Celebrating World Psoriasis Day in an Era of New Treatments

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The Burden of Psoriasis Report estimated that there are 73,000 patients with the skin condition psoriasis in Ireland, suggesting a prevalence of 2% and at least 9,000 patients living with severe disease[1]. The treatment of psoriasis has been revolutionised by the introduction of new biological therapies and more than any other skin condition, the treatment armentarium for patients with psoriasis has expanded significantly. It is not unrealistic to proffer clear skin to many patients who have lived with this stigmatizing condition all their lives. Across the therapeutic categories reduction in Psoriasis Area and Severity Index, a clinical measure of psoriasis has increased from 75% clearance (PASI 75) to 100% clearance (PASI 100). In an interesting proof – of concept, these therapies have also led to increased understanding of the pathogenesis of psoriasis with key pathways and cytokines identified.

Anti – TNF therapy:

Etanercept subcutaneously was approved for the treatment of psoriasis by the FDA in 2004, followed by Infiximab intravenously in 2006 and Adalimumab subcutaneously in 2008. Etanercept 50 mg twice weekly resulted in achievement of Psoriasis Area and Severity Index PASI75 at week 12 in 47–49% of patients compared with placebo, PASI75 response rate; at week 24 response was 59% (last observation carried forward)[2]. Infliximab administered at 5 mg/kg at week 0, 2, and 6 resulted in PASI75 responses at week 10 of 75.5% and 80% compared with 1.9% and 3.0% with placebo[3]. Adalimumab 80 mg week 0 followed by 40 mg at week 1 and then every other week, 71% achieved a PASI75 response at week 16 compared with 7% in the placebo group[4]. An extension of the phase III study (open label), showed that 76% of patients with at least a PASI75 response at week 16 and 33, maintained PASI75 after 160 weeks of continuous treatment (measured as last observation carried forward)[5]. Certolizumab is the newest TNF inhibitor to be licensed for the treatment of psoriasis in 2018, in patients treated with certolizumab 400 mg, 74.5 % of patients achieved PASI 75 at week 16 and 54.6% of those treated with certolizumab 200mg[6]. Certolizumab is the only member of this class to be licensed for use during pregnancy, an important consideration in patients of childbearing age.

Anti Il12/IL-23 inhibition:

Psoriasis was the first indication for which ustekinumab was licensed by the FDA in 2009 and paved the way for the development of targetted therapies for psoriasis. In phase III studies, treatment with ustekinumab 90 mg on week 0 and 4 resulted in PASI75 responses at week 12 of 66.4% and 75.7%, respectively, compared with 3.1% and 3.7% in the placebo group[7]. With continuous treatment, 90 mg every 12 weeks, similar PASI75 responses were reached in the two studies, 78.5% and 78.6%, at week 28[8].

Anti IL-17 therapy:

Secukinumab was the first IL-17A inhibitor approved in 2015 for treatment of patients with psoriasis and in phase III studies, the proportion of patients who achieved PASI75 at week 12 was 75.9–86.7% with secukinumab 300 mg (administered once weekly for 4 weeks starting at week 0, then every 4 weeks[9-11]. In a subsequent head to head study of secukinumab versus ustekinumab, After 52 weeks of treatment, the proportions of patients (secukinumab versus ustekinumab) with a PASI90 response were 76% versus 61% and the proportions with a PASI100 response were 46% versus 36%[12].

Ixekizumab which also targets anti-IL-17A was licensed the following year in 2016 and two phase III studies of ixekizumab 160 mg as starting dose followed by 80 mg every 2 weeks were 87.3% of patients achieved PASI 75 and 89.7% at week 12. Sixty – eight percent of patients achieved PASI 90 and 37.1% PASI 100[13].

Brodalumab which interacts with IL-17RA is the third member of this class and was licensed in 2017 , 83 – 86 % of patients achieved PASI 75[14,15]. Efficacy was compared with ustekinumab was measured at the level of a PASI100 achievement at week 12, with 44% of patients treated with Brodalumab achieved PASI 100[16].

With this group of treatments for the first time clear or almost complete clearance of psoriasis was being discussed as an endpoint of clinical trials and an attainable goal for patients.

Anti-IL-23 therapy:

Guselkumab, an IL-23p19 neutralizing antibody, was approved by the FDA in July 2017 and results from phase III studies have been published, both controlled for placebo as well as for adalimumab. The largest absolute differences were seen at PASI90: Guselkumab 100 mg week 0 and 4 and then every 8 weeks, resulted in a PASI90 response at week 16 of 73.3%[17,18]. This has been followed by Tildrakiazumab in 2018, with efficacy at week 12, 64% and 62% of patients in the 100 mg and 200 mg groups, respectively, attained PASI-75[19].

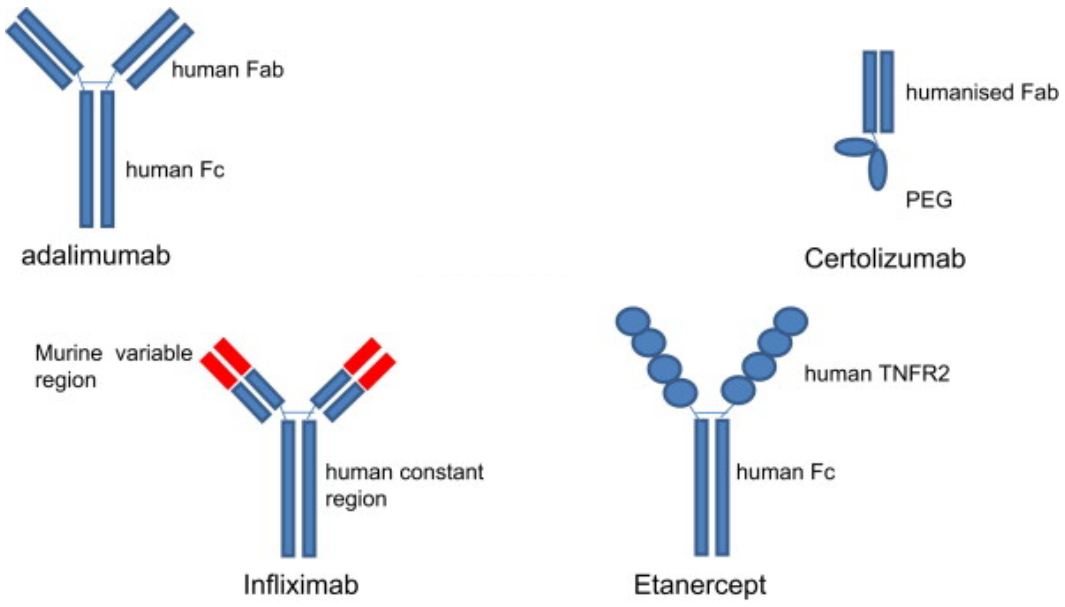

Fig 1: Anti TNF therapy for Psoriasis

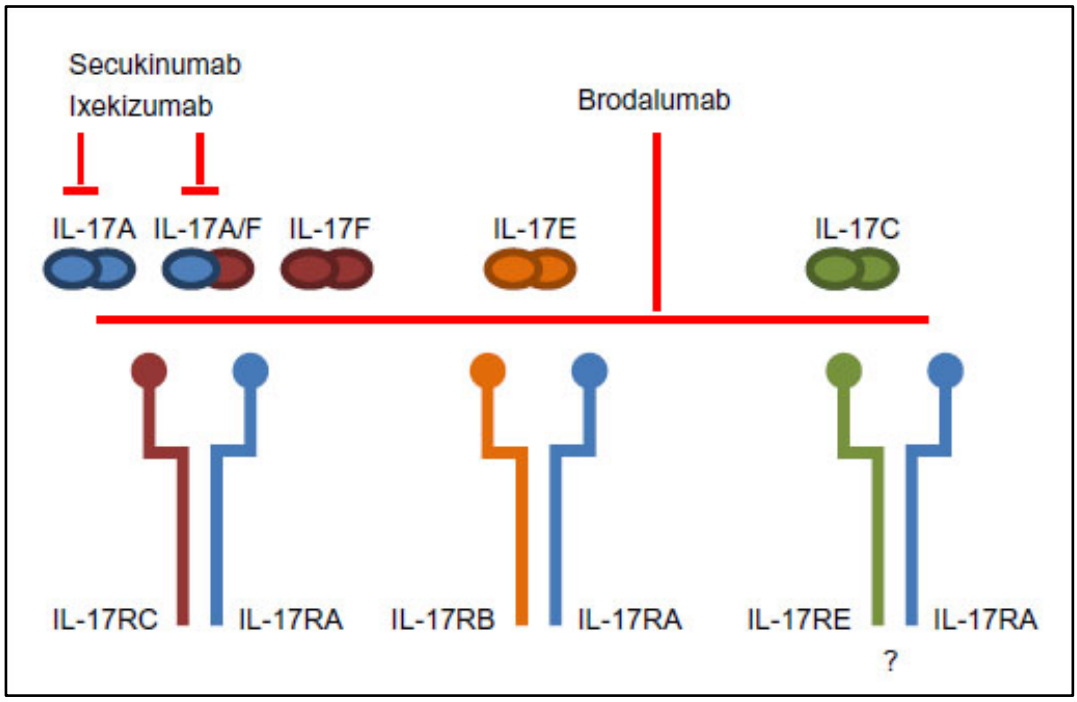

Fig 2: Anti IL-17 treatments for Psoriasis

Risaknkizumab another antibody targeting the IL-23 pathway was licensed by the FDA in 2019, in Phase III trials with ustekinumab as a comparator PASI 90 was achieved by 75.3% of patients receiving risankizumab and PASI 100 by 35.9% of patients treated[20].

New treatments in the pipeline:

Clinical trials are ongoing in the development of new injectable, oral and topical treatments for psoriasis, patients and clinicians will have a wider choice of treatments. This rapid expansion of treatments for psoriasis has as stated previously, enhanced our understanding of the disease. Research is also ongoing to identify predictors of treatment response in psoriasis patients. (PSORT) consotrium aims to better understand determinants of response to biologic therapies and stratify patients accordingly.

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