Liquid biopsy testing in metastatic or advanced breast cancer patients during the COVID-19 pandemic

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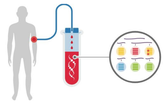
INTRODUCTION

Project ACTT



> 3100 patients

> 470 oncologists

170+ institutions

1710 mutation positive reports

1190 total actionable results

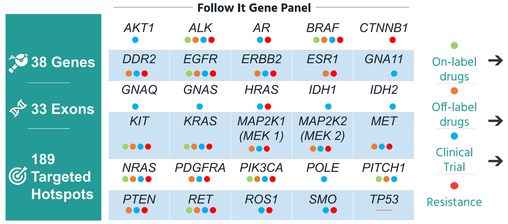
1197 breast cancer patients

*numbers reflect November 2022; we continue to provide testing for patients.

- Response to COVID-19 reduced access to cancer testing and care, but liquid biopsy was an alternative to inaccessible or cancelled tissue biopsies
- Free liquid biopsy cancer testing of ctDNA using the Follow It™ assay which focuses on 189 actionable genomic targets across 38 genes
- Funded by federal government and industry partners
- Eligibility: locally advanced or metastatic cancers (primarily: breast, lung, colon)
- Aimed to localize and democratize cancer testing with minimally invasive methods

Methods

- Blood was drawn in two 10 mL Streck™ DNA BCTs and sent to the CAP/CLIA/DAP accredited Imagia Canexia Health laboratory for testing using the clinically validated Follow It™ liquid biopsy assay
- Plasma was isolated with double spin protocol and cfDNA extracted using an optimized Promega Maxwell RSC method, amplified with a multiplex, amplicon based 30 or 38 gene panel, and sequenced on an Illumina MiSeq or NextSeq 550
- In-house bioinformatics pipeline called SNVs, indels, and copy number amplifications



- SNVs ≥ 0.7% or 0.4% VAF, indels ≥ 5% or 0.5% VAF
- Copy number gains ≥ 4 (9 genes)
- Mean depth: NextSeq ~40,000x, Miseq ~10,000x

Results

Actionability

1214 total breast cancer samples

15 were repeat testing

39% of samples submitted

586 reports with pathogenic ctDNA mutations

48% of results

438 reports with actionable results

36% of total results

77% of mutation positive results

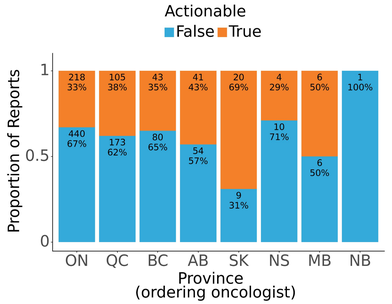
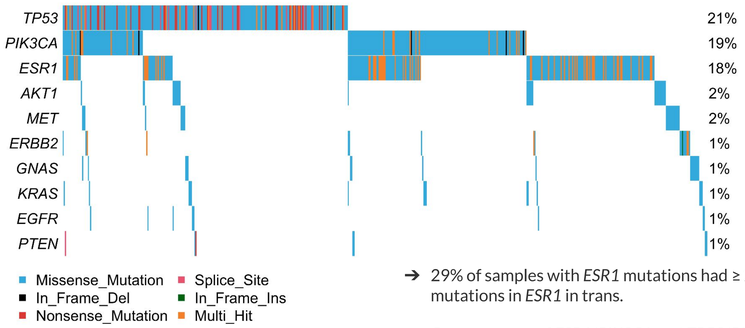


Fig 1. Actionability of breast cancer results. Actionability is defined as having at least one tier 1 or tier 2 mutation (having strong or potential clinical significance) present in a report.

Mutations



- 29% of samples with *ESR1* mutations had ≥ 2 mutations in *ESR1* in trans.
- Co-occurence of *ESR1*/*PIK3CA* and *TP53*/*PIK3CA* ($p < 0.001$)

Fig 2. Occurrence of top 10 mutated genes in samples. Samples presented as columns across genes, colored bars indicate presence and type of mutation found in that gene. Percentages are of all samples sequenced.

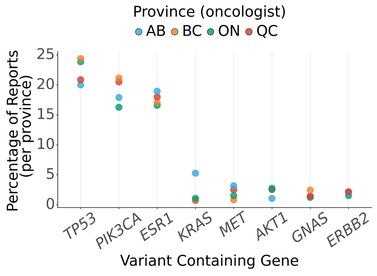


Fig 3. Province specific occurrence of genes on reports for provinces with the most reports. Data limited to genes on > 1% of reports across all provinces.

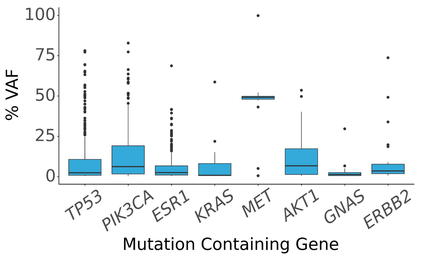
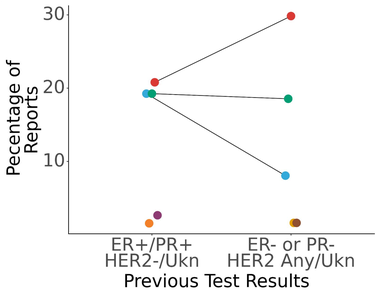


Fig 4. Variant allele frequencies of SNV and indel mutations for genes most commonly found across provinces.



- For ER/PR + and HER2 -/unknown samples with ctDNA, 63% of them were *ESR1* and/or *PIK3CA*.

Fig 5. Top 5 most commonly mutated genes in samples where hormone receptor test results were known. Ukn = status unknown.

Conclusions

- ctDNA testing lead to actionable results in ~36% of breast cancer samples, with pathogenic mutations identified in 48%
- *PIK3CA* mutated, ER+/HER2- tumors are predicted to respond to alpelisib (FDA/Health Canada approval)[1]
- *ESR1* mutations are associated with acquired resistance to antiestrogen therapies[2]
  - The samples with multiple ESR1 mutations may indicate resistance subclones

Partners

References: [1]Fritsch et al. 2014. Mol. Cancer Ther.; [2]Fribbens et al. 2016. J. Clin. Oncol.