PD-1 and PD-L1 checkpoint inhibitor immunotherapies: options for subsidy consideration for multiple cancer types

General/overall comments

Please note, comments that are beyond the scope of PD-1 and PD-L1 checkpoint inhibitor immunotherapies: options for subsidy consideration for multiple cancer types will not be considered

Specific responses

Please insert your comments against the consultation questions below.

Question 1

What do you/your organisation see as the potential advantages of the PBAC considering the PD-1 and PD-L1 checkpoint inhibitors for multi-tumour listings?

In general, this class of medication has better tolerability and durability over chemo regardless of tumour type.

Question 2

What do you/your organisation see as the potential disadvantages of the PBAC considering the PD-1 and PD-L1 checkpoint inhibitors for multi-tumour listings?

Length of treatment and monitoring will become astoundingly high over time if more and more indications are approved. Finding the patients most likely to respond or better respond will be critical through diagnostic testing.

Question 3

What is urgent unmet clinical need? How should it be established? For which patient groups?

Based on evolving clinical trials and evidence for new indications these populations with unmet medical needs will need to be incorporated into coverage plans.

Question 4

What is the minimum level of evidence of effectiveness that you/your organisation think should be required before a PD-1 and PD-L1 checkpoint inhibitors is considered for subsidy for a particular kind of cancer? Why?

For those therapies that have identified subgroups, use an approved diagnostic assay to provide evidence that a certain patient population respond better than others.

Question 5

Do you/your organisation think it is possible for the PBAC to be able extrapolate, or apply, the evidence of effectiveness of a checkpoint inhibitor in one kind of cancer to another kind of cancer, or from late stage cancer to early stage cancer? Why? How?

No, multiple clinical trials have shown that different responses in different patient populations across different cancer types (note the multiple failures on gastric cancer – not responding well to immunotherapies), need proper patient population, a valid result from and approved diagnostic assay, and therapy

Question 6

Do you/your organisation think it is possible for PBAC to satisfy itself that treatment with a PD-1 or PD-L1 checkpoint inhibitor is cost-effective without an economic model that is specific to that kind of cancer? How?

- Is it possible to group different cancer types together based on particular characteristics that are similar, and construct a single model for the group?
- Are other approaches to establishing cost-effectiveness across cancer types possible? What are those approaches and how would they operate?

No response to first part of question. In response to bullet point #2: Est. cost effectiveness across cancer types – the answer is to utilize diagnostically selected patient populations by using an approved diagnostic assay with a valid result. In addition, using a Multi Decision Criteria Analysis (MCDA) could identify cost effect treatments.

Question 7

What do you/your organisation think is a reasonable subsidy price for Government to pay for a PD-1 or PD-L1 medicines for cancer types where the benefit is potentially very modest?

Multi Decision Criteria Analysis (MCDA) could also identify cost-effective treatments.

Question 8

Do you/your organisation think PD-1 and PD-L1 medicines should be made available to all patients whose cancers display a particular biomarker? Why? Which biomarker?

Yes. It has been proven in clinical trials that with increasing level of PD-L1 expression via IHC (e.g. VENTANA PD-L1 (SP142) Assay and VENTANA PD-L1 (SP263) Assay) patients' likelihood and magnitude of response increase across disease areas. Currently, VENTANA PD-L1 SP263 has shown concordance with other PD-L1 assays in additional to having the most drug labels associates with it (Keytruda, Optivo, Durvalumab)

Question 9

Do you/your organisation think it is appropriate for the PBAC to extrapolate the evidence from one PD-1 or PD-L1 checkpoint inhibitor to other medicines in the same class(es). This could provide patients with more choice and give Government the opportunity to negotiate better subsidy prices by utilising the competition between sponsors of medicines.

No answer

Question 10

Do you/your organisation think that different evidentiary requirements are appropriate for rare cancers? How do you think cost-effectiveness should be established in this case?

Identifying subgroups with higher likelihood of response and magnitude of response would be key.

Question 11

Do you/your organisation think PBAC should set aside one of its meetings each year to consider only PD-1 or PD-L1 inhibitors for cancer? (This would mean no other submissions for other medicines, including other cancer medicines, or other diseases would be considered at that meeting.)

Yes, due to the fast changing landscape of this field we would welcome the opportunity of a single annual meeting

Question 12

If limited evidence is available at the time of subsidy of a PD-1 or PD-L1 inhibitor for a type of cancer, what do you/your organisation think should happen afterwards?

- Should sponsors be required to collect more evidence?
- What should happen if the new evidence shows the medicine is less effective or has greater safety risks than expected?
- Should the medicine continue to be subsidised but at a price commensurate with its benefit? Should the sponsor be compelled to continue to make the medicine available even if it thinks the price is too low?

No answer

Question 13

(For industry/clinical groups) Clinical study information: (Please use the template provided for this information.)

- In what indications has your organisation completed clinical trials with a PD-1 and PDL1 inhibitor? Please include both positive and negative studies.

- In what indications is your organisation currently conducting or planning to conduct clinical trials with PD-1 or PD-L1 inhibitors? If usual PBAC processes were to be followed, when would you expect to make an application for subsidy for these indications?
- How does your organisation decide which indications to study and which to prioritise for registration or subsidy?

No answer

Question 14

Are there effective international models for multi-tumour subsidy that could be applied in Australia within the current regulatory framework?

None currently known

Question 15

(For Industry) What information can you provide regarding established international agreements for multi-tumour subsidy and how could these apply in the Australian regulatory context?

None currently known

Question 16

Is there anything else you/your organisation would like to add?

The use of PD-L1 expression as a biomarker may:
Optimize the cost-effectiveness of the treatment with immune checkpoint therapy
Decrease the overall economic impact of immune checkpoint therapy
Decrease the cost of life-year saved

Resources:

A Cost-Effectiveness Analysis of Nivolumab versus Docetaxel for Advanced Nonsquamous NSCLC Including PD-L1 Testing. J Thorac Oncol. 2016 Nov;11(11):1846-1855. Matter-Walstra K, Schwenkglenks M, Aebi S, Dedes K, Diebold J, Pietrini M, Klingbiel D, von Moos R, Gautschi O;

Correlation between PD-L1 expression and outcome of NSCLC patients treated with anti-PD-1/PD-L1 agents: A meta-analysis. Crit Rev Oncol Hematol. 2016 May; 101:75-85 Abdel-Rahman O.

Cost–effectiveness of immune checkpoint inhibitors in NSCLC according to PD-L1 expression. LUNG CANCER MANAGEMENT VOL. 5, NO. 3 Pedro Aguiar Jr, Luke A Perry, Gilberto L Lopes Jr

The effect of PD-L1 testing on the cost-effectiveness and economic impact of immune checkpoint inhibitors for the second-line treatment of NSCLC. Ann Oncol. 2017 Sep 1;28(9):2256-2263. Aguiar PN Jr, Perry LA, Penny-Dimri J, Babiker H, Tadokoro H, de Mello RA, Lopes GL Jr.

The budget impact of introducing a PD-L1 assay to select patients with metastatic NSCLC who are potential candidates for treatment with immune checkpoint inhibitors. Value in Health 2017 20:9 (A576) Sheppard B., Ahlsten M., Paolini D., Xenakis J., Zhang W.

Financial consequences of the performance of a PD-L1 test to select patients receiving second and third line treatments for non-small cell lung cancer in Italy. Value in Health 2017 20:9 (A424) Restelli U., Artale S., Pacelli V., Croce D.

An Estimate of the Economic Impact of Immunotherapy Relative to PD-L1 Expression in Brazil - An Update with Brazilian Costs. Journal of Thoracic Oncology, Volume 12, Issue 1, Supplement, 2017, Page S427 Pedro Aguiar, Ramon De Mello, Hakaru Tadokoro, Hani Babiker, Gilberto Lopes