Psoriasis Research Review™

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Issue 29 - 2016

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Abbreviations used in this issue:

BMI = body mass index; **CT** = computed tomography; **OR** = odds ratio; **VAS** = Visual Analogue Scale.

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Welcome to the twenty-ninth issue of Psoriasis Research Review.

We begin this issue with an informative study comparing coronary artery calcium in patients with psoriasis and type 2 diabetes. We then look at a study of ixekizumab for psoriasis itch and learn that ixekizumab recipients report greater improvements in itch severity, skin pain and degree of bothersomeness compared with etanercept or placebo recipients. Also in this review we investigate ixekizumab for scalp psoriasis, HLA-Cw6 homozygosity and strep throat in plaque psoriasis, coronary artery disease progression and biologic agents, psoriasis and obstructive sleep apnea, vasoconstriction with calcipotriol plus betamethasone dipropionate, the long-term clinical safety and efficacy of brodalumab, psoriasis itch VAS for psoriasis vulgaris and DLQI as a criterion for systemic agents.

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

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Comparison of coronary artery calcium scores between patients with psoriasis and type 2 diabetes

Authors: Mansouri B et al.

Summary: Three single-centre, cross-sectional studies in patients with moderate-to-severe psoriasis (n = 129; mean age 51) compared asymptomatic coronary atherosclerosis measured by coronary artery calcium (CAC; mean total Agatston score) versus patients with type 2 diabetes mellitis (n = 129; mean age 52) and healthy controls (n = 129; mean age 52). Psoriasis patients had a low Framingham Risk Score, but a high prevalence of cardiovascular and cardio-metabolic risk factors, as did patients with type 2 diabetes. Psoriasis was associated with CAC (Tobit regression ratio 0.89; $p < 0.001$) similar to that for type 2 diabetes (Tobit regression ratio 0.79; $p = 0.04$). In likelihood ratio testing, psoriasis had an incremental value in predicting CAC in a fully adjusted model ($\chi^2 = 4.48$; $p = 0.03$). There was an independent association for psoriasis in CAC (OR 2.35; 95% CI 1.12-4.94) in fully adjusted models, whereas CAC was not associated with type 2 diabetes after adding BMI to the model (OR 2.18; 95% CI 0.75-6.35).

Comment: This looks at 387 patients from a well know dermatological unit in Texas. The conclusion is that patients with psoriasis have increased CAC similar to that of patients with type 2 diabetes. The suggestion is that patients have significantly high rates of subclinical atherosclerosis, and therefore need to reduce the cardiac morbidity by the use of systemic agents.

Reference: JAMA Dermatol. 2016;152(11):1244-53

Abstract

RESEARCH REVIEW – The Australian Perspective Since 2007

Impact of ixekizumab on psoriasis itch severity and other psoriasis symptoms: Results from 3 phase III psoriasis clinical trials

Authors: Kimball AB et al.

Summary: This analysis of data from three 12-week, multicentre, double-blind, placebo-controlled, phase III clinical trials in patients with moderate-to-severe psoriasis (UNCOVER-1 [n = 1296], UNCOVER-2 [n = 1224] and UNCOVER-3 [n = 1346]) assessed the effect of ixekizumab 80 mg every two weeks (Q2W) or every four weeks (Q4W), etanercept 50 mg bi-weekly or placebo, on itch severity (numeric rating scale), skin pain (VAS) and bothersomeness of skin appearance (Psoriasis Skin Appearance Bothersomeness Instrument) caused by psoriasis. Ixekizumab recipients reported improvements in itch severity, skin pain, and degree of bothersomeness versus etanercept or placebo recipients (all $p < 0.001$). Clinically meaningful itch severity improvements were achieved by week 1.

Comment: Ixekizumab has been Therapeutic Goods Administration (TGA) approved and is known as Taltz. It is expected that it will become available on the Australian PBS in early 2017. Therefore, dermatologists need to know something about it. The first of this pair is of a review article of the three phase III studies by the usual gods of dermatology. Despite what is written in our textbooks, we all know that itch is a prevalent symptom of psoriasis. This study confirms the obvious, that if we make psoriasis better slowly, the itch goes away.

Reference: J Am Acad Dermatol. 2016;75(6):1156-61
Abstract

Sustained response with ixekizumab treatment of moderate-to-severe psoriasis with scalp involvement: results from three phase 3 trials (UNCOVER-1, UNCOVER-2, UNCOVER-3)

Authors: Reich K et al.

Summary: This analysis of the UNCOVER-1 and -2 and the open-label long-term extension (UNCOVER-3) trials assessed the effect of ixekizumab on scalp psoriasis over 60 weeks using the Psoriasis Scalp Severity Index (PSSI). In patients with baseline scalp involvement, at week 12 both PSSI 90 and PSSI 100 were achieved by more ixekizumab Q2W (81.7% and 74.6%) or Q4W (75.6% and 68.9%) recipients than placebo (7.6% and 6.7%; both $p < 0.001$) or etanercept (55.5% and 48.1%; both $p < 0.001$) recipients and these outcomes were maintained through week 60 in patients who continued receiving ixekizumab Q4W.

Comment: This is a more clinically relevant paper to the readership. Scalp psoriasis is one area that sometimes doesn't respond as well as others. This paper is using the data from the UNCOVER series of trials, which were the pivotal studies in the development and listing of this medication. It makes a point that scalp psoriasis is improved and stays improved whilst on therapy.

Reference: J Dermatolog Treat. 2016;Nov 13 [Epub ahead of print]
Abstract

HLA-Cw6 homozygosity in plaque psoriasis is associated with streptococcal throat infections and pronounced improvement after tonsillectomy: A prospective case series

Authors: Thorleifsdottir RH et al.

Summary: A prospective case series examined the outcome of tonsillectomy in 28 patients with psoriasis to see the effect of presence of the HLA-Cw*0602 allelle. HLA-Cw*0602 homozygotes had a greater improvement than heterozygous and HLA-Cw*0602-negative patients, and PASI score was reduced by 82% in the homozygotes, 42% in heterozygotes and 31% in HLA-Cw*0602-negative patients ($p < 0.001$), Psoriasis Disability Index score improved by 87% versus 38% and 41% ($p < 0.001$), and Psoriasis Life Stress Inventory score reduced by 82% versus 60% and 54% ($p < 0.001$), respectively. Onset of psoriasis was more often associated with a throat infection ($p = 0.007$) in homozygotes as was an increased frequency of streptococcal throat infections per lifetime ($p = 0.038$).

Comment: A Scandinavian study that only had 28 patients. I occasionally come across patients who develop multiple episodes of throat infection leading to a flare of, or development of, guttate psoriasis. They tried to load them up with an appropriate antibiotic as soon as they become symptomatic, but in some this management plan doesn't work. The thought then arises as to what would happen if their tonsils were removed. There is very limited data in this field. In this study, the HLA-Cw*0602 allelle would suggest that such a surgical management with tonsillectomy would lead to a significant improvement on ongoing psoriasis. It is a very small subset of patients; however, there is some evidence to show that a particular management plan would be logical and worthwhile.

Reference: J Am Acad Dermatol. 2016;75(5):889-96
Abstract

Association between changes in coronary artery disease progression and treatment with biologic agents for severe psoriasis

Authors: Hjuler KF et al.

Summary: In a prospective, single-centre, controlled, observer-blinded clinical study, the association between biological therapy and coronary artery disease progression in 28 patients with severe psoriasis (mean age 49.2 years; 71% men; mean PASI 15.4) and 28 control patients (mean age 52.8 years; 71% men; mean PASI 12.4) was examined using repeated coronary CT. Non-contrast CAC CT scores were stable in the biological therapy recipients (mean yearly CAC change -16) but progressed in controls (mean yearly CAC change 14 [$p = 0.02$]; intervention vs controls [$p = 0.02$]). Luminal narrowing in diseased segments was stable in biological therapy recipients (Wilcoxon W 76; $p = 0.39$) but increased in controls (Wilcoxon W 281; $p = 0.02$).

Comment: This study is only of a small group of 28 patients and this topic is still being developed. It is, however, a reasonable article for us to review.

Reference: JAMA Dermatol. 2016;152(10):1114-21
Abstract

Psoriasis and obstructive sleep apnea

Authors: Shalom G et al.

Summary: The comprehensive community-based medical database of Clalit Health Services was used in a case-control study to determine the association between psoriasis and obstructive sleep apnoea (OSA) using data on 12,336 psoriasis patients and 24,008 age- and sex-matched controls. OSA prevalence in psoriasis patients was higher than in controls (2.7% vs 1.5%; $p < 0.001$). Multivariate analysis suggested a significant association between psoriasis and OSA after adjustment for age, sex, ethnicity, BMI, chronic obstructive pulmonary disease, hypothyroidism, hyperlipidemia and peptic disease (OR 1.27; 95% CI 1.08-1.49; $p < 0.001$).

Comment: Again a co-morbidity issue. This scientifically validates that psoriasis and its metabolic syndrome is associated with OSA. This is a study on a large number of patients, 12,336 with psoriasis and 24,008 age- and sex-matched controls. A huge study that proves what one would all think to be given clinically. It is, however, always nice to have scientific proof for what we think should be occurring.

Reference: Int J Dermatol. 2016;55(11):e579-e584
Abstract

Enhanced vasoconstrictor potency of the fixed combination calcipotriol plus betamethasone dipropionate in an innovative aerosol foam formulation vs. other corticosteroid psoriasis treatments

Authors: Queille-Roussel C et al.

Summary: This single-centre, investigator-blinded, vehicle-controlled, intra-individual, phase I trial tested an aerosol foam formulation of fixed combination calcipotriol 50 µg/g (Cal) and betamethasone dipropionate 0.5 mg/g (BD) in 35 healthy controls. Skin blanching (visual assessment for 6 to 32 hours) with Cal/BD aerosol foam was less than clobetasol propionate 0.5 mg/g cream (mean AUC_{0-32} 2560 vs 3831; mean difference -1272; 95% CI; -1598 to -945; $p < 0.001$), but did not differ to that with BD aerosol foam (mean AUC_{0-32} 2595; mean difference -35; 95% CI -362-292) and was greater than with Cal/BD ointment (mean AUC_{0-32} 2008; mean difference = 552; 95% CI 225-878; $p = 0.001$) and fluocinolone acetonide 0.25 mg/g ointment (mean AUC_{0-32} 1981; mean difference 578; 95% CI 251-905; $p < 0.001$). Colorimetric a* and L* measurements (secondary criteria) also suggested greater reduced skin blanching with Cal/BD aerosol foam than with clobetasol propionate cream.

Comment: This product will be coming on the Australian market in 2017. It would be great for dermatologists to know about it. It would be nice to get the information from an independent cross-referenced peer reviewed journal. In this phase 1 study of a small number of patients, however, the aerosol foam is more potent and effective in our patient group. I am sure it is something we will all be using very shortly.

Reference: J Eur Acad Dermatol Venereol. 2016;30(11):1951-56
Abstract

Long-term clinical safety and efficacy of brodalumab in the treatment of Japanese patients with moderate-to-severe plaque psoriasis

Authors: Umezawa Y et al.

Summary: This extension of a phase 2 trial, tested the human anti-interleukin-17-receptor A monoclonal antibody brodalumab (KHK4827) 210 or 140 mg subcutaneously every 2 weeks in 133 Japanese patients with moderate-to-severe psoriasis who completed 52 weeks of treatment. The proportion of patients with a ≥75% reduction in PASI scores (PASI 75) was 94.4%, while the number achieving a ≥90% (PASI 90) or 100% (PASI 100) reduction were 87.5% and 55.6% with brodalumab 210 mg. Corresponding proportions in brodalumab 140 mg recipients were 78.1%, 71.2% and 43.8%. 75.0% of brodalumab 210 mg recipients achieved a ≥20% improvement in American College of Rheumatology response criteria (ACR 20), versus 37.5% of brodalumab 140 mg recipients. The most commonly reported adverse events were nasopharyngitis (35.2%), upper respiratory tract inflammation (10.3%) and contact dermatitis (9.7%).

Comment: Brodalumab was under phase III development. The original research program was terminated because of a perception of major adverse cardiovascular event (MACE) effects. There was some significant academic discussion whether this was a valid course of action; however, the company decided to halt the research program. The drug is now being further developed and reviewed. This is a review article of Japanese patients. It shows a reasonable number of patients, 145, of which 133 completed the study. The drug gives very good PASI responses. Although it is only a 52-week study, the MACE issues were not noted. We will see more studies looking at this drug. Certainly from the Australian researchers who were developing anecdotally there were minimal problems of what seemed to be a very effective agent.

Reference: J Eur Acad Dermatol Venereol. 2016;30(11):1957-60
Abstract

Reliability and validity of the Psoriasis Itch Visual Analog Scale in psoriasis vulgaris

Authors: Pedersen CB et al.

Summary: Data from two randomised, parallel-group phase III trials in patients with psoriasis vulgaris (n = 426, 463) were analysed to determine cross-sectional distribution and construct validity, longitudinal test-retest reliability, and sensitivity to change of a single-item psoriasis itch Visual Analogue Scale (VAS). Across both trials, distributional properties were acceptable. Convergent-validity correlations provided strong endorsement for construct validity, as did known-group validity tests. Longitudinal test-retest reliability and sensitivity to change also support the use of the psoriasis itch VAS in psoriasis vulgaris.

Comment: We really don't have an adequate patient initiated measurement tool. PASI of course is a government inflicted measuring tool that we have to perform and is relatively onerous and complicated. It would be nice to have a valid tool that the patients can fill in in the waiting room. For those of us who like measuring and recording patients' perceptions this is something that you should look at and read.

Reference: J Dermatolog Treat. 2016;Sep 5 [Epub ahead of print]
Abstract

DLQI as a major criterion for introduction of systemic agents in patients with mild psoriasis

Authors: Mermin D et al.

Summary: This retrospective single centre study assessed the impact of systemic treatments on Quality of Life (QoL) in patients with mild psoriasis (PASI ≤6). Patients receiving systemic therapies as a first choice treatment had higher QoL impairment, mainly due to psoriasis lesions localised on visible areas, than those receiving local and/or UV light therapies. During follow-up, systemic-therapy recipients had better PASI score and Dermatology Life Quality Index (DLQI) improvements than local and/or UV light treatment recipients.

Comment: DLQI was originally developed by the Dermatology Unit in Cardiff for dermatological diseases. It then validated a number of dermatological diseases. The TGA does not put a lot of reliability on DLQI; however, it is a well-known tool. This is a study out of France that suggests that this would be a useful way of measuring patients' responses to our systemic therapies. It well known amongst dermatologists and used in many disorders. We all await a better tool for now.

Reference: J Eur Acad Dermatol Venereol. 2016;30(11):1961-64
Abstract

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Selection of papers and comments are provided by
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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.

