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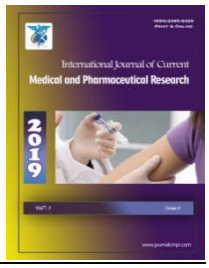

CONTINUATION OF THERAPY OF SECUKINUMAB (SEC): EVIDENCE FROM A TERTIARY REFERRAL CENTRE

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ABSTRACT

A clinical pathway was created to feed information into a clinical audit checklist, and was adopted as the patient-management model for biological therapies. From this, the data was reviewed concerning 41 patients who were receiving SEC between January 2014 and December 2018. The results for the Psoriasis Area Severity Index (PASI) and Dermatology Life Quality Index (DLQI) score which are typically reviewed at baseline and at 16 weeks to assess response to treatment.

INTRODUCTION

Abrouk *et al*., (2017) acknowledged that, regardless of the wide range of currently available treatments for psoriasis, refractory disease remains a problem.[1] Whilst the safety of Secukinumab (SEC) is well established, there are insufficient head-to-head studies currently available to compare SEC efficacy to other biologicals whose use is currently established.[2]

The 'biologicals' represent a powerful class of agents with very specific actions. They are expensive therapies placing a duty on healthcare providers to ensure they are used for the most appropriate patients. New products with novel modes of action are emerging regularly. Also as patent protection expires, owing to the complexity of manufacture and the difficulties in ensuring products from 'generic' manufacturers are identical, the concept of 'biosimilars' has emerged. To achieve the best outcomes for our patients whilst ensuring the best possible use of available resources requires novel approaches to day to day management.[3]

SEC is a fully human monoclonal antibody that selectively neutralizes interleukin IL-17A, a key cytokine involved in the development of psoriasis (PsO).[4]Superior efficacy[5]and sustainable response for up to 5 years had been reported in clinical trials.[6]In placebo-controlled trials SEC significantly improved clinical symptoms and inhibited structural progression at week 24 in patients with Psoriatic Arthritis (PsA), with and without the use of a loading dose.[7]Reporting further for the FUTURE trial group, Mease *et al*., (2018) indicated that SEC was well tolerated noting no new safety signals.[8]Consequently, it was considered to offer an effective new addition to the current therapeutic options in PsA.[9]

In the FUTURE studies, 476 patients receiving SEC achieved sustained improvement in their PsA and tolerated the treatment for 2 years.[2]Langley *et al*., (2014) concluded that, based on the findings from the ERASURE and FIXTURE randomised studies, that SEC is effective for PsO management at 12 week patient reviews, however the response varied by dose, "In the ERASURE study, the rates were 65.3% with 300 mg of SEC, 51.2% with 150 mg of SEC, and 2.4% with placebo; in the FIXTURE study, the rates were 62.5% with 300 mg of SEC, 51.1% with 150 mg of SEC, 27.2% with etanercept, and 2.8% with placebo ($P<0.001$ for each SEC dose vs. comparators)", where infection rate for SEC was higher than with placebo but similar to etanercept.[10]This conclusion confirms the finding by Bissonnette *et al*., (2018) who stated that SEC higher dose (300 mg) produced "high and sustained levels of skin clearance" improving the participants quality of life throughout and up to the 5 years follow up in patients with moderate-to-severe psoriasis.[11]This also agrees with Yang *et al*., (2018) who stated that selection of patients classified as "moderate-to-severe psoriasis" is a key consideration for the use of SEC.[12]Malakouti *et al*., (2015) also concluded that patients treated with SEC achieved "high clearance rates up to

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PASI 90 and 100 as monotherapy in cases of moderate-to-severe psoriasis", and that it is a favourable treatment option for those with have antidrug antibodies, have failed other biologic agents and those diagnosed with psoriatic arthritis or ankylosing spondylitis.[13]

However, trials are conducted under carefully controlled conditions, and for all new treatments there is a need for 'real world data'in patients with multiple pathologies, multiple other medications and those whose adherence to therapy may not be closely monitored. Further, increasing availability of 'biosimilars' in the marketplace is creating drivers to reduce costs, but in the interests of patient safety and quality of life, it is important for centres like this one, to be in a position to make realistic comparisons.[3]

METHOD AND DESIGN

The aim of this audit was to test our model for monitoring our patients to identify whether when SEC was prescribed for a patient of this department, the baseline characteristics of their condition and demographics and their clinical experience of the medication had been recorded in such a way that the department is in a position to retrospectively review their progress and any issues experienced with this medication.

This aims to provide

1. Data to audit our clinical experience with SEC in our patient population with our normal follow-up.
2. To provide baseline comparison data against which future competitor agents or 'biosimilars' could be assessed.
3. To review our ongoing audit model for future use with all biological agents in our referral service.

Patients prescribed SEC were identified from our pharmacy database and data were collected from electronic patient records between January 2014 and December 2018.

Standard

According to NICE guidelines (NICE TA350):[14,15]

1. Initiation of therapy should be as 150 mg every week
2. After 150 mg every week for 5 doses, the maintenance 150 mg every month, dose may be increased to 300 mg according to clinical response
3. SEC should be withdrawn in patients whose psoriasis has not responded adequately within 12 weeks of initial dose; further treatment cycles are not recommended.

Our normal care protocol is for the PASI and DLQI to be conducted to confirm patient eligibility for the initiation of SEC. These are 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 baseline and at 16 weeks PASI and DLQI scores to assess the response seen in real-world patients outside the clinical trials environment.

RESULTS

Forty-one patients who had been deemed appropriate for SEC treatment were identified of whom thirty-seven were males (90.24%).The mean age was 47.85 ± 11.81 (n=41). The mean baseline PASI score was 16.43 ± 5.68 (n=39) and the mean baseline DLQI was 20.26 ± 6.16. The proportion of patients that were bio-naive was 36.58% (15/41). It is not currently our routine practice to monitor adherence. Patients trained on self-injection at home.

The response to the treatment was assessed at 16 weeks. 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 plusa 5 points reduction in DLQI. PASI 75 was achieved by 84.62% (22/26), 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 patients volunteered information on adverse effects, on questioning 1/41 reported some rhinorrhoea. No reports of diarrhoea or more serious adverse effects were received.

DISCUSSION

Our early findings are reported, and appear broadly in line with the types of response seen in formal trials. It is encouraging that the patients have met and exceeded the NICE criteria to be able to continue with therapy that is proving highly effective and that the side effect profile appears to continue to be favourable.

Our routine practice does not currently include any assessment or monitoring of adherence. The clinical responses measured suggest it is reasonable, although previous studies have demonstrated resistance to self-administered injections.[16-17]Possible ways of including adherence measurement/monitoring into our care going forward are being considered.

CONCLUSION

Our data demonstrates real life clinical outcomes of SEC in a cohort of PsO patients in the real world, with more than 90% patients meeting NICE criteria to treatment continuation at 16 weeks. More research is required to assess the sustainability of efficacy in these patients beyond 16 weeks, in real time and in community living, of treatment outside of clinical controlled trials.

In the context of expensive therapies that must be justified by clinical effectiveness, and the substitution of biosimilars, an approach that allows regular audit of clinical outcomes and adverse effects is a valuable tool.

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