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Mitotic Circulating Tumor Cells Correlates with Poor Clinical Outcomes in Metastatic Breast Cancer Patients over a 3 Year Period

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ABSTRACT

Currently, the gold standard in cancer diagnosis, prognosis, and treatment is assessing cancer cell mitosis in tumor tissue biopsies, which identifies patients with more aggressive cancer subtypes that may require more tailored treatment regimens. Circulating tumor cells (CTCs), cancer cells that detach from primary tumors, enter the bloodstream, and seed metastatic sites, are a well-known non-invasive blood biomarker which can also be used to aid in stratifying metastatic breast cancer (mBC) patients with highly aggressive subtypes. Initial pilot studies have identified a particular subtype of CTCs which are undergoing mitosis that appears to correlate with very poor survival outcomes compared to non-mitotic CTCs alone. In a multi-institutional prospective study, we isolated CTCs from the blood of n=167 mBC patients to categorize mitotic CTCs and evaluate their association with progression-free survival (PFS) and overall survival (OS) over a 3 year period.

MATERIALS & METHODS

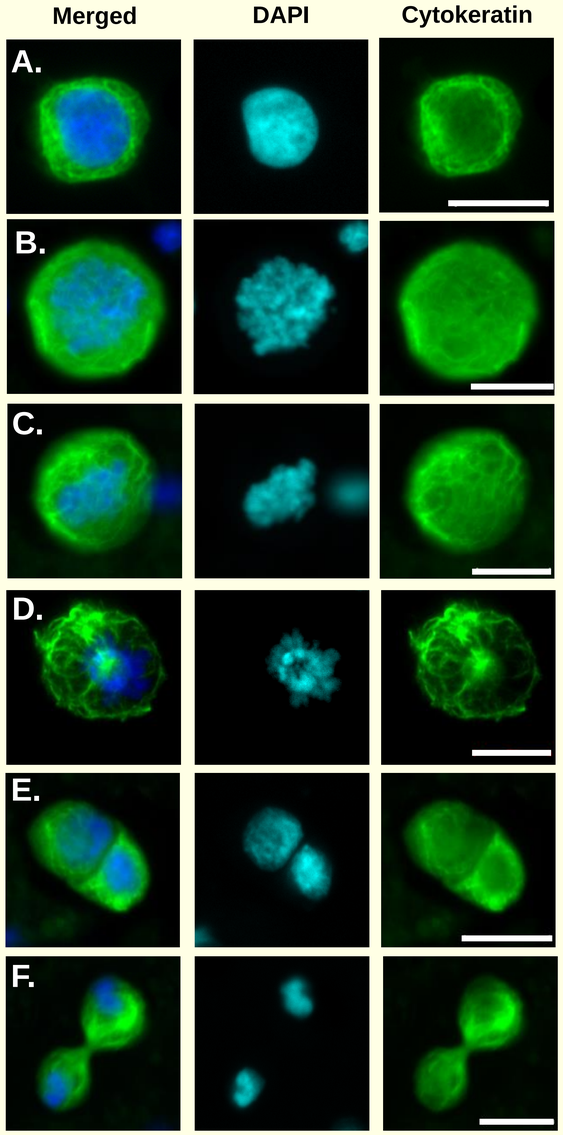
Peripheral blood samples (7.5ml) were collected from n=167 mBC patients progressing on systemic therapies and prior to new systemic therapy induction (i.e. chemotherapy n=102, hormone therapy n=13, immunotherapy n=63, targeted therapy n=62). Samples were processed using CellSieve microfilters to isolate CTCs via size exclusion and fluorescently stained for CD45, Cytokeratin, and DAPI. CTCs were imaged, enumerated, and subtyped based on the presence of ≥1 mitotic event, using previously established visual indicators (**Figure 1**). PFS and OS were assessed over 3 years by censored univariate and multivariate analyses.

REFERENCES

1. Adams DL, et al "Mitosis in circulating tumor cells stratifies highly aggressive breast carcinomas." Breast Cancer Res. 2016
2. Mu et al, Detection and Characterization of Circulating Tumor Associated Cells in Metastatic Breast Cancer" *Int. J. Mol. Sci.* 2016, *17*(10), 1665
3. Cristofanilli M, "Liquid Biopsies in Solid Tumors" *Springer Intl Publish.* 2017

Figure 1. Examples of CTCs at different stages of Mitosis

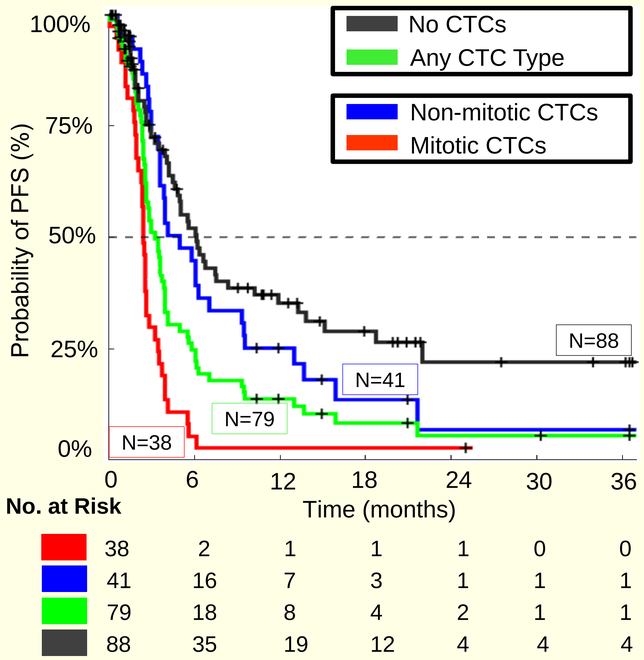
Circulating tumor cells (CTCs) isolated from patients with breast cancer at different stages of mitosis. Representative images of A) "classic" CTCs, B) prophase, C) metaphase, D) anaphase, E) telophase, F) cytokinesis. Scale bar = 10 µm.



RESULTS

- Any CTC type was found in 47% of patients (n=79/167)
- Mitotic CTCs were identified in a subset, 48% (n=38/79) of the any CTC type group.
- Patients with any CTC type were associated with poor PFS and OS versus patients without CTCs**. (Fig. 2 & Fig. 3)**
- Patients with mitotic CTCs had significantly poorer PFS and OS versus non-mitotic CTCs. **(Fig. 2 & Fig. 3)**
- 95% of patients with mitotic CTCs progressed within 6 months, regardless of systemic therapy type

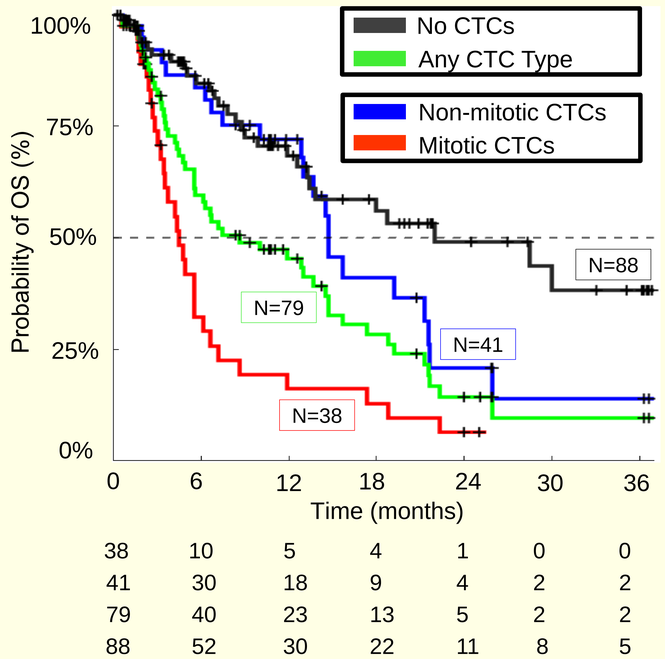
Figure 2. PFS of CTC Subtypes



No. at Risk

38	2	1	1	1	0	0
41	16	7	3	1	1	1
79	18	8	4	2	1	1
88	35	19	12	4	4	4

Figure 3. OS of CTC Subtypes



38	10	5	4	1	0	0
41	30	18	9	4	2	2
79	40	23	13	5	2	2
88	52	30	22	11	8	5

Table 1: Comparisons Between CTC Groups

Groups	HR	95% CI	P-Value	HR	95% CI	P-Value
No CTCs vs Any CTC Type	2.1	1.4-3.0	0.0002	2.4	1.5-3.7	0.0002
No CTCs vs Non-mitotic CTCs	1.4	0.9-2.2	0.2129	1.5	0.9-2.8	0.1975
No CTCs vs Mitotic CTCs	5.2	2.9-9.1	<0.0001	6.4	3.4-12.0	<0.0001
Any CTC Type vs Non-mitotic CTCs	0.7	0.4-1.0	0.0563	0.6	0.4-1.0	0.0787
Any CTC Type vs Mitotic CTCs	1.9	1.2-3.0	0.0095	1.8	1.1-3.0	0.0306
Mitotic CTCs vs Non-mitotic CTCs	3.3	1.9-5.8	<0.0001	3.0	1.7-5.4	0.0004

CONCLUSIONS

- We stratified and enumerated CTC subtypes from the blood of mBC patients and compared them to clinical outcomes.
- The detection of any CTC type indicated poor outcomes in patients.
- CTC undergoing mitosis appears to indicate highly aggressive disease with the poorest survival rates.
- Further studies are needed to expand upon the subtyping of CTCs and their correlation to therapy response.

FUNDING SOURCE

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