Dermatology Research Review™

Making Education Easy

Issue 116 - 2025

In this issue:

Abbreviations used in this issue:

BCC/SCC = basal/squamous cell carcinoma;
EGFR = epidermal growth factor receptor; **IL** = interleukin.

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Welcome to issue 116 of Dermatology Research Review.

We begin this issue with research investigating the topical application of a hedgehog inhibitor, patidegib, for treating Gorlin syndrome. There is also a study reporting that we probably don't need to be overly concerned about completely excised scalp SCCs recurring when the deep histological margin is <1mm as long as the galea aponeurotica isn't involved. Other included research has reported oncological outcomes for patients with clinically resolved cutaneous SCCs managed by watchful waiting. We conclude this issue with research we can use to reassure our patients with androgenetic alopecia that they do not need to be too concerned about any hair shedding they experience during the initial weeks of topical minoxidil treatment.

We hope you enjoy this update in dermatology research, and look forward to your comments and feedback.

Kind Regards,

Dr Warren Weightman
warren.weightman@researchreview.com.au

Topical application of the hedgehog inhibitor patidegib in patients with Gorlin syndrome

Authors: Lear JT et al.

Summary: These researchers developed a gel containing the hedgehog inhibitor patidegib for topical application, which they evaluated in a phase 2 trial in which the gel was applied to the faces of individuals with Gorlin syndrome. The participants had low patidegib concentrations in their blood after topical administration, and experienced only minimal side effects with no major effects reported. Moreover, *post hoc* analyses suggested that topical patidegib reduced both hedgehog signalling and new surgically eligible BCCs.

Comment: Oral hedgehog inhibitors have been effective in the management of Gorlin syndrome and high-risk BCCs, but there are significant side effects such as muscle cramps, dysgeusia and hair loss which often lead to discontinuation of the medication. The use of a topical hedgehog inhibitor is a novel approach. Patidegib has been used orally, but in this trial it was applied topically twice daily to the face and targeted BCCs. This was a proof-of-concept trial, but it showed that patidegib gel can reduce the size of existing BCCs and can prevent development of new BCCs. Blood drug concentrations were very low, and patients had minimal or no major side effects. Patidegib is the first topical hedgehog inhibitor to reduce the number of new BCCs, although topical sonidegib has been shown to reduce BCC size. There were several limitations of this trial, including small numbers, a short duration study period (26 weeks) and lack of histological evidence of BCC clearance. A phase 3 trial is planned to address these issues and determine the optimum length of treatment.

Reference: Br J Dermatol 2025;192:611–7
Abstract

Independent commentary by Dr Warren Weightman

Dr Warren Weightman has practiced Dermatology for more than 30 years and is currently Head of the Department of Dermatology at the Queen Elizabeth Hospital, Adelaide and a Senior Lecturer with Adelaide University. He has been Chief Censor and President of the Australasian College of Dermatologists. Dr. Weightman has been involved in clinical research and has a particular interest in treatment of actinic keratoases and superficial basal cell cancers with topical therapies including methyl aminolevulinate and photodynamic therapy, imiquimod, and ingenol mebutate. His other interests include the management of non-melanoma skin cancer in transplant patients, the use of biologics in psoriasis and other skin disorders, and the role of oral retinoids.

Management of human epidermal growth factor receptor inhibitors-related acneiform rash

Authors: Apalla Z et al.

Summary: This paper reported on the establishment of unified international guidelines regarding the management of acneiform rash due to EGFR inhibitors. Five European Academy of Dermatology and Venereology Task Force 'Dermatology for Cancer Patients' members developed an 84-statement questionnaire that was circulated to 32 international supportive oncodermatology experts to be rated on a five-point Likert scale. Strong consensus was reached for 75 of the statements, with moderate consensus reached for six; lack of robust data likely contributed to the failure to reach consensus for the remaining three. Key points included: i) considering low-dose isotretinoin for refractory grade II/III acneiform rash; ii) topical steroid-sparing agents (e.g. topical pimecrolimus) as maintenance treatment; and iii) doxycycline 100 or 200 mg/day for prophylaxis. Topical antibiotics were not recommended for prevention or treatment.

Comment: An acneiform rash is not unusual with EGFR inhibitors, and these consensus guidelines advise on optimum management, which should be individualised based on the severity and extent of the rash. Doxycycline 100–200mg daily is usually the first-line oral treatment, but it may be worthwhile using it prophylactically for 6 weeks prior to starting EGFR inhibitors. Oncologists have been reluctant to do this, as the severity of the acneiform rash is a prognostic factor. Superinfection occurs in nearly 30% of cases, so a bacterial swab is important. Mild-potency steroids should be used for face and flexures, with topical pimecrolimus and tacrolimus options for long-term use. Low-dose isotretinoin (0.3 mg/kg) should be considered for persisting or nonresponsive patients, but should not be considered as initial treatment.

Reference: J Eur Acad Dermatol Venereol 2025;39:730–41
Abstract

Low-dose isotretinoin for the management of rosacea

Authors: King A et al.

Summary: This was a systematic review with meta-analysis of data from 16 randomised or nonrandomised studies, with 1445 participants, investigating the use of low-dose isotretinoin (≤0.5 mg/kg/day) for the treatment of rosacea. Low-dose isotretinoin was found to be associated with statistically significant decreases in lesion count and erythema, with the reduction in lesion count significantly also greater when compared with topical retinoids and topical antimicrobials. Sixteen weeks after low-dose isotretinoin cessation, mean lesion count and erythema remained reduced by 70% and 47%, respectively, whereas the relapse rate at 5.5 months was 35% with worsening of rosacea occurring in 0.4% of participants. Serious adverse events occurred in 0.4% of participants.

Comment: Isotretinoin is now commonly used for moderate-to-severe rosacea, and this review and meta-analysis confirmed the effectiveness in reducing lesion count in papulopustular rosacea, but it was not effective in reducing erythema. Isotretinoin was more effective than topical retinoids and antimicrobials. Oral doxycycline was more effective for the ocular symptoms of rosacea and meibomian gland dysfunction. The mean dose of isotretinoin was 0.30 mg/kg/day, or 7.03 mg/day, and the mean duration of treatment was 18.5 weeks. Rosacea often recurs, but in this review, there was an average recurrence of 35% at 5.5 months, which is a reasonable result. A maintenance regimen was not discussed, but it is reasonable to continue isotretinoin long term if the side effects are minimal.

Reference: J Eur Acad Dermatol Venereol 2025;39:785–92
Abstract

Histological deep margins in cutaneous squamous cell carcinoma of the scalp and risk of recurrence

Authors: Verdaguer-Faja J et al.

Summary: These researchers evaluated the risk of scalp SCC recurrence after wide local excision according to histological margin depth <1 (close deep) vs. ≥1mm in a retrospective observational cohort of 295 patients with 338 SCCs. There was no significant association between close deep histological margins and an increased cumulative incidence of SCC recurrence (subhazard ratio 1.96 [95% CI 0.87–4.41]), except for when there was concurrent invasion of the galea aponeurotica (3.52 [1.24–10.01]) and for SCCs with clear but close (<1mm) peripheral margins (5.01 [1.68–14.97]).

Comment: For SCCs, wide clinical margins of 4–10mm are recommended, but when pathology is reviewed, the histological margin may be much closer. It is not uncommon to have a close deep histological margin <1mm, but this study on SCCs of the scalp showed that unless the galea was involved, there was no increased risk of recurrence. Most of the tumours were well or moderately differentiated (89%) and did not impact the results. Immunosuppression, tumour diameter >2cm and perineural invasion were independently associated with an increased risk of recurrence, so if these associations are present, re-excision would be indicated. There may be extensive cautery in a vascular area such as the scalp, which may be one reason the risk of recurrence is low. The authors recommended excision down to the galea, but if the tumour does not extend to the galea but has a deep margin <1mm, then it is reasonable to observe. These results may apply to SCC in other sites, but studies need to be done to confirm this.

Reference: J Eur Acad Dermatol Venereol 2025;39:855–64
Abstract

Efficacy of antipsychotics in delusional infestation

Authors: Tang PK et al.

Summary: Responses associated with different antipsychotics were reported in this retrospective observational analysis of 414 records from two hospitals in the UK of adults with delusional infestation, in whom 315 antipsychotic prescription events were recorded. It was found that amisulpride had the highest treatment response at 67%, followed by risperidone at 57%, quetiapine at 36%, aripiprazole at 28% and olanzapine at 25%.

Comment: Delusions of parasitosis is a difficult condition to treat, and if patients can be persuaded to take an antipsychotic, it is important to give the one most likely to have a benefit, as they may not agree to a second antipsychotic. Risperidone and amisulpride were assessed as the most effective, and both are available in Australia. Other antipsychotics such as quetiapine (36%), aripiprazole (28%) and olanzapine (25%) were not as effective, although there was a low number of patients on olanzapine, so the effectiveness of quetiapine in this study may not be accurate. Risperidone is the antipsychotic that most dermatologists have experience with, so would be recommended as the first choice in delusions of parasitosis.

Reference: J Eur Acad Dermatol Venereol 2025;39:815–22
Abstract

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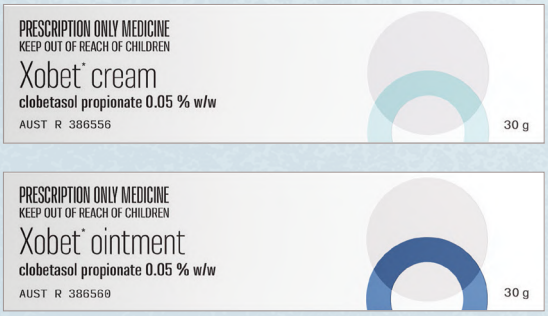

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References: 1. Xobet (clobetasol propionate) Cream Product Information, December 2023. **2.** Xobet (clobetasol propionate) Ointment Product Information, December 2023. **3.** Clobetasol Public Summary Document November 2024 PBAC Meeting. **4.** Jacobson C, Cornell RC, Savin RC. A comparison of clobetasol propionate 0.05 percent ointment and an optimized betamethasone dipropionate 0.05 percent ointment in the treatment of psoriasis. Cutis. 1986;37(3):213-220. **5.** Guttman-Yassky E, et al. Molecular signatures order the potency of topically applied anti-inflammatory drugs in patients with atopic dermatitis. Journal of Allergy and Clinical Immunology, [online] 140(4), pp.1032-1042.e13. doi:https://doi.org/10.1016/j.jaci.2017.01.027.

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Zoon balanitis: not a distinct clinicopathological entity?

Authors: Watchorn RE et al.

Summary: These authors reviewed all historical published cases of Zoon balanitis to see if the clinical or histological features of male genital lichen sclerosus had been present and overlooked. Images claiming to be Zoon balanitis and were amenable to further scrutiny were included in 66 of the published cases. Clinical signs of male genital lichen sclerosus, such as adhesions, coronal sulcus and frenulum effacement, tightening of the prepuce, constrictive posthitis, etiolation of the glans, lichenoid inflammation and sclerosis, were present in 98.5% of the scrutinised images.

Comment: Zoon balanitis and lichen sclerosus have been considered separate entities, but this article has reviewed all articles of Zoon balanitis showing clinical images. and 98.5% showed clinical evidence of lichen sclerosus. Nine percent of the manuscripts, including the original case series by Professor Johannes Jacobus Zoon, reported phimosis in patients with Zoon balanitis, and 98.5% of cases, including the original cases reported by Professor Zoon, showed signs of lichen sclerosus, such as lichenoid inflammation, attenuation of the architecture, micro-adhesions, effacement of pearly penile papules, sclerosis, adhesions or tightening of the prepuce. It is possible that Zoonoid inflammation may represent an early phase of lichen sclerosus. Treatments that are successful in Zoon balanitis are the same treatments for lichen sclerosus, such as barrier preparations, potent topical steroids and circumcision, although Diprosone OV ointment (betamethasone dipropionate) is usually used first line in lichen sclerosus and not Zoon balanitis, so Zoon balanitis may benefit more with the most potent steroid.

Reference: Clin Exp Dermatol 2025;50:731–9
Abstract

Refractory benign familial pemphigus successfully treated with dupilumab

Authors: Gozalbo AS et al.

Summary: These authors reported a case series of three patients with refractory moderate-to-severe benign familial pemphigus successfully treated with dupilumab. Over 18 months of follow-up, a decrease in pruritus and improved skin findings were seen after treatment with dupilumab in all three patients, and there were no adverse effects recorded, although one of the patients did require an increase in their dupilumab dose to achieve optimal control. The authors also reviewed previous case reports of biologic agents for treating benign familial pemphigus, and concluded that dupilumab appears to be a safe, useful option.

Comment: Benign familial pemphigus is treated with corticosteroids, calcineurin inhibitors and antimicrobial treatments, but in patients with moderate-to-severe disease, other options that have worked include retinoids, dapsone and immunosuppressives. More recently, Botox (botulinum toxin), laser, low-dose naltrexone, and Janus kinase inhibitors have been used. Dupilumab is used successfully in other nonatopic eczema indications such as bullous pemphigoid and urticaria, and was successful in benign familial pemphigus in this case study. In another recent review of 11 patients with benign familial pemphigus who were treated with dupilumab, ten showed marked improvement with dupilumab. The mechanism for dupilumab's effectiveness in treating benign familial pemphigus remains unclear. Skin barrier defects associated with benign familial pemphigus may promote type 2 inflammation, and IL-4 and IL-13 may decrease calcium influx into keratinocytes, and blocking these pathways by dupilumab leads to increased calcium, enabling formation of the proteins involved in cellular differentiation. Finally, IL-4 plays an important role in the neuromodulation of chronic pruritus, helping to control this symptom, and all three patients in this study showed a marked improvement in itch. Dupilumab is a new option for the treatment of benign familial pemphigus refractory to other treatments.

Reference: Clin Exp Dermatol 2025;50:841–4
Abstract

Oncologic outcomes for invasive squamous cell carcinoma with a clinically resolved biopsy site managed by watchful waiting

Authors: Boudreaux B et al.

Summary: Oncological outcomes were reported for a retrospective cohort of patients diagnosed with 148 cutaneous SCCs that were managed by watchful waiting for ≥12 months after determined to be clinically resolved. Local recurrence was recorded for two cases, whereas there were no cases of nodal metastasis, distant metastasis or disease-specific death. Recurrences were significantly more likely in patients who were immunocompromised (hazard ratio 12.87 [p=0.0193]) and those with rheumatological diseases (16.18 [p=0.0075]).

Comment: This study looked at observing a biopsy proven SCC if it resolved clinically before re-excision. Of 148 tumours in this study, apart from two cases of local recurrence, there was no recurrence over at least a 12-month follow-up but with a median follow-up of 35 months. One hundred and seven tumours (72%) were <10mm at initial diagnosis, and 71 (48%) were located on the head and neck. Histopathologically, 90% were well differentiated, 83% had at least one positive peripheral margin, and none were noted to have perineural invasion. Ninety-five percent had a shave biopsy with only 1% undergoing a punch biopsy and the remainder not specified. As the majority were well differentiated, it is possible several of these were keratoacanthomas. There are some patients who have contraindications for further surgery or whose life expectation is limited, but watchful waiting is also an option in otherwise well patients with clinical resolution. Dermatologists may be more comfortable if the SCC is well differentiated, but a positive margin is not a reason to re-excise if clinically clear.

Reference: J Am Acad Dermatol 2025;92:801–6
Abstract

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3D total-body photography in patients at high risk for melanoma

Authors: Soyer HP et al.

Summary: Adults at high risk of developing a primary or subsequent melanoma were randomised to usual care (6-monthly online surveys) with (n=158) or without (n=156) 3D-total-body photography in person and sequential digital dermoscopy imaging via teledermatology at 0, 6, 12, 18 and 24 months. There were 905 excisions performed in 122 intervention group participants and 622 in 104 control group participants, with histopathologically confirmed melanoma in 4% and keratinocyte cancer in 26%. Compared with the control group, the intervention group had a higher mean number of lesions (any type) excised (5.73 vs. 3.99 per person [p=0.02]), and lower melanoma detection and incidence rates (35% vs. 64% and 2.03 vs. 3.62, respectively). The intervention group also had a numerically but not statistically significantly lower 1-year melanoma rate per person (0.08 vs. 0.16), as well as lower average rates of keratinocyte cancers (0.86 vs. 0.42) and excision/biopsy (2.01 vs. 1.39) per person.

Comment: Although 3D-total-body photography combined with sequential dermoscopy is a new and potentially more accurate way to detect changes in moles or new lesions in patients at high risk of melanoma, these patients, compared with the control group, had an increased number of excisions but fewer melanoma excisions and more excisions of keratinocytes carcinomas and benign lesions. It may be that, by chance, fewer melanomas occurred in the intervention group, which would explain the reduced melanoma excision rate. As it detected more keratinocyte carcinomas, it was effective in detecting early changes of skin cancer, but as there were more benign lesions, the diagnostic accuracy needs to be improved. 3D-total-body photography was not cost effective in this study. Limitations of the study included junior clinicians checking the skin in the intervention group, so more experienced clinicians may affect the results and reduce the rate of benign excisions. Studies with larger numbers of patients and for longer periods and with the use of AI may improve these results, so further studies are needed to determine the role of 3D-total-body photography.

Reference: JAMA Dermatol; Published online Mar 26, 2025
Abstract

Whether the transient hair shedding phase exist after minoxidil treatment and does it predict treatment efficacy?

Authors: Bi L et al.

Summary: Hair shedding with 24 weeks of topical 2% or 5% minoxidil use was reported in this retrospective study of 49 patients with androgenetic alopecia. Hair shedding increased temporarily during the first 12 weeks of minoxidil treatment, but continued for longer with 2% minoxidil than with 5% minoxidil. There was a correlation detected between the severity of hair shedding and trichoscopy test improvement with 5% minoxidil but not with 2% minoxidil. The maximum relative amount of hair shedding was significantly associated with improvements in BASP classification for both strengths of minoxidil.

Comment: Hair shedding is commonly seen after topical minoxidil, which can continue for the first 12 weeks. In this study, 5% minoxidil showed increased shedding at 4 weeks but had returned to normal by 8 weeks. This study showed that the severity of hair shedding was correlated with subsequent improvement, but only with the 5% strength and not the 2% strength. This was thought to be due to 5% minoxidil having an increased effect in shifting from telogen to anagen. The maximum shedding in the 5% group also showed a strong positive correlation with improvement in average hair diameter, as well as the proportion of terminal hairs, which is consistent with previous studies. Patients are often very concerned about the initial increased hair loss and may be reluctant to start minoxidil because of this, but this study can reassure them that those with most hair shedding have the best long-term result.

Reference: J Dermatolog Treat 2025;36:2480739
Abstract