.^{20,21} In these patients, monitoring of transaminases and viral markers with or without antiviral prophylaxis can be chosen following negativity or positivity of HBV-DNA, also considering patient's risk factors and after referral to the infectivologist and/or hepatologist.^{20,21} HBV prophylaxis should be started at least 2 weeks before the introduction biological therapy and continued up to 6 months after biologic discontinuation.^{20,21}

Currently, the evidence on the safety of anti-IL-23 drugs in patients affected by HBV is scant. In particular, in literature, there are only three cases of a patient with HBV history treated with tildrakizumab.^{18,19} Gargiulo et al reported two male patients with HBV history (patient 1: HBcAb positive, HBsAb negative, HBsAg negative, HBV-DNA undetectable; patient 2: HBcAb positive, HBsAb positive, HBsAg negative, HBV-DNA undetectable) successfully treated with tildrakizumab without receiving prophylaxis for HBV infection and monitoring HBV reactivation up to 52 weeks.¹⁸ Similarly, Ch'en et al reported the case of a man with HBcAb positive, HBsAb negative, HBsAg positive and HBV-DNA undetectable successfully treated with tildrakizumab and with a follow-up of 42 weeks.¹⁹

To the best of our knowledge, our case is the first reporting a female patient affected by moderate-to-severe psoriasis and with chronic HBV infection undergoing prophylaxis, successfully treated with tildrakizumab without reporting hepatitis reactivation. Even if limited, our case seems to confirm available evidence about the safety of anti-IL-23, particularly tildrakizumab, on patients with chronic HBV infection undergoing prophylaxis.

Conclusion

Psoriasis management is moving towards a personalized approach.³⁰ In this context, the treatment of patients with a positive hepatitis B screening should be evaluated case by case. Even if limited, our case suggests the safety of tildrakizumab also in patients with chronic HBV infection undergoing prophylaxis, suggesting this drug as a valuable option in these subjects. Certainly, further studies are needed to point out a tailored-tail approach in this class of patients.

Ethics Statement

The patient signed a written consent form for the publication of medical data. The consent for the publication of images was included with the patient's consent. Institutional approval was not required.

Consent Statement

Informed consent was provided by the patient for publication of the case.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

There is no funding to report.

Disclosure

The authors declare no conflicts of interest in this work.

References

- Gudjonsson JE, Elder JT. Psoriasis: epidemiology. *Clin Dermatol*. 2007;25(6):535–546. doi:10.1016/j.clindermatol.2007.08.007
- Megna M, Potestio L, Fabbrocini G, et al. Treating psoriasis in the elderly: biologics and small molecules. *Expert Opin Biol Ther*. 2022;22(12):1503–1520. doi:10.1080/14712598.2022.2089020
- Megna M, Potestio L, Ruggiero A, et al. Guselkumab is efficacious and safe in psoriasis patients who failed anti-IL17: a 52-week real-life study. *J Dermatolog Treat*. 2022;33(5):2560–2564. doi:10.1080/09546634.2022.2036674
- Valenti M, Narcisi A, Pavia G, Gargiulo L, Costanzo A. What Can IBD specialists learn from IL-23 trials in dermatology? *J Crohns Colitis*. 2022;16(Supplement_2):ii20–ii29. doi:10.1093/ecco-jcc/ijac023
- Megna M, Potestio L, Camela E, et al. Ixekizumab and brodalumab indirect comparison in the treatment of moderate to severe psoriasis: results from an Italian single-center retrospective study in a real-life setting. *Dermatol Ther*. 2022;35(9):e15667. doi:10.1111/dth.15667
- Ryu HH, Lee EY, Shin K, et al. Hepatitis B virus reactivation in rheumatoid arthritis and ankylosing spondylitis patients treated with anti-TNFalpha agents: a retrospective analysis of 49 cases. *Clin Rheumatol*. 2012;31:931–936. doi:10.1007/s10067-012-1960-1
- Trépo C, Chan HL, Lok A. Hepatitis B virus infection. *Lancet*. 2014;384(9959):2053–2063. doi:10.1016/S0140-6736(14)60220-8
- Nicoletta B, Alessandra N, Nevena S, et al. Management of psoriatic patients in biologic treatment associated with infectious comorbidities. *Postepy Dermatol Alergol*. 2020;37(3):417–421. doi:10.5114/ada.2020.96155
- Perez-Alvarez R, Diaz-Lagares C, Garcia-Hernandez F, et al. Hepatitis B virus (HBV) reactivation in patients receiving tumor necrosis factor (TNF)-targeted therapy: analysis of 257 cases. *Medicine*. 2011;90:359–371. doi:10.1097/MD.0b013e3182380a76
- Duncan JR, Orlowski TJ, Elewski BE. Safety of guselkumab in hepatitis B virus infection. *Dermatol Online J*. 2019;25(10). doi:10.5070/D32510045827
- Qin H, Liu N, Hu Y, et al. Safety and efficacy of secukinumab in psoriasis patients infected with hepatitis B virus: a retrospective study. *Eur J Dermatol*. 2022;32(3):394–400.
- Chiu HY, Hui RC, Huang YH, et al. Safety profile of secukinumab in treatment of patients with psoriasis and concurrent hepatitis B or C: a multicentric prospective cohort study. *Acta Derm Venereol*. 2018;98(9):829–834. doi:10.2340/00015555-2989
- Megna M, Fabbrocini G, Gallo L, et al. A case of chronic HCV infection reactivation in a psoriasis patient treated with guselkumab. *Curr Drug Saf*. 2022;17(4):390–392. doi:10.2174/1574886317666220307112926
- Koike Y, Fujiki Y, Higuchi M, et al. An interleukin-17 inhibitor successfully treated a complicated psoriasis and psoriatic arthritis patient with hepatitis B virus infection and end-stage kidney disease on hemodialysis. *JAAD Case Rep*. 2019;5(2):150–152. doi:10.1016/j.jdc.2018.11.016
- Megna M, Patruno C, Bongiorno MR, et al. Hepatitis virus reactivation in patients with psoriasis treated with secukinumab in a real-world setting of Hepatitis B or Hepatitis C infection. *Clin Drug Investig*. 2022;42(6):525–531. doi:10.1007/s40261-022-01163-5
- Peccerillo F, Odorici G, Pellacani G, et al. Secukinumab: a positive outcome in a patient with severe psoriasis and HBV-HCV co-infection. *Dermatol Ther*. 2018;31(4):e12601. doi:10.1111/dth.12601
- Song EJ, Whitman P, Samsel J. The use of ustekinumab and guselkumab in a pediatric psoriasis patient with active hepatitis B infection. *JAAD Case Rep*. 2020;14(8):37–39.
- Gargiulo L, Pavia G, Valenti M, et al. Safety of biologic therapies in patients with moderate-to-severe plaque psoriasis and concomitant viral hepatitis: a monocentric retrospective study. *Dermatol Ther*. 2022;12(5):1263–1270. doi:10.1007/s13555-022-00726-w
- Chen PY, Farrer S, Miranda-Cacdac L, et al. The use of interleukin 23 inhibitors in patients with chronic hepatitis B infection: a case series. *JAAD Case Rep*. 2022;30:1–4. doi:10.1016/j.jdc.2022.09.023
- Gisoni P, Fargnoli MC, Amerio P, et al. Italian adaptation of EuroGuiDerm guideline on the systemic treatment of chronic plaque psoriasis. *Ital J Dermatol Venerol*. 2022;157(1):1–78. doi:10.23736/S2784-8671.21.07132-2
- Piaserico S, Messina F, Russo FP. Managing psoriasis in patients with HBV or HCV infection: practical considerations. *Am J Clin Dermatol*. 2019;20:829–845. doi:10.1007/s40257-019-00457-3
- Strand V, Balsa A, Al-Saleh J, et al. Immunogenicity of biologics in chronic inflammatory diseases: a systematic review. *BioDrugs*. 2017;31:299–316. doi:10.1007/s40259-017-0231-8
- Ruggiero A, Camela E, Potestio L, et al. Drug safety evaluation of tildrakizumab for psoriasis: a review of the current knowledge. *Expert Opin Drug Saf*. 2022;21(10):1249–1257.
- Megna M, Potestio L, Fabbrocini G, et al. Tildrakizumab: a new therapeutic option for erythrodermic psoriasis? *Dermatol Ther*. 2021;34(5):e15030. doi:10.1111/dth.15030
- Megna M, Tommasino N, Potestio L, et al. Real-world practice indirect comparison between guselkumab, risankizumab, and tildrakizumab: results from an Italian 28-week retrospective study. *J Dermatolog Treat*. 2022;33(6):2813–2820. doi:10.1080/09546634.2022.2081655
- Ruggiero A, Potestio L, Cacciapuoti S, et al. Tildrakizumab for the treatment of moderate to severe psoriasis: results from a single center preliminary real-life study. *Dermatol Ther*. 2022;35(12):e15941. doi:10.1111/dth.15941
- Megna M, Cinelli E, Gallo L, et al. Risankizumab in real life: preliminary results of efficacy and safety in psoriasis during a 16-week period. *Arch Dermatol Res*. 2022;314(6):619–623. doi:10.1007/s00403-021-02200-7
- Yang K, Oak ASW, Elewski BE. Use of IL-23 inhibitors for the treatment of plaque psoriasis and psoriatic arthritis: a comprehensive review. *Am J Clin Dermatol*. 2021;22(2):173–192. doi:10.1007/s40257-020-00578-0
- Megna M, Potestio L, Ruggiero A, et al. Risankizumab treatment in psoriasis patients who failed anti-IL17: a 52-week real-life study. *Dermatol Ther*. 2022;35(7):e15524. doi:10.1111/dth.15524
- Camela E, Potestio L, Ruggiero A, et al. Towards personalized medicine in psoriasis: current progress. *Psoriasis*. 2022;1(12):231–250. doi:10.2147/PTT.S328460

Clinical, Cosmetic and Investigational Dermatology**Dovepress****Publish your work in this journal**

Clinical, Cosmetic and Investigational Dermatology is an international, peer-reviewed, open access, online journal that focuses on the latest clinical and experimental research in all aspects of skin disease and cosmetic interventions. This journal is indexed on CAS. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/clinical-cosmetic-and-investigational-dermatology-journal>