maintrac

Circulating Tumor Cells
Interpretation of Cell Numbers

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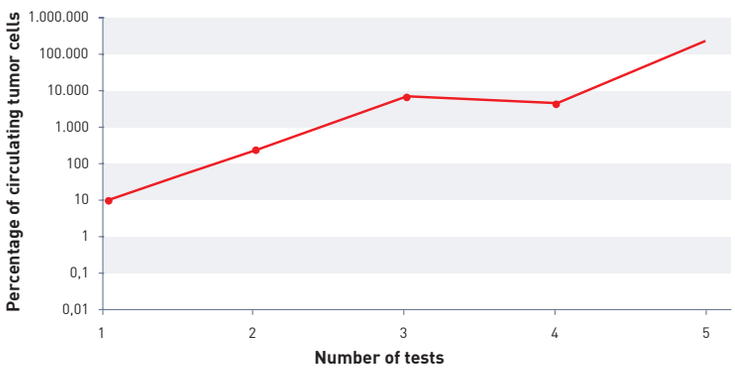
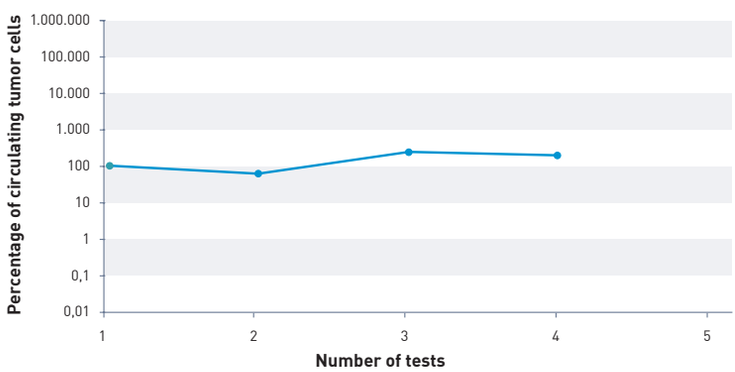
Typical Cell Number Dynamics

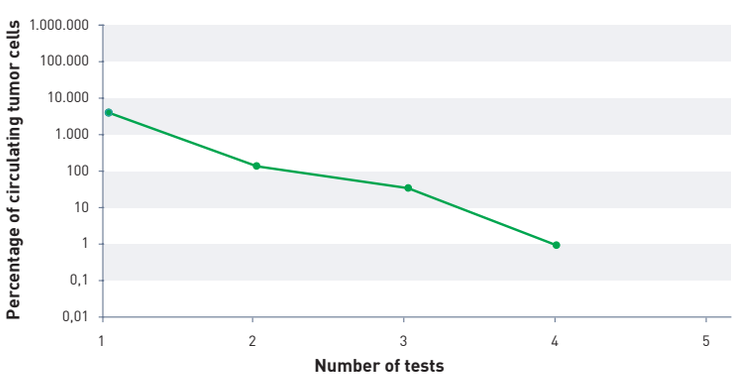
Increasing number of circulating tumor cells



Constant numbers of circulating tumor cells



Decreasing numbers of circulating tumor cells



Individual Cell Numbers

The total number of circulating tumor cells can differ significantly from patient to patient.

Basic Values

The first measurement always serves as a basic value. This number has usually no prognostic relevance.

Threshold

maintrac uses no specified threshold when determining the number of CETCs. Studies have shown that even small tumors may have a high number of CETCs that are released into the bloodstream and vice versa.

Questions about treatment

The medical laboratory is available for any questions you may have about your treatment on +49 (0) 921 850 200 or via email on maintrac@laborpachmann.de

Neoadjuvant Therapy

the tumor has not yet been removed; therapy is applied primarily to reduce the size of the tumor.

Neoadjuvant Chemotherapy

Decrease in Cell Numbers

Initially there is usually a rapid reduction in the number of peripherally circulating tumor cells. However, if the tumor tissue disintegrates, this can result in a massive increase in the number of circulating epithelial tumor cells (release of CETCs from the shrinking tumor even if pathologic complete remission is achieved). Therapy should be continued until a reduction of CETCs is achieved again, possibly also postoperatively.

Increase in Cell Numbers

The disintegration of tumor tissue often leads to a massive increase in the number of cells (release of CETCs from the shrinking tumor even if pathologic complete remission is achieved). In this case, therapy should be modified until a decrease in CETCs is visible. The number of cells should be further monitored in the postoperative situation.

Neoadjuvant Endocrine Treatment

Decrease in Cell Numbers

A slow, continuous decrease in the number of cells can frequently be monitored over a longer period of time. A release of CETCs is usually not observed. Otherwise the same principles as above are valid.

Increase in Cell Numbers

A slow, continuous increase in cell numbers over a period of time indicates ineffectiveness of therapy. The treatment should be modified until a decrease in CETCs is visible. The number of cells should be further monitored in the postoperative situation.

**Explanation:*
CETC = circulating epithelial tumor cells

Adjuvant Therapy

is applied after complete surgical excision of the primary tumor with no evidence of metastases found by imaging techniques.

Adjuvant Chemotherapy

Decrease in Cell Numbers

A decrease in the number of CETCs usually occurs after the first 1–2 cycles. The number of cells should further decrease until the end of chemotherapy (decrease by factor 10 or two times in succession) or remain low. This correlates with a favorable course of disease (90–95% breast cancer patients are recurrence-free 4–5 years after treatment).

However, if the number of circulating epithelial tumor cells increases again after the first cycles until the end of therapy, this indicates an unfavorable prognosis and a change in therapy should be considered. Even if the treatment is successful, sometimes no CETCs can be detected throughout and several weeks after therapy. Where appropriate, the efficient therapy should be continued.

Constant Cell Numbers

Although, in some cases, CETCs (mainly in estrogen-receptor positive tumors) may not respond to chemotherapy, they have a low growth tendency, which correlates with a favorable course of disease.

Increase in Cell Numbers

If cell numbers continuously increase in spite of adjuvant therapy or reincrease after an initial decrease, this indicates that therapy is not or no longer effective. Without a change in therapy, this correlates with an unfavorable course of disease. Treatment should be changed (possibly after testing the cytotoxic efficiency of the drugs). If there is an increase in cell numbers by a factor of at least 10, recurrences occur in 65–70% of breast cancer patients within the first 5–6 years.

Adjuvant Endocrine Treatment

Decrease in Cell Numbers

During adjuvant endocrine treatment there is often a slow, continuous decrease in the number of cells can frequently be monitored over a long period of time (years). CETCs are usually not completely eliminated, but become quiescent (dormancy). A continuation of therapy is recommended.

Throughout anti-hormonal therapy heavy fluctuations of cell numbers may occur in some patients due to patient's compliance. Regular intake is recommended to be checked as these patients may particularly benefit from antihormonal therapy.

In premenopausal patients, several recent studies from 2016 have shown that pituitary blockade with gonadotropin-releasing hormone (GnRH) analogues can lead to insufficient estrogen suppression. This may also be a reason for the heavy fluctuations in cell numbers.

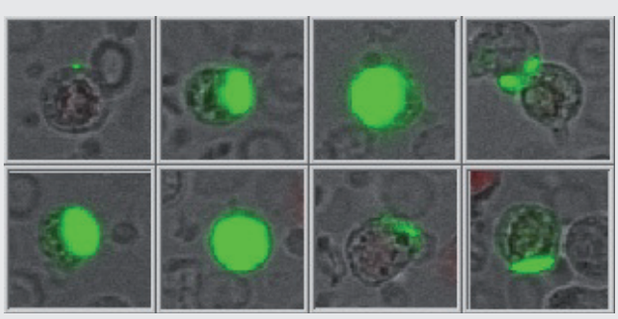
Constant Cell Numbers

Under adjuvant endocrine treatment cell numbers can remain constant even over years. This is associated with a good prognosis.

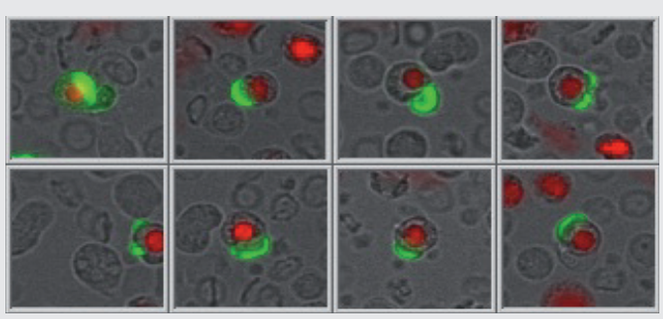
Increase in Cell Numbers

A slow, continuous increase in cell numbers over a long period of time indicates a lack of therapy efficacy. Treatment should be changed (e.g., from tamoxifen to aromatase inhibitors, or vice versa).

Typical vital and dead cells from a patient sample:



Vital tumor cells are stained green.



Dead tumor cells are additionally stained red..

Metastatic Situation

many small and/or large foci are already present.

Decrease in Cell Numbers

As soon as cell numbers decrease in conjunction with a reduction of the metastases, the therapy is effective. However, if the therapy results in the destruction of the tumor tissue, surviving cells can be washed out. Although the tumor (metastases) shrinks, there may be an increase in the number of tumor cells in blood. Therapy should be continued until there is a renewed decrease in cell numbers.

If CETCs decrease but the metastases remain unaltered, or even continue to grow, this indicates that the concentration of the drug in blood is sufficiently high and the circulating tumors cells respond to therapy. However, a high intratumoral pressure in the tumor/metastasis may avert a sufficiently high concentration of the medication. This is the most frequent reason for therapy failure.

A sudden decrease in cell numbers without or shortly after treatment can be a sign that an indication that the CETCs remigrate into the metastases (self-seeding). In short-term surveillance, a rapid rerise of CETC numbers is almost always observed. Further diagnostic measures are recommended.

Constant Cell Numbers

If cell numbers in the metastatic situation remain unchanged, metastases stay stable. This situation can be achieved with metronomic therapy.

Increase in Cell Numbers

Whenever cell numbers increase prior to the expansion of metastases, therapy is not effective and should be changed after sensitivity testing of the drugs. If there is a massive increase in cell numbers due to CETC washout and simultaneous reduction of the size of metastases, therapy should be continued until also a decrease in cells numbers in blood is achieved.

If cell numbers remain permanently high (> 5,000 cells/ml), continuous monitoring by imaging techniques is recommended, also in cases with a decrease in cell numbers.

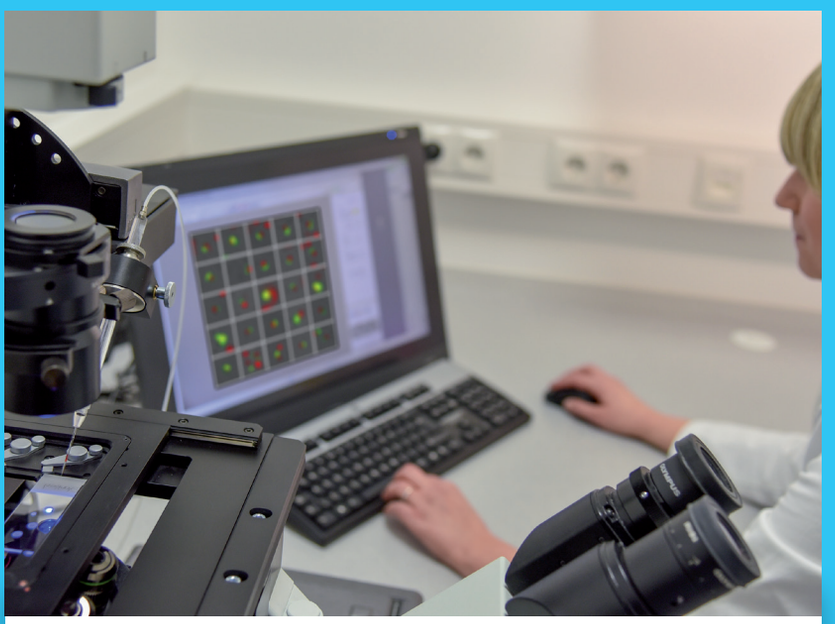
No Epithelial Cells Detectable

In some cases, CETCs are no longer detectable in patients with advanced metastasis. One hypothesis is that the cells are in epithelial-mesenchymal transition (EMT) . Another is that the cells have already migrated to existing metastases (self-seeding). The determination of the circulating cancer stem cells (tumor spheres) using stemtrac® can be helpful here.

1 Francart ME, Lambert J, Vanwynsberghe AM, Thompson EW, Bourcy M, Polette M, Gilles C. Epithelial-mesenchymal plasticity and circulating tumor cells: Travel companions to metastases. Dev Dyn 2018, 247:432-450.
2 Kim MY, Oskarsson T, Acharyya S, Nguyen DX, Zhang XH, Norton L, Massagué J. Tumor self-seeding by circulating cancer cells. Cell 2009, 139:1315-1326.

Your Notes

Your competent partner
in oncology and hemostaseology.



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Since 2005, maintrac is performed by the DIN EN ISO 15189 accredited specialized medical laboratory Dr. Pachmann.

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