Australian Government
Medical Services Advisory Committee

STAKEHOLDER MEETING MINUTES - FINAL

SENTINEL LYMPH NODE BIOPSY FOR INTERMEDIATE THICKNESS AND THICK MELANOMA

Wednesday 7 November 2018

Attendees

Meeting attendees included members of the Medical Services Advisory Committee (MSAC); clinicians with experience and expertise in clinical oncology, pathology, dermatology and clinical genetics; representatives of the applicant; representatives from consumer organisations; and representatives from the Department of Health.

1. Meeting open – welcome and introduction

The MSAC Chair opened the meeting at 9:10 am.

The Chair thanked participants for attending and clarified that the stakeholder meeting was not an MSAC decision-making forum, but would inform MSAC's reconsideration of the issues raised by MSAC at its July 2018 consideration of Application 1485: sentinel lymph node biopsy (SLNB) for intermediate thickness and thick melanoma. MSAC's advice would then be considered by the Government.

The key objective of the meeting was to seek input from clinicians on whether it would be possible to:

- establish risk equivalence criteria (i.e. the SLNB result that equates to the same melanoma risk as for the patients in the recent trials of newly emerging adjuvant therapies) that would qualify a patient for access to adjuvant therapies
- be confident that this would form a reasonable basis for extrapolated evidence of predictive effect.

The Chair reminded participants that this was a confidential discussion. The outcomes of the meeting would be provided to all attendees for input before being published on the MSAC website. The Chair indicated that these minutes would not attribute any of the discussion to any identified individual.

Conflicts of interest

The Chair noted the conflicts of interest declared.

2. Background – recent MSAC consideration and key discussion points

At its July 2018 meeting, MSAC did not accept the rationale to have a fee increase for an SLNB-specific MBS item, compared to the current non-specific MBS items that this service is currently being claimed under, when there was insufficient basis provided to discern any

difference in patient health outcomes or clinical management as a consequence of using SLNB compared to not using it.

MSAC deferred its advice to request further clarification of the patient selection criteria for the emerging role of adjuvant treatment of melanoma and the role of SLNB in selecting patients for such treatment. MSAC considered that it would be helpful to:

- further discuss this application with the Oncology Clinical Committee from the MBS Review Taskforce
- seek input from the Medical Oncology Group of Australia (MOGA), the Royal College of Pathologists of Australasia (RCPA) and melanoma surgeons.

The Chair noted that SLNB is now being seen as a prerequisite for determining access by some patients to adjuvant therapies for melanoma. MSAC's decision on this issue has flow-on effects for the Pharmaceutical Benefits Advisory Committee consideration of these adjuvant therapies, making a coordinated approach essential.

3. Summary of discussion

Guideline recommendations for SLNB

Participants noted that the latest Cancer Council *Clinical practice guidelines for the diagnosis and management of melanoma* state that:

> Sentinel lymph node biopsy should be considered for all patients with melanoma greater than 1 mm in thickness and for patients with melanoma greater than 0.75 mm with other high risk pathological features to provide optimal staging and prognostic information and to maximise management options for patients who are node positive.

Therefore, the indication for this application should be broadened to all melanoma greater than 1 mm thick, and melanoma at least 0.8 mm thick in the presence of ulceration. Participants noted this was also consistent with international guidelines.

Participants noted that the AJCC staging system had also been updated in 2017 to state that, for a patient with this indication to be staged appropriately, they must have SLNB. Participants noted that the AJCC system is evidence based and draws on a database of more than 40,000 melanoma patients, around 20% of whom are Australian.

In relation to the definition of SLNB positivity and how samples are handled, participants noted that the Cancer Council guidelines provide detailed guidance on handling sentinel lymph nodes and provide commentary on how the pathologist should assess an SLNB and report its results. These guidelines refer to detection of involved lymph nodes using immunohistochemistry however some subjects (11%) in the MSLT-II trial were identified as SLNB positive using PCR (more sensitive). Participants noted there were no pathologists present at this stakeholder meeting, and the Department agreed to connect with this group to seek their input. In particular MSAC will need advice on the method (immunohistochemistry or PCR based) of assessment of lymph nodes and the definition of positive (for each method).

Access, equity and education issues

Participants noted the wide variation in access to SLNB across Australia. It was reported that around 45% of patients in New South Wales who are indicated for SLNB actually receive it, and only 18% of patients in Queensland. Access to appropriate surgeons and quality

lymphoscintigraphy are particularly difficult in rural and remote areas, although it was noted that an education program is being developed to upskill providers in lymphoscintigraphy. Participants considered that an education program was highly appropriate to ensure availability of relevant expertise, particularly if there is increased uptake of SLNB after the creation of a specific MBS item in the context of melanoma.

Participants noted that a previous barrier to access was that SLNB did not affect survival outcomes. The relevance of SLNB in clinical management has changed because a positive SLNB will now inform suitability for adjuvant therapy for some patients, which significantly increases overall survival. However, it was noted that the relevant adjuvant trials mostly enrolled patients with macrometastatic disease (who have a poor prognosis). The impact of adjuvant treatment on individuals with SLNB positivity has not been comprehensively addressed. Hence a key point for discussion at the meeting was to explore the risk equivalence of the SLNB positive group with the group with higher risk disease (see below).

MBS item descriptor and proposed fee

The applicant proposed that a single MBS item would be appropriate. The item descriptor would specify all melanoma greater than 1 mm thick, and melanoma at least 0.8 mm thick in the presence of ulceration.

Regarding the proposed fee, participants noted that SLNB for melanoma can be complex (particularly for head and neck melanoma), but this varies case by case. The applicant proposed that a single fee would be appropriate, equivalent to the fee for MBS item 30299 (SLNB for breast cancer). However, it was requested that multiple items could be claimed if SLNB was required at multiple different sites (e.g. axilla, and head and neck).

Risk equivalence

Participants noted that the clinical trials of adjuvant therapy enrolled few patients who would be identified by the proposed SLNB listing. Rather, most patients in the trials had higher-risk disease. This is additionally complicated by the changes in the staging system (from Version 7 to Version 8), so that, in particular, a patient who was Stage IIIA in the trials would not necessarily be representative of Stage IIIA patients using the current system (with SLNB). Participants considered that it was likely that the hazard ratios for adjuvant therapy outcomes were similar across those who had macrometastatic disease and those who had micrometastatic disease.

Participants considered that the current system identifies more patients as being SLNB–positive for Stage IIIA than would have been enrolled in the trials, and this improves their prognosis by reducing their baseline risk of disease recurrence and survival. If constant hazard ratios across reduced baseline risks can be assumed, then this reduces their expected absolute improvements in the recurrence and survival outcomes. Participants therefore agreed that not every person with a positive SLNB would require or be suitable for adjuvant therapy. Participants noted that, although immunotherapy (and targeted therapy) has substantial survival benefits, it is also associated with substantial adverse events. For this reason, participants agreed that it would be undesirable to expose a large number of people to a course of adjuvant immunotherapy/targeted therapy when their risk of recurrence is small.

Trigger for access to adjuvant therapy

Participants acknowledged the difficulty in determining a threshold for access to adjuvant therapy when the evidence is uncertain and still being generated. However, it was noted that

data show a clear separation in survival curves between Stage IIIA and higher stages, so Stage IIIA may be a natural threshold for access to adjuvant therapy. It was advised that all patients diagnosed via SLNB as being Stage IIIA or more with the current system would be referred to a medical oncologist.

Participants also advised that all treatment decisions must be made by the patient in consultation with their medical oncologist to weigh up the potential benefits and harms for that patient. Participants noted that eligibility criteria in MBS and PBS listings would apply to the entire population, but that decisions to undertake biopsy and initiate treatment would still need to be made at the individual level.

Patient preferences

Participants noted that patients understand that sentinel lymph node status is an important prognostic indicator, and knowledge of an SLNB result can help them plan their lives. The psychological benefits to the patient of a negative SLNB should not be underestimated; similarly, a positive SLNB that might provide access to a clinical trial can also provide psychological benefits. Participants also noted that patients often have a very strong fear of recurrence and are frequently willing to accept serious adverse effects from adjuvant therapy for only a small benefit.

Participants also noted the importance of balancing the need to treat patients with effective therapies, but not to overtreat, as is now being debated in the context of adjuvant chemotherapy of breast cancer. Participants agreed that patients need to be fully informed of the risks and benefits of any intervention, whether further investigation or treatment.

Other comments

Participants considered that utilisation data would be important to understand how SLNB is used in the Australian population, but that this may be difficult to obtain given the non-specific MBS items that are currently used for billing purposes. It was noted that the lack of a specific MBS item may send a message to the community that SLNB is not needed. As a result, patients may not present until a later stage. The lack of a specific MBS item also fuels misinformation about SLNB and melanoma.

4. Meeting close

The Chair invited each attendee to make any further comment. Participants were then thanked for their valuable insights and it was hoped that they found the meeting informative.

The meeting closed at 10:20 am.