

Ustekinumab in the Treatment of Moderate to Severe Lower Extremity Psoriasis: A case series

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People that endure moderate to severe plaque psoriasis regularly report social and personal discomforts that impair their quality of life. When topical therapy, phototherapy, and common oral medications such as methotrexate and cyclosporine have failed, targeted systemic therapies (biologics) have become increasingly more common. The purpose of this case series was to examine the use of Ustekinumab (Stelara™) for moderate to severe plaque psoriasis to the lower extremity. Four individuals (3 males, 1 female) ranging in age from 16 to 66 years with a prior history of ineffective conventional therapy for their lower extremity plaque psoriasis were selected for this study. After reviewing each patient's medical history they received their first injections at the Temple University Foot and Ankle Institute during March-June 2010. Patient progress was based on the clinical PASI score (Psoriasis Area and Severity Index), which was calculated at each visit. After 16 weeks of treatment, clinical regression of moderate to severe lower extremity plaque psoriasis was noted in three of the four cases. At 52 weeks, it was noted in all four cases. Ustekinumab is a fully human monoclonal antibody that binds with high specificity and affinity to the shared cytokine subunit p40 found in both IL-12 and IL-23. In turn, this decreases the differentiation of T-cells, an important phase in the pathogenesis of psoriasis. This protein selective targeting allows the physician increased mechanisms to combat plaque recalcitrant palmo-plantar psoriasis. More importantly, it provides the patient a new and proven means to control their own quality of life when other psoriatic treatments have failed. In this case series, ustekinumab injections show an effective method of controlling chronic and recalcitrant plantar psoriasis.

Key Words: Psoriasis, Ustekinumab, Stelara, P40 Subunit, PASI

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Psoriasis is a chronic skin disorder affecting roughly 2% of the United States population, capable of causing social and psychological distress.¹ Chronic plaque psoriasis (psoriasis vulgaris) is the most common presentation of psoriasis.²

It represents over 80% of psoriatic cases and commonly presents as an erythematous plaque covered with a white silvery scale. Traditionally, these plaques are found on the scalp, elbows, knees, and lower back in a well-demarcated pattern.²⁻³ Presentations of psoriasis can be labeled as mild, moderate, and severe depending on the amount of body surface area affected.

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Ustekinumab (Stelara™) is a recently FDA approved “biologic” treatment for moderate to severe plaque psoriasis. It is a human monoclonal antibody that binds with a high specificity and affinity to the shared p40 subunit found in both IL-12 and IL-23; inhibiting their receptor-mediated signaling. Inhibition at this step in the inflammatory cascade enables suppression of both Th1 and Th17.^{4,5}

Two separate phase III trials found ustekinumab both safe and effective for moderate to severe psoriasis versus a placebo. A starter dose of 45mg is given subcutaneously in the physician’s office, followed by another 45mg dose at week four. Following the second dose, the injections are then given every twelve weeks. 90 mg doses are substituted at the same intervals for patients weighing greater than 100kg.⁶⁻⁷

The physician’s decision to treat a patient with a biologic such as ustekinumab will be based on the patient’s previous medication history and failure rate. Generally, patients with plaque psoriasis are treated with topical medications first (corticosteroids, Vitamin D analogs, moisturizers), followed by either administration of UVA (with psoralen) or narrowband UVB or oral medications (methotrexate, cyclosporine).⁸ Ultimately, if the patient failed most of the treatment regimens above, a biologic is further considered after reviewing the patient’s medical history and surface area of body affected.

When the patient has both hands and feet affected by plaque psoriasis, this only represents 2% body surface area; however, the quality of life affected by this presentation can be labeled as a moderate presentation of the disease and be eligible for biologic therapy.

To date, there are relatively few therapeutic clinical trials that address palmo-plantar psoriasis specifically. In this case series, four patients are reported who received injections of ustekinumab for their plantar plaque psoriasis after all conservative treatments failed.

Materials and Methods

Four individuals (3 males, 1 female) ranging in age from 16 to 66 years old received their first ustekinumab injections at the Temple University Foot and Ankle Institute during March-June 2010 and have continued to be monitored to the present day. Patient progress was based on the clinical picture, which included the PASI score (Psoriasis Area and Severity Index), that was calculated at each visit using an online calculator (<http://pasi.corti.li/>). This index measures the severity of erythema, induration, and desquamation of the specific area of the body being studied.⁹

Case 1:

A 66 year-old African American female presented with a three year history of palmo-plantar plaque psoriasis. She had been on the biologic efalizumab (Raptiva®) from 9/2008 to 4/2009 when it had been removed from the market. Efalizumab had effectively treated her palmo-plantar psoriasis. When she discontinued using efalizumab, she was managed topically with urea 40% emulsion (Umecta®), betamethasone/calcipotriene ointment (Taclonex®), and hyaluronic acid sodium salt 0.2% (Bionect®) for one year effectively until the fissures in the plantar aspect of her feet would no longer respond to the topical medications. (Fig. 1) The fissures caused her great pain and inability to be as active as she had been. The patient wished to retry a biologic medication. Appropriate blood work and TB skin testing were obtained prior to starting the medication.

The first dose of ustekinumab (45 mg) was injected in the office on 6/2010 followed by the second dose of 45 mg one month later and every three months thereafter. At 52 weeks, 6/2011, she reported that she felt the medication was working and no longer had painful fissures. (Fig. 2)



Figure 1 At baseline, first injection, PASI score: 7.0.



Figure 2 At 52 weeks, PASI score: 5.6.

Case 2:

A 43 year-old male presented to the surgical faculty for severe left ankle pain. It was determined a tibiototalocalcaneal (TTC) fusion should be performed, but the patient had a rash all over his body, especially over the proposed incision site. (Fig. 3) The patient was being managed for his psoriasis and psoriatic arthritis with etanercept (Enbrel®) for several years, but realized it was not helping his skin and joint inflammation anymore. The patient was referred to the main author for management of the psoriatic plaques in order to proceed with the proposed surgery. The patient discontinued the etanercept and agreed to try topical medications (triamcinolone 0.1% ointment and Neosalus™) for a few months.



Figure 3 At first injection, PASI score: 12.9.



Figure 4 At week 4, PASI score: 6.3.

The patient wished to retry a biologic because he wanted to have the TTC fusion done as soon as possible. After all of the appropriate tests were completed, the patient had the first dose of ustekinumab (90 mg) on 5/2010. The patient did extremely well and was able to have the surgery without complication. (Fig. 4) The patient's rheumatologist did add methotrexate to his ustekinumab regimen to continue control of the psoriatic arthritis. Case 2 achieved PASI-64 at 16 weeks and PASI-70 at one year.

Case 3:

A 63 year-old healthy, active male presented with a chronic, fissuring, and painful rash on his hands and feet, but also complained of lesions on his lower leg and scalp. After a biopsy confirmed it was plaque psoriasis, the patient was started on a topical treatment regimen consisting of calcipotriene (Dovonex®) cream and halobetasol ointment to be applied to the lower legs and feet.



Figure 5 At baseline, initial injection, PASI score: 13.2



Figure 7 At baseline, initial injection, PASI score: 8.8



Figure 6 At 52 weeks, PASI score: 0.6



Figure 8 At 52 weeks, PASI score: 0.8

This had mild effect. In 6 weeks when the patient's skin flared, he was placed on cyclosporine. This also had a mild effect on his skin disease. After the appropriate tests were completed, the patient began to receive ustekinumab injections on 3/2010. At the one-month follow-up, the patient was able to walk in regular shoes without pain due to the resolution of the fissures in his feet. He continues to receive ustekinumab injections to the present day. Case 3 achieved PASI-77 at 16 weeks and PASI 95 at one year. (Figs. 5 and 6)

Case 4:

A 16 year-old male patient who had a 10-year history of psoriasis presented after efalizumab was removed from the market. His psoriasis flared and negatively impacted his quality of life. The main author placed him on etanercept as there were clinical trials using this biologic in his age group. He received 50 mg/mL of etanercept weekly due to his body mass and body surface area affected. After obtaining no relief from this medication, it was discontinued for a topical therapy (betamethasone ointment and urea 40% cream) for several months.

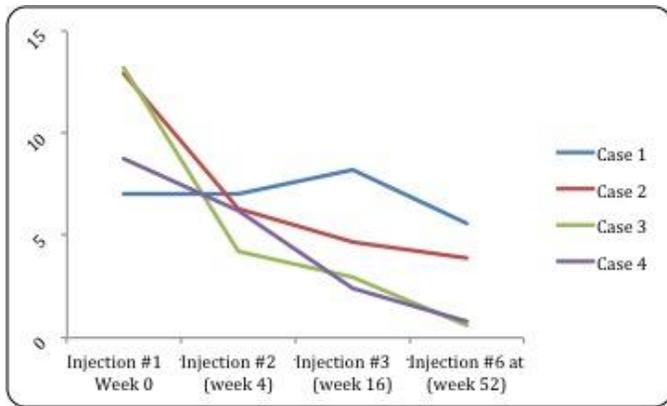


Table 1 Change in PASI over a 52 week regimen.

He and his guardian decided to re-consider biologic therapy. (Fig. 7) After the appropriate tests were taken, the patient began ustekinumab on 5/2010 and at the one-month follow up, his hands and knees showed resolution of the plaques. Over time, his feet also showed complete resolution (Fig. 8) and due to his age and lack of long-term data, he recently discontinued injecting the medication with no rebound of the lesions. Case 4 achieved a PASI-73 at 16 weeks and PASI-90 at one year.

Discussion

In order to quantify the results seen, subjects were assessed using the PASI scoring system. This score combines the surface area involved based on the severity of erythema (redness), induration (thickness), and desquamation (scaling). The body is divided into four main areas for scoring: the head, trunk, upper extremities and lower extremities. The severity of the above criteria are scored separately for each of the four areas and then combined into one final score.⁹

For each case presented here, a baseline PASI score is assigned at week zero which was the patient's initial injection. Subsequent scores were recorded at weeks 4, 16, and 52 for comparison with baseline values. A reduction of 75% in the PASI score is commonly referred to as PASI 75 and is considered a successful benchmark for clinical study.

A 2004 study by Carlin, et al., suggests that this score may be too stern, risking failure for possible therapeutic treatments. Their study found that a PASI score of 50 equated to a meaningful change in a person's life and may serve as a more appropriate benchmark than a PASI 75.¹⁰

All four patients in this study reported they were extremely satisfied with their improvement from baseline by week 52. By week 16, three out of the four patients in this study had well surpassed the 50% improvement benchmark and had no plateaus in their improvement. Patients 3 and 4 exceeded PASI 90 by week 52 correlating with a physician global assessment (PGA) of clear to almost clear skin.

Case 1 responded least to the ustekinumab injection series. She saw her baseline symptoms worsen 17% prior to injection number three given at week 16, and then improve by 33% from week 16 to week 52. It's difficult to ascertain the cause of her slow improvement; however, the location of her palmo-plantar plaque may be to blame. In general, palmo-plantar plaque psoriasis requires more potent topical medications to break down the scale and inflammation that the thickened and more traumatized skin in that area generates.

PASI scores cannot take into account quality of life. Patients with great clinical improvement may not be satisfied if their sense of shame or discomfort is not adequately mitigated. Likewise, patients who fail to meet statistical benchmarks often perceive their treatment as being largely superior to what their PASI score indicates. In case 1, she had suffered with palmo-plantar plaque psoriasis for three years and was seeking restoration of her active lifestyle. At week 52 she had experienced merely 20% improvement, or PASI 20. Yet, her painful plantar fissures subsided, allowing the return to her normal daily activity and her wanting to continue the injection therapy. (Table 1)

Conclusion

Given the difficult nature of treating psoriasis, it is important to consider the many therapeutic options available on the market today for each patient on an individual basis. This is particularly true when considering palmo-plantar lesions. In this case series, ustekinumab injections show an effective method of controlling chronic and recalcitrant plantar psoriasis. Further studies would be helpful to better evaluate its therapeutic use and the results of this study.

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