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Abbreviations used in this issue:

HR = hazard ratio; IGA = Investigator Global Assessment; IL = interleukin; LTBI = latent tuberculosis infection; PASI = Psoriasis Area and Severity Index; PPGA = Palmoplantar Psoriasis Area Severity Index; PPPASI = Palmoplantar Psoriasis Physician Global Assessment; PsA = psoriatic arthritis; RA = rheumatoid arthritis; RR = risk ratio; TSA = Therapeutic Goods Administration; TNF = tumour necrosis factor.

Welcome to issue 40 of Psoriasis Research Review.

First up we review a study investigating the impact of previous biologic use on the efficacy and safety of brodalumab and ustekinumab in patients with moderate-to-severe plaque psoriasis. Following on, we investigate a French study looking at the safety and efficacy of biologic therapies in psoriatic patients with alcoholic cirrhosis. Other papers included in this review cover the topics of incident liver disease in psoriasis, psoriatic arthritis (PsA), and rheumatoid arthritis (RA), calcipotriol/betamethasone aerosol foam for plaque psoriasis, apremilast for moderate-to-severe palmoplantar psoriasis, etanercept biosimilar efficacy in chronic plaque psoriasis and latent tuberculosis in patients treated with TNF inhibitors.

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

Impact of previous biologic use on efficacy and safety of brodalumab and ustekinumab in patients with moderate-to-severe plaque psoriasis: Integrated analysis of AMAGINE-2 and AMAGINE-3

Authors: Papp KA et al.

Summary: The impact of previous biologic exposure on efficacy and safety of brodalumab and ustekinumab in moderate-to-severe plaque psoriasis was investigated in two placebo- and ustekinumab-controlled phase III clinical trials (AMAGINE-2 and AMAGINE-3). During a 12-week induction phase, patients received brodalumab 210 mg every two weeks (Q2W; n = 1236) or 140 mg Q2W (n = 1239), ustekinumab 45-90 mg (depending on body weight) on day 1 and week 4 (n = 613) or placebo (n = 624). Overall, 493 patients had received prior biologics including 334 (27%) brodalumab 210 mg Q2W and 159 (26%) ustekinumab recipients; 150 brodalumab Q2W recipients had failed ≥1 previous biologic as had 62 ustekinumab recipients. At week 12, the efficacy of brodalumab was similar in patients with or without previous biologic exposure; PASI 100 was achieved by 40.9% of biologic-naïve and 39.5% of biologic-experienced patients, compared with 21.1% and 17.0% of ustekinumab recipients, respectively (both p < 0.001). Among brodalumab recipients in whom prior biologics were successful, 41.7% achieved PASI 100 compared with 32.0% of those in whom prior biologics had failed, while corresponding values were 21.1% and 11.3% for ustekinumab recipients. Previous biologic therapy did not have an influence on the tolerability of either agent, both of which were well tolerated.

Comment: Now we have more biologics available to us than ever previously. Many patients with severe psoriasis in the Australian community are on or have been exposed to a prior biologic. Study data regarding the impact of previous biologic exposure on efficacy and safety is necessary. Brodalumab is not yet available in Australia but it is coming, possibly towards the end of 2019. Ustekinumab is our present market leader, most likely because of the dosing frequency. Brodalumab gave higher PASI 100 or complete clearance at week 12 compared to ustekinumab. Certainly this is my experience of the newer IL-17s, I find them more efficacious and in many cases quicker in onset. What I found interesting in this study was that 12% of the brodalumab group and 10% of the ustekinumab group had reported previously failing a biologic. For brodalumab there was no difference in the clinical response whether patients had been previously exposed or not to a biologic. Once again, there were no safety signs in this study group.

Reference: Br J Dermatol. 2018;Feb 28 [Epub ahead of print]

Abstract
Risk of incident liver disease in patients with psoriasis, psoriatic arthritis, and rheumatoid arthritis: A population-based study

Authors: Ogdie A et al.

Summary: This longitudinal cohort study examined the risk of incident liver disease in psoriasis (n = 197,130), PsA (n = 12,308), and RA (n = 54,251) using data from 1994 to 2014 from The Health Improvement Network (THIN), a UK population-based electronic primary care medical records database. The adjusted HRs for any liver disease were elevated in psoriasis and PsA patients with and without systemic therapy (psoriasis patients HRs 1.97 and 1.37, PsA patients HRs 1.67 and 1.38, respectively) and elevated in RA patients without systemic therapy (HR 1.49), but not with systemic therapy (HR 0.96). The risk of incident non-alcoholic fatty liver disease was highest in patients with psoriasis and PsA patients prescribed systemic therapy (HRs 2.23 and 2.11, respectively), while the risk of cirrhosis was greatest among psoriasis patients prescribed systemic therapy (HR 2.62) and in PsA patients not prescribed systemic therapy (HR 3.15). A stepwise increase in the prevalence of liver disease and cirrhosis was observed with increasing body surface area affected by psoriasis (p for trend < 0.001).

Comment: More on liver. Dermatologists feel that we have far more liver issues with our psoriatic patients than we do with our atopic patients. Some drugs, for example methotrexate are used as systemic therapy in both. This is an American study out of the University of Pennsylvania assessing liver disease, non-alcoholic fatty liver disease and cirrhosis in a very large number of patients. The matched control group consisted of almost 1.3 million patients. Therefore, a very believable study. Incident non-alcoholic fatty liver disease was highest in patients with cutaneous psoriasis who had been prescribed systemic therapies. The risk of cirrhosis was highest in the same groups. The prevalence of liver disease and cirrhosis increases in the systemic therapy cohort in association with increasing body surface area. That is, the fatter they are the more likely they are to have fatty liver and/or cirrhosis. This is a study that confirms my clinical suspicions and findings.


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 4-week, open-label, prospective, non-controlled, observational, non-interventional, study at 87 German sites assessed the efficacy and tolerability of the new aerosol foam of calcipotriol 50 µg/g plus betamethasone dipropionate 0.5 mg/g (Cal/BD foam, Enstilar®) in 410 psoriasis vulgaris patients (56% male) under daily practice conditions. Investigator Global Assessment (IGA) at baseline revealed mild psoriasis in 41.81%, moderate psoriasis in 49.63% and severe psoriasis in 8.31% of patients. An IGA of clear or almost clear was achieved by 49% of patients at week 4, while the mean PASI was reduced from 10.4 to 5.2 (p < 0.0001) and the mean affected body surface area from 12.91% to 7.55%. Among those with severe IGA, 43% achieved treatment success (IGA = 0/1 and ≥2-step improvement). Adverse events were absent in 93% of the patients.

Comment: I have included this paper for our readers as Enstilar® is now prescribable and on the PBS in Australia. In 2017, there was a manufacturing and supply issue. Previously my patients had been able to fill their scripts with ease at any pharmacy. For dermatology prescribers who wish to understand more about the drugs they are using I am sure Leo Pharma will be more than happy to provide a full article for their review. This paper notes that after 4 weeks of treatment, 49% of patients received an IGA of almost clear. The average PASI scores went from 10.4 to 5.2. More interestingly 43% of patients with severe investigator global assessments of cutaneous psoriasis achieved treatment success. 93% of patients showed no adverse event. Certainly this is a medication that I have been using more frequently in my practice and patients are happier with the outcome.

Reference: Dermatology 2017;233(6):425-34

Abstract

AIMING FOR CLEAR?


a RESEARCH REVIEW publication

PP-JX-AU-0309. ELT0217/V1/DPR.
Apremilast for the treatment of moderate-to-severe palmoplantar psoriasis: results from a double-blind, placebo-controlled, randomized study

Authors: Bissonnette R et al.

Summary: This double-blind, placebo-controlled, randomised study assessed the efficacy and impact on quality of life and work productivity of apremilast for the treatment of moderate-to-severe palmoplantar psoriasis in 100 patients randomised to either apremilast 30 mg twice daily or placebo for 16 weeks; from week 16 to 32 apremilast 30 mg twice daily was administered. At week 16, there was no significant difference in the proportion of patients achieving a Palmoplantar Psoriasis Physician Global Assessment (PPPGA; primary endpoint) of 0/1 between patients randomised to apremilast (14%) and placebo (4%; p = 0.1595). However, by 32 weeks, 24% of patients receiving apremilast achieved a PPPGA of 0/1 and apremilast was superior to placebo in achieving a Palmoplantar Psoriasis Area Severity Index (PPPASI) 75 (apremilast 22%; placebo 8%; p = 0.0499), in improving PPPASI (apremilast -7.4; placebo -3.6; p = 0.0167) and Dermatology Life Quality Index score (apremilast -4.3; placebo -0.8; p = 0.0004), and in reducing activity impairment (apremilast -11.0; placebo 2.5; p = 0.0063).

Comment: Palmoplantar psoriasis is a not an uncommon variant that poses difficulties in my practice. Very rarely do I get a patient that responds to topical therapy. Apremilast is TGA approved but not on the PBS. It is an agent that may become PBS funded in the future. This study assessed 100 patients out of Montreal, Canada with moderate-to-severe palmoplantar psoriasis. At 16 weeks, there was no significant statistical difference. At 32 weeks, 24% of patients achieved a PGA of 0/1. Results on apremilast have always been mild and a little slow. Its safety profile, however, is such that it doesn’t require any systemic monitoring. If this drug were to become available it will be a second- or third-line therapeutic choice.


Multiple switches between GP2015, an etanercept biosimilar, with originator product do not impact efficacy, safety and immunogenicity in patients with chronic plaque-type psoriasis: 30-week results from the phase 3, confirmatory EGALITY study

Authors: Gerdes S et al.

Summary: This analysis of data from the randomised controlled phase III EGALITY study in 531 patients with plaque-type psoriasis examined the effects of repeated switching between the etanercept biosimilar GP2015 and etanercept. Mean PASI scores at baseline did not differ between patients who underwent multiple switches versus those on continuous treatments. PASI 50, PASI 75 and PASI 90 response rates, percentage change from baseline PASI scores and all other efficacy parameters did not differ between pooled-switched and pooled-continued treatment groups across all time points. Treatment-emergent adverse event rates including injection site reactions did not differ between the pooled-switched (36.7%) and pooled-continued (34.9%) groups. No patients were positive for binding anti-drug antibodies during the treatment period analysed.

Comment: Biologic Prescribers are going to be exposed more frequently to biosimilars. The Federal Government has introduced streamlining for biosimilars but not for the originator drugs. Equally it will become harder to control what is dispensed by pharmacists. These are reasons that we need to understand biosimilars better. This is a German study looking at a biosimilar for entanercept. This is a medication no longer frequently used for cutaneous psoriasis in Australia. The concern of switching from one biosimilar to another is these are not identical products and immunogenicity leading to loss of efficacy or the development of immunological side effects (e.g., urticaria, injection site reactions etc. may occur). In this study there were three consecutive treatment switches within the first 30 weeks of treatment. They concluded that there were no effects in the short term on clinical data and no positivity for binding anti-drug antibodies was noted.

Rates of latent tuberculosis infection in patients treated with TNF inhibitors for psoriasis: a retrospective chart review

Authors: Lee EB et al.

Summary: This retrospective analysis of 138 patients with psoriasis receiving TNF inhibitor therapy between 2004 and 2017 examined the incidence of latent tuberculosis infection (LTBI) and active tuberculosis. In 99 biologic-naïve patients, 14 tested positive for LTBI before starting TNF inhibitor therapy and five developed LTBI during therapy; one biologic-naïve patient developed LTBI followed by active tuberculosis. In 39 non-naïve patients, three had LTBI prior to biologic therapy, and one developed LTBI during treatment.

Comment: We are all screening our patients with Quantiferon Gold and chest x-rays prior to the use of biologics. Many, especially the younger practitioners and registrars, are screening patients when systemic therapies are being prescribed as a routine. I wonder with the newer biologic agents whether the tuberculosis issue will be relevant. I suspect our investigation profile will change over the next 5-10 years. Certainly I have many patients originating from countries like South America and the Philippines. Many travel, work or have partners who come from high endemic tuberculosis areas. It never ceases to amaze me which patients I pick up with latent tuberculosis (i.e., positive Quantiferon Gold). In this study of 99 biologic-naïve patients, 14 had LTBI before starting biologic therapy. Five developed LTBI during TNF inhibitor therapy. One patient developed LTBI and then went on to active tuberculosis.

Reference: J Dermatol Treat. 2018;Mar 22 [Epub ahead of print]

A systematic review and meta-analysis of the efficacy and safety of the interleukin (IL)-12/23 and IL-17 inhibitors ustekinumab, secukinumab, ixekizumab, brodalumab, guselkumab, and tildrakizumab for the treatment of moderate to severe plaque psoriasis

Authors: Bilal J et al.

Summary: This meta-analysis examined data from 24 randomised placebo-controlled trials to assess the use of interleukin (IL)-12/23, IL-17, and selective IL-23 inhibitors in moderate-to-severe plaque psoriasis. The RRs (all p < 0.00001) for achieving PASI-75 and PGA/GA 0/1 in ustekinumab recipients were 20.2 (95% CI 13.8-29.5) and 14.6 (95% CI 10.4-20.3) for a 90 mg dose and 13.7 (95% CI 8.5-22.3) and 9.8 (95% CI 5.7-16.9) for a 45 mg dose. For secukinumab the RRs were 17.7 (95% CI 12.4-25.2) and 26.1 (95% CI 16.1-42.5) for 300 mg and 15.4 (95% CI 10.8-21.9) and 20.9 (95% CI 12.8-34.1) for a 150 mg dose. For ixekizumab the RRs were 18.2 (95% CI 10.6-31.2) and 18.8 (95% CI 10.4-34.2) for a dosage of 80 mg every 4 weeks and 19.8 (95% CI 11.1-35.5) and 20.4 (95% CI 11.0-37.8) for 80 mg every 2 weeks. With brodalumab the RRs were 14.8 (95% CI 9.9-22.2) and 21.9 (95% CI 15.5-31.0) for a 210 mg dose and 11.6 (95% CI 7.8-17.2) and 16.6 (95% CI 11.7-23.5) for a 140 mg dose. Guselkumab had RRs of 12.4 (95% CI 8.9-17.3) and 10.8 (95% CI 7.9-14.9) at 100 mg. For tildrakizumab the RRs were 11.5 (95% CI 7.5-17.6) and 11.0 (95% CI 6.4-18.7) for a 200 mg dose and 11.0 (95% CI 7.2-16.9) and 10.0 (95% CI 6.5-15.6) for a 100 mg dose. There was an increased risk of withdrawal due to toxicity for ixekizumab versus placebo.

Comment: This is a study that tries to systematically analyse the agents we are presently using as well as some of the newer ones in development. Guselkumab will be with us this year. Brodalumab possibly next year and tildrakizumab in 2020. Safety recordings showed there was a slightly increased risk of withdrawal due to toxicity with ixekizumab compared to the placebo arm. As there are limited head-to-head studies it is very difficult to compare one biological with the other. I would encourage regular prescribers of biologics to get a copy of this paper before they make their own conclusions as to which biologic they will be supporting as their first- and second-line options.

Reference: J Dermatol Treat. 2018;Mar 13 [Epub ahead of print]

Epidemiological survey from 2009 to 2012 of psoriatic patients in Japanese Society for Psoriasis Research

Authors: Ito T et al.

Summary: This paper reports on the most recent annual epidemiological survey conducted by the Japanese Society for Psoriasis Research, which included data on 9290 psoriatic cases (2009-12). The sex ratio favoured males by a 2:1 margin (6281 [67.6%] male; 3009 [32.4%] female). Psoriasis vulgaris made up 85.6% of all cases, psoriasis arthropathica 0.6%, psoriasis guttate acuta 3.2%, Zumbusch-type generalised pustular psoriasis 1.6% and psoriasis erythroderma 1.5%. Psoriasis arthropathica and psoriasis guttate acuta had their highest prevalence in patients aged <65 years. Compared to previous surveys (1982-2001; 2002-08) there was an increased number of comorbid diabetes and/or arthritis cases. Treatment typically involved topical corticosteroids (89.7%) and vitamin D3 ointments (78.0%; significantly increased since previous surveys), and 33.3% of patients were receiving systemic treatment, including cyclosporin (33.6%), etretinate (19.5%), methotrexate (6.6%), infliximab (11.4%), adalimumab (10.9%) and ustekinumab (6.2%). Phototherapy was used by 30.9% of patients, and this survey identified a shift from psoralen plus ultraviolet A therapy in previous surveys to narrowband ultraviolet B therapy (84.5% of phototherapy).

Comment: Australia is a multicultural society. Certainly I do not have a large number of Japanese patients. For those who are academically curious it is interesting to learn about the pattern of psoriasis presenting in this homogenous genetic group. In their study, they evaluated 9290 patients. Items I found of interest were a male/female ratio of 2.08:1. The presence of erythrodermic psoriasis in 1.5% and generalised pustular psoriasis in 1.8%. These seem to be higher than what I see in my practice, however, we have no comparable Australian data. Amongst the systemic therapy cyclosporine was prescribed in 33.6% of patients and methotrexate only in 8.6%. This is probably a ratio that is different to what we use in our practice. Phototherapy was used in 30.9% of patients, which is quite high for a pigmented group of patients.

Reference: J Dermatol. 2018;45(3):293-301

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RESEARCH REVIEW—The Australian Perspective Since 2007
Intentional and unintentional medication non-adherence in psoriasis: The role of patients’ medication beliefs and habit strength

Authors: Thorneloe RJ et al.

Summary: This “real-world” study examined self-reported non-adherence to systemic therapies in 811 psoriasis patients enrolled in the British Association of Dermatologists Biologic Interventions Register, and assessed factors associated with non-adherence. In total, 617 patients self-administering systemic therapy, of whom 22.4% reported being “non-adherent” (12% intentionally, 10.9% unintentionally). Oral conventional systemic agent recipients were more likely to be non-adherent than etanercept or adalimumab recipients (29.2% vs 16.4%; p < 0.001). Latent profile analysis suggested three discrete groups were represented in a categorical latent variable model. All three groups had strong beliefs about the need for systemic therapy, but differing levels of concern about their medication. Group 1 (26.4%) had the strongest concerns, Group 2 had moderate concerns (61%), and Group 3 (12.6%) had the weakest concerns. Membership of Group 1 was associated with unintentional non-adherence (OR 2.27; 95% 1.16-4.47), while weaker medication-taking routine or habit strength was associated with intentional non-adherence (OR 0.92; 95% CI 0.89-0.96).

Comment: This is a study out of Manchester looking at the British Biologic Interventions Register. 811 patients were included. In their group, 22.4% were classified as non-adherent (12% intentionally and 10.9% unintentionally). Patients using conventional oral systemic therapies are more likely to be non-adherent compared to their biologic group. Their patients were divided into three groups by assessing the patient’s strong beliefs about the need for systemic therapy. The groups differed in their level of medication concerns. Those patients with the highest level of concerns about medication were more likely to not adhere to the medication prescription schedule. Medication beliefs and habits are modifiable targets for strategies to improve adherence in psoriasis. This is sort of logical with what we see in practice. There are many mechanisms that we clinicians use to motivate our patients to follow the prescribed therapy. What we dermatologists need is training on mechanisms to motivate and manipulate our patients into being more compliant.


Abstract

RESEARCH REVIEW—The Australian Perspective Since 2007

PBS INFORMATION: Authority required. For the treatment of severe chronic plaque psoriasis. Refer to PBS Schedule for full authority information.

Please click here to review the full Product Information before prescribing.

mNRI: Modified Non-responder Imputation; NRI: Non-responder Imputation; PASI: Psoriasis Area Severity Index.


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