Skin Cancer Research Review™

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Issue 10 - 2022

In this issue:

Abbreviations used in this issue:

ALM = acral lentiginous melanoma; **BCC** = basal cell carcinoma; **CI** = confidence interval; **CNN** = convolutional neural network; **CT** = computed tomography; **CTLA-4** = cytotoxic T-lymphocyte–associated antigen 4; **FGD** = fluoro-2-deoxy-D-glucose; **MCC** = Merkel cell carcinoma; **OS** = overall survival; **PD-(L)1** = programmed cell death protein-(Ligand)1; **PET** = positron emission tomography; **PFS** = progression-free survival; **RECIST** = Response Evaluation Criteria in Solid Tumours; **SCC** = squamous cell carcinoma.

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Welcome to issue 10 of Skin Cancer Research Review.

Salvage combination therapy consisting of ceralasertib plus durvalumab may be a therapeutic option for patients with immunotherapy-resistant advanced/metastatic melanoma after failure of front-line anti-programmed cell death protein (PD)/PD-ligand (L)1 therapy with a Korean phase 2 trial reporting anti-tumour activity in mucosal, acral and cutaneous melanoma subtypes with a tolerable toxicity profile. Further data in larger patient cohorts are eagerly awaited to confirm these results. Positron emission tomography (PET) has demonstrated utility in evaluation of response to PD-1 inhibitor therapy and long-term prognostication in metastatic melanoma in a study from the Melanoma Institute Australia reported in *Annals of Oncology*. PET may replace the current standard of computed tomography (CT) as the preferred imaging modality in this indication, particularly given its utility for evaluation of residual lesions. In the realm of non-melanoma skin cancer, the clinical and molecular factors of unresectable advanced Merkel cell carcinoma (MCC) associated with clinical response to PD-1 immune checkpoint inhibitors is investigated, the combination of a Hedgehog inhibitor induction regimen with concurrent radiotherapy looks promising for advanced basal call carcinoma (BCC) and low-dose acitretin is an efficacious chemoprevention strategy for keratinocyte carcinomas after solid organ transplant.

We hope you find these and the other selected studies interesting, and look forward to receiving any feedback you may have.

Kind Regards,

Dr David Simpson

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Clinical and molecular characteristics associated with response to therapeutic PD-1/PD-L1 inhibition in advanced Merkel cell carcinoma

Authors: Spassova I et al.

Summary: Spassova et al retrospectively investigated clinical and molecular factors associated with clinical response to PD-(L)1 immune checkpoint inhibitors in patients with unresectable advanced MCC. The study cohort was comprised of 114 patients (72% male) with histopathologically confirmed MCC who received single-agent avelumab, nivolumab or pembrolizumab treatment in the front- to third-line setting at one of 10 German centres or one Swedish centre between May 2018 and July 2020. Primary tumours were located predominantly on the head and neck or extremities and disease was mostly metastatic (stage M0-M1a/b/c, 85%). Disease control with at least stable disease by Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1 criteria was achieved by 65% of the entire cohort (n=74) consisting of mostly objective responses (complete or partial, n=54). Higher rates of objective responses and disease control were observed after anti-PD-1 therapy with pembrolizumab or nivolumab compared to anti-PD-L1 therapy with avelumab (56% vs 39% and 72% vs 58%, respectively). Achievement of at least disease control significantly impacted both progression-free survival (PFS) and overall survival (OS) with dismal clinical outcomes in patients who did not respond to therapy (PFS, 12.1 vs 1.4 months; OS, 15.9 vs 3.9 months). The absence of concomitant immunosuppression and fewer tumour-involved organ systems were associated with a favourable response to therapy on Bayesian cumulative ordinal regression model analysis. Analysis of tumour tissue prior to immune checkpoint inhibition with multiplexed immunohistochemistry identified dense intratumoral infiltrates of CD8+ effector and central memory T cells as molecular characteristics portending favourable therapeutic response.

Comment: Immune checkpoint inhibitors are being used in a variety of cancers and their effectiveness is often associated with the mutational burden and immunogenicity of the tumour. The authors have previously examined these factors in MCC and found that the central memory T cell activity and tumour infiltrating cell density were more important indicators of a favourable prognosis. The presence of CD8+ T cells was linked to an improved response rate and absence of immunosuppression and only one metastatic location were associated with a favourable outcome. Age less than 70, elevated lactate dehydrogenase and C-reactive protein were associated with a worse response to immune checkpoint therapy. Merkel Cell polyomavirus positivity was not a significant factor. Interestingly, the response to PD-L1 therapy (avelumab) was significantly inferior to PD-1 inhibitor therapy (nivolumab and pembrolizumab).

Reference: J Immunother Cancer 2022; (1):e003198

Abstract

The anatomical distribution of non-melanoma skin cancer: A retrospective cohort study of 22303 Australian cases

Authors: Khalid A et al.

Summary: This single-centre study from the Flinders Medical Centre in South Australia utilised a customised phrase algorithm to quantify anatomic non-melanoma skin cancer locations by cancer type in a cohort of patients (n=22,303) who had their cancer excised in a five-year period spanning 2012 to 2017. The cohort consisted predominantly (80%) of excisions in the head and neck region. BCC was more common on the scalp, periocular and nasal regions while squamous cell carcinoma (SCC) was mostly found on the lip, neck and scalp. Gender and age-related patterns were identified including higher rates of ear BCC and scalp SCC in males and higher rates of lip and leg cancers of either histology in females. The proportion of forehead BCC excisions had a positive correlation with age. The authors concluded that although gender and age account for some of the variation in anatomic distribution between non-melanoma cancer types other factors were also influential.

Comment: Non-melanoma skin cancer is known to have a predilection for areas of the body with high ultraviolet light exposure but some areas appear more affected than others. This large study of hospital-treated cases showed that even in the same general area there are differences in both frequency and type of non-melanoma skin cancer (BCC vs SCC) in particular subunits of that region. Those areas with chronic exposure are more likely to be the site of SCC, as expected, but differences such as more BCCs in the anterior scalp and more SCCs in the rest of the scalp were found. SCCs were found not only on the scalp but also the nasal dorsum, lower lip and lateral neck whilst BCCs were more common on the rest of the nose, upper lip, eyelid margins and forehead. In a community setting these findings might show a lower incidence of head and neck tumours since many of these more complicated excisions might be referred to hospital but the large size of this study adds important data to non-melanoma skin cancer distribution.

Reference: ANZ J Surg 2021;91(12):2750-56
Abstract

Hedgehog inhibitor induction with addition of concurrent superficial radiotherapy in patients with locally advanced basal cell carcinoma: A case series

Authors: Weissman J et al.

Summary: Hedgehog inhibitor therapy in combination with involved field radiotherapy may offer a novel treatment paradigm for patients with locally advanced BCC with this small US retrospective case series reporting a high complete response rate with a manageable toxicity profile. Analysis was based on 12 consecutive patients (median age 68 years; 75% male) with unresectable locally advanced Brigham and Women's stage T2b/T3 tumours who underwent Hedgehog inhibitor induction monotherapy with either oral sonidegib 200 mg/day or vismodegib 150 mg/day plus concurrent superficial radiotherapy (electron-beam or photon) initiated at the time of maximal tumour shrinkage (approximately 2-3 months) at the Comprehensive Cancer Centres of Nevada. The median duration of induction therapy was 3.6 months in patients who received sonidegib and 5.5 months for vismodegib. The median duration of radiotherapy was 31 days at which time Hedgehog inhibitor therapy was also terminated. A complete response was achieved by all patients with a relapse rate of 16.6% (2/12). A prolonged PFS was reported for almost 90% of the cohort (three-year PFS, 88.8%). There were no treatment discontinuations due to adverse events. Three-quarters of patients experienced mild (grade 1-2) adverse events attributed to Hedgehog inhibitor therapy and two-thirds mild skin toxicity to radiotherapy.

Comment: Patients presenting with large, neglected BCCs present challenges due to invasion into surrounding tissues and the likelihood of cosmetically disfiguring results if cure or local control is to be achieved. Mutations in the Hedgehog signalling pathway are implicated in the development of BCCs, both sporadic and inherited (such as in Gorlin's syndrome). Sonedigib and vismodegib are oral medications which inhibit Hedgehog pathway signalling and have been used in the rare metastatic BCCs as well as the more common locally advanced, unresectable BCCs but their use is limited by adverse effects such as loss of taste as well as a lack of durable response. This retrospective analysis looked at the results from initially treating with a Hedgehog pathway inhibitor and at the point of maximal tumour shrinkage superficial radiotherapy was added whilst continuing the Hedgehog pathway inhibitor until the end of the radiotherapy course. At the 40-month mark PFS was 89% which offers an excellent option for this tricky group of patients.

Reference: Oncologist 2021;26(12):e2247-53
Abstract

Monitoring patients at risk for melanoma: May convolutional neural networks replace the strategy of sequential digital dermoscopy?

Authors: Winkler J et al.

Summary: This cross-sectional study compared convolutional neural networks (CNNs) to sequential digital dermoscopy for differentiation between melanoma and nevi in high-risk patients. Two CNNs and 26 dermatologists were assessed for accuracy of melanoma detection using a four-image set comprised of one melanoma image and three nevi images from each of 59 patients (total 239 images). The CNNs correctly classified 15.3% and 13.6% of image sets with sensitivities ranging from 25.4%-28.8% and specificities of 92.7%-75.7%. Sensitivity was improved to 44.1%-49.2% by the addition of sequential digital dermoscopy follow-up. The average accuracy of the dermatologists was 40.1%. The study authors concluded that to be of use in clinical practice CNNs would need to be able to incorporate dynamic change data from sequential digital dermoscopy.

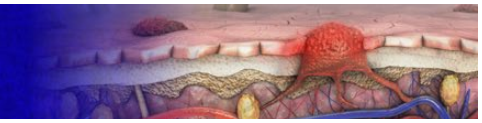
Comment: There has been a lot of interest in using CNN artificial intelligence systems to diagnose skin cancer and some studies have shown it to be at least equivalent to dermatologists. Monitoring patients with high-risk skin phenotypes is time consuming and can result in problems when patients fail to return for follow-up. Comparing image sets assessed by either dermatologists or two CNNs failed to show a superiority of CNN over dermatologists. The CNNs only correctly diagnosed a minority of the melanomas in the baseline images but this improved with the follow-up ones. The study was biased toward the dermatologists because they were informed that only one of the four images was a melanoma which gave them a one in four chance of being correct by chance. Using a combination of highest CNN score and dermatology opinion the sensitivity increased to 78.2%. When excised, over 50% of the melanomas were invasive, ranging from 0.2-1.3 mm Breslow thickness and this illustrates another problem with sequential digital dermoscopy - you may be spending time and resources watching a melanoma become invasive rather than treating it!

Reference: Eur J Cancer 2022;160:180-88
Abstract

Skin Cancer Research Review™

Independent commentary by Dr David Simpson

Dr David Simpson is a skin cancer doctor on the Sunshine Coast in Queensland. He has a masters degree in Skin Cancer Medicine from the University of Queensland and is a teaching assistant on the MMed program.



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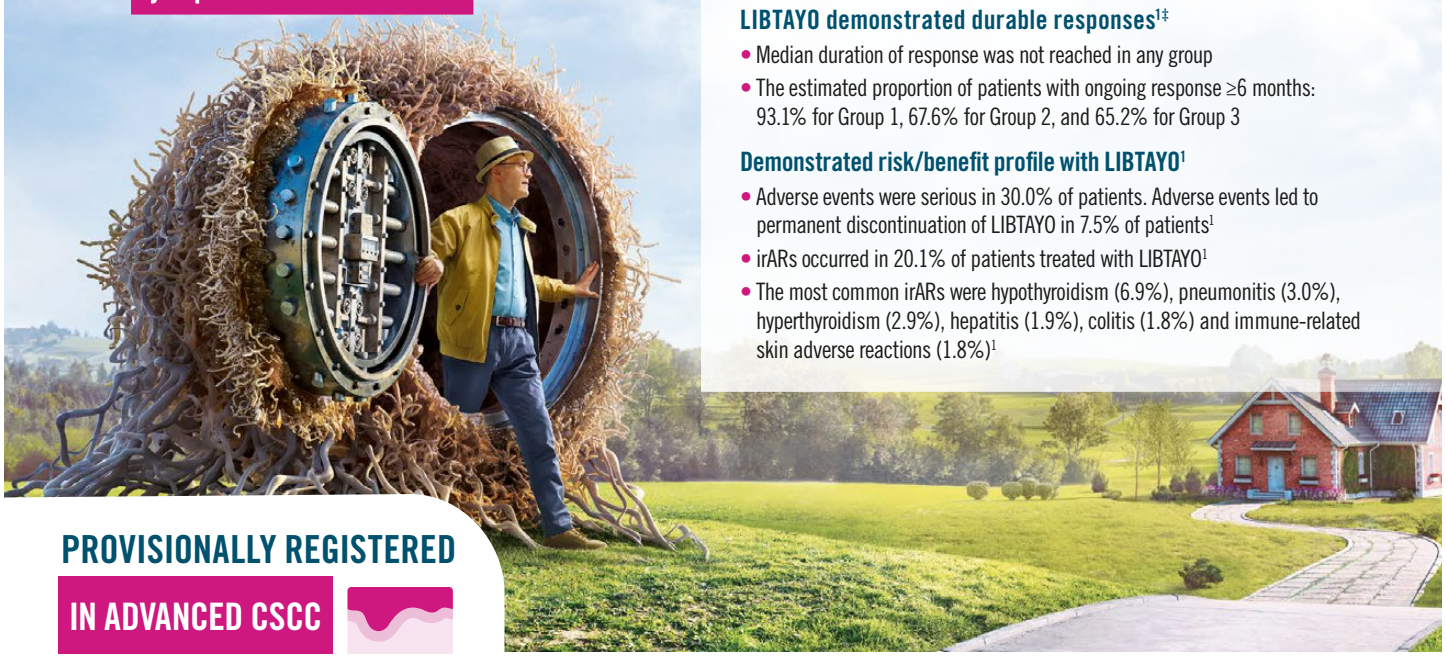

For patients with advanced cutaneous squamous cell carcinoma (CSCC).[1]

LIBTAYO demonstrated clinically meaningful responses[1]*

- **49.2% ORR** (95% CI, 35.9%-62.5%) for Group 1† **(mCSCC)**
- **43.6% ORR** (95% CI, 32.4%-55.3%) for Group 2† **(laCSCC)**
- **41.1% ORR** (95% CI, 28.1%-55.0%) for Group 3† **(mCSCC)**

LIBTAYO demonstrated durable responses[1]‡

- Median duration of response was not reached in any group
- The estimated proportion of patients with ongoing response ≥6 months: 93.1% for Group 1, 67.6% for Group 2, and 65.2% for Group 3

Demonstrated risk/benefit profile with LIBTAYO[1]

- Adverse events were serious in 30.0% of patients. Adverse events led to permanent discontinuation of LIBTAYO in 7.5% of patients[1]
- irARs occurred in 20.1% of patients treated with LIBTAYO[1]
- The most common irARs were hypothyroidism (6.9%), pneumonitis (3.0%), hyperthyroidism (2.9%), hepatitis (1.9%), colitis (1.8%) and immune-related skin adverse reactions (1.8%)[1]

PROVISIONALLY REGISTERED IN ADVANCED CSCC

LIBTAYO as monotherapy has **provisional approval** in Australia for the treatment of adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma (mCSCC or laCSCC) who are not candidates for curative surgery or curative radiation.[1]

The decision to approve this indication has been made on the basis of objective response rate (ORR) and duration of response from single arm clinical studies. The sponsor is required to submit further clinical data to confirm the clinical benefit of the medicine.[1]

▼ This medicinal product is subject to additional monitoring in Australia due to provisional approval. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

PBS Information: This product is not listed on the PBS

Study 1540 was a phase 2, pivotal, open-label, multicentre study that enrolled 193 patients with mCSCC or laCSCC, with a combined median follow-up of 9.4 months. Treatment may be continued until disease progression, unacceptable toxicity, or completion of planned treatment. The primary endpoint was confirmed ORR as assessed by ICR. Secondary endpoints included DOR, PFS, OS, and CR rate.[1]

LIBTAYO demonstrated an acceptable risk/benefit profile in clinical studies of 1,078 patients with advanced solid malignancies including 219 advanced CSCC patients who received LIBTAYO monotherapy.[1]

The recommended dose is 350 mg of LIBTAYO every 3 weeks (Q3W) administered as an intravenous infusion over 30 minutes. Treatment may be continued until disease progression or unacceptable toxicity.[1]

*Data cutoff was 20 September 2018 for Groups 1 and 3 and 10 October 2018 for Group 2.[1]

†In Groups 1, 2, and 3, median durations of follow-up were 16.5 months, 9.3 months, and 8.1 months, respectively.[1]

‡Based on Kaplan-Meier estimates.[1]

CR=complete response; CSCC=cutaneous squamous cell carcinoma; DOR=duration of response; ICR=independent review committee; ORR=objective response rate; OS=overall survival; PFS=progression-free survival.

Reference: 1. LIBTAYO® (cemiplimab) Approved Product Information. December 2021.

Please review full Product Information before prescribing. Full Product Information is available at here or by contacting Sanofi Medical Information on 1800 818 806.

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Sanofi and Regeneron are collaborating in the global development and commercialisation for LIBTAYO® (cemiplimab).

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Date of preparation: January 2022. MAT-AU-2102060

Phase II study of ceralasertib (AZD6738) in combination with durvalumab in patients with advanced/metastatic melanoma who have failed prior anti-PD-1 therapy

Authors: Kim R I et al.

Summary: This Korean single-centre, open-label, non-randomised phase 2 trial (NCT03780608) reports preliminary anti-tumour activity of the combination of ceralasertib plus durvalumab in immunotherapy-resistant advanced/metastatic melanoma. A total of 30 adult patients with a histologically confirmed diagnosis of metastatic melanoma refractory to or relapsed following anti-PD-(L)1 therapy were enrolled into the study and received 28-day cycles of 1500 mg durvalumab every four weeks plus 240 mg certalasertib twice-daily on days 15-28, continued until disease progression or unacceptable toxicity. At data cut-off on January 11, 2020 with a 14.5-month median follow-up the objective response rate by modified RECIST 1.1, the primary outcome measure, was 31%, consisting entirely of partial responses (n=9). A further nine patients had stable disease leading to a disease control rate of 63.3%. Responses were achieved in patients with mucosal, acral and cutaneous melanoma subtypes. The median duration of response was 8.8 months, and PFS 7.1 months. There were fourteen deaths with a median OS of 14.2 months. Exploratory analyses identified homologous recombination deficiency as a potential marker of therapeutic efficacy with superior PFS (hazard ratio 0.17; 95% confidence interval [CI], 0.02-1.43; p=0.064).

Comment: Ceralasertib is a novel DNA damage repair agent which acts via inhibition of the serine/threonine ATR (ataxia telangiectasia and Rad 3 related protein). During normal DNA replication ATR is recruited at stalled replication forks which can progress to double strand breaks if not repaired. By combining this new agent with a PD-L1 immune checkpoint inhibitor (durvalumab) it was hoped that patients who had already failed checkpoint inhibitor therapy might still achieve a durable response. The overall response rate was 30% with a disease control rate of 63% and a PFS of 7.1 months. The OS was 14.1 months. Many cancers rely on proteins such as ATR to control replicative stress on the uncontrollably dividing tumour cells and so targeting this may be an alternative way to target these cells.

Reference: Ann Oncol 2022;33(2):193-203
Abstract

FDG-PET to predict long-term outcome from anti-PD-1 therapy in metastatic melanoma

Authors: Dimitriou F et al.

Summary: Dimitriou and colleagues from the Melanoma Institute Australia at The University of Sydney in New South Wales provide five-year follow-up data comparing two imaging modalities for prognostication of outcome following anti-PD-1-based treatment for metastatic melanoma. The study retrospectively included 104 patients who received immune checkpoint inhibitor therapy with an anti-PD-1 inhibitor as a monotherapy (67%) or in combination with anti-cytotoxic T-lymphocyte–associated antigen 4 (CTLA-4; ipilimumab) therapy and underwent standard CT plus [18F]2-fluoro-2-deoxy-D-glucose (FDG)- PET at baseline and at one-year follow-up. Previously published data at one-year indicated that assessment of metabolic response using FDG-PET provided more accurate prediction of disease progression than CT (Tan A et al. *Ann Oncol* 2018;29[10]:2115-2120). At a median follow-up of 61 months from one-year PET, rates of PFS in patients with a complete or partial response by RECIST criteria using CT were 93% and 76%, respectively. In contrast, PFS rates in patients with a complete or non-complete metabolic response by European Organisation for Research and Treatment of Cancer (EORTC) criteria for PET were 90% and 54%. Five-year OS rates for complete versus partial (metabolic) response were 100% vs 91% by CT and 96% vs 87% for PET. The authors concluded that most patients derived a sustained clinical benefit from anti-PD-1 ± anti-CTLA-1 treatment and that compared to standard CT imaging, PET was better for assessing residual lesions enabling superior long-term progression prediction.

Comment: PD-1 checkpoint inhibitor therapy is proving to have excellent durable responses and in a previous study this team showed that the degree of metabolic response seen on PET scans was a better predictor of prognosis than using CT scans. In the previous study, whilst only 28% had a complete response according to CT, 75% had a complete metabolic response on PET scanning. In this longer-term follow-up the authors have shown continuing responses after five-years from the one-year PET scan and the metabolic response rate has proved to be a better predictor of PFS and OS. Complete metabolic response indicates an excellent long-term prognosis and does not appear to be related to duration of therapy or CT response rate.

Reference: Ann Oncol 2022;33(1):99-106
Abstract

Sentinel lymph node biopsy positivity in patients with acral lentiginous and other subtypes of cutaneous melanoma

Authors: Cheraghlou S et al.

Summary: This retrospective cohort study extracted data from the US National Cancer Database to examine the risk of sentinel lymph node melanoma metastasis from the rare acral lentiginous (ALM) histopathologic subtype of malignant melanoma. Of the 60,148 cases of *AJCC Cancer Staging Manual, 8th edition* (AJCC-8) stage 1-3 malignant melanoma (median age 64 years; 42.5% female) diagnosed between 2012 and 2015 in the database, 1.6% were ALM subtype (n=959). Evaluation of the risk of sentinel lymph node positivity by histologic subtype by adjusted multivariable logistic regression analysis revealed that the ALM subtype had the greatest risk with almost double the odds compared to the superficial spreading melanoma subtype (odds ratio 1.9; 95% CI, 1.59-2.28). The highest risk for sentinel lymph node positivity was found in stage 1B and 2 ALM disease, with positivity rates of 18.39% and 39.53%, respectively.

Comment: ALM is a rare subtype which is not thought to be related to ultraviolet light exposure and may be linked to trauma or chemical exposure. This study examined over 60,000 cases of melanoma and assessed the likelihood of positive sentinel lymph node biopsy. Whilst nodular melanoma had the highest rate of sentinel lymph node positivity in thin tumours ALM had the highest rate in all tumours of stage 1B and upwards. Histologic predictors for a positive SLN were associated more with nodular melanoma than ALM and it may be that ALM doesn't follow the classic stepwise progressive of invasion leading to distant spread and other unknown factors are to blame. In this study 26.5% of stage 1B ALM cases did not undergo sentinel lymph node biopsy despite the average Breslow thickness being 2 mm. The high rate of sentinel lymph node positivity for ALM and the aggressive behaviour compared to that expected from the histopathological features suggests that ALM patients would benefit from increased sentinel lymph node biopsy and subsequent therapy if indicated.

Reference: JAMA Dermatol 2022;158(1):51-8
Abstract

Melanoma of the nail apparatus: An analysis of patients' survival and associated factors

Authors: Seyed Jafari S et al.

Summary: Total digit amputation may not be necessary in all cases of nail apparatus melanoma according to results from this European retrospective cohort review published in *Dermatology*. The study included 30 patients with a single, primary localised histopatholically confirmed nail apparatus melanoma. The five- and ten-year OS rates were 85.6% and 73.4%, respectively. Factors identified as associated with superior outcome included thin tumours (in situ or Breslow thickness <1 mm) and primary tumour located in the hand with patients with thinner tumours having superior five-year disease-free survival and OS compared to patients with thicker tumours (90% vs 58.3% and 94.1% vs 55.6%, respectively). Half of the cohort were treated with tumour excision and full-thickness skin graft covering and had a 100% survival rate at five-years.

Comment: Nail apparatus melanoma has an uncertain aetiology, similar to the uncertainty regarding ALM, and has also been regarded as a site with a worse prognosis. This paper looks at a retrospective case series and lacks specific data regarding the association of each factor but the main findings were that patients treated with wide local excision and skin grafting did no worse than those treated with amputation and that NAM on the hand had a much better prognosis than on the foot. Breslow thickness greater than 1 mm and the presence of tumour infiltrating lymphocytes were associated with a worse prognosis. Whilst they conclude that amputation may be unnecessary based on these findings it is unclear whether those patients treated with amputation as well as those with foot tumours and those with tumour-infiltrating lymphocytes had more advanced tumours at diagnosis.

Reference: Dermatology 2022;238(1):156-60
Abstract

Low-dose acitretin for secondary prevention of keratinocyte carcinomas in solid-organ transplant recipients

Authors: Solomon-Cohen E et al.

Summary: This retrospective case-crossover study from an Israeli specialised dermatology clinic in a transplantation centre assessed the efficacy of low-dose acitretin for prevention of secondary keratinocyte carcinoma in patients after a solid-organ transplant. Analysis was based on 34 solid-organ transplant recipients who developed at least one keratinocyte carcinoma after transplant and subsequently received two-years of acitretin 10 mg/day. A significantly lower mean new keratinocyte carcinoma rate was found during acitretin treatment compared to the two-year pre-treatment period (1.7 vs 3.6; treatment effect -53%; p=0.002). This efficacy was consistent across tumour types (SCC and BCC).

Comment: Solid-organ transplant patients suffer from high levels of keratinocyte carcinomas – SCC, BCC and intraepidermal carcinoma – due to their long-term immunosuppressive medication. Systemic retinoids have been shown to be effective at reducing this disease burden but tolerability is limited by adverse reactions including xerosis, dry mucous membranes, dry chapped lips, skin fragility, hair loss, hyperlipidaemia and liver function test abnormalities. The standard dose is 25-50 mg daily but by lowering this to 10 mg daily the authors managed to provide a significant reduction in keratinocyte cancers with no clinically significant adverse effects reported by the study group.

Reference: Dermatology 2022;238(1):161-66
Abstract

Clinical and dermatoscopic predictors of squamous cell carcinoma of the lips: a case-control, multicentric study

Authors: Lallas A et al.

Summary: Lallas et al retrospectively evaluated the clinical and dermatoscopic morphology of lip lesions from SCC in comparison to those from actinic cheilitis and inflammatory lesions to identify differentiating features. Images from 107 histologically confirmed SCC lesions were compared to images from 70 controls. Dermatoscopically, lip SCC lesions were characterised by scales, white halos, white clods and ulceration with polymorphic vessels. Clinical predictors of lip SCC included an exophytic appearance and hyperkeratosis (odds ratios 43 and 4, respectively).

Comment: SCC of the lip is an important diagnosis to make since this location has an increased propensity for lymph node metastasis and a delayed diagnosis will result in a larger excision with worse cosmetic and functional outcomes. When assessing a lip lesion on the vermillion the main objective is to discriminate between actinic cheilitis, which can be treated with non-surgical methods, and invasive lip SCC which will require wide excision or radiotherapy. Other diagnoses such as systemic lupus erythematosus, chronic discoid lupus, lichen planus and eczematous cheilitis should also be considered. Lip SCCs were most likely to have an exophytic clinical appearance but may be flat and hyperkeratosis was a frequent feature. Dermatoscopically, white halos and scale were common to both lip SCC and actinic cheilitis and so not useful to distinguish between them. Lip SCCs had white clods – not white circles because this feature is only seen in follicles, which are absent on the vermillion – ulceration and both linear and hairpin vessels. Actinic cheilitis can have areas of erosions rather than full thickness ulceration but biopsy is advised if there is any doubt. In addition, actinic cheilitis' has whitish structureless areas with scales and halos in the vermillion and radially-arranged telangiectasia surrounding the areas of erosion. Summing it up - Amilio Llalas described the classic lip SCC case to be an elderly male with a scaly exophytic lesion on the lower lip, dermatoscopically displaying ulceration, white clods and linear and hairpin vessels.

Reference: J Eur Acad Dermatol Venereol 2022;36(2):222-27
Abstract

