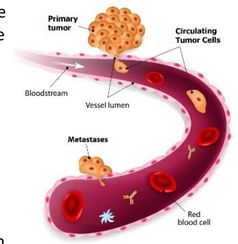
Assessing the impact of real-time serial circulating tumor cell results on the management of patients with metastatic breast cancer

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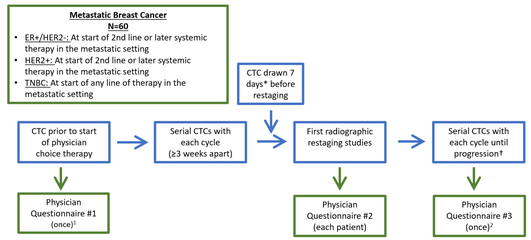
Background

The FDA-cleared CellSearch® Circulating Tumor Cell (CTC) assay is a minimally-invasive liquid biopsy approved for metastatic disease monitoring.[1] In metastatic breast cancer (MBC), prospective phase III data supports a positivity threshold of ≥5 CTC.[2] Positive CTCs (≥5 CTCs) at baseline (BL), persistent CTC positivity, and increases in CTC count over time outperform serum tumor markers such as CA 27-29 and CA 15-3 and predict radiographic disease progression.[3-5] Nevertheless, CTC enumeration has not been utilized broadly in real-world clinical practice.



Design

The ACT-MBC study is **A** Prospective Observational Impact Study of **C**irculating **T**umor Cells (CTCs) in **M**etastatic **B**reast **C**ancer (MBC) in which patients receive CTC enumeration and biomarker testing. Provider perception of CTC testing is measured with questionnaires at BL (PQ1), at each patient's restaging visit (PQ2), and at study end (PQ3). The study also evaluates if CTC results correlate with response assessment and disease progression as defined by standard of care imaging, and whether CTC results influence the timing of radiographic assessment. The study includes metastatic Hormone Receptor (HR)+/HER2- and HER2+ (after protocol amendment from 9/2024 onwards) patients who are starting ≥2nd line and metastatic Triple Negative (TN) patients at any line of systemic therapy. Treatment was determined by the treating provider.



Baseline Characteristics Patients

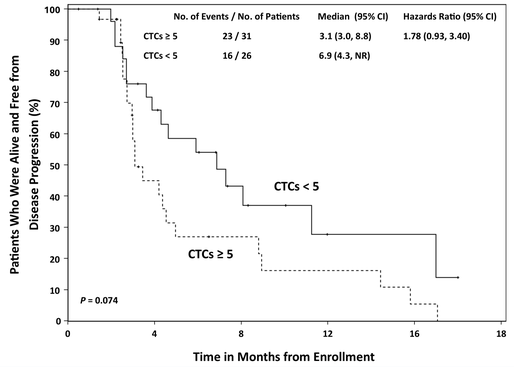
Of the 63 patients who signed informed consent, 3 subjects were deemed to be screen failures. Patient characteristics of the remaining 60 enrollees are shown below:

Characteristics	<5 CTC*	≥5 CTC	Total
No. of patients	29	31	60
Age, years, median (range)	64 (32, 82)	67 (41, 92)	66 (32, 92)
Histology			
Ductal	27 (93.1%)	18 (58.1%)	45 (75.0%)
Lobular	1 (3.4%)	10 (32.3%)	11 (18.3%)
Other	1 (3.4%)	3 (9.7%)	4 (6.7%)
Subtype (IHC)			
HR positive, HER2 negative	21 (72.4%)	27 (87.1%)	48 (80.0%)
HER2 positive	1 (3.4%)	0 (0.0%)	1 (1.7%)
Triple negative	7 (24.1%)	4 (12.9%)	11 (18.3%)
Lines of therapy			
0	2 (6.9%)	1 (3.2%)	3 (5.0%)
1-2	16 (55.2%)	15 (48.4%)	31 (51.7%)
3 or more	11 (37.9%)	15 (48.4%)	26 (43.3%)

* The 3 patients who were missing baseline CTCs were included in the <5 CTC group.

Prognostic Impact of CTCs

Of the 57 pts who had baseline CTCs, 50 completed the study, while 7 (all <5 CTCs) are still on study. Progression-free survival curves according to baseline CTC category are shown below for these 57 pts:



Provider Baseline Characteristics

Of the 31 participating providers, 15 enrolled at least one patient and completed PQ2 data. Of those, 8 of 15 (53.3%) practiced in Rochester (research/university hospital), while 3, 2, and 2 providers practiced in Mankato, Eau Claire, and Albert Lea (community hospitals), respectively. 11 of 15 (73.3%) providers were MDs, while the remaining 4 providers were clinical nurse practitioners.

Provider perspective on CTCs in the management of MBC

The 15 providers completed PQ2 for a total of 54 patients after 1st restaging visit. The median number of patients per provider was 2 (range: 1 to 15).

- Of the 54, 2 pts did not have a baseline CTC result.
- Of the remaining 52 patients, 27 had a baseline CTC ≥5.
- **For these 27 patients, the median % change from baseline at 1st follow CTC result was -60.0% (Q1 = -93.0%, Q3 = 70.8%).**

The provider perspective on CTCs in the management of MBC is based on 47 patients from 14 providers, where the provider indicated having CTC results available before the restaging visit:

- ***83.0%** (90% CI: 70.4%, 95.5%) agreed or strongly agreed that assessing **CTCs enhanced their ability to determine response to therapy**.*
- ***72.3%** (90% CI: 55.9%, 88.8%) agreed or strongly agreed that the **CTC results helped guide their decision to continue or change therapy.***

Conclusions

The ACT-MBC analyses show that oncologists in academic and community practice responded that **serial CTC assessments enhance ability to determine response of therapy, and guide decisions to continue or change treatments.**

Additionally, provider perception on the general usefulness of CTCs increased when using serial CTCs while managing patients.

Provider perception of CTCs pre- vs post-intervention

The providers' perception of the general usefulness of CTCs is assessed in questionnaires pre(PQ1) and post-intervention (PQ3). For the 14 (of 15) providers who also completed both PQ1 and PQ3, we created summary ('shift') tables for each of the questions regarding CTC usefulness. McNemar's test was used to assess the degree of evidence of a shift in the "Agree" / "Strongly Agree" direction post-intervention. Green cells highlight "Agree" / "Strongly Agree" results pre- and post-intervention; **emboldened results** highlight responses with change in provider perception between PQ1 and PQ3.

*"Persistently elevated CTCs (≥5) after initiation of new systemic therapy **indicates that a patient is not responding to treatment**."*

(*P*-value = 0.034)

Pre-intervention response (PQ1)	Post-intervention response (PQ3): Agree / Strongly Agree	Strongly Disagree / Disagree / Neutral	Total
Agree / Strongly Agree	6	**1**	7 / 14 (50.0%)
Strongly Disagree / Disagree / Neutral	**7**	0	7
Total	13 / 14 (92.9%)	1	14

*"Serially assessing **CTCs is a useful biomarker** in monitoring MBC."*

(*P*-value = 0.025)

Pre-intervention response (PQ1)	Post-intervention response (PQ3): Agree / Strongly Agree	Strongly Disagree / Disagree / Neutral	Total
Agree / Strongly Agree	8	**0**	8 / 14 (57.1%)
Strongly Disagree / Disagree / Neutral	**5**	1	6
Total	13 / 14 (92.9%)	1	14

- ***92.9% of providers agreed or strongly agreed that serially assessing CTCs is a useful biomarker in monitoring MBC** (increased by 35.8% from pre- to post-intervention).*

*"Pts with ≥5 CTCs/7.5 mL have a **worse prognosis** than pretreatment pts with <5 CTCs."*

(*P*-value = 0.180)

Pre-intervention response (PQ1)	Post-intervention response (PQ3): Agree / Strongly Agree	Strongly Disagree / Disagree / Neutral	Total
Agree / Strongly Agree	8	**1**	9 / 14 (64.3%)
Strongly Disagree / Disagree / Neutral	**4**	1	5
Total	12 / 14 (85.7%)	2	14

*"The results of a BL CTC test will **influence my choice of systemic therapy** for a pt with MBC."*

(*P*-value = 0.257)

Pre-intervention response (PQ1)	Post-intervention response (PQ3): Agree / Strongly Agree	Strongly Disagree / Disagree / Neutral	Total
Agree / Strongly Agree	1	**2**	3 / 14 (21.4%)
Strongly Disagree / Disagree / Neutral	**5**	6	11
Total	6 / 14 (42.9%)	8	14

References

1. Cristofanilli et al, NEJM 2004
2. Bidard et al, JCO 2024
3. Liu et al, JCO 2009
4. Bidard et al, Lancet Oncol 2014
5. Cristofanilli et al, Clin BC 2007

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