Monitoring treatment efficacy using personalised circulating-tumour DNA panels in patients with metastatic breast cancer

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Background & objectives

Systemic anti-cancer therapy aims to delay disease progression, improve survival and to reduce cancer-related symptoms in patients with metastatic breast cancer (MBC). Treatment response is normally evaluated using radiographic imaging every 3-4 months. As a result, patients with long-term stable disease will undergo multiple unnecessary scans, whereas other non-responders will continue treatment for several months before disease progression can be confirmed. Therefore, there is a need for improved methods to monitor disease and treatment efficacy in MBC patients, preferably also including molecular information.

The overall aim of this study is to determine the clinical value of blood-based biomarker analysis for disease monitoring in MBC patients.

Methods

The PDM-MBC trial (NCT04597580) includes patients with stage IV breast cancer, receiving first line therapy with an aromatase inhibitor and a CDK4/6 inhibitor (n=100). Patients undergo routine imaging and study samples are collected at baseline and then serially until disease progression. To detect and quantify circulating tumour-DNA (ctDNA) we used SiMSen-Seq and tailor-made ctDNA panels that detect patient-specific mutations selected from sequencing of tumour tissue. Biomarker analysis also includes the tumour marker cancer antigen 15-3 (CA15-3).

Results

So far, ctDNA has been analysed in 17 patients by using tailor-made panels and ctDNA has been detected at baseline in 14 (82%) of the included patients. ctDNA positive patients had on average 3 mutations (1-7) with panel sizes ranging from 4 to 13. Preliminary data show that changes in ctDNA levels are associated with disease status and that biomarker changes forego the response seen on imaging. Compared to CA15-3, ctDNA appears to be superior in predicting disease progression.

Conclusion

We have developed an experimental approach to monitor personalised and blood-based biomarkers in stage IV breast cancer. The implementation and use of liquid biopsy-based analysis has the potential to guide and complement routine imaging.