Melanoma Research Review™

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Issue 45 - 2021

In this issue:

Abbreviations used in this issue:

ANNs = artificial neural networks; **AUROC** = area under the receiver operating characteristic; **CNN** = convolutional neural network; **CPI** = checkpoint inhibitor; **CR** = complete response; **CTLA4** = cytotoxic T-lymphocyte-associated protein-4; **DDR** = DNA damage repair; **EMT** = epithelial–mesenchymal transition; **IFA** = incomplete Freund's adjuvant; **IRR** = immune response rate; **LPV** = long peptide vaccine; **MEP** = minimal epitope; **MIA** = Melanoma Institute Australia; **MR** = Mitotic rate; **NNB** = number needed to biopsy; **ORR** = objective response rate; **OS** = overall survival; **PD-1** = programmed death 1; **PD-L1** = programmed death ligand 1; **PFS** = progression-free survival; **PR** = partial response; **SLN** = sentinel lymph node; **SN** = sentinel node; **SNBs** = sentinel node biopsy; **Tet**; tetanus helper peptide; **TILs** = tumour-infiltrating lymphocytes; **TLR** = toll-like receptor; **UV** = ultraviolet.

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Welcome to the 45th issue of Melanoma Research Review.

This month's Research Review has three articles related to SNB of melanoma. One looks at whether artificial intelligence networks make them redundant. Another upgrades nomograms that help in deciding whether they are needed, and a third questions the accuracy of histopathology reporting that surgeons rely on to carry out SNBs. A study suggesting that adoptive immunotherapy with TILs may become practical is reviewed. A commentary is also included that points to possible new agents for treating mucosal melanoma and treatment resistant melanoma that deserves attention. Immunotherapy of cancers with long antigenic peptides has had some success in cervical cancers. A study of these in melanoma is reviewed which shows how difficult such studies are in multi-institutional settings. A very experienced group have also taken up the question of whether starting with single agent anti-PD1 followed by anti-CTLA4 plus anti-PD1 for relapse is just as good as the combination up front. Finally, a New Zealand study suggests that teledermoscopy has merit in diagnosing melanoma.

Kind Regards,

Professor Peter Hersey

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Deep learning approach to predict sentinel lymph node status directly from routine histology of primary melanoma tumours

Authors: Brinker TJ, et al

Summary: The researchers aimed to develop a digital biomarker that can predict lymph node metastasis non-invasively from primary melanoma tumours. They digitised H&E slides from primary melanoma tumours with known sentinel node (SN) status (150 SN positive/265 SN negative). Two hundred ninety-one slides were used to train artificial neural networks (ANNs) and 124 slides were used to test the ability of the ANNs to predict sentinel status. ANNs were trained and/or tested on data sets that were matched or not matched between SN-positive and SN-negative cases for patient age, ulceration and tumour thickness. The researchers concluded the best accuracy was achieved by an ANN that was trained and tested on unmatched cases (61.8% ± 0.2%) area under the receiver operating characteristic (AUROC). In contrast, ANNs that were trained and/or tested on matched cases achieved (55.0% ± 3.5%) AUROC or less.

Comment: *Does looking at the primary by artificial intelligence make SLN biopsy unnecessary?*

Risk factors known to be associated with positive lymph node status (SLN+) in melanomas are increasing Breslow thickness and ulceration, younger age, mitotic rate (MR), and the level of tumour-infiltrating lymphocytes (TILs). There is a clinical need to predict SLN status non-invasively, reproducibly and with high accuracy, especially for subgroups of patients with high-risk factors for surgery and multiple comorbidities. Recently, deep learning–based ANNs have proven their potential in skin cancer image analysis as well as digital pathology for melanoma. Distant visceral recurrence was also predicted from digitised sections of the primary tumour using a combination of precomputed features, a convolutional neural network (CNN) and a recurrent neural network. This study aimed to develop a deep learning–based digital biomarker to predict the likelihood of SLN+ from digitised H&E slides using whole slide images of primary tumours.

The results show that SN status can be predicted to some extent using CNN-based image analysis; mostly by detecting morphological equivalents of features that are already known to correlate with lymph node status, namely, tumour thickness, ulceration, and patient age. Reasons for inaccuracy included epithelial–mesenchymal transition (EMT) changes that were too rare for the CNN to use. In addition, some tumour cells may have the ability to spread into the lymph nodes downstream of the primary tumour. Only one slide per case was analysed, and superficially spreading melanomas may be highly heterogenous. The area of the tumour or cell clone going to spread is uncertain so that areas of relevance may have been missed. They conclude that additional studies are required to confirm the results and to improve the prediction to increase clinical applicability. (*SLN biopsy looks to be with us for a while longer!*)

Reference: Eur J Cancer 2021 Sep;154:227-234
Abstract

Predicting sentinel node positivity in patients with melanoma: External validation of a risk-prediction calculator (the Melanoma Institute Australia nomogram) using a large European population-based patient cohort

Authors: El Sharouni MA, et al

Summary: The investigators performed further validation of the Melanoma Institute Australia (MIA) nomogram in predicting SN positivity using a European national patient cohort. Of the 3,049 patients from the Dutch Pathology Registry who met the eligibility criteria, 23% (691) were SN positive. The investigators reported validation of the MIA nomogram (including the parameters Breslow thickness, ulceration, age, melanoma subtype and lymphovascular invasion) showed a good C-statistic of 0.69 with excellent calibration (R2 = 0.985, P = 0.40). The negative predictive values (NPVs) of 90.1%, found at a 10% predicted probability cutoff for having a positive SN biopsy, implied that by using the nomogram, a 16.3% reduction in the rate of performing an SN biopsy could be achieved with an error rate of 1.6%. They also noted validation of the MIA nomogram considering MR as present or absent showed a C-statistic of 0.70.

Comment: *Is that sentinel lymph node biopsy really necessary?*

Sentinel node status is an important predictor of survival outcome in patients with melanoma. It can however sometimes lead to complications such as infection, seroma and lymphoedema. Consequently, various prediction models have been used to select patients for SN biopsy to ensure that those most likely to be SN positive undergo the procedure, while those most likely to be SN negative are not.

The MIA nomogram for predicting SN status (available at www.melanomarisk.org.au) was shown to be more accurate than the previously published online calculator of risk of SN positivity that was developed at the Memorial Sloan Kettering Cancer Center more than 15 years ago. The improvement was achieved by replacing body site and Clark level with MR, melanoma subtype and lymphovascular invasion status. It was externally validated using data from the MD Anderson Cancer Center. The aim of this study was to externally validate the MIA nomogram using a nationwide population-based dataset from a third continent.

They considered the strength of this study was that it was population-based so confirming its general applicability. It was limited in that the Dutch dataset did not include the number of mitoses in the primary melanoma, only their presence or absence. Nevertheless, they found that the nomogram still resulted in significant reduction in unnecessary SN biopsies. They conclude that the MIA nomogram can thus be recommended for clinical practice internationally to guide clinical decision making and counsel patients by informing them whether or not an SN biopsy procedure is likely to provide useful information that may influence management. The information may also guide follow-up recommendations.

Reference: Br J Dermatol 2021 Aug;185(2):412-418
Abstract

Histopathologic synoptic reporting of invasive melanoma: How reliable are the data?

Authors: Taylor LA, et al

Summary: The study explored variability in the assessment and reporting of critical characteristics of invasive melanomas. One hundred fifty-one pathologists interpreted 41 invasive melanoma cases. There was complete agreement among all reviewers for 22 of the 41 cases (54%) on Breslow thickness dichotomised at 0.8 mm, with pairwise agreement ranging from 49% to 100% across the 41 cases. There was complete agreement for "no ulceration" in 24 of the 41 cases (59%), with pairwise agreement ranging from 42% to 100%. Tumour transected at base had complete agreement for 26 of the 41 cases (63%), with pairwise agreement ranging from 31% to 100%. Mitotic rate (MR) had complete agreement for 17 of the 41 cases (41%), with pairwise agreement ranging from 36% to 100%. Regression saw complete agreement for 14 of 41 cases (34%), with pairwise agreement ranging from 40% to 100%. Lymphovascular invasion, perineural invasion, and microscopic satellites were rarely reported as present.

Comment: *Can you really trust the histopathology report on the primary melanoma?*

This US study addressed variability in the assessment and reporting of critical characteristics of invasive melanomas that are used by clinicians to guide patient care. The results demonstrated striking variability in the histopathological reporting of melanoma that they believe had not had attention in the literature.

Particular problems were reporting including Breslow thickness, MR, ulceration, regression, and microscopic satellites. For example, although lympho-vascular and perineural invasion demonstrated rates of complete agreement among pathologists at 78% and 90%, respectively there was complete agreement for only 44% of cases on the presence of microscopic satellites, which is incorporated into the AJCC model as a lymph node (N) staging criterion and prognostic factor.

They noted that although stage T1a melanomas have more favourable outcomes than thicker melanomas and are not subject to official recommendations for SLN mapping, 21% of T1a lesions in this study were still considered to have a less favourable prognosis by participating pathologists. On scrutiny of the data, participants were more likely to estimate a poor prognosis for T1a lesions when they were associated with increased numbers of mitotic figures. In this study, MR, categorised as 0, 1, or 2/mm^2, had complete agreement for only 17 of the 41 cases (41%). Many other inconsistencies were noted. They considered this work served to alert pathologists and clinicians to the existence of variability in reporting these prognostic factors. *Maybe Australian pathologists could publish a reply?*

Cancer 2021 Sep 1;127(17):3125-3136
Abstract

Lifileucel, a tumor-infiltrating lymphocyte therapy, in metastatic melanoma

Authors: Sarnaik AA, et al

Summary: This phase II open-label, single-arm, multicentre study included patients with advanced melanoma previously treated with checkpoint inhibitor/s (CPIs) and BRAF ± MEK targeted agents. Sixty-six patients received a mean of 3.3 prior therapies (anti-programmed death 1 [PD-1] or programmed death ligand 1 [PD-L1]: 100%; anti-cytotoxic T-lymphocyte-associated protein-4 (CTLA4): 80%; BRAF ± MEK inhibitor: 23%). Patients received a nonmyeloablative lymphodepletion regimen, a single infusion of lifileucel, and up to six doses of high-dose interleukin-2. Lifileucel was produced from harvested tumour specimens in 22-days. The objective response rate (ORR) was 36%, with two complete responses (CRs) and 22 partial responses (PRs). Disease control rate was 80%. Median duration of response was not reached after 18.7-month median study follow-up. In the primary refractory to anti-PD-1 or PD-L1 therapy subset, the ORR and disease control rate were 41% and 81%, respectively.

Comment: *Is adoptive autologous T cell immunotherapy now a practical treatment choice in Australia?*

This article received a detailed commentary by Dr Paul Chapman in the Journal of Clinical Oncology *(Chapman PB. Targeting tumor-rejection antigens in melanoma with tumor-infiltrating lymphocytes. J Clin Oncol. 2021 Aug 20;39(24):2640-2642)* and the following are extracts from that excellent review.

"Tumor-infiltrating lymphocytes were presumed to be enriched for T cells recognising specific tumor-rejection antigens and as originally envisioned by Rosenberg et al, *(Rosenberg SA, et al: Use of tumor-infiltrating lymphocytes and interleukin-2 in the immunotherapy of patients with metastatic melanoma. A preliminary report. N Engl J Med 319:1676-1680, 1988)* could potentially be expanded and reinfused into the patient without having to identify each patient's specific tumour-rejection antigen. TIL were expanded in vitro and reinfused with relatively high-dose interleukin 2 (IL-2) (720,000 IU/kg every 8 hours) to maintain TIL viability".

Sarnaik et al, now report the results of essentially a phase II trial with lifileucel, an autologous TIL product that can be prepared in 22 days. For each patient, a tumour biopsy was shipped to the sponsor and TIL were expanded using IL-2 and anti-CD3 monoclonal antibody OKT3. The TIL product was cryopreserved and sent back to the investigator for infusion. Patients received standard nonmyeloablating chemotherapy with cyclophosphamide and fludarabine before TIL infusion. After infusion, patients receive IL-2, 600,000 IU/kg q8-12 hours for six doses, although the median number of doses actually administered was 5.5. Of the 78 patients who underwent tumour harvest, 66 (85%) were able to receive lifileucel. This distinguishes lifileucel from the previous TIL studies in which the proportion of patients harvested who were actually treated was either not reported or was relatively low. Given the short turnaround time of lifileucel and the high proportion of harvested patients actually treated, the patients in this study are less highly selected than in previous TIL studies. As in the previous TIL studies, the patients in this trial were all heavily pre-treated having received a mean of 3.3 prior lines of therapy. All patients had been treated with anti–PD1 or anti-PDL1 therapy and most had received anti-CTLA4 therapy.

The main finding from the trial was that two patients had a CR and 22 had a PR for an ORR of 36%. Although the median progression-free survival (PFS) was only 4.1 months for all 66 patients, among the 24 responding patients, an estimated 70% remained relapse-free at 12 months, indicating that responses have been relatively durable.

Lifileucel may be a reasonable treatment option for patients with melanoma who progress on CPI therapy, although few of the past TIL patients had received prior CPIs. If patients resistant to CPIs are also less sensitive to TIL therapy, this could explain the relatively low CR rate seen on this trial. Overall, only a small minority of the 66 treated patients were relapse-free at 12 months but further follow-up will tell us more about the durability of the responses.

Reference: J Clin Oncol 2021 Aug 20;39(24):2656-2666
Abstract

Pembrolizumab plus ipilimumab following anti-PD-1/L1 failure in melanoma

Authors: Olson DJ, et al

Summary: This prospective clinical trial evaluated pembrolizumab plus low-dose ipilimumab after anti-PD-1/L1 immunotherapy failure, in advanced melanoma. Prior treatments included 60 on anti-PD-1 antibody alone and 10 on anti-PD-1/L1 antibody-based combinations. The median length of prior treatment with anti-PD-1/L1 antibody was 4.8 months; 13 patients had progressed in the adjuvant setting.

Patients received pembrolizumab 200 mg plus ipilimumab 1 mg/kg once every 3 weeks for four doses, followed by pembrolizumab monotherapy. The authors reported five CRs and 15 partial responses, with ORR of 29%. The median PFS was 5.0 months, and the median overall survival (OS) was 24.7 months. The median duration of response was 16.6 months. The authors noted there was no difference in median time on prior anti-PD1/L1 or time to PD1 + CTLA4 initiation between responders and non-responders. Furthermore, responses occurred in PD-L1-negative, non-T-cell-inflamed, and intermediate tumour phenotypes. Grade 3-4 drug-related adverse events occurred in 27% of patients.

Comment: *Do you get the same treatment outcome by starting with monotherapy with anti-PD1 and switching to the combination if patients fail?*

This was a prospective study on 70 patients with metastatic melanoma. It was testing the hypothesis that combined PD-1 and CTLA4 inhibition can be effective after progression on a prior anti-PD-1/L1. The use of this combination in the second line might also theoretically spare the higher toxicity rate for patients who only required single-agent anti-PD-1 therapy for disease control. Toxicity was mitigated by treatment with low dose ipilimumab at 1mg/kg rather than 3mg.

Responses to pembrolizumab plus low-dose ipilimumab were observed predominantly among PD-L1–negative and intermediate to non-T-cell–inflamed tumours in archival FFPE samples. This contrasted with upfront anti-PD1 where responses were seen in inflamed IFN gamma associated activation. This led to the observation that these (good TIL) patients were probably excluded from the relapsed group. They considered that a limitation of the study was lack of a clear consensus to define progression on anti-PD1. In 79% of patients 2 scans were used to confirm progression but in others it was based on clinical judgement.

Nevertheless, the study demonstrated durable long term responses in PD1 failed patients after treatment with the combination. It was associated with minimal toxicity and appeared superior to salvage treatment with anti-CTLA4 at 3 mg/kg. A clinical trial would be needed to confirm the findings.

Reference: J Clin Oncol 2021 Aug 20;39(24):2647-2655
Abstract

Independent commentary by Peter Hersey, FRACP, D Phil

Peter Hersey is an honorary Professor of Immuno Oncology in the University of Sydney and a faculty member of the Melanoma Institute Australia. He has conducted a number of phase I to III trials of immunotherapy in melanoma, including use of modified peptide antigens and dendritic cell vaccines. He has taken a leading role in studies investigating properties of melanoma cells that make them resistant to treatment and new treatment approaches to overcome these properties. He is generally recognized as a pioneer of immunotherapy for melanoma in Australia, and has participated in most of the key clinical trials on immunotherapy with immune checkpoint inhibitors. He continues translational research on melanoma in the Centenary Institute as joint holder of a NHMRC program grant on melanoma.

Pyrexia in patients treated with dabrafenib plus trametinib across clinical trials in BRAF-mutant cancers

Authors: Schadendorf D, et al

Summary: The authors characterised the incidence, patterns and management of pyrexia in patients receiving dabrafenib plus trametinib in clinical trials. The trials included in the analysis were: phase II registration trial in advanced NSCLC (n = 82), phase III COMBI-AD study in resectable stage III melanoma (n = 435) and phase III COMBI-d and COMBI-v studies in unresectable or metastatic melanoma (n = 209 and n = 350, respectively). They found among the 1,076 patients enrolled in the clinical trials, 61.3% developed pyrexia, 5.7% developed grade 3/4 pyrexia and 15.6% developed a protocol-defined serious pyrexia event. Among the 660 patients with pyrexia, 33.0% had 1 occurrence, 19.8% had 2 occurrences and 47.1% had ≥3 occurrences. It was noted the incidence of pyrexia was highest early in treatment and decreased with time on treatment. The most common and effective management strategy was temporary dose interruption of dabrafenib or trametinib.

Comment: *Revision of a common side effect from treatment with dabrafenib and trametinib.*

This subject has been extensively reviewed in a number of articles. The authors, however, aimed to present a comprehensive analysis of pyrexia to better characterise the incidence, patterns and management of pyrexia in patients treated with dabrafenib plus trametinib in the controlled trial setting using data from phase II and phase III clinical studies. They draw attention to algorithms that have proven useful in management. The pathogenesis gets brief mention which is unfortunate as further treatment initiatives depend on a better understanding of the cause of pyrexia.

Reference: Eur J Cancer 2021 Aug;153:234-241
Abstract

Phase I study of ceralasertib (AZD6738), a novel DNA damage repair agent, in combination with weekly paclitaxel in refractory cancer

Authors: Kim ST, et al

Summary: Ceralasertib is an oral inhibitor of the serine/threonine protein kinase ataxia telangiectasia and Rad3-related (ATR) protein. The study cohort of 57 patients with solid tumours enriched for melanoma (33 who failed prior PD1/L1 treatment) were enrolled in ceralasertib dose cohorts ranging from 40 mg QD to 240 mg BD plus weekly paclitaxel. The recommended phase II dose was established as ceralasertib 240 mg BD days 1-14 plus paclitaxel 80 mg/m2 on D1, D8, D15 every 28 days. In the full analysis set of 57 patients, the ORR was 22.6%. In 33 patients with melanoma, resistant to prior anti-PD1 therapy, the ORR was 33.3%. In the melanoma subset, the median PFS was 3.6 months, the median duration of response was 9.9 months, and the median OS was 7.4 months. The most common toxicities were neutropenia (68%), anaemia (44%), and thrombocytopenia (37%).

Comment: It is unusual for very early studies to be reviewed in Melanoma Research Reviews but there are three reasons why this particular study is of particular interest. Firstly, the agent of interest is a DNA damage repair (DDR) inhibitor. This class of agent in general have not previously attracted interest in melanoma. Secondly, the patients responding in this phase 1 trial were the hardest patients to treat. All were immune checkpoint inhibitor resistant and included mucosal melanoma that have low response rates to most treatments. The third reason is the possible mechanism of action. The expression of PD-L1 appeared to be a possible biomarker which raises the question whether the treatment was due to immune responses. If DNA is not repaired, it might be seen as a neoantigen by the immune system. PD-L1 is however, attracting interest not only as a ligand for PD-1 but in its ability to enter the nucleus and upregulate innate death pathways. Evaluation of this DDR inhibitor is at an early stage but certainly worth keeping an eye on.

Reference: Clin Cancer Res 2021 Sep 1;27(17):4700-4709
Abstract

Phase I/II trial of a long peptide vaccine (LPV7) plus toll-like receptor (TLR) agonists with or without incomplete Freund's adjuvant (IFA) for resected high-risk melanoma

Authors: Patel SP, et al

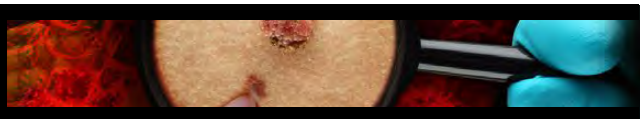
Summary: This clinical trial evaluated safety and immunogenicity of a novel long peptide vaccine in combinations of IFA and agonists for TLR3 and TLR7/8. Participants (n =50) with resected stage IIB-IV melanoma were vaccinated with seven LPVs from tyrosinase, gp100, MAGE-A1, MAGE-A10, and NY-ESO-1, each containing a known minimal epitope (MEP) for CD8+ T cells, plus a tetanus helper peptide (Tet). Patients were enrolled to one of seven adjuvant combinations. Vaccines were administered at weeks 1, 2, 3, 6, 9, 12. The authors reported CD8+ T cell immune response rate (IRR) to MEPs was 18%, less than in prior studies using MEP vaccines in IFA. In addition, the CD8+ T cell IRR trended higher for IFA-containing adjuvants (24%) than adjuvants containing only TLR agonists (6%). Overall T cell IRR to full-length LPV7 was 30%; CD4+ T cell IRR to Tet was 40%, and serum Ab IRR to LPV7 was 84%. These IRRs also trended higher for IFA-containing adjuvants (36% vs 18%, 48% vs 24%, and 97% vs 60%, respectively). There was one dose-limiting grade 3 toxicity (injection site reaction). All other treatment-related adverse events were grades 1-2.

Comment: *Do melanoma peptide vaccines work in a multi-institutional setting?*

This was an adjuvant study on 50 patients initiated by Craig Singluff, one of the most experienced peptide vaccine researchers. The patients were mainly resected stage III melanoma patients treated at two institutions: University of Virginia (31 patients) and the MD Anderson Cancer Center (19 patients). The aim was to assess the safety and immunogenicity of seven long peptides plus IFA, the TLR3 agonist polyICLC, and/or a TLR7/8 agonist resiquimod in seven different adjuvant combinations, using an adaptive study design. The long peptides represented portions of melanocytic differentiation antigens and cancer-testis antigens, each 29–31 amino acids long, and each incorporating a defined MEP for CD8 T cells. The central hypothesis was that vaccination with the long peptide vaccine (LPV7) would induce stronger T cell responses to the MEPs than observed in prior vaccines with MEPs themselves.

Without going into the detailed results, the outcomes were very disappointing for the investigators in that immune responses were no better than their previous studies with short peptides. It appears the main problem was the lack of any responses in the MD Anderson patients even though all the assays were carried out by Dr Slingluff in Virginia. They conclude that the study provides direction toward optimised cancer vaccine approaches by demonstrating safety and immunogenicity of seven new long peptides and the safety and immunogenicity of vaccination with IFA+polyICLC. The role of same-site vaccination in the outcome they considered deserved further investigation.

Reference: J Immunother Cancer 2021 Aug;9(8):e003220
Abstract



The association between citrus consumption and melanoma risk in the UK Biobank

Authors: Marley AR, et al

Summary: This prospective, population-based cohort study explored the association between citrus consumption and melanoma risk among 1,592 cases and 197,372 controls from the UK Biobank. Citrus consumption data were collected via questionnaires. After adjusting for potential confounders, participants in the highest category of total citrus intake (> 2 servings per day) had a significantly increased risk of melanoma (OR 1·63) relative to those with no consumption. It was also noted fair- or very fair-skinned participants with high citrus consumption had an even greater melanoma risk (OR 1·75).

Comment: *Does that orange drink in the morning really increase the incidence of melanoma?*

The basis for this study was the increasing incidence of melanoma in many countries and the question of whether dietary factors may be contributing to this. They review the reason for considering citrus consumption as follows "Several melanoma risk factors have been established, including exposure to ultraviolet (UV) radiation from the sun; having fair skin, fair hair, light-coloured eyes or the inability to tan, the use of solariums or sunlamps; and a history of sunburn during adolescence.

Psoralen, a type of furocoumarin used in photochemotherapy using oral psoralen and UVA radiation, is also known to be photocarcinogenic. Naturally occurring in nature as part of a plant's natural defence against pathogens, psoralens are abundantly found in citrus products, leading to the hypothesis that citrus consumption may increase melanoma risk due to psoralen photocarcinogenicity."

They conclude "our current analysis, based on a large, prospective, population-based cohort, found that high citrus consumption was associated with a significantly increased risk of melanoma. These findings support previous evidence of the photosensitivity and photocarcinogenicity of psoralens and support the hypothesis that high consumption of psoralen-rich foods may increase melanoma risk. Although this is biologically plausible, further investigation is needed to confirm the findings, particularly those that support potential effect modification by skin colour. Further investigation and confirmation of these findings could lead to updated sun exposure guidance and improved melanoma risk-reduction strategies."

Reference: Br J Dermatol 2021 Aug;185(2):353-362
Abstract

Real-world outcomes of melanoma surveillance using the MoleMap NZ telemedicine platform

Authors: Greenwald E, et al

Summary: This real-world study assessed the effectiveness of MoleMap NZ as a melanoma early detection program. The community-based teledermoscopy program uses expert review of total body photography and close-up and dermoscopic images of skin lesions that are suspicious for malignancy. The investigators reviewed 2,108 melanocytic lesions recommended for biopsy/excision by MoleMap NZ dermoscopists between January 2015 and December 2016. Pathologic diagnoses were available for 1,571 lesions. Of these, 1,303 (83%) lesions were benign and 260 (17%) lesions were diagnosed as melanoma, for a melanoma-specific benign:malignant ratio of 5.0:1. The number needed to biopsy (NNB) to obtain 1 melanoma was 6. Among melanomas with available tumour thickness data (n = 137), 92% were <0.8 mm (range in situ to 3.1 mm), with in situ melanomas comprising 74%.

Comment: *Are face to face consultations needed to diagnose primary melanoma?*

Teledermatology, the delivery of dermatologic care through information and communication technology, uses non-invasive imaging techniques to provide remote specialist dermatology services either to other health care professionals or to patients directly.

Patients referred (or self-referred) to MoleMap NZ attend an in-person visit at 1 of 44 clinics in New Zealand. A trained and certified nurse melanographer reviews the patient's history, takes total body photographs, performs a total body skin examination with dermoscopy, and takes clinical and dermoscopic images of individual nevi that meet prespecified criteria. The diagnosing dermoscopist reviews the images and provides management recommendations for any concerning lesions. The patient's primary provider (e.g., primary care physician, dermatologist, or surgeon) obtains all recommended biopsy specimens.

"While a comparison between the performance of MoleMap NZ and in-person visits with a dermatologist or other health care provider was not a studied outcome of this paper, the number of lesions excised per melanoma (NNB) estimates are lower than the NNB published for practitioners in Australia (NNB 23-30), The estimated melanoma-specific benign:malignant ratio for MoleMap NZ teledermatologists was 5.0:1. This is comparable to published benign:malignant ratios of in-person visits to pigmented lesion clinics, which range from 4.3:1 to 5.4:1."

Limitations-25% of patients were excluded because of missing pathologic diagnoses; Tumour thickness data were available for 53% of the melanomas, so these data may not accurately describe the overall tumour thickness data for the MoleMap NZ screening program. They conclude this real-world study of MoleMap NZ, a community-based teledermoscopy program, suggests that it has the potential to increase patients' access to specialist expertise via telemedicine. Additional studies are needed to more accurately define its efficacy. *Well - interesting results!*

Reference: J Am Acad Dermatol 2021 Sep;85(3):596-603
Abstract