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Tildrakizumab in the treatment of moderate-to-severe hidradenitis suppurativa

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Title: Tildrakizumab in the treatment of moderate-to-severe Hidradenitis Suppurativa

Short running title: Tildrakizumab for HS

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Conflict of interest

Prof Varigos had received an unrestricted research grant from Sun Pharma, outside the submitted work and Prof Varigos have been on the advisory board for Sun Pharma.

A/Prof Kern is a site principal investigator for clinical trials from AbbVie (NCT03926169) and UCB Biopharma (EudraCT 2019-002551-42).

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

Research letter

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Research letter

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Editor

Hidradenitis Suppurativa is a chronic, recurrent inflammatory disease of hair follicles characterised by painful abscesses, nodules, sinus tracts and scarring on the apocrine gland-bearing skin[1]. An overexpression of interleukin (IL)-23 by macrophages infiltrating lesional skin and the T-cell helper 17 pathway appear to be important in the pathogenesis of Hidradenitis Suppurativa[2]. Tildrakizumab is a humanised monoclonal antibody which targets the p19 subunit of IL-23[1]. Although it is intuitive that blockage of the IL-23 pathway by tildrakizumab should improve disease severity in Hidradenitis Suppurativa, there is currently no published data documenting this response.

We present a case series of five patients with moderate-to-severe Hidradenitis Suppurativa who were treated with tildrakizumab 100mg injections at weeks 0 and 4 and 200mg every 4 weeks thereafter. This dosing regimen was based on a similar analogy with adalimumab, where Hidradenitis Suppurativa patients receive a higher dose compared to chronic plaque psoriasis patients. Tildrakizumab was accessed through a compassionate pathway from Sun pharma who did not contribute to the study design or conduct. Treatment response was measured using the total abscess and nodule count, Dermatology Life Quality Index (DLQI) and visual analogue scale (VAS) for

pain at baseline and weeks 8 and 20. Patients were commenced on tildrakizumab instead of adalimumab based on past studies demonstrating superior efficacy and better tolerability in tildrakizumab over a tumour necrosis alpha inhibitor (etanercept) for chronic plaque psoriasis[3]. A three-year open label extension study with adalimumab also showed that the Hidradenitis Suppurativa clinical response (HiSCR) was only maintained in 52.3% of patients receiving weekly injections, suggesting the need to explore other biologic agents as an alternative[4].

The mean age for patients was 43 years with a range between 28 to 61 years (Table 1). Three patients (60%) were male. Two patients (40%) were current smokers, two patients (40%) were ex-smokers and one patient (20%) never smoked. Two patients have diabetes mellitus and two patients report wearing tight clothing and excessive sweating. Four patients (80%) had Hurley Stage III disease and one patient (20%) had Hurley stage II disease. The most common sites of involvement were the axilla and groin. Prior to starting tildrakizumab, two patients received prior biologic therapy and all patients had systemic therapy. All patients were on concomitant medications at baseline. Interestingly, three patients ceased all concurrent treatment at their last clinic visit.

All patients demonstrated an improvement in their Hidradenitis Suppurativa abscess and nodule count at week 8 compared to their baseline (Table 2), with a mean reduction of 16.8 ($p = 0.04$). Two patients reported ongoing improvement at their week 20 visit with one patient demonstrating a slight increase in her abscess and nodule count, albeit, still much lower compared to her baseline count. The first patient had ceased tildrakizumab after week 8 due to pregnancy.

Four patients also reported measurable quality of life improvement via the DLQI and three patients had reduction in pain symptoms via the VAS at week 8 compared to baseline, although, the difference did not reach statistical significance (DLQI, mean difference = 8.0, $p = 0.46$;VAS, mean difference = 1.2, $p = 0.64$). Three patients who had attended their week 20 visit reported ongoing improvement in their pain scores.

Our patients did not experience common side effects of tildrakizumab including upper respiratory tract infections, injection site reactions and diarrhoea[5]. There were no serious adverse effects or any haematologic, hepatic or renal laboratory abnormalities. The pregnant patient also reported no pregnancy complications or any foetal abnormalities.

There were no identifiable changes to patients' risk factors for Hidradenitis Suppurativa during the study including smoking status and physical risk factors such as wearing tight clothing and excessive sweating. Patients' weight also did not deviate by more than two kilograms from baseline at each visit.

The limitations of this study include the lack of a control group, small sample size, missing patient data, short duration and potential confounders such as the use of concomitant medications which may be responsible for some of the improvement observed in patients commenced on tildrakizumab. Two patients also changed their oral antibiotics whilst on tildrakizumab, making it difficult to determine if the improvement in severity scores were due to the new antibiotics or tildrakizumab.

Despite this, our study further consolidates that tildrakizumab and other IL-23 inhibitors may be new promising treatment options for Hidradenitis Suppurativa. Larger studies with a control group over a longer duration are needed to validate the results of this study, assess drug survival and the time required for tildrakizumab to reach maximum efficacy.

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Table 1. Patient demographic data

Patient	Age (years)	Gender	Smoking history	Obesity (BMI > 30)	Physical risk factors	Diabetes	Hidradenitis Suppurativa location	Hurley stage	Prior treatment for Hidradenitis Suppurativa	Concurrent Hidradenitis Suppurativa treatment at baseline	Concurrent treatment at most recent visit (no. months)
1	28	F	Current	No	Tight clothing	No	Axilla, groin, gluteal	III	Short courses of doxycycline, intralesional steroids	Doxycycline, amoxycillin	Rifampicin, clindamycin (2)
2	61	M	Current	Yes	Nil	No	Axilla, groin, scalp, post-auricular	III	Rifampicin, minocycline, cephalexin, isotretinoin	Doxycycline	Nil (5)
3	41	M	Ex-smoker	No	Excessive sweating	Yes	Auricular	II	Doxycycline	Clindamycin	Nil (2)
4	34	F	Ex-smoker	No	Nil	No	Axilla, groin	III	Erythromycin, adalimumab	Doxycycline, oral contraceptive pill	Rifampicin, Topical resorcinol (5)
5	50	M	Never	Yes	Nil	Yes	Axilla, groin, gluteal, thighs, scrotum	III	Clindamycin, vancomycin, meropenem methotrexate, anakinra, infliximab	Prednisolone	Nil (5)

BMI, Body Mass Index

Table 2. Patients' abscess and nodule count, DLQI and VAS pain scores at baseline, week 8 and week 20 post commencing tildrakizumab

Patient	Most recent patient visit (no. of weeks)	Total abscess and nodule count w0/w8/w20	DLQI w0/w8/w20	VAS w0/w8/w20
1	8	20/7/-	24/9/-	7/3/-
2	20	25/14/2	30/28/NA	9/7/2
3	8	13/3/-	NA/NA/-	0/0/-
4	20	12/1/4	3/2/NA	3/4/0
5	20	45/6/5	27/13/19	10/9/7

DLQI, Dermatology Life Quality Index; VAS, Visual Analogue Scale; NA, not available; W, weeks.