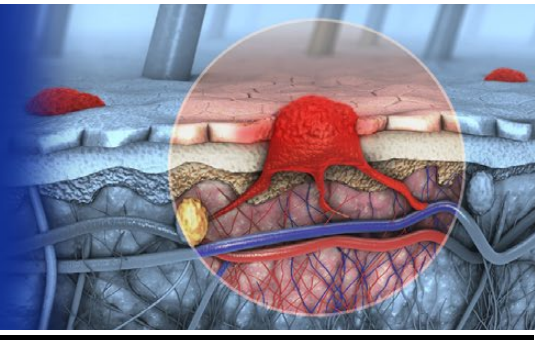
Melanoma Practice Review™



Making Education Easy

Issue 11 - 2022

In this issue:

Abbreviations used in this issue:

ct = circulating tumour; **CTCL** = cutaneous T-cell lymphoma; **MBS** = Medicare Benefits Schedule; **RT** = radiation therapy.

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Welcome to the 11th issue of Melanoma Practice Review.

This Review covers news and issues relevant to clinical practice in melanoma. It will bring you the latest updates, both locally and from around the globe, in relation to topics such as new and updated treatment guidelines, changes to medicines reimbursement and licensing, educational, professional body news and more. And finally, on the back cover you will find our COVID-19 resources, and a summary of upcoming local and international educational opportunities including workshops, webinars and conferences.

We hope you enjoy this new Research Review publication and look forward to hearing your comments and feedback.

Kind Regards,

Dr Janette Tenne

Editor

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Clinical Practice

Systemic therapy for melanoma: ASCO guideline rapid recommendation update

A rapid update to the ASCO guideline on systemic therapy for melanoma adds a new strong recommendation to offer tebentafusp to patients with previously untreated HLA-A*02:01–positive metastatic uveal melanoma. Tebentafusp consists of an affinity-enhanced T-cell receptor fused to an anti-CD3 effector that recruits T cells to target cells expressing the target antigen, glycoprotein 100. For all other patients with uveal melanoma, there is no recommendation for or against any specific systemic therapy, and clinical trial enrolment should be considered where possible.

The update follows the US Food and Drug Administration (FDA) approval of tebentafusp for patients with previously untreated HLA-A*02:01–positive metastatic uveal melanoma. The drug was approved in Australia in June.

The recommendation is based on the significant 1-year overall survival benefit observed with tebentafusp compared with standard therapy (pembrolizumab, ipilimumab, or dacarbazine) in the phase 3 IMCgp100-202 trial (73% vs 59%, respectively). The tebentafusp group also had a statistically significant increase in 6-month progression-free survival compared with standard therapy (31% vs 19%, respectively).

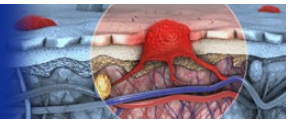
Although the frequency of grade 3 and 4 adverse events was 2.6-fold higher with tebentafusp, toxicity became more manageable over time, with only 2% of patients discontinuing due to adverse events. The higher disease control rate with tebentafusp compared with standard therapy may be responsible for the improved progression-free survival and overall survival, according to the authors, despite the low objective response rate (9% vs 5%, respectively). Additional studies are required to understand the relationship between clinical benefit and tumour response with tebentafusp or similar agents in advanced uveal melanoma.

J Clin Oncol. 2022;40(21):2375-7

The European Society of Gynaecological Oncology, the International Society for the Study of Vulvovaginal Disease, the European College for the Study of Vulval Disease and the European Federation for Colposcopy consensus statements on pre-invasive vulvar lesions

This joint consensus statement aims to improve the quality of care for patients with vulvar squamous intraepithelial neoplasia, vulvar Paget disease in situ, and melanoma in situ. An excisional procedure must always be adopted for differentiated vulvar intraepithelial neoplasia, while both excisional and ablative procedures can be used for vulvar high-grade squamous intraepithelial lesions. Ablative procedures can be considered for anatomy and function preservation; to exclude malignancy, several biopsies should be taken before the procedure. For vulvar high-grade squamous intraepithelial lesions, imiquimod or cidofovir can be considered. Imiquimod for vulvar Paget disease showed promise in recent studies. A 2 cm margin is considered necessary in surgical approaches. A wide local excision with 1 cm free surgical margins is recommended for melanoma in situ. Women should be seen on a regular basis for clinical assessment, including biopsy of any suspicious areas after treatment of preinvasive vulvar lesions.

J Low Genit Tract Dis. 2022;26(3):229-44



Efficacy of radiotherapy combined with immune checkpoint inhibitors in patients with melanoma

This was a systematic review and meta-analysis assessing the efficacy of radiotherapy combined with immune checkpoint inhibitors in patients with melanoma. The review included 624 patients from 12 studies (mostly retrospective analyses). The authors found radiotherapy combined with immune checkpoint inhibitors had a higher overall response rate compared with immune checkpoint inhibitors alone (35.0% vs 20.4%), however, there was no overall survival advantage. There was no statistically significant difference between 6-month (P=0.13) and 12-month overall survival (P=0.69). There was no significant difference in progression-free survival at 6 months (P=0.08), but there was a significant difference at 12 months (P=0.005). It was noted there were no serious adverse effects with the combination. The authors concluded that more prospective studies are warranted.

Melanoma Res. 2022;32(2):71-8

Association of radiation therapy with risk of adverse events in patients receiving immunotherapy

Both radiotherapy and immunotherapy are cornerstones of cancer management. For many cancers multimodality treatment provides improved outcomes to sequential therapies, however little data is available on the use of immune checkpoint inhibitors sequentially with radiation therapy. This pooled analysis of trials in the US Food and Drug Administration database finds no increased rate of adverse events in patients who receive concurrent radiation therapy and immunotherapy. Analysis was based on patient-level data from 68 prospective trials including over 16 thousand patients with rates compared between patients who were administered an immune checkpoint inhibitor (atezolizumab, avelumab, cemiplimab, durvalumab, ipilimumab, nivolumab or pembrolizumab) sequentially within 90 days of radiotherapy (n=1,733) or immunotherapy without radiotherapy (n=13,956).

Exploratory analyses found that the frequency and severity of adverse events were comparable with immunotherapy, regardless of prior radiotherapy, with an average difference in adverse events of 1.2% (0% difference for neurologic adverse events; 8% difference for fatigue) and this finding was consistent in a propensity score-matched analysis. The authors concluded that there is no evidence of any safety concerns with the combination of radiotherapy and immunotherapy, with the caveat that the observation remains to be confirmed in a clinical trial.

JAMA Oncol. 2022;8(2):232-40

Hydrochlorothiazide: An update on a common drug which increases skin cancer in immunocompetent patients

This presentation from the Australasian College of Dermatologists 2022 Annual Scientific Meeting assessed hydrochlorothiazide use and skin cancer risk based on 17 studies investigating one or multiple skin cancers. Hydrochlorothiazide is a thiazide diuretic and first-line treatment for hypertension. All studies investigating squamous cell carcinoma (SCC) identified an increased risk as did six of eight studies in basal cell carcinoma (BCC). Fewer studies investigated melanoma; four studies showed an increased risk and two showed no change in melanoma risk. A study undertaken in Australia identified an increased risk in both SCC and melanoma. One study showed a decrease in melanoma and non-melanoma skin cancer risk. The authors concluded that risk of BCC or SCC continues to increase the longer a patient is on hydrochlorothiazide, but this dose-dependent relationship is not observed for melanoma.

Abstract

Associations of thiazide use with skin cancers

This systematic review and meta-analysis assessed the relationship between thiazide use and skin cancer risk based on 25 case-control or cohort studies of hydrochlorothiazide, bendroflumethiazide, and indapamide use that included nearly 18 million participants. Hydrochlorothiazide use was associated with an increased risk of melanoma (OR 1.11), non-melanoma skin cancer (NMSC; OR 1.16), and squamous cell carcinoma (OR 1.32), which was associated with high cumulative hydrochlorothiazide doses. Hydrochlorothiazide was associated with melanoma subtypes including superficial spreading (OR 1.18), nodular (OR 1.23), and lentigo maligna (OR 1.33) melanoma. Associations of hydrochlorothiazide with increased risk of NMSC and melanoma were only observed in non-Asian countries. There was no meaningful increased skin cancer risk associated with bendroflumethiazide or indapamide.

BMC Med. 2022;20(1):228

Cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life years for 29 cancer groups from 2010 to 2019

A systematic analysis for the Global Burden of Disease Study 2019 reports that in the nine-year period since the last iteration in 2010 there has been a significant increase in the global burden of malignant cancer. There has been an approximately 20% increase in incidence, morbidity and mortality of cancer, ranking second only to cardiovascular diseases for magnitude of burden across all three measures and well above other disease groups including maternal and neonatal disorders and respiratory infections.

Analysis included data from vital registration systems, cancer registries and verbal autopsy reports from 204 countries and territories. The total global incident cancer cases in 2019 was estimated to be 23.6 million, a 26.3% increase from 18.7 million in 2010. Cancer-related mortality was 10 million, a 20.9% increase from 8.29 million cancer deaths in 2010 and a 2% increase in the proportion of total deaths (17.7% from 15.7%). Cancer-related disability-adjusted life years (DALY; life years lost plus years lived with disability) in 2019 was estimated at 250 million, a 16% increase from 2010.

The cancers with the greatest contribution to DALY worldwide were lung (18.3%), colorectal (9.7%), stomach (8.9%), breast (8.2%) and liver (5.0%). The pattern of change over time was notably different by sociodemographic index. In more developed areas (higher sociodemographic index), whilst the overall burden of cancer increased, age standardised incidence remained the same and age standardised mortality fell, suggesting higher cancer incidence due to an aging population, with improving cancer outcomes. Areas of lower sociodemographic index demonstrated the largest increases in cancer incidence and mortality rates, suggestive of disparities in cancer prevention, screening and treatment. This is valuable information for policymakers and those interested in improving cancer outcomes around the world.

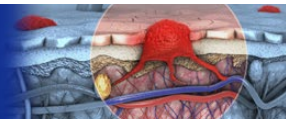
JAMA Oncol. 2022;8(3):420-44

Regulatory News

MBS news

The MBS has introduced seven new items (31377 to 31383) for the excisions of clinically suspected melanoma and amended six existing items (31371 to 31376) to ensure clarity regarding appropriate claiming for melanoma excision services.

Read more here



News in Brief

Defining the validity of skin self-examination as a screening test for the detection of suspicious pigmented lesions

Previous studies have demonstrated the value of patient-led surveillance after treatment of melanoma. This systematic review and meta-analysis pooled estimates of skin self-examination diagnostic accuracy for the detection of suspicious pigmented lesions based on three studies (all at risk of bias) that included 553 participants. For detecting suspicious pigmented lesions, skin self-examination had pooled sensitivity of 59%, pooled specificity of 82%, a summary diagnostic odds ratio of 5.88, and an AUC of 0.71. The findings of this study support the role of skin self-examination in the detection of suspicious pigmented lesions.

Dermatology. 2022;238:640-8

Circulating tumour DNA monitoring and early treatment for relapse: Views from patients with early-stage melanoma

Circulating tumour DNA (ctDNA) is a novel, blood-based biomarker being evaluated as a surveillance strategy after curative surgery in melanoma and other cancers. These authors conducted semi structured telephone interviews with 25 patients with early-stage melanoma to ascertain their views on the use of ctDNA monitoring and early treatment for relapse. The responses indicated that ctDNA monitoring would add service value, with respondents describing regular ctDNA monitoring during follow-up as more reassuring, more 'scientific' than skin checks and preferable to scans. It was noted that patients wanted to know when to expect test results in order to manage their anxiety, with a positive result seen as an opportunity to ensure treatment is received early.

Br J Cancer. 2022;126:1450-6

Experiences of resuming life after immunotherapy and associated survivorship care needs: A qualitative study among patients with metastatic melanoma

This qualitative study explored the survivorship care needs following immunotherapy in metastatic melanoma survivors. A focus group and interview including 20 patients revealed the need for psychosocial supportive care in addition to medical care for patients as well as their close relatives. The authors found that having reliable and easily accessible sources of information when facing uncertainty could help the patient's overall experience of treatment and resuming life after treatment. These findings highlight the need for a single point of contact and individual survivorship care plan to help the patient make an easier transition into mainstream life after successful treatment. Healthcare professionals should take these findings into account in daily practice.

Br J Dermatol. 2022;187(3):381-91

Rainbow pattern: a dermoscopic sign of invasive melanoma

The rainbow pattern is used to describe the bluish-reddish colouration that can be observed alongside various colours of the rainbow spectrum under polarised light dermoscopy. While initially thought to be specific to Kaposi sarcoma, it has now been reported to be observed in both benign and malignant skin lesions. These researchers evaluated the frequency and presentation of the rainbow pattern in 1100 dermoscopic images of different melanocytic and nonmelanocytic cutaneous neoplasms. Of 245 malignant melanomas and 855 non-malignant melanoma neoplasms, the rainbow pattern was evident in 9.4% and 5.1%, respectively. It was found that the rainbow feature in malignant melanomas was usually associated with other dermoscopic criteria of malignant melanoma and was located in a focal and eccentric area, compared with a typical diffuse, isolated presentation in non-malignant melanoma neoplasms.

Clin Exp Dermatol. 2022;47:529-33

Cutaneous T-cell lymphoma is associated with increased risk of lymphoma, melanoma, lung cancer, and bladder cancer

This systematic review included ten studies reporting on 12 cohorts of patients with cutaneous T-cell lymphoma (CTCL). Across these studies, 5.9-16.8% of patients developed second malignancies in 2.1-5.4 years from CTCL diagnosis, with males particularly affected. A meta-analysis revealed that the standardised incidence ratio was 2.2 for all malignancies, specifically 15.3 for Hodgkin lymphoma, 5.0 for non-Hodgkin lymphoma, 3.1 for melanoma, 1.7 for bladder cancer and 1.7 for lung cancer. A high index of suspicion is needed to avoid delays in the diagnosis and management of CTCL. The findings of this study emphasise the importance of a timely diagnosis in order to initiate screening for second malignancies associated with CTCL and minimise their morbidity burden.

J Am Acad Dermatol 2021;85:1418–28

COVID-19 Resources

The Australasian College of Dermatologists
Cancer Australia
European Academy of Dermatology and Venereology
American Academy of Dermatology
European Society of Medical Oncology
American Society of Clinical Oncology

Conferences, Workshops and CPD

Please click on the links below for upcoming local and international melanoma meetings, workshops and CPD.
The Australasian College of Dermatologists - Events
DermNet New Zealand - Conferences
MOGA - Events
COMS - Conferences and Meetings on Dermatology

Research Review Publications

Melanoma Research Review with Profs Michael Henderson and Peter Hersey

Skin Cancer Research Review with Dr David Simpson

Dermatology Research Review with Dr Warren Weightman and Clinical Prof Saxon D Smith

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