New treatment for tackling plaque psoriasis

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Secukinumab (Cosentyx) is licensed for the treatment of moderate to severe plaque psoriasis. Here, Steve Chaplin presents the clinical data relating to its efficacy and Drs Susan O’Gorman and Trevor Markham discuss its place in therapy.

KEY POINTS
- Secukinumab (Cosentyx) is a monoclonal antibody for the treatment of adults with moderate to severe plaque psoriasis who are suitable for systemic therapy
- The recommended dosage is 300mg weekly (as two subcutaneous injections) for four doses then monthly
- In clinical trials, secukinumab improved psoriasis severity scores in significantly more patients than etanercept and the response was maintained in most patients at one year
- The most frequent adverse event is infection, usually mild to moderate upper respiratory tract infection
- Secukinumab costs £1218.78 for two 150mg injections

Steve Chaplin

NICE guidance on the management of psoriasis recommends referral to a specialist for adults with severe psoriasis or if topical therapies are unsuccessful.¹ Treatment options then include phototherapy or systemic therapy, initially with a non-biological agent (methotrexate, ciclosporin, acitretin). If this is unsuccessful, further options include biological therapy with adalimumab, infliximab, etanercept or ustekinumab (a monoclonal antibody that targets interleukins (IL) 12 and 23).

Secukinumab

Secukinumab is a monoclonal antibody that targets IL-17A, a proinflammatory cytokine expressed on various cells, including keratinocytes, that is up-regulated in psoriatic skin plaques. It is licensed for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy and should be prescribed under the guidance and supervision of an appropriately experienced physician.

The recommended dose is 300mg by subcutaneous injection (given as two injections of 150mg) at weeks 0, 1, 2 and 3 then monthly from week 4. Secukinumab is supplied as a prefilled syringe and a prefilled pen (SensoReady), both of which contain a single dose of 150mg. Treatment should be reviewed after 16 weeks and discontinued if there is no response but patients with a partial response may subsequently improve.

No dose adjustment is recommended for older people; secukinumab has not been studied in patients with renal or hepatic impairment. There is a risk of exacerbation of Crohn’s disease and an increased risk of infection, notably non-serious mucocutaneous candida infection.

Clinical trials

ERASURE (Efficacy of Response and Safety of Two Fixed Secukinumab Regimens in Psoriasis; n=738) and FIXTURE (Full Year Investigative Examination of Secukinumab vs Etanercept Using Two Dosing Regimens to Determine Efficacy in Psoriasis; n=1306) were double-blind, placebo-controlled trials lasting 52 weeks.² Eligibility criteria included moderate to severe plaque psoriasis poorly controlled with topical treatments, phototherapy, systemic therapy or a combination of therapies. Patients scored ≥12 on the Psoriasis Area and Severity Index
(PASI) (means 21–24) and had ≥10 per cent of body surface area involved (means 30–35 per cent). Some 50 to 60 per cent of patients had previously received a systemic therapy, including a biological agent in 13 (FIXTURE) and 30 (ERASURE) per cent. These trials included a 150mg dose of secukinumab administered once weekly for five weeks then every four weeks; patients randomised to treatment with etanercept received 50mg twice weekly for 12 weeks, then once weekly.

The coprimary endpoints were the proportion of patients with a reduction of ≥75 per cent in the Psoriasis Area-and-Severity Index (PASI) score (PASI 75) and a response of clear or almost clear by clinician’s global assessment, both at 12 weeks.

The proportions of patients achieving PASI 75 were significantly greater with 300mg secukinumab (77 and 82 per cent) than with placebo (5 per cent) or etanercept (44 per cent) (p<0.001 for all comparisons) (see Figure 1). This was matched by the response by clinician’s global assessment (63 and 65 per cent vs 2 and 3 per cent with placebo and 27 per cent with etanercept; p<0.001). Secukinumab improved itch, pain and scaling compared with placebo. Almost complete clearance (PASI 90) at 12 weeks occurred in 54–59 per cent of patients treated with 300mg secukinumab and 21 per cent with etanercept. Dermatology-related quality of life improved significantly more with secukinumab. A PASI 75 response was maintained at 52 weeks in 80–84 per cent of patients with 300mg secukinumab and 73 per cent with etanercept.

These response rates were matched when patients self-administered secukinumab, with slightly higher PASI 75 response rates using an autoinjector (87 vs 3 per cent with placebo) than with a prefilled syringe (76 vs 0 per cent).3

**Adverse effects**
Common adverse events in clinical trials included infections (47.5 per cent over 52 weeks, 1.2 per cent serious), most of which were upper respiratory tract infections but also included oral herpes.

Other common adverse events included rhinorrhea (1.2 per cent), urticaria (0.6 per cent) and diarrhoea (4.1 per cent). Mild, transient neutropenia occurred in 0.5 per cent of patients treated with secukinumab; there was no relationship with dose or timing of infection.

**References**

**Declaration of interests**
Steve Chaplin has none to declare.

*Steve Chaplin is a pharmacist who specialises in writing on therapeutics*

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Biological therapy is an important addition to the dermatologist's armamentarium in the treatment of severe plaque psoriasis, in patients who are unsuitable for, or have not gained sufficient benefit from the non biological agents, such as methotrexate or fumaric acid esters.

There are two groups of biological agents that target tumour necrosis factor (TNF); the anti-TNF monoclonal antibodies such as infliximab and adalimumab, and the soluble TNF receptor etanercept. The PASI 75 response seen with etanercept at 12 week ranges from 49 (US Psoriasis Pivotal Trial) to 57 per cent (ACCEPT study). These are lower than those seen with the anti-TNF monoclonal antibodies with a PASI 75 seen in 71 (REVEAL)–79.6 per cent (CHAMPION) of patients after 16 weeks of adalimumab and a PASI 75 of 80 (EXPRESS) – 88 per cent (SPIRIT) at week 10 of treatment with infliximab.

Ustekinumab targets IL-12 and IL-23 and a PASI 75 response is seen in 66–76 per cent of patients after 12 weeks of treatment (PHOENIX 1, PHOENIX 2, ACCEPT).

IL-17 acts downstream of IL-23 and Secukinumab targeting IL-17A, has proven to be highly efficacious for the treatment of chronic plaque psoriasis. At week 12, 77–82 per cent of patients achieved PASI 75 (Fixture, Erasure), demonstrating superior efficacy to etanercept at that time point (Fixture, p<0.001). This PASI 75 response was maintained at 52 weeks in 80–84 per cent of patients with secukinumab. The PASI 90 score with secukinumab has additionally been impressive, with 54–59 per cent of patients achieving this at week 12, representing almost complete clearance, while the percentage reaching PASI 100 at the same time point is between 24 and 29 per cent. An advantage of secukinumab is that once the patient is established on it, following an injection at week 0, 1, 2, 3, the frequency of administration is then monthly.

Although no long-term data on safety exists for secukinumab, short-term data suggests that it is well tolerated. Infections were common while on treatment (47.5 per cent over 52 weeks), while only 1.2 per cent were considered serious. The most common infections seen were upper respiratory infections, but oral herpes was also seen. Other adverse events included mild transient neutropenia (0.5 per cent), urticaria (0.6 per cent), rhinorrhoea (1.2 per cent) and diarrhoea (4.1 per cent).

Secukinumab has been licensed for the treatment of moderate to severe psoriasis, meaning that it could be used as a first line systemic agent in psoriasis, however given the lack of long-term safety data, it is likely initially to be used when agents such as methotrexate, fumaderm or the more established biologics have failed.

### Declaration of interests
None to declare.

Dr Susan O’Gorman is an SpR and Dr Trevor Markham is a dermatology consultant at Galway University Hospital.

### POEMS

**Can cognitive behavioral therapy be successfully delivered in the primary care setting?**

**Bottom Line**
Cognitive behavioral therapy (CBT), delivered in the primary care setting to patients with anxiety or depression, is at least as effective as usual treatment, including medication, for these disorders. The UK has made a concerted effort to train healthcare professionals in CBT because of its safety and efficacy. Embedding the delivery of CBT in the primary care setting makes sense and would make it more convenient for patients. (LOE = 1a)

**Reference**

**Study Design:** Systematic review

**Setting:** Outpatient (primary care)

**Allocation:** Unknown

**Synopsis**
Although CBT is a highly effective treatment for anxiety, depression, and several other disorders, access to practitioners skilled in its use may be limited. Therefore, researchers have developed and tested approaches to CBT (eg, self-help, telephone-based, computerised, and one-on-one) that are able to be delivered in the primary care setting. In this well-done systematic review, the authors identified 29 studies of CBT delivered in the primary care setting or to primary care patients compared with no treatment or usual treatment, or studies that compared CBT plus usual treatment to usual treatment alone. Most studies enrolled patients with anxiety or depression; some studies enrolled patients with both. CBT was most commonly delivered by psychologists or therapists working in a primary care clinic, but was also delivered by physicians, other healthcare professionals, and via a computer in some studies. Seven studies that compared CBT with no primary care treatment found a clinically and statistically significant benefit to CBT, especially for anxiety symptoms and especially if delivered by computer. Fourteen studies compared CBT with usual treatment, which could include other approaches to counseling or medication. These also found a significant effect favoring CBT, especially for anxiety and when delivered one-on-one in the primary care setting. In this group of studies, only three looked at computerised approaches; two found no benefit and one found a substantial benefit. The number of sessions of CBT ranged from two to 12.