

# Trial Watch

## CIRCULATING TUMOUR CELLS

Three press releases from the 33rd Annual Cancer Therapy and Research Center–American Association of Cancer Research San Antonio Breast Cancer Symposium indicate that the presence of circulating tumour cells (CTCs) is prognostic for cancer recurrence and poor survival in women with early- and late-stage breast cancer.

Results from SUCCESS, a randomized Phase III trial, which is assessing the effect of docetaxel and gemcitabine as adjuvant therapies in patients with early-stage breast cancer, indicate that women with one to four CTCs in their blood after surgery, but before receiving adjuvant chemotherapy, have an 88% increased risk of early disease recurrence and a 91% increased risk of death from this disease. Women who had five or more CTCs in their blood sample had a fourfold increased risk of disease recurrence and a threefold increased risk for death. The presence of CTCs before treatment was an independent predictor for both disease-free (hazard ratio (HR) 1.88) and overall survival (HR 1.91). However, additional prospective, randomized trials are required to verify these initial findings.

In a second trial involving 21 women with metastatic breast cancer at diagnosis, who were treated with high-dose chemotherapy followed by autologous stem cell transplantation, the presence of CTCs before or after therapy was a clear indicator of poor outcome. Hui Gao and colleagues from the MD Anderson Cancer Center, Texas, USA, found that the growth factors used to mobilize haematopoietic progenitor cells from the bone marrow for use in autologous transplant also mobilized CTCs from the bone marrow. Some of these cells had undergone epithelial–mesenchymal transition and had a phenotype that could be missed by standard CTC detection assays. Six of the women in this study had CTCs in their blood prior to transplant, and nine had CTCs 1 month after the transplant. Women with more than five CTCs prior to transplant were likely to have shorter overall survival, and those with more than five CTCs after transplant were likely to have both shorter relapse-free survival and shorter overall survival. Interestingly, both lead researchers from these two trials were quoted as having found stem cell-like CTCs in the population of CTCs isolated from women in these trials.

In the third study, Jean-Yves Pierga and colleagues prospectively assessed 267 women from five different cancer centres in France who presented with metastatic breast cancer and were treated with first-line chemotherapy. They were assessed for the expression of three different serum tumour markers (CA15.3, CEA and LDH) and the numbers of CTCs in 7.5 ml of blood taken before treatment, before the second treatment cycle, at clinical evaluation of disease response and at tumour progression. This direct comparison of serum markers and CTCs showed that the presence of CTCs is an independent marker of progression-free survival and overall survival, and that persistently high levels of CTCs before the second round of treatment is a strong and early predictive marker of poor progression-free survival.

### WEB SITES

CTRC–AACR San Antonio Breast Cancer Symposium: <http://www.sabcs.org/>