

# Circulating Tumor Cells in non-Metastatic Triple Negative Breast Cancer

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# Triple Negative Breast Cancer (TNBC)

- Tumors lack estrogen and progesterone receptor expression, HER2 amplification
- 10-20% of breast cancer patients
- Younger age- pre menopausal
- Poorer prognosis than non-TNBC
- Hispanic and African-American women
- Not candidates for targeted therapies

# Circulating Tumor Cells in non-Metastatic Breast Cancer

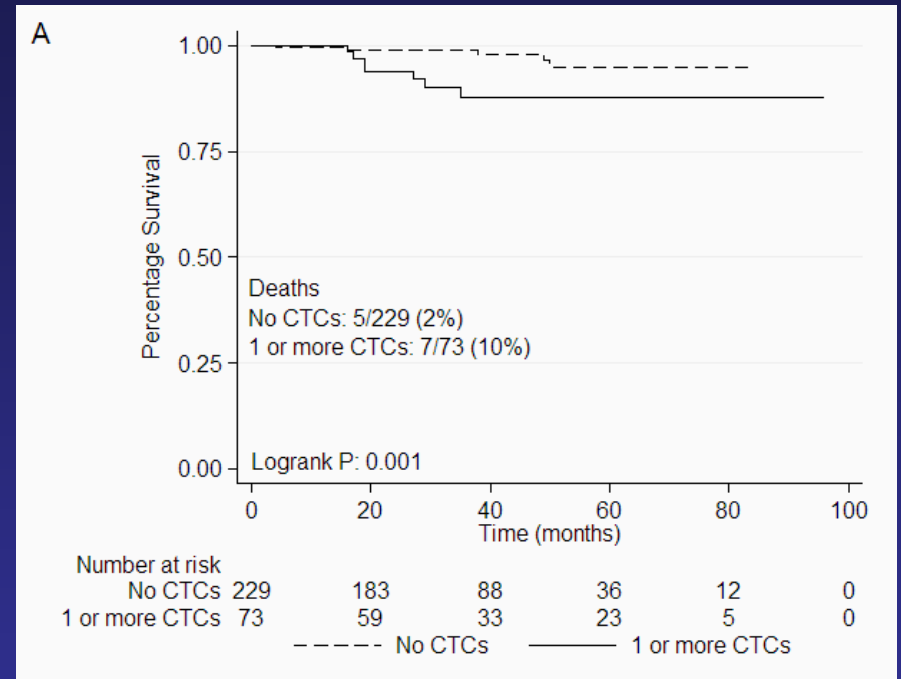
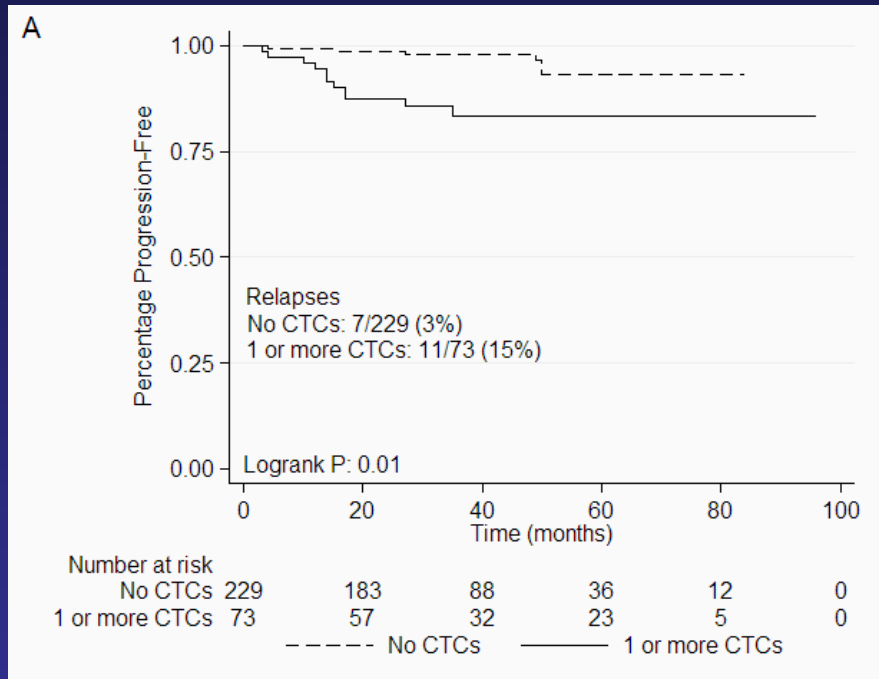
Bidard, et al. *Ann Oncol*. 2010 Apr;21(4):729-33

- (REMAGUS 02 trial)  $\geq 1$  CTC before the start of systemic chemotherapy predicted decreased metastasis-free and overall survival in stage II/III breast cancer patients

Rack, et al. *Cancer Res* 2010 70(24 suppl): Abstract S6–5

- (SUCCESS trial)  $\geq 1$  CTCs before systemic treatment predicted decreased disease-free and overall survival in breast cancer patients with node-positive or high risk node-negative disease

# CTCs in Chemo-naïve BC Patients



## Progression free Survival

One or more CTC vs. no CTCs

P=0.01

## Overall Survival

One or more CTC vs. no CTCs

P≤0.001

# Hypothesis and Aims of the Study

Given the aggressive nature of TNBC, we hypothesized that the presence of CTCs would predict worse progression-free and overall survival in non-metastatic TNBC patients.

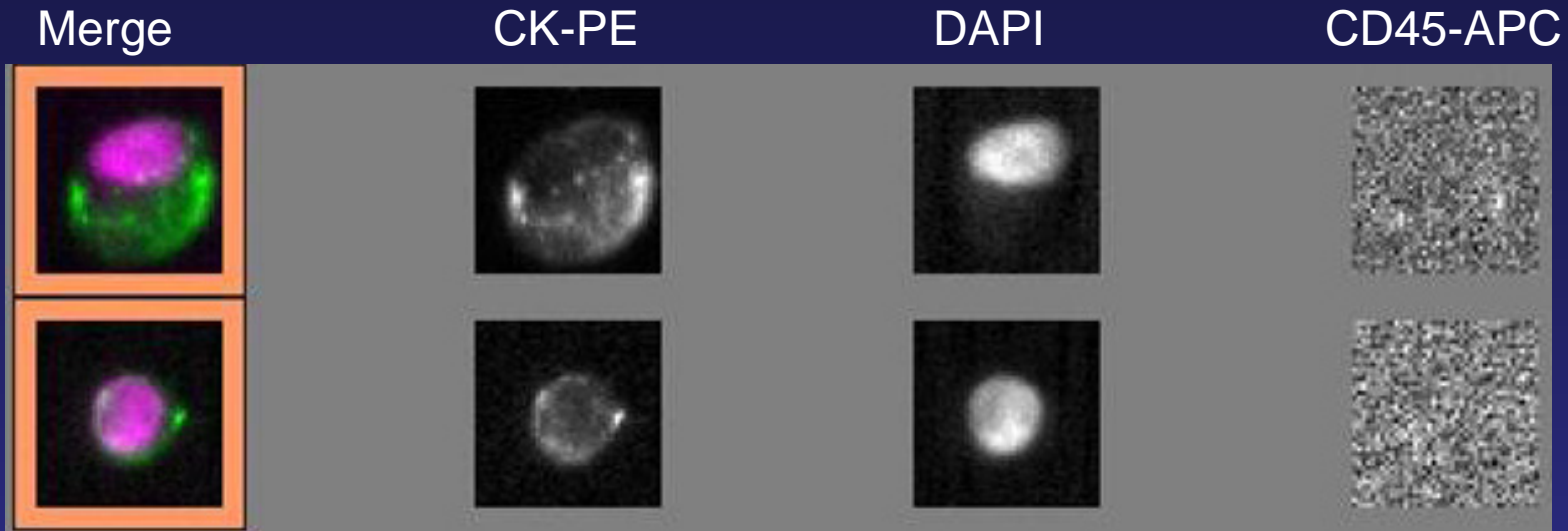
## Aims:

1. Identify if CTC presence is associated with standard prognostic factors (tumor size, grade, axillary lymph node status).
2. Determine if CTCs predict outcome in non-metastatic TNBC patients.

# Patients

- 80 non-metastatic TNBC patients seen at UT MD Anderson Cancer Center
- Mean Age: 54 (29 – 80) years
- Pre-Menopausal: 70%
- 53% received NACT prior to CTC assessment
- Median Follow up: 40 months

# CellSearch<sup>®</sup> CTC assay



- 7.5 mL Blood is collected in a CellSave<sup>®</sup> tube and processed within 96 hours
- EpCAM+ cells are immunomagnetically enriched
- Isolated cells are fluorescently stained with:
  - DAPI
  - anti-Cytokeratin (CK) 8,18, 19-PE
  - anti-CD45-APC

# CTC Positivity in TNBC

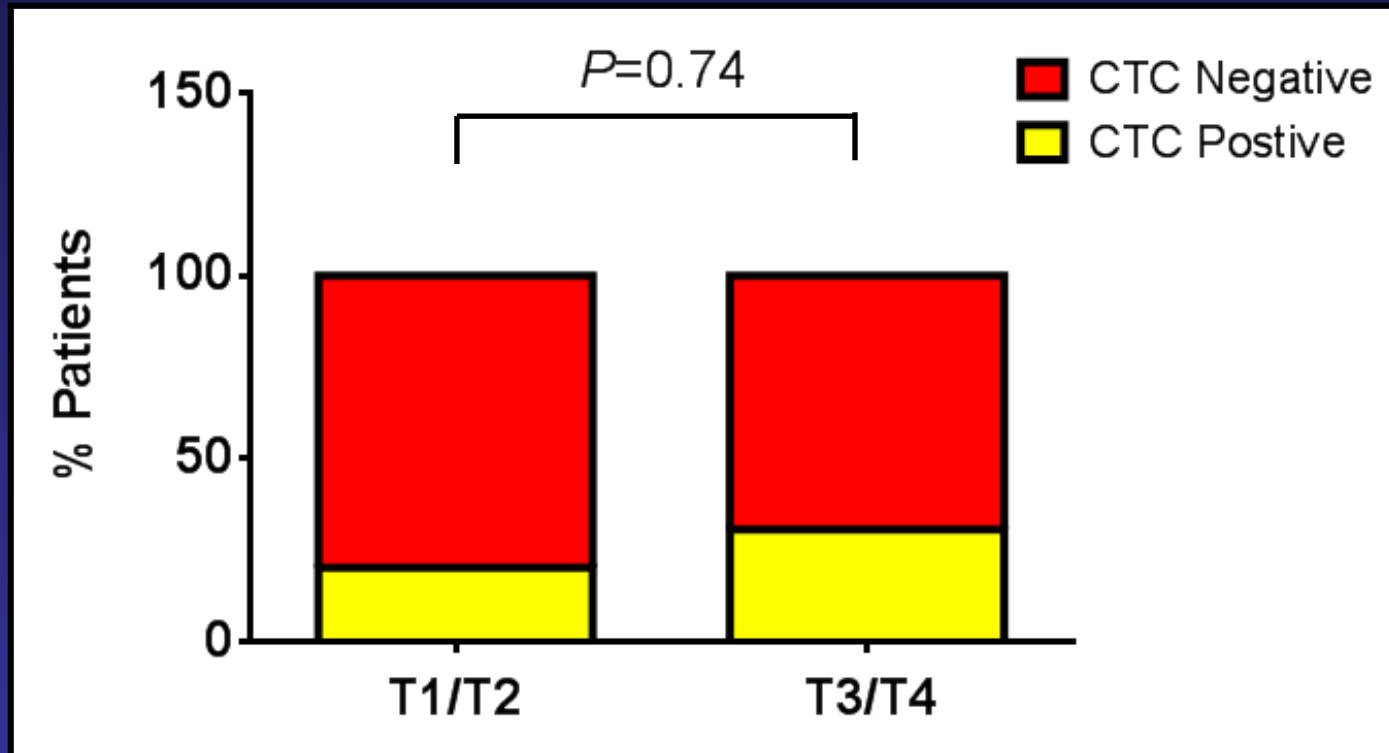
	<b>CTC + Patients</b>	<b>%</b>
<b>Non-TNBC</b>	<b>96/420</b>	<b>23%</b>
<b>TNBC</b>	<b>19/80</b>	<b>24%</b>



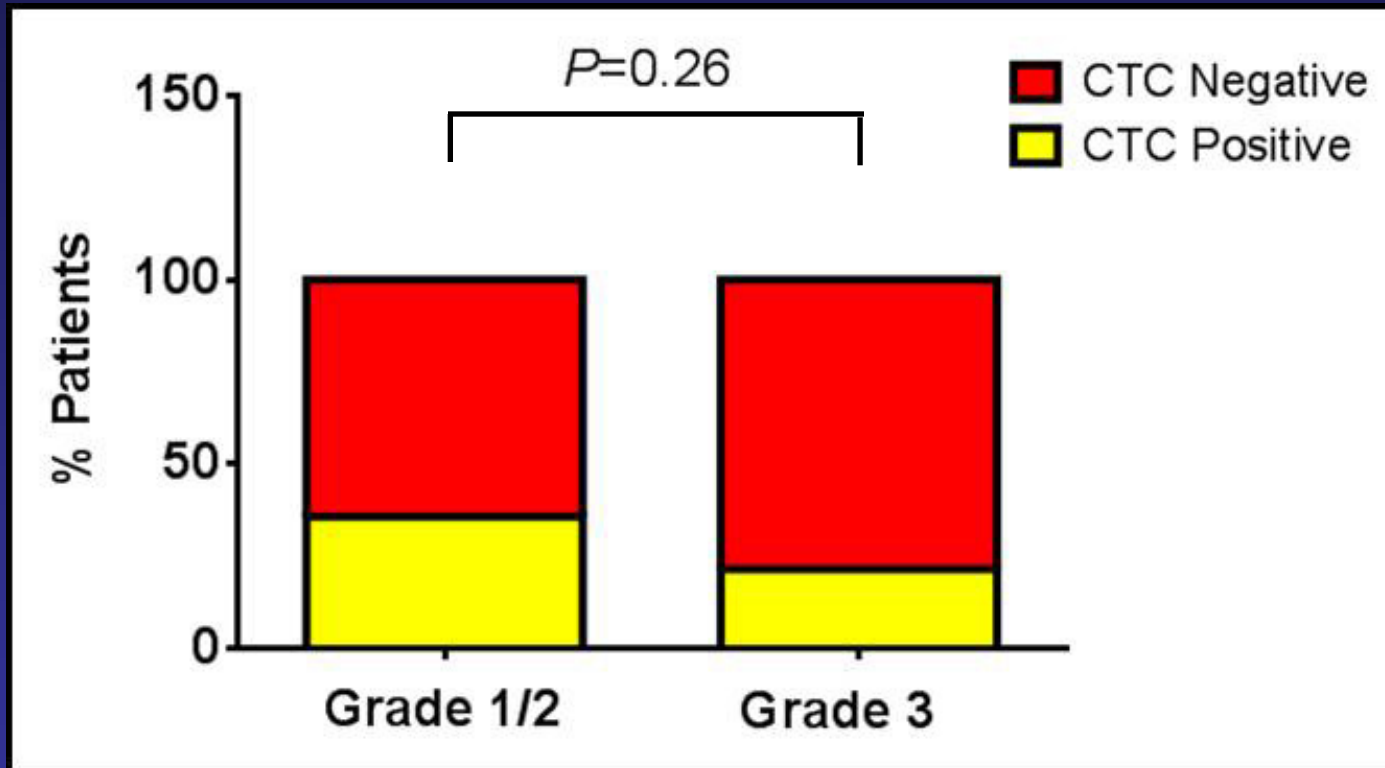
# TNBC and CTC Positivity

Variables	Overall Cohort Number of Subjects	1 or more CTC		P value
		Positive	Negative	
<b>Tumor Size</b>				
<2 cm (T1)	22 (28%)	4 (21%)	18 (30%)	0.74 <sup>^</sup>
2 cm – 5 cm (T2)	32 (40%)	7 (37%)	25 (41%)	
>5 cm (T3)	8 (10%)	3 (16%)	5 (8%)	
Skin / Chest wall infiltration (T4)	18 (22%)	5 (26%)	13 (21%)	
<b>Pathologic Nodal Status</b>				
Node negative	35 (44%)	7 (37%)	28 (46%)	0.37
1-3 Lymph nodes	26 (32%)	5 (26%)	21 (34%)	
> 3 lymph nodes	19 (24%)	7 (37%)	12 (20%)	
<b>Histologic Tumor Grade</b>				
Low Grade (Grade 1)	3 (4%)	3 (16%)	0 (0%)	0.26 <sup>#</sup>
Intermediate Grade (Grade 2)	11(14%)	2 (11%)	9 (15%)	
High Grade (Grade 3)	65 (81%)	14 (74%)	51 (84%)	
<b>Neoadjuvant Chemotherapy</b>	42 (53%)	9 (47%)	33 (54%)	0.61

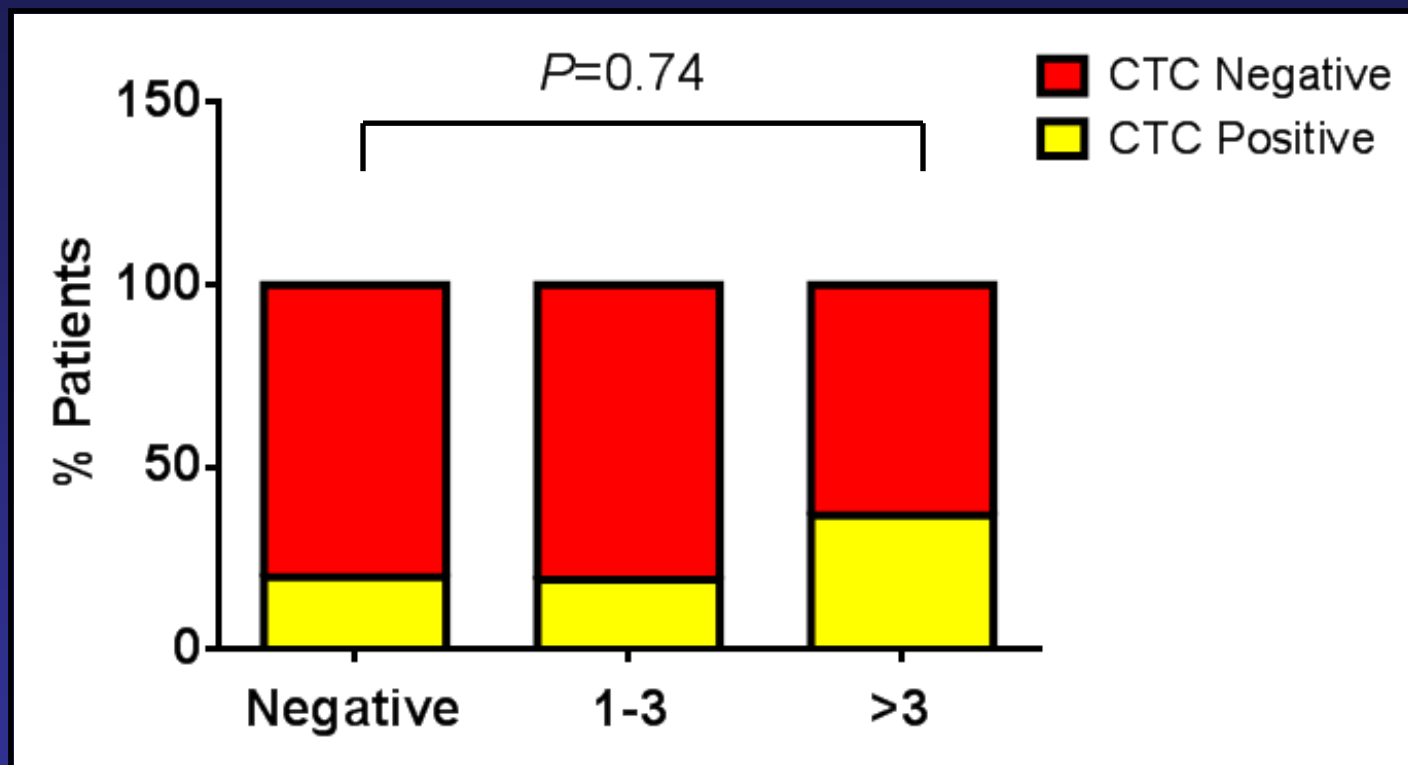
# CTC Positivity and Tumor Size



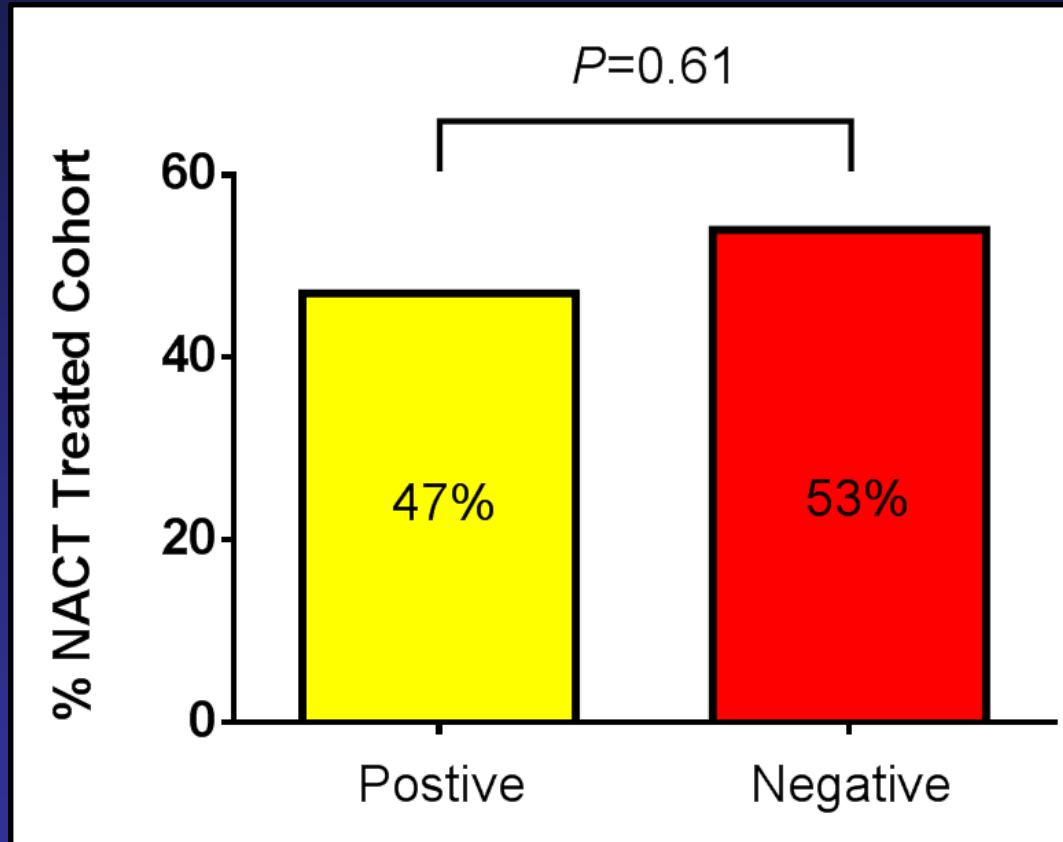
# CTC Positivity and Tumor Grade



# CTC Positivity and Lymph Node Status



# CTC Positivity in NACT Treated Patients



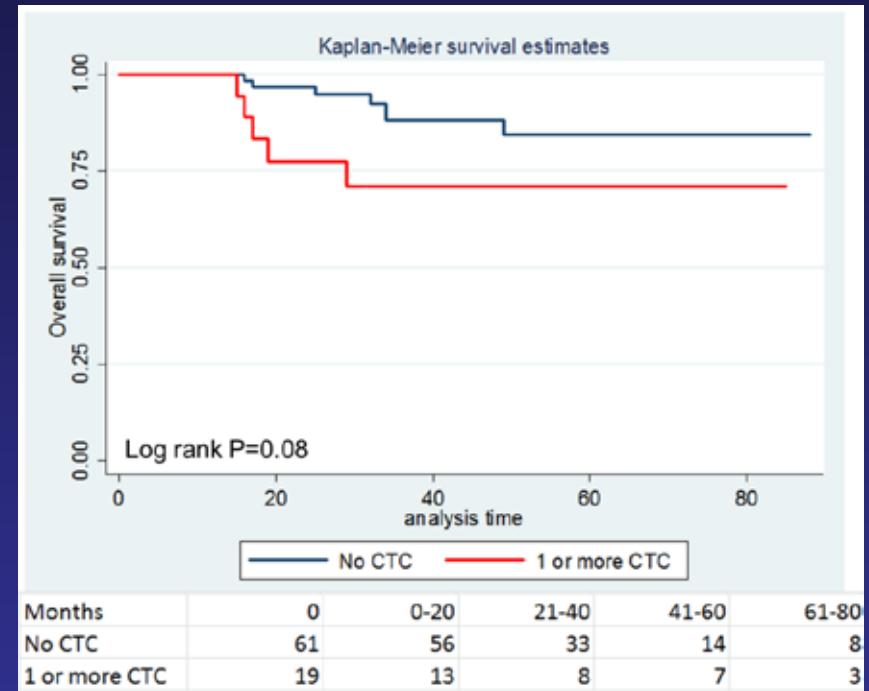
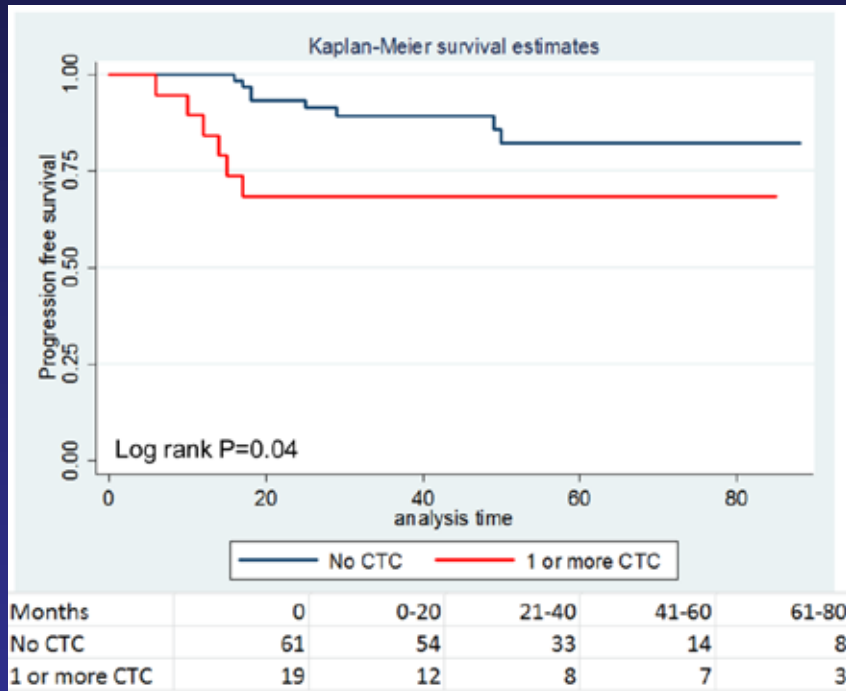
# CTCs and Progression-free Survival

Variable		Number	Relapses (Percent)	Relapse free Survival proportion at 2-years	P Value by log-rank test
<b>By Number of Circulating Tumor Cells</b>					
<b>One or more CTCs</b>	+	19	6/19 ( <b>32%</b> )	68%	<b>0.04</b>
	-	61	8/61 (13%)	93%	
<b>Two or more CTCs</b>	+	6	3/6 (50%)	50%	0.02
	-	74	11/74 (15%)	90%	
<b>Three or more CTCs</b>	+	4	3/4 (75%)	25%	≤0.0001
	-	76	11/76 (14%)	90%	

# CTCs and Overall Survival

Variable		Number	Deaths (Percent)	Overall Survival proportion at 2-years	P Value by log- rank test
<b>By Number of Circulating Tumor Cells</b>					
<b>One or more CTCs</b>	+	19	5/19 (26%)	77%	0.08
	-	61	7/61 (11%)	97%	
<b>Two or more CTCs</b>	+	6	3/6 ( <b>50%</b> )	67%	<b>0.01</b>
	-	74	9/74 (12%)	94%	
<b>Three or more CTCs</b>	+	4	3/4 (75%)	50%	≤0.0001
	-	76	9/76 (12%)	94%	

# CTCs in Non-Metastatic TNBC Patients



## Progression Free Survival

One or more CTC vs. no CTCs

P=0.04

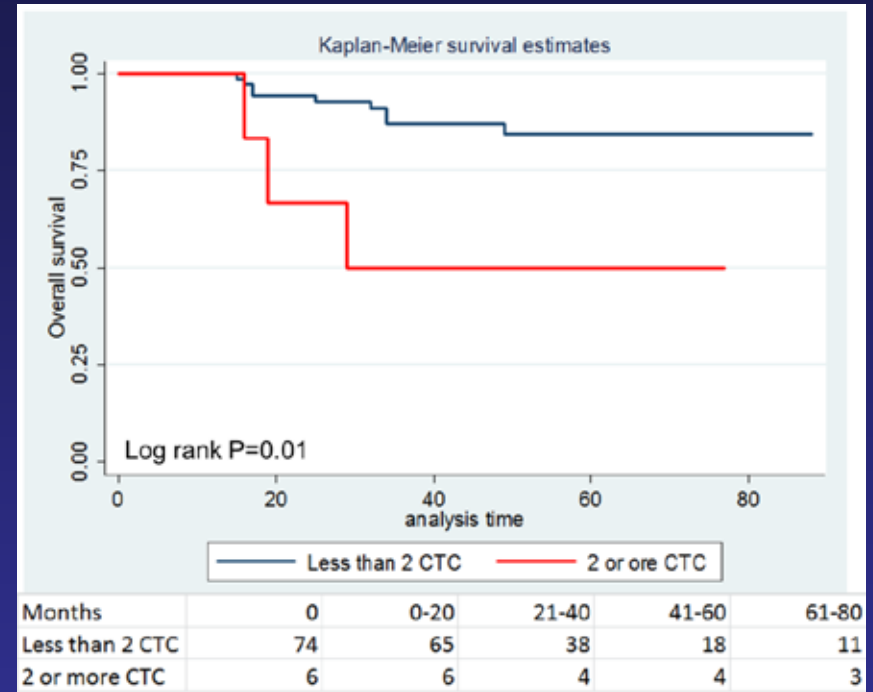
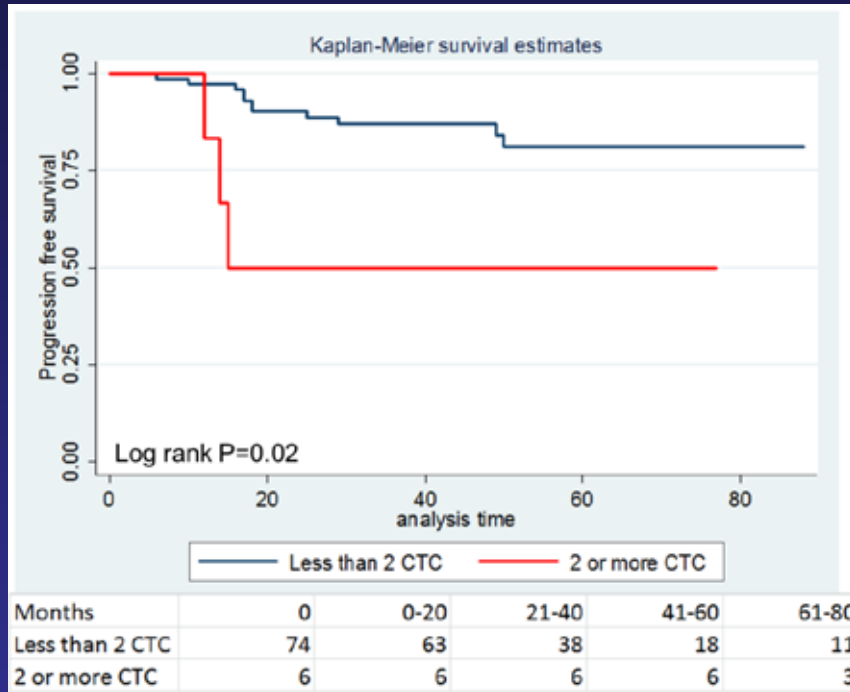
## Overall Survival

One or more CTC vs. no CTCs

P=0.08



# CTCs in Non-Metastatic TNBC Patients



## Progression Free Survival

Two or more CTCs vs. one or less CTCs

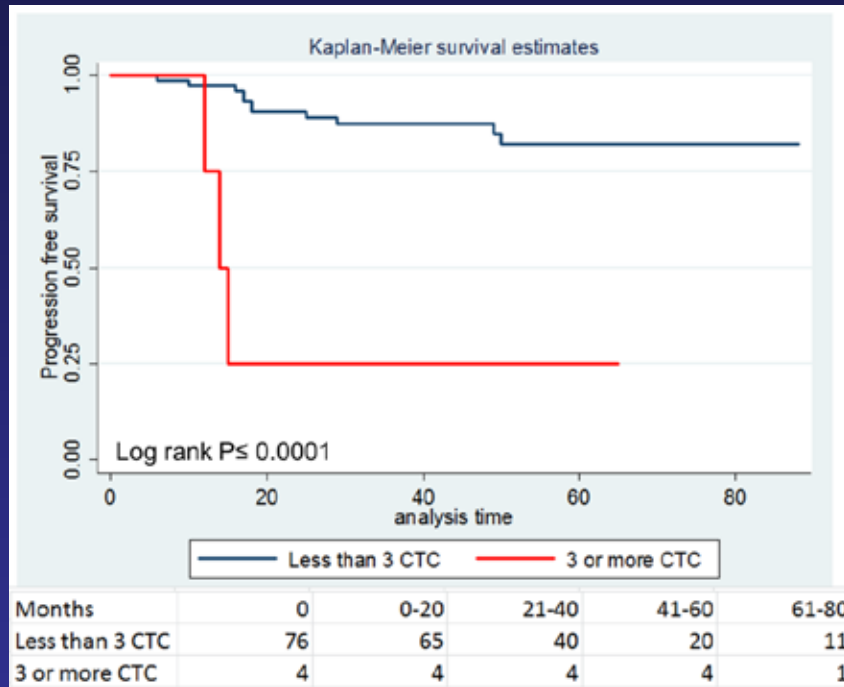
P=0.02

## Overall Survival

Two or more CTCs vs. one or less CTCs

P=0.01

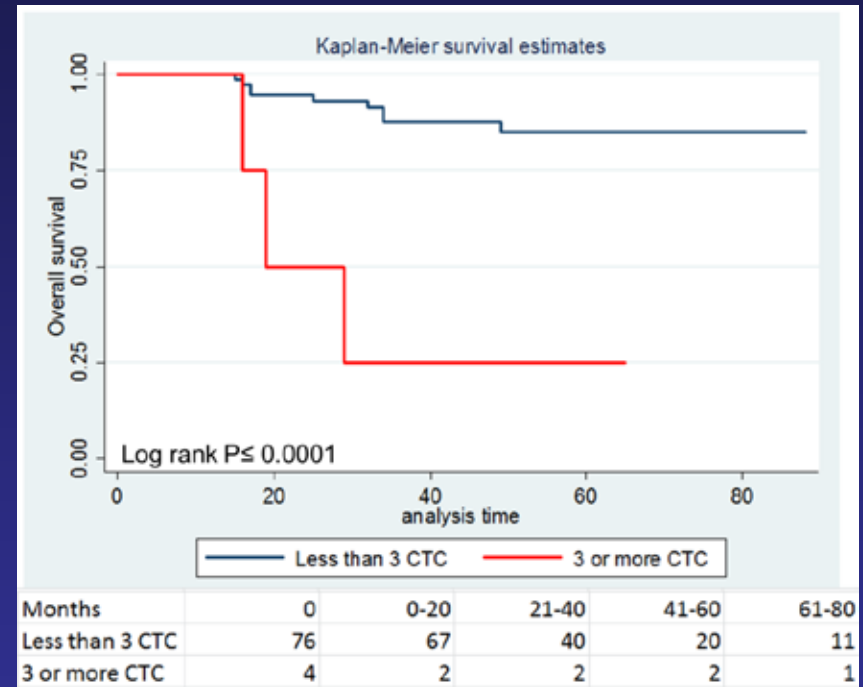
# CTCs in Non-Metastatic TNBC Patients



## Progression Free Survival

Three or more CTCs vs. two or less CTCs

$P \leq 0.001$



## Overall Survival

Three or more CTCs vs. two or less CTCs

$P \leq 0.001$

# Progression Free Survival and $\geq 2$ CTCs

PFS	Hazard Ratio
Tumor > 2cm	2.99
1-3 Lymph Nodes	0.66
3+ Lymph Nodes	4.55
Tumor grade 3	1.38
$\geq 2$ CTCs	4.31

# Overall Survival and $\geq 2$ CTCs

OS	Hazard Ratio
Tumor > 2cm	2.35
1-3 Lymph Nodes	0.86
3+ Lymph Nodes	4.84
Tumor grade 3	1.22
$\geq 2$ CTCs	4.48

# Conclusions

- CTCs can be detected in 24% of operable TNBC patients
- CTC detection is not associated with tumor size, grade, or axillary lymph node status
- Two or more CTCs predicts decreased progression-free and overall survival in TNBC

# Future Studies

- Continued enrollment to determine if one or more CTC predicts outcome
- Characterization of CTCs to identify therapeutic targets
- Collaboration with Dr. Dave Hoon involving nucleic acid assessment in pair-matched serum samples

# Acknowledgements

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