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CTC prognostic significance in non- muscle invasive bladder cancer Results from a prospective study

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The rationale for serial monitoring of patients using the CELLSEARCH® CTC Test

Use the CELLSEARCH® CTC Test to make more informed decisions about treating patients with metastic breast (mBC), prostate (mPC),* and colorectal (mCRC) cancer at initiation of treatment and throughout the continuum of therapy.

Clinical trial results
Case studies

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Case studies

Monitoring patients with metastatic cancer throughout treatment is critical to making informed clinical decisions. However, current methods for monitoring patients with mBC, mPC and mCRC are not without limitations, controversies, and uncertainties.[1-5]

The CELLSEARCH® CTC Test is the only clinically validated, FDA-cleared system that captures, isolates, and enumerates the number of circulating tumor cells (CTCs) before and during treatment with high sensitivity and specificity. As an adjunct to standard monitoring methods, monitoring patients with the CELLSEARCH® CTC Test can help keep you informed of your patient's status based on real-time predicted prognosis. Evaluation of CTCs at any time during the course of therapy allows assessment of patient prognosis and is predictive of progression-free survival and overall survival.[6]

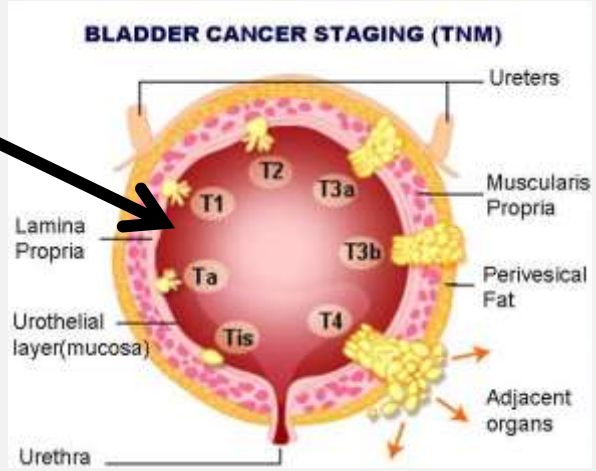
CELLSEARCH® CTC TEST results should be used in conjunction with all clinical information derived from diagnostic tests (eg, imaging or laboratory tests), physical examination and complete medical history, in accordance with appropriate management procedures. Please see instructions for use for indications and limitations of the CELLSEARCH® CTC Test as a monitoring aid in management of mBC, mPC, and mCRC.

clinical utility of CTC enumeration yet to be proven

There is a broad agreement that CTC as prognostic marker may be more beneficial in **early-stage** cancer particularly in those tumor types characterized by **high progression rate and lack of prognostic markers**

BLADDER CANCER

Non - muscle invasive (Ta, T1, CIS)	**74%**
Muscle invasive (T2-T4)	**18%**
Metastatic (M1)	**8%**



Recurrence rate > 50%
Progression rate 20-40%

Micrometastatic disease

European Association of Urology

Platinum Priority – Editorial and Reply from Authors

Referring to the article published on pp. 423–430 of this issue

How Well Can You Actually Predict Which Non–Muscle-Invasive Bladder Cancer Patients Will Progress?

Richard J. Sylvester *

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EUROPEAN UROLOGY 49 (2006) 466–477

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Bladder Cancer

Predicting Recurrence and Progression in Individual Patients with Stage Ta T1 Bladder Cancer Using EORTC Risk Tables: A Combined Analysis of 2596 Patients from Seven EORTC Trials

Richard J. Sylvester [a,*], *Adrian P.M. van der Meijden* [b], *Willem Oosterlinck* [c], *J. Alfred Witjes* [d], *Christian Bouffioux* [e], *Louis Denis* [f,1], *Donald W.W. Newling* [g,2], *Karlheinz Kurth* [h,3]

Need for improving current predictive tools

Conservative treatment
(transurethral resection)

Radical treatment
(cystectomy)

2011

Annals of Oncology 23: 2352–2356, 2012
doi:10.1093/annonc/mdr619
Published online 20 February 2012

Prognostic value of circulating tumor cells in nonmuscle invasive bladder cancer: a CellSearch analysis

P. Gazzaniga[1*], A. Gradilone[1], E. de Berardinis[2], G. M. Busetto[2], C. Raimondi[1], O. Gandini[1], C. Nicolazzo[1], A. Petracca[1], B. Vincenzi[3], A. Farcomeni[4], V. Gentile[2], E. Cortesi[5] & L. Frati[1]

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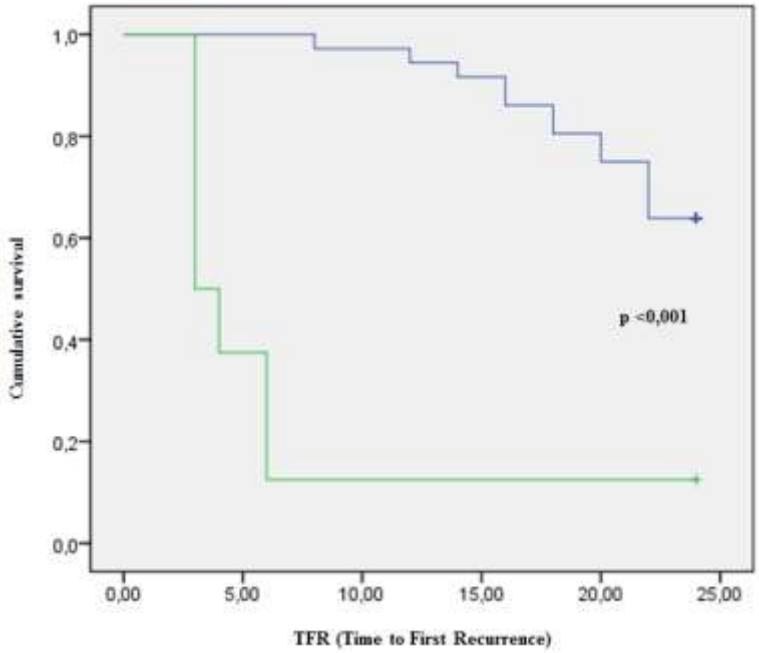


CTC were detectable in 8/44 patients (18%).

Presence of at least 1 CTC /7.5 mL significantly associated to shorter time to first recurrence (6.5 versus 21.7 months, $P < 0.001$).

Median time to progression was not reached, due to the short follow-up period.

PROSPECTIVE SINGLE-CENTER TRIAL

CTC prognostic significance in non- muscle invasive bladder cancer
Results from a prospective study

Primary objective:

to correlate CTC presence to ***progression of disease*** in T1G3 bladder cancer

Patients and methods

130 patients enrolled from January 2010 to January 2013

Inclusion criteria:
T1
G3
Candidate to TURB+ BCG

98 pt. suitable

Follow up time: 36 months
Median follow up time: 24.3 months (range: 4-36).

Blood draw (7.5 mL) for CTC enumeration by CellSearch® immediately before transurethral resection procedure

unpublished data

Patients population and CTC detection rate

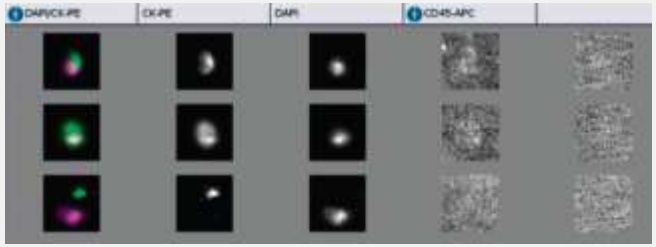
Patients	Total (N=98)	CTC negative (N=82)	CTC positive (N=16)	P
Age (years)	74.0 (66.8-78.0)	73.0 (66.0-78.0)	76.5 (68.5-80.0)	0.173
Gender (male)	92 (93.9%)	79 (96.3%)	13 (81.2%)	0.053
Time between TURBT and BCG therapy (months)				1.0
1-2 weeks	0	0	0	
3-4 weeks	98 (100%)	82 (100%)	16 (100%)	
>1 month	0	0	0	
Cis positive	19 (19.4%)	9 (11.0%)	10 (62.5%)	<0.001
Tumor multifocality	74 (75.5%)	58 (70.7%)	16 (100%)	0.010
Tumor size				0.010
<1 cm	24 (24.5%)	24 (29.3%)	0	
1-3 cm	49 (50.0%)	41 (50.0%)	8 (50.0%)	
>3 cm	25 (25.5%)	17 (20.7%)	8 (50.0%)	
Lymphovascular invasion	13 (13.3%)	6 (7.3%)	7 (43.8%)	0.001
Stage				1.0
I	98 (100%)	82 (100%)	16 (100%)	
II-IV	0	0	0	
Circulating tumor cells				<0.001
0	82 (83.7%)	82 (100%)	0	
1	12 (12.2%)	0	12 (75.0%)	
>1	4 (4.1%)	0	4 (25.0%)	
Local recurrence	39 (39.8%)	26 (31.7%)	13 (81.2%)	<0.001
Progression	20 (20.4%)	5 (6%)	15 (93.0%)	<0.001

CTC positive 16%

mean number: 1

range: 1-50

= 0	82/98	84%
= 1	12/98	12%
>1	4/98	4%



unpublished data

Patients	Total (N=98)	CTC negative (N=82)	CTC positive (N=16)	P
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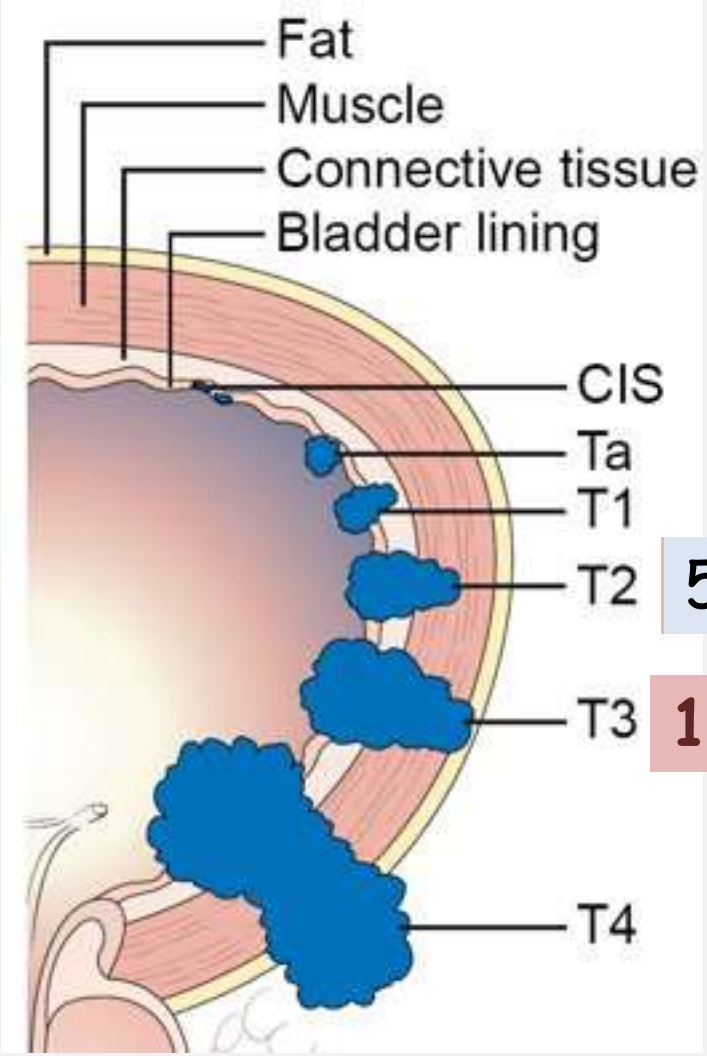
CTC -

CTC +



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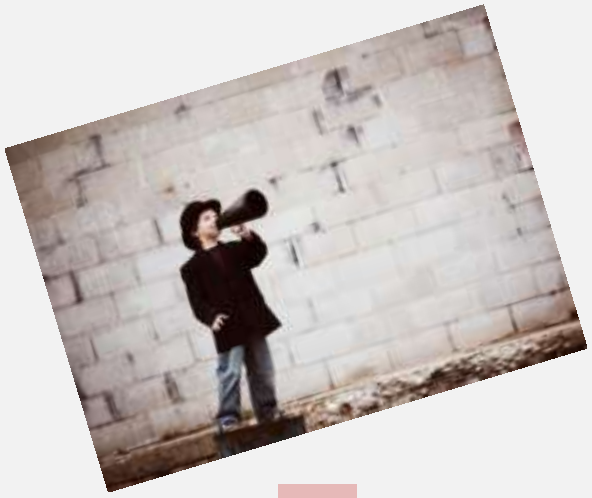


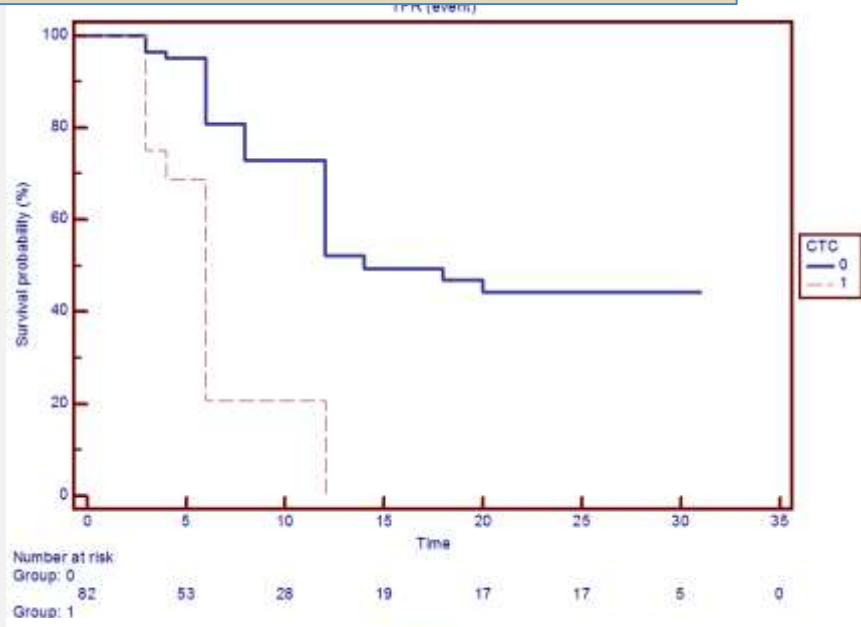
2

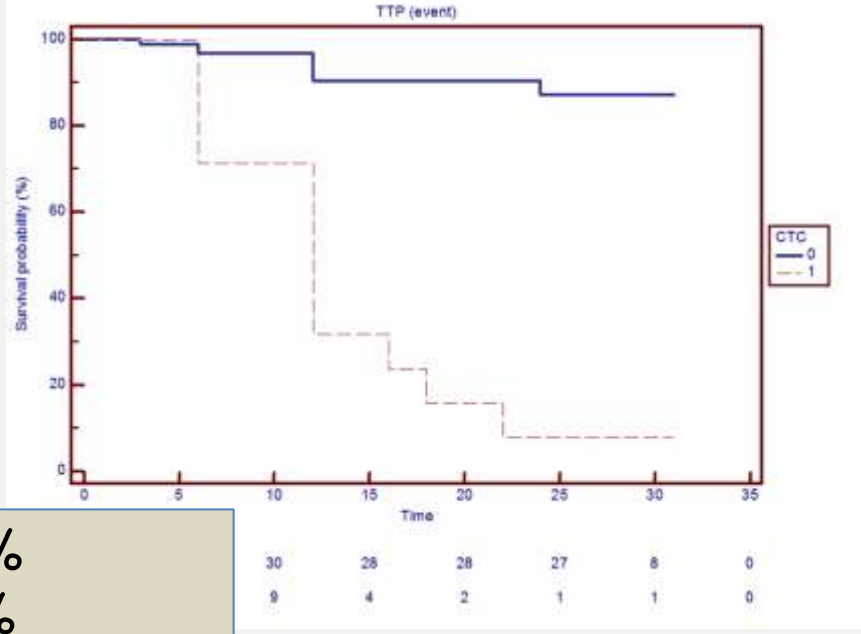
overt metastasis

unpublished data

TFR and TTP in CTC+ vs CTC-

Variables	Bivariate analysis	
	HR (95% CI)	P value
Time to first recurrence		
Age	1.04 (1.00; 1.09)	0.048
Male gender	0.53 (0.16-1.74)	0.295
Cis positivity	4.79 (2.39; 9.61)	<0.001
Tumor multifocality	14.26 (1.95; 104.07)	0.009
Tumor size	1.25 (0.81-1.95)	0.314
Lymphovascular invasion	3.75 (1.87; 7.51)	<0.001
Circulating tumor cell positivity	4.74 (2.31-9.72)	<0.001
Time to progression		
Age	1.06 (0.99; 1.13)	0.079
Male gender	0.27 (0.08; 0.94)	0.040
Cis positivity	10.24 (3.52; 29.80)	<0.001
Tumor multifocality	30.28 (0.24; >100)	0.168
Tumor size	3.21 (1.47; 7.01)	0.003
Lymphovascular invasion	3.98 (1.45; 10.91)	0.007
Circulating tumor cells ≥1	12.11 (4.06; 36.10)	<0.001





NPV 95%
PPV 75%

CTC in non- metastatic bladder cancer (CellSearch): 18-30%

Prognostic value of circulating tumor cells in nonmuscle invasive bladder cancer: a CellSearch analysis

P. Gazzaniga[1*], A. Gradilone[1], E. de Berardinis[2], G. M. Busetto[2], C. Raimondi[1], O. Gandini[1], C. Nicolazzo[1], A. Petracca[1], B. Vincenzi[3], A. Farcomeni[4], V. Gentile[2], E. Cortesi[5] & L. Frati[1]

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BJUI

Detection of circulating tumour cells in peripheral blood of patients with advanced non-metastatic bladder cancer

Michael Rink, Felix K.H. Chun, Sarah Minner*, Martin Friedrich†, Oliver Mauermann†, Hans Heinzer§, Hartwig Huland§, Margit Fisch, Klaus Pantel† and Sabine Riethdorf†

*Department of Urology, University Medical Centre Hamburg-Eppendorf, *Department of Pathology, University Medical Centre Hamburg-Eppendorf, †Institute of Tumour Biology, University Medical Centre Hamburg-Eppendorf, §Martini-Clinic, Prostate Cancer Centre, University Medical Center Hamburg-Eppendorf, Hamburg, †Department of Urology, HELIOS Hospital Krefeld, Krefeld, Germany*

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available at www.sciencedirect.com
journal homepage: www.europeanurology.com

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European Association of Urology

Bladder Cancer

Prognostic Role and HER2 Expression of Circulating Tumor Cells in Peripheral Blood of Patients Prior to Radical Cystectomy: A Prospective Study

Michael Rink[a,e,], Felix K. Chun[a,*], Roland Dahlem[a], Armin Soave[a], Sarah Minner[b], Jens Hansen[a], Malgorzata Stoupiec[c], Cornelia Coith[c], Luis A. Kluth[a], Sascha A. Ahyai[a], Martin G. Friedrich[d], Shahrokh F. Shariat[e,f], Margit Fisch[a], Klaus Pantel[c], Sabine Riethdorf[c]*

All T1G3
TTP not reached

Heterogeneity in stage (T1-T4) and treatments
Limited sample size

Lights

shadows

Strict selection of a population
extremely homogenous for:
Stage
Grade
Treatment
Risk score

variable follow-up (with some patients providing data only for 4 months)

Single centre design

CTC in early bladder cancer: Key point

Which clinical information?

The presence of at least 1 CTC/7.5mL is associated to high risk of progression to muscle invasive and metastatic disease

The PPV of the test is significantly higher than that of EORTC risk score

Conservative treatment (transurethral resection)

Radical treatment (cystectomy)

Systemic treatment ???

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May help the individual therapeutic decision-making process in non muscle invasive bladder

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Thanks for the attention!