Australian Government

Department of Health

Targeted Consultation Survey on MSAC Application 1669

KRAS G12C variant testing to determine eligibility for PBS-subsidised sotorasib second-line therapy in patients with locally advanced or metastatic non-small cell lung cancer

This feedback survey relates to the application form and Population, Intervention, Comparator and Outcome (PICO) Confirmation for new and amended requests for public funding (including but not limited to the Medicare Benefits Schedule (MBS)).

Please use this template, to prepare your feedback on the application form and/or the PICO Confirmation. You are welcome to provide feedback from either a personal or group perspective for consideration by the Department of Health when the application is being reviewed.

The data collected will be used to inform the Medical Services Advisory Committee (MSAC) process to ensure that when proposed healthcare interventions are assessed for public funding in Australia, they are patient focused and seek to achieve best value.

This feedback survey should take approximately 15 minutes to complete.

You may also wish to supplement your responses with further documentation or diagrams or other information to assist the Department in considering your feedback.

Thank you for taking the time to provide valuable feedback.

Responses may be provided to the MSAC, its subcommittees, a health technology assessment group and the applicant. Should you require de-identification please contact the Consumer Evidence and Engagement Unit (details below).

While stakeholder feedback is used to inform the application process, you should be aware that your feedback may be used more broadly by the applicant.

Please reply to the Consumer Evidence and Engagement Unit:

Email: commentsMSAC@health.gov.au

Postal: MDP 910 GPO 9848 ACT 2601

PART 1 – PERSONAL AND ORGANISATIONAL INFORMATION

1. Respondent details

Name:

Email:

Phone No:

2. Is the feedback being provided on an individual basis or by a collective group?

☐ Individual
☒ Collective Group

If individual, specify the name of the organisation you work for

If collective group, specify the name of the group

Australian Genomics

3. How would you best identify yourself?

☐ General Practitioner
☐ Specialist
☐ Researcher
☐ Consumer
☐ Care giver
☒ Other

If other, please specify

Project officer for Australian Genomics, in consultation with senior program administrators, clinicians, researchers and community representatives from Australian Genomics.

PART 2 – CLINICAL NEED AND PUBLIC HEALTH SIGNIFICANCE

4. Describe your experience with the medical condition (disease) and/or proposed intervention and/or service relating to the application form

Australian Genomics is an Australian Government initiative supporting genomic research and its translation into clinical practice. Through broad engagement and a national collaborative approach, it achieves two key objectives: to improve efficiency, reach and timeliness of genomic research projects, and to support Commonwealth, State and Territory health departments in the implementation of genomics research outcomes by refining and communicating evidence to inform policy development.

Australian Genomics engages with current and emerging government policy and priorities to identify gaps and opportunities, to support policy and action for integrating genomic technologies into the health system. By interfacing with consumers, government, industry and global genomics initiatives, Australian Genomics drives change and growth in the sector.

Australian Genomics has investigated clinical implementation of genomic testing into a range of rare disease and cancer diseases. This had included a Somatic flagship, that investigated clinically actionable variants in a range of cancer types using the Comprehensive Cancer Panel (391 cancer gene panel) at the Peter MacCallum Cancer Centre. This study, on non-resectable solid tumours (including non-small cell lung cancer (NSCLC)) also investigated the implementation of treatment changes in patients after their genomic result.

Additionally, an Australian Genomics Lung Cancer Diagnosis flagship has investigated the methodology of endobronchial ultrasound lymph node aspirates for nucleotide extraction and whole genome / whole exome sequencing technologies, to guide lung cancer treatment. Australian Genomics also engages with their Community Advisory Group which includes members who have personal experience with disease types such as cancer.

5. What do you see as the benefit(s) of the proposed medical service, in particular for the person involved and/or their family and carers?

Without the proposed medical service, this subset of patients would not have the opportunity to be identified as suitable for second line sotorasib treatment of NSCLC. An early diagnosis of the driver mutation (if there is one) will lead to accurate and early intervention with targeted therapy**.**

Recent studies have indicated a response rate of 37.1% for sotorasib in NSCLC, the majority who had previously received platinum-based chemotherapy and PD-1 or PD-L1 therapies (Skoulidis *et al*., 2021). Although the population of patients is often at an advanced age (median age of onset in studies is reported at 70 years of age (Howlader *et al*., 2013), sotorasib provided a durable clinical benefit in terms of tumour shrinkage and disease control (Skoulidis *et al*., 2021).

We have also had direct responses from a consumer perspective that:

"I was diagnosed with NSCLC in June 2014, and fortunately had NGS which determined that I had the ALK fusion and was ALK Positive, this led to immediate treatment with targeted therapy.

I understand that the KRAS gene can be included within the same panel of tests as tested my tumour for EGFR/ALK and ROS1 without the need for any additional tissue sample. I also understand that there is a targeted treatment available for this mutation.

Having regard to the cost of targeted treatments it is vital from a consumer perspective that:

1. those patients who will benefit from the targeted therapy receive it as quickly as possible, and
2. other expensive treatments which will not be effective are avoided, particularly having regard to the adverse side effects commonly associated with cancer treatments.

Given the large % of NSCLC patients harbouring the KRAS mutation I believe that it is unethical not to screen for this mutation at the same time."

Taken together, we believe that the proposed service and treatment will provide considerable hope for the patient, their family and carers, and offer stabilisation of quality of life.

6. What do you see as the disadvantage(s) of the proposed medical service, in particular for the person involved and/or their family and carers?

If the test is not reimbursed, then there will be inequity of testing and ultimately treatment due to cost issues.

Skoulidis *et al*., (2020) reported a relatively high proportion of side effects – adverse events in almost 70% of patients, with almost 20% experiencing a grade 3 event (side effects include nausea, fatigue and liver damage). The relevant advantage of positive treatment effects versus side effects would have to be well communicated to patients with suitable support during treatment as appropriate.

Relevant counselling and support services for patient and other family members should be available as standard of care through respective oncology services.

It is also noted that in there is a risk of acquired resistance when using a targeted therapy. Although there is limited testing of sotorasib resistance in NSCLC, acquired resistance has been documented in lung cancer driver oncogene targeted treatment. As indicated by Dunnett-Kane *et al*., (2021), sotorasib will induce acquired resistance, although further work is required to determine the mechanism. This acquired resistance risk would need to be incorporated into any treatment plan.

7. What other benefits can you see from having this intervention publicly funded on the Medicare Benefits Schedule (MBS)?

As indicated by Skoulidis *et al*., 2021, there was an objective response in 37.1% of phase 1 study patients (n=126).

There is always the potential to detect the disease early through testing which may lead to the ability to resect and or extend the life expectancy of patients.

Generally, there would be considerable reduction in financial burden to the family. Additionally, there may be a reduction in financial cost to the health system / potential increase in quality-adjusted life years, however there is a lack in data in this area due to the recent approval of the drug.

8. What other services do you believe need to be delivered before or after this intervention, e.g. Dietician, Pathology etc?

We understand this service will mainly be delivered through oncology services, in conjunction with sample collection by a respiratory physician. We strongly suggest that counselling services are also made available.

PART 3 – INDICATION(S) FOR THE PROPOSED MEDICAL SERVICE AND CLINICAL CLAIM

9. Do you agree or disagree with the proposed population(s) for the proposed medical service as specified in Part 6a of the application form?

- [x] Strongly Agree
- [ ] Agree
- [ ] Disagree
- [ ] Strongly Disagree

Specify why or why not:

The figure of 13% of tumour from NSCLC patients having the G12C subtype is well supported in the literature.

10. Have all the associated interventions been adequately captured in Part 6b of the application form?

- [ ] Yes
- [x] No

Please explain:

We believe more clarity is required around the type of testing offered in this application. The PCR based *therascreen* KRAS RGQ PCR kit (Qiagen) is offered as an option for KRAS testing. As noted, most Australian laboratories utilise NGS technologies (e.g. a multigene capture panel) for MBS item 73337 and this provides a degree of flexibility for future analysis. We feel this needs to be clarified as there are implications given the often limited nature of tumour tissue.

11. Do you agree or disagree that the comparator(s) to the proposed medical service as specified in Part 6c of the application form?

☐ Strongly Agree
☒ Agree
☐ Disagree
☐ Strongly Disagree

Please explain:

The comparators of no test and current second-line therapy are appropriate, also citing the existing MBS item number 73337.

12. Do you agree or disagree with the clinical claim made for the proposed medical service as specified in Part 6d of the application form?

☒ Strongly Agree
☐ Agree
☐ Disagree
☐ Strongly Disagree

Specify why or why not:

The test will offer targeted treatment and potentially greater progression free and overall survival (Skoulidis *et al*., 2021), that is currently not offered as standard of care.

PART 4 – COST INFORMATION FOR THE PROPOSED MEDICAL SERVICE

13. Do you agree with the proposed MBS item descriptor, as specified in Question 53 of the application form?

- ☐ Strongly Agree
- ☒ Agree
- ☐ Disagree
- ☐ Strongly Disagree

Specify why or why not:

In general, we agree with the item descriptor however have two notes:

1) We note that in application 1660 (METex14 testing in NSCLC) both pathology and genetic services were named – we believe genetic services should also be added to the current application descriptor wording

2) As noted in other parts of this survey, we believe the application would benefit around further details concerning minimum requirements for testing (either NGS or PCR based) in the form of a "full submission dossier"

14. Do you agree or disagree with the proposed MBS fee, as specified in Question 53 of the application form?

- ☐ Strongly Agree
- ☒ Agree
- ☐ Disagree
- ☐ Strongly Disagree

Specify why or why not:

It is referenced in the application that there were challenges in determining the cost of the test in Australian labs. We suggest further cost estimates from overseas to guide the cost of $397.35. There is also no reference of the difference between PCR and NGS technologies, and possible downstream health economics of each respective method.

PART 5 – ADDITIONAL COMMENTS

15. Do you have any additional comments on the proposed intervention and/or medical condition (disease) relating to the proposed medical service?

Further to comments in the above (Part 3, Q10), we believe more time is required on summarizing the minimal standards of the KRAS G12C mutation. It is mentioned in several places that most Australian diagnostic laboratories surveyed use NGS technologies for determining KRAS G21C status. However, more consideration on the merits of multigene NGS panel technology versus PCR based test (such as the *therascreen* KRAS RGQ PCR kit (Qiagen) is warranted). For example, tumour multigene NGS panels may offer more flexibility with the ability to investigate other genes related to NSCLC. It also offers options in terms of reanalysis. Indeed, Mosele *et al*. (2020), state that the European Society for Medical Oncology recommend routine use of tumour multigene NGS on tumour samples in advanced non-squamous NSCLC. They also site moderate cost effectiveness of targeted/multigene NGS panels (Tan *et al*,. 2020; Steuten *et al*., 2019). Based on this evidence, we believe that NGS technology would be a better technology for KRAS G12C variant testing, and result in more consistent workflows across Australian laboratories.

As outlined by Sherwood *et al*., (2017) the decision on what technology to use also depends on the clinical context – if other genes need to assess in parallel there are benefits to using multigene NGS panels. In relation to the discussion above, there is also the possibility of liquid biopsy testing in the future, which would help address the issue of limited tumour availability (see review by Vessies *et al*., 2020).

Finally, we also note recent research points to benefits of using a combination of sotorasib and another covalent inhibitor, adagrasib (Addeo *et al*., 2021). We would suggest considering a review of this combination therapy (noting recent FDA approval).

16. Do you have any comments on this feedback survey? Please provide comments or suggestions on how this process could be improved.

More structured responses to 6a and 6b are suggested – for example if sufficient evidence is given for various points (e.g. health benefits, effectiveness of treatment etc).

<u>Again, thank you for taking the time to provide valuable feedback.</u>

References

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