

# CIRCULATING TUMOR CELLS OR STEM TUMOR CELLS FROM PERIPHERAL BLOOD AS A PROGNOSTIC MARKER FOR THE CLINICAL COURSE OF PATIENTS WITH BREAST CANCER



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## PURPOSE

The last few years many researchers support the idea that the majority of metastases and relapses in cancer progression is promoted by a population of cells which is called Circulating Tumor Cells (CTCs). CTCs are a distinct population of cancer cells that have been detached from the primary tumor and flow into the blood or lymphatic circulation, able to generate a secondary tumor. They are characterized by their potential to disseminate and proliferate as a metastatic lesion and by their ability to stimulate angiogenesis. Thus, CTCs can be considered as the progenitors of relapses. This indicates that they may include in their subpopulation of cells, all the hallmarks of cancer stem cell-like (CSC-like) cells, as CSCs have the ability to give rise to a new tumor. The pluripotency, the ability to self-renew by asymmetric cell division as well as the resistance to chemotherapy are some of their special hallmarks. Studying all the above using molecular markers (nanog, oct3/4, sox2, etc) the population of CSCs can be identified in a heterogeneous cancer population with aggressive behavior (blood and/or tissue sample).

## MATERIALS AND METHODS

Blood sample from 58 patients who suffered from breast cancer (between I and IV stage according to TNM classification) has been used in order to identify, isolate, quantify and analyze the quality of CTCs and by extension, the presence of CSCs inside this population. The first panel of the experiments included a flow cytometric and sorting – based method as well as positive and/or negative cell selection by using hematologic, epithelial, endothelial and tumor stem cell origin markers (CD45, CD30, panCK, c-MET, nestin, etc). The second panel included a gene's expression analysis assay by using end-point and quantitative real-time PCR. For reliable and precise results all the experiments were performed in duplicates by using positive and negative controls. In addition, it has been requested from the medical centers, a clinical assessment of the patients in order to discover their response rate to chemotherapeutics. Collecting all these data, a correlation between the CSCs population and the progress of the disease was made by using statistically evaluation methods.

## CONCLUSIONS

*From the present analysis, it was proven that apart from the well – characterized population of CTCs, a new entity of cells (CSCs), may play a key role in the recurrence, expansion and resistance of the disease and as a result this small population may be a prognostic marker in cancer development.*

## REFERENCES

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## RESULTS

From the 58 patients of the initial sample population only the 39 of them have completed the assessment experiments. It has been proved that the population of CTCs was increased over 75% in those who had rapid progression of the disease. In this group of patients as well as in the group of patients who had partial response to chemotherapy, after the comparison between the CSCs number (which were in MET phase) with the number of CTCs, it was found that the CSCs were in a higher ratio.

| 39 patients in total          | COMPLETE RESPONSE | PARTIAL RESPONSE | STABLE DISEASE | PROGRESS OF DISEASE | UNKNOWN |
|-------------------------------|-------------------|------------------|----------------|---------------------|---------|
| Stage I                       |                   |                  | 1              |                     | 1       |
| Stage II                      |                   | 1                | 9              |                     |         |
| Stage III                     | 2                 | 2                | 2              |                     | 1       |
| Stage IV                      |                   | 2                | 1              | 3                   | 1       |
| UNKNOWN                       | 3                 | 1                | 5              | 1                   | 3       |
| CTCs over cut off point       | 1                 | 3                | 8              | 3                   | 2       |
| CSCs present over 50% of CTCs | 0                 | 2                | 14             | 4                   | 4       |

Table 1. Response rate of the 39 breast cancer patients.

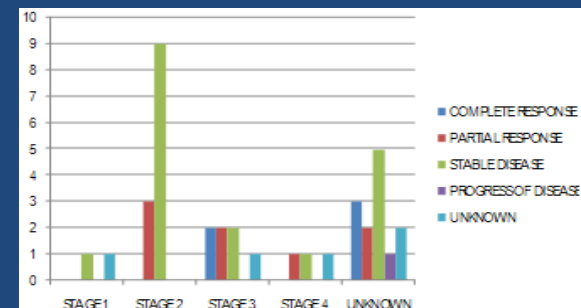


Table 2. Response rate of the 39 breast cancer patients