MOGA

Oncology Drugs and Treatments Advocacy and Access Activities Report 2019

Acknowledgements

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Introduction:

The Medical Oncology Group of Australia is the national professional organisation for Australian medical oncology; and, a specialty society of the Royal Australasian College of Physicians. The Association maintains strong advocacy and lobbying positions that support international, best clinical practice at all times including the best available standard of care for our patients. This report provides a brief overview of the Association's main activities in oncology drugs, treatment and professional issues advocacy and lobbying in 2019.

Drug and Treatment Submissions:

- MOGA developed and submitted responses on the oncology drugs listed for consideration on the agendas for each of the PBAC's 2019 meetings (March, July and November); see Appendix 1. A number of special issue submissions on administrative and process matters were also put forward for PBAC consideration.

Positive Regulatory Advocacy Outcomes:

- Harmonisation of Authority Required (Streamlined) listings across public and private hospital PBS items for the Section 100 Highly Specialised Drugs Program.
- Pemetrexed de-restricted by PBAC to allow for use in first line treatment for advanced or metastatic lung cancer (adenocarcinoma) and allowing for use in first line treatment of NSCLC. Thereby aligning with standard treatment options in Lung Cancer Management Guidelines.
- Removal of the requirement for 3-monthly cardiac function testing for patients on anti-HER2 therapies recommended by the PBAC.
- Streamlined Authority for pazopanib for soft tissue sarcoma.
- Extending the listing for pegfilgrastim.
- Extending the Medicare rebates for breast MRI scans and PET Scans. The rebate for MRIs was extended to patients requiring a breast MRI as part of their diagnostic scans or pre-surgery. The rebate for PET scans was extended to patients with metastatic or suspected metastatic breast cancer to assist in determining cancer stage.

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Ongoing unresolved regulatory Issues:

- Listing of adjuvant bisphosphonate (zolendronic acid (Zometa)) for post-menopausal women with EBC.
- Remove requirement for patients with BRAF mutated melanoma to have "progressed following treatment with a BRAF inhibitor (with/without a MEK inhibitor)".
- PBS listing of infliximab to treat immunotherapy induced colitis.
- PBS listing of ondansetron to allow a longer course of prescription.
- Listing of entecavir for Hepatitis B prophylaxis in patients undergoing cancer therapy included on the PBS. The new national guidelines relating to Hepatitis B prophylaxis include recommendations for the use of drugs that are not PBS listed such as entecavir.
- Increase repeat prescriptions for alectinib and crizotinib.
- Listing and access to older oncology drugs without TGA registration such as dacarbazine for Hodgkin's lymphoma and other malignancies.
- Access to more detailed listings information in PBAC applications to facilitate the Oncology Drugs Working Group's scoring using the ESMO model.

Other Drug and Policy Issues:

- MOGA participated in the special PBAC Stakeholder meetings to discuss options for PBS listing of PD-1 and PDL-1 checkpoint inhibitor immunotherapies for multiple cancer types and also made a comprehensive submission on this matter in August last year. Subsequently MOGA has provided further feedback to the PBAC on broad PBS listing for PD-(L)1 inhibitors for NSCLC. MOGA Lung Cancer Expert Group advised that the difference between the stage 3 curable adjuvant and stage3/4 is still an issue to highlight and have different implications for re-treatment. This complex matter is still an area of MOGA focus and continues to be monitored.

- MOGA welcomed the focus on cancer that both major parties articulated as part of the Federal Election 2019 campaign. The issues generated by the campaign served as a catalyst for MOGA to develop a new Position Statement, "A National Cancer Strategy for Australia", to articulate what the profession considered to be the top national priorities. This included adopting a realistic approach to the fact that the national health dollar will

always be subject to limitations and must be strategically applied to ensure the best possible outcomes for patients and clinicians, and a commitment to addressing the financial toxicity experienced by Australian cancer patients.

- MOGA's input to the consultation on "Tackling Mental Ill-Health in Doctors and Medical Students-A National Framework", supported the need for an Australian framework and a reform agenda which positions the wellbeing of the medical profession as a national priority.

- MOGA has been consulting as part of the Victorian State Government's "Review of Assisted Reproductive Treatment" which focuses on the regulatory framework for assisted reproductive treatment.

- MOGA was an active partner in the development and endorsement of the new Australian Consensus Statement and recommendations for the management of hepatitis B during cancer therapy. Given the number of people undergoing cancer therapy and the burden of hepatitis B in Australia, several thousand people are likely to be at risk of hepatitis B reactivation each year, this important statement will directly benefit Australian cancer patients.

- MOGA circulated two Members' alerts to provide timely, advice to members of the Association with their clinical practice. The first, on MammaPrint® (70 gene signature) test for EBC in relation to the MSAC decision on the public funding of the test to alert clinicians to potential patient concerns and treatment issues that could arise from the MSAC decision and to guide them in their advice to patients. The second alert, also from the Breast Experts, focused on the TGA's Hazard Alert and the international product recall of textured breast implants and tissue expanders.

- MOGA's Top 5 low-value practices and interventions developed as part of "Evolve" were launched in mid-May. This initiative led by the College of Physicians aims to drive high-value, high-quality care in Australia and New Zealand. "Evolve" identifies a specialty's Top Five clinical practices that, in particular circumstances, may be overused, provide little or no benefit or cause unnecessary harm. The MOGA guidelines are also part of the NPS MedicineWise Choosing Wisely Australia initiative. These new recommendations provide the latest evidence-based advice on tests and treatments for cancer patients and provide a guide for best practice in palliative care oncology.

- The Victorian Voluntary Assisted Dying Act 2017 commenced operation on 19 June 2019. The issue has also been debated this year in the Western Australia and the Northern Territory. It is important that all our members understand any new laws concerning VAD and the potential implications for their practice that come into force in Australia. MOGA maintains a watching brief on this important legislative issue.

- Over the last three years MOGA has responded to a number of requests relating to dihydropyrimidine dehydrogenase deficiency (DPD) toxicity and testing. Uridine triacetate (Vistogard) was approved by the US FDA in 2015 for patients who exhibit early-onset severe or life-threatening 5-FU/capecitabine toxicities or present with an overdose. Access to uridine triacetate is supported by eviQ but there is no Australian supplier and MOGA continues to advocate for a co-ordinated response to establish a single national repository for the supply and distribution of Vistogard in Australia; and, supported the recommendation that the Peter MacCallum Cancer Centre act as the national repository for the supply and distribution. MOGA has written to the US supplier to articulate the latter recommendation. We have also highlighted that the issue of cost to enable access on a national level needs to be considered, as Vistogard is not funded through the PBS. MOGA is of the view that few oncology facilities in Australia would be able to offer routine DPD testing, and the associated barriers as well as costs to the patient preclude support for DPD testing as the standard care for all patients before starting fluoropyrimidine chemotherapy in Australia. DPD Testing is not the standard of care for patients before starting fluoropyrimidine chemotherapy. Australian medical oncologists do not generally use or recommend DPD testing and the test is not included on the Australian MBS and, is therefore not rebated. DPD testing is not recommended by eviQ. Despite emerging evidence on DPD Testing, major practical barriers remain that preclude routine DPD testing in Australia, including, genetic testing is difficult to interpret and is not necessarily reflective of enzymatic deficiency nor are genetic abnormalities when identified necessarily predictive of all cases of life-threatening toxicity. At this time the Association recommends and promotes ongoing education around the use of fluoropyrimidines including the monitoring and management of toxicity in clinical practice.

- Over the last 4 years MOGA has actively participated in the consultation process and provided advice to the MBS Taskforce on oncology and related specialist items as part of the national Review. Follow up on the profession's response to the Oncology Recommendations announced in late 2018 was deferred until 29 September when MOGA participated in a Stakeholder Meeting convened by the Department of Health to consider the MBS Review – Chemotherapy Recommendations. The meeting focused on the recommendations for the removal of numerous items (such as item 13945 – Accessing long-term implanted drug delivery devices) and the introduction of three new items, including a new Chemotherpapy oral item (139XX.1) which will require an MSAC assessment and submission to be developed by the professional craft groups. The Committee also recommended that the supervision and administration of antineoplastic agents be extended to oral antineoplastic agents (including tyrosine kinase inhibitors but not hormone therapy or bisphosphonates). MOGA will continue to be proactive in working with the Review to resolve the oncology recommendations. MOGA also responded to the Specialist and Consultant Physician Consultation Clinical Committee Report from the MBS Review Taskforce. The Report's recommendations have significant implications for the way specialist and consultant physicians who work in the private sector, or whose patients receive MBS rebates, work in the future. The proposal will see a reduction in more than 60% of attendance items and these will be replaced with new time-based standard attendance schedule fees. The Review has recommended a move away from initial and subsequent consultations, differential rebates for specialists and consultant physicians and additional payments for complex planning, to a time-based structure similar to that applied in general practice. This consultation is still in progress and is being closely monitored.

- In September the Health Department's Provider Benefits Integrity Division commenced a systematic review of claims made to the MBS and wrote to 106 providers (58 medical oncologists) requesting they review their claims for MBS Items 14221, 13954 and 15275. In 2011-2012 MOGA had extensive discussions with the Department and addressed concerns about the item numbers under consideration. MOGA has given considerable time to assist with the MBS Review, and have agreed with the Department that moving forward, the item number 13945 will no longer exist but be replaced by a new item. It is assumed that will occur when the recommendations are agreed to by the Minister.

- The Health Department have also recently advised the Association that they intend to conduct Medicare Compliance Audits on Medical Practitioners over the next two years (commencing October 2019), in relation to a specific group of item numbers Group T9 Items 51300 – 51318; Group A15 Items 721 – 880; Groups A3 and A4 Items 99 – 133. MOGA plans to monitor this activity and support its members throughout the process.

- MOGA contributed to the AMA's Consultation on "Informed Financial Consent-Collaboration between Doctors and Patients". MOGA endorsed the position that the medical profession needs to be proactive about informing patients about out of pocket costs and, the need for transparent and informed financial consent between physicians and their patients. MOGA highlighted that Cancer treatment is a complex and often lengthy pathway, pinpointing specific areas where patients can incur significant costs. While the RACP has taken on board MOGA's recommendations, the AMA determined to develop a more generic guideline document. Plans are in place to develop a speciality specific set of guidelines and advice that will complement those produced by the AMA.

- The Australian medical oncology profession, MOGA and the RACP are represented by Dr Steer joined the Department of Health's "Out of Pocket Costs Transparency Working Group" that is developing a national searchable website to allow the public to access information on the costs of specialist services.

- Development and endorsement of the Prostate Cancer Foundation of Australia's Position Statement on "Screening for Distress and Psychosocial Care for Men with Prostate Cancer and Monograph: A Psycho social Care Model for Men with Prostate Cancer". In October MOGA appointed Dr Siobhan Ng as our nominee to the Foundation's new Multi-disciplinary Expert Panel Group to help develop a new prostate Cancer Distress Screening Tool for Clinicians.

Appendix 1

Table 1: Highest priority for PBS listing

Drug(s)	Comparator(s)	Pivotal Trial(s)	Disease/indication	OS benefit	PFS/DFS benefit	Less toxic	QOL benefit	ESMO-MCBS[1]
Dabrafenib/Trametinib	Placebo	COMBI-AD[2-4]	Adjuvant treatment of resected BRAF V600 mutation positive stage III melanoma	Data immature	Yes	No	No	**A**
Nivolumab	Ipilimumab	Checkmate 238[5,6]	Adjuvant treatment of resected stage III or IV melanoma	Data immature	Yes	Yes	No	**A**

Table 2: High priority for PBS listing

Drug(s)	Comparator(s)	Pivotal Trial(s)	Disease/indication	OS benefit	PFS/DFS benefit	Less toxic	QOL benefit	ESMO-MCBS[1]
Atezolizumab + Bevacizumab (+platinum-based chemotherapy)	Bevacizumab + platinum-based chemotherapy	IMpower 150[7]	EGFR/ALK wildtype, non-squamous metastatic NSCLC	Yes	Yes	No	No	**3**
Cabozantinib	Sunitinib	CABOSUN[8]	Untreated Stage IV clear cell RCC	No	Yes	No	Yes[9]	**3[a]**
Pembrolizumab	N/A	Keynote 164[10]	Locally advanced or metastatic CRC in patients with MSI-H or dMMR tumours, who have progressed following prior treatment	Unknown	Unknown	Unknown[b]	Unknown	**2[c]**

Pertuzumab (+Trastuzumab +Chemotherapy)	Trastuzumab + Chemotherapy	APHINITY[11]	Adjuvant treatment of HER-2+ LN+ early breast cancer	Unknown	Yes	No	No	**A**

[a]Randomised phase II trial; QOL benefit was seen in a post-hoc analysis and so therefore score NOT upgraded to 4

[b]Likely to be less toxic but no randomised data compared to standard of care (chemotherapy/targeted therapy).

[c]ESMO-MCBS Form 3 (orphan drug/rare tumour) used so may increase to a score of 3 when median duration of response is known.

Table 3: Other supported applications

Drug(s)	Comparator(s)	Pivotal Trial(s)	Disease/indication	OS benefit	PFS benefit	Less toxic	QOL benefit	ESMO-MCBS[1]
Abemaciclib (+ Aromatase inhibitor)	Aromatase inhibitor	MONARCH 3[12,13]	Non-premenopausal patients with HR+, HER2- locally advanced or metastatic breast cancer	Data immature	Yes	No	Unknown	**3[a]**
Atezolizumab + Bevacizumab (+platinum-based chemotherapy)	Bevacizumab + platinum-based chemotherapy	IMpower 150[7]	EGFR/ALK mutation positive non-squamous metastatic NSCLC after progression on a TKI	Yes	Yes	No	No	**Cannot be scored[b]**
Bevacizumab	N/A	Friedman et al.[14] BELOB[15] CABARET[16] AVAREG[17]	Relapsed or recurrent GBM	Unknown	Unknown	No	Unknown	**2**
Neratinib	Placebo	ExteNET[18-20]	Extended adjuvant treatment of patients with early-stage HER2+ breast cancer who have received prior adjuvant trastuzumab based therapy	Data immature	Yes	No	No	**A**

[a]May increase to an ESMO-MCBS score of 4 when overall survival data matures

[b]EGFR/ALK mutation sub-group in the IMpower trial was an exploratory analysis so the ESMO-MCBS cannot be applied

[i] MOGA has provided two scores. If Durvalumab in this setting is considered a potentially curative treatment, then it scores an A. If it is considered a non-curative treatment then it scores a 3 based on PFS, however this is highly likely to increase to a 4 once the OS data is mature enough to determine the median OS difference between the Durvalumab and placebo arms.

[ii]No direct comparisons of Nivolumab + Ipilimumab vs BRAF/MEK inhibitors as 1st line treatment in the BRAF mutated population
[iii]Upgraded to a 4 as PFS difference at 2 years was >10% and plateau of PFS curve in treatment arm
[iv]Upgraded to a 4 as QOL improvement demonstrated in pivotal trial

Table 1: Highest priority for PBS listing

Drug(s)	Comparator(s)	Pivotal Trial(s)	Disease/indication	OS benefit	PFS/DFS benefit	Less toxic	QOL benefit	ESMO-MCBS[1]
Dabrafenib/Trametinib	Placebo	COMBI-AD[2,3]	Adjuvant treatment of resected BRAF V600 mutation positive stage III melanoma	Data immature	Yes	No	No	**A**
Durvalumab	Placebo	PACIFIC[4,5]	Stage III NSCLC (after definitive chemoradiation)	Yes	Yes	No	No	**A** OR **3**[i]
Nivolumab	Ipilimumab	Checkmate 238[6,7]	Adjuvant treatment of resected stage III or IV melanoma	Data immature	Yes	Yes	No	**A**
Osimertinib	Gefitinib/Erlotinib	FLAURA[8]	1st line treatment of advanced EGFR mutated NSCLC	Data immature	Yes	Yes	No	**4**[ii]
Pembrolizumab	Placebo	Keynote-054[9]	Adjuvant treatment of Stage III or Stage IV malignant melanoma after surgical resection	Data immature	Yes	No	No	**A**
Pembrolizumab (+ chemotherapy)	Chemotherapy	Keynote-189[10,11] QOL analysis[12]	EGFR/ALK/ROS-1 wildtype, non-squamous NSCLC	Yes	Yes	No	Yes[iii]	**5**

[i] MOGA has provided two scores. If Durvalumab in this setting is considered a potentially curative treatment, then it scores an A. If it is considered a non-curative treatment then it scores a 3 based on PFS, however this is highly likely to increase to a 4 once the OS data is mature enough to determine the median OS difference between the Durvalumab and placebo arms.
[ii] Will increase to a 5 if mature data demonstrates an improvement in OS
[iii] Data presented at ASCO ASM 2018. Although this QOL analysis is in abstract form only, it was a pre-specified analysis from the Keynote-189 trial and there was a statistically significant improvement in global QOL on a validated scale.

Table 2: High priority for PBS listing

Drug(s)	Comparator(s)	Pivotal Trial(s)	Disease/indication	OS benefit	PFS/DFS benefit	Less toxic	QOL benefit	ESMO-MCBS[1]
Apalutamide (+ ADT)	ADT	SPARTAN[13] QOL analysis[14]	Non-metastatic castrate resistant prostate cancer	Data immature	Yes	No	No	**3**[iv]
Atezolizumab (+ chemotherapy)	Chemotherapy	Impower133[15] QOL analysis[16]	Extensive stage small cell lung cancer	Yes	Yes	No	No[v]	**3**

[iv] Will increase to a 4 if mature data demonstrates an improvement in overall survival.

[v] Data presented at ESMO Immuno-Oncology Congress 2018. There is a suggestion of improvement in QOL however it is unclear from the abstract if there is a statistically significant difference in global QOL. The score therefore has not been upgraded to a 4.

Table 3: Other supported applications

Drug(s)	Comparator(s)	Pivotal Trial(s)	Disease/indication	OS benefit	PFS/DFS benefit	Less toxic	QOL benefit	ESMO-MCBS[1]
Cabozantinib	Placebo	CELESTIAL[17] QOL analysis[18]	Advanced HCC (after sorafenib)	Yes	Yes	No	No[vi]	**3**
Ramucirumab (+Paclitaxel)	Paclitaxel	RAINBOW[19] QOL analysis[20]	Metastatic gastric cancer (after progression with platinum/5-FU based chemotherapy)	Yes	Yes	No	No	**2**
Regorafenib	Placebo	RESORCE[21] QOL analysis[22]	Advanced HCC (after sorafenib)	Yes	Yes	No	No	**3**

[vi]Data presented at the ASCO GI cancers symposium 2019. This data suggests there is an increase in QALYs with cabozantinib in this setting. However as this is a post-hoc analysis and it has not been published in full, the score has not been upgraded to a 4.

Abbreviations used: **ADT** = androgen deprivation therapy; **ALK** = anaplastic lymphoma kinase; **ASCO** = American Society of Clinical Oncology; **ASM** = Annual Scientific Meeting; **DFS** = disease free survival; **EGFR** = Epidermal Growth Factor Receptor; **ESMO-MCBS** = European Society for Medical Oncology Magnitude of Clinical Benefit Scale; **GI** = gastrointestinal; **HCC** = hepatocellular carcinoma; **NSCLC** = non-small cell lung cancer; **OS** = overall survival; **PFS** = progression free survival; **QOL** = quality of life.

Table 1: Highest priority for PBS listing

Drug(s)	Comparator(s)	Pivotal Trial(s)	Disease/indication	OS benefit	PFS/DFS benefit	Less toxic	QOL benefit	ESMO-MCBS[1]
Durvalumab	Placebo	PACIFIC[2,3]	Stage III NSCLC (after definitive chemoradiation)	Yes	Yes	No	No	**A** (or **3**[i])
Nivolumab + Ipilimumab	Trial: Nivolumab OR Ipilimumab (PBS – BRAF/MEK inhibitors)	Checkmate 067[4]	BRAF mutated unresectable stage III/IV melanoma	Unknown	Unknown	Unknown	Unknown	**Unable to be scored**[ii]
Olaparib	Placebo	SOLO1[5]	Maintenance treatment of advanced high grade epithelial ovarian, fallopian tube or primary peritoneal cancer, in class 4 or 5 BRCA1/2 mutation positive patients who are in response to platinum-based chemotherapy.	Data immature	Yes	No	No	**4**[iii]
Pembrolizumab	Placebo	Keynote-054[6]	Adjuvant treatment of Stage III or Stage IV malignant melanoma after surgical resection	Data immature	Yes	No	No	**A**
Talazoparib	Chemotherapy	EMBRACA[7]	Germline BRCA mutated HER2-negative advanced breast cancer who have been previously treated with a taxane and/or an anthracycline	Data immature	Yes	No	Yes	**4**[iv]
Trastuzumab Emtansine	Trastuzumab	KATHERINE[8]	Adjuvant treatment of patients with HER2+ early breast cancer with residual disease following neoadjuvant treatment with HER2 targeted therapy.	Data immature	Yes	No	No	**A**

[i] MOGA has provided two scores. If Durvalumab in this setting is considered a potentially curative treatment, then it scores an A. If it is considered a non-curative treatment then it scores a 3 based on PFS, however this is highly likely to increase to a 4 once the OS data is mature enough to determine the median OS difference between the Durvalumab and placebo arms.

[ii] No direct comparisons of Nivolumab + Ipilimumab vs BRAF/MEK inhibitors as 1st line treatment in the BRAF mutated population

[iii] Upgraded to a 4 as PFS difference at 2 years was >10% and plateau of PFS curve in treatment arm

[iv] Upgraded to a 4 as QOL improvement demonstrated in pivotal trial

Table 2: High priority for PBS listing

Drug(s)	Comparator(s)	Pivotal Trial(s)	Disease/indication	OS benefit	PFS/DFS benefit	Less toxic	QOL benefit	ESMO-MCBS[1]
Atezolizumab (+ chemotherapy)	Chemotherapy	Impower133[9] QOL analysis[10]	Extensive stage small cell lung cancer	Yes	Yes	No	No[v]	**3**
Lorlatinib	Trial: no comparator (PBS – chemotherapy)	Solomon et al[11]	ALK+ metastatic NSCLC (after previous treatment with one or more ALK inhibitors)	Unknown	Unknown	Unknown[vi]	Unknown[vi]	**3[vii]**

[v]Data presented at ESMO Immuno-Oncology Congress 2018. There is a suggestion of improvement in QOL however it is unclear from the abstract if there is a statistically significant difference in global QOL. The score therefore has not been upgraded to a 4.

[vi]Likely to be less toxic and improve QOL compared to chemotherapy and so could potentially be upgraded to a 4 but there is no randomised data compared to standard of care (chemotherapy).

[vii]Form 3 used (orphan drug where PFS/ORR are outcomes in trial)

Table 3: Other supported applications

Drug(s)	Comparator(s)	Pivotal Trial(s)	Disease/indication	OS benefit	PFS/DFS benefit	Less toxic	QOL benefit	ESMO-MCBS[1]
Brigatinib	Trial – Crizotinib (PBS – Alectinib)	ALTA-1L[12]	ALK+ advanced/metastatic NSCLC (1st line)	Data immature	Yes	No	Yes[13]	Unable to be scored as treatment arm has not reached median
Neratinib	Placebo	ExteNET[14-16]	Extended adjuvant treatment of patients with early-stage HER2+ breast cancer who have received prior adjuvant trastuzumab based therapy	Data immature	Yes	No	No	**A**
Trifluridine with Tipiracil	Placebo/BSC	TAGS[17]	Metastatic gastric cancer who have been previously treated with, or are not considered candidates for, currently available therapies	Yes	Yes	No	No	**3**

[viii]Treatment arm has not reached median in pivotal trial.

Abbreviations used: **ALK** = anaplastic lymphoma kinase; **CRC** = colorectal cancer; **DFS** = disease free survival; **EGFR** = Epidermal Growth Factor Receptor; **ESMO-MCBS** = European Society for Medical Oncology Magnitude of Clinical Benefit Scale; **GBM** = glioblastoma multiforme; **HR** = hormone receptor; **LN** = lymph node; **dMMR** = mismatch repair deficient; **MSI-H** = microsatellite instability-high; **NSCLC** = non-small cell lung cancer; **OS** = overall survival; **PFS** = progression free survival; **QOL** = quality of life; **RCC** = renal cell carcinoma; **TKI** = tyrosine kinase inhibitor