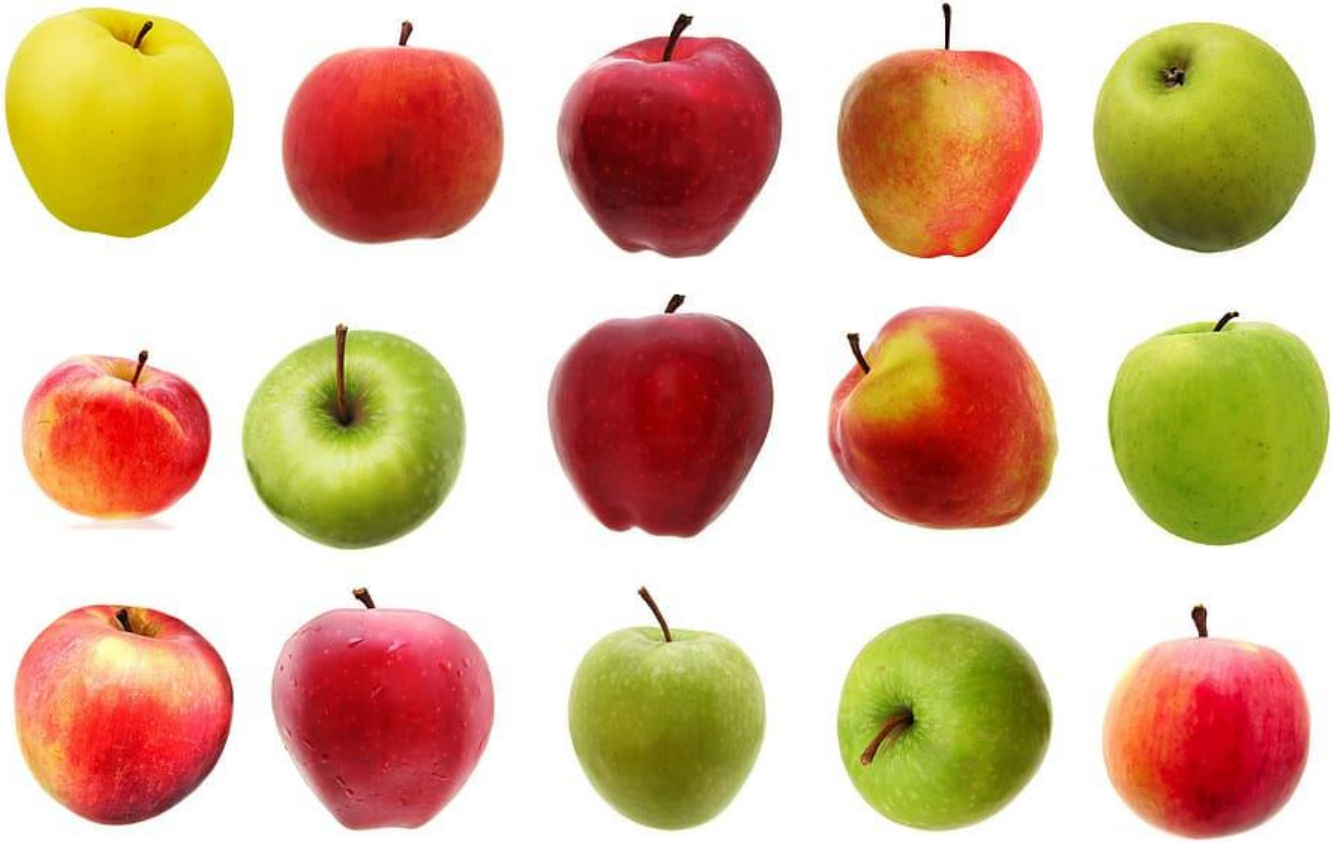
The Q-IMPROvE (Queensland- IMplementation of PRecision Oncology in brEast cancer) pilot study.

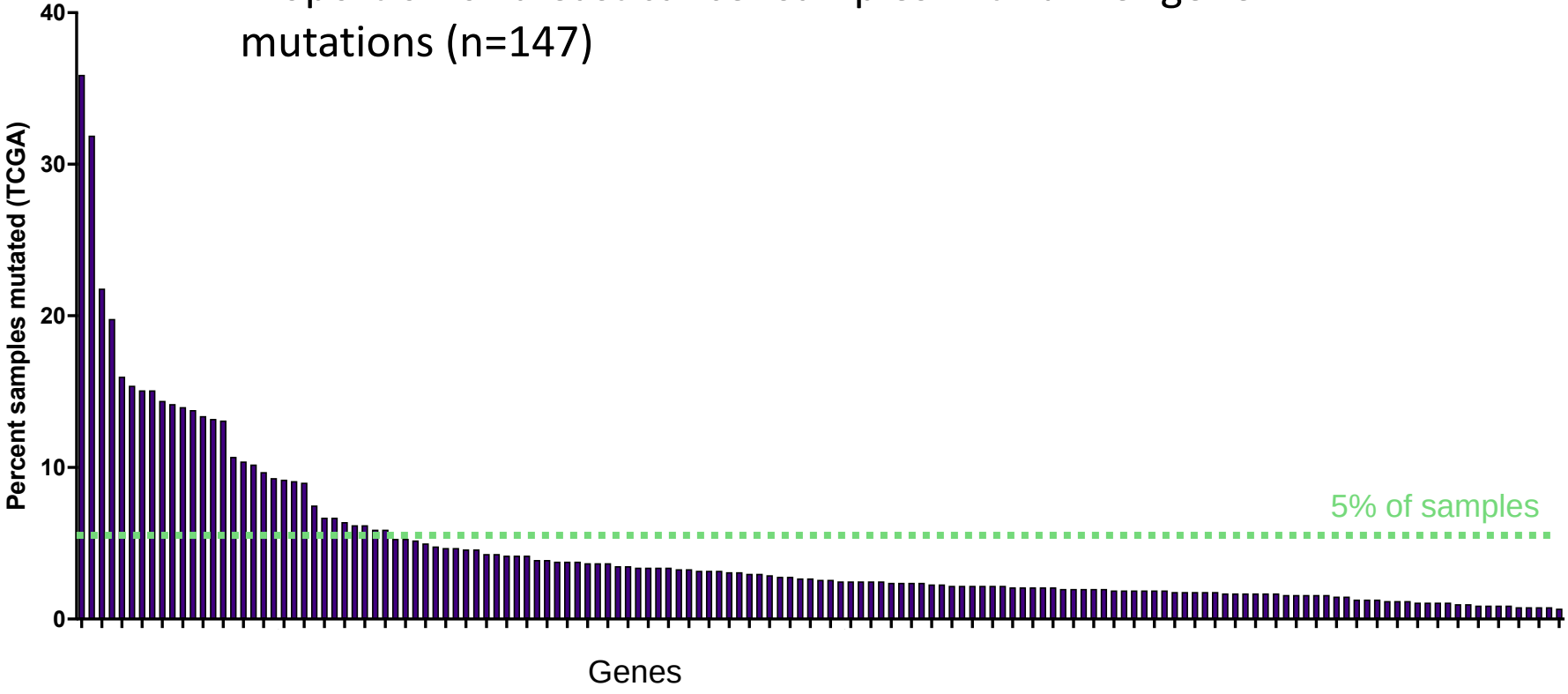
Dr Amy McCart Reed
UQCCR

Comparing apples with apples



No two breast cancer genomes are the same

Proportion of breast cancer samples with driver gene mutations (n=147)



Is Breast cancer ready for genomic medicine?

Feature	Actionability
Mutations (n=147) →	Familial cancer; drugs
TMB →	>10 mut/Mb = pembrolizumab
CNA →	*ERBB2; CCND1*
Mutation signatures →	PARPi

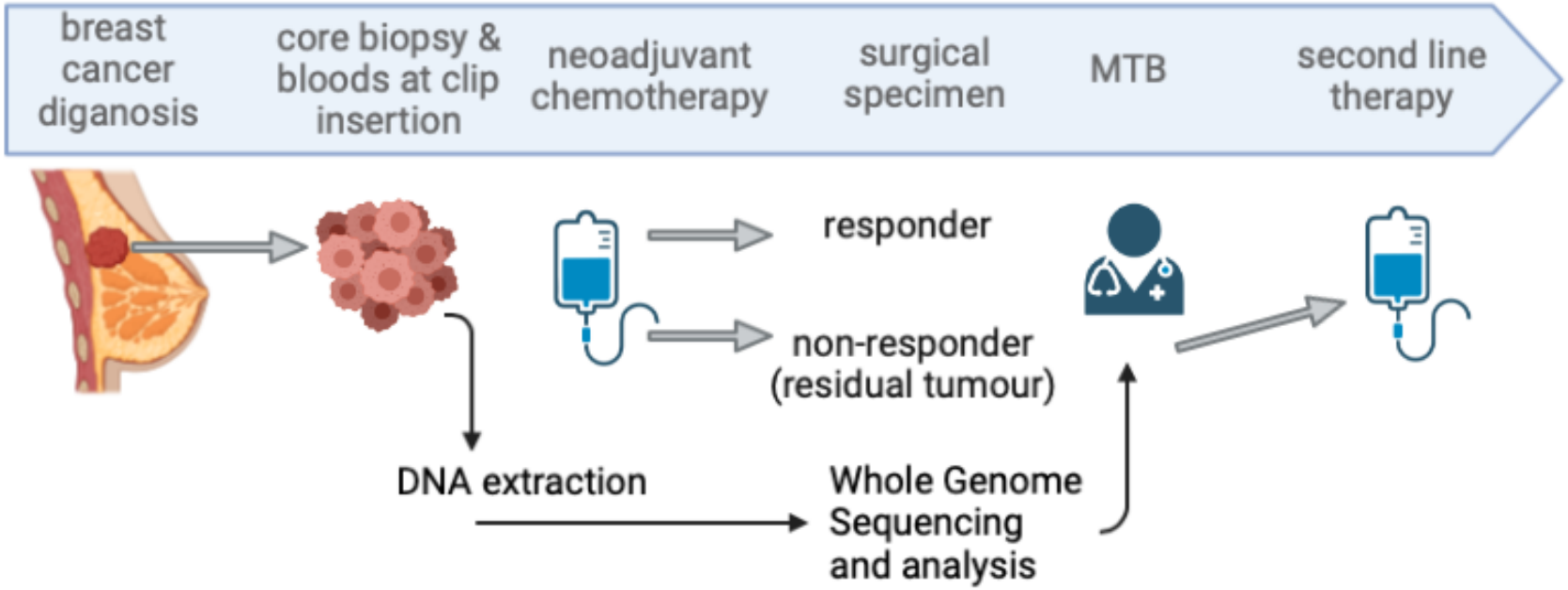
Q-IMPROvE

Innovation

- integration of genomics research within the clinic

Goals

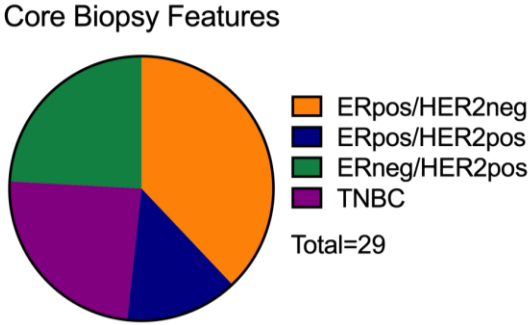
- to establish a framework for routine clinical genomics in BrCa
- to determine if WGS can inform second-line decision making
    - trials? therapy change? pharmacogenomics?
- Funding for pilot trial (n=30)

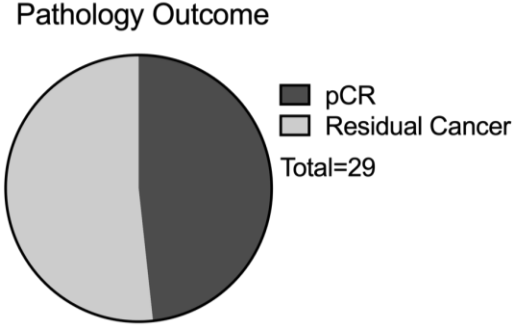


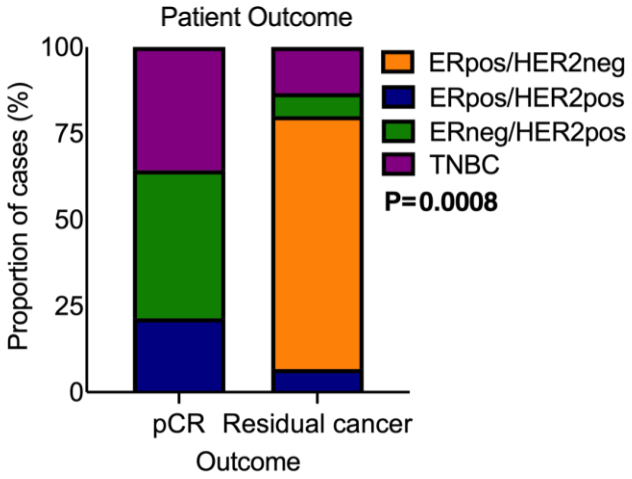
Adjuvant therapy- surgery prior to chemotherapy
**Neoadjuvant therapy- chemotherapy prior to surgery*

Sample work flow

The Q-IMPROvE cohort







What did we report on?

Somatic

- 147 breast cancer driver genes
- Chromosome scale changes

Germline

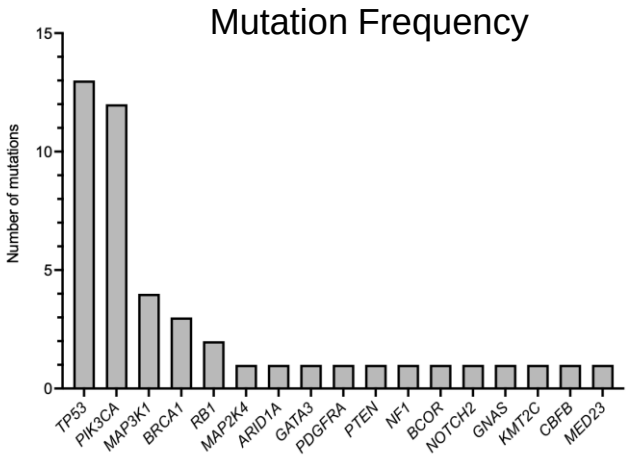
- restricted to panel of clinically actionable breast cancer alterations
- *BRCA1*; *BRCA2; TP53; ATM* (c.7271T>G);

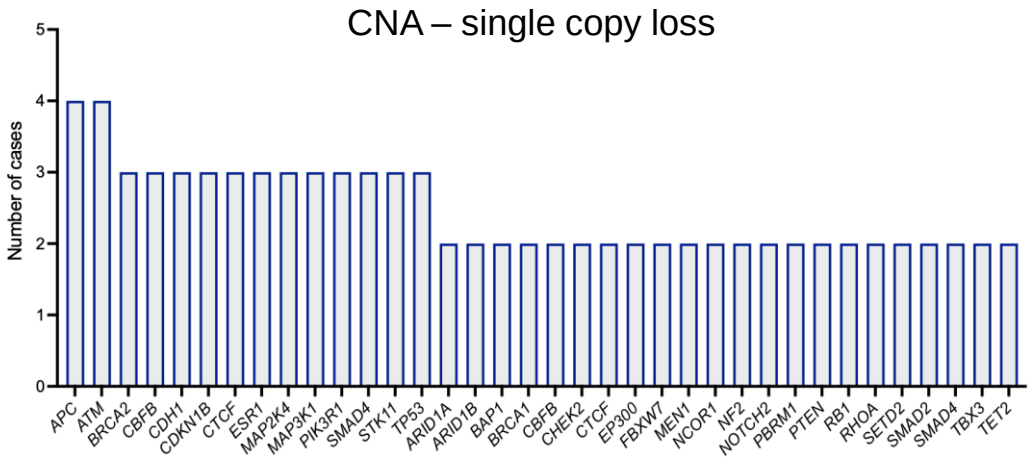
CHEK2 (truncating only); *PALB2* (truncating only)

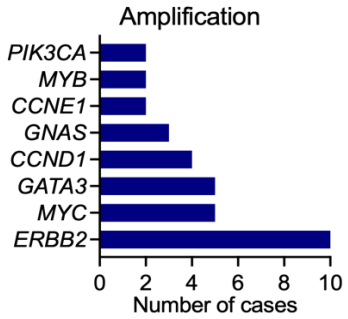
- Pharmacogenomics loci including *DPYD*

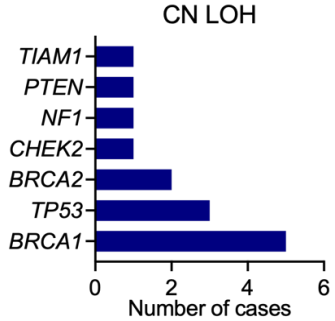
Signatures

What did we report from the tumours?







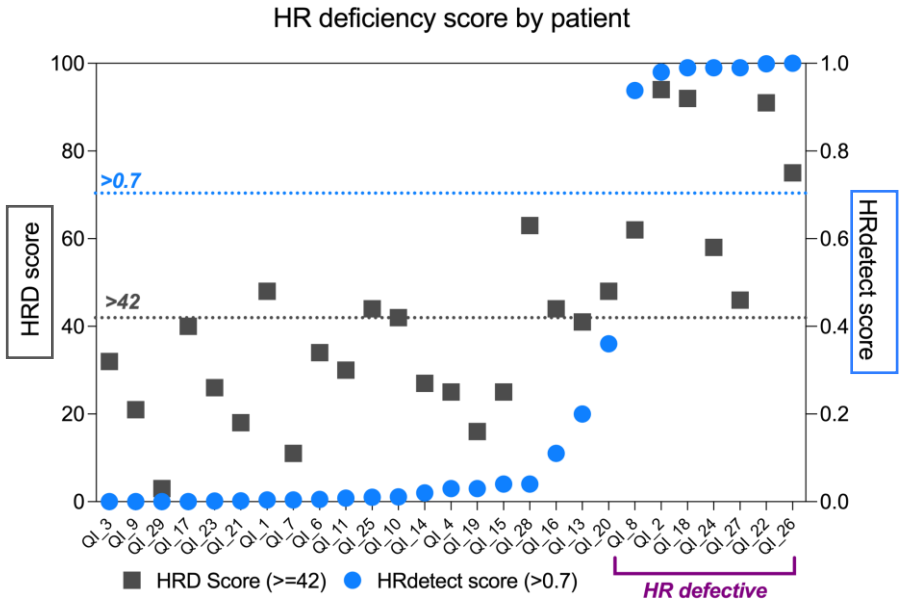


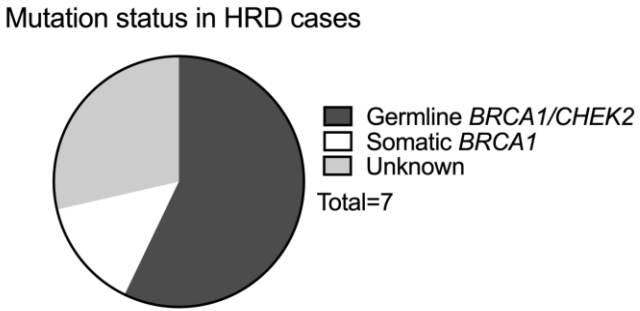
What did we find in the germline?

Age	Existing Genetic Health referral for BrCa panel*	Germline Status at recruitment	WGS germline finding	Putative somatic second hit	WGS Somatic finding of interest	New referral to Genetic Health
25-35	Y	.	.	CNLOH *TP53*	*TP53* p.Cys135Tyr	Yes
	Y	*BRCA1 mutant*	*BRCA1* p.Asn1355LysfsTer10	.	.	.
	Y	.	.	.	.	.
45-55	Y	.	.	.	.	.
	Y	.	.	.	.	.
	Y	*BRCA1 mutant*	*BRCA1* p.Gly1348AsnfsTer7	Copy loss *BRCA2*	.	.
	Y	.	.	.	.	.
	N	.	*BRCA1* p.Val627SerfsTer4	.	.	Yes
	N	.	*CHEK2* p.Gln20Ter	CNLOH *CHEK2*	.	Yes
60+	Y	.	.	CNLOH *BRCA1*	.	.

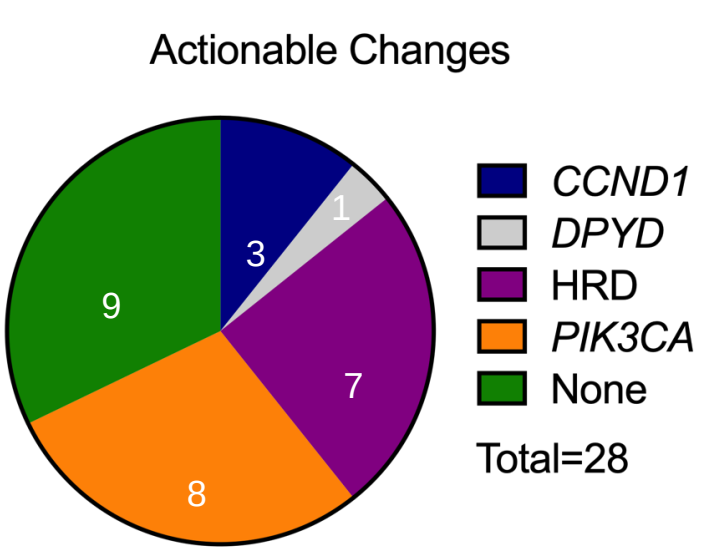
*local clinical, germline breast cancer panel comprises: *ATM* (c.7271T>G); *BRCA1*; *BRCA2; CHEK2* (truncating only); *PALB2* (truncating only); *TP53*.

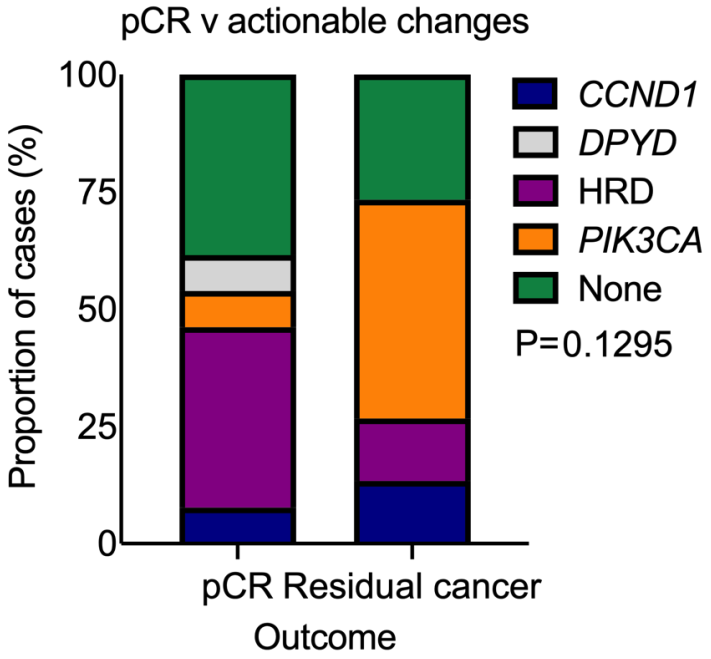
Were signatures important?





What did we find overall?





*Capivasertib CAPItello-291 Phase III

Where to next?

Genomics Health Futures Mission

Whole Genome Sequencing in high-risk breast cancer patients.

- aim to extend Q-IMPROvE nationally, and integrate a research program

A National Program

BREAST CANCER TRIALS

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The patients and their families

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