Pattern of access to genomically-linked therapies associated with pan-cancer biomarkers in advanced cancer patients: Insights from the Australian Molecular Screening and Therapeutics (MoST) Program

Christine E Napier [1,2], Frank Lin [3,4,5], Subotheni Thavaneswaran [3,4,6], Lucille Sebastian [2], John Grady [1,2], Maya Kansara [7], Milita Zaheed [1,4], John Simes [3], Mandy L Ballinger [1,2], David M Thomas [1,2]

[1]Centre for Molecular Oncology, UNSW, Sydney, Australia; [2]Omico, Sydney, Australia; [3]NHMRC Clinical Trials Centre, University of Sydney, Australia; [4]School of Clinical Medicine, UNSW Sydney, Australia; [5]Department of Medical Oncology, Prince of Wales Hospital, Sydney, Australia; [6]The Kinghorn Cancer Centre, St. Vincent's Hospital Sydney, Australia; [7]Genomic Cancer Medicine Laboratory, Garvan Institute of Medical Research, Sydney, Australia

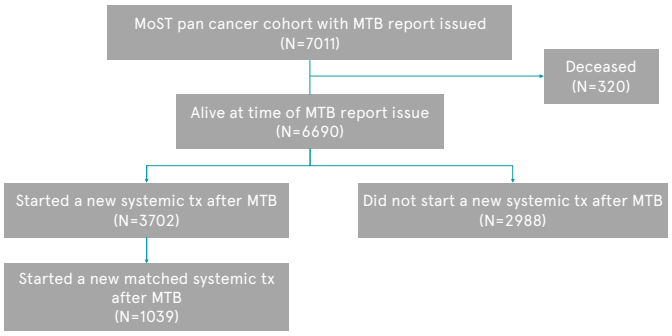
Background

- Comprehensive genomic profiling (CGP) can reveal tumour-agnostic biomarkers that are potentially targetable across a range of cancer types, including rare (<6/100,000 population) and less common (6-12/100,000 population) cancers (RLCC). Common cancers occur in >12/100,000 population.
- The prevalence of genomic biomarkers and their actionability has not been well characterised, particularly in RLCC.
- Real-world Australian data on methods of accessing genomically-matched therapies is unclear.

Methods

- The Molecular Screening and Therapeutics (MoST) Program (ACTRN12616000908437) is a nationwide precision oncology platform.
- Patients were eligible if they had a RLCC with no standard treatment options or advanced common cancers on last line therapy.
- CGP was conducted on archival tumour samples via panels such as Illumina's TST170 and TSO500, and Foundation One CDx.
- This study focused on therapeutically significant genomic biomarkers, including high tumour mutational burden (TMB-H; TMB > 10), microsatellite instability (MSI-H), *BRAF* V600E, oncogenic alterations in *ERBB2*, or fusions in *NTRK1-3* and *RET*, and access to molecular tumour board (MTB)-based therapy recommendations.
- The cohort included 7011 patients, with ≥6 months of clinical follow up to June 2024.

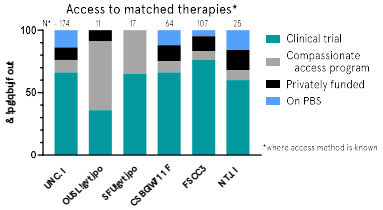
Cohort



	MTB report issued (N, %)	Alive @ MTB report issued (N, %)	Started tx after MTB (N, %)	Started matched tx after MTB (N, %)
Total	7011	6690	3702	1039
Age				
<20	24 (0.3)	23 (0.3)	15 (0.4)	6 (0.6)
20-34	418 (6)	400 (6)	252 (6.8)	75 (7.2)
35-44	716 (10)	688 (10)	398 (11)	119 (12)
45-54	1228 (18)	1166 (17)	664 (18)	165 (16)
55-64	1917 (27)	1827 (27)	1051 (28)	325 (31)
65-74	1935 (28)	1844 (28)	970 (26)	267 (36)
75-84	737 (11)	707 (11)	340 (9.2)	80 (7.7)
≥85	36 (0.5)	35 (0.5)	12 (0.3)	2 (0.2)
ECOG @ referral to MoST				
0	3205 (46)	3140 (47)	1927 (52)	551 (53)
1	3484 (50)	3275 (49)	1667 (45)	453 (44)
2+	323 (3.6)	208 (3.1)	70 (1.9)	20 (1.9)
Unknown	70 (1.0)	67 (1.0)	38 (1.0)	15 (1.4)
Gender				
Female	3714 (53)	3562 (53)	2000 (54)	573 (55)
Tumour rarity				
Rare	4783 (68)	4571 (68)	2494 (67)	669 (64)
Less common	303 (4.3)	282 (4.2)	148 (4.0)	35 (3.4)
Common	1925 (27)	1837 (27)	1060 (29)	335 (32)
Regionality				
Urban	6269 (89)	5988 (90)	3335 (90)	947 (91)
Rural	742 (11)	702 (10)	367 (10)	92 (8.9)

Access to matched therapies

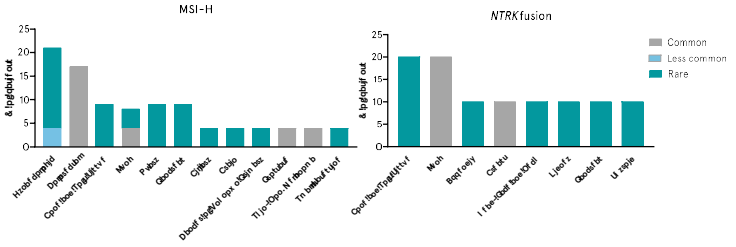
- Biomarkers linked to matched therapies are predominantly by either clinical trials or compassionate access programs. A minority of matched therapies were privately funded. Over the course of the program, PBS indications for immunotherapy, *BRAF* and *ERBB2*-directed therapies have expanded based on supportive clinical trial evidence.



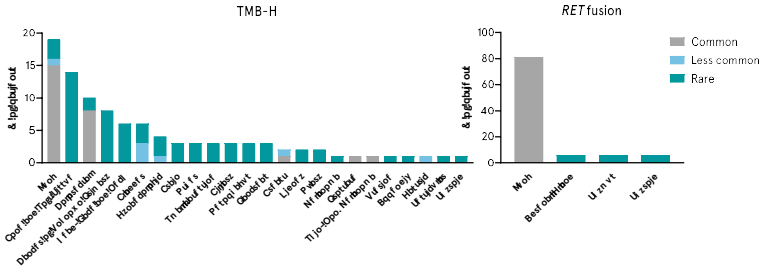
Biomarker	Biomarker identified (N)	Started matched tx after MTB (N, %)	Lines of matched tx (N)
TMB-H	424	154 (36)	212
NTRK fusion	14	10 (71)	12
RET fusion	24	16 (67)	18
BRAF V600E	184	70 (38)	76
ERBB2	372	109 (29)	131
MSI-H	75	23 (31)	25

Notes:
- TMB-H is not a TGA-approved/ PBS-reimbursed indication for immunotherapy use.
- *ERBB2* detected by CGP is not approved for use to access PBS-funded therapy (IHC/FISH required).
- *BRAF* V600E colorectal cancer would be considered predicted but assigned.
- MSI-H patients may also be mismatch-repair deficient (dMMR), which confers PBS-reimbursement.

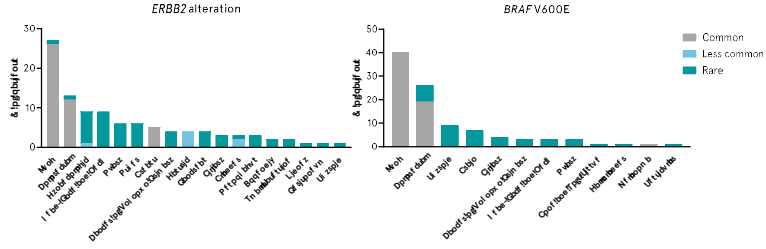
- A greater proportion of patients with rare cancers who had either *NTRK* fusions or MSI-H received matched therapies than patients with common cancers.



- Patients with a TMB-H RLCC received a greater proportion of immunotherapy therapies.
- Access to selective *RET* inhibitors was dominated by common non-squamous non-small cell lung cancers.



- Over half of all patients that accessed a matched therapy targeting either *ERBB2* or *BRAF* V600E had lung or colorectal cancer.



Conclusions

- CGP confirms identification of tumour-agnostic biomarkers associated with approved targeted therapies in common cancers, where reimbursed standard panels are used as standard in Australia.
- CGP extends the identification of patients who may be benefit from biomarker-directed therapies based on a tumour-agnostic approach where a current reimbursed indication may not exist, highlighting the utility of molecular characterisation in this group of patients.
- Clinical trial participation, with inclusion of RLCC, is an important modality for access to biomarker-dependent matched therapies by Australian patients.

We thank the patients and their families for participating in this research.
Omico is a non-profit, nationwide network of research and treatment centres that facilitates, supports and promotes clinical trials and is funded by the Australian Federal Government.
Supported by MSD, Merck Sharp & Dohme (Australia) Pty Limited.