Exploring the interplay between tumor burden and liquid biopsy longitudinal evaluation in Hormone Receptor-positive, HER2-negative metastatic breast cancer (MBC)

E-Poster 293P
Abstract #4159

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BACKGROUND

- Liquid biopsy, including circulating tumor DNA (ctDNA), is gaining momentum in MBC characterization and monitoring.
- The aim of this study was to explore the interplay between ctDNA and serum biomarkers with respect to metastatic spread and tumor burden.

METHODS

- A total of 83 patients (pts) with luminal-like MBC treated with first line endocrine therapy and CDK4/6 inhibitors were characterized for ctDNA through droplet digital PCR at baseline (BL) and after three months, at the first radiological evaluation (E1).
- Associations between clinicopathological characteristics, ctDNA and serum biomarkers were tested through Kruskal-Wallis test.
- Variations between BL and E1 were tested through Wilcoxon sign-rank test.

Table 1. Patients' characteristics.

	BL	E1
≥ 3 mte_sites	31%	25%
Bone metastasis	72%	68%
Liver metastasis	29%	28%
Lung metastasis	22%	22%

RESULTS

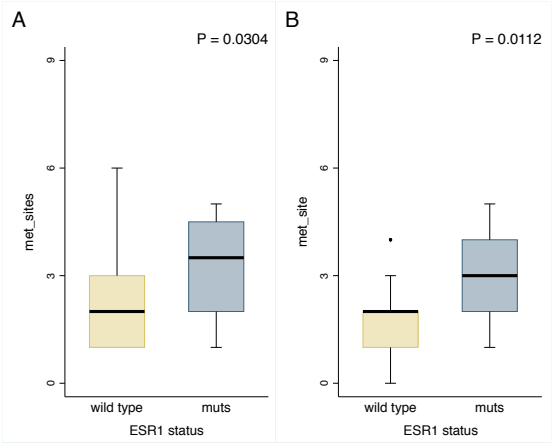


Figure A-B. ESR1 status the baseline (A), at the first radiological evaluation (B)

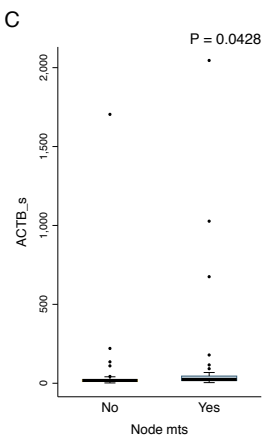
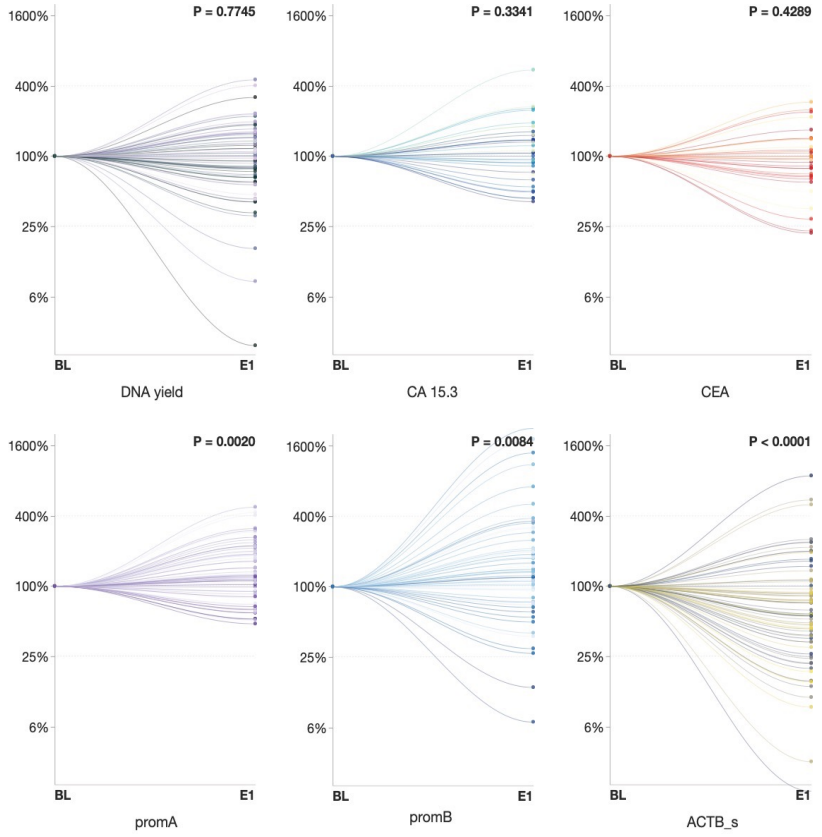


Figure C. At the baseline

Table 2. Liquid biopsy: ctDNA median values.

	BL (IQR)	E1 (IQR)
DNA yield	24.12 ng (18.36 - 39.24)	23.52 ng (17.52 - 33.96)
ACTB-s	19.5 ng (12 - 36)	12.5 ng (8 - 24)
ACTB-m	2 (0.5 - 4)	1 (0.5 - 2)
ACTB-l	10 (7 - 17)	5.5 (3.5 - 10.5)
Methylation of ESR1 prom A	36.75% (25 - 42.5)	44% (33 - 51.5)
Methylation of ESR1 prom B	24% (11 - 37.5)	38.75% (29 - 50)

- **At baseline**, ctDNA-detected ESR1 mutations (muts) and PIK3CA muts were found in 11% and in 28% of pts, respectively. ESR1 muts were associated with liver metastases (mts) ($P < 0.0001$) and a higher number of metastatic sites (met_sites) ($P = 0.0304$). ACTB short fragments (ACTB_s) were significantly higher in pts with node mts ($P = 0.0428$).
- **At the first radiological evaluation**, liver mts, serosal mts and higher met_sites were associated with ESR1 muts (respectively, $P < 0.0001$, $P = 0.038$ and $P = 0.0112$). Liver mts were also associated with higher methylation of ESR1 promoter B (promB) ($P = 0.046$).
- In pts that did not progress at E1, met_sites and ACTB_s significantly decreased at E1 vs BL (respectively, $P = 0.0005$ and $P < 0.0001$). A significant increase was observed for methylation of ESR1 promA and B (respectively, $P = 0.00139$ and $P = 0.0084$), while no significant changes were observed for CEA, CA15.3 and total ctDNA yield.



CONCLUSIONS

The present study showed a strict association between ctDNA, tumor burden and metastatic pattern in luminal-like MBC. Changes in biomarkers were consistently observed at the different timepoints, further supporting ctDNA as a key tool for disease monitoring.

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No potential conflicts of interest were reported by the first and presenting author

Study sponsored by Ricerca Finalizzata Italian Ministry of Health and by AstraZeneca