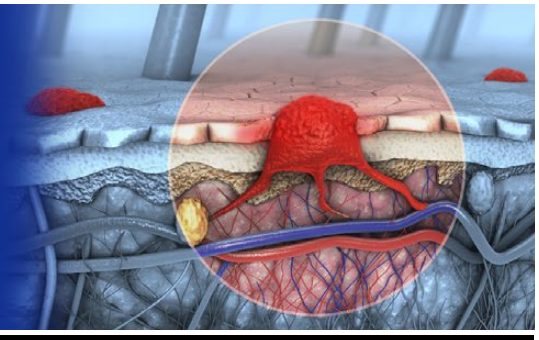
Melanoma Practice Review™



Making Education Easy

Issue 7 - 2021

In this issue:

Abbreviations used in this issue:

EXPeRT = European Cooperative Study Group for Pediatric Rare Tumors
PARTNER = Paediatric Rare Tumours Network - European Registry
TGA = Therapeutic Goods Administration

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Welcome to the 7th 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 Research Review publication and look forward to hearing your comments and feedback.

Kind Regards,

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Clinical Practice

Outcomes of COVID-19 in patients with cancer: Report from the National COVID Cohort Collaborative

The US NCATS' National COVID Cohort Collaborative (N3C) is a centralised database representing the largest multicentre cohort of COVID-19 cases and controls in the US. These authors evaluated characteristics of cancer patients within N3C and identified risk factors for mortality from COVID-19.

Among 4,382,085 patients from 50 US medical centres, a cohort of 398,579 patients aged ≥ 18 years with cancer were identified. The patients had a COVID-19–positive or COVID-19–negative diagnosis between January 1, 2020, and March 25, 2021.

Among the N3C cancer cohort, 63,413 (15.9%) were COVID-19–positive. The most common cancers were skin (13.8%), breast (13.7%), prostate (10.6%), haematologic (10.5%), and gastrointestinal cancers (10%).

All-cause mortality was significantly associated with COVID-19 positivity (HR 1.20; 95% CI 1.15 to 1.24) after adjusting for all other potential risk factors. Older age (>65 years), male gender, increasing comorbidities, haematologic cancer, and recent cytotoxic therapy were associated with higher mortality in COVID-19 patients with cancer. COVID-19–positive patients who received recent immunotherapies or targeted therapies did not have significantly higher risks of overall mortality from COVID-19.

J Clin Oncol. 2021;39(20):2232-46

Cutaneous melanoma in children and adolescents: The EXPeRT/PARTNER diagnostic and therapeutic recommendations

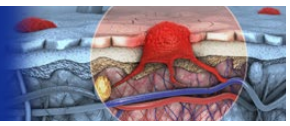
This article describes recommendations for the diagnosis and treatment of children and adolescents with cutaneous melanoma established by the European Cooperative Study Group for Pediatric Rare Tumors (EXPeRT) within the EU-funded project termed PARTNER (Paediatric Rare Tumours Network - European Registry).

Cutaneous melanoma is rare in children and consequently, there is a lack of evidence and clinical expertise. The diagnosis and treatment of paediatric melanoma is often difficult, and there are no standard therapies or paediatric guidelines. Accordingly, young patients are often managed as adults, but there is concern regarding their access to clinical trials and new therapies, which greatly improve survival outcomes for advanced melanoma.

The key recommendations are:

- Due to the rarity of the disease in children and the complexity of the approach to its treatment, discuss paediatric patients in multidisciplinary teams that include both paediatric oncologists and specialists in adult melanoma.
- Enrol patients in prospective trials (if available).
- Propose collection of data in national–international databases to patients and their caregivers.
- Develop an effective international collaboration between paediatric and adult melanoma groups in order to ease the transfer of potentially effective new therapeutics from the adult to the paediatric setting.

Pediatr Blood Cancer. 2021;68 Suppl 4:e28992



Demographics and trends in paediatric melanoma in the United States

Paediatric melanoma is relatively uncommon. This paper identified 1903 cases of paediatric melanoma using the US National Cancer Database, which captures approximately 70% of all cancer diagnoses in the US, from 2004 to 2016.

The mean age was 12.4 years. Most cases were in white females. The most common anatomic location was the trunk (31.1%). Comparing subtypes by age, there was an increased proportion of nodular and epithelioid and spindle cell tumours in pre-teen children and a higher percentage of superficial spreading tumours in teenagers. The most common stage was 0 or I (56.9%).

The number of melanoma cases over the 13-year period trended downward, while no significant trend in melanoma deaths was identified. The 5-year all-cause survival was greater than 90% for stages 0 to III (higher than in adults) and decreased to 34.4% for stage IV melanoma.

Pediatr Dermatol. 2021 Jul 11

Not all melanomas are created equal: a review and call for more research into nodular melanoma

This systematic review identified the common clinical and pathologic features of nodular melanoma. This subtype of melanoma often does not meet the classic ABCD criteria for diagnosing melanomas due to its lack of radial growth phase. Nodular melanoma accounts for 16% to 25.6% of melanoma cases and is associated with a higher case-fatality rate and a worse prognosis for thin melanomas when compared with other melanoma subtypes. Nodular melanoma is more common in older men and the head/neck region. Interestingly, this subtype is seen more commonly with the "non-nevus" melanoma pathway, and thicker nodular melanomas are seen in patients aged >50 years with a lower total body nevus count.

Nodular melanomas are more likely to demonstrate a higher Breslow thickness at diagnosis, increased mitotic rate, and less regression on histology. *NRAS* mutations have been identified more commonly in nodular melanoma compared with superficial spreading melanomas. Although greater Breslow depths with nodular melanoma are related to fatality, the nodular melanoma subtype itself is an independent predictor for decreased melanoma-specific survival and accounts for 44% of fatal melanomas. This suggests that nodular melanomas may possess a unique tumour biology that inherently makes them more aggressive than other subtypes. This observation is timely with the advent of gene-expression profiling (GEP) for melanoma. Dermatologists may want to consider utilizing GEP for nodular melanoma in conjunction with pathologic staging procedures. Having this knowledge may help provide tailored treatment strategies for nodular melanoma that could positively change survival outcomes.

Further studies are needed in primary nodular melanoma to evaluate the potential role of GEP in guiding therapeutic conversations. Furthermore, additional research is necessary to determine the molecular features leading to the aggressive nature of nodular melanoma and to optimize the early diagnosis and management of patients with nodular melanoma.

Br J Dermatol. 2021 Apr 16

Pulmonary metastatic melanoma: current state of diagnostic imaging and treatments

While malignant melanoma largely occurs in the skin, it has also been described in other organs, including the lung. Primary malignant melanoma of the lung accounts for 0.01% of all primary lung tumours. The pathophysiology of pulmonary malignant melanoma of the lung is not well understood and its management is not clearly defined. Guidelines for surveillance imaging in melanoma patients vary widely and are based mainly on expert consensus rather than evidence. These authors performed a literature search on current clinical practice in this setting with an emphasis on diagnostic imaging and therapeutic modalities to guide healthcare professionals in the management of patients with a high index of suspicion.

Primary malignant melanoma of the lung and metastatic melanoma to the thorax can have a wide range of radiographic presentations. CT, MRI and PET-CT scans are useful in staging and monitoring treatment responses. Chest CT is the least expensive option, and the most sensitive imaging technique for pulmonary malignancies in extracutaneous melanoma. The most common findings on chest CT are solitary or multiple pulmonary nodules.

When selecting the optimum therapeutic strategy, consider the clinical and histological features of the lesion, patient characteristics, and the body area involved. There have been substantial advances in treatment options including immunotherapy that inhibits the MAPK pathway and surgical metastasectomy with adjuvant radiotherapy.

The *BRAF* inhibitors vemurafenib and dabrafenib are approved for use in advanced melanoma. Trametinib, a highly potent *MEK* inhibitor has also shown activity in patients with *BRAF*-positive melanoma. Furthermore, some patients with metastatic melanoma have c-kit signalling mutations; however, limited efficacy has been shown with imatinib. Combined immunotherapy with the PD-1 inhibitor nivolumab and CTLA-4 inhibitor ipilimumab has demonstrated success in improving survival in malignant melanoma patients compared with either therapy alone.

Surgical metastasectomy is indicated for patients with limited pulmonary involvement usually indicative of an isolated and/or focal mass. Previous evidence in patients with complete resections of their pulmonary metastases have shown improved 5- and 10-year survival rates of 22% and 16%, respectively. Palliative radiotherapy is also important in the control of metastatic melanoma.

New treatment approaches, including additional molecular targets have also shown promise. Nanomicelles engineered to carry siRNA to target the NF-κB signalling pathway showed a significant decrease in metastatic pulmonary nodules in animal models. IL-33 has demonstrated modulation of pulmonary metastases in mice with primary breast cancer. Trials using therapeutic vaccines are also ongoing.

Melanoma Management. 8 Jul 2021

Evolving treatments and future therapeutic targets in desmoplastic melanoma

This was a review on the future therapy of desmoplastic melanoma, a rare and histopathologically distinct type of melanoma that is a subvariant of spindle cell melanoma.

Desmoplastic melanoma is most often caused by chronic sun exposure, and usually occurs in the elderly. The incidence of desmoplastic melanoma is described as less than 4% of cutaneous melanomas. Because desmoplastic melanoma is mostly dermal and usually amelanotic, early diagnosis is difficult. It may often be misdiagnosed as a number of benign and malignant nonmelanocytic spindle cell tumours.

According to the authors, the future of desmoplastic melanoma lies in better targeted therapies and greater penetration into the tumour leading to better responses to therapeutic agents. Current standard treatment options are surgical excision, sentinel lymph node biopsy, systemic chemotherapy and radiation therapy. Desmoplastic melanoma carries a particularly high mutation burden when compared to other melanomas and several genetic mutations associated with desmoplastic melanoma have shown it to be responsive to targeted therapies. Furthermore, whole exome sequencing has led to the discovery of additional genetic mutations that may provide future targets. New advancements in nanotechnology have delivered hope that there are better therapeutic delivery options for patients with desmoplastic melanoma that provide higher infiltration of the tumour by the drug. Finally, retrospective studies have demonstrated promising response rates to PD-L1 inhibitors in patients with advanced desmoplastic melanoma giving hope that checkpoint inhibitors may be important in future regimens for the treatment of advanced desmoplastic melanoma.

Melanoma Management. 17 Jun 2021

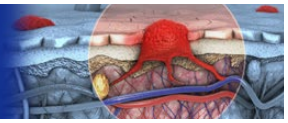
Regulatory News

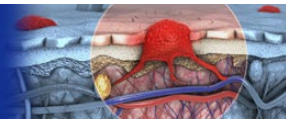
Neutrogena aerosol sunscreen recall - Possible presence of benzene

Johnson & Johnson Pacific Pty Ltd is recalling all batches of Neutrogena Ultra Sheer Body Mist Sunscreen Spray SPF 50+ (aerosol sunscreen), AUST L 202301, because benzene has been detected in some batches in Australia. All batches with an expiry date of 30th August 2023 or earlier should not be used.

Benzene is a human carcinogen. It is not an ingredient in this sunscreen but is sometimes used in the manufacturing processes. The TGA requires a limit of benzene below a concentration of 2 parts per million. Johnson & Johnson detected benzene at concentrations less than 3 ppm in two of 17 batches supplied in Australia.

Read more here





News in Brief

Melanoma in situ: A critical review and re-evaluation of current excision margin recommendations

This was a review of evidence for clearance margins for melanoma in situ. Most guidelines recommend 5-10 mm clinical margins. However, due to the high incidence of subclinical extension of melanoma in situ, particularly of the lentigo maligna subtype, wider margins are often required. The review identified 31 non-randomised studies and no randomised clinical trials. The studies were mostly retrospective reviews of single centres using Mohs micrographic surgery for lentigo maligna or staged excision for treatment of melanoma in situ on the head/neck. The studies showed a need for clinical margins > 5 mm and often > 10 mm, in contrast to current guidelines. However, it is not clear whether wider margins are necessary for all melanoma in situ subtypes.

Adv Ther. 2021;38(7):3506-30

Re-defining the role of surgery in the management of patients with oligometastatic stage IV melanoma in the era of effective systemic therapies

Although previously the mainstay of treatment, the role of surgery for asymptomatic oligometastatic stage IV melanoma has changed in the era of immunotherapies. Whether to treat with upfront surgery or immunotherapy is dependent on individual patient and tumour factors and needs to be discussed at specialist melanoma multidisciplinary meetings. Ultimately, prospective randomised trial evidence is required to resolve uncertainties.

Eur J Cancer. 2021;153:8-15

Oral manifestations in melanoma patients treated with target or immunomodulatory therapies

This review described the key oral adverse events occurring in melanoma patients treated with targeted therapies or immunotherapy. The main oral toxicities occurring with BRAF/MEK/TKI inhibitors are gingival hyperplasia, pigmentation disorders, and squamo-proliferative lesions, while the principal oral adverse events occurring with CTLA-4 or PD1 inhibitors are lichenoid reactions, immuno-bullous reactions, and xerostomia. Such events are often misdiagnosed and under-reported, with the oral cavity not routinely evaluated during clinical practice. However, the symptoms related to oral toxicity are important as they may represent the first sign of a severe systemic reaction, cause challenges with nutrition, and/or impact patients' quality of life. Examination of the oral cavity is recommended during the evaluation of oncology patients.

J Clin Med. 2021;10(6):1283

Impact of shave biopsy on diagnosis and management of cutaneous melanoma

This systematic review and meta-analysis looked at the impact of shave biopsy on melanoma staging, treatment recommendations, and prognosis. Among 14 articles from 2010 to 2020, a total of 3713 patients had melanoma diagnosed on shave biopsy. Meta-analysis showed a positive deep margin in 42.9% of shave biopsies. Tumours were restaged in 7.7% of patients after wide local excision, with 2.3% of patients requiring further treatment - either additional wide local excision and/or sentinel lymph node biopsy. There was no impact on local recurrence or survival among the studies analysed between shave biopsy and other biopsy modalities.

Ann Surg Oncol. 2021 Mar 29:1–9

COVID-19 Resources

The Australasian College of Dermatologists
Clinical Oncology Society of Australia
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
COSA - Events
MOGA - Events
COMS - Conferences and Meetings on Dermatology

Research Review Publications

Melanoma Research Review
with Professor Michael Henderson and Peter Hersey
https://tinyurl.com/y95oloy7

Skin Cancer Research Review
with Dr David Simpson
https://tinyurl.com/y9v4htzj

Dermatology Research Review
with Dr Warren Weightman and Clinical Assoc Prof Saxon D Smith
https://tinyurl.com/y7b6m4e3

Speaker Series – Merkel cell carcinoma masterclass
https://tinyurl.com/svj6ay4t

Study Review – Patient-reported outcomes with resected, high-risk melanoma
https://tinyurl.com/56v6mwu3

ACD 2021 Conference Review
https://tinyurl.com/k5zunmkw

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