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Abbreviations used in this issue:

- aOR = adjusted odds ratio
- IL-17 = interleukin 17
- OR = odds ratio
- PASI = Psoriasis Area and Severity Index
- PBS = Pharmaceutical Benefits Scheme
- TB = tuberculosis
- TNF-α = tumour necrosis factor alpha

Welcome to issue 34 of Psoriasis Research Review.

The factors influencing choice of first-line biological therapy for psoriasis in the UK and France were investigated in the first two studies reviewed in this issue. In the French study we discover the most common biologics to be adalimumab, etanercept, ustekinumab and infliximab. Following on we review two studies looking at male fertility in untreated psoriasis and psoriasis treated with TNF-α and fumaric acid esters. Also in this issue we address the issues of psoriasis and suicidality, the association between psoriasis and depressive symptoms, the difference between psoriasis severity in men and women, early psoriasis relapse after stopping brodalumab and the use of methotrexate in psoriasis.

We hope you find the latest issue of Psoriasis Research Review stimulating reading and look forward to any feedback.

Kind Regards,

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Identification of factors that may influence the selection of first-line biological therapy for people with psoriasis: a prospective, multicentre cohort study

Authors: Davison NJ et al.

Summary: This study from the Psoriasis Stratification to Optimise Relevant Therapy (PSORT) consortium aimed to identify factors influencing selection of first-line biological therapy in people with psoriasis using multinomial logistic regression on 2012-15 data (n = 3040) from the British Association of Dermatologists Biologic Interventions Register. Factors identified by this analysis included weight, employment, country of registration, baseline disease severity and history of psoriatic arthritis. The analysis also revealed a change in prescribing behaviour over the period of study.

Comment: See below

Abstract

Factors associated with the choice of the first biologic in psoriasis: real-life analysis from the Psobioteq cohort

Authors: Sbidian E et al.

Summary: Data from the French prospective, observational Psobioteq cohort study were analysed using a multinomial logistic regression model adjusted on year of inclusion (2012-16) to determine factors associated with choosing first-line biological treatment for 830 patients (mean age 46.6 years; 318 [38.3%] female) with moderate-to-severe psoriasis. The most common biologics were adalimumab (n = 355; 42.8%), etanercept (n = 247; 29.8%), ustekinumab (n = 194; 23.4%) and infliximab (n = 34; 4.0%). Patients were more likely to receive adalimumab if they had severe psoriasis (baseline PASI) or psoriatic arthritis than to receive etanercept (aOR 0.42; 95% CI 0.16-1.07) or ustekinumab (aOR 0.15; 95% CI 0.04-0.52). If patients had a positive screening for latent TB they were more likely to receive ustekinumab than adalimumab (aOR 2.39; 95% CI 1.04-5.50). Younger patients were also more likely to receive ustekinumab, and those with chronic obstructive pulmonary disease were more likely to receive ustekinumab or etanercept than adalimumab.

Comment: There are a number of biological agents available on our PBS that we can use in appropriate patients. I predict that there will be another 3-4 joining this table in the next 36 months. Both of these papers, one British and the other French, address the question of what factors to assess in the decision-making process. The British look at the presence of psoriatic arthritis, patient weight, employment status, country of registration and baseline disease severity. The French study does not address the newer IL-17 agents and looks at the last 4 years of biologic prescribing. Adalimumab is more likely to be used in severe psoriasis as defined by baseline PASI as well as in the presence of psoriatic arthritis compared to etanercept and ustekinumab. Ustekinumab is more likely to be used in the presence of a positive screening for latent TB. This drug was also prescribed to more younger patients. Adalimumab is given less in the presence of chronic obstructive pulmonary disease. There was a trend to prescribe etanercept in the presence of cardiovascular comorbidities, metabolic syndrome and in patients with a history of cancer.

Abstract
Untreated psoriasis impairs male fertility: a case-control study

Authors: Caldarola G et al.

Summary: This Italian case-control study assessed gonadal function in 50 psoriatic males to determine the effect of systemic inflammation on fertility and compared them to 50 controls. Decreases in testosterone and sex hormone-binding globulin were observed in psoriasis patients versus controls and estradiol levels were increased. Total sperm count, sperm motility and the proportion of morphologically normal spermatozoa were reduced in patients versus controls. Soluble urokinase-type plasminogen activator receptor (suPAR) levels were increased in patients versus controls and were elevated above reference limits. Ultrasound indices of accessory gland inflammation were observed in 35 psoriasis patients but not in controls.

Comment: Both these papers look at fertility in male patients. This issue has until now not been discussed in previous Psoriasis Research Reviews. The Italian study compared 50 biologic patients with controls measuring hormone levels, sperm count, sperm mobility and percentage of spermatozoa with normal pathology. In their conclusion they suggest that untreated psoriasis may impair male fertility. It is considered that this impact is due to systemic inflammation on the hormonal profile and on sexual accessory gland inflammation. The German study assessed male fertility and sperm quality. Only 27 patients were studied from which 101 semen specimens were obtained. They concluded that an overall cluster analysis showed adalimumab, secukinumab, and ustekinumab were comparable in terms of high efficacy and tolerability. Ixekizumab and infliximab were differentiated by very high efficacy but poorer tolerability. The lack of longer-term controlled data limited their analysis to short-term outcomes. Trial performances also do not equate to real-world, long-term safety and effectiveness data.

Comment: See below

Reference: Dermatology. 2017; Jun 9 [Epub ahead of print] 

Influence of TNF-alpha inhibitors and fumaric acid esters on male fertility in psoriasis patients

Authors: HeppF et al.

Summary: This German single-centre, open-label, prospective study aimed to determine the effect of TNF-α inhibitors, fumaric acid esters and disease activity status on fertility and sperm quality in 27 male psoriasis patients (101 semen specimens) with a mean baseline PASI score of 11.05. Semen was analysed at baseline and every 3 months during treatment. Normozoospermia without any other abnormal seminal values was observed in 14.8% of patients, while ≥1 sperm/seminal abnormality was observed in the other 85.2% of patients; two patients had azoospermia. Sperm parameters indicating genital tract inflammation were observed in 48.1% of patients. TNF-α inhibitors and fumaric acid esters had no negative effects on relevant sperm parameters.

Psoriasis and suicidality: A systematic review and meta-analysis

Authors: Singh S et al.

Summary: The next two articles have some linkage. This US systematic review and meta-analysis examined the relationship between psoriasis and suicidality using Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines in literature published between 1946 and 2017. In total, 18 studies (n = 1,767,583) were identified that included 330,207 psoriasis patients. Random effects modelling indicated a pooled OR for suicidal ideation of 2.05 (95% CI 1.54-2.74) and a pooled OR for suicide attempts (combined attempted and completed suicides) of 1.26 (95% CI 1.13-1.40) among psoriasis patients. Subgroup analysis illustrated that psoriasis patients were more likely to attempt (OR 1.32; 95% CI 1.14-1.54) and complete (OR 1.20; 95% CI 1.04-1.39) suicide than those without psoriasis. A greater likelihood of suicidality was associated with more severe psoriasis and younger age.

Reference: J Invest Dermatol. 2017; 137(9):1646-54

The association between the clinical diversity of psoriasis and depressive symptoms: the HUNT Study, Norway

Authors: ModalsliEH et al.

Summary: This analysis linked data from the population-based 3rd Nord-Trøndelag Health Study (HUNT3; n = 37,833) to prescription and population data to determine associations between depressive symptoms and inverse psoriasis, psoriasis severity and psoriasis duration. A weak association was identified between any psoriasis and the prevalence of depressive symptoms (aOR 1.12; 95% CI 0.97-1.28). The association was stronger when psoriasis was characterised by inverse anatomical distribution (OR 1.32; 95% CI 1.02-1.70), requirement for systemic psoriasis medication (OR 1.47; 95% CI 1.00-2.17) and longer disease duration (OR 1.33; 95% CI 1.09-1.64). Conversely, when there was no inverse psoriasis distribution, no requirement of systemic medication, or shorter disease duration, psoriasis was not meaningfully associated with depressive symptoms.

Comment: This is a study out of Norway where the population-based HUNT3 Study was linked to the Norwegian Prescription Database and Statistics Norway. Depressive symptoms were assessed using the Hospital Anxiety and Depression Scale (HADS). Their conclusion was that depressive symptoms do not seem to be a major concern amongst subjects with psoriasis in the general Norwegian population. Clearly there is a significant difference between Norway and America.


Quantitative evaluation of biologic therapy options for psoriasis: A systematic review and network meta-analysis

Authors: Jabbar-Lopez ZK et al.

Summary: This network meta-analysis of direct and indirect evidence on biologic efficacy and tolerability, and hierarchical cluster analysis of outcomes was conducted on data from randomised controlled trials of licensed biological psoriasis treatments (adalimumab, etanercept, infliximab, secukinumab, ustekinumab, ixekizumab) to assess relative efficacy and tolerability. All the licensed biologics demonstrated efficacy when compared with placebo or methotrexate at 3-4 months. Cluster analysis indicated that adalimumab, secukinumab and ustekinumab had similar efficacy and tolerability, but that ixekizumab and infliximab had high efficacy but poorer tolerability.

Comment: This study comes out of London. It is a systematic review and network meta-analysis of therapeutic options. They discuss the lack of head-to-head randomised controlled trials making choosing between the different biologic agents difficult on scientific grounds. MEDLINE, PubMed, Embase and Cochrane were searched for randomised controlled trials of licensed biologic treatments for skin psoriasis. The study group performed a network meta-analysis to identify direct and indirect evidence comparing biologics with one another, methotrexate or placebo. They concluded that an overall cluster analysis showed adalimumab, secukinumab, and ustekinumab were comparable in terms of high efficacy and tolerability. Ixekizumab and infliximab were differentiated by very high efficacy but poorer tolerability. The lack of longer-term controlled data limited their analysis to short-term outcomes. Trial performances also do not equate to real-world, long-term safety and effectiveness data.


A systematic review and network meta-analysis to assess relative efficacy and tolerability of adalimumab, etanercept, infliximab, secukinumab, ustekinumab, ixekizumab, and placebo. They concluded that an overall cluster analysis showed adalimumab, secukinumab, and ustekinumab were comparable in terms of high efficacy and tolerability. Ixekizumab and infliximab were differentiated by very high efficacy but poorer tolerability. The lack of longer-term controlled data limited their analysis to short-term outcomes. Trial performances also do not equate to real-world, long-term safety and effectiveness data.

Abstract
The Cosentyx Efficacy

He was so excited to have been given a greater opportunity to achieve clear skin*1

*At week 52, PASI 100 responses to secukinumab and ustekinumab were 45.9% and 35.8% respectively (p=0.0103). Primary study endpoint was achieved with secukinumab demonstrating superiority in PASI 90 response (79%) to ustekinumab (57.6%; p<0.0001) at Week 16.

That’s Cosentyx

PBS Information: Section 85 Authority Required for the treatment of severe chronic plaque psoriasis, active ankylosing spondylitis and severe psoriatic arthritis.
Refer to PBS Schedule for full Authority information.

See approved Product Information before prescribing. Approved Product Information available on request.
For the most up-to-date Product Information, go to: https://www.novartis.com.au/products/healthcare-professionals
Severity of psoriasis differs between men and women: A study of the clinical outcome measure Psoriasis Area and Severity Index (PASI) in 5438 Swedish register patients

Authors: Hägg D et al.

Summary: This Swedish cross-sectional study used data from a national registry for systemic treatment of psoriasis (PsoReg; n = 5438) to examine sex differences in psoriasis severity using the gold standard PASI measure and examined the elements of the PASI score. Overall, and across all ages, women had lower median PASI scores (5.4) than men (7.3; p < 0.001). Itemised PASI analyses confirmed that women had lower scores than men across all body areas except for the head.

Comment: This is an interesting article out of Sweden. This is a cross-sectional study based on the national registry for systemic treatment of psoriasis. They had 5438 patients entered in this database. Differences in the PASI score and its elements at enrolment were tested by multivariable ordinal logistic regressions. Their results show that women had statistically significantly lower median PASI scores (5.4) than men (7.3). This was consistent across all ages. There were no differences in the use of medications prior to enrolment that may have caused this difference between the sexes. This is an interesting study, which may explain why in most biologic studies there is an excess in males.


Abstract

Early relapse of psoriasis after stopping brodalumab: a retrospective cohort study in 77 patients

Authors: Masson Regnault M et al.

Summary: This retrospective, multicentre cohort study (n = 77) examined the pattern of psoriasis recurrence (request from patient to initiate a new treatment) after the abrupt interruption of brodalumab drug development by Amgen in June 2015. At discontinuation, 67 (87%) patients had reached PASI90, all 77 patients relapsed after 9 months follow-up with a median time to relapse of 46 days; 73 patients presented with plaque psoriasis, one with erythrodermic psoriasis, and three with pustular psoriasis. In seven patients without a previous history of psoriatic arthritis, relapse was associated with inflammatory joint pain suggestive of psoriatic arthritis. In eight patients with limited relapse, topical treatment controlled the condition; 43 patients received a biological, two were included in an investigational clinical trial and 15 received conventional systemic agents.

Comment: Biologic agents targeting IL-17 are very effective at clearing moderate-to-severe psoriasis. The newest drugs have been targeted at this site. There is limited information regarding the frequency and pattern of psoriasis relapse upon treatment cessation. We can expect that brodalumab will be a prescribable product in Australia within 12-18 months. It is a small study in which 77 patients were followed up. Their conclusion was that cessation of brodalumab is associated with a rapid relapse of psoriasis with some patients experiencing a rebound. They have recommended that treatment with IL-17 antagonists is not stopped abruptly even in patients who experience complete clearance of psoriasis. All their patients relapsed after follow up of 9 months. The median time to relapse was 46 days. One patient relapsed with erythrodermic psoriasis and three of their 77 with pustular psoriasis. Among seven patients who had no previous history of psoriatic arthritis, their relapse was associated with inflammatory joint pain.


Abstract

Effectiveness and safety of methotrexate in psoriasis: an eight-year experience with 218 patients

Authors: Cabelló Zurita C et al.

Summary/Comment: A study of 218 patients of which methotrexate was administered in 67% as the first systemic treatment. The average treatment duration was 17.2 months. In this study group, 33.5% achieved a reduction of PASI of 75% at week 12, 34.9% at week 16, 44.7% at week 24, and 52.8% at week 48. These results are a little higher than what I am used to. 3.3% had to discontinue because of analytical hepatic (2.8%) or renal (0.5%) abnormalities. Only one patient experienced severe interstitial pneumonitis. No liver biopsies were required. Methotrexate is a cheap drug with impressive clinical results.

Reference: J Dermatolog Treat. 2017;28(5):401-05

Abstract