

Abstract

BACKGROUND: Circulating tumor cells (CTCs) are accepted as surrogate markers for tumor response and linked to shorter survival in castration-resistant prostate cancer (CRPC) patients¹. Thus, detection of CTCs has become an important addition to the clinical care toolbox. The only FDA approved method, the CellSearch[®] prognostic kit, captures only epithelial cell adhesion molecule (EpCAM)-positive CTCs and suffers from low yield of CTCs and limited capacity to perform molecular analysis. The CellSearch[®] profile kit also relies on EpCAM to enrich CTCs but ApoCell integrates laser scanning cytometry (LSC) to perform molecular and genetic analysis of CTCs^{2,3}. This study compared CTC recovery by the CellSearch[®] prognostic kit and the CellSearch[®] profile kit in CRPC patients. We assessed the use of CTCs as a prognostic factor for clinical monitoring of CRPC patients in real time and evaluated the association between CTC number, laboratory and clinical characteristics, and overall survival (OS).

METHODS: CTCs were enumerated using the CellSearch[®] prognostic kit and the CellSearch[®] profile kit in 24 CRPC patients. A side by side comparison was performed on two 7.5 mL blood samples collected from each patient. Clinical variables included metastatic site(s) and number, Gleason score, PSA, CEA, chromogranin A, NSE, alkaline phosphatase, LDH, sedimentation rate, and C-reactive protein. The probability of patient survival over time was estimated by the Kaplan-Meier method.

RESULTS: Overall, higher CTC counts were obtained by the CellSearch[®] profile kit and LSC method compared to the CellSearch[®] prognostic kit.

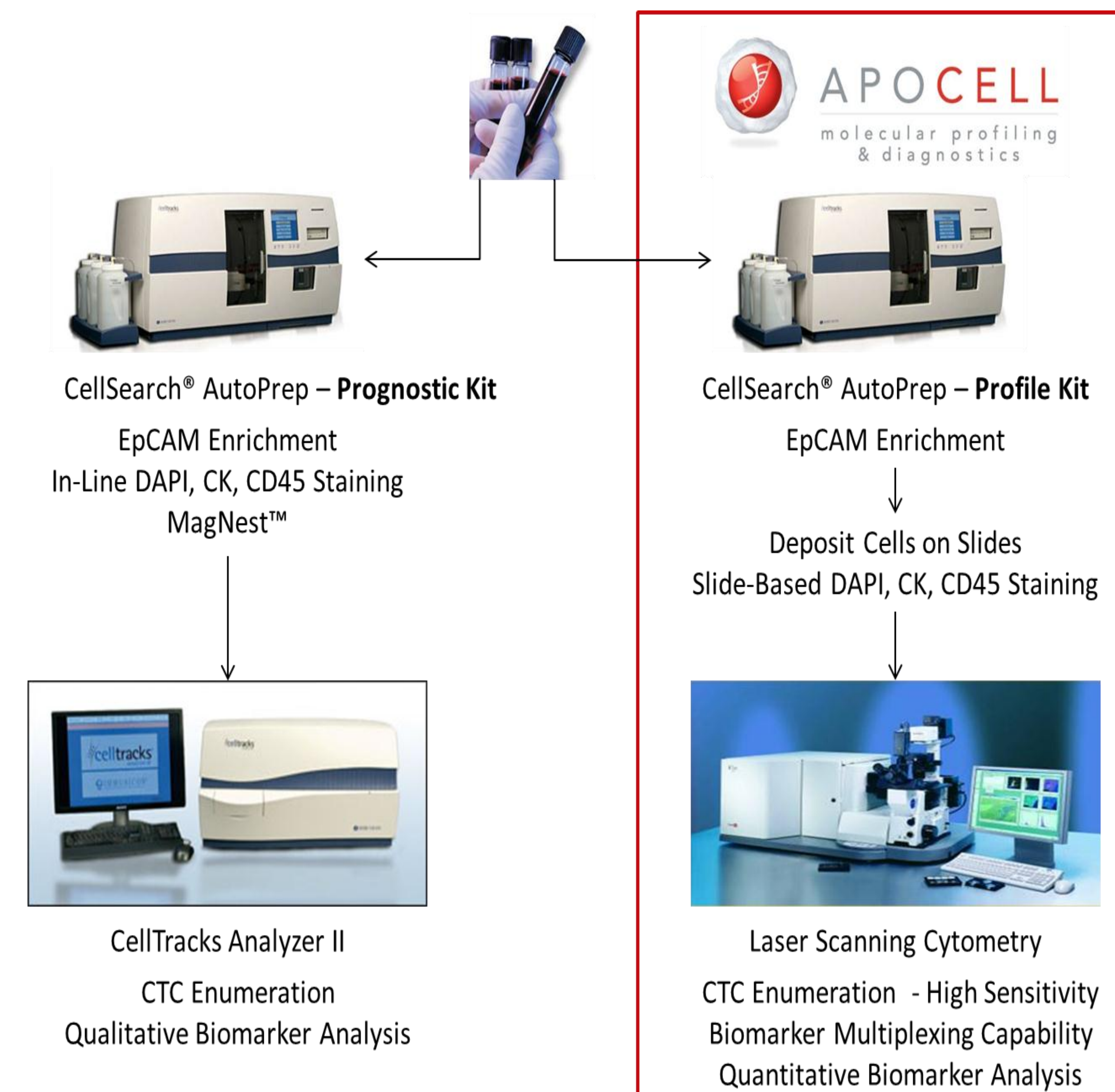
CONCLUSIONS: CTC enumeration by the integrated CellSearch[®] profile kit and LSC yielded improved CTC recovery compared to the standard method. CTC counts correlated with disease severity and support the use of CTCs as predictors of OS. We will present a comparison of CTC enumeration with a correlation to clinical variables.

Patient Characteristics

Characteristics	No. (%)
Median Age	68.3
Age Range	47-85
Gleason	
7	4
8	5
9	12
10	1
N/K	2
No. Metastatic Sites	
1	14
2	8
3	2
Metastatic Sites	
Bone	17
Lymph Node	15
Lung	3
Liver	1
No. Prior Therapy	
1	17
2	7

Table 1. Patient characteristics

CTC Analysis Methods



CTCs Predict Overall Survival

	CellSearch [®] Prognostic*			CellSearch [®] Profile + LSC		
	<5	5-99	≥100	<5	5-99	≥100
Patients Enumerated	19	3	1	7	8	9
Median CTCs (Range)	0 (0-4)	42 (40-70)	-	0 (0-0)	37 (8-79)	209 (119-1314)
Patients Alive	14	0	-	2	6	7
Patients Dead	5	3	1	5	2	2
Median OS (Range)	13.05 (2.82-21.20)	4.44 (0.89-6.25)	-	12.42 (0.89-13.05)	- (4.67-21.20)	- (2.63-9.87)

*1 n/a

Table 2. Side-by-side comparison of the CellSearch[®] prognostic kit and the CellSearch[®] profile kit in 24 CRPC patients.

Overall Survival Probability – CellSearch[®] Prognostic

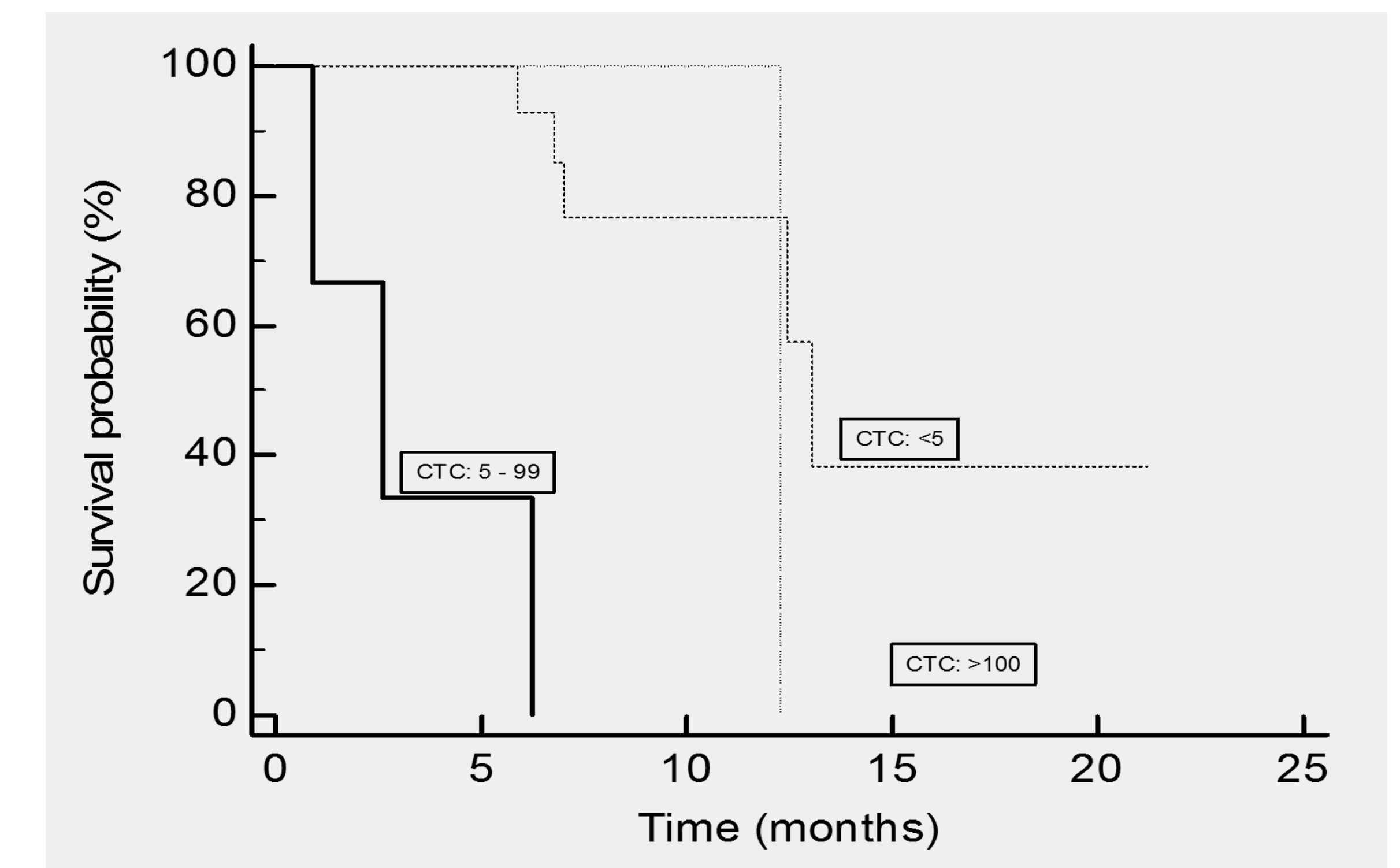


Figure 1. Overall survival of 23 patients using the CellSearch[®] prognostic kit.

Overall Survival Probability – CellSearch[®] Profile + LSC

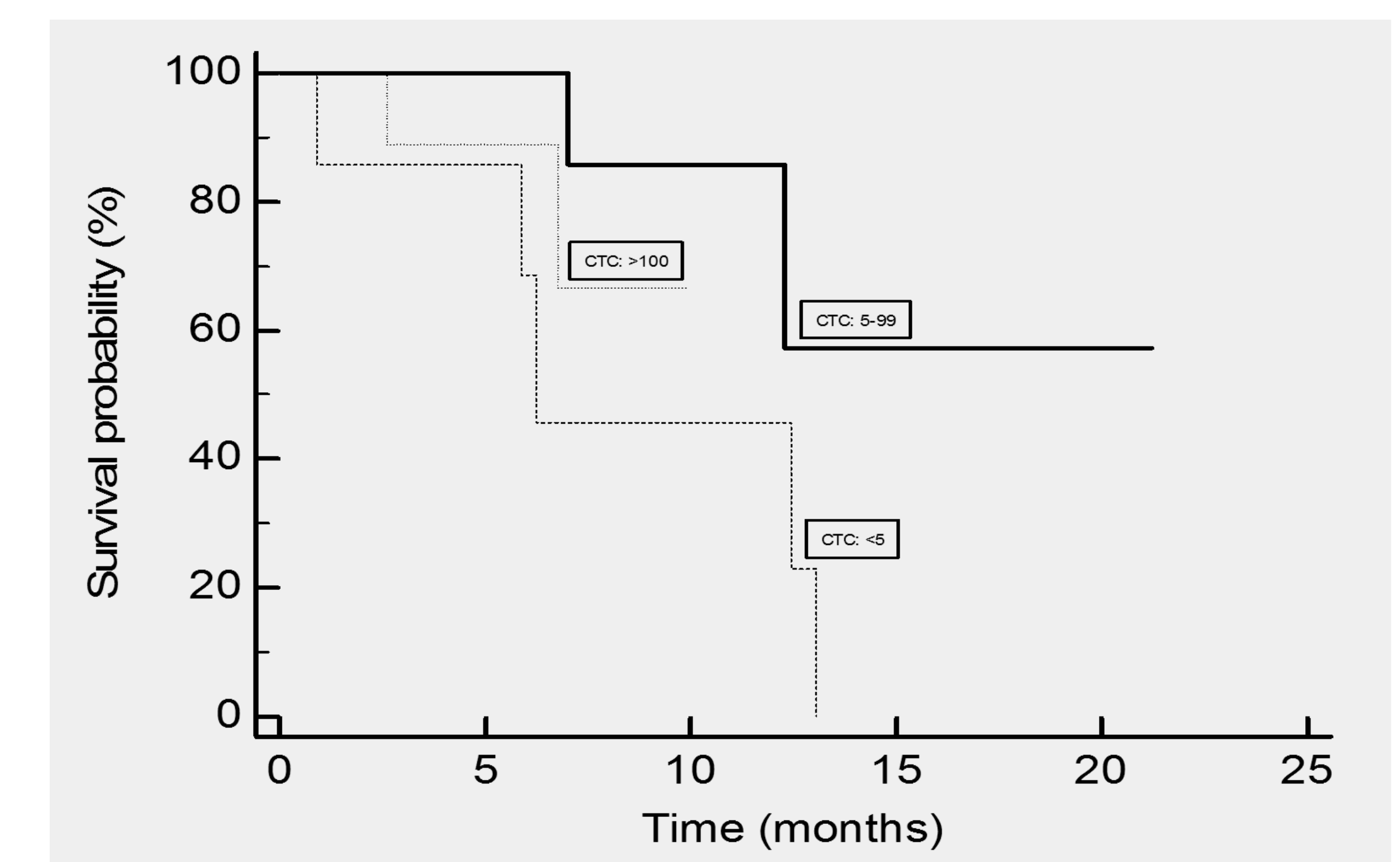


Figure 2. Overall survival of 24 patients using the CellSearch[®] profile kit plus laser scanning cytometry.

Conclusions

- Baseline CTCs are predictive of patient survival and are significantly correlated with clinical characteristics in prostate cancer patients.
- CTC enumeration by the integrated CellSearch[®] profile kit and LSC method yielded improved CTC recovery compared to the standard CellSearch[®] prognostic method.
- CTC counts correlated with disease severity and support the use of CTCs as predictors of OS.
- Our study confirms previous findings that support the use of CTC enumeration as a prognostic biomarker for prostate cancer patients.

References

- 1) JS de Bono, Scher HI, Montgomery RB, et al. Circulating tumor cells predict survival benefit from treatment in metastatic castration-resistant prostate cancer. Clin Cancer Res 2008;14:6302-6309.
- 2) Flores LM, Kindelberger DW, Ligon AH, et al. Improving the yield of circulating tumour cells facilitates molecular characterisation and recognition of discordant HER2 amplification in breast cancer. Br J Cancer 2010; 102 (10):1495-502.
- 3) Melnikova VO, Liu W, Zhang Y, et al. Development of a new, highly sensitive assay for CTC detection based on the CellSearch[®] CTC profile kit enrichment and laser scanning cytometry analysis. In AACR 101st Annual Meeting; April 17-21, 2010; Washington, DC. Abstract number 2687.