

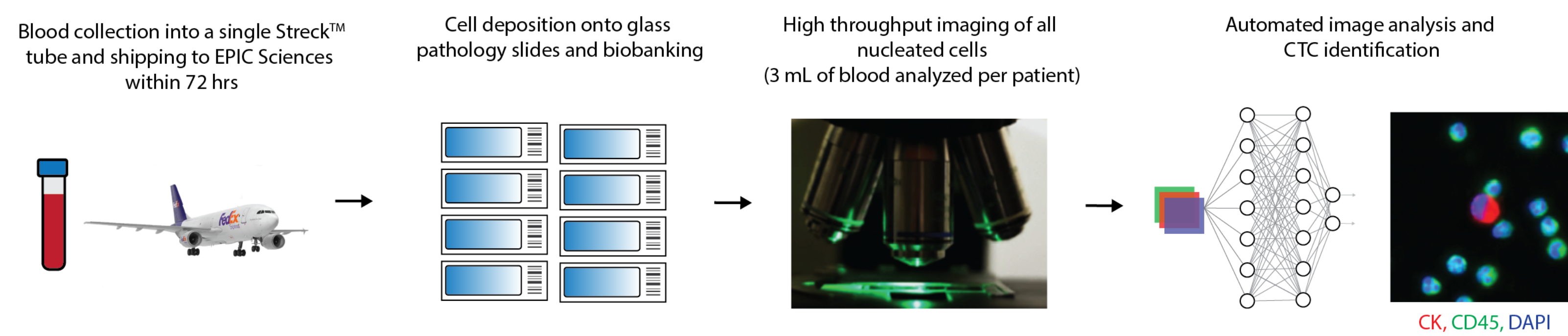
Abstract #312459: Clinical Significance Of CTC Enumeration Using The Epic Sciences Platform In Metastatic Castration Resistant Prostate Cancer (mCRPC) Patients Treated With AR Signaling Inhibitors

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BACKGROUND

- Circulating Tumor Cell (CTC) number has been shown to be prognostic for survival pre- and post-therapy for use as an aid to monitoring breast, colorectal and prostate cancers. Historically, CTCs are counted as any cell in 7.5 mL of blood that is captured by EpCAM, is CD45-, and expresses cytokeratin's (CK)¹.
- Here we report the prognostic significance of CTCs detected using the enrichment-free EPIC Sciences platform in mCRPC patients prior to treatment with an AR signaling inhibitor. CTC were counted from 3 mL of blood for this analysis and defined as any CK+, CD45- cell with an intact DAPI+ nucleus.

The Epic Sciences CTC Detection Platform

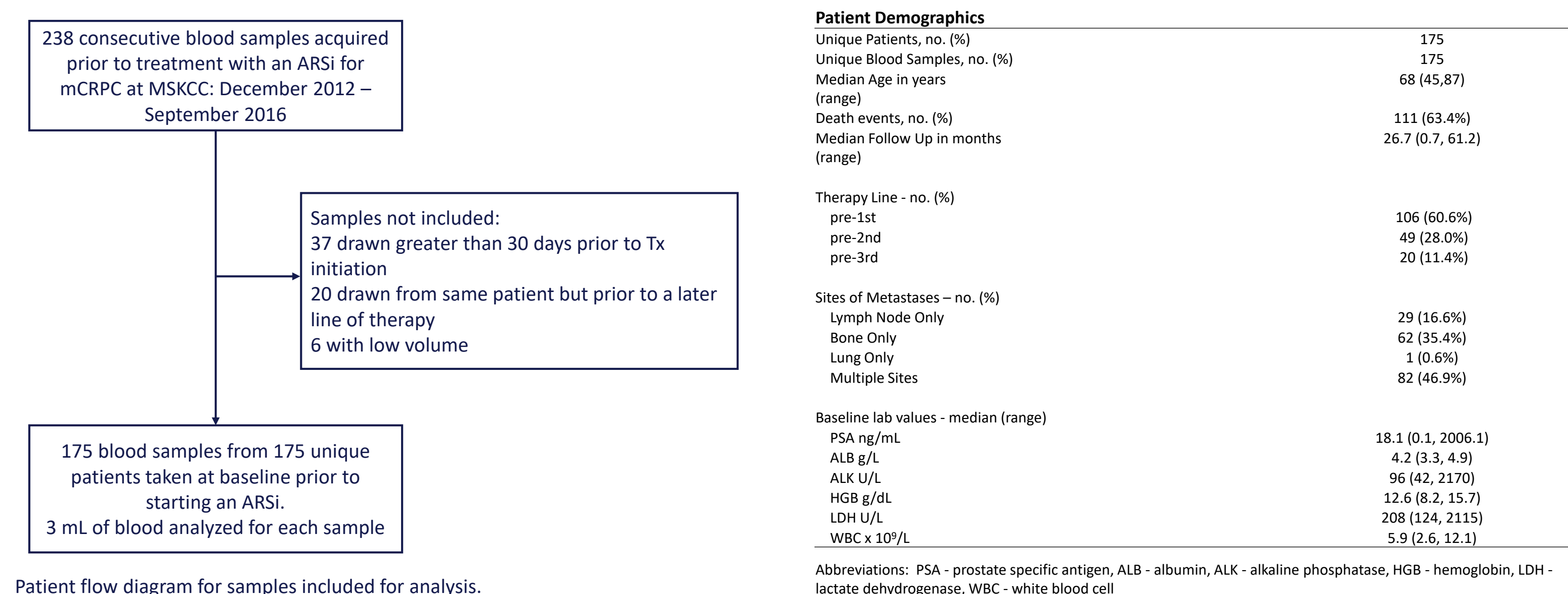


Circulating Tumor Cell Definition

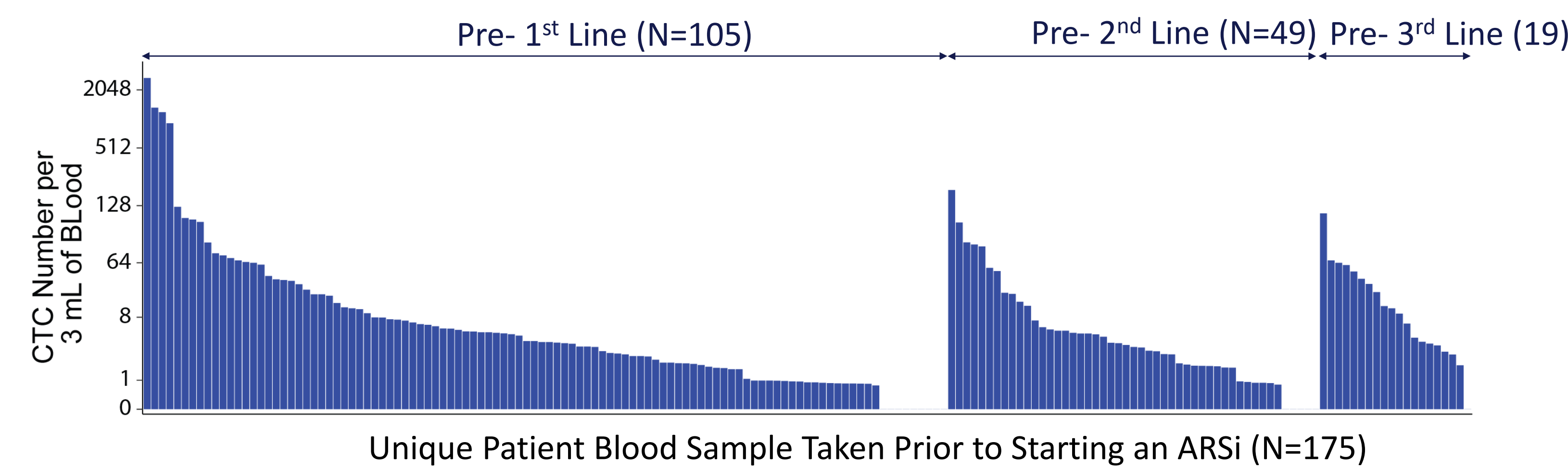
- Has epithelial lineage (CK+)
- No leukocyte lineage (CD45-)
- Has an intact nucleus (DAPI+)
- Clusters of CTCs are counted as 1 event
- The reported CTC number is from or per 3 mL of blood
- Median turn-around-time is 4 days from blood collection

Workflow schematic of the Epic Sciences platform and definition of a CTC in this analysis. Within 72 hours of collection, red-cells are lysed and nucleated cells are plated onto glass pathology slides and can be stored long-term at -80 C. At analysis slides are stained with DAPI, CK, and CD45. Each cell image is automatically processed and CTCs are detected *in silico*. 3 mL of blood is analyzed per patient.
 Reference: Werner *et al*. Analytical Validation and Capabilities of the Epic CTC Platform: Enrichment-free Circulating Tumour Cell Detection and Characterization J Circ Biomarkers 2015. PMID: 28936239

Patient Selection And Demographics



CTCs Were Detected in >90% of mCRPC Patient Blood Samples in the 1st, 2nd, and 3rd Line Settings Prior to Initiation of an AR Signaling inhibitor (ARSi)

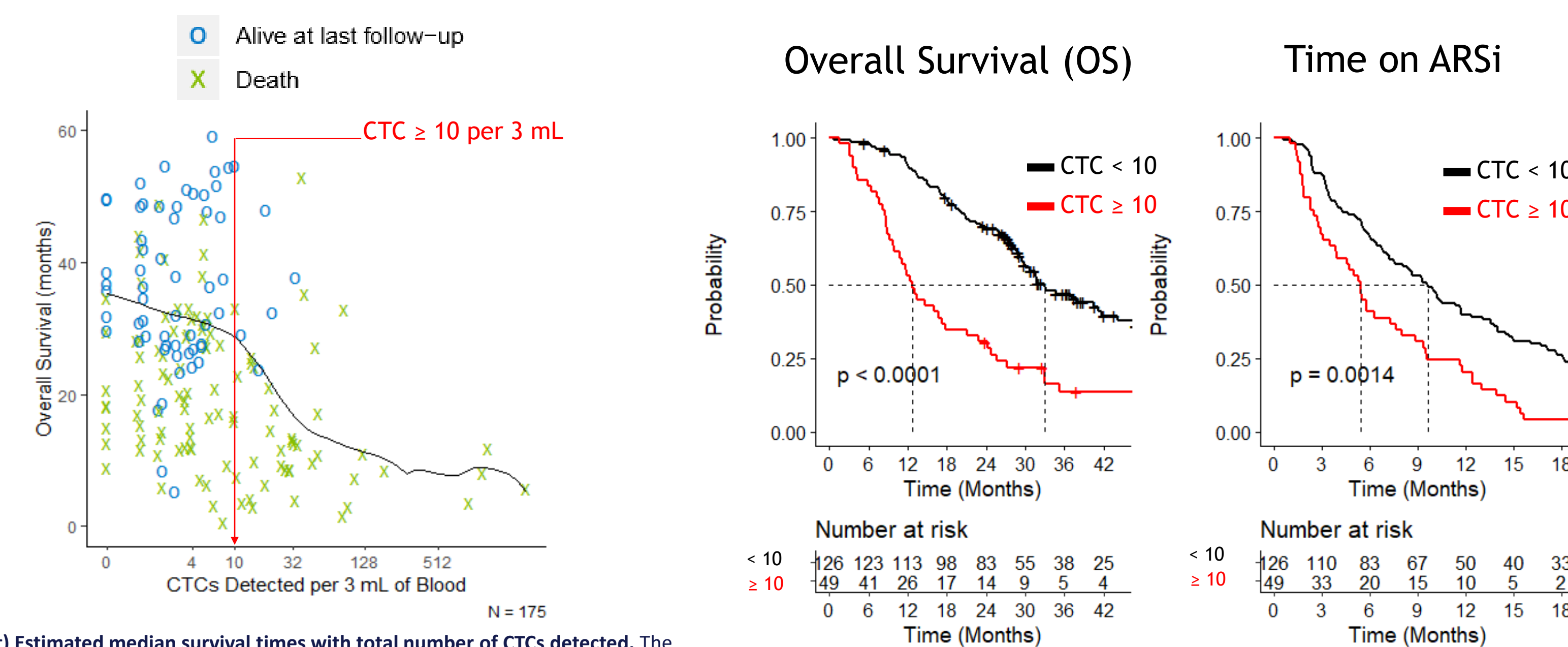


CTC count and incidence by line of therapy. CTC number reported per 3 mL of blood analyzed.

Therapy Line	CTC incidence no. (%)	#CTCs detected median (range)
pre 1st	97/106 (91.5%)	4 (0-3090)
pre 2nd	44/49 (90.0%)	4 (0-200)
pre 3rd	19/20 (95.0%)	11 (0-95)

Abbreviations: CTC – Circulating Tumor Cell

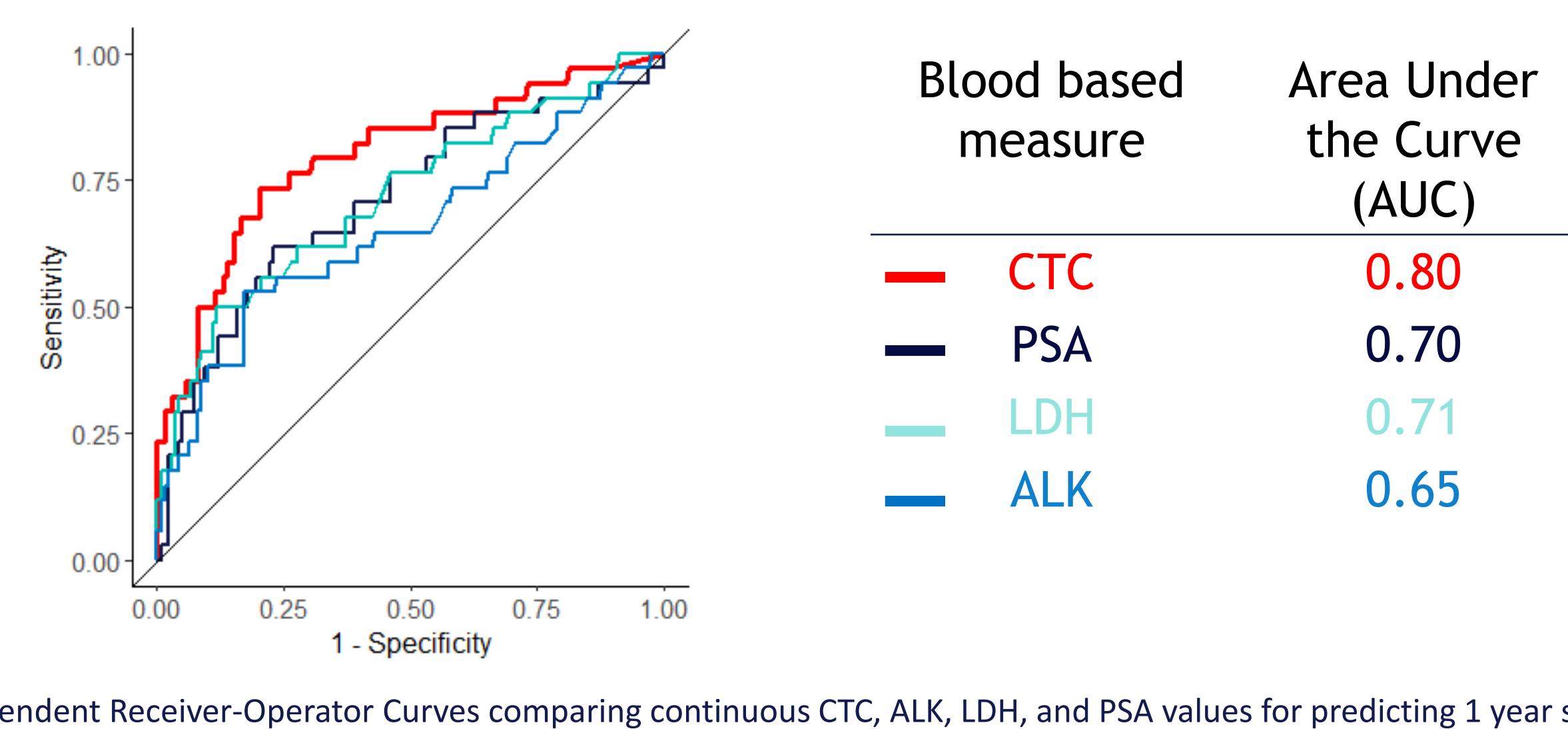
Patients With High CTC Counts Have Shorter Survival and Shorter Time on ARSi Treatment



Left) Estimated median survival times with total number of CTCs detected. The solid lines indicate the estimated median survival times using a gaussian kernel density estimate. The "o" refers to censored events, while the "x" indicates a death event. CTC number is the number of CTCs detected in the 3 mL of blood analyzed.

Right) Kaplan-Meier analysis of CTC-High (≥10 CTCs in 3 mL) and CTC-Low (<10 CTCs in 3 mL).

CTC Number Considered as a Continuous Variable Had the Highest AUC for Predicting 1 year Survival Relative to PSA, LDH, and Alkaline Phosphatase



Time-dependent Receiver-Operator Curves comparing continuous CTC, ALK, LDH, and PSA values for predicting 1 year survival.

CTC Number Determined on the Epic Sciences Platform is Prognostic For Survival and Time on ARSi Treatment for mCRPC patients

The association of CTCs number with overall survival and time on drug in univariate and multivariable Cox PH modeling

		CTC Number High vs. Low	
		CTC < 10	CTC ≥ 10
CTC Frequency	Number of Men (%)	126 (72%)	49 (28%)
Overall Survival (OS)	Median OS (months; 95% CI)	31.9 months (29.5 - 44.1)	12.9 months (10.0 - 22.9)
	HR* (95% CI)	2.7 (2.0 - 4.3); p < 0.001	
	HR** (95% CI)	2.3 (1.5 - 3.8); p < 0.001	
Time on ARSi	Median Time On ARSi (months; 95% CI)	9.6 months (7.5 - 11.7)	5.4 months (3.8 - 8.0)
	HR* (95% CI)	1.7 (1.2 - 2.4); p = 0.002	
	HR** (95% CI)	1.4 (0.9 - 2.0); p = 0.1	

*univariate HR; ** HR adjusted for Line of Therapy, Age, LDH, ALK, PSA

Patient Demographics	CTC < 10	CTC ≥ 10
Therapy Line - no. (%)		
pre-1st	78 (61.9%)	28 (57.1%)
pre-2nd	38 (30.2%)	11 (22.4%)
pre-3rd	10 (7.9%)	10 (20.4%)
Sites of Metastases – no. (%)		
Lymph Node Only	25 (19.8%)	4 (8.2%)
Bone Only	48 (38.1%)	14 (28.6%)
Lung Only	1 (0.8%)	0 (0%)
Multiple Sites	52 (41.3%)	30 (61.2%)
Baseline lab values - median (range)		
PSA ng/mL	15.4 (0.5, 1191.7)	45.8 (0.1, 2006.1)
ALB g/L	4.2 (3.4, 4.9)	4.1 (3.3, 4.6)
ALK U/L	88 (42, 342)	138 (54, 2170)
HGB g/dL	12.9 (8.2, 15.7)	11.7 (9.2, 14.2)
LDH U/L	202 (124, 427)	259 (139, 2115)
WBC x 10 ⁹ /L	5.8 (2.6, 10.8)	5.8 (3, 12.1)

Abbreviations: PSA - prostate specific antigen, ALB - albumin, ALK - alkaline phosphatase, HGB - hemoglobin, LDH - lactate dehydrogenase, WBC - white blood cell

CONCLUSIONS

1. >90% of blood samples from 1st-3rd line mCRPC patients taken prior to starting an Androgen Receptor Signaling inhibitor contained detectable CTCs (CK+, CD45- negative cells) in the 3 mL analyzed.
2. CTCs detected on the Epic Sciences platform are prognostic in mCRPC patients about to start an Androgen Receptor Signaling inhibitor (ARSi).
3. Patients with low CTCs had longer time on an ARSi, suggesting that CTC counts determined on the Epic Sciences platform could be used to identify patients more likely to have greater benefit.
4. The results warrant prospective testing of CTC values on the Epic Sciences platform as a baseline prognostic tool as ongoing studies evaluate the CTC count biomarker as a response monitoring tool.

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