SKIN

IN-DEPTH REVIEWS

A Review of Biologics and Other Treatment Modalities in HIV-Associated Psoriasis

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ABSTRACT

Psoriasis poses a significant challenge to dermatologists, and comorbid conditions may further exacerbate that challenge. This is especially true for conditions that compromise a patient's immune status—such as human immunodeficiency virus (HIV)—as many of the most potent medications in the psoriasis armamentarium rely on immunomodulation. Moreover, patients with HIV are often not included in clinical trials because of their immunocompromised state. Therefore, most treatment recommendations rely on limited evidence derived from case reports and case series. This article reviews the current literature regarding management of HIV-associated psoriasis, with a particular focus on the relatively recent use of biologic agents in this population. Though there is a risk of compounding patients' suppressed immune status, the reports to date have demonstrated promise in treating HIV-associated psoriatic disease, and these agents may play a role in managing appropriately selected patients.

INTRODUCTION

Psoriasis is a common, chronic inflammatory condition caused by hyperproliferation and abnormal maturation of keratinocytes in the dermis. This results in erythematous plaques and papules with a silver scale, most commonly on the knees, elbows, scalp, and extensor surfaces of the limbs.
While mild to moderate psoriasis can be managed with topical treatments and phototherapy, more pervasive and severe disease often necessitates the use of systemic agents. Traditionally, acitretin, cyclosporine, and methotrexate were the only available systemic agents, but biologics are now becoming the first-line therapy for moderate to severe psoriasis.

Dermatologists are increasingly using biologics to treat psoriasis, owing to their high efficacy, but these potent medications are not administered without consideration of their risks. By nature of their immune-regulating molecular mechanisms, biologic agents often result in a relatively immunosuppressed state. Their use can be particularly challenging in patients who are immunosuppressed at baseline, such as transplant recipients or HIV patients. According to the NIH, about 2.2% of the United States population suffers from psoriasis, and this prevalence is similar if not

increased in HIV-positive patients. Moreover, psoriasis in patients suffering from HIV can be more severe, often correlating with the degree of a patient's immunosuppression.[1] Similarly, psoriatic arthritis is also noted to be more severe in this population.[2] Thus, these patients are often in need of the most efficacious systemic therapy to manage the severity of their psoriatic disease, yet their comorbid HIV-status relatively contraindicates one of the most potent classes of medication in the psoriasis armamentarium.

Data regarding the use of biologic agents in treating psoriasis in HIV patients is limited, as these patients are often not included in clinical trials. However, a continually growing number of case reports reveals an important role for these agents in treating HIV-associated psoriasis without significant detriment to patients' immune status. In this review, we discuss the challenges and considerations warranted in treating psoriasis in the HIV population, with a particular focus on biologics and the role they may play in treating psoriatic disease in HIV-positive patients.

HIV ASSOCIATED PSORIASIS & ANTI-RETROVIRAL THERAPY

New onset psoriasis may be the presenting feature of HIV infection. In patients already suffering from psoriasis, HIV infection may exacerbate their course, resulting in more chronic, severe, and recalcitrant disease.[3] Thus, diligent management by a dermatologist is of the utmost importance in caring for these patients.

Given the crucial role of T-cells in psoriasis pathogenesis[4] and the T-cell depletion that typically characterizes HIV infection, the correlative relationship between these two diseases seems somewhat paradoxical at first glance. However, it is suggested that CD8+ T-cells and the interferon-γ they produce are largely involved in psoriatic lesions[5,6] while CD4+ T-lymphocytes are those destroyed in HIV. The relative imbalance between CD4 and CD8 cells that results from HIV-mediated CD4+ T-cell destruction is suggested to play a role in HIV-associated psoriasis, among other changes in the lymphocyte population and the relative amounts of various cytokines they produce.[7]

Accordingly, by protecting CD4+ cells and mitigating the impact of this lymphocyte imbalance, antiretroviral therapy (ART) may be an essential component of an HIV-associated psoriasis treatment regimen. Moreover, ART may also have a secondary benefit by combating the effects of the pro-inflammatory cytokine TNF-α[2], believed to contribute to both HIV and psoriasis pathogenesis. Mechanistic hypotheses aside, while the nature of the biomolecular relationship between HIV and psoriasis continues to be explored, the clinical evidence is strongly suggestive of ART's utility in managing HIV-associated psoriasis. There are a notable number of reports supporting the use of ART in combating HIV-associated psoriasis[5,8,9,10,11], even administered as monotherapy.[12]

It should be noted that while ART has demonstrated success in treating HIV-associated psoriasis, the degree to which it responds varies from patient to patient. Nonetheless, patients whose psoriatic disease does not respond to antiretrovirals should strongly consider continuing on an optimal ART regimen under the care of a qualified infectious disease specialist. These medications are a cornerstone of HIV

management, and suppressing viral replication will help protect against the other pernicious ramifications of CD4+ T-cell depletion[13], including other HIV-related dermatologic conditions.

TOPICAL THERAPY

In addition to managing a patient's immune status, first-line treatment for mild HIV-associated psoriasis relies on targeted modalities such as topical agents, as is recommended in the general population. Commonly used medications include topical corticosteroids, calcipotriol[14], tazarotene, and a variety of formulations combining two of the abovementioned medications.[2] By nature of their limited and localized effects, topical medications pose little risk of compounding the immunosuppressive state in HIV. Overall, they can be safely used in this population and the adverse effect profile is the same as would be expected in the general population.

PHOTOTHERAPY

Limitations of topical therapy include lack of potency, limited field coverage, and inconvenience of application, especially if disease is more widespread. Accordingly, first-line treatment for moderate to severe psoriatic disease in patients who are averse to topical agents includes ultraviolet phototherapy, which inhibits cell proliferation and inflammation.[2,7] Reports of cases treated with psoralen and ultraviolet A (PUVA) or ultraviolet B (UVB) have demonstrated clinical improvement of HIV-associated psoriasis.[15,16,17,18] Although some animal and in vitro studies have noted possible activation of HIV by UV radiation[19], most reports suggest safe use in clinical practice without detriment to CD4+ T-cell counts or increases in viral load.[18,20]

TRADITIONAL SYSTEMIC AGENTS

Traditional systemic agents serve as possible options for patients intolerant of and/or unresponsive to ART, topical agents, and phototherapy. Traditional systemic agents include acitretin, methotrexate and cyclosporine. Among these agents, acitretin has the notable advantage of not causing or exacerbating immunosuppression. In a 20-week study of 11 HIV-positive patients with moderate to severe psoriasis treated with 100mg of acitretin, 4 patients achieved greater than 75% reduction in their Psoriasis Area and Severity Index (PASI) score, with another 2 achieving 51-75% reduction.[21] Side effect profile of retinoids, including dryness, hypertriglyceridemia and hepatotoxicity remains the same in HIV population, but clinicians should be especially vigilant in monitoring for pancreatitis, as its risk can be increased in combination with certain ART medications.[2]

Methotrexate has been used successfully to treat psoriasis for over half a century, but its immunosuppressive and hepatotoxic effects are of particular concern in the HIV population. A handful of case reports have documented effective treatment with methotrexate[22,23], but weighing the risks of immunosuppression against the therapeutic benefits is critical, as it has been notably associated with an increased risk of opportunistic infections.[23] Therefore, methotrexate is traditionally reserved for the most severe cases of HIV-associated psoriasis and should be used cautiously with close collaboration of a dermatologist and infectious disease specialist.[7,23]

Similarly, there are a handful of case reports of successful cyclosporine use in HIV patients with psoriasis. While cyclosporine is also immunosuppressive, there has been no notable increase in opportunistic infections with its use.[24,25] In fact, it is hypothesized that cyclosporine's ability to prevent T-cell activation may slow the destruction of immune cells by HIV.[25] Nonetheless, cyclosporine should be administered judiciously in this population. If given, trough serum levels should be monitored, especially in patients whose HIV regimens contain protease inhibitors or other medications used for opportunistic infection prophylaxis, as these agents can increase bioavailability of cyclosporine.[26]

BIOLOGICS

The past decade has seen a paradigm shift in psoriasis pathogenesis leading to development of highly efficacious and safe biologic agents. In the two decades since etanercept was first approved for treatment of rheumatoid arthritis, biologic agents have continually demonstrated efficacy in treating a wide variety of ailments across the vast spectrum of medical specialties.

However, their use in the HIV population is a more nuanced matter. Data regarding biologic use in HIV patients is scarce owing to their relative recency and lack of clinical trials, making blanket recommendation algorithms difficult to generate. Theoretically, anti-TNF-α biologic agents could have several desirable roles in HIV-associated psoriasis. In addition to contributing to the inflammation underlying psoriasis, TNF-α may also contribute to HIV disease progression. Though its exact role in HIV pathogenesis is not certain, TNF-α is overexpressed at all stages of HIV infection, and it is hypothesized to enhance HIV expression and replication through NF-κB signaling and assist in CD4+ lymphocyte programmed cell death.[27] It may also underlie the manifestations of fever, fatigue, and cachexia in the setting of advanced HIV/acquired immunodeficiency syndrome (AIDS).[7] TNF-α blockade can thus serve several purposes in patients with HIV-associated psoriasis.

On the other hand, TNF-α is also an essential inflammatory mediator of the immune system, and its suppression should be handled cautiously in the setting of systemic immunodysfunction secondary to HIV infection.[27] In the general population the iatrogenic TNF-α suppression resulting from these biologic agents leaves patients more susceptible to infectious insult, and it is not clear to what extent this phenomenon is potentiated in HIV-positive patients.

Despite these concerns, a growing number of case reports have demonstrated success with anti-TNF-α and other biologic agents in treating HIV-associated psoriasis. Moreover, the vast majority of cases demonstrate no detriment to CD4 lymphocyte counts, serum viral loads, overall immune status, and susceptibility to infection. In fact, CD4 count increased in a majority of patients following treatment. Tables 1-3 summarize the reports to date utilizing common anti-TNF-α therapies in treating refractory HIV-associated psoriasis.

Adalimumab is a human monoclonal antibody that binds and prevents the activity of solubilized and bound TNF-α (Table 1). A couple of case reports in just the last few years have demonstrated safe and successful use of this drug in treating psoriasis refractory to other modalities. Lindsey et al notes complete clearance of a

patient's psoriasis after failing numerous treatments.[1] The patient was treated for 30 months and experienced no adverse effects.

Etanercept is a soluble receptor fusion protein that binds solubilized TNF-α and prevents its interaction with cell surface receptors (Table 2); it has been used most frequently among the biologic agents in the HIV-associated psoriasis literature. Mikhail et al reported that not only did the psoriasis resolve in one patient, but his presenting leukocytosis and fevers normalized as well.[28] Linardaki et al and Di Lernia et al met similar success, notably without aggravating their respective patients' hepatitis C coinfection.[29,30] Bardazzi et al discusses the largest case series hitherto in the literature on biologic treatment of HIV-associated psoriasis, in addition to the longest follow-up.[31] He concludes that more evidence is necessary, but preliminary data support the use of these medications with appropriate monitoring. It is worth mentioning the report of fatal infection in the etanercept report by Aboulafia et al that ultimately resulted in the patient's death.[32]

Infliximab, is a chimeric monoclonal antibody that has higher affinity for TNF-α and hence a higher potency (Table 3).[33] Indeed, Cepeda et al demonstrated successful use of infliximab for treatment of psoriasis in HIV patients who insufficiently responded to etanercept.[34] Sellam et al similarly reported a few cases whose skin and debilitating psoriatic arthritis responded favorably upon addition of infliximab to their methotrexate regimen.[35]

As evidenced by these cases, the vast majority of patients responded well to biologics intervention, with no deleterious effect on CD4 count, viral load, or immune status.

In addition to the anti-TNF-α agents, other biologics also seem promising in HIV-associated psoriasis. Several reports cite successful use of ustekinumab, which was well-tolerated by patients (Table 4).

Ustekinumab targets other inflammatory immune-regulating cytokines, notably IL-12 and IL-23. Having agents with alternative molecular mechanisms and targets can be beneficial, as Wieder et al demonstrated treatment success using ustekinumab after failing several anti-TNF-α agents.[37] Saeki et al also administered ustekinumab after the patient did not respond to numerous medications, including adalimumab.[38] Similar to TNF-α inhibitors, however, ustekinumab should be reserved for severe cases, as IL-12 and IL-23 play a role in warding off opportunistic infections in the HIV population.[39]

Overall, while the success of biologics has been encouraging, due to the theoretical immunosuppressive risks, current recommendations favor their use only for cases that are unresponsive to other therapies.[2] Anti-TNF-α therapy may promote opportunistic infections and increase the risk of lymphoproliferative malignancies that result from HIV-induced immune-dysregulation, as well as possibly reactivating latent tuberculosis, a potential complication present even in the general immunocompetent population while on biologic agents.[42] Further research is necessary, and concomitant antiretroviral regimens are recommended to reduce the risk of developing complications during treatment with these potent agents.[2,7,35]

Table 1. Adalimumab

Report	Cohort	Treatment	Results
Lindsey et al.[1], 2014	• 49 y.o. male with PsO, PsA, HIV on ART • Minimally responsive to acitretin, phototherapy, and topical agents • CD4: 127 • VL: 14,649	• Loading dose of 80mg, followed by 40mg every other week • 30 months course	• Therapy yielded complete clearance of skin disease and near complete resolution of joints • Last viral load undetectable • Transient decrease in CD4 count managed with change in ART regimen
Bardazzi et al.[31], 2017	• 2 patients with HIV and moderate-to-severe PsO • Both failed CSA therapy • Patient 1 CD4: 472, not on ART • Patient 2 CD4: 725, on ART	• Loading dose of 80mg, 40mg at week 1, then 40mg every 2 weeks thereafter	• Both patients reached 75% reduction in PASI • No adverse effects, including infections • Transient, clinically insignificant reduction in CD4 • Patient 1 CD4: 456 • Patient 2 CD4: 800

Table 2. Etanercept

Report	Cohort	Treatment	Results
Aboulafia et al.[32], 2000	• 45 y.o. male with HIV on ART, PsO and debilitating PsA • Failed corticosteroids, hydroxychloroquine, minocycline • CD4: 20; VL: 14,000	• 25 mg twice weekly for 8 weeks	• Dramatic improvement of skin and joint disease • CD4 and viral counts remained stable • However, recurrent microbial infections requiring ABX led to cessation of therapy
Linardaki et al.[29], 2007	• 42 y.o. male with HIV on ART, HCV, PsO, PsA and hemophilia A • Failed MTX and CSA • CD4: 380; VL: 4,100	• 25 mg twice weekly for 2 years (ongoing)	• Complete remission of PsO within 1 month • No change in liver panel • CD4 > 450; VL: undetectable
Mikhail et al.[28], 2008	• 32 y.o. male with von Zumbusch pustular PsO, PsA, and HIV on ART • Failed topical	• 50 mg weekly (ongoing)	• Complete remission of skin within 4 weeks, though mild recurrence noted • CD4: 633; VL: undetectable • No infectious episodes

	treatment • CD4: 435; VL: < 75		
Di Lernia et al.[30], 2013	• 51 y.o. male with widespread PsO, HIV on ART, HCV, and alcoholism • Failed corticosteroids, acitretin, CSA, phototherapy • PASI: 13.4 • CD4: 200-499; VL: 7,930	• 50 mg twice weekly for 12 weeks, then 50 mg weekly • 132 weeks	• PASI reduced to 6.2 • CD4 remained stable; VL: undetectable • No significant infectious episodes • Mild relapses of PsO managed with topical therapy
De Simone et al.[6], 2016	• 50 y.o. male with PsO, HIV on ART, and HCV • Failed acitretin and topicals • Previous HBV infection • PASI: 24.2 • CD4: 445	• 50 mg twice weekly for 12 weeks, then 50 mg weekly • 6 months (ongoing)	• PASI reduced to 1.8 • No significant change in viral load, CD4 count, HCV viral load, and liver tests • No HBV reactivation • Mild relapses of PsO managed with topical therapy
Bardazzi et al.[31], 2017	• 4 patients with HIV and moderate-to-severe PsO • All failed CSA therapy • Patient 1 CD4: 486, not on ART • Patient 2 CD4: 1000, on ART • Patient 3 CD4: 265, on ART • Patient 4 CD4: 870, on ART	• 50 mg twice weekly for 12 weeks, then 50 mg weekly	• All patients reached 75% reduction in PASI • No adverse effects, including infections • Transient reduction in CD4 • Patient 1 CD4: 491 • Patient 2 CD4: 1000 • Patient 3 CD4: 350 • Patient 4 CD4: 885

Table 3. Infliximab

Report	Cohort	Treatment	Results
Bartke et al.[36], 2004	• 46 y.o. male with PsO, PsA, and HIV on ART • Failure of acitretin, MTX, corticosteroids, phototherapy and	• Infliximab 3 mg/kg loading does, at 2 weeks and 6 weeks	• Rapid response of skin and joints within 2 days • Serum HIV RNA remained undetectable during treatment • CD4: 107

	topicals • CD4: 193		
Sellam et al.[35], 2007	• Patient 1 had HIV on ART, PsO, PsA, debilitating arthritis, sacroilitis, 2º syphilis, and urethritis; PsO failed topicals, prednisone, and MTX • Patient 1 CD4: 425; VL: <50 • Patient 2 had HIV on ART, PsO, and PsA; PsO failed topicals, acitretin • Patient 2 CD4: 16; VL: 300,000	• Patient 1: 20mg at weeks 0, 2, 6 and then every 8 weeks • Total of 15 infusions • Received infliximab in addition to continued MTX • Patient 2: 2 mg/kg at weeks 0, 2, 6 and then every 8 weeks • Total of 25 infusions • Received infliximab in addition to continued MTX	• Both Patients had dramatic improvement of skin and joint disease • CD4 and VL largely unchanged • No adverse effects nor infectious episodes • Patient 1 experienced escape phenomenon, managed with increase in dosing frequency
Cepeda et al.[34], 2008	• Review of 8 HIV patients with rheumatic disease refractory to other treatment • Of 8, 3 had PsA and PsO • Patient 1 CD4: 750; VL: 22,148, not on ART • Patient 2 CD4: 268, VL: <50, on ART • Patient 3 CD4: 446, VL: < 400, on ART	• All psoriatic patients received some combination of biologic agents, adding to the regimen if the previous agent was insufficient (Etanercept 25 mg twice weekly, adalimumab 40 mg every other week, infliximab 5 mg/kg every 6-8 weeks) • While some had moderate responses to adalimumab and etanercept, response to infliximab was satisfactory across all patients • Treatment durations from 13-55 months	• All 3 PsO patients has near-complete clearing of skin • Patient 1 CD4: 741; VL: 54,227 • Patient 1 had transient increase in viral load responsive to temporary discontinuation and subsequent resumption of medication • Patient 2 CD4: 417; VL: <50 • Patient 2 had facial abscess responsive to ABX • Patient 3 CD4: 456; VL: <400

Table 4. Ustekinumab

Report	Cohort	Treatment	Results
Paparizos et al.[40], 2011	• 61 y.o. male with HIV and PsO • Unresponsive to ART, acitretin, phototherapy, MTX, CSA and etanercept • PASI: 11.9 • CD4: 429; VL: < 50	• 45 mg at weeks 0, 4, and 16 • Maintenance dose of 45 mg every 12 weeks (ongoing)	• PASI reduced to 2.7 at week 12 • Achieved 90% reduction by week 18 • Increase in CD4 • No adverse effects
Wieder et al.[37], 2014	• 39 y.o. male with HIV on ART, PsO, and PsA • Failed topicals, phototherapy, MTX, acitretin, hydroxyurea, etanercept, adalimumab, golimumab • PASI: 48 • CD4: 847; VL: undetectable	• Total of six 45-mg doses and one 90-mg dose • Erratic dosing schedule due to poor patient compliance	• PASI reduced to 19 • CD4 remained stable and viral load remained undetectable • Only notable side effect were genital condylomata acuminate, also present before treatment
Saeki et al.[38], 2015	• 47 y.o. male with HIV on ART and plaque PsO • Failed UVB, CSA, etretinate, adalimumab • PASI: 15.1; it decreased to 1.7 with adalimumab, but then increased to 9.7 • CD4: 602; VL: 29	• 45 mg every 3 months • 4 months (ongoing)	• Sustained PASI reduction to 0.8 • No adverse effects or change in CD4; VL < 20
Bardazzi et al.[31], 2017	• 4 patients with HIV and moderate-to-severe PsO • All failed CSA therapy • Patient 1 CD4: 523, on ART • Patient 2 CD4: 537, on ART • Patient 3 CD4: 186, on ART	• 45 mg at week 0 and week 4, and every 12 weeks thereafter	• All patients reached 75% reduction in PASI • Transient reduction in CD4 • Relapses were noted in 2 patients, managed by addition of phototherapy • Patient 1 CD4: 454 • Patient 2 CD4: 606 • Patient 3 CD4: 330 • Patient 4 CD4: 610

	• Patient 4 CD4: 535, on ART		
Carpentieri et al.[41], 2017	• 4 patients with HIV on ART and PASI values ranging from 16.2 to 19 • Failed traditional systemic therapies	• Not specified	• All experienced 75% reduction in PASI score • Well-tolerated • CD4 count increased in 3 patients

Abbreviations:
ABX = antibiotics, ART = Antiretroviral therapy, CD4 = CD4+ T-cell count in cells/mm^3, CSA = cyclosporine, HBV = hepatitis B virus, HCV = hepatitis C virus, MTX = methotrexate, PASI = psoriasis area severity index, PsO = psoriasis, PsA = psoriatic arthritis, VL = Viral Load in copies/mL, WBC = white blood cell count, y.o. = years old

CONCLUSION

Unfortunately, there are no randomized controlled trials assessing the efficacy and safety of commonly used psoriasis treatments in the HIV population. Most data are derived from anecdotal evidence such as case reports and case series.[2] With that said, these isolated reports, particularly those on biologics, are slowly coalescing into a more robust literature that can help guide clinicians in determining the most appropriate treatment for psoriasis in HIV-positive patients.

Psoriasis in its own right, particularly if severe, poses numerous challenges to dermatologists, and these are only compounded in the HIV population. Psoriasis in HIV patients should be treated as per guidelines of National psoriasis foundation and require the coordinated interdisciplinary care of dermatologists and infectious disease specialists.[2]

Additional studies are necessary to further explore the utility of these potent agents in treating HIV-associated psoriasis, but the reported cases thus far have been promising.

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References:

1) Lindsey SF, Weiss J, Lee ES, et al. Treatment of severe psoriasis and psoriatic arthritis with adalimumab in an HIV-positive patient. *J Drugs Dermatol*. 2014;13:869-871.
2) Menon K, Van Voorhees AS, Bebo BF Jr, et al. Psoriasis in patients with HIV infection: from the medical board of the National Psoriasis Foundation. *J Am Acad Dermatol.* 2010;62:291.
3) Mallon E, Bunker CB. HIV-associated psoriasis. *AIDS Patient Care & Stds*. 2000;14:239-46
4) Monteleone G, Pallone F, MacDonald TT, et al. Psoriasis: from pathogenesis to novel therapeutic approaches. *Clin Sci (Lond).* 2010;120(1):1-11.
5) Fischer T, Schwörer H, Vente C, et al. Clinical improvement of HIV-associated psoriasis parallels a reduction of HIV viral load induced by effective antiretroviral therapy. *AIDS*. 1999;13:628.
6) De Simone C, Perino F, Caldarola G, et al. Treatment of psoriasis with etanercept in immunocompromised patients: Two case reports. *J Int Med Res*. 2016;44:67-71.
7) Morar N, Willis-Owen SA, Maurer T, et al. HIV-associated psoriasis: pathogenesis, clinical features, and Management. *Lancet Infect Dis.* 2010;10:470-78.
8) Kaplan MH, Sadick NS, Wieder J, et al. Antipsoriatic effects of zidovudine in human immunodeficiency virus-associated psoriasis. *J Am Acad Dermatol.* 1989; 20:76.
9) Duvic M, Crane MM, Conant M, et al. Zidovudine improves psoriasis in human immunodeficiency virus-

positive males. *Arch Dermatol.* 1994;130:447.
10) Mahajan VK, Sharma NL, Sarin S, et al. Triple antiretroviral therapy improves psoriasis associated with human immunodeficiency virus infection: a clinico-therapeutic experience. *J Eur Acad Dermatol Venereol*. 2008;22:1017.
11) Mamkin I, Mamkin A, Ramanan SV. HIV-associated psoriasis. *The Lancet Infectious Diseases*. 2007;7:496.
12) Vittorio Luigi De Socio G, Simonetti S, Stagni G. Clinical improvement of psoriasis in an AIDS patient effectively treated with combination antiretroviral therapy. *Scand J Infect Dis.* 2006; 38:74.
13) Günthard HF, Saag MS, Benson CA, et al. Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults: 2016 Recommendations of the International Antiviral Society-USA Panel. *JAMA.* 2016;316:191.
14) Gray JD, Bottomley W, Layton AM, Cotterill JA, Monteiro E. The use of calcipotriol in HIV-related psoriasis. *Clin Exp Dermatol.* 1992;17:342-3.
15) Breuer-McHam J, Marshall G, Adu-Oppong A, et al. Alterations in HIV expression in AIDS patients with psoriasis or pruritus treated with phototherapy. *J Am Acad Dermatol.* 1999; 40:48.
16) Meola T, Soter NA, Ostreicher R, et al. The safety of UVB phototherapy in patients with HIV infection. *J Am Acad Dermatol.* 1993; 29:216.
17) Ranki A, Puska P, Mattinen S, et al. Effect of PUVA on immunologic and virologic findings in HIV-infected patients. *J Am Acad Dermatol.* 1991;24:404-10.
18) Pechère M, Yerly S, Lemonnier E, et al. Impact of PUVA therapy on HIV viremia: a pilot study. *Dermatology*. 1997; 195:84.
19) Cavard C, Zider A, Vernet M, et al. In vivo activation by ultraviolet rays of the human immunodeficiency virus type 1 long terminal repeat. *J Clin Invest.* 1990; 86:1369.
20) Fotiades J, Lim HW, Jiang SB, et al. Efficacy of ultraviolet B phototherapy for psoriasis in patients infected with human immunodeficiency virus. *Photodermatol Photoimmunol Photomed.* 1995;11:107-11.
21) Buccheri L, Katchen BR, Karter AJ, Cohen SR. Acitretin therapy is effective for psoriasis associated with human immunodeficiency virus infection. *Arch Dermatol.* 1997;133:711.
22) Masson C, Chennebault JM, Leclech C. Is HIV infection contraindication to the use of methotrexate in psoriatic arthritis? *J Rheumatol.* 1995;22:2191.
23) Maurer TA, Zackheim HS, Tuffanelli L, et al. The use of methotrexate for treatment of psoriasis in patients with HIV infection. *J Am Acad Dermatol.* 1994;31:372-5.
24) Allen BR. Use of cyclosporin for psoriasis in HIV-positive patient. *Lancet*. 1992;339:686.
25) Tourne L, Durez P, Van Vooren JP, et al. Alleviation of HIV-associated psoriasis and psoriatic arthritis with cyclosporine. *J Am Acad Dermatol*. 1997;37:501.
26) Rosmarin DM, Lebwohl M, Elewski BE, et al. Cyclosporine and psoriasis: 2008 National Psoriasis Foundation Consensus Conference. *J Am Acad Dermatol*. 2010; 62:838.
27) Calabrese LH, Zein N, Vassilopoulos D. Safety of antitumor necrosis factor (anti-TNF) therapy in patients with chronic viral infections: hepatitis C,

hepatitis B and HIV infection. *Ann Rheum Dis.* 2006;65:983-9

28) Mikhail M, Weinberg JM, Smith BL. 2008. Successful treatment with etanercept of von Zumbusch pustular psoriasis in a patient with human immunodeficiency virus. *Arch. Dermatol.* 144:453– 456.

29) Linardaki G, Katsarou O, Ioannidou P. Effective Etanercept Treatment for Psoriatic Arthritis Complicating Concomitant Human Immunodefiency Virus and Hepatitis C Virus Infection. *J Rheumatol*. 2007;34(6):1353-5.

30) Di Lernia F, Zoboli G, Ficarelli E. Long-term Management of HIV/Hepatitis C Virus Associated with Etanercept. *Indian J Dermatol Venereol Leprol*. 2013;79(3):444.

31) Bardazzi F, Magnano M, Campanati A, et al. Biologic Therapies in HIV-infected Patients with Psoriasis: An Italian Experience. *Acta Derm Venereol*. 2017;97(8):989-990.

32) Aboulafia DM, Bundow D, Wilske K, et al. Etanercept for the treatment of human immunodeficiency virus-associated psoriatic arthritis. *Mayo Clin Proc.* 2000; 75:1093.

33) Scallon B, Cai A, Solowski N, et al. Binding and functional comparisons of two types of tumor necrosis factor antagonists. *J Pharmacol Exp Ther*. 2002; 301:418-26.

34) Cepeda EJ, Williams FM, Ishimori ML, et al. The use of anti-tumour necrosis factor therapy in HIV-positive individuals with rheumatic disease. *Ann Rheum Dis.* 2008; 67:710.

35) Sellam J, Bouvard B, Masson C, et al. Use of infliximab to treat psoriatic arthritis in HIV-positive patients. *Joint Bone Spine.* 2007; 74:197.

36) Bartke U, Venten I, Kreuter A, et al. Human immunodeficiency virus-associated psoriasis and psoriatic arthritis treated with infliximab. *Br J Dermatol.* 2004; 150:784.

37) Wieder S, Routt E, Levitt J, et al. Treatment of Refractory Psoriasis with Ustekinumab in an HIV-Positive Patient: A Case Presentation and Review of the Biologic Literature. *Journal of Psoriasis and Psoriatic Arthritis*. 2014;20(3):96-102.

38) Saeki H, Ito T, Hayashi M, et al. Successful treatment of ustekinumab in a severe psoriasis patient with human immunodeciency virus infection. *J Eur Acad Dermatol Venereol*. 2015;29:1653-1655.

39) Yannam GR, Gutti T, Poluektova LY. IL-23 in infections, inflammation, autoimmunity and cancer: possible role in HIV-1 and AIDS. *J Neuroimmune Pharmacol.* 2012;7:95-112.

40) Paparizos V, Rallis E, Kirsten L, Kyriakis K. Ustekinumab for the treatment of HIV psoriasis. *J Dermatolog Treat*. 2012;23:398.

41) Carpentieri A, Silvestris R, Mascia P, et al. Evaluation of Efficacy and Safety of Biological Therapy in Patients with Psoriasis and HIV Coinfection. *J Am Acad Dermatol*. 2017;76(6):AB128.

42) Patel RV, Weinberg JM. Psoriasis in the Patient with Human Immunodeficiency Virus, Part 2: Review of Treatment. *Cutis*. 2008;82(3):202-10.