CTC Phenotyping and Genotyping in Breast Cancer – an Update.

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CTC enumeration is prognostic in several epithelial malignancies, including breast, prostate, color-rectal, and lung. In breast cancer, the presence of compared to the absence of detectable CTC is associated with worse, although not absolute risk of subsequent distant recurrence[1,2]. Furthermore, in metastatic breast cancer (MBC), ≥5 CTC/7.5 ml whole blood (WB) at baseline portends a shorter progression free and overall survival (OS), and perhaps more importantly failure to reduce elevated CTC levels below this cutoff after one cycle of therapy, especially first line chemotherapy, is associated with a median OS of <13 months.

These results suggest that CTC enumeration, alone, is insufficient to exploit the full potential of CTC enrichment/purification. We have reported development of a CTC-endocrine therapy index (CTC-ETI), which we proposed might be helpful to determine if patients with estrogen receptor (ER) positive MBC have endocrine therapy refractory disease. Our preliminary data demonstrated remarkable CTC-phenotypic heterogeneity, and a prospective trial addressing this issue is now complete. We have also reported equally remarkable genetic heterogeneity among single CTC form the same patients, and <100% concordance with next generation sequencing performed on tissue biopsies collected in a similar time frame as the CTC[3]. We are now moving towards more intensive phenotyping and genotyping for prognosis, prediction of response to targeted therapies, monitoring patients to detect late relapse and for determination of pharmacodynamic effects in clinical trials, and to gain greater insights into tumor biology and resistance to therapies.

Selected References

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