Welcome to issue 50 of Psoriasis Research Review.

Highlights of the Dutch evidence- and consensus-based guideline on psoriasis 2017 are now available and are a worthwhile read for those treating psoriatic patients. The guideline includes sub-sections on the treatment of paediatric patients and the management of patients during pregnancy. In this issue we also take a look at the persistence of treatment with biologics for patients with psoriasis in a real-world setting in France, and discover that approximately 85% of patients who discontinue their first biologic resume systemic treatment of some form in the following year, with 85% restarting a biologic. Other topics in this issue include cause-specific mortality in patients with psoriasis and psoriatic arthritis (PsA), psychiatric morbidity and suicidal behaviour in psoriasis patients, the development of IBD in patients with psoriasis, the long-term use of acitretin in psoriasis, and onychomycosis in nail psoriasis.

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

Highlights of the updated Dutch evidence- and consensus-based guideline on psoriasis 2017

Authors: van der Kraaij GE et al.

Summary: This article provides a summary of the 2017 updated Dutch psoriasis guideline. This guideline is based on the Dutch Society of Dermatology and Venerology guideline and the European Dermatology Forum guideline on the treatment of psoriasis, as well as newer literature. This article focuses mainly on patients with moderate-to-severe psoriasis and highlights the most important aspects of systemic therapy in patients with psoriasis. The summary aims to provide a useful manual for daily clinical practice and includes recommendations for screening, monitoring and treatment. A concise physician decision aid for treating patients with biologics and the small molecule inhibitor apremilast is also included.

Comment: The fashion for having individual national guidelines is starting to abate. There are no Australian guidelines for the treatment of psoriasis. The Australian Psoriasis Collective of which I am a member has published a number of articles on the medical therapy of psoriasis in the Australian Journal of Dermatology. I found this article interesting as it has sub-sections on the treatment of paediatric patients and pregnancy, which are niche populations with very limited research. For those truly interested in psoriasis and treatments I would recommend getting a copy of this article and reviewing it in depth. It is a worthwhile paper to assess.


Abstract

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Perspective of treatment with biologics for patients with psoriasis: a real-world analysis of 16,545 biologic-naive patients from the French National Health Insurance database (SNIRAM)

Authors: Sibidian E et al.

Summary: This nationwide population-based cohort study, involving biologic-naive adult patients (n = 16,545; mean age 48.6 years; 57.3% male) with psoriasis registered in the French National Health Insurance database (SNIRAM) between 2008 and 2016, assessed the long-term persistence of biologics used to treat psoriasis in a real-life setting. All included patients had received a first prescription of etanercept, infliximab, adalimumab or ustekinumab. During a mean follow-up of 3.6 years, there were 9988 treatment discontinuations. A biologic treatment persistence rate of 61.9% for the first year, 33.3% for the third year and 22.6% for the fifth year was shown by Kaplan-Meier survival analyses. The persistence rate was higher for ustekinumab than for the other biologics. Approximately 85% of patients, having discontinued their first biologic, resumed systemic treatment of some type in the following year (85% of these cases restarted a biologic).

Comment: The reader is only able to review published data on psoriasis and biologics. Most of these come from studies that are sponsored by the pharmaceutical industry. There are limitations with this type of information as the patients who are selected in these trials are relatively free of confounding medical complaints. The so-called real-world problems of patients with multiple medications and multiple diseases in those who require treatment always lead to clinical conundrums. This paper reviews the French National Health Insurance database between 2008 and 2016. 16,545 out of 874,549 patients were biologic naive. There were 9988 treatment discontinuations. The biologic agents they utilised were etanercept, infliximab, adalimumab and ustekinumab. Of this list ustekinumab is the only agent that Australian dermatologists have been using with enthusiasm. The others have not been frequently utilised in Australia for many years particularly because of their poor persistence and lack of sufficient response or difficulty in administration. It therefore doesn’t surprise me that the conclusion was that biologics are less effective in real-life non-selective populations than physicians have been led to believe. The clinical patient group never does as well as the trial group for the reasons listed above. Why did I select this paper for this review? The comment I wish to make is that trial data are helpful. Any data are useful in clinical practice. We need to be critical in reviewing what is presented to us. This statement also includes whatever I write.


Abstract

Psychiatric morbidity and suicidal behaviour in psoriasis: a primary care cohort study

Authors: Parisi R et al.

Summary: To examine psychiatric comorbidity, psychotropic medication and risk of suicidality in people with psoriasis, data from the Clinical Practice Research Datalink, with linkage to Hospital Episode Statistics and Office for National Statistics mortality records, were analysed for 56,961 psoriasis patients and 876,919 matched patients without psoriasis. The deprivation-adjusted HR suggested a lower suicide risk in people with psoriasis (HR 0.59; 95% CI 0.41-0.85). Risk of suicide varied with age, being lower in people with psoriasis diagnosed after 40 years of age (HR 0.38; 95% CI 0.21-0.66), but no difference in those diagnosed before 40 years of age was evident (HR 0.92; 95% CI 0.58-1.46). Conversely, there was an increased risk of self-harm associated with psoriasis (HR 1.15; 95% CI 1.04-1.27).

Comment: A paper from the Chris Griffiths Manchester Unit looking at psychiatric morbidity. Clinicians understand that patients with chronic debilitating disease have psychiatric morbidity. In the development of new systemic agents for psoriasis there is a heavy emphasis on screening patients with pre-existing psychiatric and addiction issues. There is monitoring of depression and suicidality at every visit. This paper showed no increase in risk of suicide. There have been biologic agents withdrawn from development because some of these monitoring tools highlighted a potential increase in depression rates. There seems to be a difference in papers from America where there is a lot more depression in trial patients than in Europe. Presently this issue is like isotretinoin and the treatment of acne. My clinical impression is that systemic and especially biologic agents do not increase the risk of depression, however, I am not absolutely convinced this is so. This is a further paper for those who are interested in how our patients feel. Certainly it supports the view point that I am not making my patients psychological status worse.


Abstract

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Risk of first-time and recurrent depression in patients with psoriasis: a population-based cohort study

Authors: Egeberg A et al.

Summary: This analysis of Danish administrative registers (1997-2016) examined the incidence and risk of new and recurrent depression over up to 20 years of follow-up in 247,755 patients with psoriasis (topical treatment n = 220,721 [mid]; systemic non-biologicals n = 24,771 [moderate]; biological therapy n = 2263 [severe]) matched 1:1 with controls. In adjusted models, the HRs of depression were 1.19 (95% CI 1.17-1.20) for mild psoriasis, 1.19 (95% CI 1.15-1.23) for moderate psoriasis and 1.50 (95% CI 1.23-1.84) for severe psoriasis. The greatest risk occurred in those with severe psoriasis aged 40-50 years. Concurrent IBD was associated with increased risk of depression.

Comment: This paper follows on from the last article. It comes out long w

Associate Professor of papers and comments are provided by Clinical Research Revie

Abstract


Incidence and risk of inflammatory bowel disease in patients with psoriasis—A nationwide 20-year cohort study

Authors: Egeberg A et al.

Summary: An analysis of a 20-year Danish national cohort (n = 235,038) of patients with psoriasis and a 1:1 matched reference group examined the incidence rates of Crohn’s disease (CD) and ulcerative colitis (UC). CD or UC developed in <1% of psoriasis patients during follow-up. CD incidence rates were highest in younger women with psoriasis and in patients with concurrent PsA. Men with psoriasis had high incidence rates of UC versus non-psoriasis controls. In patients receiving topical treatment, the CD adjusted HR (aHR) was 1.84 (95% CI 1.47-2.29), in those receiving systemic non-biological therapy it was 2.38 (95% CI 1.62-3.49). No CD cases occurred during biological therapy. UC aHR was 1.49 (95% CI 1.29-1.72) for topical, 1.53 (95% CI 1.14-2.01) for systemic non-biological and 1.22 (95% CI 0.93-1.63) for biological therapy.

Comment: Another long study out of Scandinavia looking at a 20-year nationwide cohort of 235,038 Danish patients with a matched reference group. IBD became pertinent with the IL-17 class of biologic treatments. In this paper, the authors found less than 1% of psoriasis patients developed IBD during follow up. Younger women and patients with concurrent PsA were more likely to develop CD. UC was more likely to develop in men. In summary this paper highlights that our patient group is more likely to develop IBD. It seems to be no signal that any particular medication group is more likely to be


Long-term safety and drug survival of acitretin in psoriasis: a retrospective observational study

Authors: Chularojanamorn L et al.

Summary: This single-centre, retrospective observational analysis (2012-17) examined long-term safety, drug survival, and factors associated with the survival of acitretin (mean cumulative dose 19.28 mg/day) in 104 psoriasis patients receiving acitretin for >1 (n = 73), 3 (n = 39), 5 (n = 24) or 10 (n = 6) years. Most adverse events were mild and tolerable; nine patients withdrew due to adverse events. Cirrhosis or uncontrolled hyperlipidaemia was not observed in any patient and drug survival rates at 1, 2, 3, 4, and 5 years were 79%, 69.5%, 61.2%, 57.6% and 53.5% respectively. There were no differences in drug survival in patients stratified for obesity, metabolic syndrome or dyslipidemia.

Comment: With so many publications on newer biologics, some of the more established agents can easily be forgotten. Acitretin is a drug that we all use. Certainly in my practice it is third to fourth in line. This is a study that comes out of Thailand that raises important pharmacoeconomic points. Five years of adult patients were tracked in a central Bangkok hospital. Only 104 patients comprised the cohort with a mean treatment duration of 3.2 years. The cumulative dose was relatively low compared to my patients. Being a Thai study I would expect the participants to be of far lighter weight than what I see in my office. <10% of patients withdrew due to side effects, no patient developed cirrhosis or uncontrolled hyperlipidaemia. They had no difference between patients who were obese, had metabolic syndrome or dyslipidaemia compared to those who didn’t. I read this data to support the statement that acitretin is unlikely to cause significant liver or lipid problems. More importantly, those patients who have liver issues, obesity or metabolic syndrome do not seem to have any increased risk either. The presence of fatty liver or dyslipidaemia is not a contraindication to the use of acitretin long term.


Elderly psoriatic patients under biological therapies: an Italian experience

Authors: Ricceri F et al.

Summary: An Italian, retrospective, multicentre review examined the use of biological therapies (adalimumab 31.2%, ustekinumab 28.9%, etanercept 20.3%, secukinumab 15%, infliximab 3%, golimumab 1%, certolizumab pegol 0.6%) in 266 elderly (>65 years) psoriatic patients. PASI score at baseline had a mean of 16.5, which was reduced after treatment duration of 3.2 years. The cumulative dose was relatively low compared to my patients. Being a Thai study I would expect the participants to be of far lighter weight than what I see in my office. <10% of patients withdrew due to side effects, no patient developed cirrhosis or uncontrolled hyperlipidaemia. They had no difference between patients who were obese, had metabolic syndrome or dyslipidaemia compared to those who didn’t. I read this data to support the statement that acitretin is unlikely to cause significant liver or lipid problems. More importantly, those patients who have liver issues, obesity or metabolic syndrome do not seem to have any increased risk either. The presence of fatty liver or dyslipidaemia is not a contraindication to the use of acitretin long term.


Selection of papers and comments are provided by Clinical Associate Professor Kurt Gebauer MBBS, FACD, FACP

Clinical Associate Professor Kurt Gebauer has been practicing dermatology for 20 years in Australia. Dr. Gebauer has a busy private practice located in Fremantle and can also be found lecturing locally and internationally on different medical topics. As a contributing author on many publications, Dr. Gebauer is a well-known authority on dermatological conditions. Along with his dermatology practice Dr. Gebauer also participates in clinical research studies in order to offer new and innovative treatments for dermatological conditions including acne, atopic dermatitis, psoriasis, actinic keratoses, onychomycosis, and skin cancer.
Psoriasis, metabolic syndrome and cardiovascular risk factors. A population-based study

Authors: Fernández-Armenteros JM et al.

Summary: This observational and cross-sectional analysis used data from a Spanish hospital/priory care database (n = 398,701; 6866 with psoriasis; 499 with moderate-severe psoriasis) to assess classic cardiovascular risk factors and the metabolic syndrome, and to determine associations with severity compared to non-psoriatic individuals. Psoriasis patients had a greater prevalence of traditional cardiovascular risk factors including: type 2 diabetes mellitus (13.9% vs 7.4%; OR 2.01), dyslipidaemia (28.8% vs 17.4%; OR 1.92), arterial hypertension (31.2% vs 19.0%; OR 1.93), obesity (33.7% vs 28.1%; OR 1.30), altered fasting basal glycaemia (21.4% vs 15.1%; OR 1.54), low HDL cholesterol (38.1% vs 32.3%; OR 1.29), hypertriglyceridaemia (45.7% vs 32.2%; OR 1.55) and waist circumference (75.7% vs 72.3%; OR 1.19). The metabolic syndrome was also more prevalent in psoriatic patients (28.3% vs 15.1%; OR 2.21), and psoriatic patients had a greater prevalence of ischaemic heart disease (3.3% vs 1.8%; OR 1.87) and vascular cerebral accidents (1.8% vs 1.2%; OR 1.55). Cardiovascular risk factors did not differ between psoriasis severities.

Comment: A Spanish database containing 398,701 individuals of which 6866 had psoriasis and 499 (7.3%) of these had moderate-severe psoriasis. The data was as expected. Psoriatic patients had a higher prevalence of ischaemic heart disease, vascular cerebral accidents and the standard comorbidity risk factors (e.g. blood sugar, cholesterol etc). There were no statistical differences between psoriasis severity and cardiovascular comorbidities. There was a significant nonlinear relationship with age and sex. This paper confirms a lot of our understanding about comorbidities. As our ability to improve skin is markedly increased with newer medications both topical and predominantly systemic, the comorbidities of our patients in my view are becoming more relevant. I do make efforts to discuss with patients lifestyle factors and diet. Some of the companies have been providing practitioners with access to psychologists, dieticians, gym facilities etc., for patients on biologic therapy.


Abstract

Factors associated with onychomycosis in nail psoriasis: a multicenter study in Pakistan

Authors: Tabassum S et al.

Summary: This matched case-control study examined the secondary fungal infection of dystrophic psoriatic nails in 477 participants (159 cases; 318 controls) over 2 years. Fungal cultures were significantly more common in cases versus controls (p < 0.001) with approximately one-third of psoriatic patients with nail involvement having concomitant fungal infection. The most frequent species identified was Candida parapsilosis. Univariate analysis indicated that BMI, Nail Psoriasis Severity Index (NAPSI) scoring, socioeconomic status, elevated diastolic blood pressure, smoking status, psoriasis in first-degree relatives and disease duration >10 years were significant factors. Multivariate logistic regression suggested independent factors were low-to-middle socioeconomic status, a history of psoriasis in a first-degree relative, current smoker, and obesity.

Comment: A study out of Pakistan looking at psoriatic nail disease. Clinically when presented with nail disease I always tell my patients that there is absolutely no way that I can clinically confirm whether they have psoriasis, dermatophyte or traumatic nail disease. I may be clinically suspicious but I am not convinced. This patient group of 477 participants of which 159 had psoriasis were reviewed. They found one-third of psoriatic patients had nail involvement with concomitant fungal infection. The most frequent species identified was C. parapsilosis. Whether C. parapsilosis is a pathogenic organism in onychomycosis, or a commensal in practice, is up to the reader to decide.


Abstract