Real-time liquid biopsy assessment in early-stage breast cancer: methylation based-ctDNA analysis and CTCs detection as potential predictors of response to neoadjuvant therapy

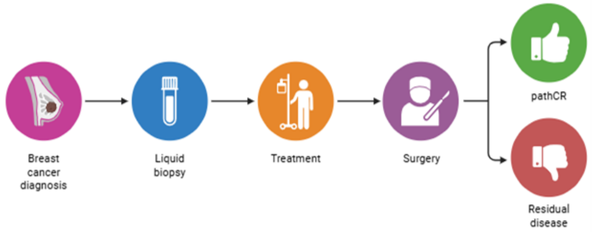
C. Gianni[1], I. Azzali[2], L. Pontolillo[3], B. Pastò[4], E. Nicolo'[5], M. Serafini[5], N. Bayou[5], M. Velimirovic[6], A. J. Medford[7], M. D. Lipsyc-Sharf[8], A. Davis[9], C. Reduzzi[5], A. Musolino[1], A. Bardia[8], M. Cristofanilli[5]

1 Medical Oncology and Breast Unit, IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori", Meldola, ITALY, 2 Biostatistics and Clinical Trials Unit, IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori", Meldola, ITALY, 3 Policlinico Agostino Gemelli, Università Cattolica del Sacro Cuore, Roma, ITALY, 4 Department of Medicine (DMED), University of Udine, Udine, ITALY, 5 Department of Medicine, Division of Hematology-Oncology, Weill Cornell Medicine, New York, NY, 6 Department of Medicine, Cleveland Clinic, Cleveland, OH, 7 Medicine, Mass General Cancer Center, Boston, MA, 8 Division of Hematology/Oncology, UCLA David Geffen School of Medicine, Los Angeles, CA, 9 Division of Oncology, WashU Medicine, St Louis, MO.

SAN ANTONIO BREAST CANCER SYMPOSIUM
DECEMBER 10–13, 2024
SABCS.ORG

Background

In early-stage breast cancer (EBC), liquid biopsy may help refine risk stratification and therapeutic decision-making. Historically, the detection of circulating tumor cells (CTCs)>1/7.5 ml has a strong prognostic value for high risk of relapse, but rarely are detected. We explored circulating tumor DNA (ctDNA) and CTC detection at diagnosis and their association with tumor characteristics and response to neoadjuvant therapy (NAT).



Methods

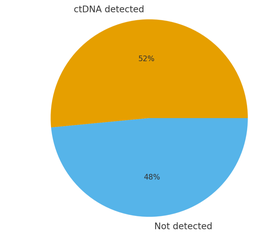
We retrospectively analyzed 40 patients with stage I–III breast cancer who underwent GR and Cellsearch testing at diagnosis. Guardant Reveal™ (GR) is a tissue-naïve, methylation-based cell-free DNA assay capable of detecting circulating tumor DNA (ctDNA) with high sensitivity, even in low-input samples. CellSearch® detects CTCs via immunomagnetic enrichment of EpCAM-positive cells and cytokeratin-based immunostaining, followed by automated enumeration. Associations between baseline ctDNA and CTC detection and clinical features—including tumor grade, stage, molecular subtype—and response to NAT were assessed.

Cohort characteristic

	Overall (n=40)
Sex, n(%)	
Female	40 (100)
Age at diagnosis	
median, Q1-Q3, min-max	45, 38-67, 28-77
T stage, n (%)	
1	11 (28)
2	19 (48)
3	7 (18)
4	3 (8)
N stage, n (%)	
0	19 (48)
1	13 (33)
2	3 (8)
3	5 (13)
Stage, n (%)	
I	7 (18)
II	23 (58)
III	10 (25)
Inflammatory Breast Cancer, n (%)	
Yes	4 (10)
No	36 (90)
Histotype, n (%)	
IDC	35 (88)
ILC	3 (8)
mixed	2 (5)
Grading, n (%)	
G1	1 (3)
G2	17 (43)
G3	22 (55)
Molecular subtype, n (%)	
TNBC	16 (40)
HR+/HER2-	17 (43)
HR+/HER2+	6 (15)
HR-/HER2+	1 (3)
Neoadjuvant therapy, n (%)	
Yes	34 (85)
No	2 (5)
Unknown	4 (10)
First test GR, n (%)	
at diagnosis (pre NAT)	30 (75)
during NAT	5 (13)
after NAT	5 (13)
Test GR	
median, Q1-Q3	1, 1-4
Follow up - months	
median, Q1-Q3	13.4, 6.4-17.9
Time between GR test – months	
median, Q1-Q3	3.2, 2.7-5.0
Time between surgery and following GR test - months	
median, Q1-Q3	3.5, 1.9-4.7

Results

Figure 1. ctDNA detection among patients tested before NAT (n=33)



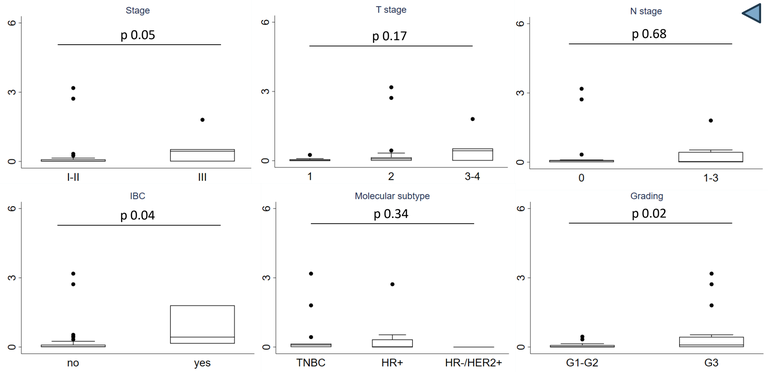


Figure 2. IBC and stage III showed a trend toward higher ctDNA tumor fraction (median methylation tumor fraction 0.43% and 0.02%, p=0.04 and 0.05, respectively).

Figure 3. Lower ctDNA levels at diagnosis were observed in patients achieving pCR (pCR vs. no pCR, median methylation tumor fraction 0.03% vs. 0.09%), although the association is not statistically significant (p=0.26).

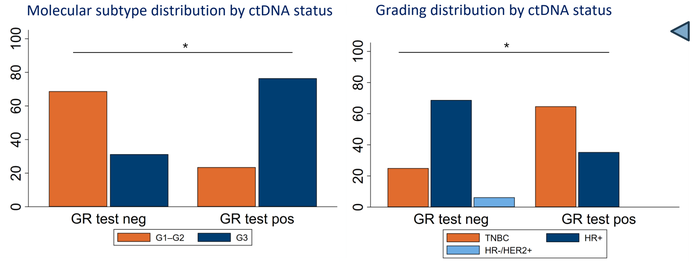
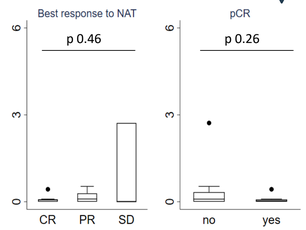


Figure 4. ctDNA detection was significantly associated with tumor grade and molecular subtype, being more frequent in G3 than G1-G2 tumors (72% vs. 27%, p=0.02), and in triple-negative and HR-positive subtypes compared to HER2-enriched (79% vs. 35% vs. 0%, p=0.04).



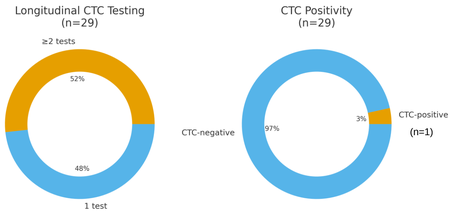


Figure 5. CTC testing overview.

At the time of analysis, no recurrences had been observed (median follow-up: 13.6 months; range 6.6–18.2 from diagnosis to last contact) and four patients are still receiving NAT.

Conclusions

In EBC, ctDNA detection using a methylation-based assay identified patients with aggressive features and potential lower likelihood of achieving pCR. The use of methylation-based ctDNA testing may hold promise as a tool to guide escalation or de-escalation strategies, supporting a more personalized approach to treatment when combined with other biomarkers such as CTCs. Further validation in larger cohorts is needed.

Contact
Caterina Gianni, MD
Medical Oncology and Breast Unit, IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori", Meldola, ITALY
Email: caterina.Gianni@irst.emr.it; cag4022@med.cornell.edu

Abstract Number: 2094
Presentation Number: PS2-09-18

This presentation is the intellectual property of the author/presenter. Contact them at caterina.gianni@irst.emr.it for permission to reprint and/or distribute.

© Poster Template by Genigraphics® 1.800.790.4001 www.genigraphics.com