Clinical trials are very much obscured by the entry requirements for the trial. An interesting comparison of drug discontinuation, effectiveness, and safety between clinical trial eligible and ineligible patients in the British Association of Dermatologists Biologic Interventions Register, undertaken by eminent dermatologists in the UK, has revealed that ineligible patients have smaller absolute PASI changes and greater serious adverse event rates versus eligible patients. Following on, we take a look at a review paper investigating the role of the microbiome in psoriasis. Other topics in this issue include calcipotriol/betamethasone aerosol foam for plaque psoriasis, methotrexate and liver cirrhosis in psoriasis patients with HBV/HCV, T-cell-mediated immune response during tofacitinib treatment, biologic treatment of recalcitrant paediatric psoriasis, mental health outcomes after biologic versus oral therapies, paediatric patients with psoriasis and psychiatric disorders, guselkumab in generalised pustular psoriasis and erythrodemic psoriasis and clinical response to methotrexate in Asian patients. We hope you find the latest issue of Psoriasis Research Review stimulating reading and look forward to any feedback.

Kind Regards,
Clinical Associate Professor Kurt Gebauer
kurt.gebauer@researchreview.com.au

Comparison of drug discontinuation, effectiveness, and safety between clinical trial eligible and ineligible patients in BADBIR

Authors: Mason KJ et al.

Summary: This study examined whether psoriasis patients in biologic clinical trials are representative of real-world populations by assessing data from the British Association of Dermatologists Biologic Interventions Register (BADBIR) on drug discontinuation, effectiveness and rates of serious adverse events between clinical trial eligible and ineligible patients receiving etanercept (Enbrel® only; n = 1509), adalimumab (n = 4000), or ustekinumab (n = 1627). In total, 839 (56%) etanercept, 2219 (56%) adalimumab, and 754 (46%) ustekinumab recipients were categorised as clinical trial eligible. The most common ineligibility criteria were diabetes mellitus (etanercept 9%; ustekinumab 12%) and non-chronic plaque psoriasis (adalimumab 4%). Ineligible patients (etanercept 24%; adalimumab 7%; ustekinumab 24%) had smaller absolute PASI changes after 6 and 12 months (adalimumab, ustekinumab), and greater serious adverse event rates versus eligible patients (etanercept IRR 1.9; 95% CI 1.4-2.6; adalimumab IRR 2.0; 95% CI 1.5-2.6; ustekinumab IRR 2.8; 95% CI 2.1-3.8). Discontinuation rates did not differ between eligible and ineligible patients.

Comment: Registry data contains information that best mimics what happens in our clinical practice. Clinical trials are very much obscured by the entry requirements for the trial. There is concern that patients who are not eligible for entry into trials have a greater risk of serious adverse events, however, this is statistically not proven. This is a study from eminent dermatologists in the UK looking at the British biologic database. Interestingly, of the 7136 patients in the study, just more than half of patients on a biologic in the UK would have been eligible as being registered for a clinical trial. The most common reason for ineligibility in this paper was diabetes. Those patients that would have been ineligible for entry into clinical trials achieved lesser improvements in PASI at 6 and 12 months. Indeed they did have significantly higher rates of severe adverse events. My interpretation of this study is that our clinic patients are more likely to have more serious adverse events and not respond as well as trial data. There is nothing in this paper that would suggest that we should not be treating such patients as we do now.


Abstract
Prospective, observational, non-interventional, multicentre study on the efficacy and tolerability of a new calcipotriol/betamethasone aerosol foam (Enstilar®) in patients with plaque psoriasis under daily practice conditions

Authors: Gerdes S et al.

Summary: This German, 4-week, open-label, prospective, non-controlled, observational study examined the use of a new aerosol foam comprising calcipotriol 50 µg/g plus betamethasone dipropionate 0.5 mg/g (Cal/BD foam, Enstilar®) in 410 adult patients with plaque psoriasis (56% male). The cohort had baseline investigator global assessment (IGA) psoriasis-severity grades of mild (41.8%), moderate (40.63%) and severe (31.39%). After 4 weeks, 49% of patients had an IGA of clear/almost clear. Mean affected body surface area decreased from 12.9% to 7.6%, and the PASI score decreased from 12.4 to 8.5 (p<0.0001). In patients with severe IGA, 43% achieved treatment success (IGA 0 or 1 and ≥2-step improvement). 7% of patients experienced adverse events.

Comment: Enstilar® is a PBS listed product. This paper reports 410 adult psoriasis patients who used it for 4 weeks in an open-label, prospective, non-controlled, observation non-interventional manner. After 4 weeks of treatment, 49% of these patients achieved an IGA of almost clear. The mean affected body surface area was significantly reduced and PASI was half. Certainly my experience seems to mimic the trial data. The base is quite popular as it spreads a long way and is not very greasy, unlike the ointment formulation. Many of my patients found it particularly good for hands, a site which I do not expect much therapeutic response with topical treatments. I appreciate that this is very much a pro-product endorsement; however, I do believe this is a product we should all be using.

Abstract

Psoriatic patients with chronic viral hepatitis do not have an increased risk of liver cirrhosis despite long-term methotrexate use: real-world data from a nationwide cohort study in Taiwan

Authors: Tang KT et al.

Summary: This Taiwanese nationwide population-based cohort study used data from the National Health Insurance Research Database to examine long-term methotrexate use and risk of chronic viral hepatitis-related cirrhosis. A total of 2417 psoriatic patients with chronic HBV and 1127 psoriatic patients with chronic HCV were identified, and over a mean follow-up of >9 years since viral hepatitis diagnosis, 125 (5%) HBV and 120 (11%) HCV patients developed liver cirrhosis. The proposition of methotrexate recipients and non-recipients that developed liver cirrhosis did not differ (4% vs 5% with HBV; 11% vs 11% with HCV).

Comment: Methotrexate is well established in dermatology both in psoriasis and eczema. Our psoriatic patients have co-morbidities that lead to fatty liver, hepatitis and extremely rarely liver failure. Those in practice for long enough who use methotrexate regularly will have some patients who have had significant medical issues. This study out of Taiwan looked at chronic viral hepatitis in association with the use of oral methotrexate. 2417 patients with chronic HBV, of which 317 were using methotrexate, and 1127 patients with HCV, of which 174 were using methotrexate, with 3-year follow up. I find the numbers of patients treated as well as the time they were treated gives this paper significant authority. Results presented above show that the long-term use of methotrexate in this population may not be associated with an increased risk of liver cirrhosis amongst psoriatic patients with chronic viral hepatitis. Clinically it is becoming easier to treat HBV and HCV. Certainly in my practice I send them off to the hepatologists for treatment first. This paper tells me that I can treat their skin disease with methotrexate, should I wish, whilst following my normal management plan. Additionally, I don’t need to worry terribly about causing the patient great harm. This is a paper that will help me sleep better at night.

Reference: J Am Acad Dermatol. 2018; May 9 [Epub ahead or print]
Abstract

T-cell–mediated immune response to pneumococcal conjugate vaccine (PCV-13) and tetanus toxoid vaccine in patients with moderate-to-severe psoriasis during tofacitinib treatment

Authors: Winthrop KL et al.

Summary: This study examined long-term tofacitinib exposure and its effects on T-cell function in 60 psoriasis patients before and after vaccination with the T-cell–dependent vaccines monovalent tetanus toxoid and 13-valent pneumococcal conjugate (PCV-13). Four weeks after vaccination, the geometric mean fold rise in 13 PCV serotypes varied from 8.3 (serotype 3) to 101.9 (serotype 6A). Results were similar in patients with and without baseline lymphotohypnia. Rises in tetanus toxoid antibody concentrations were ≥2-fold in 51 (88%) patients and ≥4-fold in 35 (60%) patients.

Comment: I have been to a number of lectures about vaccinations for our so-called immunosuppressed patients who are on systemic agents both biologic and small molecules. The Janus kinase inhibitors are a class of drugs that we will be using more of in trial first but then in clinical practice. This paper looks at tofacitinib, an agent that is used on the PBS by rheumatologists. Some of us are using it for alopecia areata and other indications. The conclusion is that most psoriasis patients who receive tofacitinib can mount a satisfactory T-cell dependent immune response to pneumococcal and tetanus toxoid vaccines. Once again, we dermatologists are being told about how toxic and immunosuppressant the drugs we use are, only to find that they are not that immunosuppressant. Again, another study that helps me sleep better at night.

Abstract

Biologic treatment of recalcitrant pediatric psoriasis: a case series from a tertiary medical center

Authors: Oliffe A et al.

Summary: This single centre, retrospective case series assessed the use of biologic agents in 10 paediatric psoriasis patients (mean age 5.75 years) with severe psoriasis treated with biological therapy from 2010 to 2016. Treatments received by these patients included etanercept (n = 9), adalimumab (n = 5), ustekinumab (n = 3) and infliximab (n = 2), with additional systemic therapy in seven cases; methotrexate (n = 5), phototherapy (n = 4), cyclosporine A (n = 1) and colchicine (n = 1). The most common discontinuation cause was secondary failure (etanercept n = 5, adalimumab n = 3). Biological treatment failure occurred in six patients and three patients failed two biological treatments; four patients are still receiving first-line biologic therapy with etanercept.

Comment: Studies in paediatric dermatoses are few. Invariably they contain small numbers. This is a case series from a tertiary medical centre where 10 patients were followed. There were more biologics per average paediatric patient than I see in my adult biologic group. The most common reason for switching was secondary failure. It would be interesting to see what would happen with the newer agents, which seem to persist over the longer term in the adult group. The conclusion is important, showing biologic therapy is effective and safe in recalcitrant paediatric psoriasis. They didn’t see anything particularly different from the adult group. This article is for those of us that treat paediatric patients. One to pull out and put in your database for when you next need to prescribe in this group.

Reference: J Dermatolog Treat. 2018; June 4 [Epub ahead of print]
Abstract

The role of the microbiome in psoriasis: moving from disease description to treatment selection?

Authors: Langan EA et al.

Summary: This review examined the role of the microbiome in psoriasis and how microbiome studies provide insights into pathogenesis and treatment selection. The review describes 16S ribosomal RNA sequencing and discusses current understanding of the cutaneous microbiome in health and disease, particularly psoriasis. Intra-individual microbiome cross-talk and potential mechanisms of interactions between skin flora and immune system function are also discussed.

Comment: The microbiome is a fascinating subject that is in its infancy in dermatology. I go to any lectures I can find on this subject and am still just as confused as when I first heard about them. An opinion paper from the gods of European dermatology. I would recommend that readers obtain the original as it is an excellent summary for where medicine is at the moment. I look forward to understanding what it is all about. Better still being able to use this information to make my patients better. That of course is a long way off.

Abstract

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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=.0103). Primary study endpoint was achieved with secukinumab demonstrating superiority in PASI 90 response (79%) to ustekinumab (57.6%; p<.0001) at Week 16 in patients with moderate-severe plaque psoriasis.

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


www.researchreview.com.au
Comparison of mental health outcomes among adults with psoriasis on biologic versus oral therapies: A population-based study

Authors: Salame N et al.

Summary: This US cross-sectional study compared the effect of biologic versus oral therapies on mental health outcomes among 2,303,534 adult patients with moderate-to-severe psoriasis. Mean Kessler 6 scores in those on biologic therapies were lower than those on oral therapies (2.72 vs 3.70; p < 0.001) as were mean Patient Health Questionnaire 2 scores (0.540 vs 0.890; p < 0.001). Multivariate linear regression models suggested that biologic therapy was associated with reductions in both Kessler 6 (p < 0.001) and Health Questionnaire 2 (p = 0.016) scores versus oral therapy.

Comment: In the May edition of this series I discussed a mental health paper, namely whether patients flare with stress. The data in that review was not sufficient to be positive or negative. This is a study from a well-known American author looking at a very large number of patients, 2,303,534 on biologic versus oral therapies. Biologic therapies are associated with reductions in psychological distress and depression when compared to oral therapy in the US adult population. This is what one would expect as biologic agents work a lot better than the oral therapies. However, there is still an ongoing question mark regarding the induction of depression by the use of biologics. In all the trials I conduct there is extensive monitoring both by the physician as well as patient questionnaires of depression. I read this paper as saying we shouldn’t be so worried and get on and treat our patients clinically as we would like.

Reference: J Dermatol Treat. 2018; May 29 [Epub ahead of print]

Pediatric patients with psoriasis and psychiatric disorders: Premorbidity and co-morbidity in a case-control study

Authors: Kara T et al.

Summary: This study, in children aged 8–16 years, examined psychiatric diagnoses before and during psoriasis in 54 paediatric psoriasis patients and 54 healthy individuals. Based on assessments using The Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime Version (K-SADS-PL), Children’s Dermatology Life Quality Index (CDLQI), Screen for Child Anxiety Related Emotional Disorders (SCARED) and Children’s Depression Inventory (CDI), one or more psychiatric diagnosis occurred in 70.3% of children with psoriasis versus 27.7% of healthy controls (p = 0.0001); 73.6% were psychiatric diagnoses in the premorbid period. Paediatric psoriasis patients had a 9.21-fold risk of anxiety (p = 0.0001) and a 6.65-fold risk of depression (p = 0.0019) versus controls.

Comment: A very rare paper, being both psychiatric and paediatric. 108 children is a reasonable number for a paediatric study, 54 with psoriasis and 54 with no skin disease. Children with psoriasis were determined to have a 9.21-fold greater risk of anxiety and a 6.65-fold greater risk of depression compared to the control group. These are more prevalent when the patient has documented extensive skin disease. This data confirms what we see in the adult patients, that when you have an awful skin disease you are anxious and unhappy. Paediatric patients have similar psychological issues to adults. However, these effects are considered likely to be more severe in the younger-aged group.

Reference: J Dermatol Treat. 2018; May 28 [Epub ahead of print]

Guselkumab, a human interleukin-23 monoclonal antibody in Japanese patients with generalized pustular psoriasis and erythrodermic psoriasis: Efficacy and safety analyses of a 52-week, phase 3, multicenter, open-label study

Authors: Sano S et al.

Summary: This Japanese, open-label, phase III study tested a human interleukin-23 monoclonal antibody, guselkumab, in patients with generalised pustular psoriasis (n = 10) and erythrodermic psoriasis (n = 11). After 16 weeks, 77.8% of generalised pustular psoriasis patients achieved treatment success as did 90.9% of erythrodermic psoriasis patients. Guselkumab consistently improved secondary end-point responses including PASI, IGA, Japanese Dermatological Association Severity Index and improvement in body surface area involvement. Quality of life (Dermatology Life Quality Index) improvements observed in patients with generalised pustular psoriasis. The most common treatment-emergent adverse event was nasopharyngitis (6/21; 28.6%).

Comment: Guselkumab is an agent that we may be prescribing on the PBS by the end of the year. Therefore, biologic users need to learn more about it. This is a Japanese paper that looks at generalised pustular psoriasis and erythrodermic psoriasis, both of which are generally excluded from clinical trials. Clinically their presentation is extremely rare. Consequently, when faced with such a patient we really have little data as to what to do. Traditionally my “go to” drug for these severe psoriasis sub-types that don’t respond to standard therapy is infliximab. This study looks at 10 patients with generalised pustular psoriasis and 11 having erythrodermic psoriasis. Small numbers, however, they are very rare diagnoses. 77.8% of pustular and 90.9% of erythrodermic patients achieved treatment success. Safety findings were consistent with the general psoriasis treatment groups. This paper would leave me to suggest that guselkumab is a logical choice in this group.


Effectiveness of and factors associated with clinical response to methotrexate under daily life conditions in Asian patients with psoriasis: A retrospective cohort study

Authors: Pongparit K et al.

Summary: This retrospective observational cohort study was conducted in 100 Asian adult psoriatic patients to assess the effectiveness of methotrexate and to identify factors associated with clinical response. Over a mean follow-up of 15.3 months, reductions in PASI score of ≥75% were achieved by 26% of patients at 3 months, 32.5% at 6 months and 45.2% at 12 months. Probability of drug survival at 12 and 24 months, by Kaplan–Meier analysis, was 68.7% and 52.1%, respectively. Male sex, BMI <25 kg/m² and absence of abdominal obesity were associated with treatment response in univariate analysis, but only male sex in multivariate analysis.

Comment: In Australia we have a very multicultural society. Most studies are based on European or American data. Asian patients are very much under represented in this group. We know with azathioprine and allopurinol that in Asians the metabolism of medications can be very different. This is an observational retrospective cohort study looking at adult psoriatic patients, 61 patients were followed for 12 months. Reduction in PASI score of at least 75 was achieved in 26% at 3 months, 32.5% at 6 months and 45.2% at 12 months. This demonstrates that methotrexate does work slowly in Asian patients, possibly slower than what I expected for my normal patient group. At 12 months, 68.7% and at 24 months 52.1% of patients were still on drug. Male sex, low BMI and the absence of abdominal obesity were factors associated with improved response. A paper that probably will not change our practice; however, it is useful to review considering that this is a drug we commonly use in all of our patients. There is limited data in different racial groups.