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Short Communication

Secukinumab efficacy and safety: Reporting on the experiences of clinicians and patients

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ABSTRACT

Secukinumab (SEC) is a human monoclonal antibody that selectively neutralizes IL-17A, a key cytokine involved in the development of psoriasis. Superior efficacy has been demonstrated in clinical trials with up to 79% of moderate-to-severe psoriasis patients achieving a PASI 90 at week 16 and 75% achieving a PASI 90 at week 52. However, the population recruited into clinical trials are different to the real-world population. The aim of this paper is to discuss the safety and efficacy of SEC based on 'real-world data' when used in patients with multiple co-morbidities and concomitant medications. Two clinical audits conducted were based on a clinical audit checklist, which was adopted and included in all patients' usual care as the patient-management model for biological therapies. Patients on SEC were identified from our pharmacy database and data was collected from electronic patient records between September 2015 and May 2018. The psoriasis area severity index (PASI) and dermatology life quality index (DLQI) were extracted at baseline and at 16 weeks. The results from the rheumatology departments of the two hospitals were then compared. A total of 135 patients' data was analysed. SEC was found to offer an efficacious real-world treatment option with response rates generally higher than observed in pivotal Phase III clinical trials. Response rates were higher in biologic naïve patients than non-naïve patients. There were no unusual safety signals; however, long-term efficacy and sustainability are yet to be established.

KEYWORDS: secukinumab, biologic therapies, psoriasis area severity index (PASI), dermatology life quality index (DLQI).

INTRODUCTION

The inflammatory infiltrate found in psoriasis-affected skin and joints has been investigated; a lymphocytic infiltrate was identified in sub-lining layer stroma of joint tissue and in the dermal papillae of the skin. This infiltrate is also in inflammatory enthesis [1]. The immunopathological changes observed in affected joints and skin appear similar: early vascular changes with uncontrolled angiogenesis and upregulated growth factors [1].

According to the Psoriasis Association, psoriatic arthritis (PsA) is a condition that affects joints "such as the knees or those in the hands and feet" as well as areas where tendons join to bone "such as the heel and lower back". Most commonly, people experience skin psoriasis before developing the arthritis, but some develop the arthritis first [2].

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Not all people diagnosed with psoriasis will experience PsA. Notwithstanding the range of treatments currently available for psoriasis, refractory disease remains a clinical problem [3]. IL-17A is a key cytokine involved in the development of psoriasis and PsA. Significant disability can be caused by both PsA and ankylosing spondylitis and both are categorised as chronic inflammatory diseases [3].

The pro-inflammatory mechanisms involved in psoriasis and PsA were described by Blauvelt and Chiricozzi (2016), explaining the rationale for targeting the IL-17 for inflammation control. The authors stated that "within the skin and joints, IL-17A acts on cellular targets, including keratinocytes, neutrophils, endothelial cells, fibroblasts, osteoclasts, chondrocytes, and osteoblasts, to stimulate production of various antimicrobial peptides, chemokines, and proinflammatory and proliferative cytokines, which, in turn, promote tissue inflammation and bone remodeling" [4].

The recent advances in their treatment started when the first tumor necrosis factor (TNF) inhibitors were launched leading to a radical improvement in the patients' quality of life [5]. However, following initial expectations of its effectiveness for all patients and for the long term, it was found that response was not universal; demonstrating the need for alternative therapeutic targets [3]. Secukinumab is a recombinant human monoclonal antibody that selectively binds to cytokine interleukin-17A (IL-17A) and inhibits the release of proinflammatory cytokines and chemokines [6]. Secukinumab, in clinical trials, demonstrated superior efficacy with up to 79% of moderate-to-severe psoriasis patients achieving a PASI 90 at week 16 and 75% achieving a PASI 90 at week 52 [7, 8]. PsA-affected skin and nails also showed significant improvement when the IL-17A was inhibited using SEC. It has a safety profile and reported efficacy in medium to long-term study data that suggests it has potential to impact treatment protocols in the near future. However, the populations recruited into clinical trials are different to the real-world population and the results may somehow differ.

In a study of 460 patients, 308 patients were assessed for SEC efficacy [9]. The authors reported that all of the efficacy study endpoints were achieved through week-156. Overall, improvements in quality of life and physical function were also sustained through week-156. They further reported that 78.1% (SEC 150 mg) and 74.8% (SEC 75 mg) of patients had no radiographic progression through week-156. Adverse events per 100 patient-years (exposure-adjusted incidence rates) for SEC 150/75 mg included serious infections (1.7/1.6), Candida infections (1.4/0.7), Crohn's disease (0/0.3), ulcerative colitis (0/0.3) and major adverse cardiac events (0.3/0.8) [10].

In the FUTURE® studies, 476 patients receiving SEC achieved sustained improvement in their psoriatic arthritis (PsA) and tolerated the treatment for 2 years [10]. A systematic review of 13 randomised controlled trials, concluded that in patients with moderate-to-severe psoriasis treated with biological agents, the mean PASI and DLQI correlate predictably and that 'a reduction in PASI of at least 75% can translate to significant quality-of-life improvement in patients treated with these therapies' [11]. Improvement of psoriasis in visible body regions has an appreciable influence on QoL improvement, and may positively affect treatment success.

Feldman *et al*. (2019) evaluated treatment patterns in PsA and initiation of therapy with biologics versus other drugs using claims data-identified biologic-naive adults with PsA from 2013 to 2016 [12]. The authors found that medication adherence was similar between biologics and others at 12 months (76.9 vs 73.4%; $p = 0.175$) when compared phosphodiesterase 4 inhibitors ($n = 381$) and matched biologic ($n = 761$) patients [12]. The Italian Medicines Agency (AIFA) categorised patients who had no previous exposure to a patented new biologic as "primary naïve" and those who had sufficient first biologic long wash-out period or using biosimilar as "secondary naïve". However, the definition of "secondary naïve" is not well established, as some authors see it as related to the type of biologics and on their mechanism of action and others see it related to the second exposure to any biologic regardless of type or mode of action [13].

This study aimed to conduct a clinical audit to assess the safety and efficacy of SEC, in all the

patients treated between September 2015 and May 2018. We compared their outcomes in two Dermatology hospital departments.

METHODS

A clinical pathway was created to feed information into an audit checklist and was adopted as the patient-management model for biological therapies. Patients on SEC were identified from the pharmacy department database and data was collected from electronic patient records between September 2015 and May 2018. Their PASI and DLQI were extracted at baseline and at 16 weeks, then all data was anonymised for further analysis. A total of 135 patients' records were included in this audit (94 patients from Burton and 41 patients from Wolverhampton).

The two sites used the same standard (NICE© TA350) [14, 15] and treatment protocol where therapy was initiated on 150 mg every week for 5 doses, then the maintenance 150 mg every month, and the dose was increased to 300 mg according to the patient's clinical response [6]. SEC was withdrawn in patients whose psoriasis has not responded adequately within 12 weeks of the initial dose as further treatment cycles are not recommended. The PASI and DLQI were conducted to confirm the patient's eligibility for the initiation of SEC. These were repeated at 11-12 weeks to establish the patient's response before continuation of therapy beyond the 12 weeks. In this audit we compared the PASI and DLQI scores at baseline and at 16 weeks to assess the response seen in real-world patients outside the clinical trials environment. The only limitation was that it is not currently our routine practice to monitor adherence, considering that patients trained on self-injection at home.

RESULTS AND DISCUSSION

Combined demographics and patient characteristics

The total number of patients was 135; age (mean ± SD): 47.92 ± 13.02 (recorded for 98 patients only). The majority were males (82 - 61%) and white British (92%); only 8% were from Asian descent. Weight was recorded in 98 patients only and the mean ± SD was 92.16 ± 22.84 and baseline PASI (mean) was 15.10 ± 7.98 (n = 130) and DLQI (mean) was 17.48 ± 7.42 (n = 131). The mean of prior systemic therapies was 1.31 which was recorded for 85 patients. There were 47.40% biologics-naive patients (64/135), and the mean ± SD for number of patients who had prior biologic therapies was 1.70 ± 1.08 [adalimumab: 44/71 (61.9%); stekinumab: 30/71 (42.2%); etanercept: 37/71 (52.1%); infliximab: 15/71 (21.13%); efalizumab: 3/71 (4.2%) and golimumab: 1/71 (1.4%)].

Burton patient response evaluation after 16 weeks

The response to the treatment at 16 weeks is presented in Table 1. Ninety patients were assessed (Bio-naive: 35 pts (39%); Bioexp: 55 pts (61%)).

Wolverhampton patient response evaluation after 16 weeks

The response to the treatment was assessed at 16 weeks (12). There was an 83.26% reduction of mean PASI score at 2.75 ± 3.21 (n = 26) and the mean DLQI score was 3.61 ± 4.53 (82.18% reduction from baseline). About 92% (24/26) of the total population met the NICE criteria for remaining on treatment, attaining at least a PASI 75 or a PASI 50 plus a 5 points reduction in DLQI. PASI 75 was achieved by 84.62% (22/26),

Table 1. The response to the treatment at 16 weeks.

	Total (%)	Bio-naive (%)	Bio-exp (%)
PASI 75	94.4	97.0	93.0
PASI 90	90.0	94.0	87.0
PASI 100	82.0	94.0	75.0

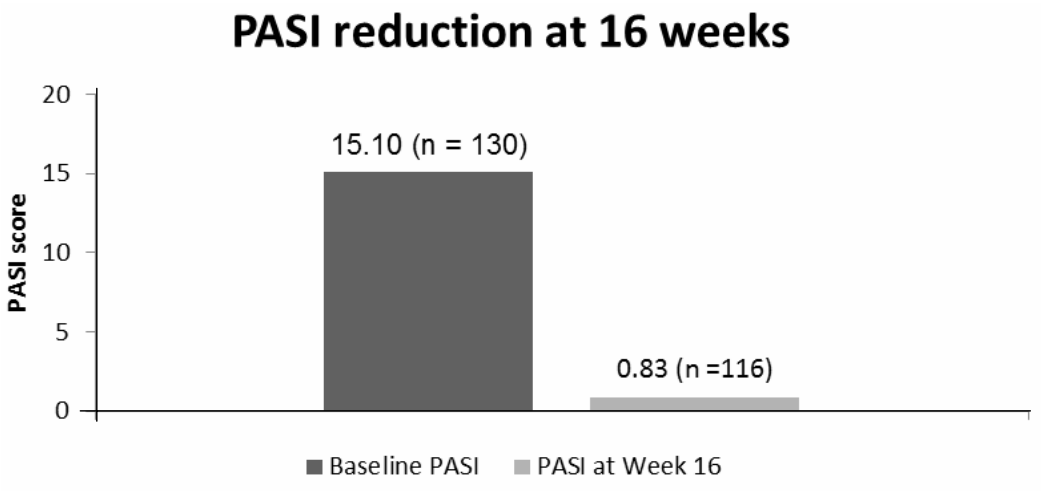

Figure 1. PASI reduction at 16 weeks.

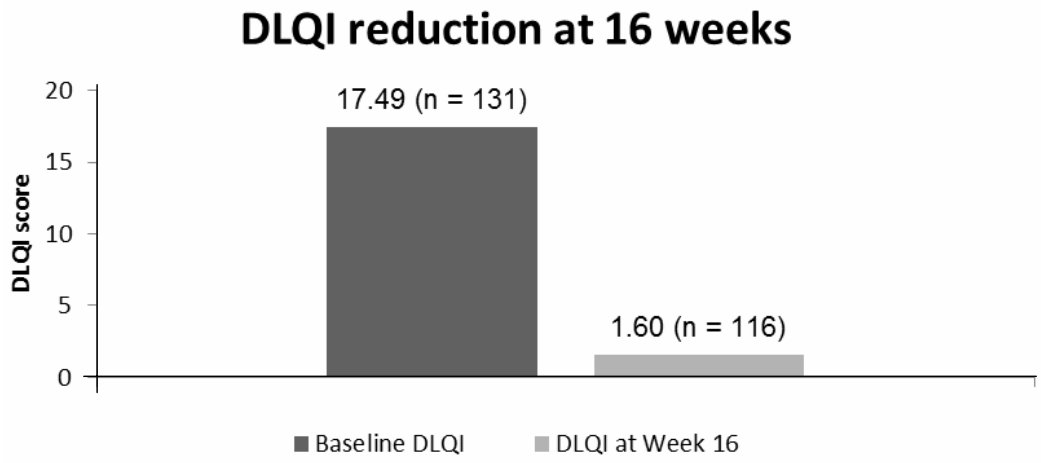

Figure 2. DLQI results observed after 16 weeks.

whereas 53.85% (14/26) of the population achieved a PASI 90 and 26.92% (7/26) achieved PASI 100. No unusual adverse events were observed. No patient volunteered information on adverse effects; on questioning 1/41 reported some rhinorrhoea. No reports of diarrhoea or more serious adverse effects were received.

Combined patients' response results

Out of all records reviewed, there was an overall 95% reduction in PASI, 90% achieved absolute PASI ≤ 3 (105/116), 94% of patients treated with SEC who were biologic naïve were able to achieve PASI 100 at Week 16 and 70% achieved absolute PASI = 0 (81/116) (Figure 1).

There was a 91% improvement in DLQI observed after 16 weeks, in comparison to the baseline (Figure 2).

No patient was withdrawn from treatment due to severe side-effects.

CONCLUSIONS

Based on the findings of this audit SEC offers an efficacious real-world treatment option, with response rates generally higher than observed in pivotal Phase III clinical trials. Common adverse events include infections (fungal, chest, upper respiratory tract), headaches, injection site pain and erythema. Response rates were higher in

biologic naïve patients than non-naïve patients. There were no unusual safety signals; however, long-term efficacy sustainability is yet to be established. The data demonstrates that, the clinical outcomes observed in our practice were comparable to the clinical trial data. More real-life data is required to assess longer term safety and effectiveness.

CONFLICT OF INTEREST STATEMENT

All authors have no financial or professional conflict of interest.

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