Melanoma Research and Therapy Special Interest Group
15 March 2018 Meeting Highlights and Recommendations

Background

The Melanoma Research and Therapy Special Interest Group is a national and inclusive multidisciplinary group of melanoma health professionals and researchers seeking:

- To achieve consensus on current issues and to seek to implement solutions to these issues, and
- To improve upon current standards of care by promoting and facilitating research in melanoma.

The inaugural meeting of the group was held in December 2017. The second meeting was held at the Auckland International Airport Novotel on 15 March 2018. Topics were:

- Sentinel node data: The results of recent international trials and how their findings might be applied in New Zealand
- Tissue banking: What currently is being collected for melanoma and how collaboration and networking throughout New Zealand might be improved.

Introduction

Dr Rosalie Stephens, chair, welcomed all to the meeting and asked all present to introduce themselves. She asked that, in light of membership being open to all who are interested, attendees to please pass on invitations to others in future.

Following brief discussion about the options for names for the group, most agreed that the current name explains accurately the nature and purpose of the multidisciplinary group. In the context of discussion about the range of professionals who may be interested in the group, a question was raised as to the number of melanoma multidisciplinary groups throughout the country, highlighting the need for a stocktake.

Topic 1: Completion Lymphadenectomy or not…The evidence
Raj Patel, Breast, Melanoma and Endocrine Surgeon, Whangarei Hospital

In his presentation Mr Patel covered the following:

- MSLT-1/Background
- Current Evidence
- Summary
- Guidelines.

MSLT-1 Trial[1]

This trial compared outcomes of patients treated with wide local excision (WLE) and SLNB (followed by immediate completion lymph node dissection [CLND] for those with a positive sentinel node [SN]) with outcomes of patients treated with WLE alone and CLND upon the development of clinically apparent disease.

The results (published in 2014) showed that for patients with nodal disease and intermediate-thickness melanoma (defined as 1.2-3.5-mm Breslow depth), early treatment following positive SLNB was associated with improved 10-year distant disease-free survival and improved 10-year melanoma-specific survival.

Because of the significantly improved melanoma specific survival and disease-free survival a SNB became the standard of care in most centres worldwide for intermediate thickness melanomas.

The question remained, however, as to whether there is any survival benefit from completion lymph node dissection versus observation when the SNB is positive for melanoma micrometastasis.

Two more recent trials have provided more guidance on this:

- DeCOG-SLT (limited in terms of lower metastatic events rates, smaller sample size and smaller study numbers)
- MSLT-2 (larger, international and randomised study).

MSLT-2 Trial[2] Findings: Immediate completion lymph-node dissection increased the rate of regional disease control and provided prognostic information. However, it did not increase melanoma-specific survival among patients with melanoma and sentinel-node metastases.

The arguments for and against CLND therefore are as follows:

FOR CLND
Some (small %) disease free survival of early CLND-nodal disease control
Improved staging + prognosis (hence potential directing for adjuvant therapy)
Requirement for intensive follow up regimen in the observation group

AGAINST CLND
No melanoma specific or overall survival benefit
No distant metastasis free survival benefit (i.e., if someone is going to have distant metatastic disease, doing a CLND will not change this)
Morbidity from CLND

Recent National Comprehensive Cancer Network Guidelines for Melanoma (Version 2.2018)[3]:

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[1] Morton DL, et al. "Multicenter Selective Lymphadenectomy Trial". *The New England Journal of Medicine*. 2014. 370(7):599-609. http://www.nejm.org/doi/full/10.1056/NEJMoa1310460

2 Faries MB, et al. "Completion Dissection or Observations for Sentinel-Node Metastasis in Melanoma. N Engl J Med 2017; 376:2211-2222
DOI: 10.1056/NEJMoa1613210. http://www.nejm.org/doi/full/10.1056/NEJMoa1613210

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https://www.nccn.org/store/login/login.aspx?ReturnURL=https://www.nccn.org/professionals/physician_gls/pdf/melanoma_blocks.pdf

For Stage IIIA and Stage IIIB/C (sentinel node positive): Primary Treatment should be:

- Active nodal basin surveillance, or
- Complete lymph node dissection (CLND).

Q&A/Discussion Points:

- It cannot be assumed that identification of nodal disease will prevent further spread; it may be indicative of distant disease; "biology is king".
- The intense follow-up required in patients who do not have CLND is likely to increase the resources (radiology and surgical outpatients clinics) required for such follow-up.
- One possibility is having clinicians undertake follow-up with surgeon performed ultrasound, rather than patients having to be referred to radiology; however, this will nevertheless require increased resources.
- Some patients will still want to have CLND; it is hard to convince some to opt for observation.
- It's acknowledged that CLND can be a therapeutic process rather than a prognostic one.
- Potential side-effects of CLND are numbness and lymphodoema, with a potential significant reduced quality of life; like many operations, there exist complications/risks.
- The studies presented have changed surgical thinking; as a result, it is important that the Melanoma Standards recommendations be reviewed/changed.
- MelNet could raise this matter with the Ministry of Health by writing a letter to Richard Martin as Chair of the Melanoma Standards Working Party; this letter should summarise the current evidence.
- These discussions highlight the need for frequency of PET and CT scanning to be reviewed; currently there is little evidence to support a specific PET CT follow-up regimen.
- Observation of patients (without CLND) in itself has major implications for resources; surgical outpatient clinics including ultrasound every 6months may be difficult for patients, especially those who live in rural areas.
- The question was raised as to the absence of evidence to support follow-up at alternative intervals, e.g. months.
- One option might be for the Auckland regional MDM to undertake a sub-study of the Science Challenge Study.
- Might surveillance be undertaken by the patient's GP?

Key conclusions/recommendations:

- The Melanoma Standards relating to completion CLND with a positive SNB should be reviewed.
- MelNet to write a letter, as outlined above, highlighting that although CLND detects disease it does not offer a survival benefit.
- The issue of surveillance (PET CT in particular) should be discussed at the next meeting.

Topic 2: Tissue Banking

Introduction: Professor Mike Eccles
University of Otago

Mike Eccles introduced the topic of tissue banking by identifying the need for a national collection of melanoma tissue in New Zealand, especially as melanoma is a rapidly evolving field.

Currently melanoma tissues and data are proposed to be used in at least two studies that will include DHBs from both North and South islands. These include the National Science Challenge, HRC and Maurice Wilkins Centre projects. There is potentially an advantage in "sharing" analysis of a melanoma tissue with other researchers carrying out future unspecified research, enabling more opportunity to do better research and making the best use of available resources.

One option would be to establish an alliance between the Auckland Regional Tissue Bank and the Cancer Society Tissue Bank (Christchurch). Decisions would be required regarding platforms, standardized protocols and Governance.

Presentation: Dr Cherie Blenkiron, Senior Research Fellow, Department of Molecular Medicine and Pathology, University of Auckland
Science and Ethics Advisor for the Auckland Regional Tissue Bank

Cherie provided an overview of the Te Ira Kawai – The Auckland Regional Tissue Bank

- Includes various tumour types
- The tissue is collected from 3 DHBs, with each having its own ethics approval process
- The collection includes blood, frozen and archived (eg formalin-fixed paraffin-embedded) tissues, as well as (albeit less commonly) finger nails and so on.
- The consent form is generic
- There has been some difficulty in establishing standardisation of storage.

Issues identified by the Tissue Bank:

- There is variability in clinical genetic testing in the Auckland region; the testing is not systematically used, and the type of test used also varies from region to region.

Questions raised by Cherie and in discussion:

- Should there be one specific recommended genetic test (eg BRAF mutation) on metastatic melanomas as a standard practice in NZ? (Note, a comment from Mike – routine BRAF testing of stage III or IV melanoma is not the case, at least in the SDHB).
- Should clinical testing include a panel of driver gene mutations rather than BRAF alone?
- Should New Zealand use the same kind of testing as in Australia?

Possible needs identified in discussion:

- More nurse coordinators
- Capturing every stage III and IV patient as part of standards of care to be involved in clinical research
- A 'lofty goal' of requiring a blood test for analysis of circulating tumour DNA on every melanoma patient
- Increasing the sensitivity of detecting melanoma in circulating tumour DNA analysis
- Working with the Australian & NZ Melanoma Trials Group

Recommendations from discussion session:

Recommendation/vision proposed by Cris Print: That every stage III or stage IV melanoma patient in New Zealand be offered the opportunity to be involved in a clinical trial or translational research. This could be the driving force for establishing a national tissue bank/blood tests, etc.

Recommendations of the Queenstown Research meeting need to be revisited. These include the recommendation that an article be submitted to the New Zealand Medical Journal.

Others who could potentially be informed/involved include GPs (via NZMA CME meetings), GPs working with DHBs, nurses (via Kai Tiaki monthly journal), Dermatological Nurses Association, National Cancer Co-ordinators in Wellington.

There is a need to work with consumers/patient representatives, e.g., Paul O'Neil who spoke at the Queenstown meeting. Melanoma New Zealand could be the mechanism for communication and involvement of patients.

Possible topics for the next meeting:

Follow-up and surveillance of patients
Use of PET
MDMs and equity of access
BRAF testing
Clinical trial update
Updates of research
Melanoma high risk assessment tool

Recommendations from the next meeting could be reported to the Melanoma Summit.

Cris Print announced two fellowships with the University of Auckland. The MelNet e-newsletter may be one avenue for publicising.

Possible dates for next meeting: Could be the day before the Melanoma Summit (Thursday 1 November) or a Friday in October (which may be more suitable for clinicians than a Thursday).