Melanoma Research and Therapy Special Interest Group meeting

Highlights and recommendations

Background

The seventh meeting of the Melanoma Research and Therapy Special Interest Group was held via Zoom on Friday 27 November 2020. Topics were:

- Advocating for funded adjuvant treatment in New Zealand
- Melanoma research: an update from MASC Trials

Chaired by Dr Jody Jordan, the meeting was attended by 26 health professionals comprised of oncologists, researchers, nurses, surgeons, health promoters, general practitioners and industry representatives.

Acknowledgements

MelNet would like to thank the presenters and all those who took the time out of their busy schedules to attend this meeting.

Topic 1: Advocating for funded adjuvant treatment in New Zealand

Presentation from Jody Jordan (Medical Oncologist, Hawke's Bay District Health Board) on unfunded systemic therapies for melanoma.

Presentation summary

- Nine drugs have been approved since 2011 for non-resectable metastatic melanoma. Four of these have been approved in the adjuvant setting and two funded by Pharmac for advanced disease (Nivolumab and Pembrolizumab).
- ASCO and ESMO guidelines state:
    - BRAF wild type: Ipilimumab + Nivolumab, single agent PD-L1, clinical trial, isolated limb perfusion
    - BRAF mutated: BRAF/MEK inhibition (Vemurafenib + Cobiimetinib, Dabrafentib + Trametinib, Encorafenib + Binimetinib) or treatment as per BRAF wild type
- Advocating for PHARMAC funding for BRAF targeted treatment for metastatic BRAF+ melanoma
    - Approximately 50% of melanomas have a BRAF V600 mutation.
    - BRAF inhibition produces rapid tumour regression. The addition of MEK inhibition reduces resistance and decreases cutaneous toxicity compared with single-agent BRAF inhibition.
    - BRAF targeted therapy has a 60 – 80% response rate, rapid response, is generally well tolerated and given orally. However it is not funded, expensive, needs to be continued to get a response and only works in 50% of melanoma patients.
    - Vemurafenib + Cobiimetinib costs approximately $10k per month, with a cap of $52,000. Dabrafentib + Trametinib costs approximately $5k per month with no cap.
- Advocating for PHARMAC funding for adjuvant therapy for resected stage III melanoma
    - The EORTC 1325-MG/Keynote-054 Trial evaluated pembrolizumab versus placebo in 1019 patients with resected high-risk stage III melanoma. Results showed that pembrolizumab adjuvant therapy

provided a sustained and clinically meaningful improvement in relapse free survival consistently across subgroups.
    - Overall survival data is not yet mature.

Questions and discussion

- **Advocating for Pharmac funding for BRAF targeted treatment for metastatic BRAF+ melanoma**
    - Maurice Wilkins Centre are working with the Auckland Phase I Cancer Trials Unit to initiate a clinical trial for the use of VGF + BRAF. Pre-clinical models have been shown to work effectively in mutant and wild type melanoma. Articles describing these results have been submitted to journals for publication. This trial may be a way to deliver treatment to patients and generate interest from Government and PHARMAC. The main barrier is currently obtaining drug company buy in.
    - Submissions cannot be made for the whole class – a specific combination must be selected.
    - Equity for Maori and Pacific is the biggest consideration in drug funding decisions at present, so melanoma is unlikely to be a priority.
    - Rosalie Stephens has made an unsuccessful clinician submission to PHARMAC previously.
    - Given the above two points, the group agreed not to proceed with a submission at this point in time.
- **Advocating for PHARMAC funding for adjuvant therapy for resected stage III melanoma**
    - Submissions for Pembrolizumab and BRAF/MEK options were discussed:
        - Pembrolizumab is in the current funding structure. BRAF/MEK is not.
        - There may be more appetite for a tablet treatment (BRAF/MEK) than an infusion (Pembrolizumab).
        - Infusions are time consuming for already stretched oncology services.
        - Chronic toxicities are common with BRAF/MEK.
        - 2019 PTAK minutes stated a submission for PD-L1 was declined based on a lack of survival data. The company won't resubmit for another 1 – 2 years once survival data is available.
        - BRAF/MEK data shows an overall survival advantage.
    - The group agreed not to proceed with a PD-L1 submission until survival data is available.
    - The group expressed interest in proceeding with a submission for BRAF/MEK but agreed inequity across the country in BRAF testing may be a stumbling block and should be addressed first.
    - The group agreed BRAF testing should be part of the standard pathological assessment and included in the Melanoma Guidelines – it helps to characterize a patient's melanoma and inform discussion on self-funded treatment options.
    - The group agreed a national picture of BRAF testing is required.

Action points

1. Collate data on BRAF testing standards across the country and circulate to group by email (Jody Jordan)
2. Review Melanoma Guidelines in relation to BRAF testing and provide feedback where required (Jody Jordan)
3. Discuss next steps at next meeting.

Topic 2: Melanoma research: an update from MASC Trials

Part A: Presentation from Professor Mark Shackleton (Chair, MASC Trials) on recent updates, vision and future opportunities for MASC Trials.

Presentation summary

- MASC Trials is undergoing a dynamic period of change and opportunity:
    - Governance restructure in 2020.

    - A new CEO (Aileen Boyd) has been appointed.
    - The current CEO (Libby Paton) will conclude her role on 11 December 2020.
- The organisation has transitioned its academic partnership from University of Sydney to Monash University. This agreement will be in place until 2025.
- A formal process has been developed for new research ideas. These are initially reviewed through discipline specific advisory groups, then a Scientific Advisory Committee translates viable ideas into protocols in preparation to seek grant funding.
- The MASC Trials Annual Scientific Meeting is being held virtually on 3 December 2020 (7:00pm-9:30pm NZT). Research highlights and future direction will be covered.
- MASC Trials is keen to increase New Zealand engagement. Attendees were encouraged to join the organisation and discipline specific advisory groups (email hello@masc.org.au).

Part B: Presentation from Associate Professor David Gyorki (Trial Management Committee) on the Melanoma Margins Trial (MelMarTii).

Presentation summary

- Current national guidelines for excision margins for primary cutaneous melanoma vary worldwide (from 1cm to 3cm). There is little data to show the difference in disease free survival for small v wider excisions.
- MelMarTii is a Phase III randomized controlled trial designed to assess the difference in disease free survival for patients treated with 1cm excision margin compared to a 2cm margin for stage II primary melanoma. Secondary objectives are to determine the impact of the narrower excision on risk of long-term pain, improved quality of life, reduced side effects, economic impact on health services and society**.**
- The trial is being led out of Australia but run in multiple centres worldwide. The trial is currently open in Canada, Norfolk, Norwich, and multiple sites in the USA (through internal funding). Funding applications are at an advanced stage in the UK, USA, Ireland and the Netherlands.
- The Phase III trial aims to recruit 3000 patients worldwide over five years. Inclusion criteria is:
    - Older than 18 years at the time of consent
    - Diagnosed with stage II primary invasive cutaneous melanoma.
    - Breslow thickness greater than 2mm or 1 – 2 mm with ulceration. There is no maximum thickness.
    - Uninterrupted 2cm margin.
    - Life expectancy of at least 5 years from time of diagnosis.
- Participants are stratified by stage, age, gender and country. Disease free survival is the single end point.
- Follow up visits are recommended at 3, 6, 12, 18 and 24 months, then annually from years 3 – 10.
- New Zealand involvement is welcomed (contact Study Chair, Professor Michael Henderson, Michael.henderson@petermac.org). Waitemata DHB will be included as a site in future.

Part C: Presentation from Associate Professor Victoria Mar (Principal Investigator) on the SMARTI Trial.

Presentation summary

- Research on artificial intelligence for melanoma diagnosis is promising but has limitations:
    - It is conducted in an artificial environment; there is reduced accuracy of algorithms when tested in a real-world clinical setting
    - There is a lack of clinical context for dermatologists who are often only given an image of a lesion from which to make a diagnosis; accuracy improves with clinical information.

- The SMARTI trial aims to evaluate the performance of an artificial intelligence algorithm (SMARTI) compared to that of a teledermatologist assessment. It will also evaluate the impact of SMARTI on the appropriateness of skin cancer management decisions, the safety of SMARTI for skin cancer detection and the feasibility of implementing SMARTI for skin cancer detection and management prior to conducting a larger trial in primary care.
- The SMARTI convolutional neural network has been developed by MoleMap and Monash eResearch. It is trained to assess dermoscopic and macroscopic lesion images as benign, uncertain or malignant. Dermatologists also assess lesion images as benign, uncertain or malignant then assign a management decision to leave, manage (monitor), manage (biopsy/excision), treat (elective) and treat (essential non-surgical).
- During the lead-in phase 299 lesions were assessed. Provisional results show:
    - Sensitivity and specificity are in line with previous studies.
    - AI has moderate agreement with dermatologists' lesion classification.
    - AI appears to err on the side of caution.
    - AI is only as good as the lesions it has been trained on.
    - External factors (like sight) can influence decision making – AI can be helpful in providing an unbiased view.
- The pilot study is recruiting from seven Melbourne sites. A New Zealand site (led by Amanda Oakley) is included in the study. It will assess approximately 400 lesions. Recruitment is almost complete.
- One attendee enquired about effectiveness of AI with different skin tones. AI may not perform as well in tones it is not familiar with – it is important that it is tested and trained in the population it will be used in. The New Zealand study will include skin of colour.

Next meeting

- The group agreed hybrid virtual/in-person meetings work well: face-to-face provides an opportunity to network and Zoom helps maximise the number of people who can attend.
- The group agreed the frequency of meetings was about right.
- The next meeting will be held as part of the New Zealand Melanoma Summit in September 2021 and will provide in-person and virtual options.