HRD Testing in Ovarian Cancer

Improving treatment with molecular biomarker screening

Organisation Name: Peter MacCallum Cancer Centre

Presenter: Dr Andrew Fellowes

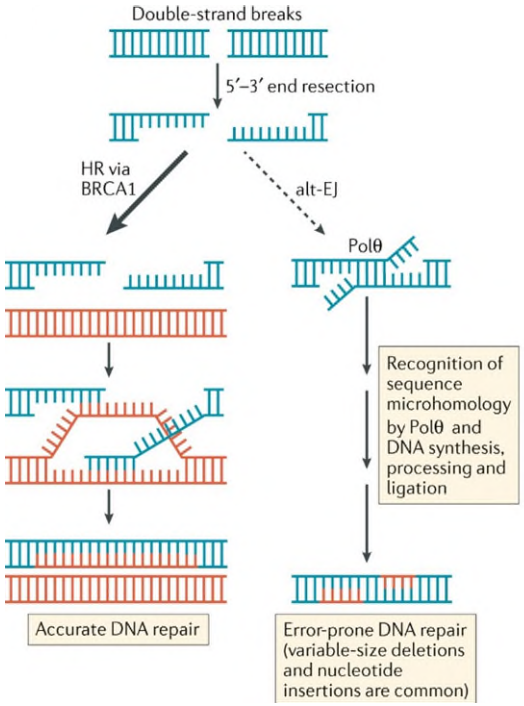
andrew.fellowes@petermac.org

PPA National Forum, Innovations Plenary
Tasmania 2023

Aim of this Innovation

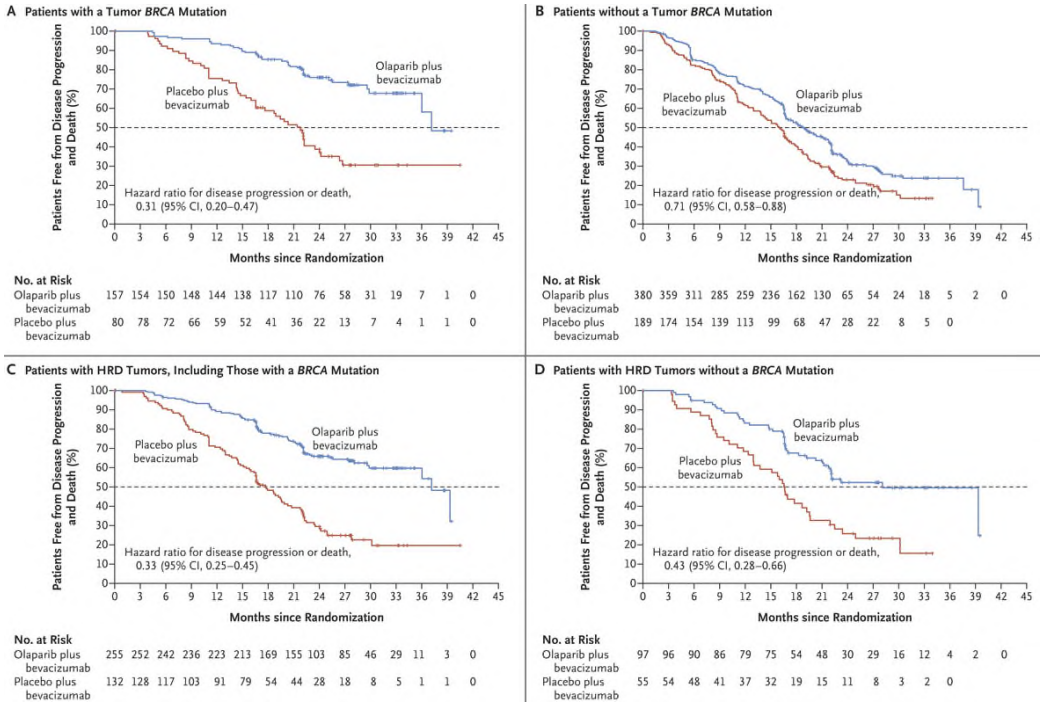
- We aimed to implement a companion diagnostic assay for the detection of Homologous Recombination Deficiency (HRD) in newly diagnosed high grade epithelial ovarian carcinoma
- At project commencement in 2020, no TGA '*companion diagnostic*' classification existed, and no FDA approved HRD companion diagnostic could be operated by Australian laboratories
- Anticipating clinical demand for HRD services and encouraged by collaboration with industry, we set about generating data for submission to NATA/TGA supporting the validity of a novel assay to detect HRD in ovarian cancer
- Maintenance PARP inhibitors have driven a paradigm shift in treatment of high-grade ovarian cancer. Long term survival data from SOLO1 and PAOLA1 clinical trials demonstrate 46% patients remain disease free beyond 5 years (compared to 10% on standard therapy)
- HRD as a molecular biomarker of response to targeted therapy is an example of the '*personalised medicine*' paradigm. By providing a timely, accurate measurement of the HRD status from a patient's diagnostic or interval debulking specimen, we hope to drive improved survival for Australian ovarian cancer patients.
- MBS listing for HRD as a companion diagnostic for PARP inhibitor maintenance therapy is due Q4 2023

HRD and PARP inhibitors



HRD arises due to deficiency of factors (notably BRCA1 or BRCA2) involved in double-strand break repair

Ashworth et al. Nat Rev Clin Oncol. 2018



HRD is associated with increased survival in patients who receive Olaparib, independent of BRCA mutation status

Ray-Coquard et al. N Engl J Med 2019

Genomic Testing in Ovarian Cancer

Public Pathology AUSTRALIA

Measuring Genomic Instability Identifies More Women with HRD

Testing Paradigm	Specimen	Origin	Gene Panel	
Detect the cause of HRD	Blood	Germline	BRCA1/2	13-18% BRCA mutations
			Other HRR genes	~23% HRR mutations
	Tissue	Germline & Somatic	BRCA1/2	~20–25% BRCA mutations
			Other HRR genes	~31% HRR mutations
Detect the effect of HRD				~50% Genomic Instability

Percent of women positive by each class of test

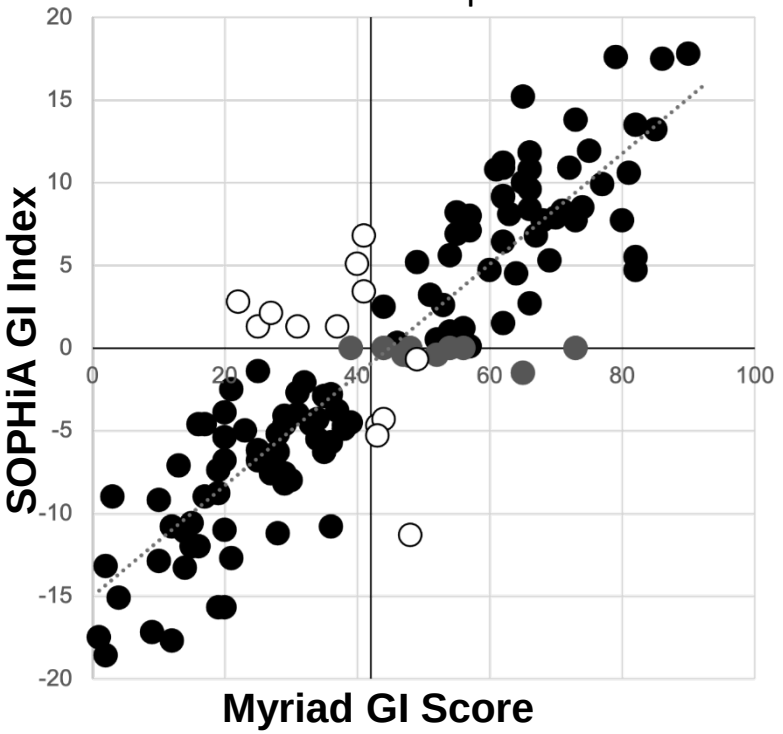
Key Changes Implemented

We designed a validation strategy to compare HRD classification by our test method to a reference method using 132 histologically confirmed high grade serous/endometroid ovarian FFPE samples

Test Method: *SOPHiA Genetics HRD Solution*
Reference Method: *Myriad myChoice HRD*

		SOPHiA HRD: Positive	SOPHiA HRD: Negative	
Myriad myChoice	Positive	**TP** 63	**FN** 5	68
	Negative	**FP** 8	**TN** 56	64
		71	61	**132**

PPA=93% **(Sensitivity)**
NPA=88% (Specificity)
PPV=89%
OPA=90% **(Accuracy)**



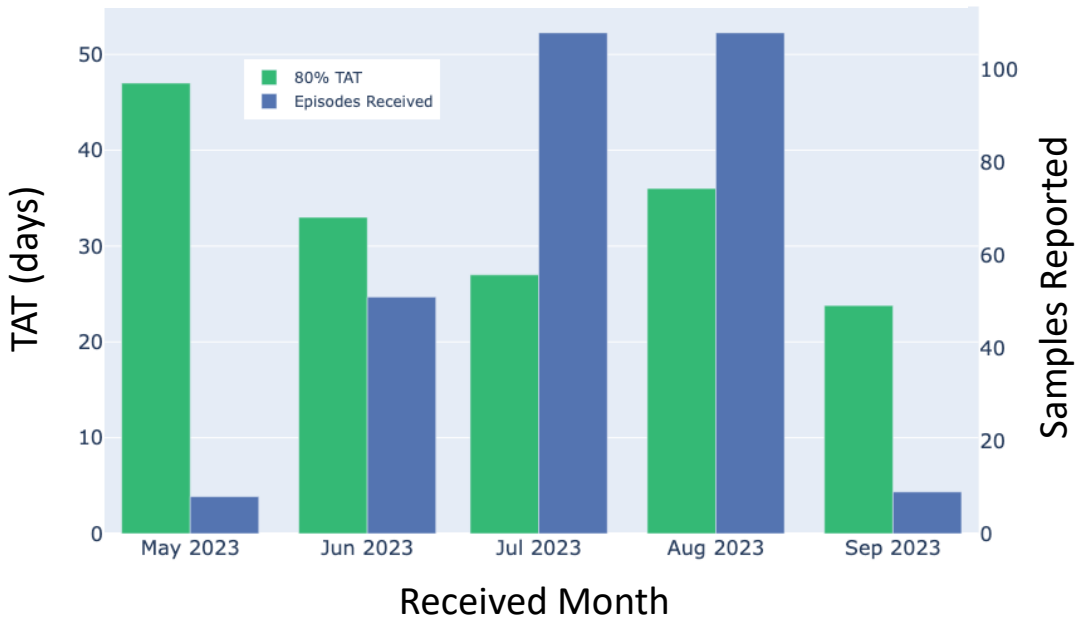
Peter Mac received NATA accreditation for GI testing in May 2023

Community First, Always.

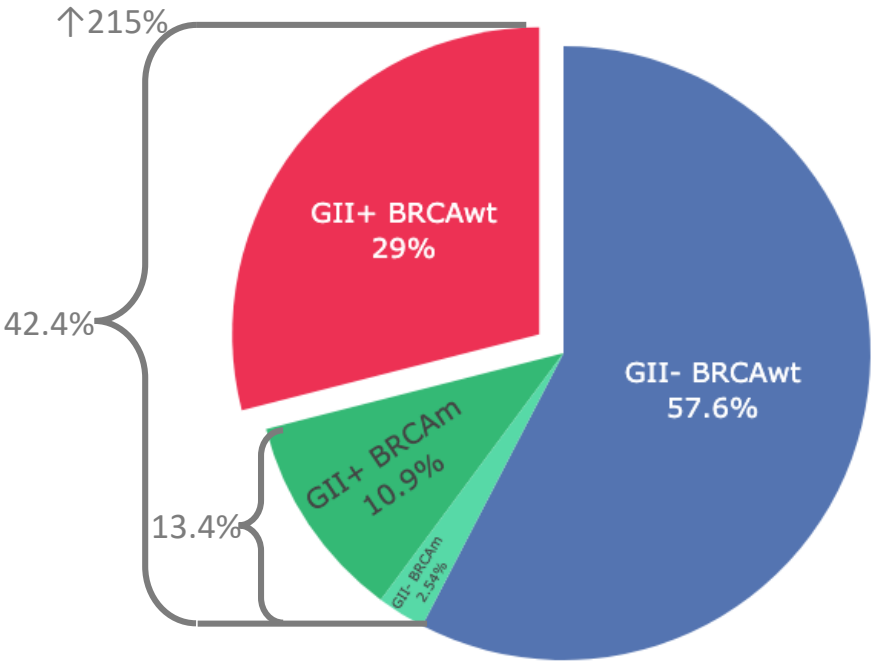
Outcomes so Far

Service offered from: June 2023
Clinical samples reported: 278

80th Percentile TAT (days) and Number of Samples



BRCA / GI Agreement



Community First, Always.

HRD Testing in Ovarian Cancer

Peter MacCallum Cancer Centre

Problem: Provide a timely, accurate measurement of the HRD status from a patient's diagnostic or interval debulking specimen

Solution: Proved non-inferiority between our test method (SOPHiA Genetics HRD Solution) and reference method (Myriad myChoice HRD)

Results: Testing high grade serous ovarian cancer using an HRD assay has increased PARPi predictive yield by 215% over BRCA testing alone

Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

Community First, Always.