Melanoma Research and Therapy Special Interest Group meeting

Highlights and recommendations

Background

The sixth meeting of the Melanoma Research and Therapy Special Interest Group was held via Zoom on Friday 26 June 2020. Topics were:

- National melanoma immunotherapy database
- PHARMAC Special Authority criteria: Temporary removal of specified dose regimen for nivolumab and pembrolizumab during COVID crisis
- Collaborative use of new genomic technologies to monitor melanoma

Chaired by Dr Jody Jordan, the meeting was attended by 36 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: National melanoma immunotherapy database

Part A: Presentation from Vanessa Wong (Research Fellow, Walter and Eliza Hall Institute of Medical Research (WEHI) and Medical Oncologist, Ballarat Health) on WEHI clinical registries and registry based randomised controlled trials.

Presentation summary

- WEHI have established prospective, comprehensive clinical registries across multiple tumour types. Patient data is collected at over 30 sites throughout Australia and internationally.
- WEHI partner with BioGrid for a user intuitive online data platform. Data is owned and controlled by local clinicians, and deidentified before being linked to the registry.
- Each registry has:
    - a clinician defined standard data set
    - comprehensive data collection and linkage – field are generally mandatory fields and multi-choice to increase the likelihood of obtaining complete data.
    - addressed ethics, privacy, security, ownership and authorship
    - an easy to use online platform and standardised look and feel
    - focuses on consecutive patient enrolment
    - allows for interpretation for real world data and has the ability to follow treatment received and patient outcomes.
- Registry based randomised controlled trials:
    - utilise data in the registry – currently aimed at improving the use of available therapies
    - can compare trial patients to individual arms of the trial as well as other patients in the registry
    - cost 10% of the usual trial cost, have a lower workload and only collect relevant information.

- Melanoma:
    - is a new tumour stream led by Miles Andrews and supported by research fellow Shehara Mendis and research nurse Tina Cavicchiolo.
    - will commence recruitment of 200 stage III and IV retrospective patients (2019/20) in the next couple of months. This is sponsored by pharma
    - Will commence prospective recruitment in 2021.
    - Will be able to look at data such as sequencing of treatment, variation of treatment across sites and toxicity management.

Part B: Presentation from Alexander Dunn, (Systemic Anti-Cancer Therapy Project Manager, Cancer Control Agency) on the Systemic Anti-Cancer Therapy Project.

Presentation summary

- The Systemic Anti-Cancer Therapy Project (SACT NZ) will establish a national collection of treatment data for all adult public and private SACT treatments, and develop associated analysis and reporting capability in order to drive consistency, quality and equity in SACT treatment and support resource planning.
- **Stage 1: Agreeing standardised terminology and naming conventions for regimens currently in use**
    - to be done across each of 15 tumour streams.
    - Where possible, these will align with eviQ.
    - Tranche 1 (bowel, lung, prostate, breast and supportive care medications) is due to be completed in October 2020.
    - Tranche 2 is planned to commence in early 2021.
    - NZ Universal List of Medicines (NZULM) has been identified as the best place to host regimen definitions. SACT NZ and NZULM are developing the infrastructure and processes to create, maintain, validate and present all adult SACT regimens.
- **Stage 2: Development of detailed reporting requirements to track equity, quality, consistency and efficiency**
- **Stage 3: Design and build of the SACT IT system**
    - Automated extraction and sending of data from oncology systems to the Cancer Control Agency
    - Automated data validation for 'bad data' to be fixed
    - Linking of data with other national data such as diagnostics, surgery, radiation and outcomes to form a whole view of the patient journey
    - Flexible 'self service' dashboarding portals for clinicians and stakeholders
- Stage 4: BAU
    - Regular data quality reporting to clinicians to ensure it is at a high level and makes sense
    - Maintenance of regimen libraries
    - Flexible and evolving reports to meet changing information needs
- Other Cancer Control Agency projects:
    - Structured pathology and radiology reporting
    - Capture and collection of patient reported outcomes and experiences
    - Capture of MDM data
    - Radiation oncology treatment collection

Questions and discussion

- **SACT's engagement and buy in from DHBs**: Alex advised this project is being driven by DHBs through medical oncology working groups, not imposed from the top down.
- **Patient control over data in WEHI registry**: Peter Gibbs advised that the project has a 'waiver of consent' as data is deidentified. The opt out rate for data that does require consent is low.
- **Data entry:** Peter advised that WEHI data is entered by data officers and medical students based at hospitals. It is also extracted manually. WEHI is moving to a remote data entry system which can be accessed offsite

from a hospital. It was noted that it would be expensive to do this type of data entry in NZ without significant funding. SACT would be automated, pulling data from existing systems so would not require manual data entry.

- **WEHI data coverage:** Peter advised they focus on collection from consecutive patients. They have a breadth of patients across public/private/urban/regional sites.
- **WEHI funding:** Peter advised that funding is an ongoing challenge. Pharma funding is the biggest resource, however they have no control over the data collected or how it is used. Funding also sources from philanthropy and grants. Where funding isn't available, clinicians support data entry at no cost.
- **WEHI data misuse:** Each registry has a management committee who are required to approve each data query to ensure it is relevant and appropriate, as well as identify opportunities for collaboration. No hospitals or clinicians are named in data reports.
- **Capture of response, tolerability and toxicity data:** Peter advised that WEHI captures relevant data that informs clinician decision making. It is difficult to capture adverse event data, however the reason why treatment finishes or is changed is recorded. Response rate is not captured but clinician assessed response rate is captured which gives an indication of efficacy.
- **Use of MOSAIQ in NZ:** Participants discussed the use of MOSAIQ in NZ for alignment of data. It was noted that the use of MOSAIQ is not compulsory. SACT would be solution agnostic so would not exclude those DHBs who do not use the MOSAIQ system.
- **Pilot project: Retrospective analysis of 100 melanoma patients**
    - WEHI are happy for NZ to participate in the melanoma registry (free of charge). Cost of data entry would need to be covered by New Zealand.
    - SACT is a long-term project which will leverage electronic data entered into frontline clinical systems. As part of the development process, they will look at six years retrospective data across Dunedin, Christchurch and Mid Central sites (at a minimum) to assess completeness, accuracy and gaps. Participants noted that data from Auckland would be required to ensure representation across the country.
    - There was some appetite to undertake a parallel process for a set of 100 retrospective patients. Funding for this has been provisionally agreed by PHARMA. This type of retrospective analysis would require participation from a range of cancer centres across NZ and would iron out kinks in data collection, give outcome data/treatments over time and would feed into the SACT project once up and running.

Action points

- Meeting Chair to determine individual interest in participating in retrospective analysis
- Meeting Chair to set up 'retrospective working group' to discuss next steps and define scope
- Meeting Chair to continue dialogue with SACT project

Topic 2: PHARMAC Special Authority Criteria

The group discussed PHARMAC's temporary removal of specified dose regimen for nivolumab and pembrolizumab during COVID crisis.

Feedback on changes included:

- Didn't switch infusion schedule
- Started 3 weekly then switched to 6 weekly.
- Had a mix of patients who stayed on 3 weekly and others who changed to 6 weekly
- Utilised 6 weekly
- Appreciated the relaxed rules around assessing response and scanning.

Overall there was no significant enthusiasm to lobby for the new infusion schedule to remain.

Topic 3: Collaborative use of new genomic technologies to monitor melanoma

Presentation from Cris Print (Professor, University of Auckland) on new genomic technologies to monitor melanoma.

Presentation summary

- Circulating tumour DNA (ctDNA) is getting close to the standard of care in diagnosis, tumour evolution and ability to predict a response to treatment.
- Metastatic melanoma is well suited to ctDNA marker technologies due to the high frequency of mutations in a small number of defined genes and the frequent unavailability of primary tumour tissue samples for genomic analysis.
- Studies are starting to demonstrate validity of ctDNA markers in melanoma, but clinical utility has not yet been demonstrated, particularly in New Zealand.
- Potential clinical utility is wide ranging:
    - a more holistic assessment of therapeutic response
    - prognostic information during immunotherapy
    - indication of relapse or residual disease
    - identification of appropriate therapy in stage III patients
    - as a supplementary disease marker in rural patients unable to easily travel for CT scans
- A pilot study of stage III and stage IV melanoma patients in Auckland is nearing completion. For the patients receiving immune checkpoint inhibitor therapy, mutations in multiple genes were detected in approximately one third of patients. In several cases, the original biopsy identified a range of genes none of which were targetable, however blood did. In post-surgical patients, detectable ctDNA appears to drop after surgery but slower than expected.
- Three technologies to detect ctDNA in melanoma have been assessed (ddPCR, Mass Spectroscopy and DNA sequencing). ddPCR was found to be the most reliable and sensitive. Use of a melanoma specific Ampliseq HD sequencing panel allows for a wider range of melanoma mutations to be covered.
- The ability to identify ctDNA mutations at clinics in remote locations (e.g. marae) may help to address rural cancer care inequities. In a sample of 15 patients, samples collected in “cell-save” preservative tubes one week prior to analysis showed no significant difference in the number of ctDNA molecules detected per ml of plasma compared with freshly collected samples.
- Currently looking to set up the next generational test in Auckland – a 500 gene cancer panel that can measure tumour mutational burden of ctDNA at an affordable cost.

Questions and discussion

Participants discussed potential clinical utility in New Zealand. Key points included:

- Reduction of inequity - Research to determine if Maori have the same mutation profile as non-Maori hasn’t been undertaken but would assume a bias would be found. Blood tests instead of scans would have positive effects.
- Adjuvant therapy and treatment in stage III and IV resected patients – the time point at when to give systemic therapy.
- Mixed response to treatment
- Treatment beyond progression and a new site of disease
- Potential to collaborate with database project and Maurice Wilkins Centre clonal diversity project.

Next meeting

- Participants agreed the next meeting should be held at the end of November via Zoom (for accessibility).
- Friday is a good day and a start time of 10 am works well.
- Advanced notice is required to organise schedules.