Real world results of liquid biopsy in stage 4 solid tumors and potential "clinical actionability"

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BACKGROUND

Plasma based next-generation sequencing (NGS) of circulating cell-free DNA (cfDNA) and cfRNA is a minimally invasive technique available in the clinic, also known as a "liquid biopsy". When tumor tissue is exhausted, a new tumor biopsy is contraindicated, and/or there has been intervening targeted therapy, a liquid biopsy may serve a unique niche. Here we report initial liquid biopsy results from stage 4 solid tumors using the Circulogene Theranostics Personalized Gene Profile (CGP, 50-gene panel) on cfDNA and cfRNA. CGP uses proprietary in situ enrichment with an input volume of 20 uL plasma for cfDNA and 400 uL for cfRNA per case.

METHODS

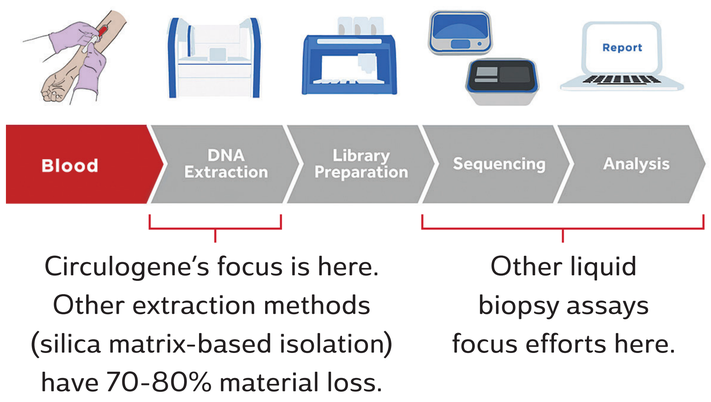
DNA mutations detected and, where available, PD-L1 expression, ALK, and ROS1 fusions in RNA were retrospectively compiled from CGP ordered at a single center. To be considered clinically actionable and commercially available (CA), the biomarker had to have demonstrated clinical efficacy in human cancer prospective trials using the biomarker and commercially available drug that can target that biomarker. To be considered a clinical trial possibility (CT), one of the biomarkers was required to have a drug in clinical development using the biomarker for the patient's cancer type listing on clinicaltrials.gov during the time period that CGP was ordered. Turnaround time (TAT) was calculated as the difference in calendar days between the date the sample was received at the vendor to the date of the first NGS report for that sample. A Student's t-test was applied to TAT calculations.

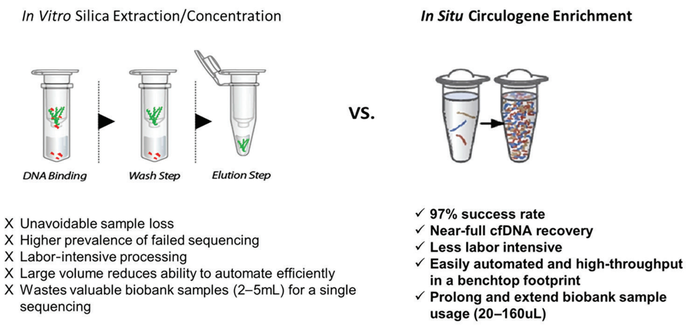
RESULTS

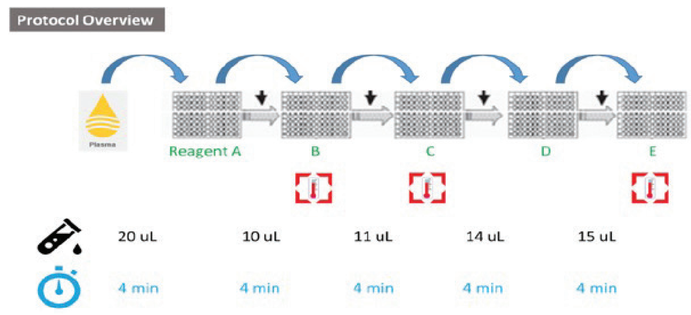
Seventy-five patients (median age 68 years, range 38-95; 35 men and 40 women) underwent CGP testing between November 2015 and October 2017. The majority of cancer types were breast, pancreatic, prostate, colon, and non-small cell lung. Most common DNA mutations recorded were TP53, PTEN, PI3KCA, and BRAF. There was a median of 3 mutations/patient (range 0-11), with a 0% sample failure rate. Overall, 10 cases had no detectable mutations (13.3%). There were six samples with PD-L1 results, and one was positive (16.7%), in the range of expected PD-L1 positivity across solid tumors. In addition to the 10 mutation negative cases, 3 cases had no potential match for CA or CT (e.g. APC, NOTCH1, SMAD4 mutations). Thus, 62 (82.7%) of cases had the potential for CA and/or CT drug identified by liquid biopsy (Table I). All samples were run within 5 days of collection. Median TAT was 7 days. Comparing 2015 to 2017 TAT results, the TAT significantly improved from a median of 12 days to a median of 6 days, respectively (p=0.0005). CGP is priced at approximately $600 per sample comparable to current reimbursement rate.

Table I. Summary of Results

Median Age (range)	68 (38-95)	
Gender	35M: 40F	
Cancer Type (%)		
Breast	14 (18.7)	
Pancreatic	12 (16.0)	
Prostate	11 (14.7)	
Colon	8 (10.7)	
Non-small cell lung	7 (9.3)	
Frequency of Common Gene Mutations*		
TP53	85	
PTEN	19	
PI3KCA	14	
BRAF	12	
# Cases Without Mutation (%)	10 (13.3)	
Median # of Mutations/Patient (range)	3 (0-11)	
*some cases may have multiple mutations in same gene		
# Cases Matched to CA and/or CT (%)	62 (82.7)	
Median TAT days for 2015 n=12 cases(range)	12 (8-27)	p=0.0005
Median TAT days for 2017 n=20 cases (range)	6 (4-15)	







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CONCLUSIONS

This analysis indicates that CGP has a high probability for identifying a potential CA or CT for a stage 4 solid tumor patient with a rapid TAT and markedly lower cost than any other commercially available NGS assays. In this real world experience, despite the low plasma sample input, there were no sample failures, suggesting CGP in situ enrichment is robust. More experience with this assay and linkage with clinical outcomes is warranted.

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