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Refractory lupus erythematosus tumidus responsive to tildrakizumab

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TITLE: Refractory Lupus Erythematosus Tumidus responsive to Tildrakizumab

RUNNING TITLE: Tildrakizumab in Lupus Erythematosus Tumidus

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KEY WORDS: Lupus Erythematosus Tumidus, Chronic Cutaneous Lupus Erythematosus, Tildrakizumab

CONFLICT OF INTEREST: Professor Rodney Sinclair was a Principal Investigator in Sun Pharma Global FZE Phase 3 Clinical Trial evaluating the efficacy and safety of tildrakizumab in moderate-to-severe Chronic Plaque Psoriasis.

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MANUSCRIPT:

A 39-year-old man presented to our clinic with a 15-year history of treatment-resistant lupus erythematosus tumidus (LET). He had no other significant past medical history. He was born in Australia with Syrian and Turkish ancestry. The diagnosis had been confirmed histologically (Figure 1). Previous treatments which had been trialled with minimal improvement included topical corticosteroids, topical calcineurin inhibitors, prednisolone and hydroxychloroquine.

Examination of the face revealed erythematous, oedematous plaques on both cheeks, more severe on the right side (Figure 2a). The absence of scale distinguishes LET from the discoid lupus variant of chronic cutaneous lupus erythematosus (CCLE). There were no plaques elsewhere on the body. There were no systemic features of lupus erythematosus.

Methotrexate 10mg weekly was commenced in addition to hydroxychloroquine 400mg daily. Concurrent intralesional triamcinolone acetonide injections were administered. After two months of treatment there was no improvement in his condition.

Routine screening investigations revealed a positive QuantiFERON-TB Gold. The patient had no symptoms or signs of tuberculosis. He was referred to an infectious diseases physician who treated him with a 6-month course of isoniazid. Following Therapeutic Goods Administration (TGA) special-access scheme approval for off-label use, tildrakizumab 100mg was injected subcutaneously at week 0 and week 4. Methotrexate and hydroxychloroquine were ceased. After two doses of tildrakizumab, there was significant improvement in the facial plaques (Figure 2b). He received his third dose of tildrakizumab at week 16. The response was sustained at week 24 and the patient was satisfied with the result. There were no adverse effects.

LET is a rare autoimmune disease which is considered a distinct subtype of CCLE. Clinical features include non-scarring erythematous, oedematous plaques in sun-exposed areas[1]. The majority of patients with LET are extremely photosensitive[1]. Histological features include perivascular and periadnexal lymphocytic infiltration and interstitial mucin deposition[1]. Kuhn et al. (2000) found that among a total of 250 patients with cutaneous forms of lupus erythematosus, 16% had characteristic clinical and histological features of LET, and thus proposed that LET is a neglected and underdiagnosed subtype of CCLE[1]. In their study,

complete resolution was achieved in all 40 patients with either systemic antimalarial therapy, topical corticosteroids, or in some cases spontaneously[1].

Tildrakizumab is a human monoclonal antibody that inhibits the p19 subunit of interleukin-23 (IL-23) and is approved by the TGA, Food and Drug Administration (FDA) and European Medicines Agency (EMA) for use in patients with moderate to severe psoriasis[2]. Human and animal studies have shown that IL-23 is plays a critical role in the pathogenesis of systemic lupus erythematosus (SLE)[3]. Ustekinumab, a monoclonal antibody targeting IL-12 and IL-23, has been shown to be efficacious in patients with subacute cutaneous lupus erythematosus and SLE[4,5]. Tildrakizumab was preferred over ustekinumab in this case due to availability, as it was provided on a compassionate basis by the manufacturer at no cost to the patient. The clinical response observed in this case report demonstrates that tildrakizumab may be a potential treatment option for refractory LET, although larger studies are needed to support this theory.

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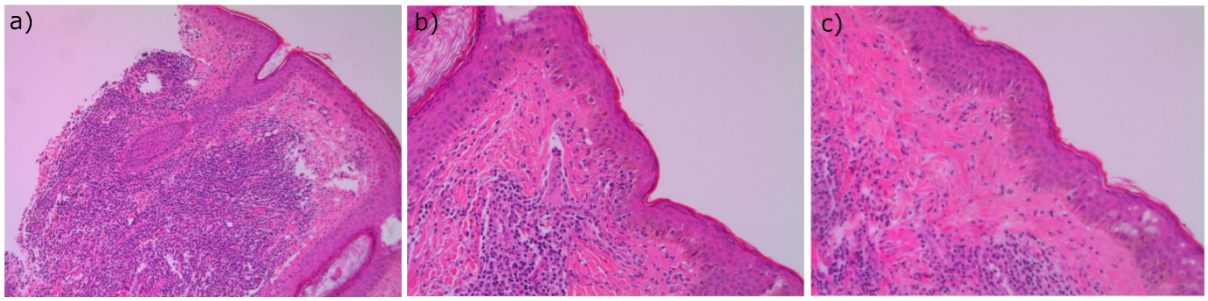
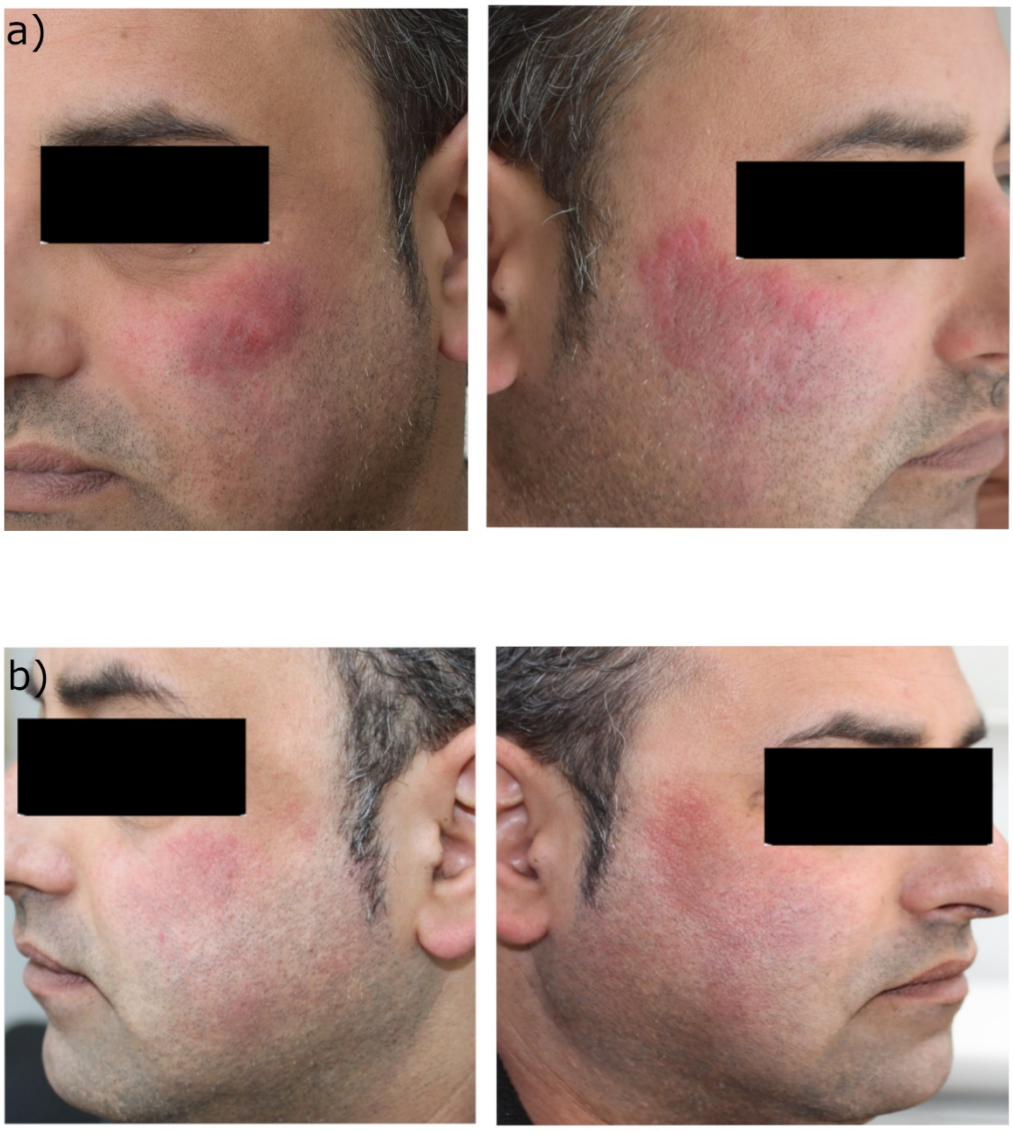
FIGURE LEGENDS

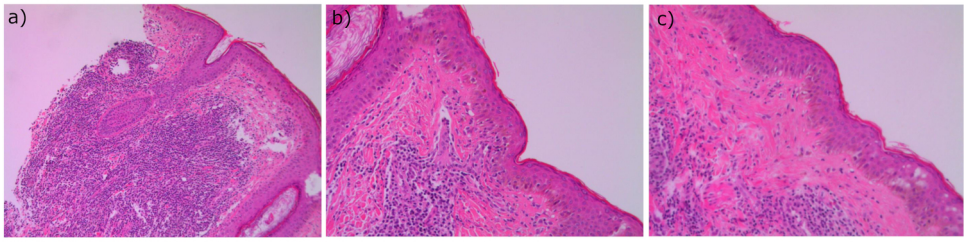
Please note that informed consent has been obtained by the patient to publish his photographs. Please see the attached consent forms.

Figure 1: Histopathological images (a) This low power (40x) haematoxylin and eosin (H&E) stain section shows brisk chronic inflammation in the dermis (b) This intermediate power (100x) H&E stained section highlights occasional late appearing lymphocytes within the epidermis with brisk perivascular chronic inflammation in the superficial dermis (c) This high power (400x) H&E stained section shows vacuolar changes at the base of the epidermis (interface changes). The superficial dermis contains a brisk chronic inflammatory infiltrate

Figure 2: (a) Facial plaques prior to tildrakizumab therapy (b) Appearance of the plaques after two doses of tildrakizumab







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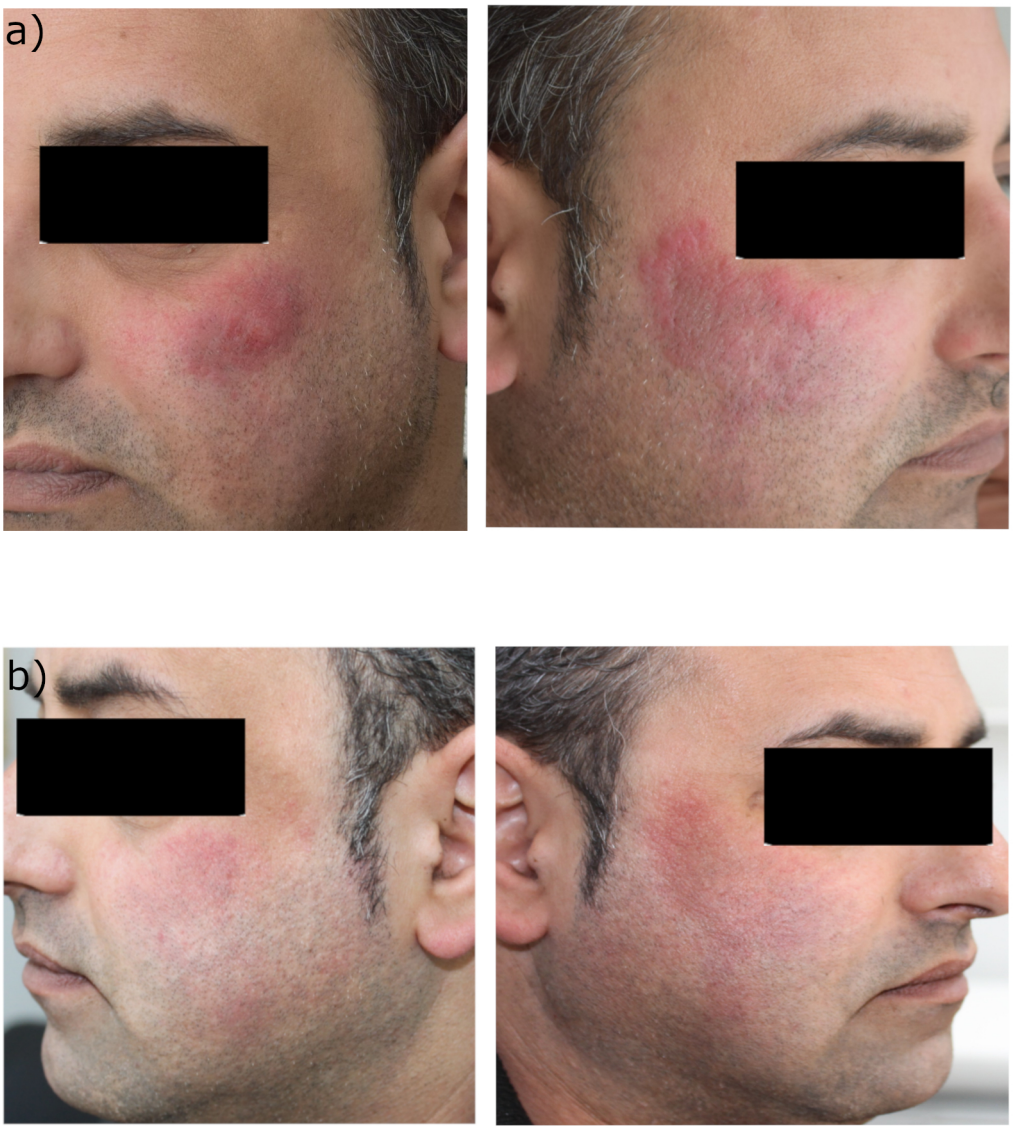

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