MelNet

Linking professionals in melanoma in New Zealand

Melanoma Research and Therapy Special Interest Group meeting

Highlights and recommendations

Background

The fifth meeting of the Melanoma Research and Therapy Special Interest Group was held the Health Promotion Agency Auckland Office on Friday 8 November 2019. Topics were:

- PHARMAC changes to funding criteria for advanced melanoma
- National immune checkpoint inhibitor database – a 'strawman' concept

The meeting was co-chaired by Professor Mike Eccles and Dr Jody Jordan.

Summary of actions and recommendations

The following recommendations and actions were made:

1. MelNet to write a formal letter to PHARMAC expressing their support for funding criteria changes.
2. Investigate the database process undertaken for pancreatic cancer.
3. Liaise with the Cancer Agency to determine their intentions around data capture, if an immunotherapy database would be part of their remit and resources available to support development and maintenance.
4. Liaise with Breast Cancer Registry to determine legalities around data being stored offshore.
5. Explore the possibility of partnering with an Australian database and costs associated with BioGrid.
6. Investigate MSD funding grants process.
7. Investigate MASC Trials funding availability.
8. MelNet to coordinate the advancement of the above recommendations.

Acknowledgements

MelNet would like to thank the three presenters and all those who took the time out of their busy schedules to attend this meeting. We would also like to acknowledge MSD NZ Ltd and the Health Promotion Agency for their support of this meeting and their ongoing support of MelNet.

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hpa health promotion agency
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Topic 1: PHARMAC changes to funding criteria for advanced melanoma

Part A: Presentation from Danae Staples-Moon (Senior Therapeutic Group Manager, PHARMAC) on the proposed amendments to funding criteria for pembrolizumab and nivolumab in the treatment of advanced melanoma.

Proposed amendments:

1. Allow medical practitioners to make Special Authority applications (both initial and renewal) on the recommendation of a medical oncologist;
2. Remove the specified number of cycles in an approval period;
3. Exclude the treatment of new patients with uveal melanoma;
4. Facilitate more appropriate clinical management of patients with evaluable but not radiologically measurable disease;
5. Allow flexibility in the dose administration schedule; and
6. Allow retreatment for patients who had previously stopped funded treatment for reasons other than disease progression or toxicity.

These amendments are expected to be in place by 1 December 2019. A notification email will be sent out to MelNet members once they are in place.

Discussion points

- These are positive changes that would be welcomed by practitioners and would result in cost savings.
- They enable clinicians to develop individualised and flexible treatment plans at their discretion and in consultation with their patient.
- There are challenges with reassessment and accessing imaging. PHARMAC noted timeframes for reassessment had been removed to allow an extra four weeks for imaging. There remains an expectation that patients are monitored and assessed as to whether treatment is still appropriate.

Part B: Presentation from Olivia Fenwick, Senior Medical Science Liaison Oncology, MSD on the pharmacokinetics behind the change to the dose administration schedule (change 5).

- The new pembrolizumab 400 mg Q6W (every 6 weeks) dosing schedule provides patients and clinicians with an additional option to the currently available dose of 200 mg Q3W (every 3 weeks). It received MedSafe approval in July 2019.
- The new regimen abdicates decision-making to the treating physician regarding:
  - if new schedule is used at all
  - if so, which patients and which timing
  - how (ie: 3-weekly check-ins via phone or F2F with registrar, CNS, NP and 6-weekly consult with medical oncology)
  - flexibiity to revert to Q3W for patients where increased monitoring desired ie: suspected pseudoprogression, toxicity
- Pharmacokinetic modeling and simulation analyses show:
  - Exposures with the 400mg Q6W dose are similar to those for the approved dose of 200 mg Q3W.
  - Trough concentrations (C_{min}) in majority of patients are within the range of C_{min} with the lowest clinically tested (and approved) dose (2 mg/kg Q3W).
  - Peak concentrations (C_{max}) are well below those observed with the highest clinically tested dose (10 mg/kg Q2W) in the pembrolizumab programme.
  - The predicted mean overall survival was similar between 400 mg Q6W and 2 mg/kg or 200 mg Q3W in melanoma and NSCLC based on E-R modeling

- The AE and efficacy profile of a higher dose of pembrolizumab (10 mg/kg) was consistent with the 2 mg/kg dose.
- A physiologically based pharmacokinetic (PBPK) model-based prediction of pembrolizumab tumor target engagement (TE) showed that at 400 mg Q6W the tumor TE profile is similar to that for 2 mg/kg or 200 mg Q3W, with all doses maintaining TE above 90% throughout the dosing interval.
- Overall, the 400 mg Q6W dosing regimen is expected to have a similar benefit–risk profile as the currently approved dosing regimens of pembrolizumab

Discussion points

- One participant asked how to respond to a patient who asked if Q6W will be as effective. The response provided stated that analysis of clinical trial data is required before this question could be answered with certainty. Data is being collected from UK and Europe from patients who have been undergoing the new regimen from March 2019. This data will provide a retrospective analysis on patient safety and efficacy.
- In New Zealand the new regimen would will useful for those in rural areas as it reduces chair time and visits to clinic.
- Clinicians in attendance agreed that Q3W was a safe starting point as it allowed close toxicity monitoring. Transfer to Q6W could be made after there was a level of confidence in toxicity and response.
- One attendee questioned how this was addressed in the Standards of Service Provision for Melanoma Patients in New Zealand. At this point there is no international or national data to support a recommendation, therefore, it is left open to clinician discretion.

Actions and recommendations

1. MelNet to write a formal letter to PHARMAC expressing their support for the changes.

Topic 2: National immune checkpoint inhibitor database

Jody Jordan briefed the group on immunotherapy treatment in New Zealand and unanswered questions. She noted that at the last Special Interest Group meeting (14 June 2019) a recommendation had been made to liaise with Melanoma Institute of Australia to understand more about their clinical database.

Information was shared on current local audits.

1. Christchurch
    - IRB-approved study passively collecting data on all patients in order to aggregate clinical data to correlate to the laboratory work. This is being conducted by a summer student.
    - Active blood collection of whole blood and plasma on pre-treatment, and trough dosing through the first several months with optional bloods at AEs. Part is banked, part is planned for analysis of anti-drug antibodies and cytokine panels.
2. Mid Central
    - Retrospective audit by registrar.
    - Hawkes Bay (subset): Excel spread sheet of prospective data entered by Oncology CNS.
3. Wellington
    - Excel database entered by two registrars.
4. Peter Mac
    - Comprehensive database which tracks information such as disease-free intervals, early diagnosis, survival outcomes, resist criteria, types of therapy, toxicity and palliative care.

- Laborious data entry process
- Moving to a new in-house database system and have invited NZ to join.

5. MIA
    - An in-house custom database that requires four data managers entering data from three hospitals.
6. Other
    - Annie Wong (Oncologist, CCDHB) shared the pancreatic cancer registry built in Excel which included information on demographics, tumour characteristics, toxicities, laboratory monitoring and impact on clinical management.
    - One attendee advised that Auckland University are developing a database for neuroendocrine patients. This philanthropically funded project will take three years and five staff.

It was noted that PHARMAC has no immediate plans to set up a data registry. To date they only collect data on treatment that has been dispensed. Nothing is collected on the level of response.

Discussion

- There is a national movement towards better data.
- A database across the immunotherapy spectrum would be useful, however melanoma is well defined and publicly funded so a useful place to start.
- There have been legislative challenges in the past about NZ data being stored offshore.
    - This is now permissible, with pancreatic cancer being used as an example.
    - If consented, approval is required through HDEC.
    - Breast cancer registry doesn't require consent
    - A BCC study didn't require consent for retrospective data but did for prospective data.
- Overall the group were enthusiastic about the concept but agreed simplicity was key.
- One participant raised a question about whether DHBs were able to share information about immune checkpoint inhibitor outcomes to allow data to be collected.
- Funding could be sought through Government or pharmaceutical company grants, however sustainability will need to be considered. One attendee suggested a levy on each drug administered similar to the levy added to prosthesis.

Actions and recommendations

2. Investigate the process undertaken for pancreatic cancer (Annie Wong)
3. Liaise with the Cancer Agency to determine their intentions, if a database like this would be part of their remit and resources available (MelNet)
4. Talk to Breast Cancer Registry to determine the legalities around data being stored offshore (Matthew Strother to identify contact)
5. Further investigate the possibility of partnering with Australia and costs associated with BioGrid (Annie Wong).
6. Investigate MSD funding grants process (Olivia Fenwick to advise Jody Jordan)
7. Investigate MASC Trials funding availability (Annie Wong)
8. Investigate DHB ability to share information about immune checkpoint inhibitor outcomes (MelNet)
9. MelNet to coordinate the advancement of the above recommendations, with the Special Interest Group being used as a forum to discuss and progress the project.