

**“Circulating epithelial tumor cells and
circulating cancer stem cells in Prostate
cancer.
Evaluation of clinical potential”**

Prof. Dr. Katharina Pachmann

AONM Webinar

2nd December 2025



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Prostate Cancer Statistical Data




Worldwide Statistics

New cases in 2022: ~1,467,854

Prostate cancer is the second most frequently diagnosed cancer in men worldwide (after lung cancer)

Deaths in 2022: ~397,430

Survival

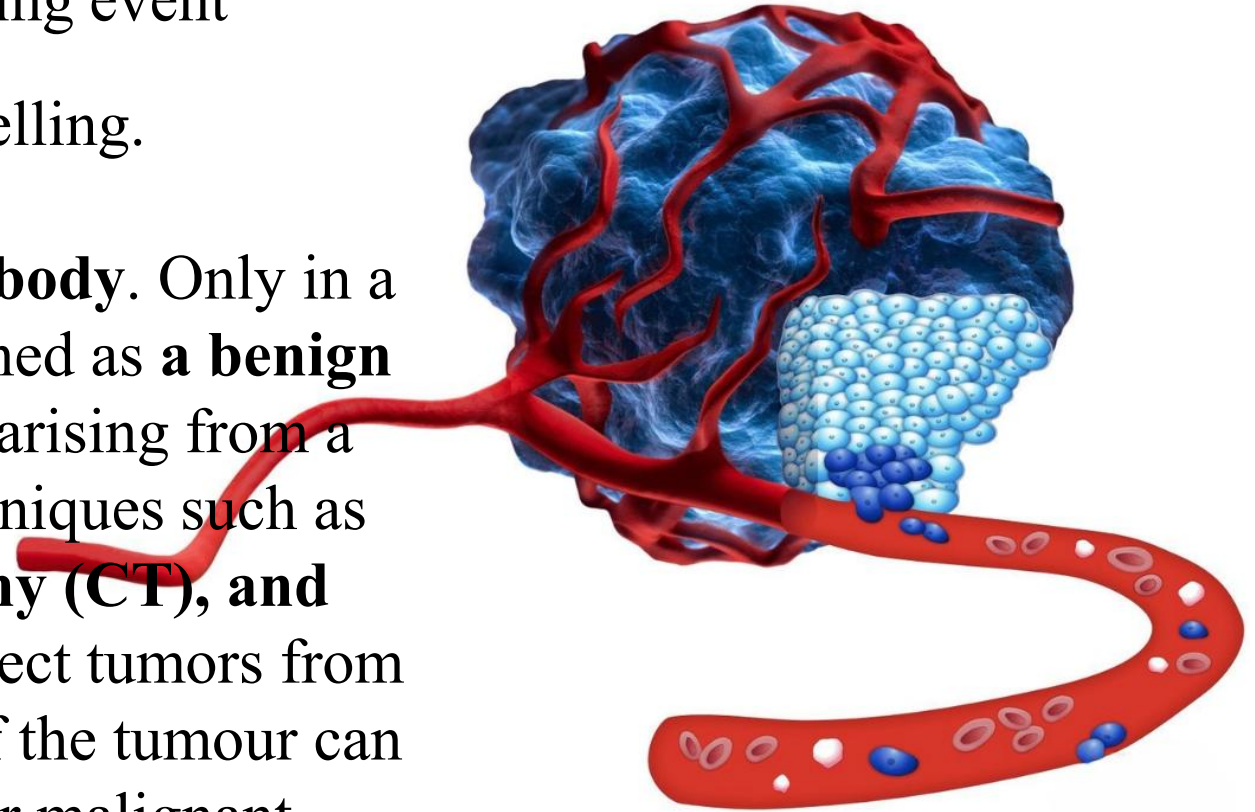
-  When prostate cancer is diagnosed at an early stage (localised or regional), the 5-year relative survival rate exceeds 99–100%
-  When the cancer is in an advanced stage (metastatic, “distant”), the 5-year survival rate drops to approximately 30–37%
-  **Risk factors:** age, family history, ethnicity, diet and life style, hormonal factors and chronic inflammation

Tumour

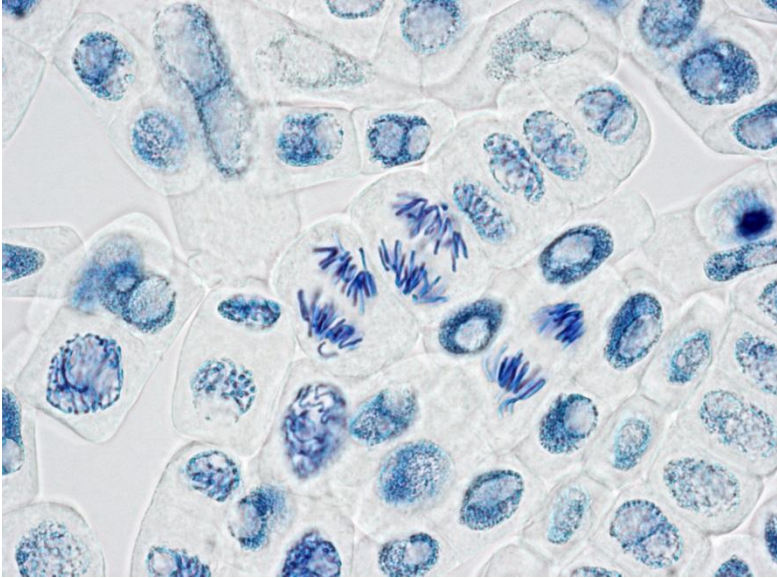
A tumour diagnosis (cancer) is a devastating event

The Latin word "*tumor*" means swelling.

It generally refers to a **mass or lesion in the body**. Only in a more specific medical sense is a tumour defined as a **benign or malignant new growth of body tissue**, arising from a **dysregulation of cell growth**. Imaging techniques such as **ultrasound, X-ray, computed tomography (CT), and magnetic resonance imaging (MRI)** can detect tumors from about 0.5 centimeters in size. The structure of the tumour can provide clues about whether it is benign or malignant. However, a **definitive diagnosis** can only be made from **tumour material analysed by pathologists (biopsy)**.



Cell growth



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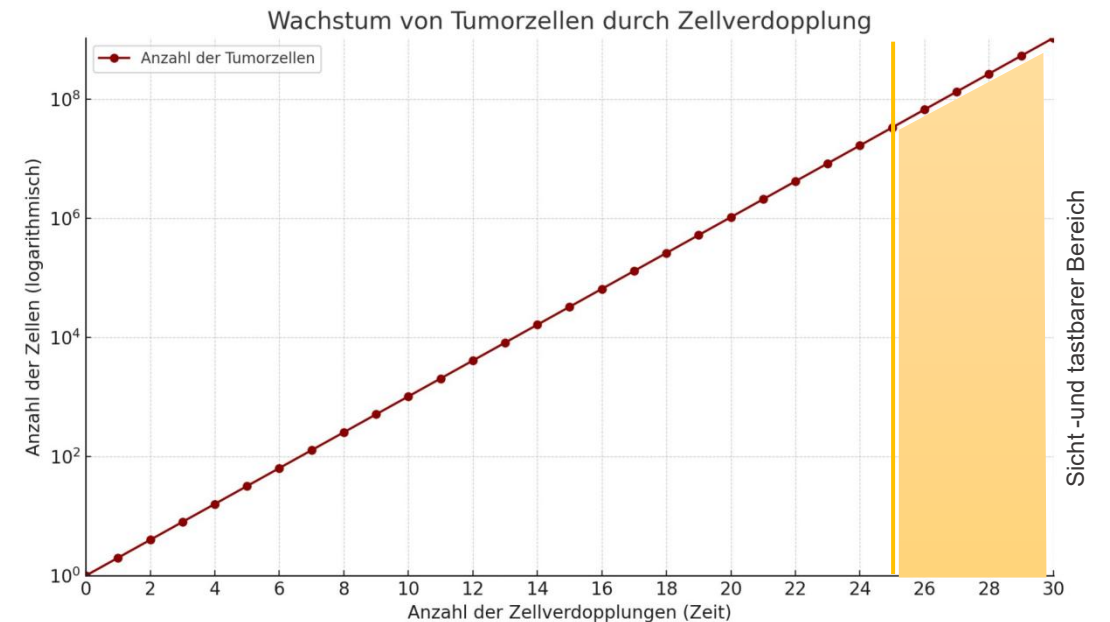
It is assumed that every cancer begins with a **single tumour cell**. The tumour cell multiplies through cell division/doubling.

They are:

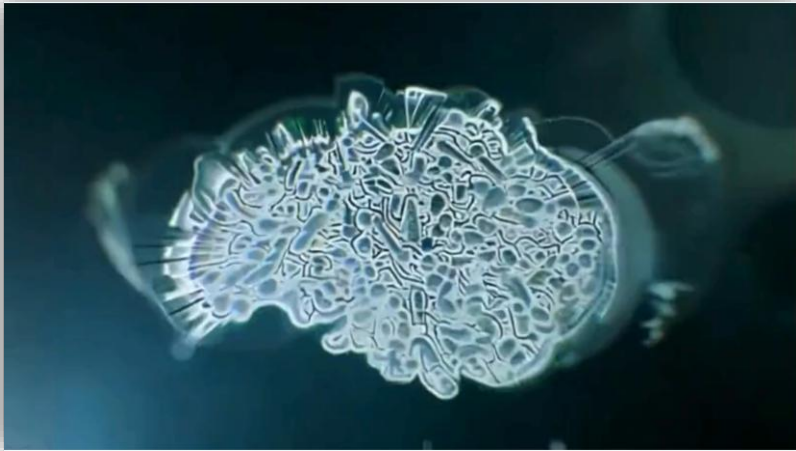
- After 10 doublings, about 1,000 cells (one thousand).
- After 20 doublings, about 1,000,000 cells (one million).
- After 30 doublings, about 1,000,000,000 cells (one billion).

A tumour of 1 centimeter contains about one billion tumor cells:

1000 × 1000 × 1000 cells.



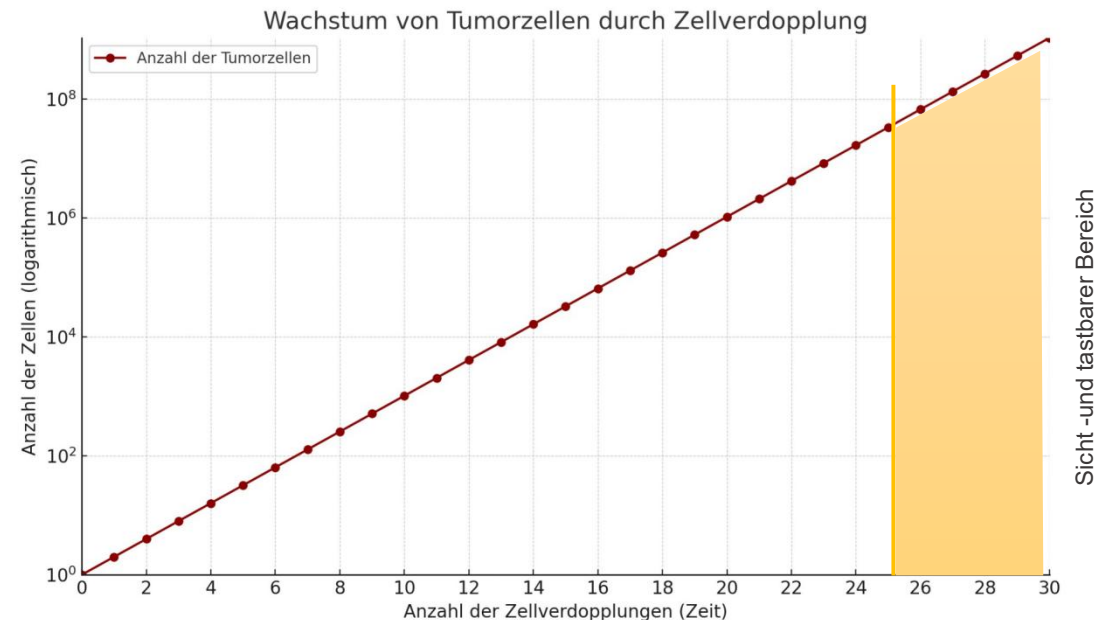
Spreading

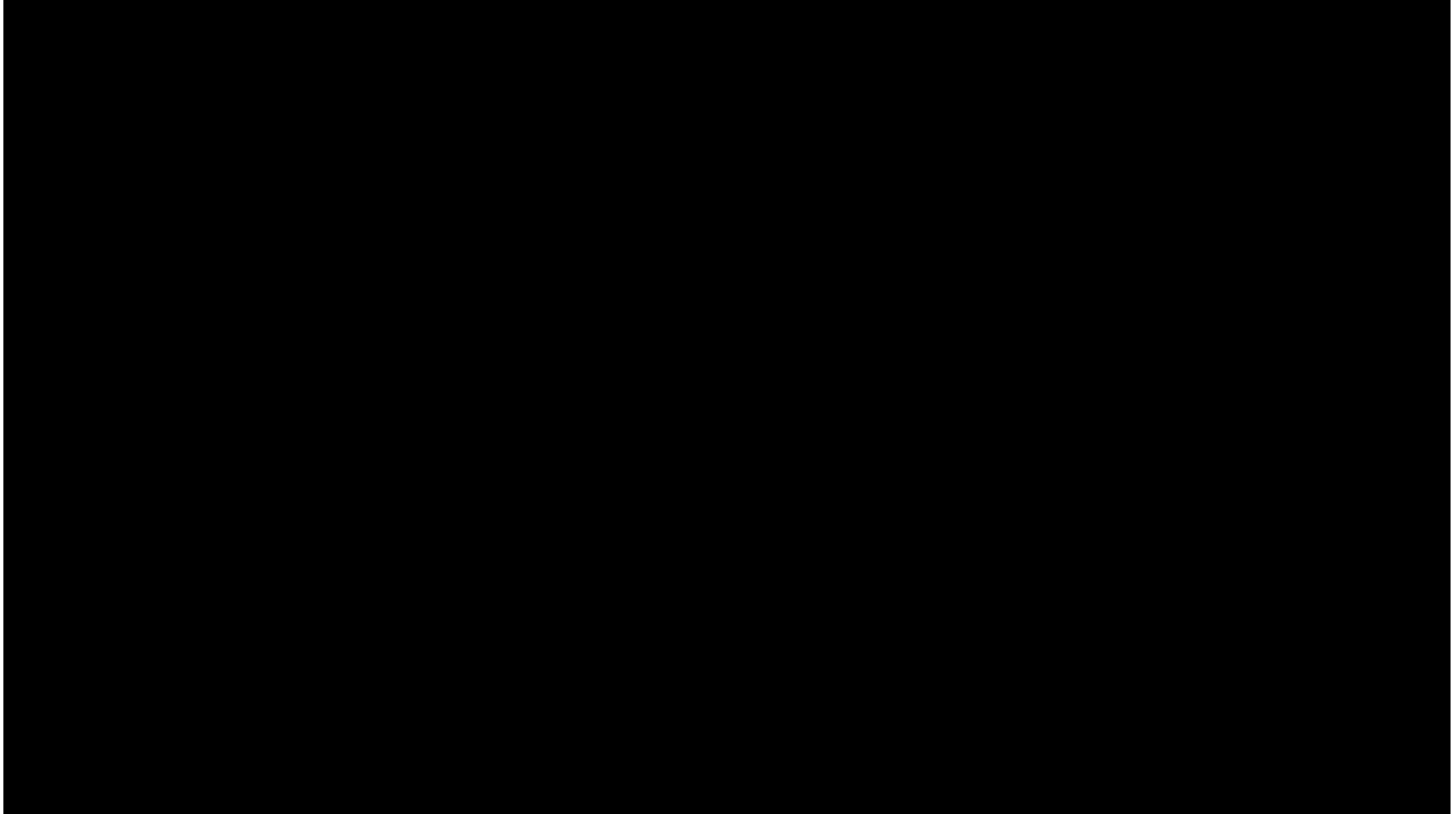


Quelle: KI-Generiertes Video Canva

A tumour of **1 millimeter** (1000×1000 cells) requires **blood supply** for further growth. Nutrients reach the tumour through the **blood vessels**, but cells can also **leave the tumour**.

These tumour cells are **in the blood**. The tumour cells circulating in the blood (**CETC/CTC**) can **remain in the bloodstream for a long time** and spread throughout the body. These cells can **exit the bloodstream at other sites**, settle, and grow into **metastases**.





Cell growth



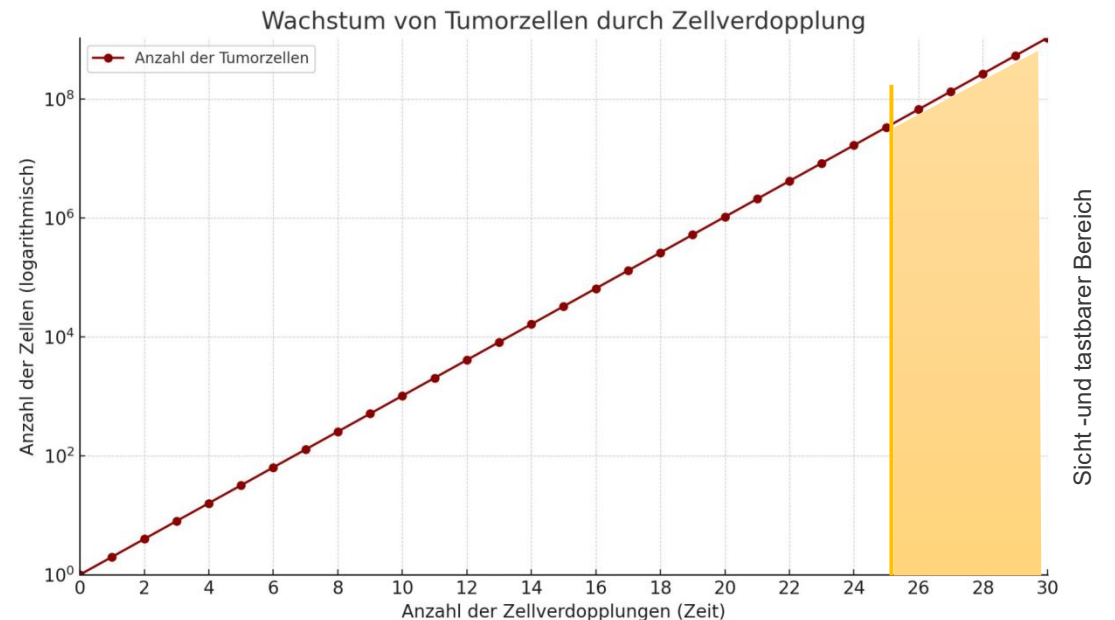
Quelle: KI-Generiertes Video Canva

Cell division/doubling can occur rapidly or slowly.

Model examples:

- **Rapid growth** – doubling of the cell number in **1 month**
- **Slow growth** – doubling of the cell number in **6 months**

A tumour of **1 centimeter (one billion tumour cells)** is detectable:
1000 × 1000 × 1000 cells.



Doubling time: fast growing tumour

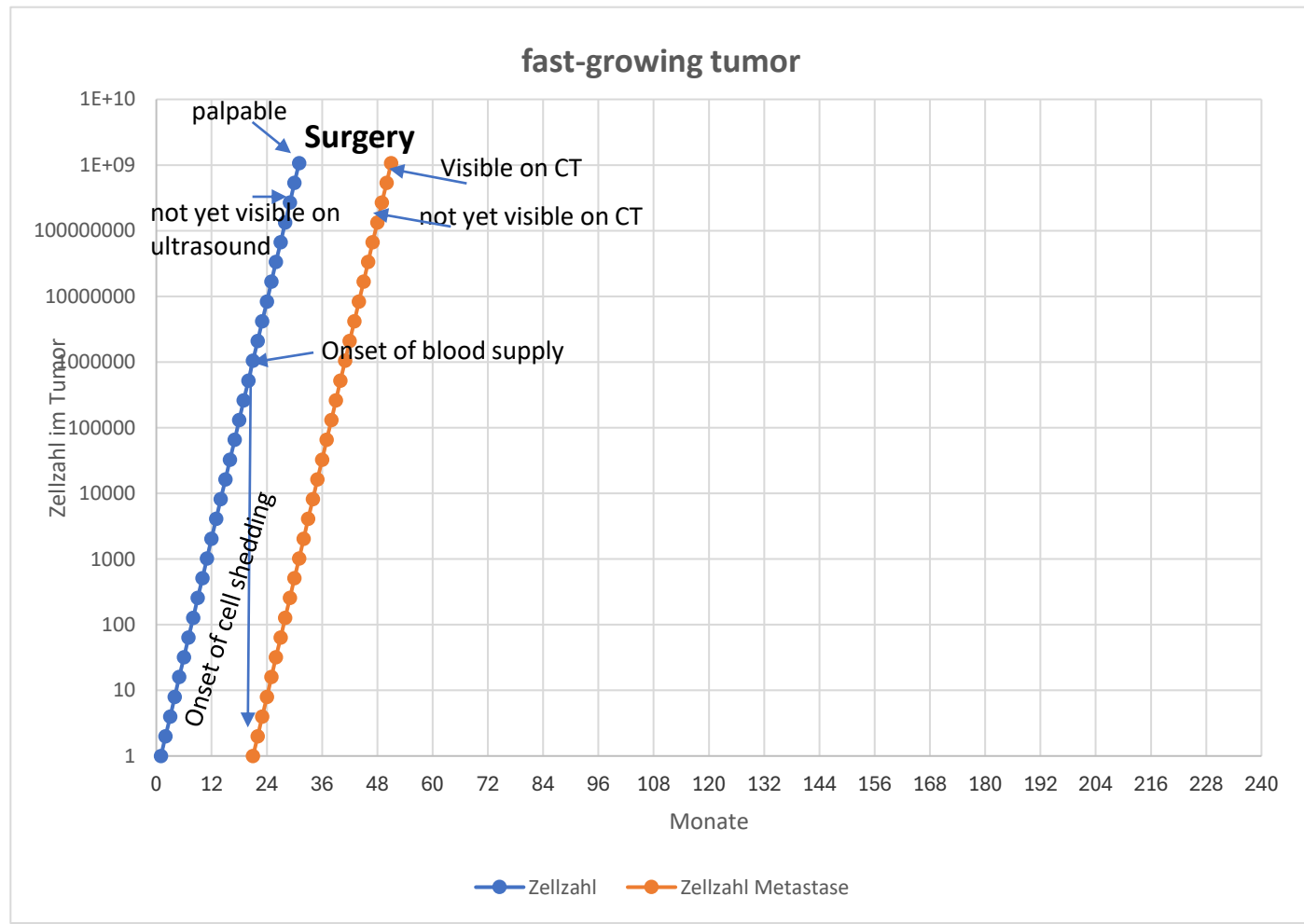
Starting from 1 malignant cell, a tumour can be detected after approximately **25 doublings**.

Prostate cancer – fast-growing tumour:

If the doubling time is about **1 month**, it may take approximately **2 ½ years** until the tumour becomes **detectable**.

Example: A patient undergoes **annual PSA testing**. No PSA increase or tumour is detected. Only a few months after the last examination, the tumour becomes clinically apparent – this can be considered an “**interval tumour**” (which is rare in prostate cancer).

If tumour cells have already been shed, settled, and grow at a similar rate as the primary tumour, **metastases** may appear about **2–3 years** after the initial diagnosis.



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Doubling time: slow-growing tumor

A tumour can be detected after approximately **25 doublings**.

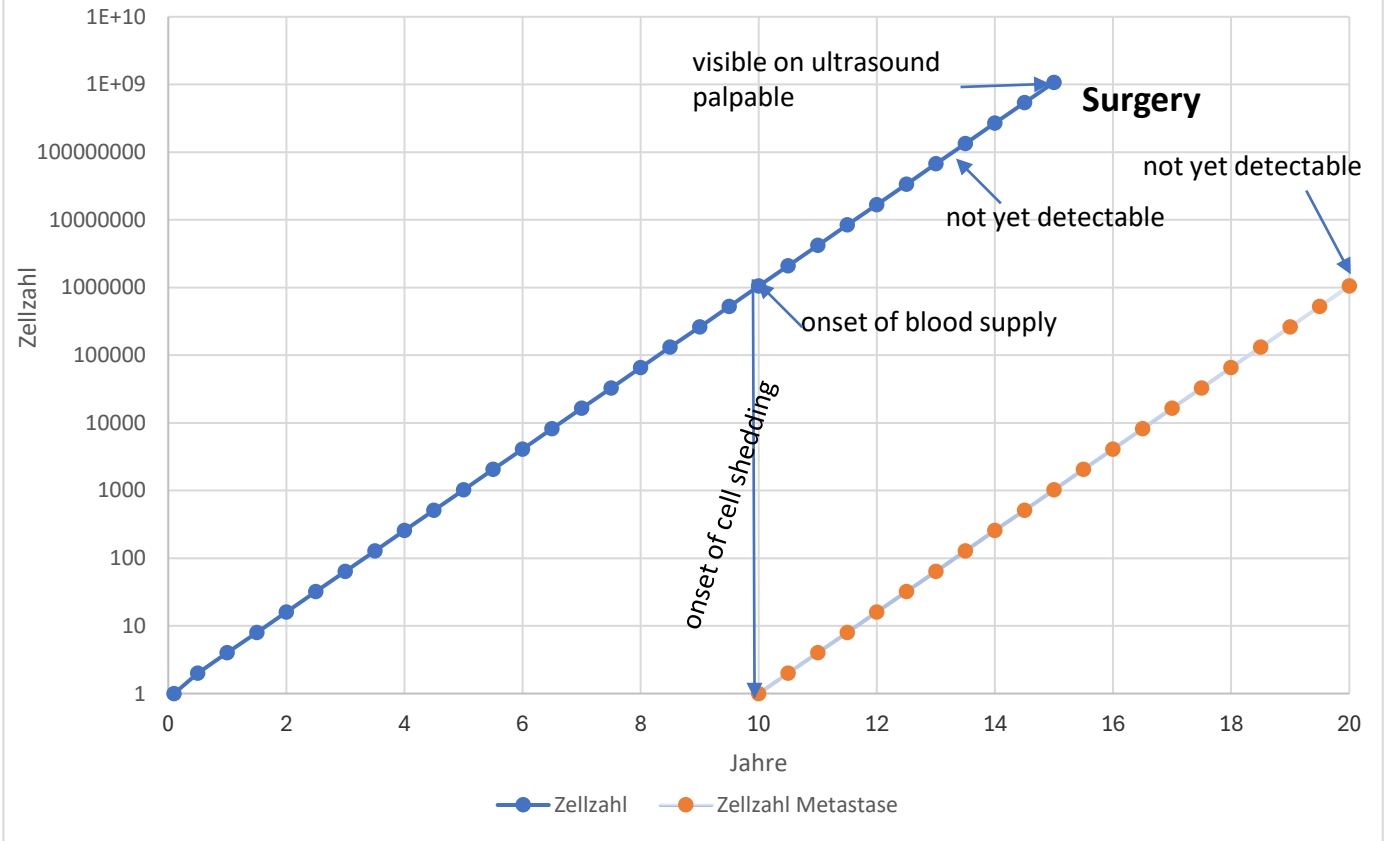
Slow-growing tumour:

With a doubling time of around **6 months**, it may take approximately **12.5 years** until a prostate tumour becomes **detectable**.

Example: A patient undergoes **annual PSA testing** and imaging. The tumor is detected during routine diagnostics. If tumour cells have already been shed, settled, and grow at a rate comparable to the primary tumour, **metastases** may remain undetectable even **10 years** after the initial diagnosis.

Based on **tumour size** alone, **it is not possible** to determine how long a **tumour** has been growing, or if and when it will **form metastases**

slow-growing prostate carcinoma

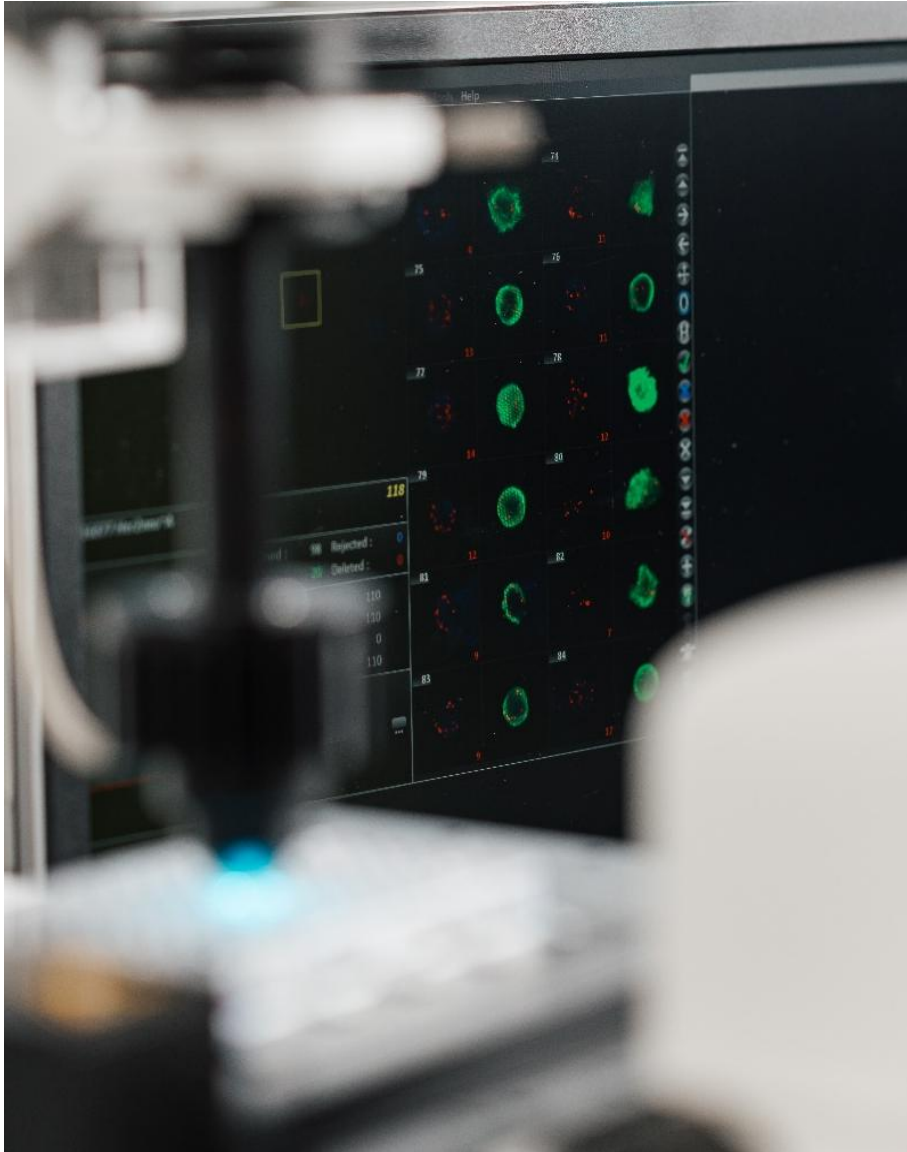


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maintrac[®] Liquid Biopsy



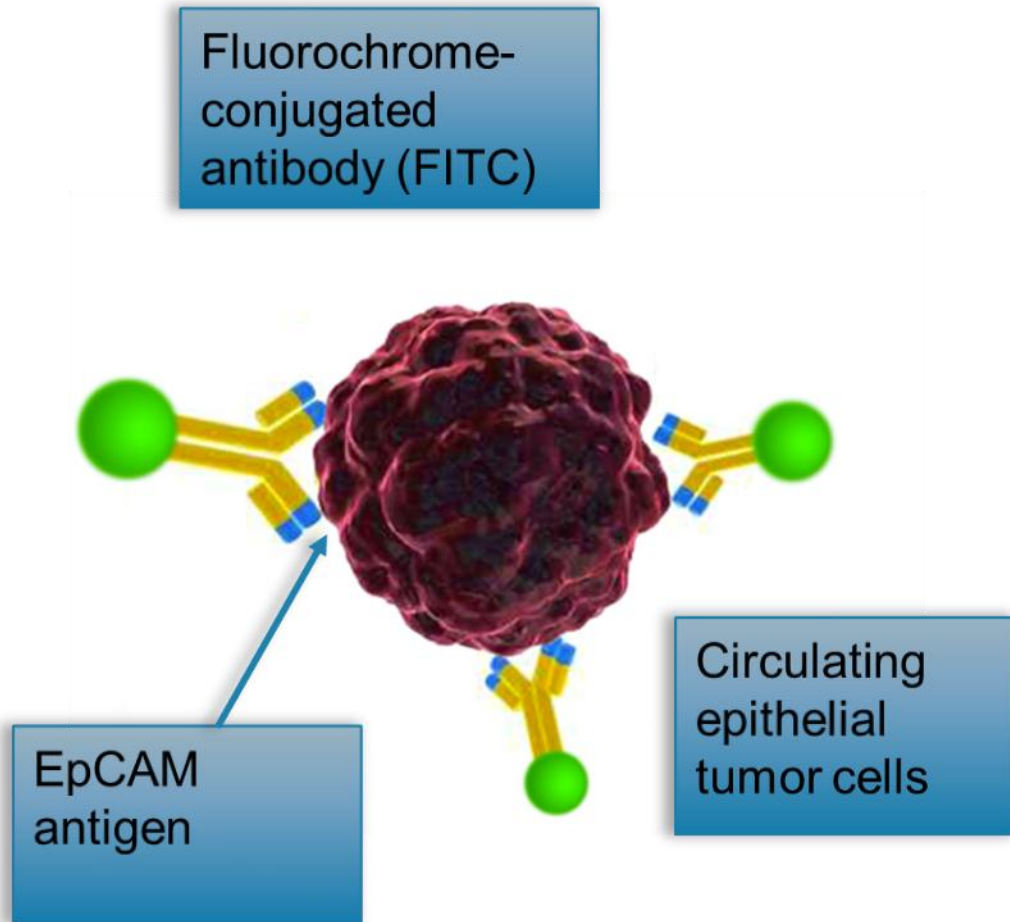
- A minimally invasive procedure that allows detection of *living circulating tumour cells*

maintrac[®] Liquid Biopsy



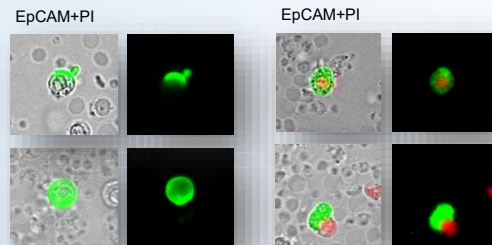
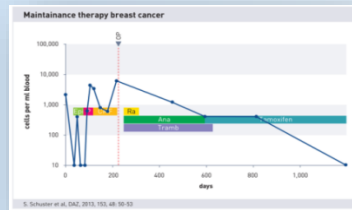
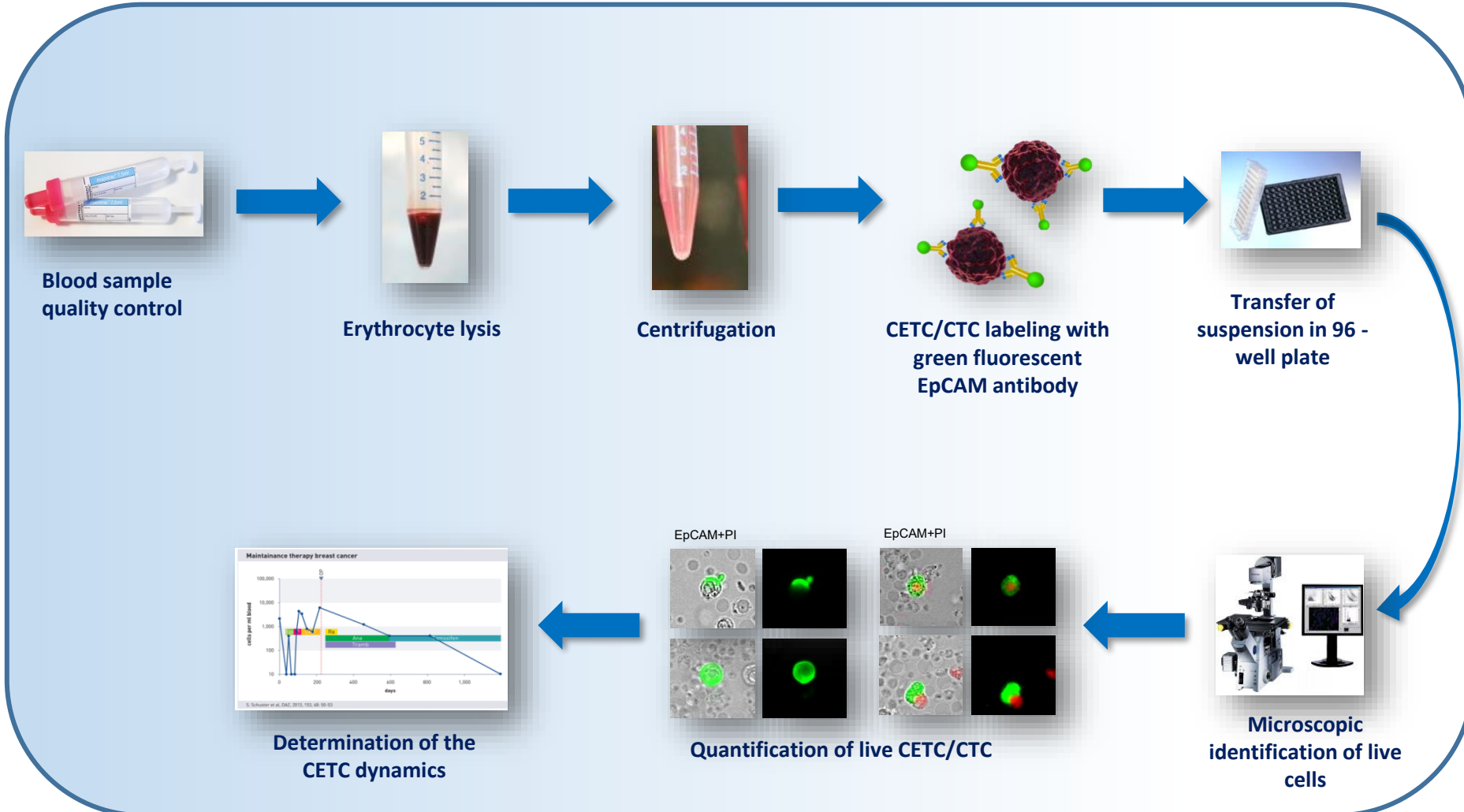
- maintrac[®] cell counting
- maintrac[®] therapeutic substance testing
- maintrac[®] therapy-relevant tumour characteristics
- stemtrac[®] tumourspheres

maintrac[®] Liquid Biopsy

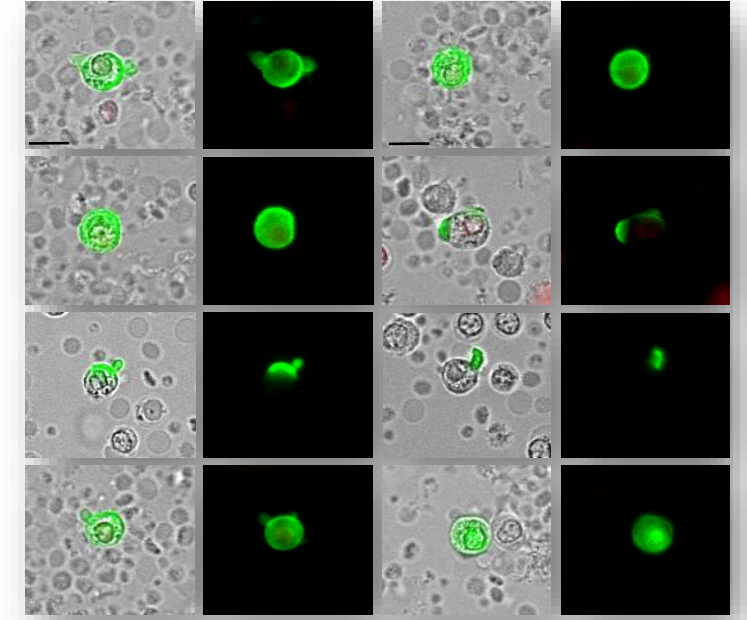
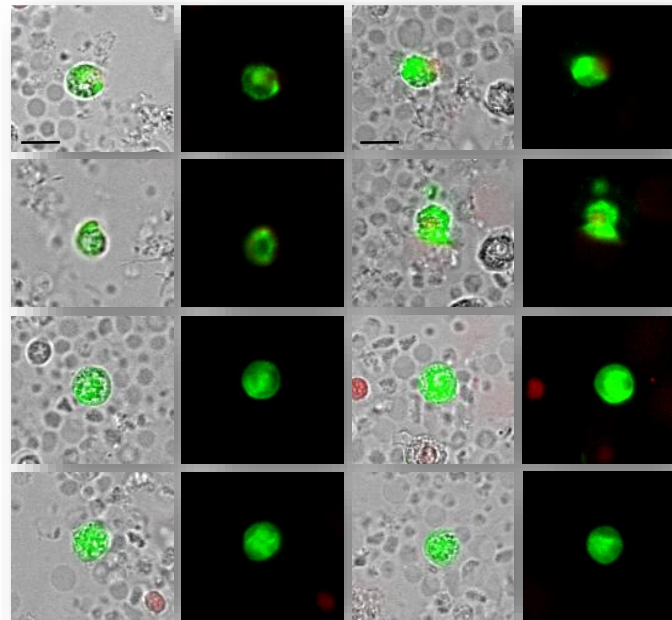
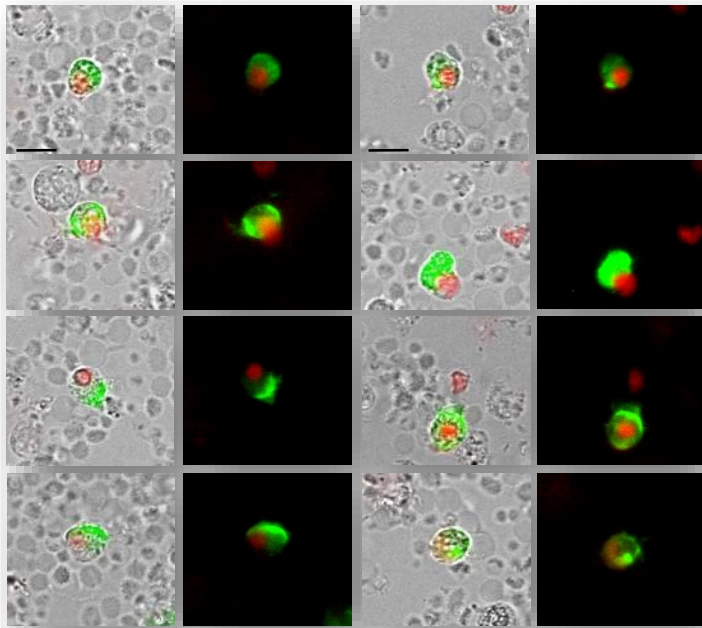


- Highly sensitive detection of CETCs/ CTCs without enrichment steps
- Can be used for all solid tumours
- Fast and reproducible
- Performed in a DIN ISO 15189 certified laboratory

maintrac[®] Workflow



maintrac[®] cell gallery



red stained nucleus= dead cell

maintrac[®] report

Test methods and results:

The automated microfluorimetric image analysis of the **epithelial cell adhesion molecule (EpCAM)**-positive cells with visual control (MAINTRAC) from **1 ml EDTA blood** resulted in following findings (detection limit is 10 cells/ml):

Examination parameter	Number of potential tumor cells			Cell fragments
	In the sample (1ml)	In circulation (5l) (in millions)	In addit. examination: % of EpCAM-pos. cells	
EpCAM	100	0.5		numerous

- the result is given in 1 ml of blood

Interpretation of the CETC numbers:

- 10-50: Minimum number of CETCs
- 50-100: Minimal to slightly elevated number of CETCs
- 150-400: Slightly elevated number of CETCs
- 450-550: Low to moderately elevated number of CETCs
- 600-1000: Moderately elevated number of CETCs
- > 1000: Considerably elevated number of CETCs

Only a more than a twofold increase is indicative of increased risk

Monitoring during or after therapy



maintrac® monitoring during or after therapy

- makes it possible to monitor therapy and directly observe tumor activity
- an additional tool for optimized and personalized therapy.

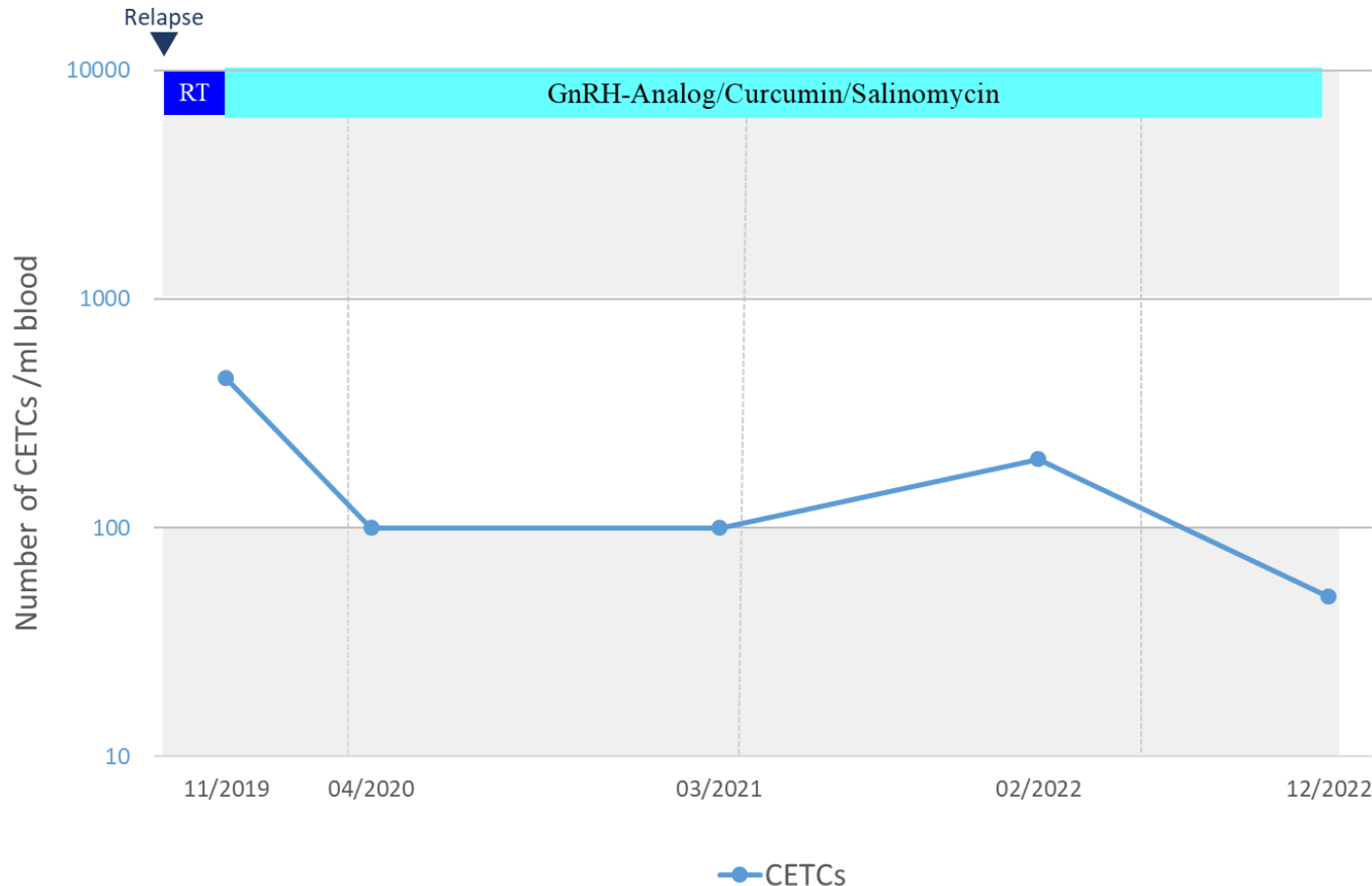


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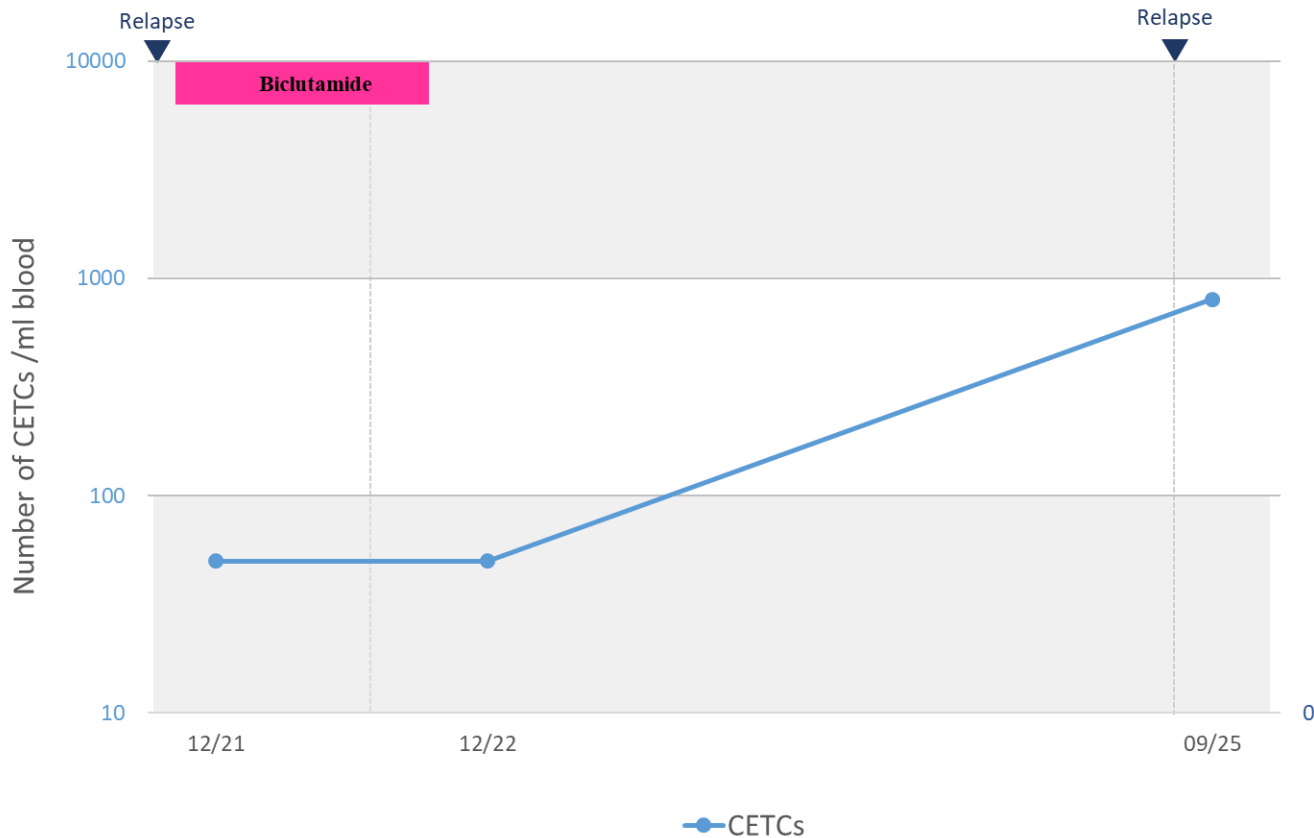
Case report I - prostate cancer



After radiotherapy, the number of CETCs/CTCs **dropped to a low level** and, during GnRH analog therapy combined with complementary treatment, **remained at a stable low level**, consistent with clinical remission

- 09/2018:
- 61 year old man diagnosed with prostate cancer
- 10/2018:
- Surgery
- pT2N0MxR1G3
- Gleason 3+3
- 09/2019:
- Relapse
- 09-12/2019:
- Radiotherapy

Case report III - prostate cancer



- 02/2007:
 - 64 year old man diagnosed with prostate cancer
 - pT3pN0M0
 - Gleason 3+4
- 03/2007:
 - Radical prostatectomy
- 03/2010 Relapse:
 - RTx
- 10/21 Biochemical relapse
 - Therapy with Bicalutamide

• During therapy with bicalutamide, **CETC/CTC** levels remained **stably low**, consistent with clinical remission. Currently, there is a massive **increase in circulating tumour cells**, which reflects **disease progression**

maintrac[®] Drug Sensitivity Testing



maintrac® Drug Sensitivity Testing

- Demonstrates the response (sensitivity) or non-response (resistance) of living circulating tumour cells from the individual patient to cytotoxic substances
- Substances can be tested in various concentrations and combinations, including under hyperthermic conditions

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Drug Sensitivity Testing



Application scenarios for therapy optimisation

- After initial diagnosis of the primary tumour, before therapy is initiated
- In a metastatic setting, prior to starting a new line of therapy
- In cases of disease progression during ongoing treatment



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Drug Sensitivity Testing

in-vitro-vitality reduction in relation to concentration and time (in%) with eutherapeutic concentrations of				
Docetaxel	75	Paclitaxel	70	The ideal is a reduction by 100% in short-term cell culture
Epirubicin	60	5-Fluoruracil	35	
Doxorubicin	45			

- The result is given as a percentage of dead CETCs
- Interpretations of drug efficacy:
 - <10% ineffectiveness of the drug
 - 10-50% marginal efficiency
 - >50% efficacy reflected in imaging scans

Natural agents suggested by the lab – you can of course use your own

<input type="radio"/> <i>Helixor A ; M ; P</i>	<input type="radio"/> <i>Further substances:</i>
<i>Please name manufacturer:</i>	
<input type="radio"/> <i>Vitamin C</i> <i>daily dose</i>	
<input type="radio"/> <i>Graviola</i>	
<input type="radio"/> <i>Iscador M; Q; U; P</i>	
<input type="radio"/> <i>DCA (Dichloracetat)</i>	
<input type="radio"/> <i>Amygdalin</i>	<input type="radio"/> <i>Combination testing:</i>
<input type="radio"/> <i>Sulforaphan</i>	
<input type="radio"/> <i>Hypericin</i>	
<input type="radio"/> <i>Curcumin</i>	
<input type="radio"/> <i>Artesunat</i>	

Prioritisation of natural agents is suggested by the results

Report on diagnostic findings on Circulating Tumor Cells (MAINTRAC)

Dear Dr.:

Many thanks for sending your examination request regarding the detection of circulating tumor cells. After Therapy.

Diagnosis:

Colon Cancer, Initial diagnosis: 08/15

- 1. Therapy: Mexico, Oasis of Hope 3 visits
Therapy: B17, Prostanalin, Xeloda, Curcumin
- 10/15-07/16: DCA, Vitamin C
- until: 10/16: Ozone, Boswellia, Hyperthermia
- 11/16: Surgery (Removal of remaining tumor 5mm)

The automated microfluorimetric image analysis of the **epithelial cell adhesion molecule (EpCAM)**-positive cells with visual control (MAINTRAC) from **1 ml EDTA blood** resulted in following findings (detection limit is at 10 cells/ml):

Examination parameter	Number of potential tumor cells			Cell fragments
	In the sample (1ml)	In circulation (SI) (in millions)	In addt. examination: % of EpCAM-pos cells	
EpCAM	500	2,5		numerous

in-vitro-vitality reduction in relation to concentration and time (in%) with eutherapeutic concentrations of				
Vitamin C	70	DCA	60	The ideal is a reduction by 100% in short-term cell culture
Amygdalin	70	Curcuma*	40	
Artesunat	95	Prostanalin*	85	
Boswellia*	60			

*provided by the patient

Curcumin appears more effective than chemotherapeutic agents for this patient

Diagnosis:

Lung Cancer, initial diagnosis: 26.06.2017

- TNM: T4 N3 M1b, Stage IV
- no Surgery
 - no Radiation therapy
 - post Complementary therapy
 - no current therapy
 - Medication: Herbal supplements

The automated microfluorimetric image analysis of the **epithelial cell adhesion molecule (EpCAM)**-positive cells with visual control (MAINTRAC) from **1 ml EDTA blood** resulted in following findings (detection limit is at 10 cells/ml):

Examination parameter	Number of potential tumor cells			Cell fragments
	In the sample (1ml)	In circulation (5l) (in millions)	In addit. examination: % of EpCAM-pos. cells	
EpCAM	150	0,75		numerous

in-vitro-vitality reduction in relation to concentration and time (in%) with eutherapeutic concentrations of				
Avastin	20	Alimta	60	The ideal is a reduction by 100% in short-term cell culture
Cisplatin	65	Vitamin C	40	
Curcumin	90	Artemisia	80	

The material for examination could be thoroughly evaluated.

Under Therapy with herbal supplements we found only a **slightly increased number of live, potentially malignant tumor cells circulating in the blood.**

In addition, there were numerous specific cell fragments detected.

Specific cell fragments occur, for example, after chemotherapy or radiation, or as part of an immune response and indicate damaged cells.

Combination of curcumin and hypericin 85% in this case

The automated microfluorimetric image analysis of the **epithelial cell adhesion molecule (EpCAM)**-positive cells with visual control (MAINTRAC) from **1 ml EDTA blood** resulted in following findings (detection limit is at 10 cells/ml):

Examination parameter	Number of potential tumor cells			Cell fragments
	In the sample (1ml)	In circulation (5l) (in millions)	In addit examination: %of EpCAM-pos. cells	
EpCAM	450	2,25		numerous

in-vitro-vitality reduction in relation to concentration and time (in%) with eutherapeutic concentrations of			
Curcumin/ Hypericin	85		The ideal is a reduction by 100% in short-term cell culture

The material for examination could be thoroughly evaluated.
After the recent surgery we found **a slightly to moderately increased number of live, potentially malignant tumor cells circulating in the blood.**
In addition, there were numerous specific cell fragments detected.
Specific cell fragments occur, for example, as part of an immune response and indicate damaged cells.

In vitro vitality reduction occurred at **Curcumin/Hypericin.**

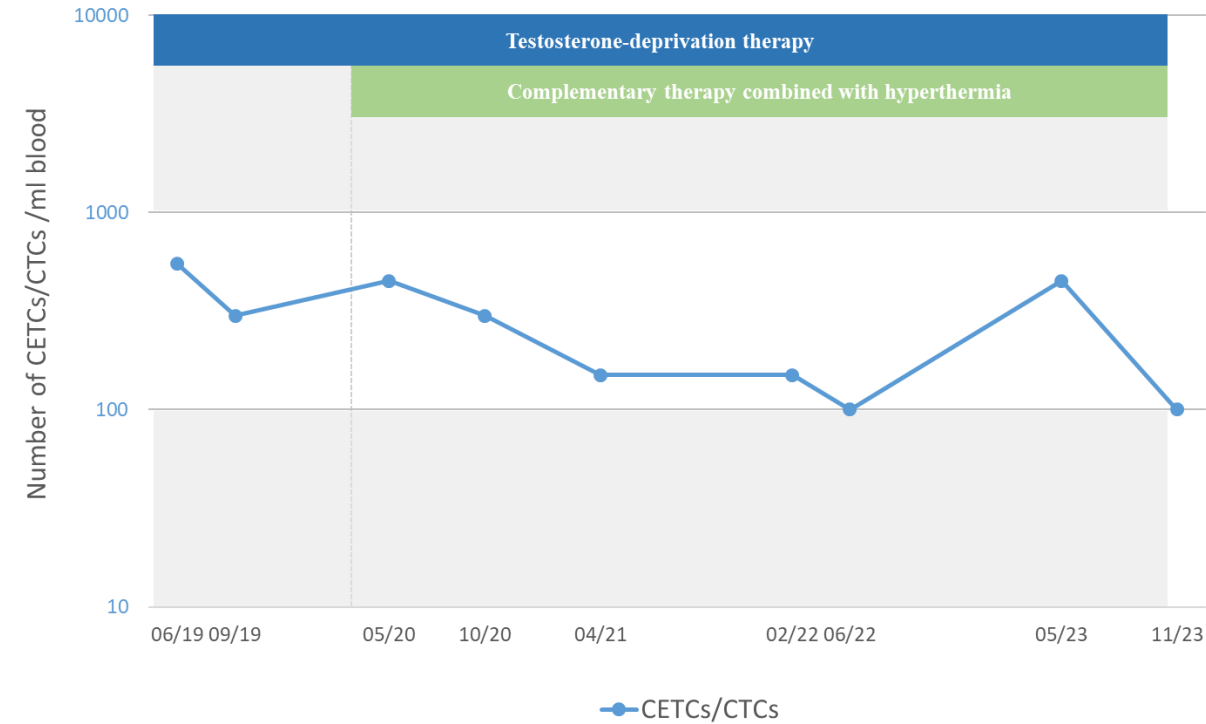
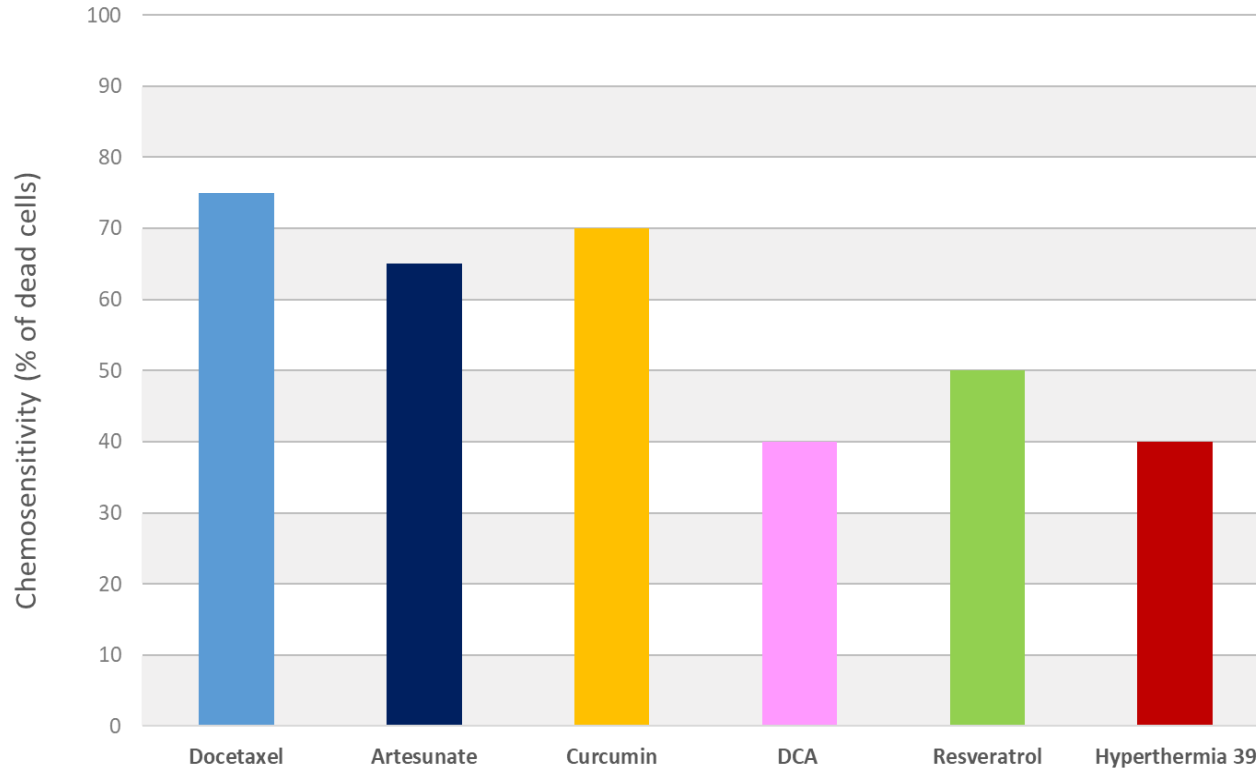
In connection with a detected tumor the cells are most probably cells from this tumor.



The current cell numbers present a basic value, only an increase in cell numbers is relevant for disease progress.

Sensitivity to agents available in three levels of concentration

in-vitro-vitality reduction in relation to concentration and time (in%) with eutherapeutic concentrations of The ideal is a reduction by 100% in short-term cell culture							
Quercetin 0,1-fold	85		Quercetin 1-fold	90		Quercetin 10-fold	99
Vitamin C 30g 0,1-fold	55		Vitamin C 30g 1-fold	75		Vitamin C 30g 10-fold	90
Artesmisinin 250mg 0,1-fold	25		Artesmisinin 250mg 1-fold	90		Artesmisinin 250mg 10-fold	98
Curcumin 450mg 0,1-fold	n.a.		Curcumin 450mg 1-fold	90		Curcumin 450mg 10-fold	n.a.

Case report III – prostate cancer



-  A 55-year-old man was diagnosed with prostate cancer and subsequently underwent local radiotherapy of the primary tumor.
-  The administration of an individualised **complementary therapy** in combination with **testosterone-deprivation therapy** resulted in a **reduction of CETCs/CTCs to stable level**, consistent with **clinical remission**.

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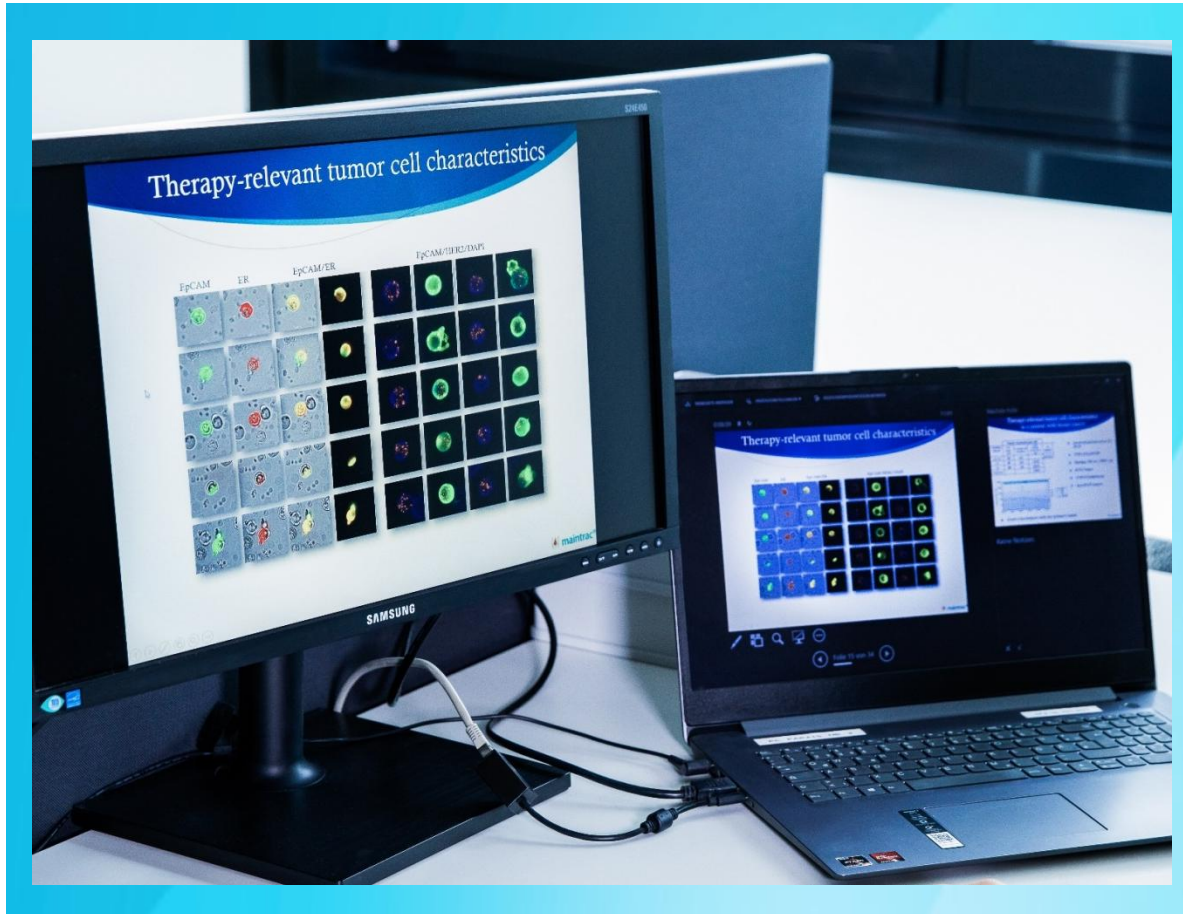
Therapy-relevant tumor cell characteristics

Therapy-relevant tumour cell characteristics



- A number of therapies only make sense if the tumour cells have corresponding characteristics
- Therapy-relevant tumour cell characteristics indicate a possible response or non-response to therapy

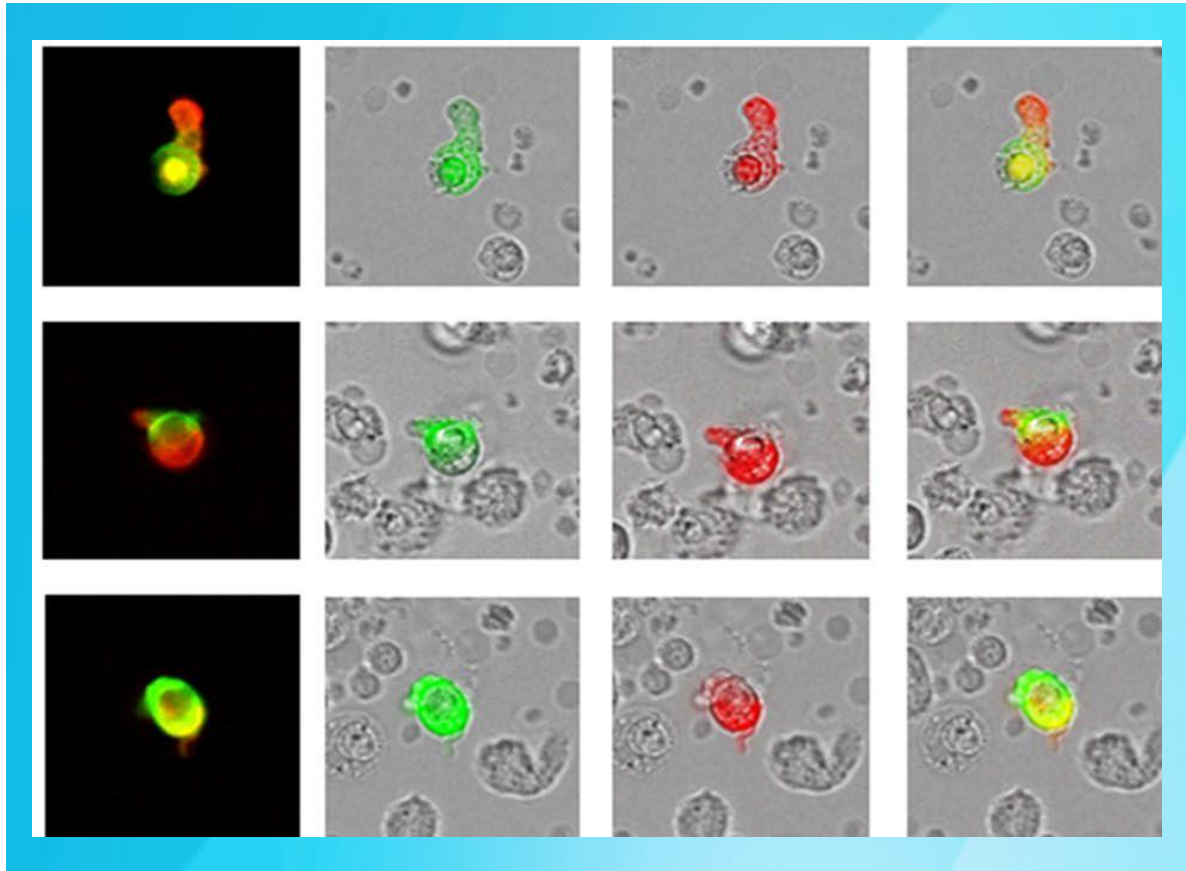
Therapy-relevant tumour cell characteristics



- Tumour characteristics can change during the course of the disease
- This can influence the effectiveness of the therapies used

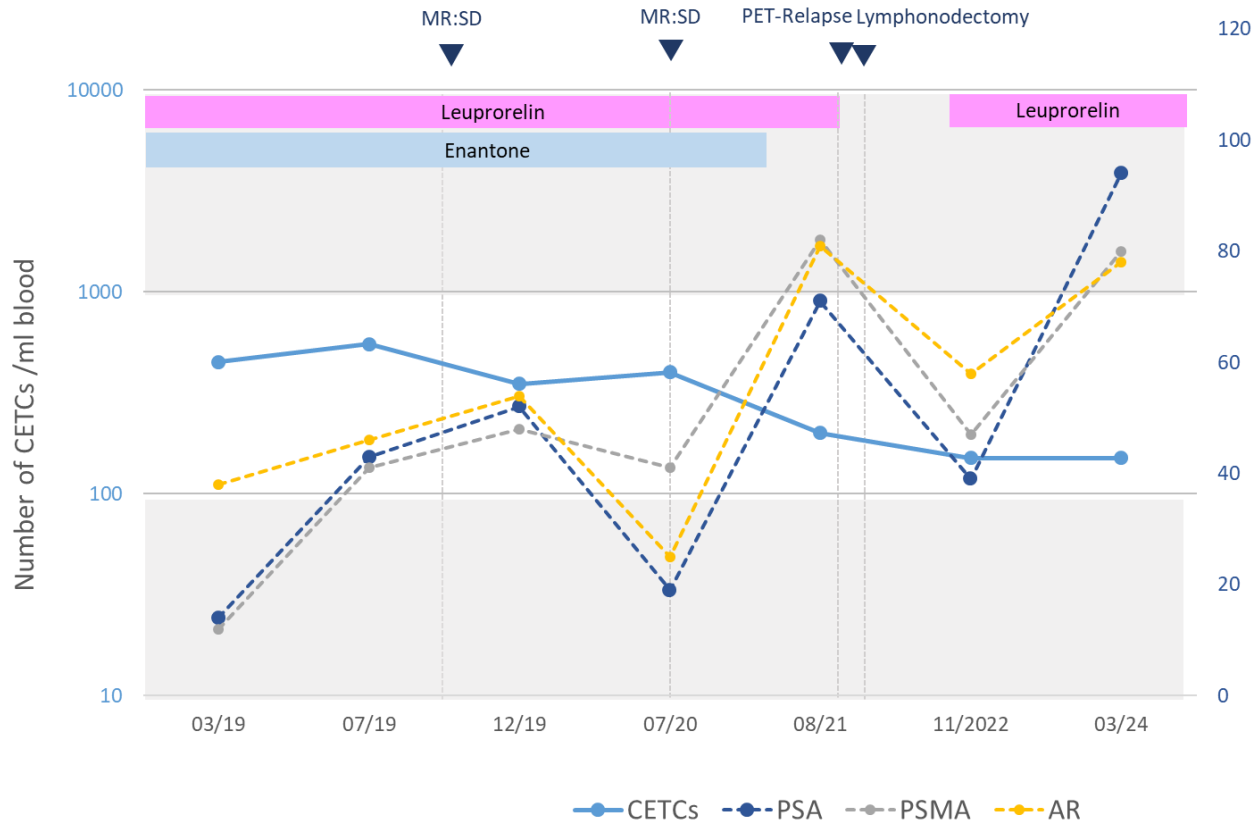
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Therapy-relevant tumour cell characteristics for prostate cancer



- Prostate-associated markers: PSA, PSMA, AR
- Immunomodulatory molecules: PD-L1, B7-H3
- Proliferation marker: Ki-67

Case report IV - prostate cancer



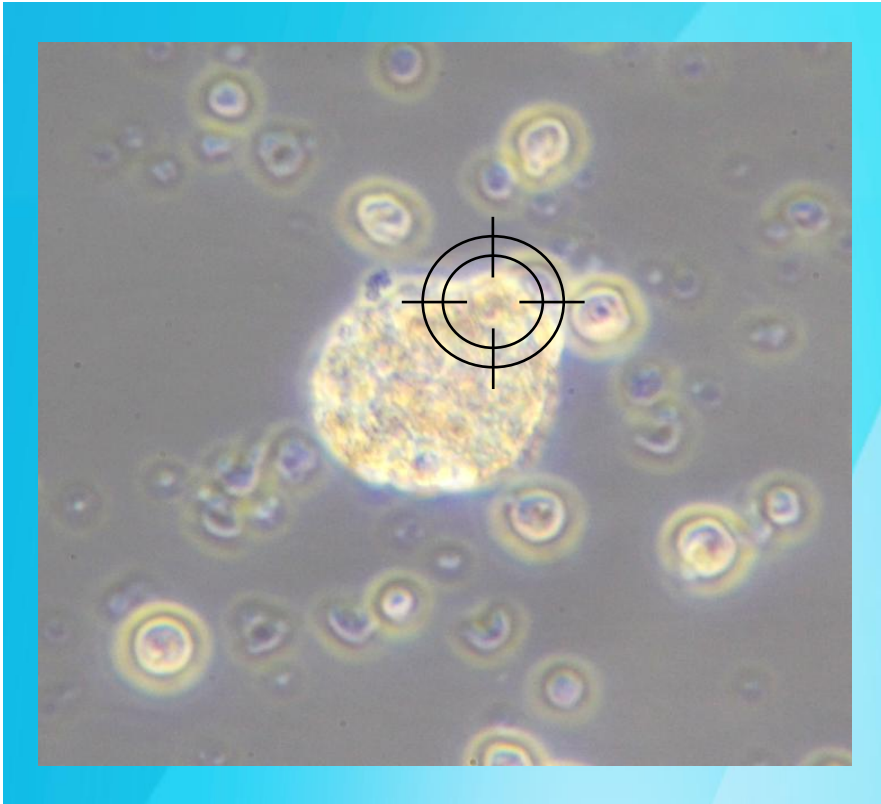
- Prostate cancer, ID: 12/10
- TNM: pT3bpN0 (Gleason Score 3+4=7)
- 04-06/11 Radiotherapy
- 11/15 Bone metastases
- 01/16 Cyberknife
- Since 05/16 Therapy with Leuprorelin und Enantone
- 09/16 Complete remission
- 01/17 Stable disease
- 10/21 PET-CT revealed a recurrence in retroperitoneal lymph nodes. This was followed by a lymphonodectomy
- Since 05/22 renewed therapy with Leuprorelin

 Significant increase in the proportion of **PSA-, PSMA- and AR-positive CETCs/CTCs** shortly before recurrence in the retroperitoneal lymph nodes

stemtrac® to assess tumor aggressiveness and risk of metastasis

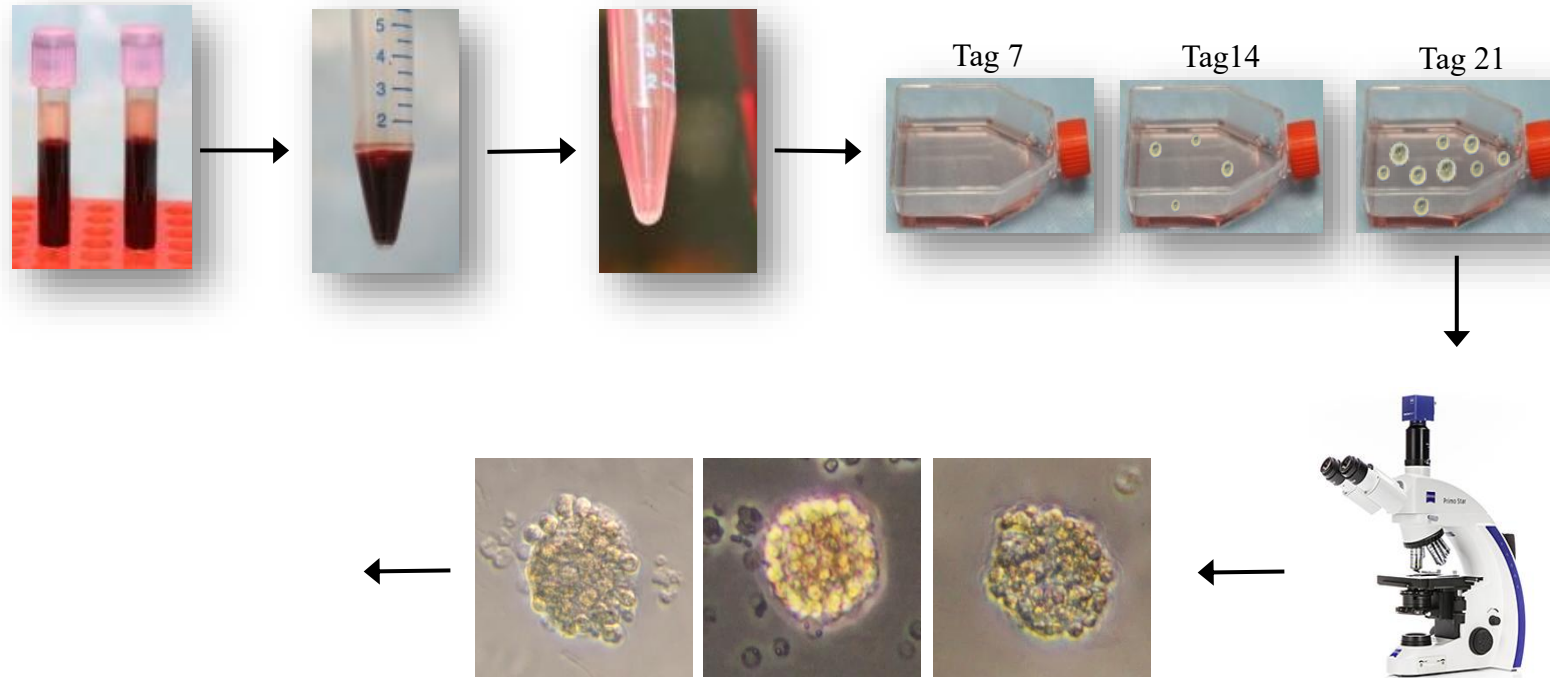
What are cancer stem cells?

Cancer stem cells (CSCs) represent a distinct subpopulation within a tumour, constituting approximately 0.1–2.0% of the tumour cell population



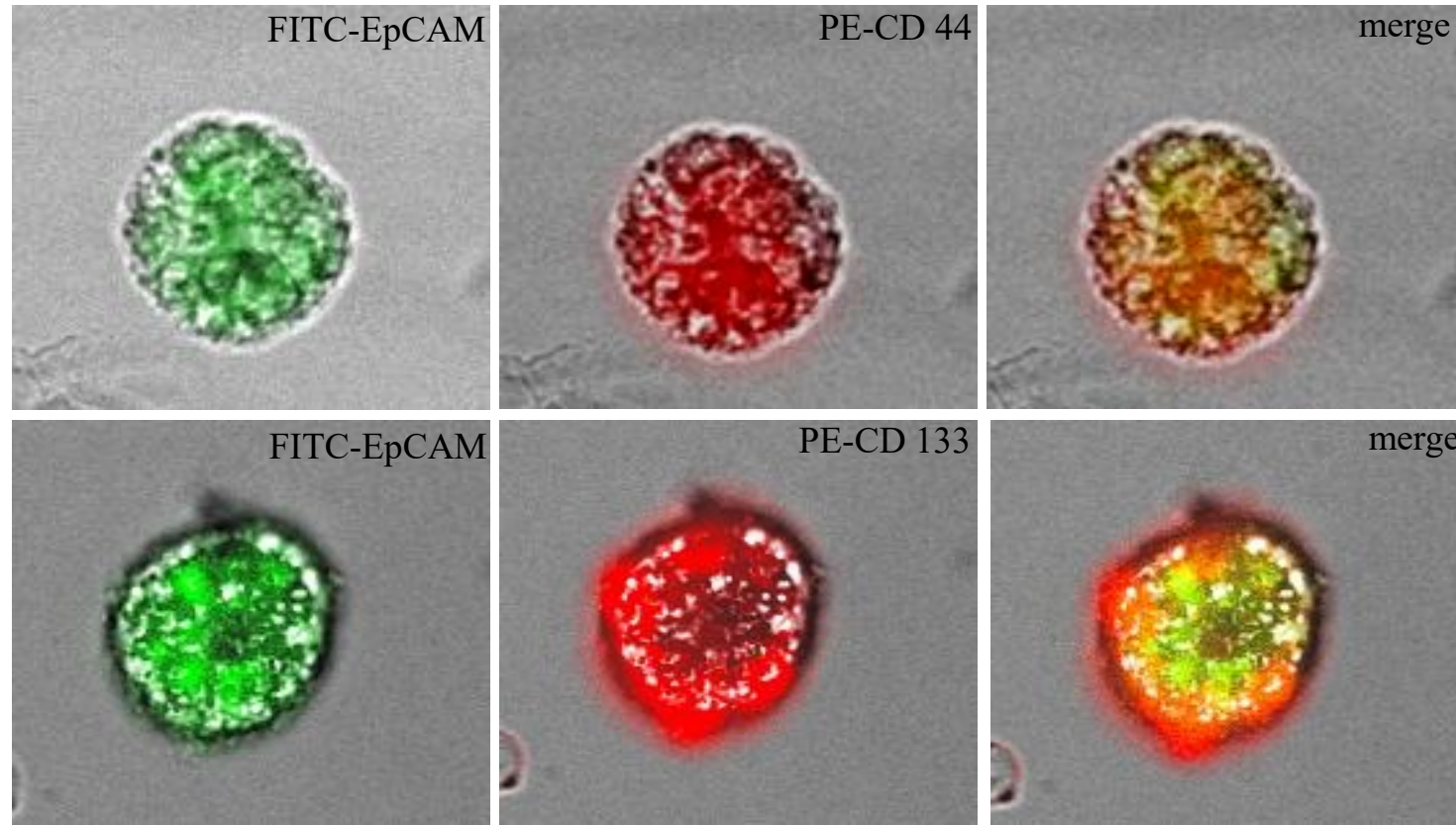
- A subpopulation of tumour cells with stem cell characteristics, including self-renewal capacity and the ability to differentiate into a heterogeneous population of cancer cells
- These cells are responsible for tumour initiation, progression, recurrence, and metastasis
- Resistant to most conventional chemo- and radiotherapies → Current treatments often ineffective
- Strategies to eradicate cancer stem cells (CSCs) → Urgent focus in cancer research

stemtrac® Tumourspheres – What is being analysed?



- ◆ We create *in vitro* specific conditions that enable *circulating cancer stem cells* to proliferate over three weeks and develop into small, spherical cell clusters known as *tumourspheres*
- ◆ We can precisely determine not only the presence but also the quantity of *circulating cancer stem* cells in the blood

Circulating cancer stem cells in a prostate cancer patient



- After three weeks, the tumourspheres are collected, labelled with specific antibodies, and counted under a fluorescence microscope

stemtrac® Tumourspheres – What are the benefits of this analysis?



Oncotarget  ONLINE ISSN: 1949-2553
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The number of tumourspheres cultured from peripheral blood is a predictor for presence of metastasis in patients with breast cancer

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Oncotarget. 2016; 7:48143-48154. <https://doi.org/10.18632/oncotarget.10174>

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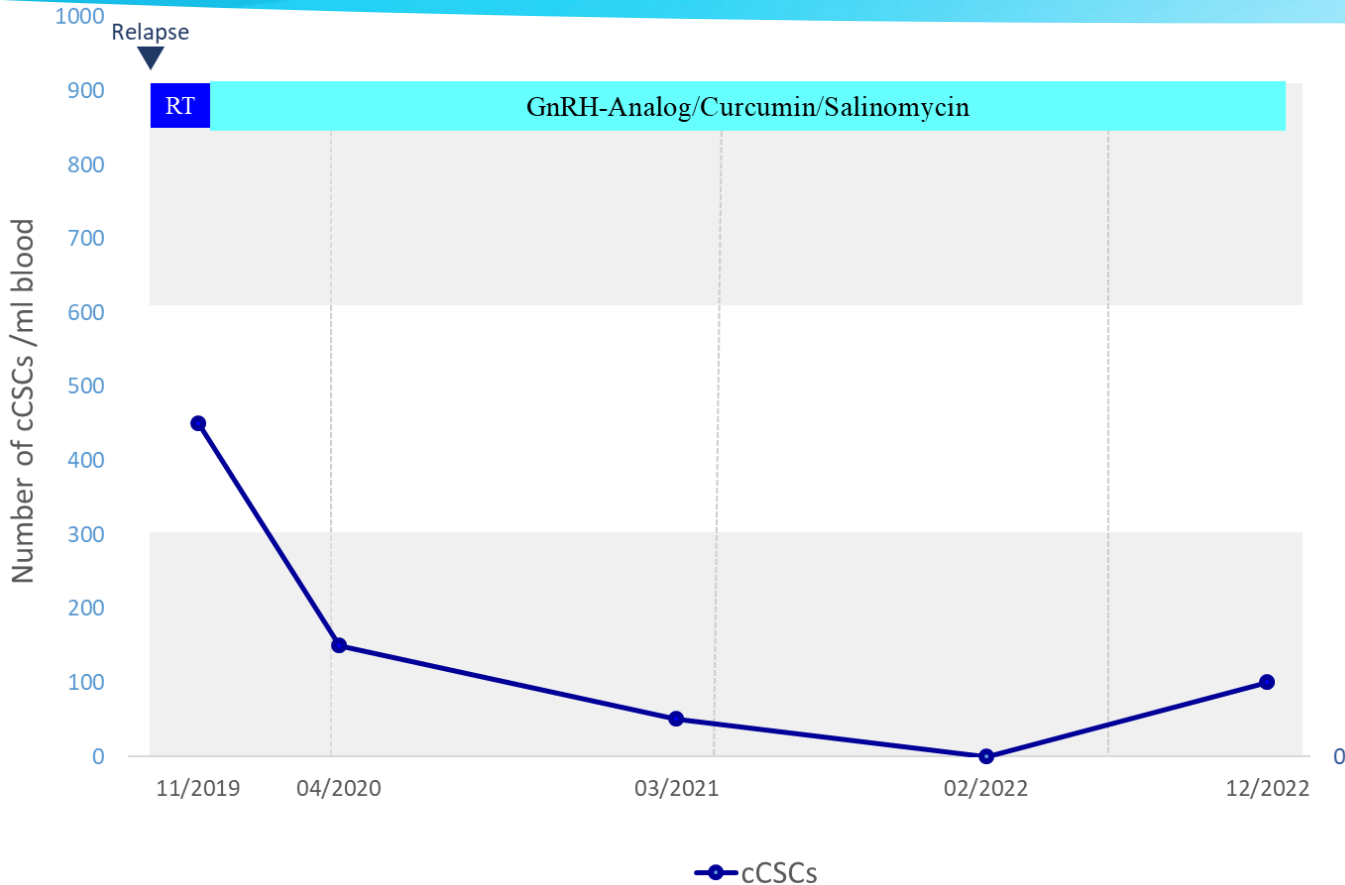
Correspondence to:
Monika Pizon, email: mpizon@simfo.de

Keywords: *breast cancer, circulating epithelial tumor cells, circulating cancer stem cells, predictor for presence of metastasis*

Received: *January 27, 2016* Accepted: *June 02, 2016* Published: *June 20, 2016*

- ◆ Assessment of the *risk for metastasis*
- ◆ Monitoring of *therapy progress*
- ◆ Early detection of a *possible relapse (recurrence)*

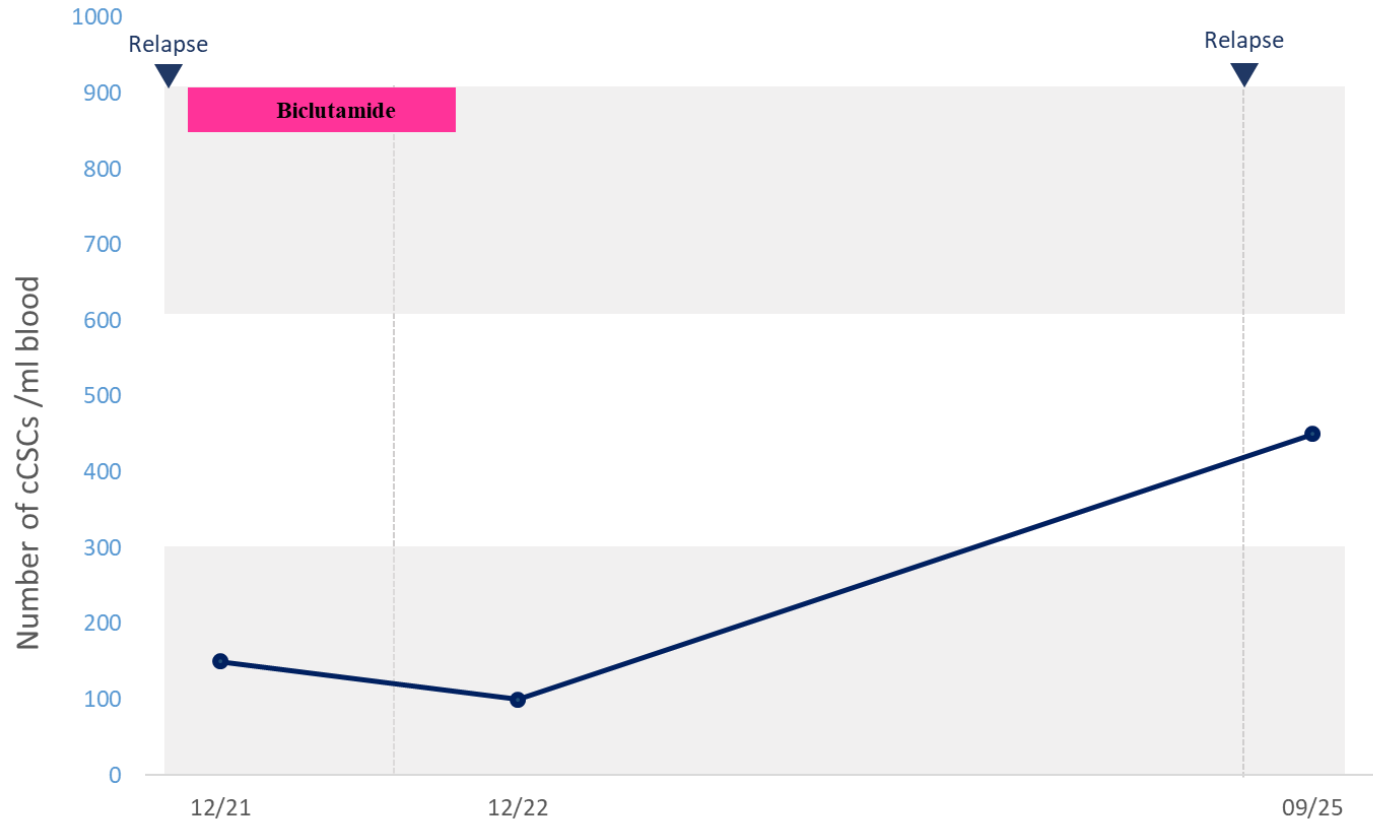
Case report V - prostate cancer














- 💧 09/2018:
- 💧 61 year old man diagnosed with prostate cancer
- 💧 10/2018:
- 💧 Surgery
- 💧 pT2N0MxR1G3
- 💧 Gleason 3+3
- 💧 09/2019:
- 💧 Relapse
- 💧 09-12/2019:
- Radiotherapy

💧 After radiotherapy and during testosterone-deprivation therapy combined with complementary therapy, **cCSCs** dropped to a **low level**, consistent with a **good treatment response** and **clinical remission**.

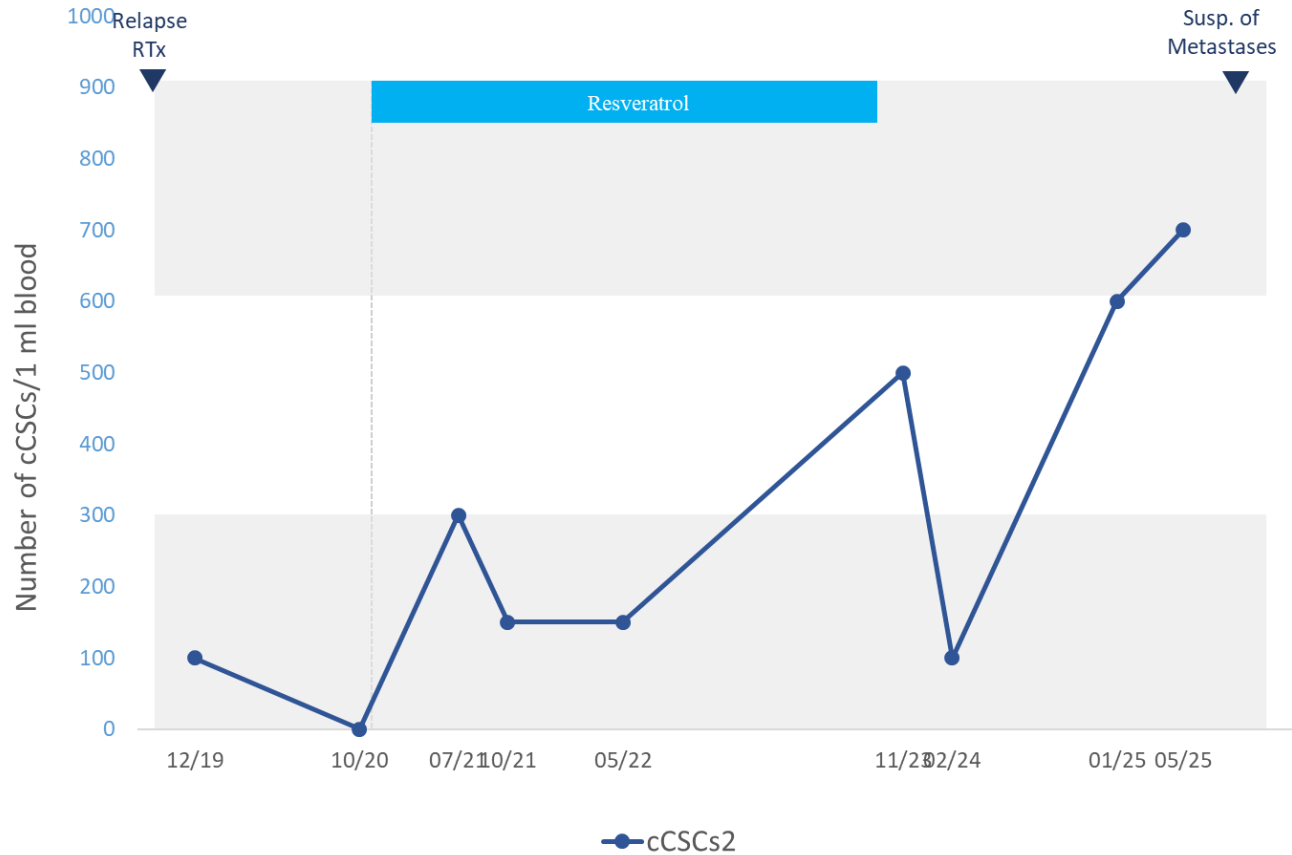
Case report VI - prostate cancer




 During therapy with **Biclutamide**, circulating cancer stem cells (**cCSCs**) were at a **low level**. **Currently**, the number of **cCSCs** has increased to **400/ml**, which is **consistent with newly diagnosed liver metastases**.

- 
02/2007:
 - 
 64 year old man diagnosed with prostate cancer
 - 
 pT3pN0M0
 - 
 Gleason 3+4
- 
03/2007:
 - 
 Radical Prostatectomy
- 
03/2010 Relapse:
 - 
 RTx
- 
10/21 Biochemical relapse
 - 
 Therapy with Biclutamide

Case report VII - prostate cancer



- 💧 10/2012:
 - 💧 59 year old man diagnosed with prostate cancer
 - 💧 pT2bpN0M0 (Gleason 3+4)
- 💧 11/2012:
 - 💧 Surgery
 - 💧 RTx
- 💧 12/2017:
 - 💧 Relapse
 - 💧 Surgery followed by RTx

💧 After surgery and radiotherapy, cCSCs dropped to a **low level** but showed a **tendency toward an unstable course** (fluctuating). The last examination revealed a **very high number of cCSCs**, suggesting the **presence of metastatic disease**. Three months later, **bone metastases** were diagnosed.

New Scientific Insights: Advancing Our Understanding



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Article

Circulating Epithelial Tumor Cells (CETC/CTC) in Prostate Cancer: Potential Prognostic Marker for the Risk of Recurrence During Radiotherapy

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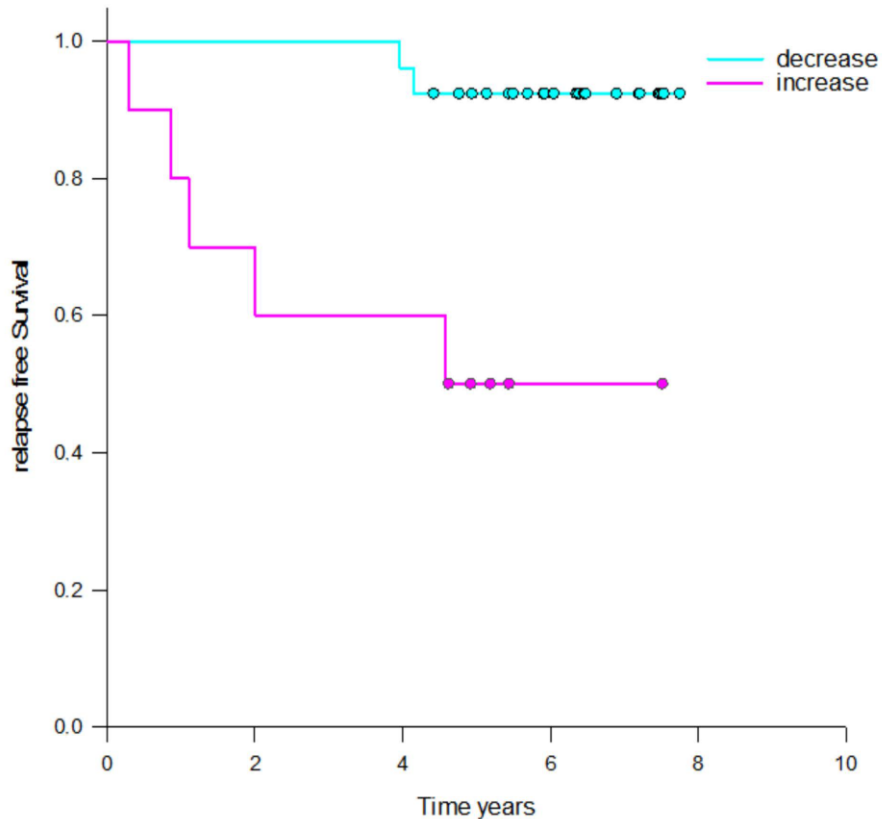
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Practical Summary

- Prostate cancer is often treated with radiotherapy (RT), but reliable biomarkers to predict recurrence after treatment are still lacking. This study evaluated whether CETCs/CTCs in blood could serve as such a biomarker.
- A total of 52 prostate cancer patients undergoing definitive, adjuvant, or salvage RT were included.
- Blood samples were collected before, during, and after RT, and CETC/CTC counts were measured using the maintrac® approach

Prognostic Value of CETCs/CTCs in Prostate Cancer During RT

Relapse free Survival Analysis



Key findings:

- CETCs/CTCs were detected in 96% of patients before or after RT
- Patients whose CETC/CTC counts decreased during RT—especially after prior surgery—had a significantly lower risk of recurrence
- An increase in CETCs/CTCs during or after RT was strongly associated with higher relapse risk (HR = 8.8; p = 0.002)
- Recurrence occurred in 36% of patients after adjuvant RT, 14% after definitive RT, and 18% after salvage RT. Changes in CETC/CTC were most predictive in the adjuvant RT group
- PSA levels measured during the study did not reliably predict relapse risk

Practical conclusion:

- Monitoring CETC/CTC levels during RT can provide valuable prognostic information and may identify patients at higher risk of recurrence more effectively than PSA

Thank you!

For further questions please contact:

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