

## **Prognostic Significance Of Early On-Treatment Evolution Of Circulating Tumor Dna In Advanced Er+/Her2- Breast Cancer**

**Abstract Submitter:** [Aaron Mamann, France\\*](#)

Co-Authors: Yoann Pradat, François-Clément Bidard, Suzette Delaloge, Sandrine Marques, Thomas Bachelot, Thibault de la Motte Rouge, Juliette Samaniego, Anne-Claire Hardy, Jerome Lemonnier, Younes Mahi, Fabrice Andre, Paul-Henry Courmede, Stefan Michiels, Elsa Bernard

\*CentraleSupélec / Institut Gustave Roussy

### **Abstract**

#### Background

Patients with advanced estrogen receptor-positive, HER2-negative (ER+/HER2-) breast cancer commonly develop resistance to treatment with hormone therapy and cyclin-dependent kinases 4/6 (CDK4/6) inhibitors. Responders cannot be distinguished from non-responders after the first cycle of treatment under current practice.

#### Objective

To assess circulating tumor DNA (ctDNA) measures at early on-treatment timepoints as prognostic markers in advanced ER+/HER2- breast cancer treated with hormone therapy and CDK4/6) inhibitors.

#### Patients and methods

Paired plasma samples were collected at baseline and early on-treatment (median 28 days) from 369 patients with advanced ER+/HER2- breast cancer treated in the PADA-1 trial with hormone therapy and a CDK4/6 inhibitor. Cell-free DNA was profiled with a 497-gene panel (Guardant360 LDT).

#### Results

Baseline ctDNA levels including the mean variant allele frequency (VAF) (progression-free survival [PFS] HR = 1.07 P<0.001, overall survival [OS] HR = 1.08 P<0.001) and the number of driver somatic mutations (PFS HR = 1.13 P<0.001 and OS HR = 1.16 P<0.001) were prognostic. Early on-treatment ctDNA dynamics including the number of driver somatic mutations with VAF>0.5% at both timepoints and the number of driver somatic mutations with a VAF increase were associated with outcomes (PFS HR = 1.39 P<0.001 and HR = 1.31 P<0.001, respectively; OS HR = 1.51 P<0.001 and HR = 1.10 P=0.02, respectively). A ctDNA-based risk model inclusive of baseline and dynamic ctDNA features was independently prognostic from RECIST in multivariable models (Test set: OS HR = 4.10 P<0.001, PFS HR = 1.86 P=0.009). The integration of ctDNA-based features in a clinical model improved survival discrimination (PFS C-index 64.7 [SD 2.5] P=0.027 & IBS 18.0 [SD 1.0] P=0.034; OS C-index 70.0 [SD 3.4] P=0.035 & IBS 12.4 [SD 1.2] P=0.011).

#### Conclusions

Early on-treatment evolution of ctDNA is prognostic in advanced ER+/HER2- breast cancer. A ctDNA-based risk model improves upon traditional RECIST and clinical features, advocating for ctDNA as a prognostic biomarker in clinical practice.

#### **Do you have any conflicts of interest?**

No, I do not have a conflict of interest.