Brief Report

Informative title:

Successful management of treatment resistant nail psoriasis with tildrakizumab

Short running title (max 40 characters):

Tildrakizumab in nail psoriasis

Key Words: Nail, psoriasis, tildrakizumab, Ilumya, biologic

Word Count: 1135

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Acknowledgements:
Tildrakizumab compassionate supply by Sun Pharma.

Conflict of Interest Statement:
Sun Pharma had no role in the study design, data collection, data analysis, interpretation of data, writing of the manuscript or publication decisions.

Patient Consent Statement:
Patients whose information and images have been used in the report, have provided their signed consent to publication.

Funding statement:
The authors received no financial support for the research, authorship, and/or publication of this article.

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Abstract

Nail psoriasis significantly impacts quality of life and is notoriously difficult to treat. Tildrakizumab, an IL-23 inhibitor, has shown significant clinical improvement in the treatment of moderate-to-severe chronic plaque psoriasis. We report 2 cases of treatment resistant nail psoriasis which showed marked improvement with the use of off-label tildrakizumab. The dosing regimen utilised was consistent with that used to treat chronic plaque psoriasis, with 100mg subcutaneously at Day 0 and Week 4, and maintenance dosing of 100mg every 12 weeks thereafter. Significant improvement at 6 and 12 months, as per the modified Nail Psoriasis Severity Index (mNAPSI) and Dermatology Life Quality Index (DLQI), was seen. There have been no tildrakizumab related side effects observed to date. Tildrakizumab appears to be an effective option in managing treatment resistant nail psoriasis.

Word Count: 129
Introduction

Nail abnormalities are common in patients with psoriasis, with a prevalence of 40-80% reported in the literature [1]. Psoriasis can affect any part of the nail, including the nail fold, nail matrix, nail bed and hyponychium. Clinical findings that are diagnostic for nail psoriasis, particularly in the finger nails, include pitting, nail bed ‘oil drops’ and onycholysis with an erythematous border [2]. In the toenails, it is often difficult to distinguish nail psoriasis from onychomycosis clinically.

Nail psoriasis is notoriously difficult to treat [2] and has been shown to have a significant impact on quality of life [3]. Radtke and colleagues found that in those with psoriasis, patients with nail involvement had significantly lower quality of life as per the Dermatology Life Quality Index (DLQI), reported a poorer state of health in the EuroQol-5 Dimension (EQ-5D) and had a higher number of days off work [3]. Despite this, in Australia severe nail psoriasis is not included as criterion for Pharmaceutical Benefits Scheme (PBS) reimbursement, in contrast to palmoplantar and facial psoriasis.

Given the anatomical structure of the nail, good penetration of therapy is fundamental for successful treatment of the condition. This frequently proves challenging with topical
therapy, and systemic therapy is often required. Biologic therapy has revolutionised the treatment of several dermatological conditions and is emerging as an effective treatment option for nail psoriasis. Both tumour necrosis factor alpha (TNF-α) inhibitors and interleukin 12 (IL-12) and or 23 inhibitors (IL-23) have shown promising results in the treatment of nail psoriasis [2].

Tildrakizumab, a humanized monoclonal antibody that selectively targets the p19 subunit of IL-23 [4], showed significant clinical improvement in moderate-to-severe chronic plaque psoriasis in the reSURFACE 1 and reSURFACE 2 clinical trials [5]. Common side effects included injection-site reactions, nasopharyngitis and fatigue. NAPSI was not captured in these trials [5]. We report 2 cases of treatment resistant nail psoriasis which showed marked improvement with the use of compassionate tildrakizumab following patient consent. The dosing regimen utilised was consistent with that used to treat chronic plaque psoriasis, with 100mg subcutaneously at Day 0 and Week 4, and maintenance dosing of 100mg every 12 weeks thereafter.

Main Text

Case 1

A 63-year-old female was commenced on tildrakizumab for a 5-year history of treatment resistant nail psoriasis predominantly affecting the toenails. The patient had previously failed treated with acitretin at a dose of 10mg daily for 10 months. The patient had no history of plaque psoriasis elsewhere on the body and no history of psoriatic arthritis. Past medical history included hypertension, hypercholesterolaemia and venous insufficiency of the lower limbs.

Modified Nail Psoriasis Severity Index (mNAPSI) performed at baseline was 44, with notable nail plate crumbling and nail bed hyperkeratosis (figure 1). Marked improvement in the nails was seen after 6 months treatment with tildrakizumab, with a reduction of mNAPSI to 13 (figure 1). After 12 months of treatment, total mNAPSI further decreased to score of 8 (figure 1), resulting in a reduction in scoring of 81.8% from baseline.
A marked reduction in DLQI scoring was also observed during the treatment period with tildrakizumab. At baseline the patient recorded a score of 16, highlighting the significant impact of nail only psoriasis on quality of life. This reduced to a score of 4 after 6 months treatment, and to a score of 3 at 12 months. 18 months following commencement of tildrakizumab the patient has continued to see improvement in her nail psoriasis with no associated side effects.

Case 2

Tildrakizumab was commenced in a 53-year-old male with a 15-year history of psoriasis affecting the nails and scalp. The patient had concomitant psoriatic arthritis with significant dactylitis. He was previously treated with methotrexate and cyclosporine with no improvement in his nail psoriasis. Past medical history was significant for gout, stable pulmonary stenosis and left pulmonary artery aneurysm.

On baseline examination, there was evidence of pitting, marked subungual hyperkeratosis, onycholysis and periungual erythema consistent with nail psoriasis (figure 2). Baseline mNAPSI score was 56 (figure 2) and Dermatology Life Quality Index (DLQI) was 19. At the 6-month mark, improvement to the toe nails was evident (figure 2). NAPSI had improved with a reduction of more than 75% from baseline, to a score of 12 (figure 2) and the patient reported marked improvement in his quality of life with a DLQI score of 8. At the 12-month mark, the patient’s nail psoriasis continued to improve with NAPSI of 7 (figure 2) and DLQI of 8. The patient has not developed any adverse event throughout the 18-month period he has remained on tildrakizumab.
Discussion

The nails are commonly affected in psoriasis which can result in significant functional impairment [2]. Unfortunately, treatment for nail psoriasis frequently proves challenging. Treatment options include topical treatments, laser therapy, phototherapy, systemic therapy and biologic therapy, depending on the clinical presentation and patient factors. In our experience topical therapy is often ineffective in severe disease, as it is difficult to achieve adequate penetration, and systemic therapy or biologic therapy is often required.

Biologic therapies which have been trialled in the treatment of nail psoriasis include tumour necrosis factor alpha (TNF-α) inhibitors and IL-12 and or IL-23 inhibitors [2]. Etanercept has shown to be efficacious in the treatment of nail psoriasis with post hoc analyses of the CRYSTEL study demonstrating a 51% improvement in NAPSI score at week 54 of treatment and 30% of patients achieving complete resolution of disease at end of treatment [6]. Adalimumab and infliximab have also illustrated success in the treatment of nail psoriasis [7], with the latter demonstrating a mean improvement of 57.2% in NAPSI after 50 weeks of
Treatment with ustekinumab, an IL-12/23 inhibitor, resulted in a reduction in NAPSI of 50% at week 24, whilst ixekizumab has also illustrated improvement in nail psoriasis [9].

Tildrakizumab is a humanized monoclonal antibody which selectively binds to the p19 subunit, inhibiting the interaction of IL-23 with its receptor [4]. IL-23 is raised in psoriasis and the activation of T helper 17 pathway promotes chronic inflammation and cytokine production resulting in keratinocyte activation and hyperproliferation characteristic of psoriasis [10]. The importance of the IL-23 and T helper 17 pathway in psoriasis has led to the development of IL-23 inhibitors [10]. More recently, a case of concomitant nail psoriasis and psoriatic arthritis, responsive to tildrakizumab over a 9 week period, has been described using the same dosing regimen [11]. Whilst no formal nail psoriasis severity scoring is outlined, there was significant improvement in patient reported joint pain and nail findings as per clinical photographs [11]. Whilst different review timepoints were used to the aforementioned case, our experience using tildrakizumab to successfully treat two cases of resistant nail psoriasis further supports the suggestion that tildrakizumab is a potential effective and safe treatment option for patients with nail psoriasis, particularly those with recalcitrant disease.

References


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Figures:
Figure 1.) Case 1 images left and right feet
Figure 2.) Case 2 images left and right feet

A) = baseline, B) = 6 months treatment with tildrakizumab, C) = 12 months treatment with tildrakizumab.
A) = baseline, B) = 6 months treatment with tildrakizumab, C) = 12 months treatment with tildrakizumab.
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Title:
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Date:
2021-06-11

Citation:

Persistent Link:
http://hdl.handle.net/11343/298639