The Treat CTC trial – a new approach targeting circulating tumor cells (CTC) in early breast cancer (EBC)

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Background

The presence of CTC in metastatic BC is associated with an impaired prognosis. Recent data have shown a reduced disease-free survival and increased risk of death in the presence of CTC in EBC. Patients with persisting CTC after (neo)adjuvant chemotherapy are at increased risk of relapse and might benefit from additional systemic treatment. Recent data have reinforced the hypothesis that trastuzumab can eliminate tumor cells by antibody dependent cell cytotoxicity (ADCC) or other immune mechanisms. Preclinical data have provided evidence that the benefit of trastuzumab may be associated with targeting cancer stem cells in a model that does not require HER2 amplification (Itthinak et al Cancer Res 2013). In a single center phase 2 study trastuzumab eliminated CTC, irrespective of the HER2 status of the primary tumor and of CTC and this was associated with reduced relapses (Georgoulis et al Ann Oncol 2012).

Methods

15 mL of blood will be processed using the CellSearchTM System. The sample will be enriched for cells expressing the epithelial-cell adhesion molecule (EpCam) with antibody-coated magnetic beads. Fluorescently labeled monoclonal antibodies specific for leukocytes (CD45) and epithelial cells (cytokeratin 8,18,19) are used. The CTC blood test will be regarded positive with ≥ 1 CTC / 15 mL of blood confirmed by central laboratory review. Additional HER2 phenotyping on CTC by immunocytochemistry will be performed.

The primary test will be a one-sided test with overall α of 0.1 to compare the trastuzumab arm to the observation arm for the CTC detection rate at week 18 (superiority test) in the intention-to-treat population. The odds ratio and its confidence interval will be estimated using a logistic regression model. The comparison of RFI, IDFS, DFS and OS will be done using a two-sided test in a proportional hazards model for cause specific hazard, adjusted for factors...