Liquid Biopsy in Cancer

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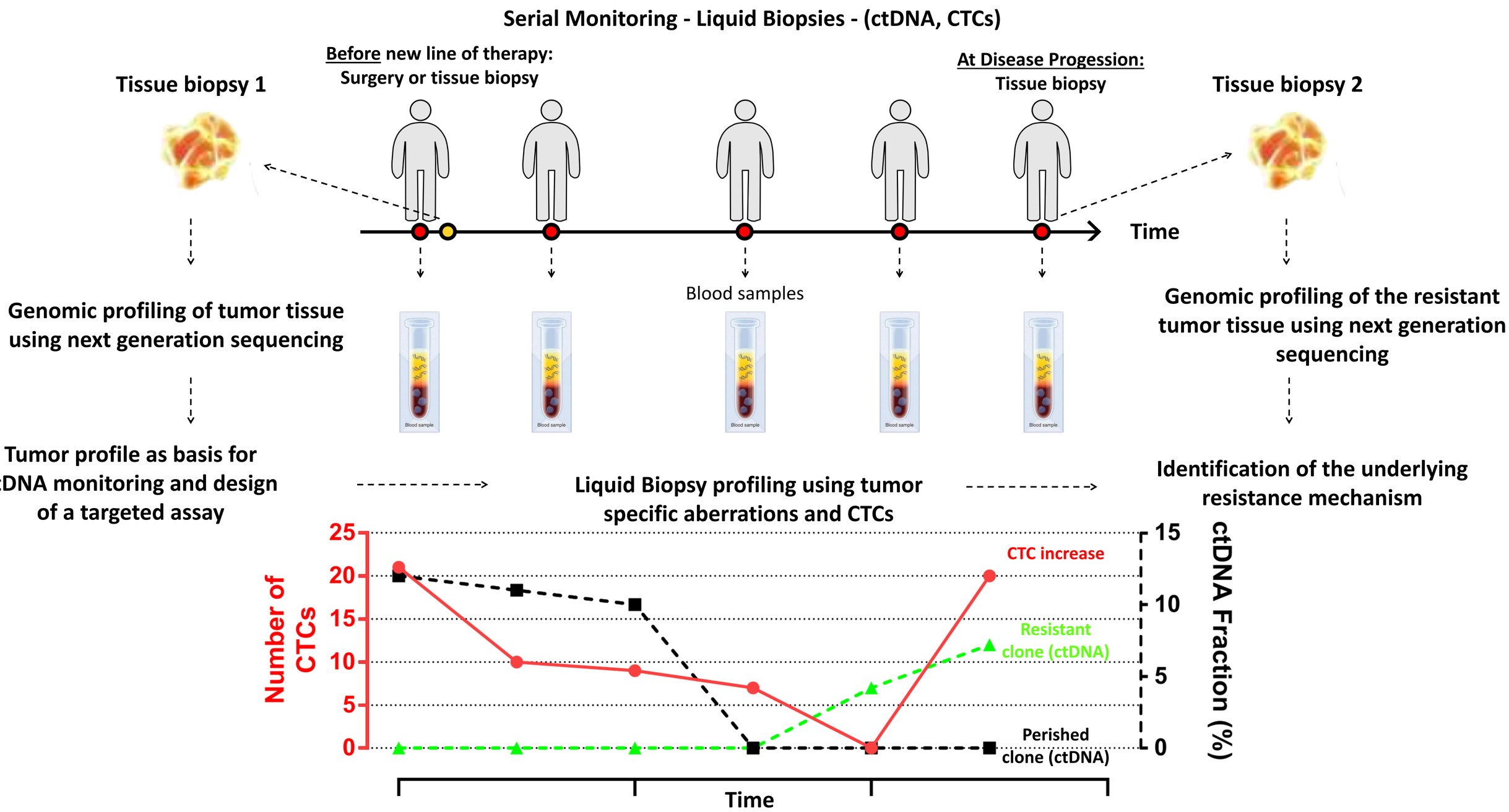
Introduction

Precision oncology aims to provide personalized treatment options by identifying, monitoring and targeting molecular aberrations of the individual patient tumor. This approach has the potential to improve clinical outcomes. In recent years **liquid biopsies**, such as circulating tumor cells (CTCs) and circulating tumor DNA (ctDNA), became very promising tools for precision oncology. Although vast amounts of scientific literature are available on liquid biopsies, controversy remains about their clinical utility, hence clinical applications remain scarce. **A major hurdle** for their widespread clinical implementation are the **lack of standardisation** and technical issues, preventing widespread use of liquid biopsies as a biomarker in a clinical routine setting

Objective

To overcome these issues of low standardisations in liquid biopsies **we propose the following objective: We will implement CEN- and ISO- compatible workflows for liquid biopsies for patients with malignant disease. We thereby focus on castration resistant prostate cancer (CRPC), colorectal cancer (CRC) and non-small cell lung cancer- (NSCLC) patients. Moreover we will investigate tissue biopsy of the metastatic sites before and after occurrence of therapy resistance.**



Methods

To achieve our objective, we will establish novel techniques, and validate technologies developed during the first CBmed funding period and implement CEN- and ISO- standard compatible workflows to isolate and analyse liquid biopsies from our patient cohort.

- Stabilisation and fixation of CTCs and other blood-derived cells, followed by downstream NGS analysis
- Setting up prospective patient cohorts of CRPC, CRC and NSCLC patients in cooperation with the Division of Oncology and the Institute of Pathology to obtain blood, primary-, metastatic-, and non-neoplastic tissue samples (if available) as reference material according to existing CEN- and ISO- standards.
- CTC enrichment/selection using different enrichment technologies, such as AdnaTest (QIAGEN), size based enrichment system (Cytogen-Smart Biopsy), Parsortix (Angle), FACS and/or novel isolation techniques for establishment and (cross-) validation of a standardized workflow for CTCs (jointly with CBmed Core Technology Immunology 1.22).
- Plasma ctDNA isolation of all patients and analysis as a (cross-) validation data set in parallel to CTCs.

Expected Outcome

- We will provide a validated workflow for the pre-analytical processing of CTCs, ctDNA and other body fluids including fine needle aspirates for NGS, RNAseq expression profiling, and proteomics. It will allow analysis of the diagnostically most relevant biomolecules (DNA, RNA, metabolome, proteome) from a single blood collection.
- We will provide a clinically validated sample-to-insight workflow for CTCs and ctDNA that complies with requirements of the EU in vitro diagnostics regulation (IVDR).
- We will have established and validated new targeted assays which can be used to investigate liquid biospies.

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References

Figure adapted from
Haber et al., Cancer Discov 2014 / Olsson et al., EMBO Mol Med 2015 / Lee et al., Nat Genet 2018

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