Outsmarting cancer, together

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Garvan Institute of Medical Research
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From genomics to clinical impact, and a sustainable future for precision oncology

Molecular screening & therapeutics

Tumour profiling to evaluate biomarker-driven treatments for patients.

Health system reform

Leading health system reform through evidence.

Omico

A national precision oncology network. Connecting leading specialists, researchers, government, industry partners and community. An innovative model for research-lead cancer care. Improving cancer outcomes for all Australians.

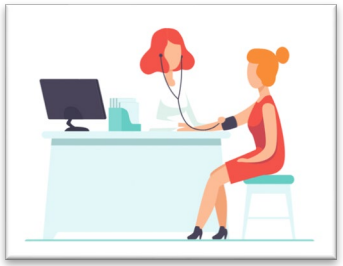
Personalised risk management

Using heritable genetic information to assess cancer predisposition and investigate clinical risk management.

Patient support & advocacy

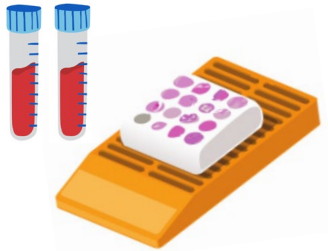
Supporting patients and families today and planning the health system for tomorrow.

Accelerating access to Comprehensive Genomic Profiling

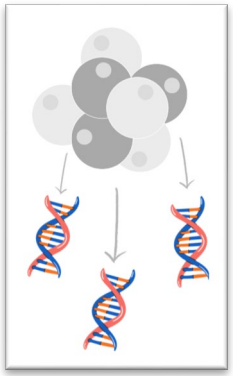


Referral from oncologist

Patient consent



Biospecimen retrieval



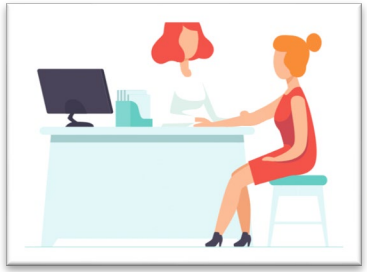
NATA Laboratory

Comprehensive genomic profiling
TSO500
Foundation CDx
IHC-based screening

Clinical trials matching

Molecular Tumour Board and report issued

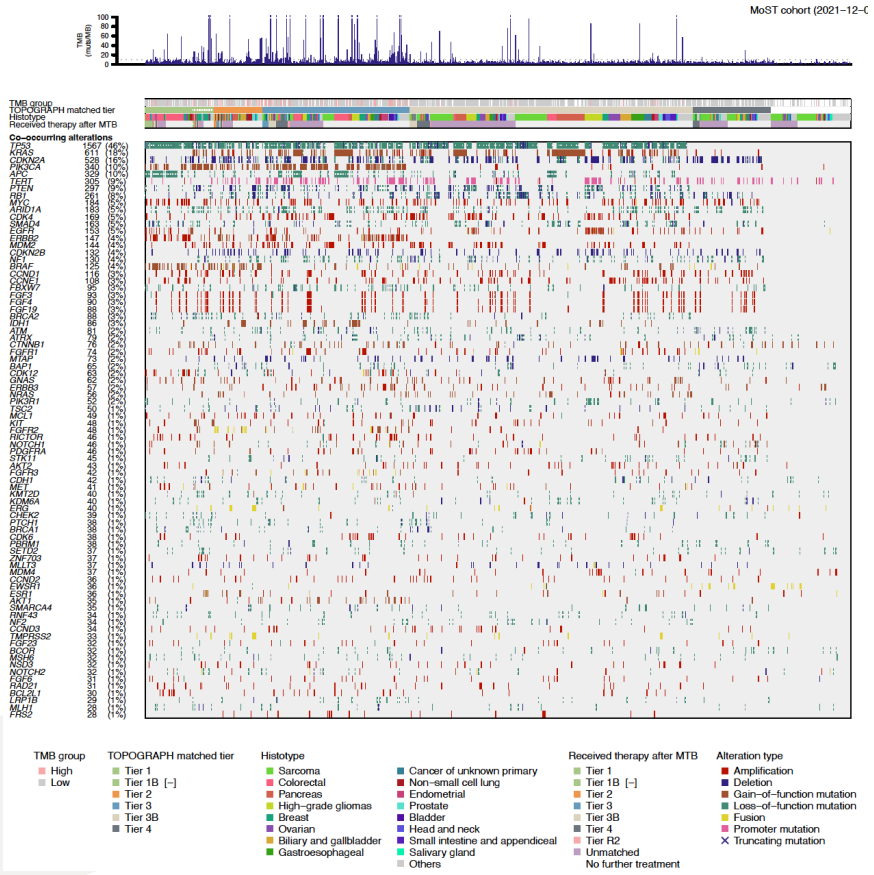
Omico Central

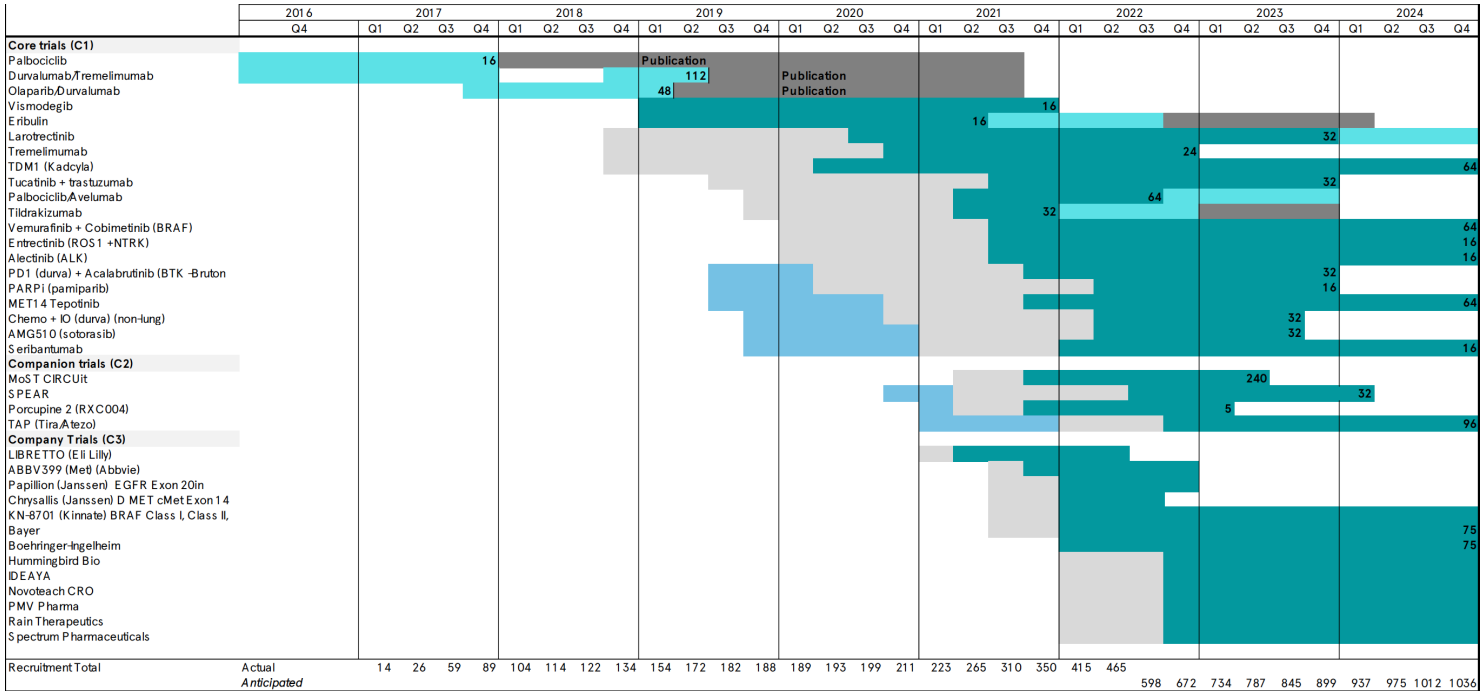


Discuss results with oncologist

Clinician

Trial portfolio: >900 patients enrolled onto biomarker-matched trials





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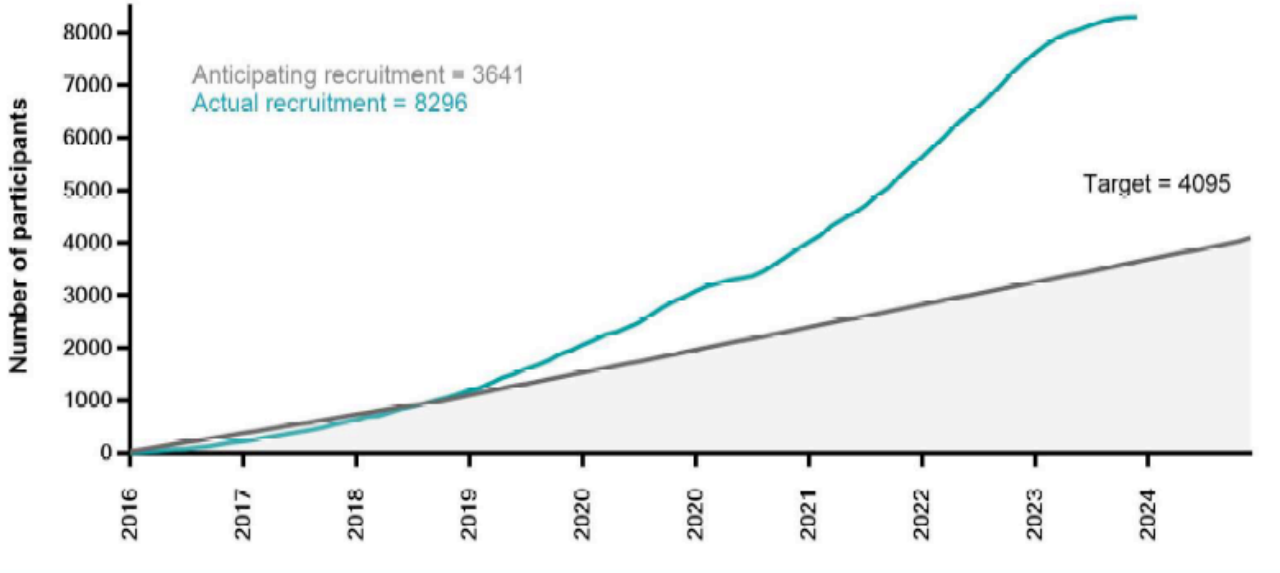
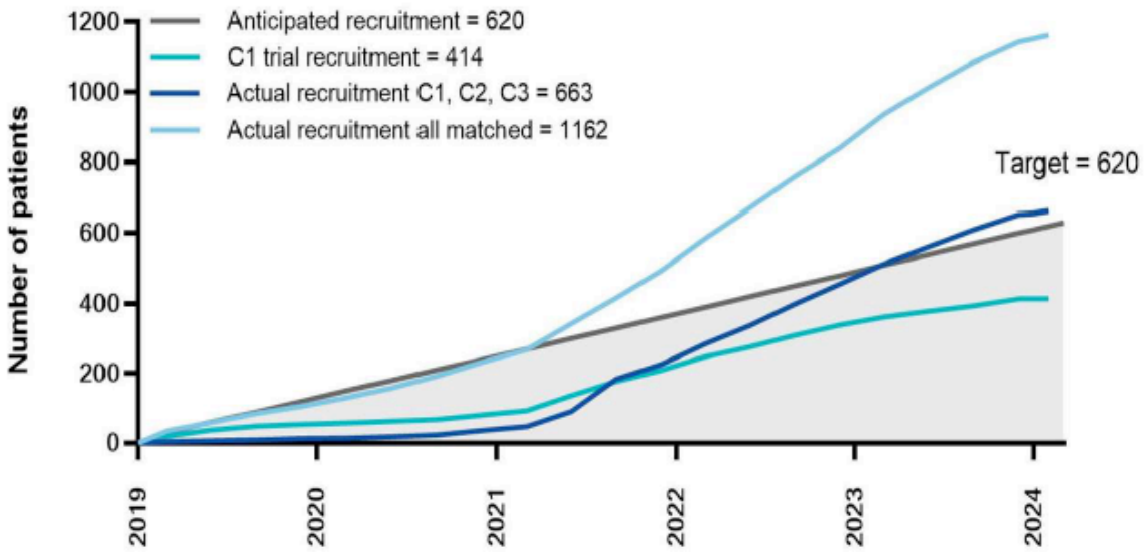
Demand for precision medicine

>800 clinicians in Australia have referred onto MoST

70% rare



Patients with tumor profiling



Patients receiving matched therapy

[1] https://hwd.health.gov.au/resources/publications/factsheet-mdcl-medical-oncology-2016.pdf

Omico’s national population screening and clinical trial network

Omico Clinical Screening Recruitment
13,000 and increasing

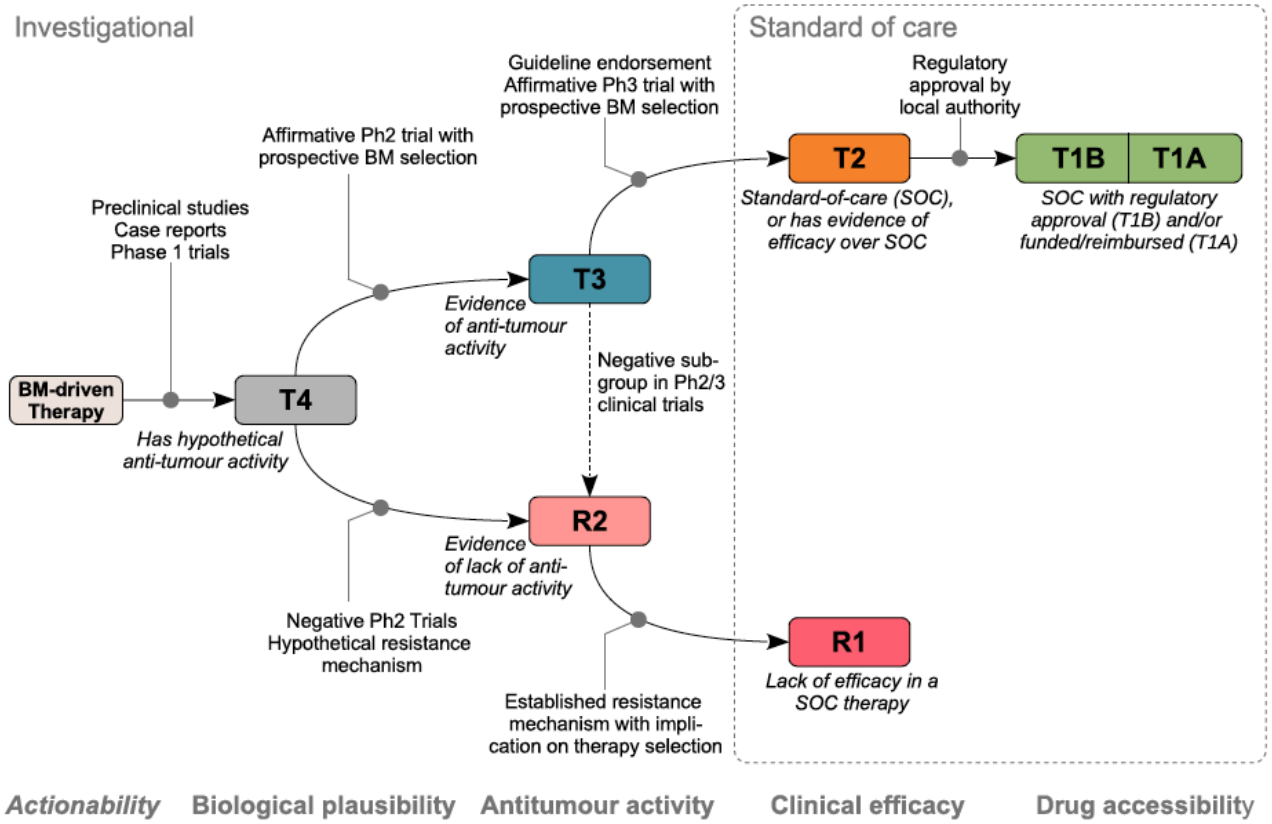
Omico National Clinical Trial Network
49 sites to date, and growing

ARTICLE OPEN

Check for updates

Criteria-based curation of a therapy-focused compendium to support treatment recommendations in precision oncology

Frank P. Lin[1,2,3✉], Subotheni Thavaneswaran[2,3,4], John P. Grady[3,4], Mandy Ballinger[3,4], Maya Kansara[3,4], Samantha R. Oakes[3,4], Jayesh Desai[5], Chee Khoon Lee[2,6], John Simes[2] and David M. Thomas[3,4✉]



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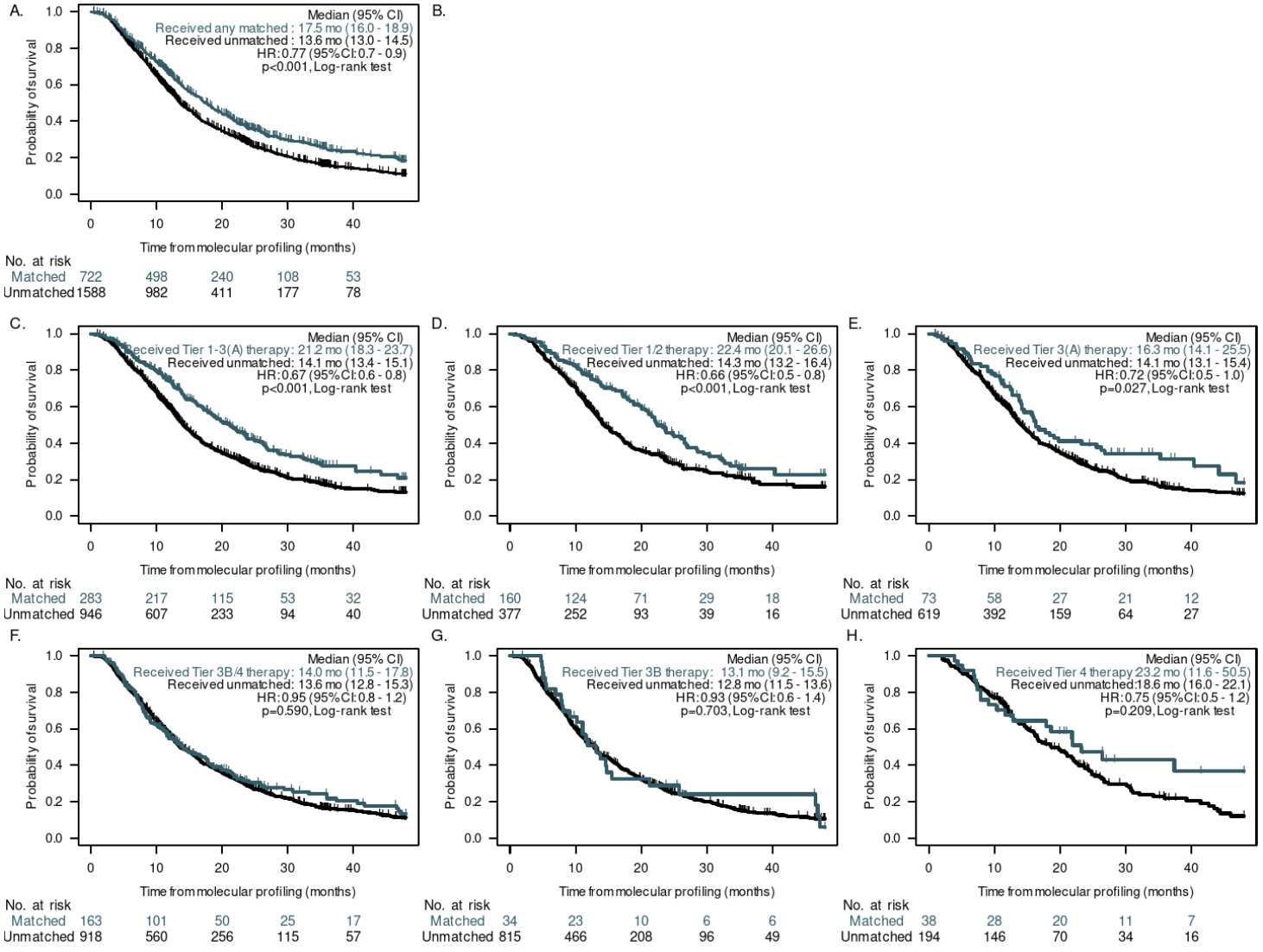
Lin et al. Criteria-based curation of a therapy-focused compendium to support treatment recommendations in precision oncology. 2022 *npj Precision Oncology*

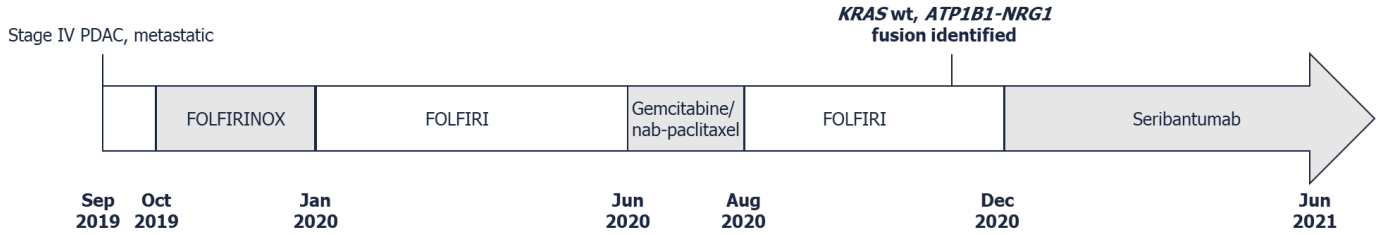
Outcomes: improved survival (update to K7700)

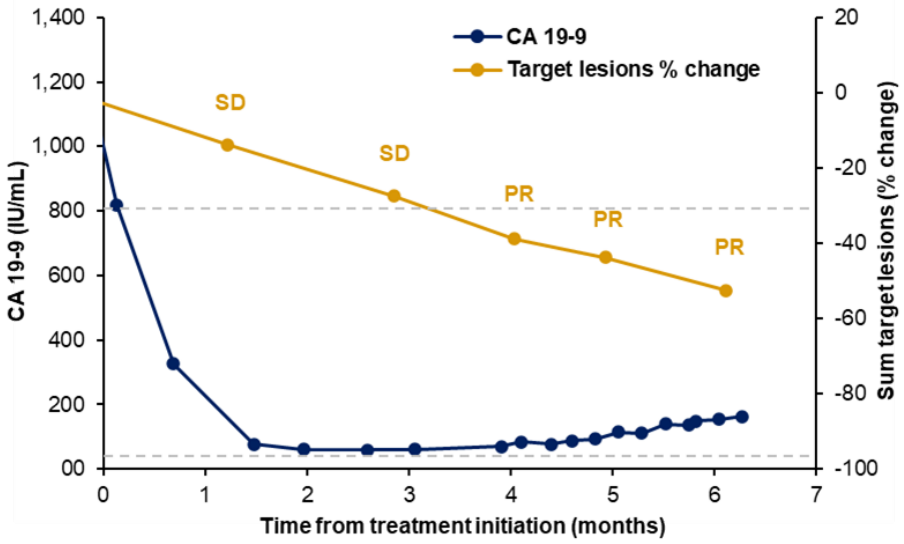


Data from MoST*

- **> 60%** of patients have had a matched treatment identified
- Of these, **37.5% have a drug target** (T1-3) which appears to result in a **doubling of survival**, provided the drug is accessible.

Case studies: NRG1 fusion in pancreas cancer





Thavaneswaran et al, JCO PO 2022

PrOSPeCT is a $190m project that will establish Australia as a regional hub for cancer drug development and build the digital economy in health analytics

PrOSPeCT (Precision Oncology Screening Platform enabling Clinical Trials) is an Omico project that will…

1

Provide broad-based access to comprehensive genomic profiling for non-curative solid or haematologic cancer patient populations – **conducting large-scale genomic screening of more than 23,000 patients**

2

Maximise opportunities in clinical trials by identifying patients for specific biomarker-dependent clinical trials – **driving the efficiency of patient recruitment and decreasing trial costs**

3

Enhance biomarker-dependent drug development by enabling advanced molecular analyses – **creating a real-world dataset and analytics platform with national scale comprising more than 23,000 patients**

PrOSPeCT will be delivered alongside a public-private consortium of partners from across the Australian genomics and clinical trials ecosystem

Major Sponsor*

Australian Government
Department of Industry, Science and Resources

Commercial Collaboration Partners

Roche
Omico.
Children's Cancer Institute
NCI AUSTRALIA

Delivery partners

Peter Mac
Peter MacCallum Cancer Centre Victoria Australia
SA PATHOLOGY
NSW Government Health Pathology
ATGC
QUT Australian Translational Genomics Centre
quantum
illumina
PathWest
Laboratory Medicine WA
BIOPLATFORMS AUSTRALIA
SYNTRO
SONIC HEALTHCARE
MICROBA
George Clinical
PRAXIS AUSTRALIA

Note: *Funding through Modern Manufacturing Initiative

CaSP Monthly Dashboard (to end August 2024)

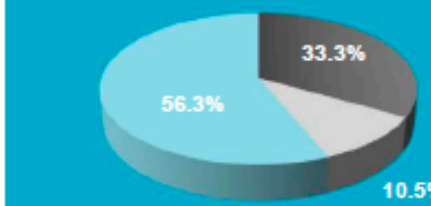
Patient Recruitment & Screening

8,399	Patients referred (CaSP and Zero)
7,059	Patients consented for screening (CaSP and Zero)
4,352	MOB (Molecular Oncology Board) reports issued
3,217 (73.9%)	Patients have had a matched therapy recommendation (Based on those with MOB report issued to date)
849	Clinicians have referred patients to CaSP

Patient Demographics & Cancer Classification

Consented pts / state (CaSP only)

State	#	Regional & rural pts
ACT	99	36%
NSW	2,337	
NT	65	
QLD	1,023	
SA	414	
TAS	331	
VIC	1,773	
WA	62	



11% have >1 primary cancer

Gender	Female	52%
Age at Diagnosis	Average	59y
	Range	9-94y

Time from patient consent to MOB report issue

	Planned	Actual (median)
Standard cases:	8-10 weeks	8.1 weeks
Urgent cases expedited:	5-6 weeks	5.9 weeks

Omico National Clinical Trial Network (ONCTN)

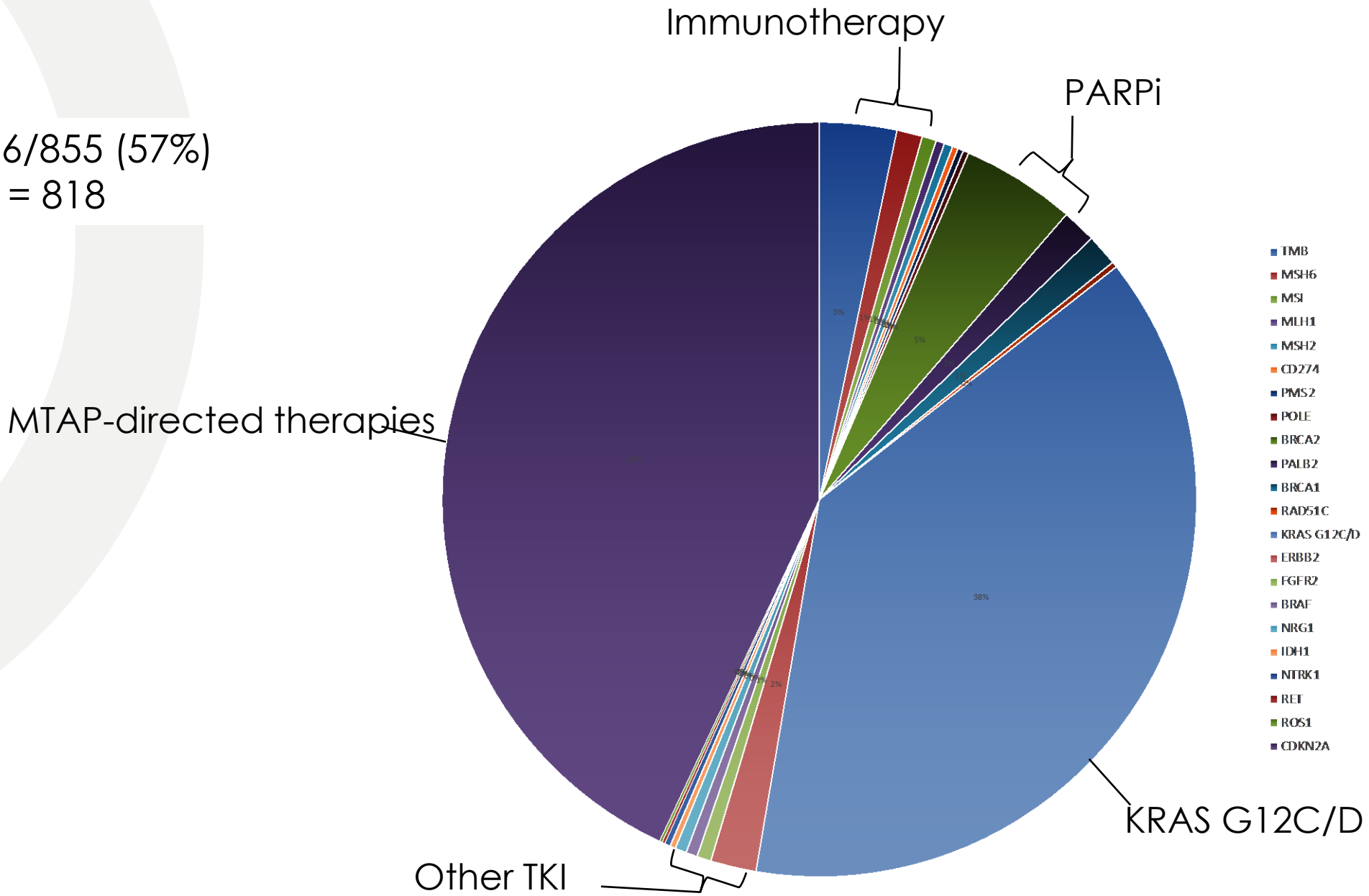
Total sites

61

State	Total	Regional
ACT	2	
NSW	26	11
NT	1	1
QLD	7	2
SA	6	1
TAS	2	
VIC	14	5
WA	3	

Pancreatic cancer

Patients = 466/855 (57%)
Drug targets = 818



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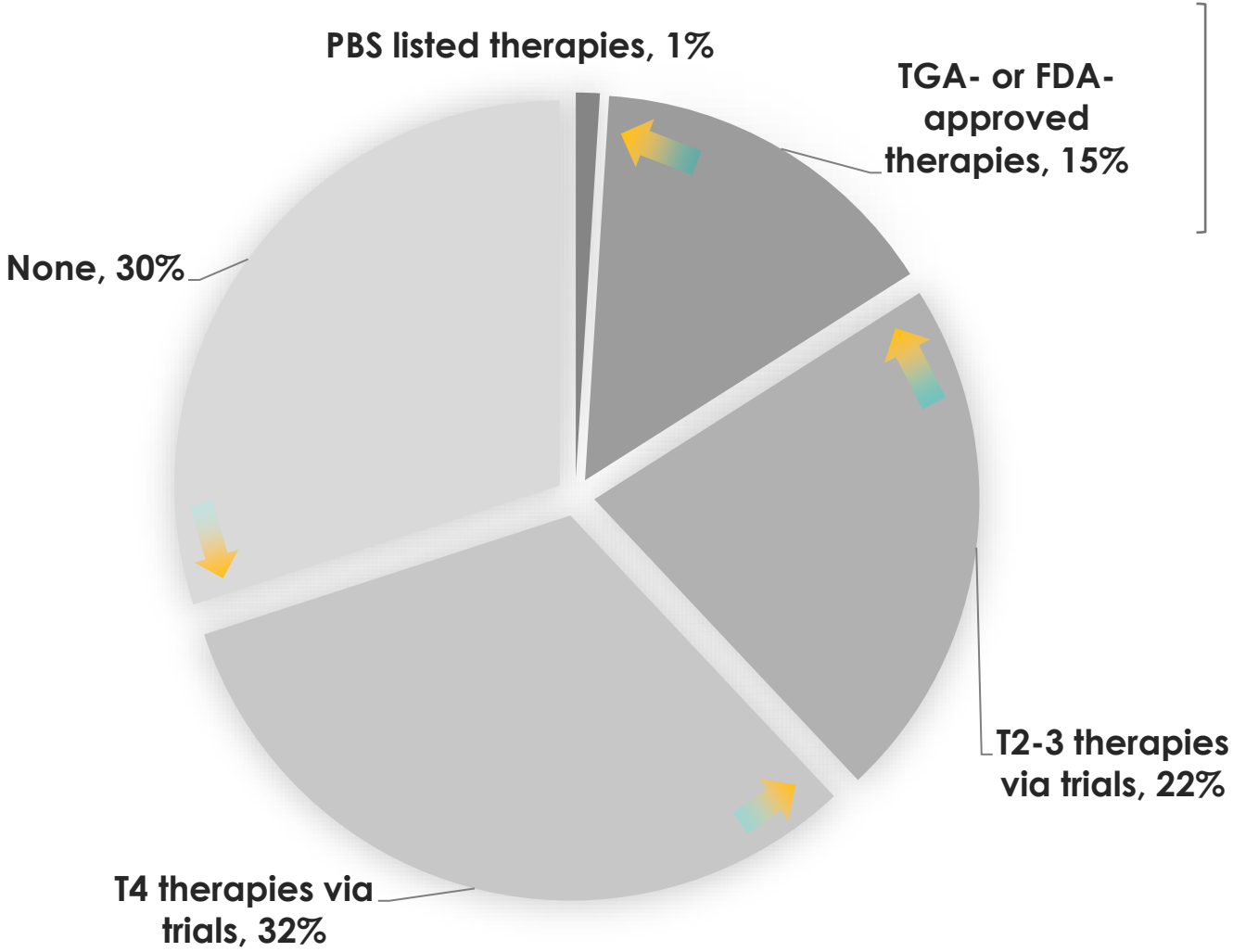
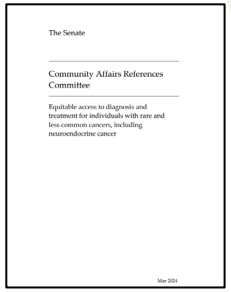


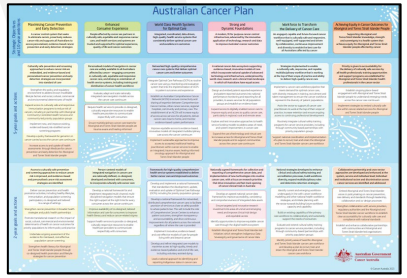
Mature therapies
Anticipated survival gain >14 months

Clinical trials
Anticipated survival gain 8 months

Health systems are challenged to deliver equity, certainty and sustainability in the face of rapid scientific advances

Public policy papers





Timely, equitable and affordable access

- Long timelines between TGA and PBS approvals exacerbated by accelerated drug development
- High unmet needs with growing and united community calls for social justice and structural equity

Strengthening HTA by reducing uncertainty

- Establish robust clinical safety, efficacy and cost-effectiveness data beyond traditional RCT paradigm
- Manage administrative and cost burden associated with increasing complexity of health innovation

Economic growth from R&D investment

- Drive economy through investment in manufacturing, clinical trials and commercialization of research
- Maintain Australia as a first-launch country for health innovation

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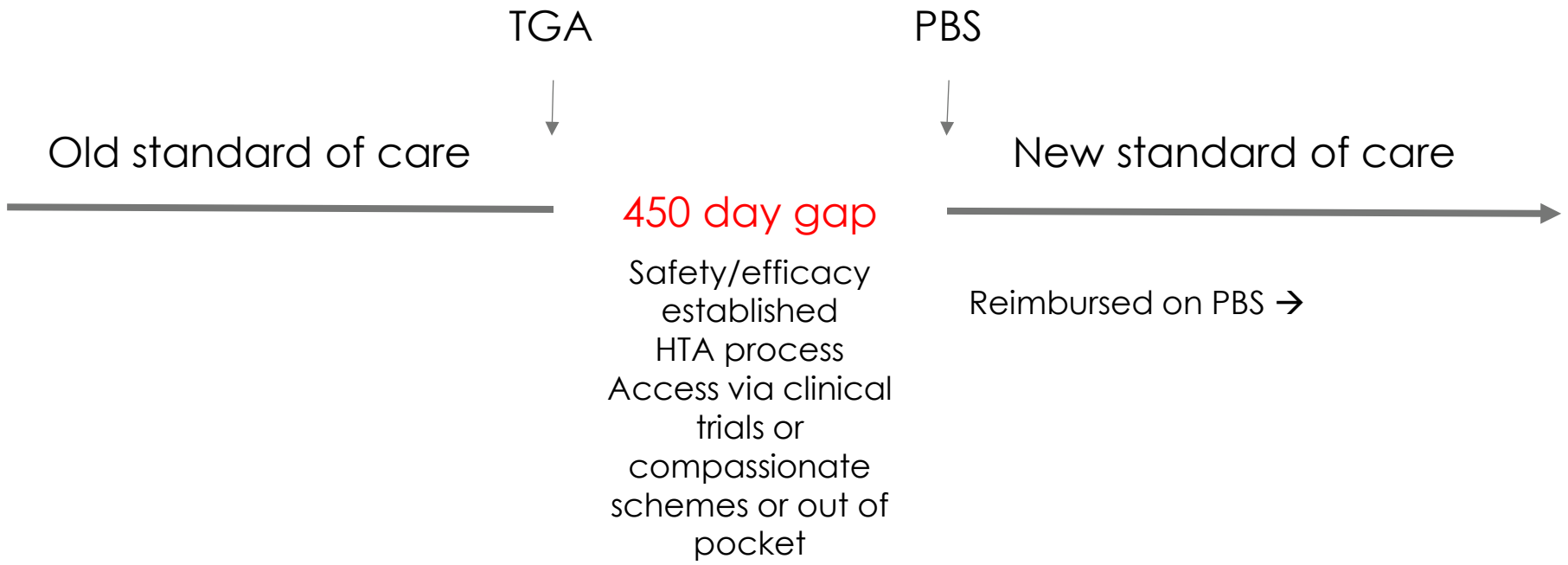
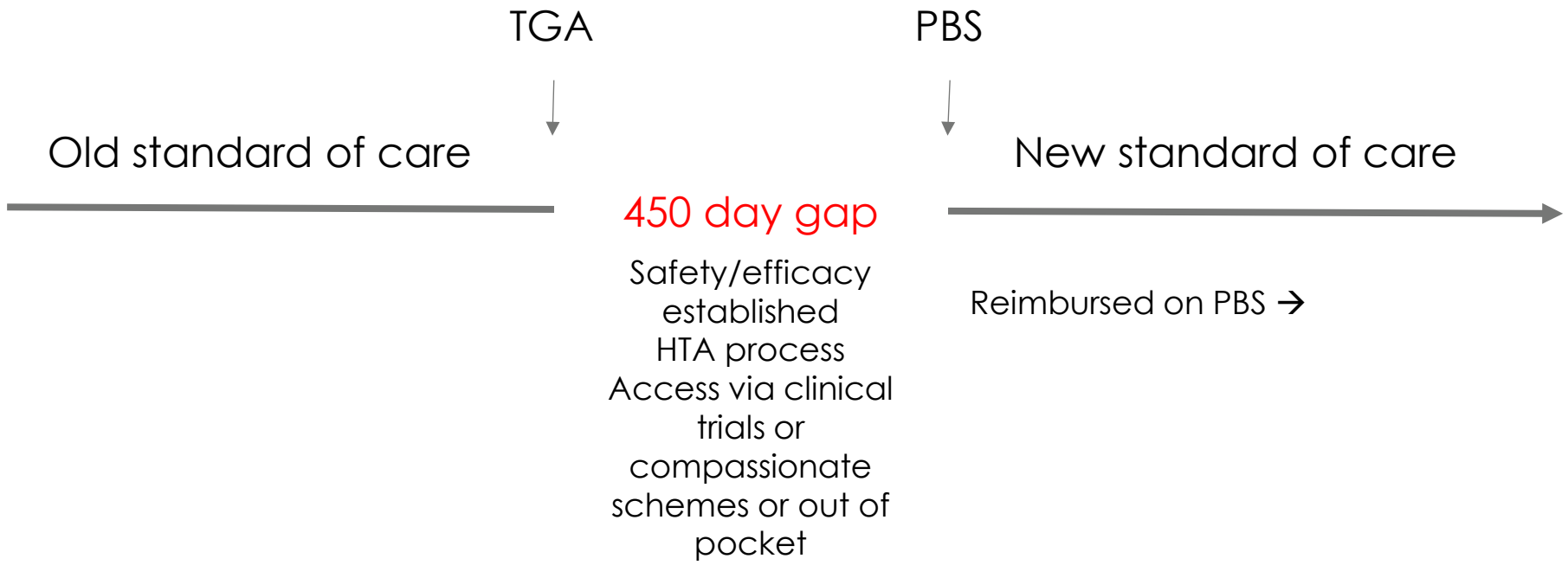
Sources: Senate Inquiry into equitable access to diagnosis and treatment for individuals with rare and less common cancers. (2023); Australian Cancer Plan, Cancer Australia (2023); Rare Cancers, Rare Diseases and Unmet need Clinical Trials initiative (2024), HTA Policy and Methods Review (2023), Intergenerational Report (2023); Medical Science Co-investment Plan (2024); MTP Connect Australia's Clinical Trial Sector (2024).


TGA
PBS
Old standard of care
New standard of care
450 day gap
Safety/efficacy established
HTA process
Access via clinical trials or compassionate schemes or out of pocket
Reimbursed on PBS →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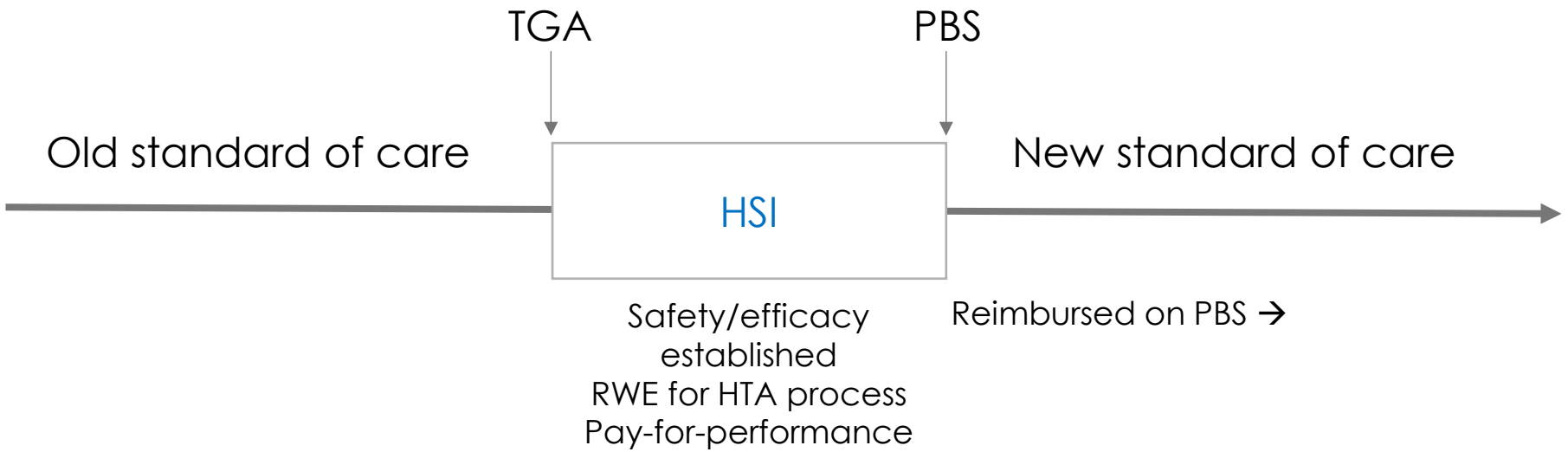
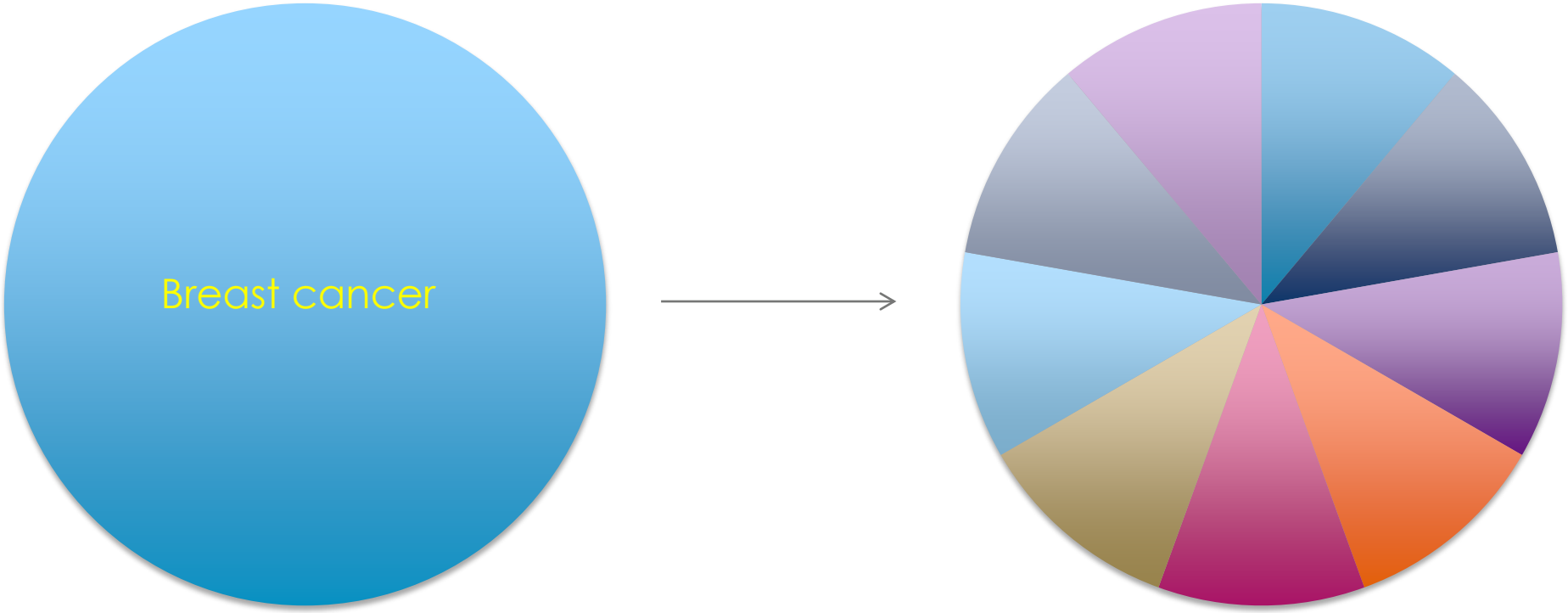
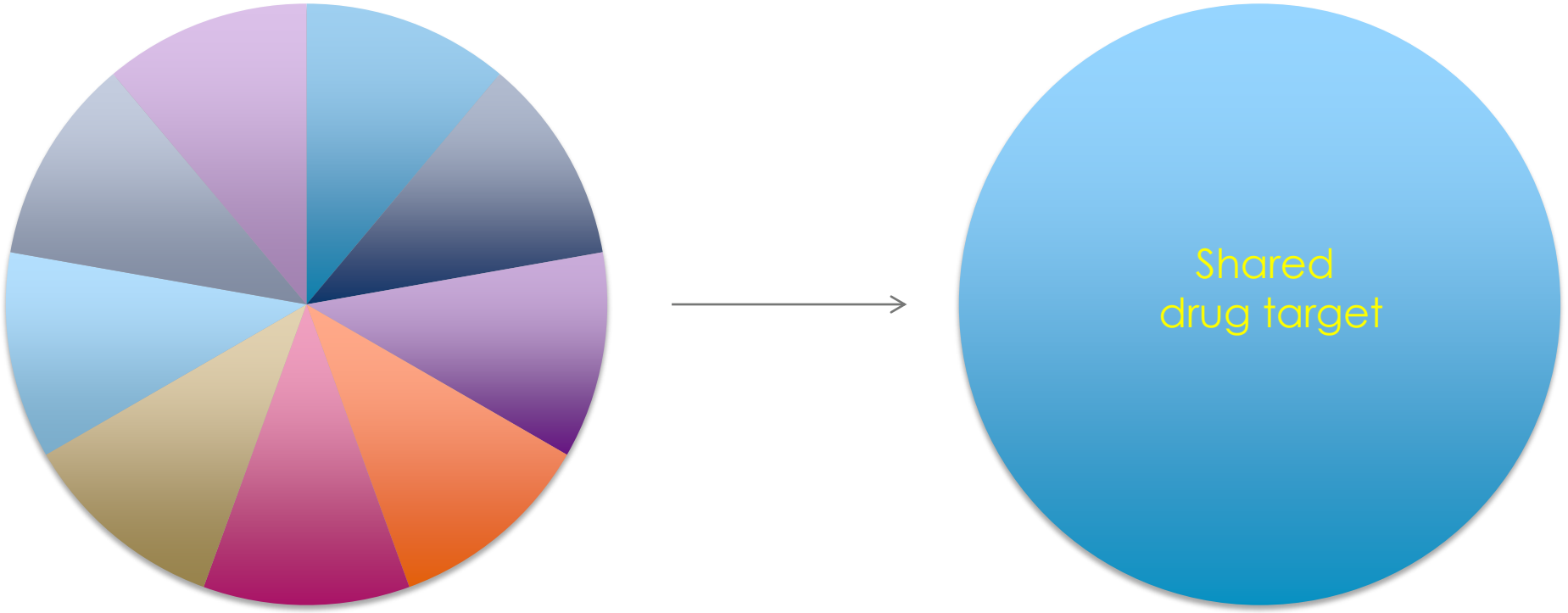

TGA
PBS
Old standard of care
HSI
New standard of care
Safety/efficacy established
RWE for HTA process
Pay-for-performance
Reimbursed on PBS →

Genomics is reshaping the cancer landscape



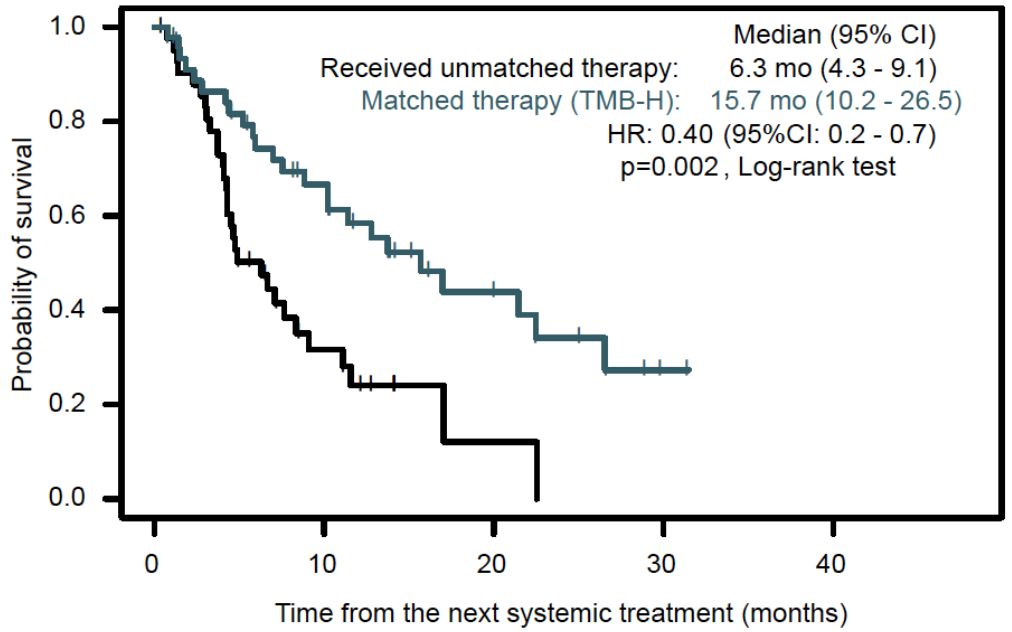
Genomics is reshaping the cancer landscape



Rare cancers

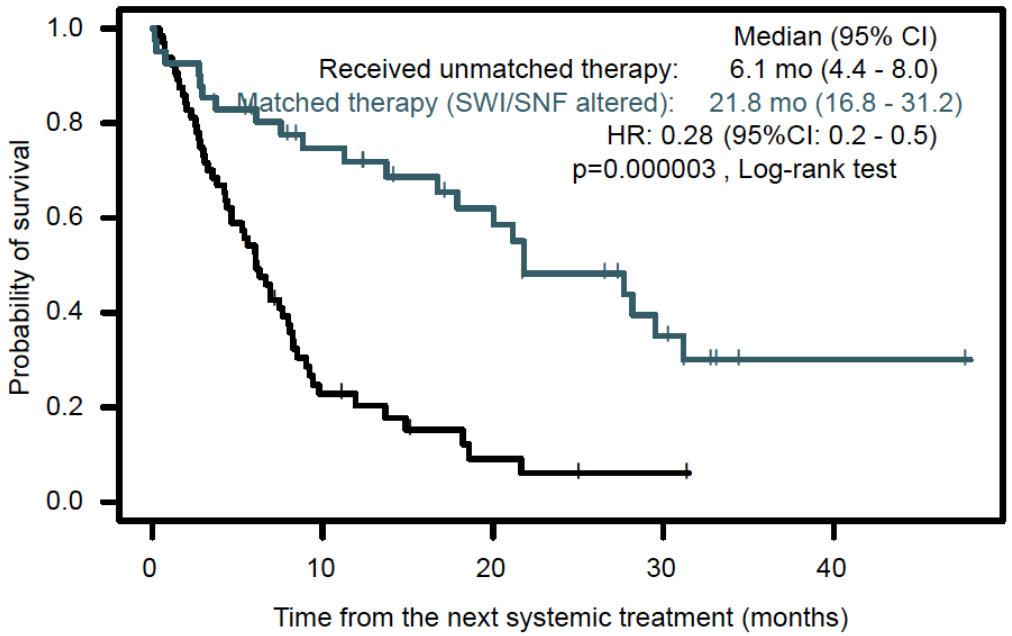
Pan-cancer biomarkers: a strategy for rare cancers

B.



No. at risk					
Unmatched	42	10	2	1	1
Matched	47	26	11	5	5

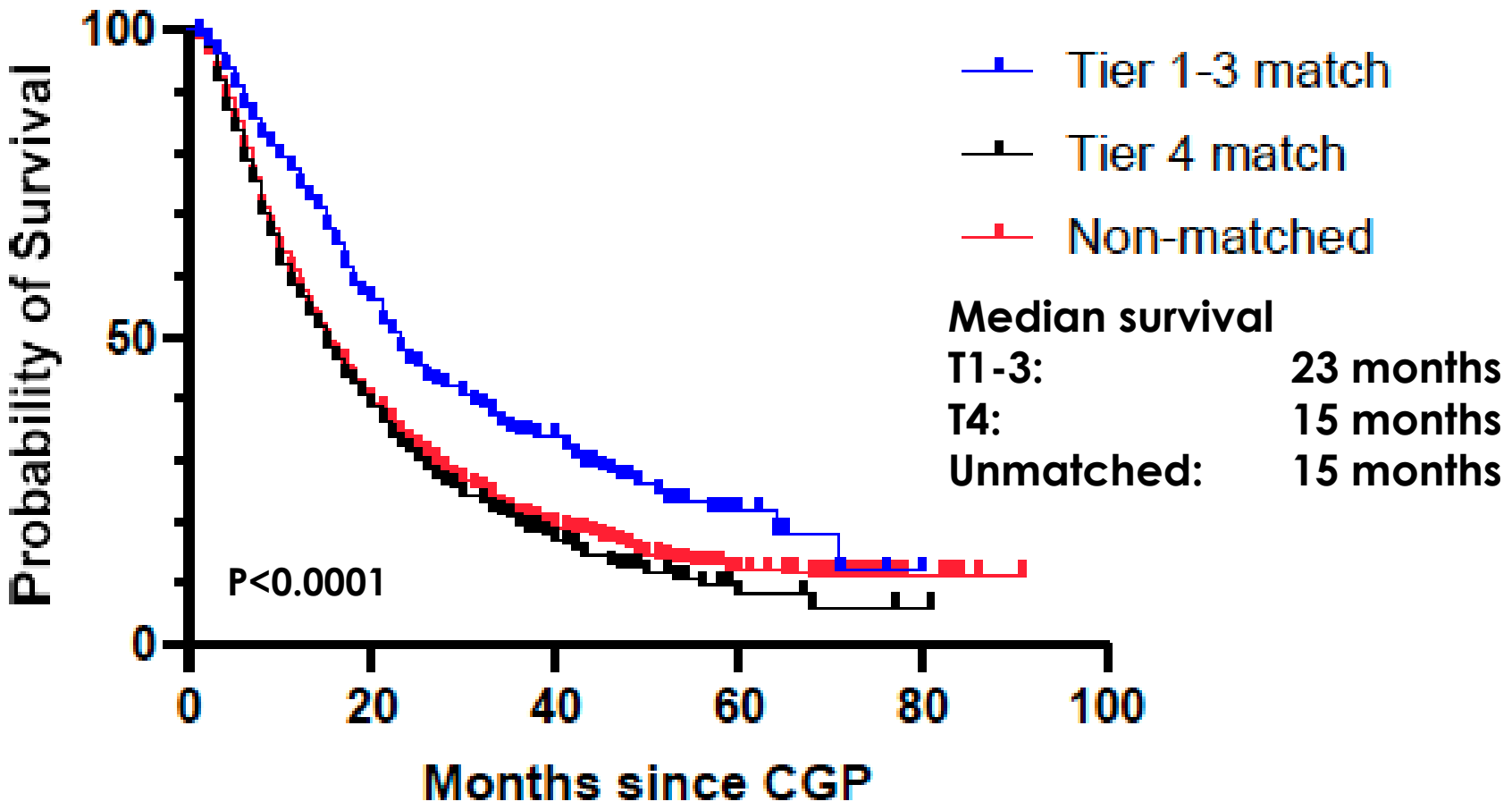
A.



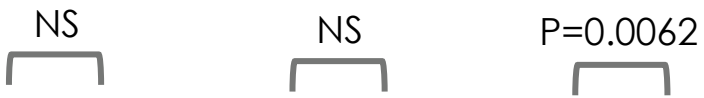
No. at risk					
Unmatched	65	13	4	3	3
Matched	41	27	19	9	7

Frank Lin

Outcomes for rare cancers in MoST



Health-related Quality of Life



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Health resource utilisation

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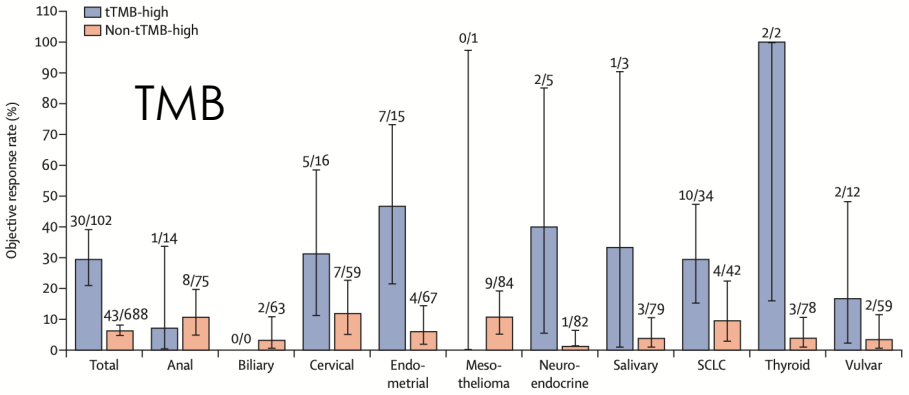
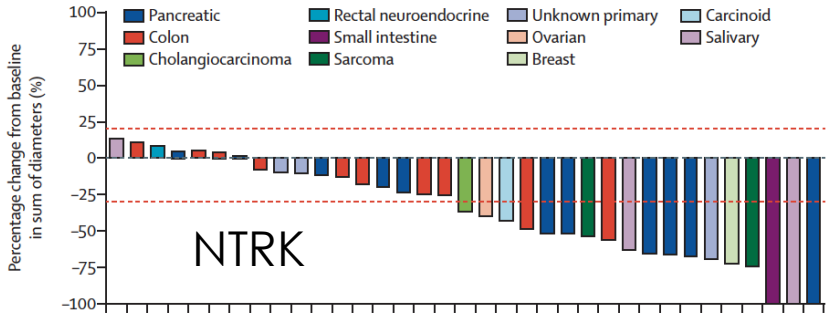
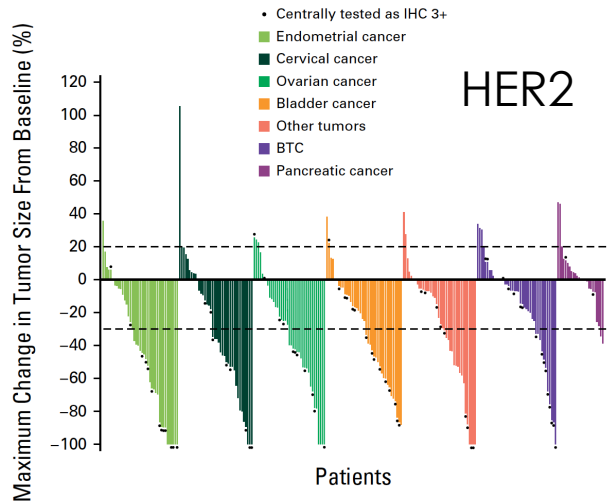
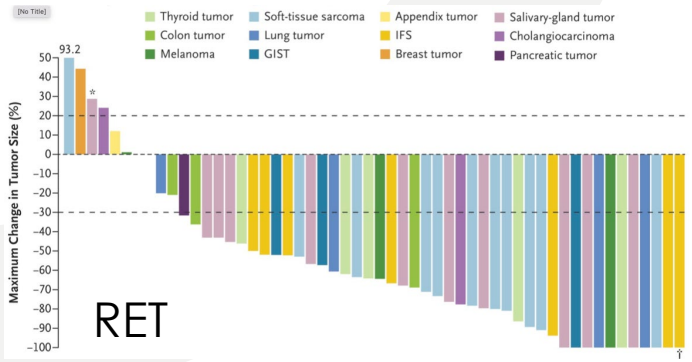
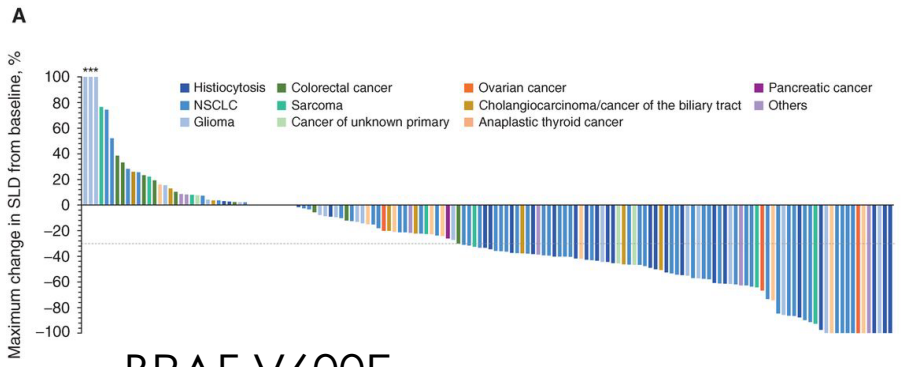
Cancer agnostic therapies

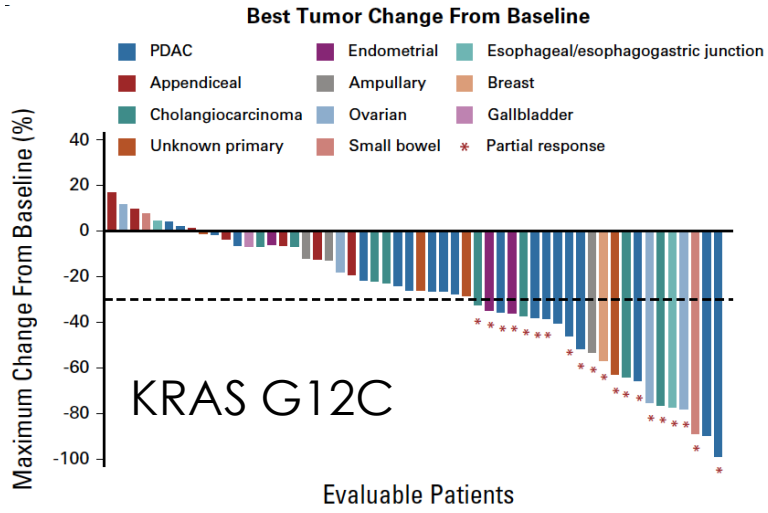












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Drilon et al, NEJM, 2018; Marabelle et al., Lancet Oncology, 2020; Subbiah et al., Cancer Discovery, 2020; Subbiah et al., Lancet, 2022; Bekaii-Saab et al., JCO, 2023

Courtesy of Roche

Biomarker-dependent drugs are becoming increasingly important in oncology

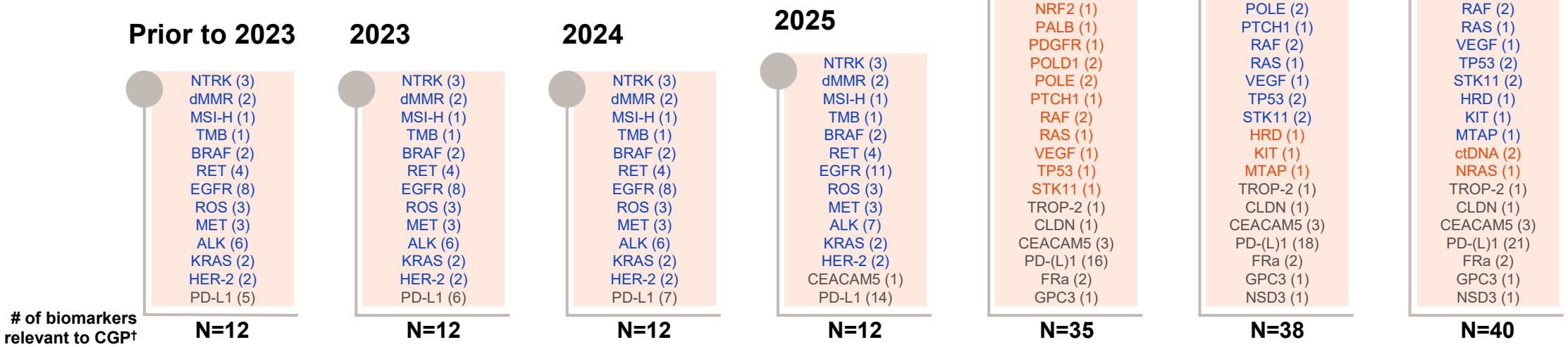
Biomarkers likely to have approved targeted therapies with tumour agnostic indications*

Analysis includes Phase 1/2, Phase 2 & Phase 3 trials initiated before April 1, 2023

= Established biomarker suitable for CGP

= New biomarker suitable for CGP

= Biomarker without immediate relevance for CGP (other detection methods more appropriate†)



*Multiple secondary sources used to cross validate information, including Trialtrove, clinicatrials.gov, EudraCT, ChiCTR; FDA approval timeline estimation based on Phase 3 primary completion date + 8 months review; analysis based on current Phase 1/2, Phase 2 and Phase 3 trials with inclusion criteria requiring patient selection based on alterations to specific biomarkers; assumption made that all ongoing trials will lead to approval; "biomarker" defined as any biological molecule found in blood or tissues that has either prognostic or predictive significance in cancer treatment, and for which the effectiveness of a therapy in a patient population defined by the detection of this molecule or molecular aberration is currently being tested or has already been approved. †Biomarkers without immediate relevance for CGP are primarily those for which detection of protein expression via IHC or other immunology approaches is more appropriate (e.g., PD-L1). CGP: comprehensive genomic profiling; ctDNA: circulating tumour DNA; dMMR: DNA mismatch repair deficiency; HRD: homologous recombination deficiency; IHC: immunohistochemistry; MSI-H: microsatellite instability-high; NSCLC: non-small cell lung cancer; TMB: tumour mutational burden.

Currently, 7 drug targets which are FDA and TGA-approved for tumour-agnostic indications

TGA-approved pan-cancer therapies and their targets

Biomarker / target	Frequency of target*	ORR (%)	Approved drug(s)	Year of FDA approval	Current Australian subsidy
dMMR	1.03%	40%	Pembrolizumab	2017	No submission to PBAC for tumour agnostic indication
			Dostarlimab	2022	As above
MSI-High	1.12%	40%	Pembrolizumab	2017	As above
TMB-high	7.91%	33%	Pembrolizumab	2020	As above
$BRAF^{V600E}$	1.62%	41%	Dabrafenib + Trametinib	2022	2019 (PBS) No submission to PBAC for tumour agnostic indication
RET fusions	0.08%	44%	Selpercatinib	2022	No
NTRK fusions	0.23%	75%	Larotrectinib	2018	2022 (PBS) for paediatric NTRK tumours
			Entrectinib	2019	No submission to PBAC for tumour agnostic indication
HER2 amp.	2.71%	61%	Deruxtecan	2024	Being submitted to TGA

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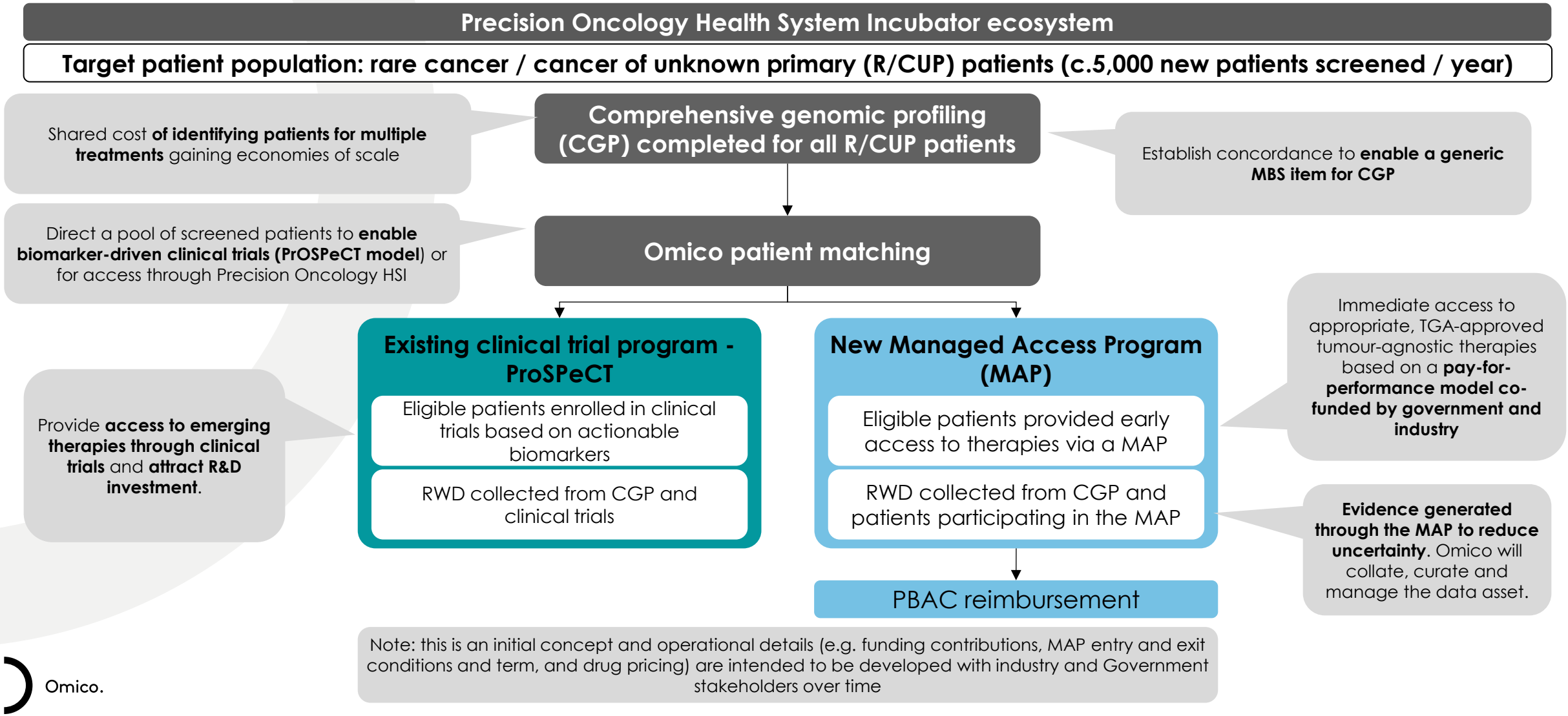
Note: * Proportion of patients screened by Omico to date that exhibit biomarker Source: Gouda MA, Nelson BE, Buschhorn L, Wahida A, Subbiah V. Tumor-Agnostic Precision Medicine from the AACR GENIE Database: Clinical Implications. Clin Cancer Res. 2023;29(15):2753-2760. doi:10.1158/1078-0432.CCR-23-0090. Also: Omico data on file.

The Precision Oncology – HSI: a unified, contained ecosystem for evaluating complex health innovations as routine care



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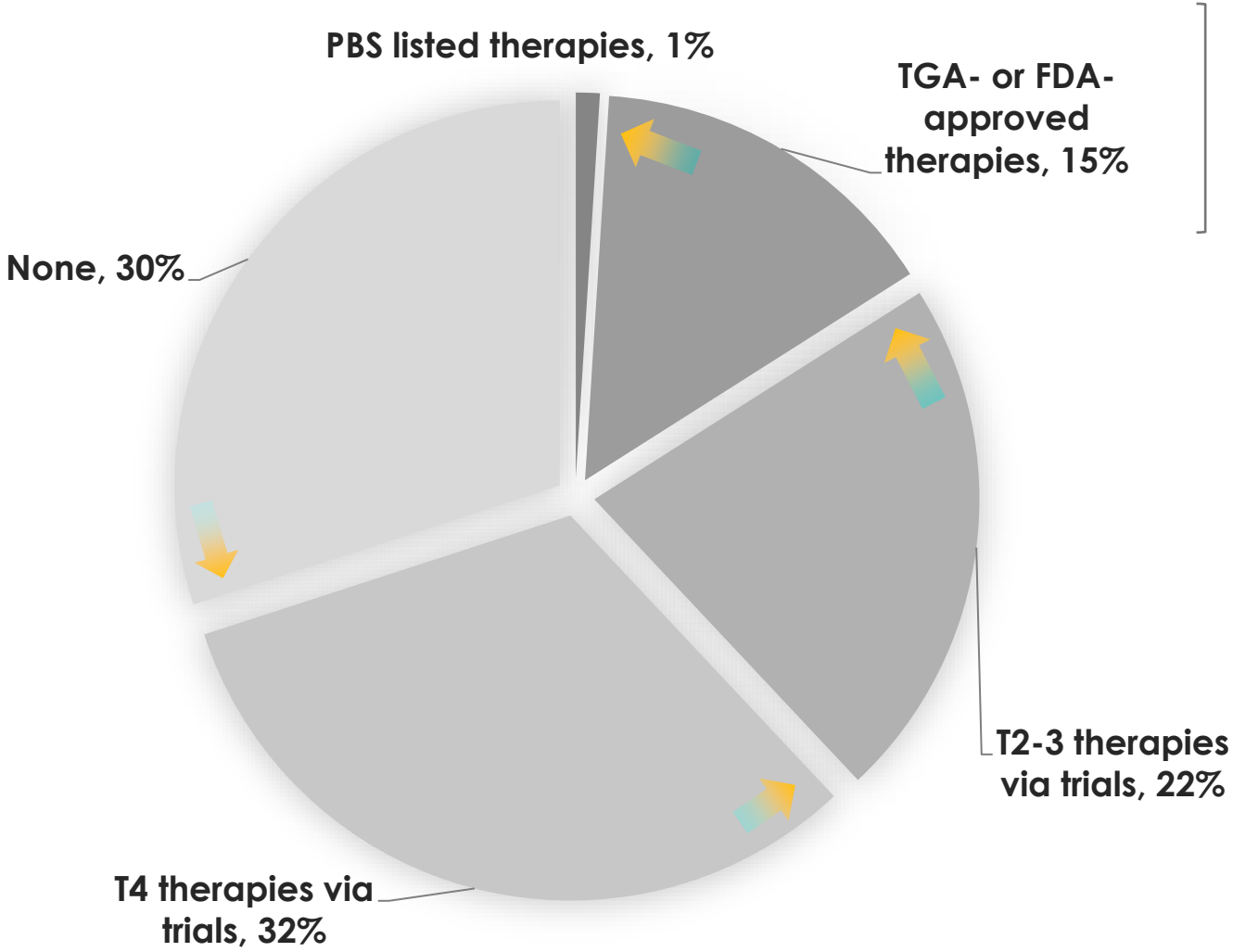
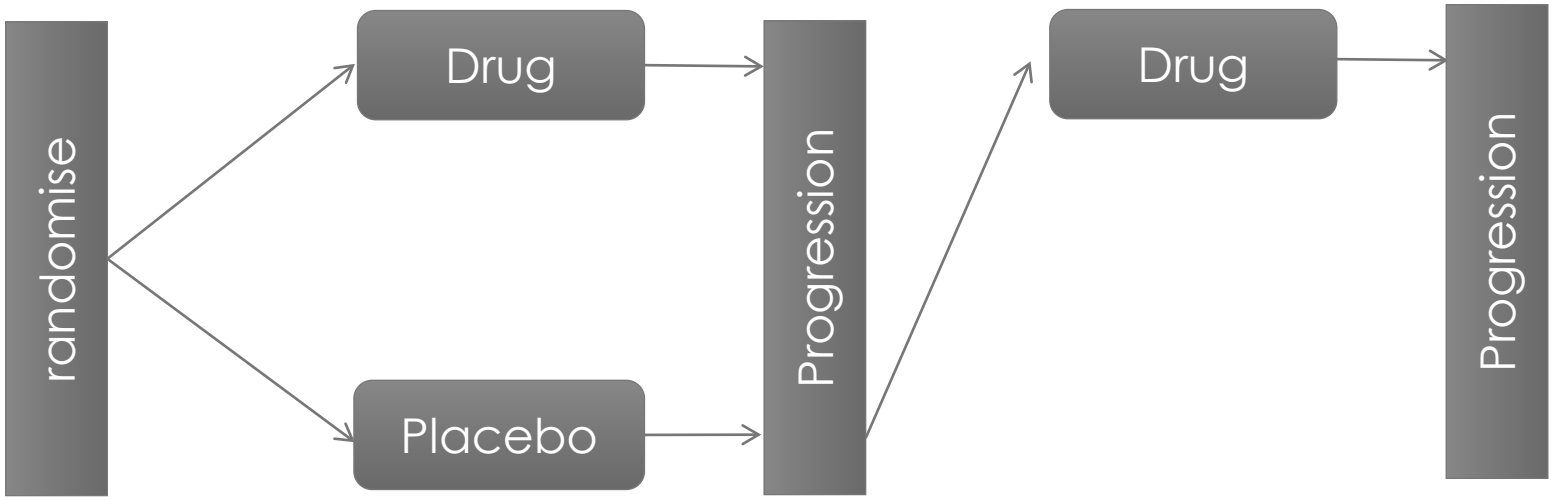


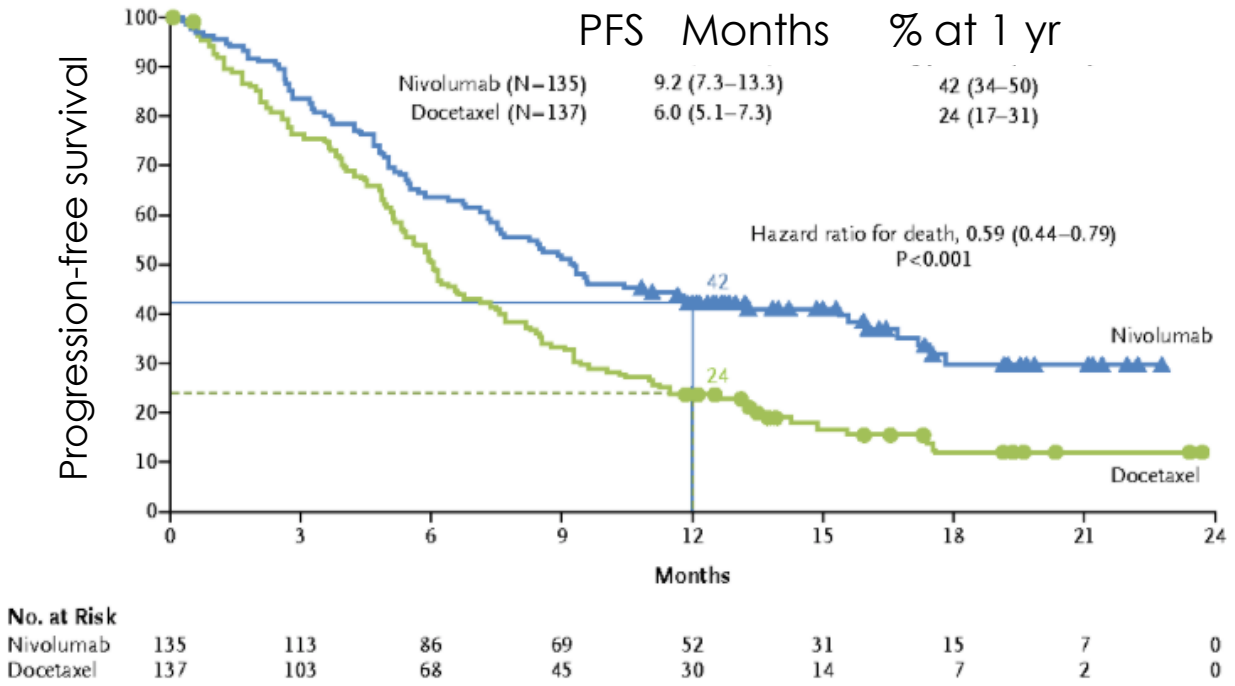
Mature therapies
Anticipated survival gain >14 months

Clinical trials
Anticipated survival gain 8 months

NSCLC



PFS Months % at 1 yr



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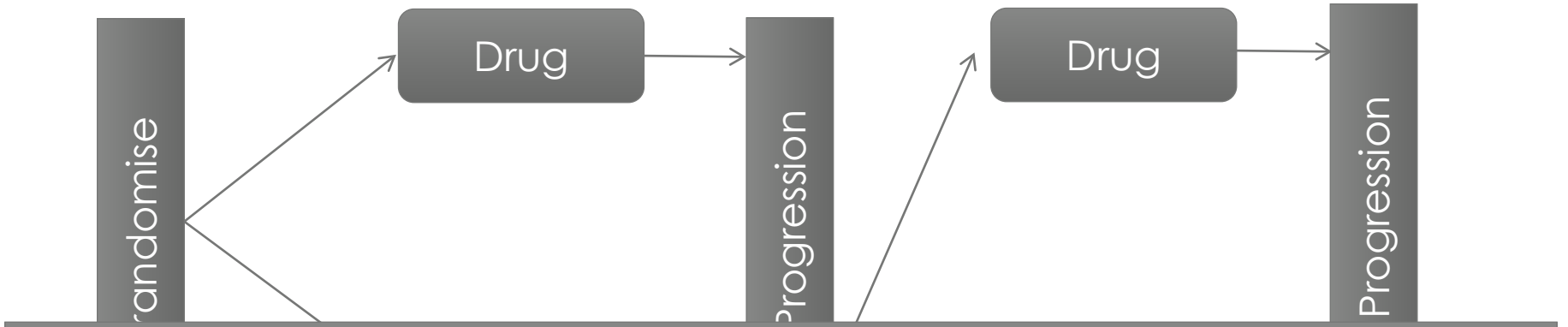
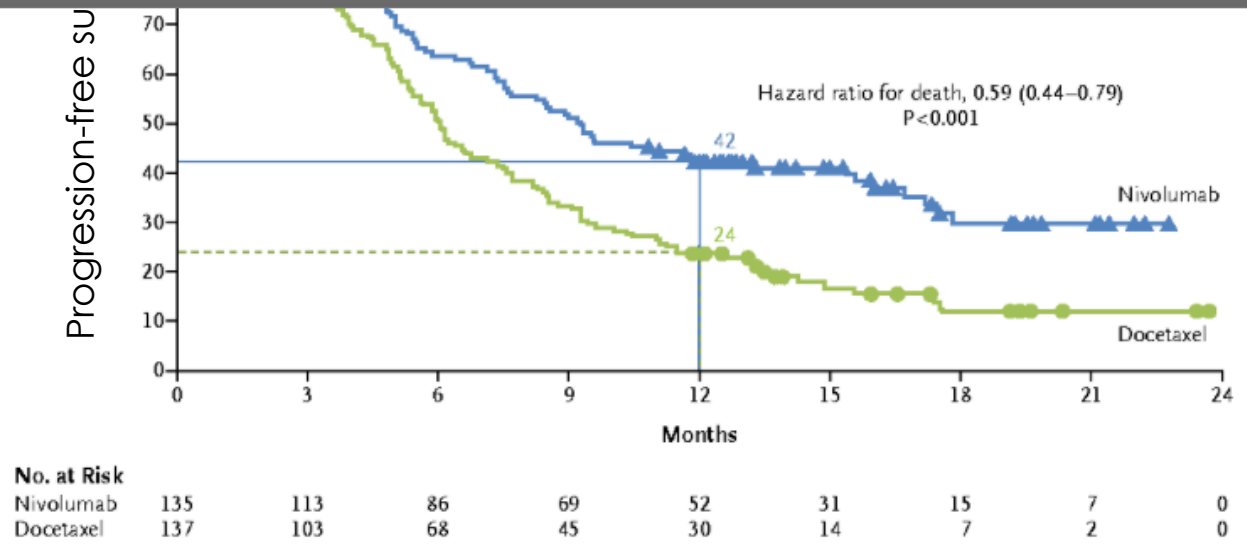
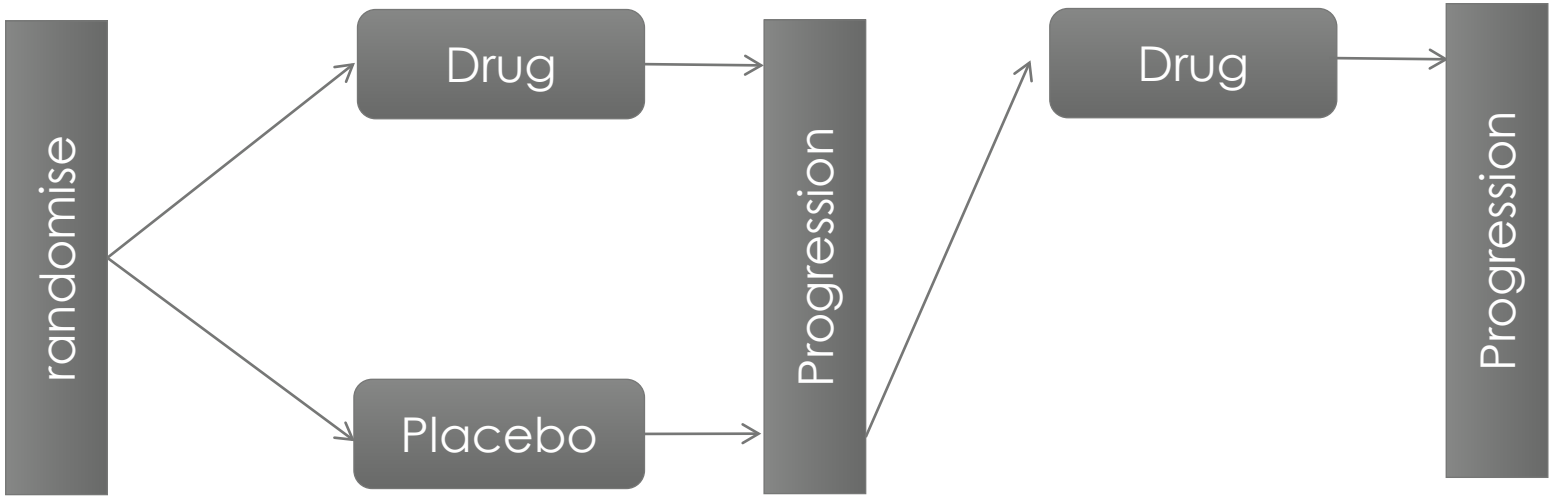
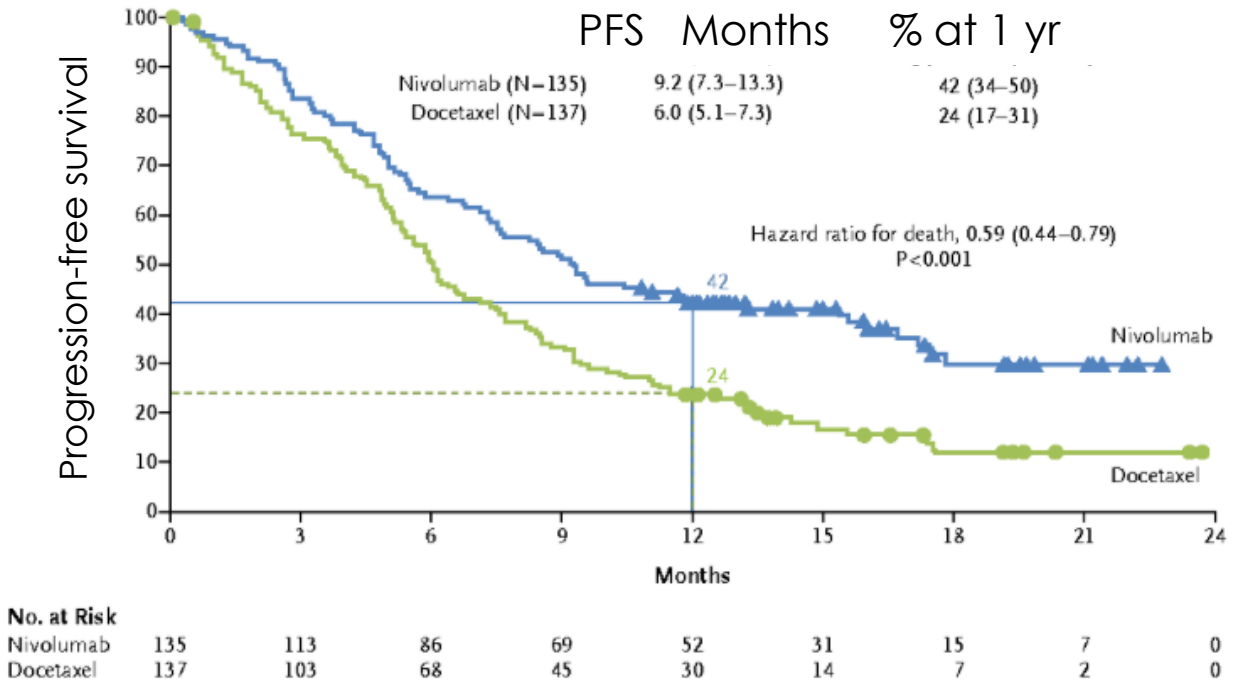


$1B PBS reimbursement and drug access for 1,000 Australians with NSCLC



Rare pan-cancer
TMB high





Rare pan-cancer
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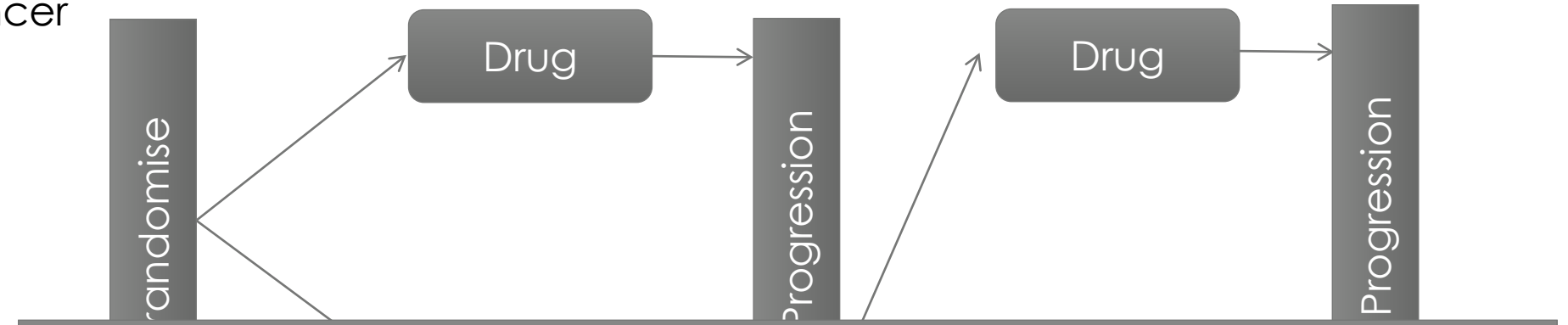
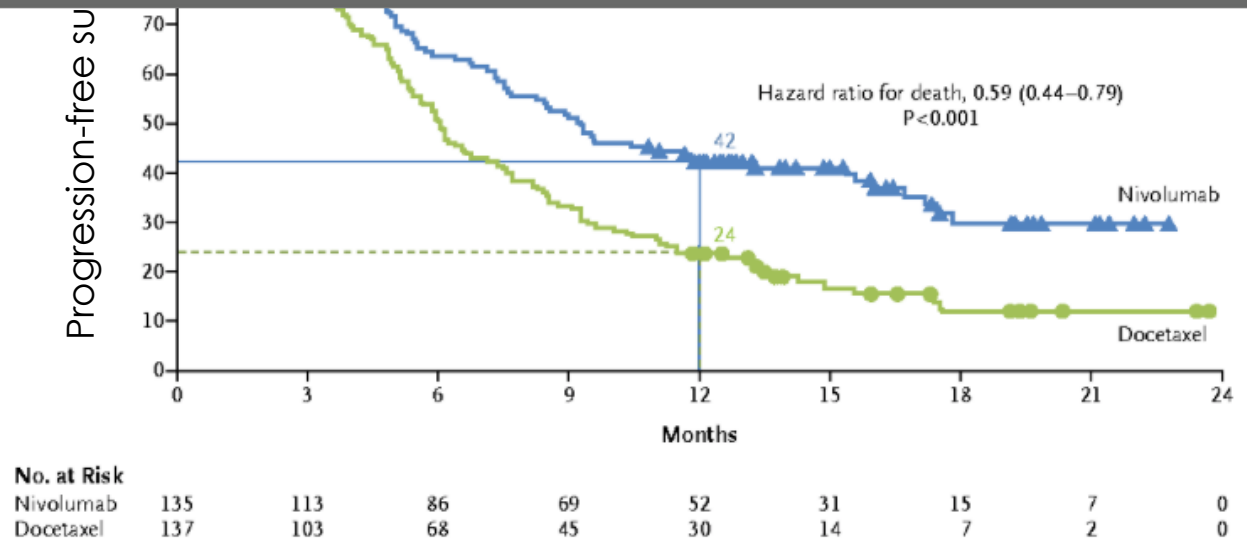
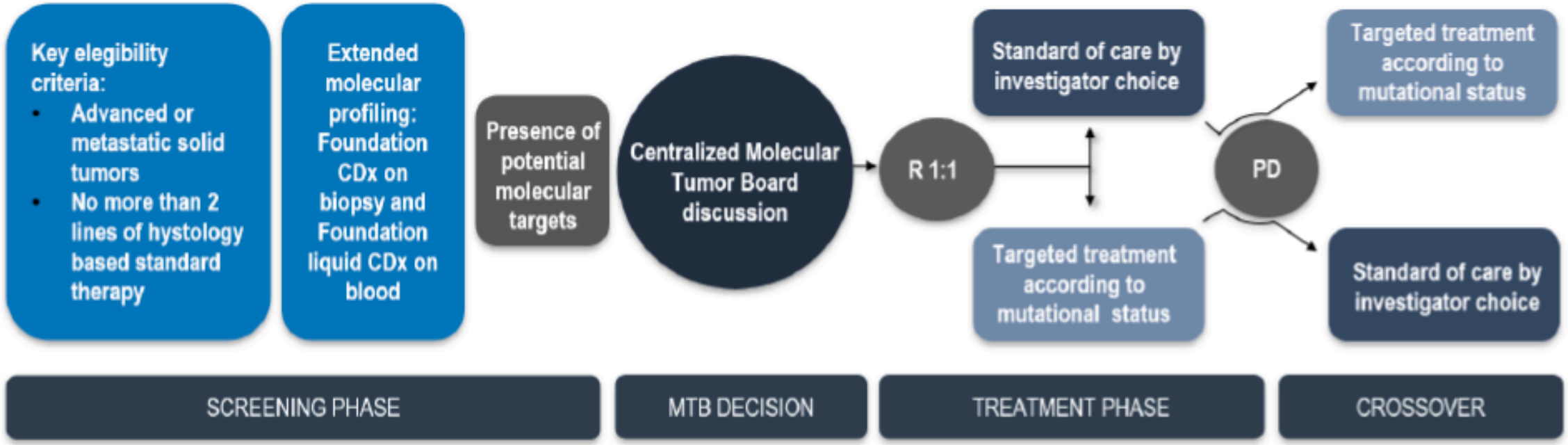


1,200 Australians with rare TMB-high cancers: we don't randomise pan-cancer



The ROME Trial:

A Randomized, Multi-basket, Phase 2, Multicentric Trial (NCT04591431)



- ✓ For each patient, we performed CGP using NGS with Foundation One, both on tissue samples and liquid biopsies. Historical samples were allowed but had to be collected within three months of patient screening
- ✓ Once molecular alterations were identified in tumor tissue or liquid biopsy, that could potentially be targeted by drugs available within the study the clinical case was reviewed by the Molecular Tumor Board (MTB)
- ✓ The MTB then decided whether to enroll the patient and proceed with randomization or to classify the case as a screening failure
- ✓ At PD crossover was planned

MTB: Molecular Tumor Board; PD: progression of disease.

PRIMARY ENDPOINT: ORR
SECONDARY ENDPOINT: PFS, TTF, TTNT, safety profile ,OS.
EXPLORATORY ENDPOINTS : PFS in homogenous subgropus of pts

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The ROME trial: Available targeted treatments and pathways

Targeted Therapy	Target pathways
Erlotinib	EGFR mutations
Trastuzumab, pertuzumab, TDM1, lapatinib	ERBB2 amplification/mutations
Everolimus	mTOR mutations, AKT mutations
Vemurafenib, cobimetinib	BRAF mutations
Alectinib, brigatinib	ALK traslocations, RET alterations
Pralsetinib*, selpercatinib*	RET alterations
Palbociclib	CDK4/6, CDKN2A/B alterations
Ponatinib	Bcr-abl traslocations
Vismodegib	SMO/PTCH1 mutations
Itacitinib	JAK mutations
Pemigatinib	FGFR1/2/3 alterations
Ipatasertib, alpelisib*	Pi3k, AKT, PTEN alterations
Entrectinib*	NTRK1/2/3 fusions, ROS1
Tepotinib	METex14, MET alterations
Talazoparib	BRCA 1/2 mutations, HRD
Immunotherapy	**Biomarkers**
Nivolumab, ipilimumab, atezolizumab	MSI, high TMB**

* Drugs included in the V4 protocol amendment in 10/2022

** high TMB defined as >10 mut/mb in solid and/or liquid NGS

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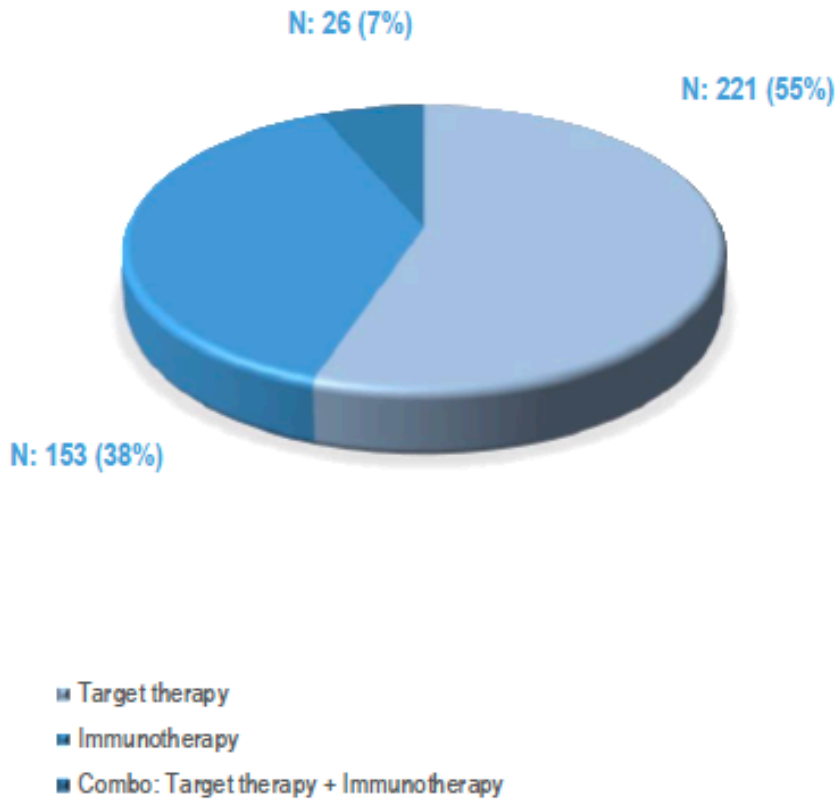
The ROME trial: treatments assigned

Nov 2020 – Aug 2023:
N: 1794 screened patients

N: 897 patients discussed in MTB

127 weekly MTB discussions

400 randomized patients



Alteration group	Therapy assigned	n
ALK/ROS1	Alectinib	4
	Entrectinib	2
Cell cycle	Palbociclib	5
Erb	TDM1	31
	Pertuzumab + Trastuzumab	12
	Trastuzumab + Lapatinib	11
	Pertuzumab + TDM1	2
	TDM1 + Atezolizumab	1
	Trastuzumab + Everolimus	1
FGFR	Pemigatinib	33
HRD	Talazoparib	7
JAK/STAT	Itacitinib	1
MET	Tepotinib	1
Other	Everolimus	2
PIK3CA/AKT/PTEN	Ipatasertib	66
	Atezolizumab + Ipatasertib	24
	Alpelisib	6
	Everolimus	3
PTCH1	Vismodegib	2
RAS/RAF/MAPK	Vemurafenib + Cobimetinib	16
	Cobimetinib	14
	Cobimetinib + Atezolizumab	1
RET	Pralsetinib	1
	Selpercatinib	1
Signature	Ipilimumab + Nivolumab	148
	Nivolumab	5

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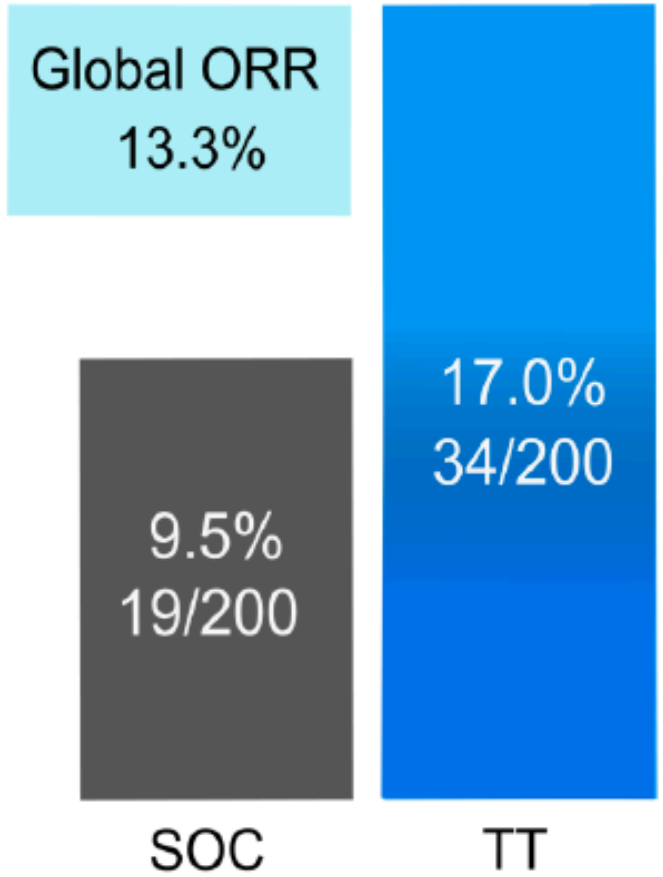
The ROME trial: characteristics of ITT population

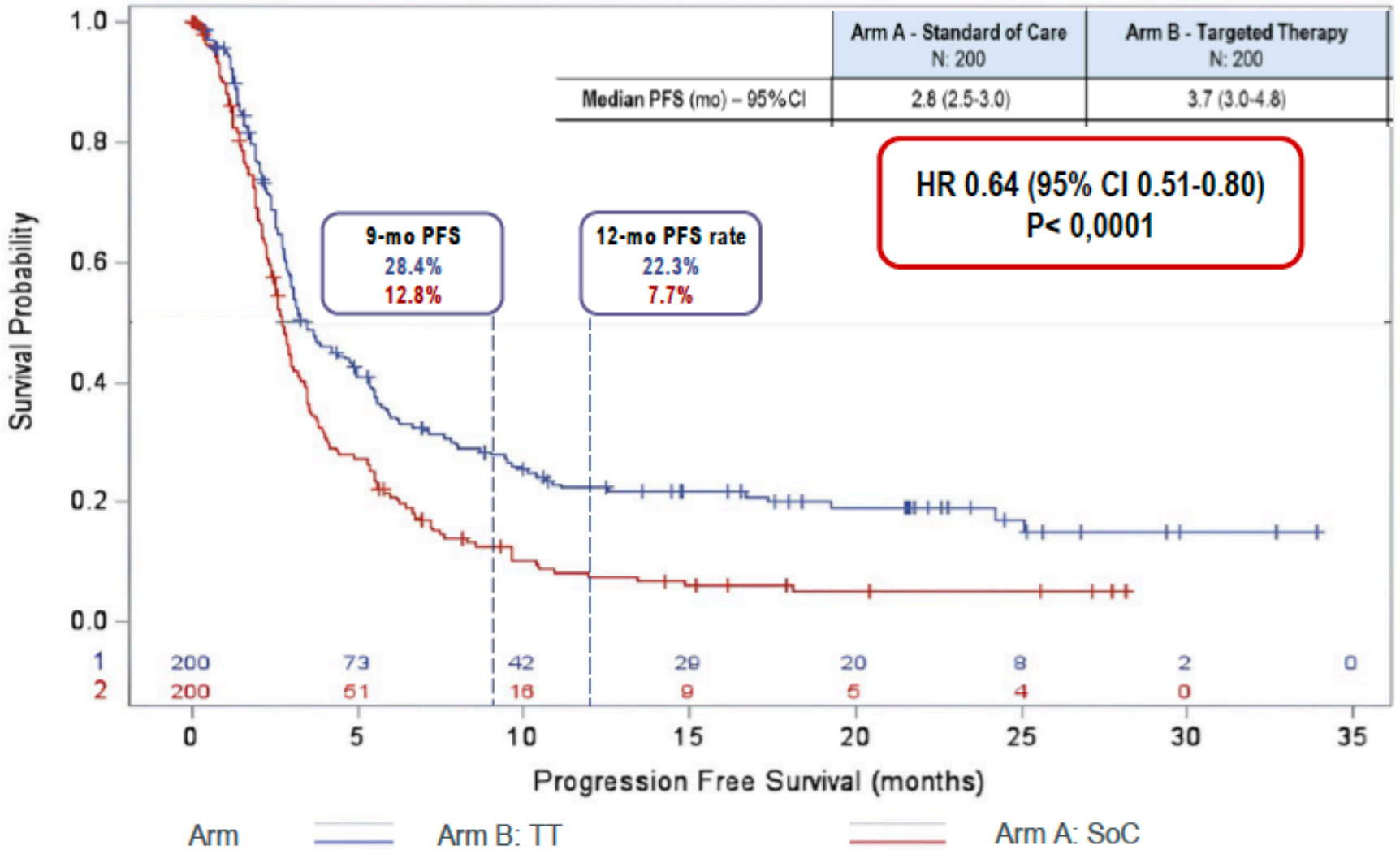
Characteristic	Overall N: 400 (%)	Arm A: Standard of Care N: 200 (%)	Arm B: Targeted Therapy N: 200 (%)
Age (years)			
median (range)	61 (22-85)	60 (34-84)	62 (22-85)
Gender			
Male	192 (48)	100 (50)	92 (46)
Female	208 (52)	100 (50)	108 (54)
Ethnicity			
Caucasian	393 (98)	197 (98)	196 (98)
Oriental	2 (0.5)	0	2 (1)
Hispanic	3 (0.8)	2 (1)	1 (0.5)
Afro-american	1 (0.1)	1 (1)	0
Other	1 (0.1)	0	1 (0.5)
Primary tumor			
Colorectal	65 (16)	31 (16)	34 (17)
Breast	39 (10)	19 (9)	20 (10)
Gastric	36 (9)	19 (9)	17 (9)
Glioblastoma	36 (9)	21 (10)	15 (7)
Biliary tract/gallbladder	36 (9)	10 (5)	26 (12)
NSCLC	35 (9)	18 (9)	17 (9)
Ovarian	18 (5)	8 (4)	10 (5)
Pancreatic	17 (4)	10 (5)	7 (4)
melanoma	13 (3)	8 (4)	5 (2)
anus	11 (2)	5 (3)	6 (3)
Other	94 (24)	51 (26)	43 (22)
Enrollment line			
Second	204 (51)	99 (50)	105 (52)
Third	196 (49)	101 (50)	95 (48)

Primary endpoint: ORR in ITT population

Best response	Arm A Standard of Care N: 200 (%)	Arm B Targeted Therapy N: 200 (%)	p value
CR	0	5 (2.5%)	
PR	19 (9.5%)	29 (14.5%)	
SD	35 (17.5%)	36 (18.0%)	
PD	147 (73.0%)	130 (65.0%)	
ORR	**9.5% [5.8-14.4]**	**17.0% [12.1-22.9]**	**0,027**



Secondary endpoint: PFS in ITT population



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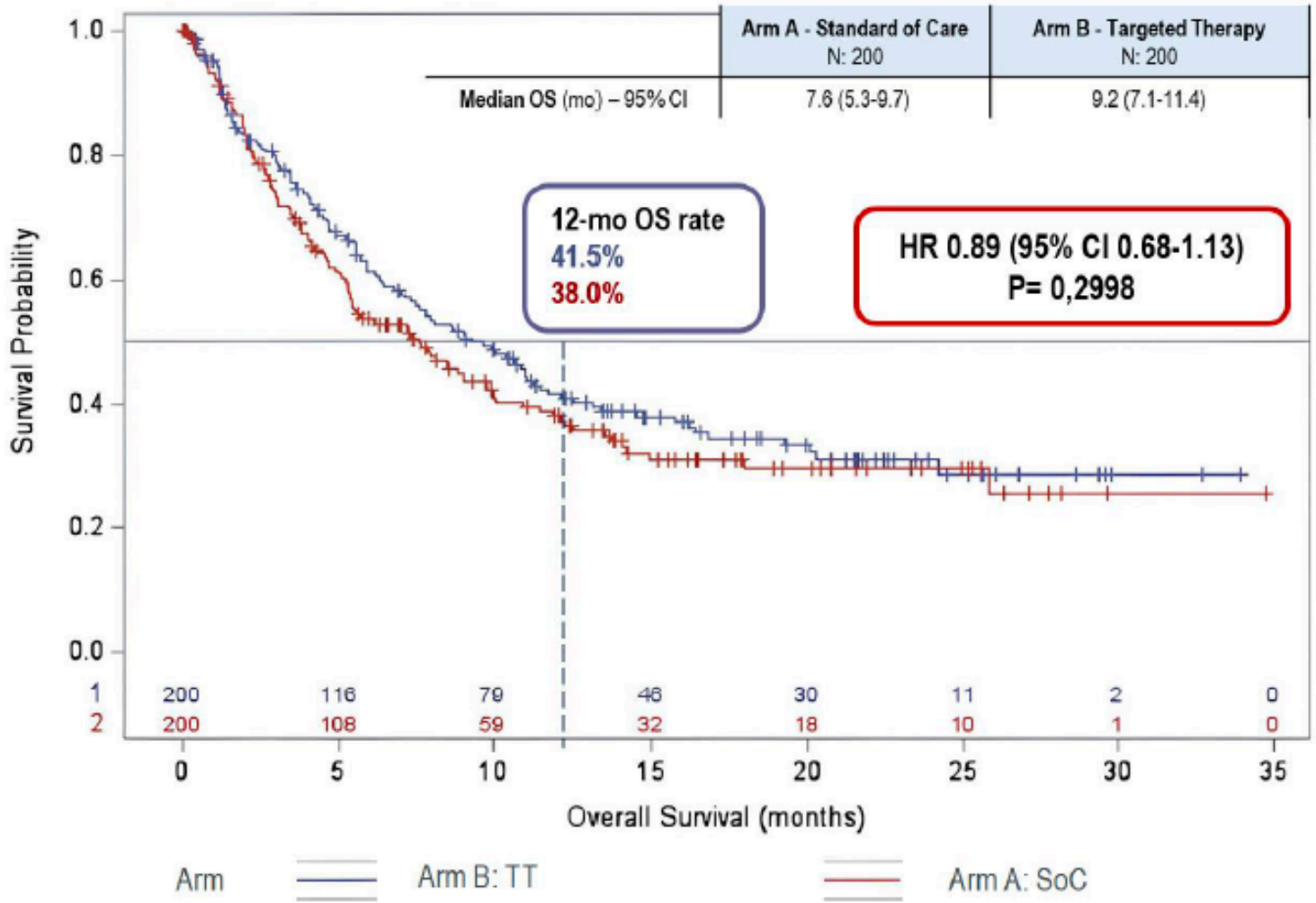
Secondary endpoint: OS in ITT population



52% SOC pts crossover

Omico.

Thank you!